ERC Implementing Arrangements

Call for Expression of Interest

2016
Almost half of the human genome is made of Transposable Elements (TEs), whose ongoing activity continually impacts our genome. However, little is known about how the host regulates TEs and their genomic and epigenomic impacts. EpiPluriRetro will advance research in a new groundbreaking concept: that TEs are active in our pluripotent genome, and that epigenetic regulation is employed therein to regulate TE activity. LINE-1 retrotransposons comprise approximately 20% of the mammalian genome, and L1 retrotransposition events can create genetic diversity by a variety of mechanisms. From acting as simple insertion mutagens to inducing other complex genomic alterations it is becoming increasingly evident that the activity of TEs is a major force driving human genome evolution. It has been demonstrated that the main mutagenic load associated with TE mobilization occurs during early human embryogenesis (i.e., our pluripotent genome). EpiPluriRetro will examine how epigenetic mechanisms influence LINE-1 retrotransposition in pluripotent cells. To do that, we will combine genetic, biochemical and genomics approaches to identify pluripotent host factors that influence the fate of LINE-1 retrotransposition. In addition, EpiPluriRetro will analyze the impact of LINE-1 insertions in our pluripotent genome and the Epimutagenic impact of new LINE-1 mobilization events in pluripotent cells. To do that, we have developed an innovative approach to analyze the effect of LINE-1 insertions within human genes without biases, including epigenetic alterations induced by a new L1 insertion. EpiPluriRetro will help to understand how the activity of TEs is controlled in our heritable genome, which will directly impact our knowledge in how new genetic diseases are generated in humans. In addition, EpiPluriRetro will allow us to describe a new concept in human biology, as we will analyze how new TE insertions can modify the chromatin status of flanking genomic regions where they insert.

Keywords of the ERC project: Epigenetics Retrotransposons, pluripotent genome, mutation, genomic instability, Stem cell biology

Keywords that characterize the scientific profile of the potential visiting researcher/s: Transposable Elements, Stem cell biology, Epigenetics
From birth to action: regulation of gene expression through transcription complex biogenesis

Transcriptional regulation of protein coding genes in eukaryotic cells requires a complex interplay of sequence-specific DNA-binding factors, co-activators, general transcription factors (GTFs), RNA polymerase II and the epigenetic status of target sequences. Nuclear transcription complexes function as large multiprotein assemblies and are often composed of functional modules. The regulated decision-making that exists in cells governing the assembly and the allocation of factors to different transcription complexes to regulate distinct gene expression pathways is not yet understood. To tackle this fundamental question, we will systematically analyse the regulated biogenesis of transcription complexes from their sites of translation in the cytoplasm, through their assembly intermediates and nuclear import, to their site of action in the nucleus. The project will have four main Aims to decipher the biogenesis of transcription complexes:
I) Investigate their co-translation-driven assembly
II) Determine their cytoplasmic intermediates and factors required for their assembly pathways
III) Uncover their nuclear import
IV) Understand at the single molecule level their nuclear assembly, dynamics and action at target genes
To carry out these aims we propose a combination of multidisciplinary and cutting edge approaches, out of which some of them will be high-risk taking, while others will utilize methods routinely run by the group. The project builds on several complementary expertise and knowledge either already existing in the group or that will be implemented during the project. At the end of the proposed project we will obtain novel results extensively describing the different steps of the regulatory mechanisms that control the assembly and the consequent gene regulatory function of transcription complexes. Thus, we anticipate that the results of our research will have a major impact on the field and will lead to a new paradigm for contemporary metazoan transcription.

Keywords of the ERC project: Gene regulation through transcription complex assembly regulation,
Keywords that characterize the scientific profile of the potential visiting researcher/s: co-translational assembly pathways, selective ribosome profiling, bioinfo analyses,
Project ID: 637733  
Project Acronym: Pentabrain  
Evaluation Panel: LS1 - Molecular and Structural Biology and Biochemistry

<table>
<thead>
<tr>
<th>Principal Investigator:</th>
<th>Dr Hugues Nury</th>
</tr>
</thead>
<tbody>
<tr>
<td>Host Institution:</td>
<td>Centre National De La Recherche Scientifique Cnrs - FR</td>
</tr>
</tbody>
</table>

**Structural studies of mammalian Cys-loop receptors**

In the brain, Cys-loop receptors mediate fast neurotransmission. They function as allosteric signal transducers across the plasma membrane: upon binding of one or more neurotransmitter molecules to an extracellular site, the receptors undergo complex conformational transitions that result in transient opening of an intrinsic ion channel. The Cys-loop family comprises receptors activated by serotonin, acetylcholine, glycine and GABA. Mammalian receptors are also the targets of a legion of psychoactive and therapeutic compounds (including nicotine, benzodiazepines, anti-emetics, general anaesthetics). Our structural knowledge is currently limited to invertebrate homologues. Atomic structures mammalian receptors are therefore acutely missing in order to understand their physiological role in molecular terms, and to be able to develop new drugs targeting them. The project proposes to decipher the operation mechanism, the pharmacology and conformational transitions of mammalian Cys-loop receptors. Starting with a solid body of preliminary results, we will obtain new high-resolution structures, taking advantage of antibody-based crystallization chaperones. We will try and record for the first time a ‘molecular movie’ of the gating conformational transition in cristallo. On the way, we will also investigate the potential of antibody-based modulators of Cys-loop receptors for biomedical applications. The applicant has solved in the past the structures of a bacterial Cys-loop receptor and of the mouse serotonin receptor. The proposed research will take place at the CNRS in Grenoble, France, in a very favourable environment for structural biology.

**Keywords of the ERC project:** membrane protein, crystallography, cryoEM, channel

**Keywords that characterize the scientific profile of the potential visiting researcher/s:**
**TOR and Cellular Homeostasis**

The Target Of Rapamycin (TOR) proteins are ser/thr kinases conserved in Eukarya. They nucleate two distinct multiprotein complexes, named TORC1 and TORC2, which regulate many, widely varying, aspects of cell and organism physiology. TOR inhibitors, such as rapamycin and derivatives, are used clinically to treat cancer, cardio-vasculature disease and to prevent organ rejection. We recently reported that both TORC1/2 are wired in feedback loops, where their downstream cellular effectors are at the same time upstream regulators. It is this feedback loop that ultimately mediates the intrinsic role of TORC1/2 in cellular homeostasis: TORC1/2 detects deviations from a steady-state condition and by means of these feedback loops returns the cell to its homeostatic situation. We propose to systematically identify the TORC1/2 homeostatic signalling loops. Subsequent characterization will focus on the signalling networks controlling intermediary metabolism. Our ultimate goal is to comprehensively unravel the TORC1/2-dependent metabolic networks composed of regulatory feedback loops which will reveal the fundamental role of the TOR Complexes as molecular devices to achieve cellular homeostasis.

**Keywords of the ERC project:** Target of Rapamycin, kinase, signaling, metabolism, complex, mass spec, phosphoproteomics

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** structure biology, signaling, biochemistry, mass spectrometry, cryo-em
Structural studies of human picornaviruses

Many picornaviruses are human pathogens that cause diseases varying in symptoms from common cold to life-threatening encephalitis. Currently there are no anti-picornavirus drugs approved for human use. We propose to study molecular structures of picornaviruses and their life cycle intermediates in order to identify new targets for anti-viral inhibitors and to lay the foundations for structure-based development of drugs against previously structurally uncharacterized picornaviruses.

We will use X-ray crystallography to determine virion structures of representative viruses from Parechovirus, Kobuvirus, Cardiovirus, and Cosavirus genera and Human Rhinovirus-C species. We will use cryo-electron microscopy to study picornavirus replication complexes in order to explain the mechanism of copy-choice recombination of picornavirus RNA genomes that leads to creation of new picornavirus species. We will determine whether picornavirus virions assemble from capsid protein protomers around the condensed genome or if the genome is packaged into a pre-formed empty capsid. Furthermore, we will investigate how picornaviruses initiate infection by analyzing genome release from virions and its translocation across lipid membrane.

A major innovation in our approach will be the use of focused ion beam micromachining for sample preparation that will allow us to study macromolecular complexes within infected mammalian cells by cryo-electron tomography. Our analysis of virion structure, cell entry, genome replication, and particle assembly will identify molecular details and mechanism of function of critical picornavirus life-cycle intermediates.

Keywords of the ERC project: virus, structure, cryo, electron, microscopy, crystallography, bacteriophage, infection, cell, entry, molecular, mechanism, picornavirus, enterovirus, human, pathogen, honeybee, tomography, protein, expression, purification

Keywords that characterize the scientific profile of the potential visiting researcher/s: structure, molecular, biology, cloning, protein, expression, purification, virus, programming, scripting
We aim to understand host cell entry of enveloped viruses at molecular level. A crucial step in this process is when the viral membrane fuses with the cell membrane. Similarly to cell–cell fusion, this step is mediated by fusion proteins (classes I–III). Several medically important viruses, notably dengue and many bunyaviruses, harbour a class II fusion protein. Class II fusion protein structures have been solved in pre- and post-fusion conformation and in some cases different factors promoting fusion have been determined. However, questions about the most important steps of this key process remain unanswered. I will focus on the entry mechanism of bunyaviruses by using cutting-edge, high spatial and temporal resolution bio-imaging techniques. These viruses have been chosen as a model system to maximise the significance of the project: they form an emerging viral threat to humans and animals, no approved vaccines or antivirals exist for human use and they are less studied than other class II fusion protein systems. Cryo-electron microscopy and tomography will be used to solve high-resolution structures (up to ~3 Å) of viruses, in addition to virus–receptor and virus–membrane complexes. Advanced fluorescence microscopy techniques will be used to probe the dynamics of virus entry and fusion in vivo and in vitro. Deciphering key steps in virus entry is expected to contribute to rational vaccine and drug design. During this project I aim to establish a world-class laboratory in structural and cellular biology of emerging viruses. The project greatly benefits from our unique biosafety level 3 laboratory offering advanced bio-imaging techniques. Furthermore it will also pave way for similar projects on other infectious viruses. Finally the novel computational image processing methods developed in this project will be broadly applicable for the analysis of flexible biological structures, which often pose the most challenging yet interesting questions in structural biology.
Mechanisms of alternative pre-mRNA splicing regulation in cancer and pluripotent cells

Alternative splicing of messenger RNA precursors is a prevalent form of gene regulation that greatly expands the coding capacity and regulatory opportunities of higher eukaryotic genomes. It contributes to cell differentiation and pluripotency and its deregulation promotes cancer progression, as evidenced by the frequent occurrence of cancer-associated mutations in splicing factors, which are also targets of anti-tumor drugs. Despite its prevalence and relevance, the underlying mechanisms of regulation remain poorly understood. This proposal aims to develop and apply systematic approaches that can allow us to carry out the equivalent of genetic analysis of splicing regulation in cancer and pluripotent cells. These technologies can help to unweave the complex network of functional interactions within the spliceosome and of the spliceosome with regulatory factors, exhaustively map the contribution of regulatory sequences and be used to investigate, with unprecedented detail, mechanisms of regulation for essentially any regulator or alternative splicing event operating in a particular cell line. Such approaches can offer a unique opportunity to address key unresolved mechanistic questions, including the molecular basis for positional effects of splicing regulatory factors (RNA Maps), the regulatory potential of the core spliceosome and the integration of alternative splicing with other cell regulatory programs. We will combine these approaches with biochemical and cellular assays to investigate detailed mechanisms of regulation relevant for the control of cell proliferation and/or pluripotency in cancer and induced pluripotent stem (iPS) cells. Progress in this area can contribute to reveal the molecular logic governing a key layer of gene regulation and has the potential to discover novel factors and regulatory circuits that trigger or modulate cell growth, differentiation and cancer progression.

Keywords of the ERC project: alternative splicing, cancer, pluripotency, regulatory networks

Keywords that characterize the scientific profile of the potential visiting researcher/s: structural biology, bioinformatics, molecular biology
Biological systems are robust to perturbations, with many genetic, stochastic and environmental challenges having no or little phenotypic consequence. However, the extent of this robustness varies across individuals, for example the same mutation or treatment may only affect a subset of individuals. The overall objective of this project is to understand the cellular and molecular mechanisms that confer this robustness and why it varies across individuals. We will address three specific questions:

1. Why do inherited mutations have different outcomes in different individuals, even when they are genetically identical and share a common environment?
2. What are the mechanisms during development that confer robustness to mechanical deformation?
3. How can the loss of robustness be exploited to specifically kill cancer cells? To address the first two questions, we will use live imaging procedures that we have developed that make the C. elegans embryo a unique animal system to link early inter-individual variation in gene expression and cellular behaviour to later variation in phenotypes. To address the third question, we will apply our understanding of genetic robustness and genetic interaction networks in model organisms to the comprehensive analysis of cancer genome datasets. The predictions from these hypothesis-driven computational analyses will then be evaluated using wet-lab experiments. Understanding and predicting variation in robustness is both a fundamental challenge for biology and one that is central to the development of personalised and predictive medicine. A patient does not want to know the typical outcome of a mutation or treatment; they want to know what will actually happen to them. The work outlined here will contribute to our basic understanding of robustness and its variation among individuals, and it will also directly tackle the problem of predicting and targeting variation in robustness as a strategy to kill tumour cells.

Keywords of the ERC project: Genomics, epigenetics, C. elegans, yeast, cancer, evolution, development

Keywords that characterize the scientific profile of the potential visiting researcher/s: Genomics, epigenetics, C. elegans, yeast, cancer, evolution, development
Why do cancers occur where they do? A genetic and evolutionary approach.

Tumorigenesis is a form of somatic evolution, a topical subject given the advent of cancer genome sequencing. However, we contend that some features of Darwinian evolution have been neglected when cancer is studied, as have some aspects of evolution that are special to cancers. For example, tumours comprise an expanding population of cells, cancers must occur within a normal human lifespan, and genotypes detrimental to growth of the tumour as a whole may be selected. These factors may render invalid the classical model in which successive mutations with large advantages arise and spread through the tumour in selective sweeps. To incorporate these neglected features and to test how tumorigenesis depends on factors such as mutation rate, selection and size constraints, we shall set up a comprehensive model of tumour growth incorporating cell birth, death, division and mutation parameters. We shall examine specific aspects of cancer-as-evolution in mice. By marking mutant clones using fluorescent proteins, we can track them and see how they persist, spread and die. We shall also determine the mutation profiles and genetic diversity of mutant clones and whole tumours in mice and humans using next-generation sequencing. Specific experiments will determine: (i) the fate of new advantageous clones arising in an existing tumour; (ii) whether new disadvantageous clones can persist in tumours; (iii) whether apparently maladaptive traits for tumour growth, such as suppressing the growth of competitors, can be selected; (iv) why do housekeeper gene mutations cause cancer in specific sites; (v) can cancer cells have too much genomic instability; and (vi) whether all cancers develop owing to driver mutations with big effects, or are there “mini-drivers” of tumorigenesis? There will be continual cross-talk between the experimental and modelling work. The results of the project will enhance our basic understanding of tumorigenesis and suggest strategies for anticancer therapy.

Keywords of the ERC project: Models of cancer evolution in mice
Keywords that characterize the scientific profile of the potential visiting researcher/s: Mathematical modelling of tumorigenesis and evolution
Chromatin dynamics during DNA replication

Chromatin assembly is a fundamental cellular process necessary for the maintenance of genome integrity and transcriptional programs. Understanding the effect of DNA replication on histone protein dynamics is also a prerequisite for understanding the role of chromatin in epigenetic inheritance. Epigenetic phenomena are thought to influence cellular differentiation and cancer formation, as well as the impact of environmental factors on early development and later predispositions to disease. While epigenetic inheritance of chromatin components is, in theory, accepted as the driver of such phenomena, chromatin state inheritance per se has only been demonstrated for a few specific cases. Not much is known about histone “inheritance” beyond the facts that bulk maternal histones distribute equally among the daughter strands and are diluted two-fold after replication with newly synthesized “unmarked” histones, and that the majority of H3/H4 tetramers do not split before reassembly. We have shown previously that maternal nucleosomes stay on average within 400bp of their original binding site, implying that any potentially heritable chromatin encoded information, has to be inherited in ~1kb blocs, as smaller nucleosome domains would rapidly be diluted by new nucleosomes.

I propose to develop high throughput systems for directly measuring movements of histones and chromatin regulators during genomic replication in S.cerevisiae to determine, how chromatin states survive the perturbations associated with replication. We will determine locus specific differences in the spread of maternal nucleosomes after replication, the effects of leading and lagging strand replication on nucleosome positioning and maternal nucleosome distribution, the renewal dynamics of posttranslational histone marks and chromatin binding proteins, and the kinetics of chromatin footprint re-establishment and gene (re)activation.

Keywords of the ERC project: epigenetic inheritance, chromatin, DNA replication, genomics, bioinformatics

Keywords that characterize the scientific profile of the potential visiting researcher/s: DNA replication, chromatin, genomics, bioinformatics
Understanding and manipulating the dynamics of chromosome topologies in transcriptional control

Transcriptional regulation of genes in eukaryotic cells requires a complex and highly regulated interplay of chromatin environment, epigenetic status of target sequences and several different transcription factors. Eukaryotic genomes are tightly packaged within nuclei, yet must be accessible for transcription, replication and repair. A striking correlation exists between chromatin topology and underlying gene activity. According to the textbook view, chromatin loops bring genes into direct contact with distal regulatory elements, such as enhancers. Moreover, we and others have shown that genomes are organized into discretely folded megabase-sized regions, denoted as topologically associated domains (TADs), which seem to correlate well with transcription activity and histone modifications. However, it is unknown whether chromosome folding is a cause or consequence of underlying gene function.

To better understand the role of genome organization in transcription regulation, I will address the following questions: (i) How are chromatin configurations altered during transcriptional changes accompanying development? (ii) What are the real-time kinetics and cell-to-cell variabilities of chromatin interactions and TAD architectures? (iii) Can chromatin loops be engineered de novo, and do they influence gene expression? (iv) What genetic elements and trans-acting factors are required to organize TADs? To address these fundamental questions, I will use a combination of novel technologies and approaches, such as Hi-C, CRISPR knock-ins, ANCHOR tagging of DNA loci, high- and super-resolution single-cell imaging, genome-wide screens and optogenetics, in order to both study and engineer chromatin architectures.

These studies will give groundbreaking insight into if and how chromatin topology regulates transcription. Thus, I anticipate that the results of this project will have a major impact on the field and will lead to a new paradigm for metazoan transcription control.

Keywords of the ERC project: Nuclear organisation; chromatin topology; Hi-C; TAD; enhancer

Keywords that characterize the scientific profile of the potential visiting researcher/s: Image analysis; Live microscopy; Nuclear organisation; chromatin topology; TAD; enhancer
Dissecting the mechanisms governing centriole formation

Centrioles are critical for the formation of cilia, flagella and centrosomes, as well as for human health. The mechanisms governing centriole formation constitute a long-standing question in cell biology. We will pursue an innovative multidisciplinary research program to gain further insight into these mechanisms, using human cells, C. elegans and Trichonympha as model systems. This program is expected to also have a major impact by contributing a novel cell free assay to the field, thus paving the way towards making synthetic centrioles. Six specific aims will be pursued:

1) Deciphering HsSAS-6/STIL distribution and dynamics. We will use super-resolution microscopy, molecular counting, photoconversion and FCS to further characterize these two key components required for centriole formation in human cells.

2) The SAS-6 ring model as a tool to redirect centriole organization. Utilizing predictions from the SAS-6 ring model, we will assay the consequences for centrioles and cilia of altering the diameter and symmetry of the structure.

3) Determining the architecture of C. elegans centrioles. We will conduct molecular counting and cryo-ET of purified C. elegans centrioles to determine if they contain a spiral or a cartwheel, as well as identify SAS-6-interacting components.

4) Comprehensive 3D map and proteomics of Trichonympha centriole. We will obtain a ~35 Å 3D map of the complete T. agilis centriole, perform proteomic analysis to identify its constituents and test their function using RNAi.

5) Regulation of cartwheel height and centriole length. We will explore whether cartwheel height is set by SAS-6 proteins and perform screens in human cells to identify novel components regulating cartwheel height and centriole length.

6) Novel cell free assay for cartwheel assembly and centriole formation. Using SAS-6 proteins on a lipid monolayer as starting point, we will develop and utilize a cell-free assay to reconstitute cartwheel assembly and centriole format.

Keywords of the ERC project: centriole, assembly

Keywords that characterize the scientific profile of the potential visiting researcher/s: cryo-electron tomography, biophysics
Unravelling cluster root development in white lupin

Plant development is continuous throughout their lifetime and reflects their ability to adapt to their environment. This developmental plasticity is very obvious in the development of the root system. Surprisingly, the fundamental mechanisms of root development have been studied into great detail but the effect of the environment on its plasticity is still largely unknown. I will use phosphate, since this nutrient has a very low mobility in soil, as a mean to study plant developmental adaptation in white lupin. This species has developed extreme adaptive mechanism to improve phosphate uptake by producing structures called “cluster roots”. They are dense clusters of lateral roots with determinate development and highly specific physiology. I will develop new tools to identify cluster root mutants in white lupin, sequence white lupin genome, perform tissues specific transcriptomics and perform full molecular characterization of selected genes. This project will also lead me to compare adaptive mechanisms between white lupin and narrow-leafed lupin, a closely related species that does not produce cluster roots. We will also test whether it is possible to transfer the ability to form cluster roots in this species. Altogether, this project will lead to a major advance in our capacity to understand how plants are able to sense and respond to their environment and how evolution has selected adaptive developmental mechanisms to improve their capacity to use limited resources. This project focuses on the most extreme developmental adaptation produced in response to phosphate starvation. It is ambitious, as it will necessitate the development of several tools. However, it is highly feasible since it builds on my previous experience and important outcome can be expected in term of crop improvement and means to reduce the use of phosphate fertilizers.

Keywords of the ERC project: Plant development, cluster roots, white lupin, adaptation.

Keywords that characterize the scientific profile of the potential visiting researcher/s: Curious, motivated, passionate.
Molecular and cellular determinants of cell monolayer mechanics

Epithelial monolayers are amongst the simplest tissues in the body, yet they play fundamental roles in adult organisms where they separate the internal environment from the external environment and in development when the intrinsic forces generated by cells within the monolayer drive tissue morphogenesis. The mechanics of these simple tissues is dictated by the cytoskeletal and adhesive proteins that interface the constituent cells into a tissue-scale mechanical syncitium. Mutations in these proteins lead to diseases with fragilised epithelia. However, a quantitative understanding of how subcellular structures govern monolayer mechanics, how cells sense their mechanical environment and what mechanical forces participate in tissue morphogenesis is lacking. To overcome these challenges, my lab devised a new technique to study the mechanics of load-bearing monolayers under well-controlled mechanical conditions while allowing imaging at subcellular, cellular and tissue resolutions. Using this instrument, my proposal aims to understand the molecular determinants of monolayer mechanics as well as the cellular behaviours that drive tissue morphogenesis. I will focus on four objectives: 1) discover the molecular determinants of monolayer mechanics, 2) characterise monolayer mechanics, 3) dissect how tension is sensed by monolayers, and 4) investigate the biophysics of individual cell behaviours participating in tissue morphogenesis. Together these studies will enable us to understand how monolayer mechanics is affected by changes in single cell behaviour, subcellular organisation, and molecular turnover. This multi-scale characterisation of monolayer mechanics will set the stage for new theoretical descriptions of living tissues involving both molecular-scale phenomena (cytoskeletal turnover, contractility, and protein unfolding) operating on short time-scales and rearrangements due to cell-scale phenomena (cell intercalation, cell division) acting on longer times.

Keywords of the ERC project: Cell Biophysics, Epithelia, Tissue mechanics, cytoskeleton

Keywords that characterize the scientific profile of the potential visiting researcher/s: Biophysicist, Epithelial Biologist, Developmental Biologist, cytoskeleton
Dissecting the cellular mechanics of contact inhibition of locomotion

Our aim is to dissect the mechanisms of contact inhibition of locomotion (CIL), a process whereby migrating cells collide and repel each other, as it is now clear that CIL is pivotal to understanding embryogenesis and pathologies such as cancer. We have developed an in vivo model using Drosophila macrophages (hemocytes), along with novel analytical tools, to examine the contact inhibition response in cells during development. We therefore have an unprecedented opportunity to address CIL in a genetically tractable organism within a physiologically relevant setting. This model has revealed that a precisely controlled CIL response is a significant driving force behind the acquisition of embryonic patterns, and recent data show that this precision requires a series of synchronized changes in cytoskeletal dynamics. Our central hypothesis is that key to this cellular ‘dance’ is mechanosensation of the collision, which integrates subsequent signaling mechanisms to choreograph the steps of the contact inhibition process. The first part of this proposal will elucidate the molecular mechanisms controlling CIL by exploiting our unique ability to live image and genetically dissect this process in Drosophila. We will also take an interdisciplinary approach to elucidate the mechanical aspects of the response, which will allow us to examine the feedback between signaling pathways and the physical forces of the CIL response. We will subsequently extend our detailed understanding of the CIL process, and our novel set of analytical tools, to mammalian cell types and model systems. This will allow us to develop new assays to directly probe the mechanics of CIL and begin to investigate the function of this underexplored process in other cell types. This in depth knowledge of the response places us in the best position to extend our understanding of CIL to new physiologically relevant scenarios that in the future will impact on human health.

Keywords of the ERC project: cell migration, contact inhibition of locomotion, drosophila morphogenesis
Keywords that characterize the scientific profile of the potential visiting researcher/s: cell migration, biophysics, development
A major role of metabolic alterations in the development of several human diseases, as diabetes, cancer and in the onset of ageing is becoming increasingly evident. This has a deep impact for human health due to the alarming increase in nutrient intake and obesity in the last decades. Fundamental aspects of how aberrant nutrient fluctuations trigger deregulated hormone levels and endocrine signals have been elucidated, being a prime example the phenomenon of insulin resistance. In contrast, how changes in nutrient levels elicit direct cell-autonomous signal transduction cascades and the consequences of these responses in physiology are less clear. The signalling circuitry of direct nutrient sensing converges with that of hormones in the regulation of the mechanistic target of rapamycin (mTOR) kinase, a driver of anabolism, cell growth and proliferation. Deregulation of mTORC1 activity underlies the pathogenesis of cancer and diabetes, and its inhibitor rapamycin is approved as an anti-cancer agent and delays ageing from yeast to mammals. In spite of its importance for human disease, our understanding of the nutrient sensing signalling pathway and its impact in physiology is largely incomplete, as only a few years ago the direct molecular link between nutrients and mTORC1 activation, the Rag GTPases, were identified. The present proposal aims to determine how the nutrient sensing signalling pathway affects mammalian physiology and metabolism, and whether its deregulation contributes to cancer, insulin resistance and aging. In particular, the objectives are: 1) To identify novel regulators of the Rag GTPases with unbiased and candidate-based approaches. 2) To establish the consequences of deregulated nutrient-dependent activation of mTORC1 in physiology, by means of genetically engineered mice. 3) To determine the impact of the nutrient sensing pathway in the effects of dietary restriction and nutrient limitation in glucose homeostasis and cancer.

Keywords of the ERC project: cancer, metabolism, mice, nutrients, mTOR, rapamycin, growth factors, Rag GTPases

Keywords that characterize the scientific profile of the potential visiting researcher/s:
Molecular Subtype Specific Stem Cell Dynamics in Developing and Established Colorectal Cancers

Annually 1.2 million new cases of colorectal cancer (CRC) are seen worldwide and over 50% of patients die of the disease making it a leading cause of cancer-related mortality. A crucial contributing factor to these disappointing figures is that CRC is a heterogeneous disease and tumours differ extensively in the clinical presentation and response to therapy. Recent unsupervised classification studies highlight that only a proportion of this heterogeneity can be explained by the variation in commonly found (epi-)genetic aberrations. Hence the origins of CRC heterogeneity remain poorly understood. The central hypothesis of this research project is that the cell of origin contributes to the phenotype and functional properties of the pre-malignant clone and the resulting malignancy. To study this concept I will generate cell of origin- and mutation-specific molecular profiles of oncogenic clones and relate those to human CRC samples. Furthermore, I will quantitatively investigate how mutations and the cell of origin act in concert to determine the functional characteristics of the pre-malignant clone that ultimately develops into an invasive intestinal tumour. These studies are paralleled by the investigation of stem cell dynamics within established human CRCs by means of a novel marker independent lineage tracing strategy in combination with mathematical analysis techniques. This will provide critical and quantitative information on the relevance of the cancer stem cell concept in CRC and on the degree of inter-tumour variation with respect to the frequency and functional features of stem-like cells within individual CRCs and molecular subtypes of the disease.

I am convinced that a better and quantitative understanding of the dynamical properties of stem cells during tumour development and within established CRCs will be pivotal for an improved classification, prevention and treatment of CRC.

Keywords of the ERC project: colorectal cancer, molecular subtypes, stem cells

Keywords that characterize the scientific profile of the potential visiting researcher/s: bioinformatics, imaging, biochemistry
Metabolic actions of brain leptin receptors signaling in type 1 diabetes

An established dogma is that insulin is absolutely required for survival. This notion has been supported by the fact that the sole life-saving intervention available to the millions affected by type 1 diabetes mellitus (T1DM; an illness caused by pancreatic β-cell loss and hence insulin deficiency) is insulin therapy. This treatment however does not restore normal metabolic homeostasis. In fact, the life-expectancy and -quality of T1DM people is worse compared to normal subjects. In part, this is due to challenging morbidities of T1DM, as for example heart disease and hypoglycemia, both of which are thought to be caused by insulin therapy itself. Indeed, owing to insulin’s lipogenic actions, this treatment likely contributes to the ectopic lipid deposition (i.e.: in non-adipose tissues) and extremely high incidence of coronary artery disease seen in T1DM subjects. Also, due to insulin’s potent, fast-acting, glycemia-lowering action, this therapy significantly increases the risk of hypoglycemia; a disabling and life threatening event. Because insulin therapy does not restore metabolic homeostasis in T1DM subjects, better intervention is urgently needed. To these ends, we and others have shown that the hyperglycemic and lethal consequences of insulin deficiency can be rescued by administration of the adipocyte-secreted hormone leptin. Not only these results challenge an established view, they also raise a fundamental biological and medical question: what are the mechanisms by which leptin improves hyperglycemia and permits survival in the context of insulin deficiency? This proposal aims at identifying the critical cellular and molecular components underlying the beneficial effects of leptin in the context of insulin deficiency. Once identified, manipulation of these components has the potential to improve life-expectancy and -quality of the millions affected by insulin deficiency (e.g.: T1DM and also some late-stage type 2 diabetics).

Keywords of the ERC project: diabetes, hypothalamus, life without insulin, new therapeutics

Keywords that characterize the scientific profile of the potential visiting researcher/s: hard worker, smart individual, strong drive to pursue an independent scientific career
**Project ID:** 639784  
**Project Acronym:** EpiTALL  
**Evaluation Panel:** LS4 - Physiology, Pathophysiology and Endocrinology

**Principal Investigator:** Dr Pieter Van Vlierberghe  
**Host Institution:** Universiteit Gent - BE

**Dynamic interplay between DNA methylation, histone modifications and super enhancer activity in normal T cells and during malignant T cell transformation**

Dynamic interplay between histone modifications and DNA methylation defines the chromatin structure of the humane genome and serves as a conceptual framework to understand transcriptional regulation in normal development and human disease. The ultimate goal of this research proposal is to study the chromatin architecture during normal and malignant T cell differentiation in order to define how DNA methylation drives oncogenic gene expression as a novel concept in cancer research. T-cell acute lymphoblastic leukemia (T-ALL) accounts for 15% of pediatric and 25% of adult ALL cases and was originally identified as a highly aggressive tumor entity. T-ALL therapy has been intensified leading to gradual improvements in survival. However, 20% of pediatric and 50% of adult T-ALL cases still relapse and ultimately die because of refractory disease. Research efforts have unravelled the complex genetic basis of T-ALL but failed to identify new promising targets for precision therapy. Recent studies have identified a subset of T-ALLs whose transcriptional programs resemble those of early T-cell progenitors (ETPs), myeloid precursors and hematopoietic stem cells. Importantly, these so-called ETP-ALLs are characterized by early treatment failure and an extremely poor prognosis. The unique ETP-ALL gene expression signature suggests that the epigenomic landscape in ETP-ALL is markedly different as compared to other genetic subtypes of human T-ALL. My project aims to identify genome-wide patterns of DNA methylation and histone modifications in genetic subtypes of human T-ALL as a basis for elucidating how DNA methylation drives the expression of critical oncogenes in the context of poor prognostic ETP-ALL. Given that these ETP-ALL patients completely fail current chemotherapy treatment, tackling this completely novel aspect of ETP-ALL genetics will yield new targets for therapeutic intervention in this aggressive haematological malignancy.

**Keywords of the ERC project:** DNA methylation, T-cell leukemia  
**Keywords that characterize the scientific profile of the potential visiting researcher/s:** bioinformatician
mTOR pathophysiology in rare human diseases

The mammalian Target Of Rapamycin (mTOR) is a master regulator of growth. mTOR is a protein kinase that exists in two distinct complexes in the cell and transduces virtually all anabolic signals from the environment: nutrients, such as glucose and amino acids, growth factor peptides, such as insulin and insulin like growth factors, oxygen, mitochondrial metabolites, energy status. mTOR is required to sustain cell responses to nutrient availability including cell growth, proliferation, macromolecule biosynthesis, and suppress autophagy. During the past ten years we have generated and characterized a wide panel of mouse mutants in the mTOR pathway. We were involved in revealing specific phenotypes that increased our knowledge of mTOR roles in pathophysiology: mutants with small cells, mutants resistant to tumorigenesis in specific tissues and after specific oncogenic insults, mutants mimicking caloric restriction and promoting longevity, mutants with muscle dystrophy, mutants with altered insulin action.

The overall goal of our research proposal for the next five years is twofold. From one hand we want to better understand fundamental processes including cell size control and organismal longevity. To this end we want to determine the molecular targets of the mTORC1/S6 kinase cassette that may explain the alterations in cell size and lifespan when these kinases are deregulated (project 1). From the other hand we want to understand and cure rare human genetic diseases that arise from pathological changes in the activity of the mTOR pathway in children or that may benefit from therapeutical intervention on this pathway. These diseases include Tuberous Sclerosis Complex, PEComas and hemangiomas (project 2), metabolic diseases (projects 3), lysosomal storage diseases (project 4). The translational approaches in this proposal will stem from a close interaction with multiple Medical Dept. in our shared research campus of the Necker Children Hospital.

Keywords of the ERC project: growth, signal transduction, metabolism, animal models, disease, nutrition, insulin, mTOR, ageing

Keywords that characterize the scientific profile of the potential visiting researcher/s: growth, signal transduction, metabolism, animal models, disease, nutrition, insulin, mTOR, ageing
Role of Liver Estrogen Receptor in female Energy Metabolism, Reproduction and Aging: What About Your Liver Sexual Functions?

In mammals, the liver is the peripheral integrator of nutrient availability and energetic needs of the entire organism. We recently demonstrated that dietary amino acids (AA) activate liver Estrogen Receptors (ER) and that, in case of food scarcity, the lowered circulating AA decrease liver ER activity and reduce IGF-1 synthesis with the consequent blockage of the estrous cycle.

Here, we hypothesize that in females liver ERα is also a sensor of the endogenous signalling induced by transitions among reproductive stages and a key organizer for the changes required to adapt energy metabolism to reproductive necessities. Thus, we propose that in mammals liver ERα is regulated by reproductive functions and that, in case of ovary malfunctioning, the altered estrogenic signalling causes metabolic impairment leading to local and perhaps systemic disruption of energy homeostasis.

To demonstrate our theory, we will explore: i) the molecular pathways activating liver ERα and the related ERα transcriptome by genome-wide analytical tools; ii) the hepatic metabolism and the systemic consequences of liver ER pharmacological and genetic manipulations by means of metabolomic technologies; iii) the association between altered signalling on liver ER and the onset of metabolic disorders; iv) the molecular interactions between ER and PPAR activity and the effect of estrogens on liver autophagy.

WAYS research is facilitated by a series of tools such as ER conditional KO, reporter mice, arrays of genes known as target of liver ERα, and others generated by our laboratory in collaboration with EU groups in previous EU programs.

The vision of the liver as a functional unit with reproductive organs constitutes a paradigm shift in our understanding of woman physiology; thus, the full comprehension of liver ERα activity and regulation will be a critical step for the conception of new therapies for several diseases affecting women including the metabolic syndrome or the non-alcoholic steatosis.

Keywords of the ERC project: hormone action, estrogen, women health, transcription regulation, energy metabolism, microglia

Keywords that characterize the scientific profile of the potential visiting researcher/s: molecular biology, cell biology, animal biology, molecular imaging
Mitochondria, Peroxisomes and Lysosomes - the "menage a trois" of cellular metabolism

The metabolic roles of mitochondria, peroxisomes and lysosomes are well established. Numerous genetic defects affecting the function of these organelles result in a wide spectrum of metabolic diseases. The involvement of these organelles in signalling pathways is receiving increasing attention. Furthermore, interactions between them and other cellular components have been elucidated. Evidence is now emerging that dysfunction in mitochondria, peroxisomes or lysosomes causes secondary perturbations in the other two organelles. The fundamental hypothesis presiding to this proposal is that mitochondria, peroxisomes and lysosomes form an interdependent network (MitoPexLyso), which is likely to have fundamental roles in cell biology, metabolism and metabolic diseases.

To test this hypothesis and elucidate the role of the MitoPexLyso network in physiology and disease, we will employ state-of-the-art imaging and systems biology approaches. First, we will uncover how dysfunction of each MitoPexLyso organelle affects the network. We will test if mitochondrial dysfunction can trigger lysosome biogenesis, and also systematically address how perturbations in one organelle affect the other two. Second, we will identify signalling pathways sensing perturbations on the MitoPexLyso network, and elucidate their pathologic significance, both in cell lines and in animal models of metabolic diseases. Third, we will test a novel strategy to cure mitochondrial diseases: enhanced removal of damaged mitochondria through increased lysosomal autophagic capacity. We will generate a novel mouse model with higher lysosomal capacity in the skeletal muscle, and use a mouse model of mitochondrial myopathy, to test this premise in vivo.

This proposal addresses key questions in cell biology and metabolism, and will lay the foundation for a new field of “organelle networks” which will profoundly impact our understanding of metabolism and metabolic diseases and drive future research endeavours.

Keywords of the ERC project: organelle communication, mitochondria, peroxisomes, lysosomes, autophagy, signaling, genomics

Keywords that characterize the scientific profile of the potential visiting researcher/s: organelle communication, mitochondria, peroxisomes, lysosomes, autophagy, signaling, genomics
How do cortical circuits process sensory stimuli that leads to perception? Sensory input is encoded by complex interactions between principal excitatory neurons and a diverse population of inhibitory cells. Distinct inhibitory neurons control different subcellular domains of target principal neurons, suggesting specific roles of different cells during sensory processing. However, the individual contribution of these inhibitory subtypes to sensory processing remains poorly understood. This is mainly due to the technical challenges of recording the activity of identified cell types in-vivo, in response to quantified sensory stimuli. Therefore, I propose a novel approach based on four pillars: 1) An optically accessible circuit in the superficial layers of the cortex, comprised of inhibitory cells expressing the serotonin receptor 5HT3a, and the distal dendrites of pyramidal neurons. 2) A novel combination of electrophysiology and 3D two-photon imaging to simultaneously record the activity of morphologically identified 5HT3a cells and their dendritic targets. 3) A head-fixed perceptual decision task, whereby mice use their whiskers to determine the location of an object, allowing an accurate description of the sensory stimulus. 4) The integration of experimental data and computer models to gain mechanistic insights into circuit functions. The 5HT3a cells and the distal dendrites of pyramidal neurons receive ‘top-down’ contextual information from other cortical areas that is essential for constructing meaningful perceptions of sensory stimuli. Thus I hypothesize that 5HT3a cells influence sensory perceptions by controlling the excitability of the pyramidal cell distal dendrites that integrate top-down and sensory input. Thus, I will not only reveal novel functions of inhibitory neurons, I will also shed light on how top-down and sensory input is integrated, and I will provide novel methods to test the functions of other cell types in normal mice and disease models.

Keywords of the ERC project: In-vivo Ca2+ imaging, sensorimotor integration, barrel cortex, neural inhibition, mouse behavior, computational neuroscience

Keywords that characterize the scientific profile of the potential visiting researcher/s: in-vivo patch clamp recordings, neural tracing, in-vivo imaging, extracellular recordings, mouse behaviour.
Neurons and blood vessels rely on common guidance signals to wire into elaborate neural and vascular networks that are closely juxtaposed and interdependent: vascular supply of oxygen and nutrients is essential to sustain the high metabolic rate of the nervous system, and conversely neural control of vascular tone is crucial for circulatory homeostasis. However, it remains unclear how the nervous and vascular systems establish an intimate physical and functional relationship. This proposal seeks to reveal the developmental mechanisms that link neuronal connectivity and vascularization of the nervous system, focusing on the interactions between vascular endothelial cells and spinal motor neurons that control locomotion, respiration and autonomic responses. Motor neuron diseases and a variety of other neurodegenerative conditions are precipitated by vascular abnormalities. Thus, understanding the molecular basis of neurovascular crosstalk may offer novel therapeutic opportunities.

My group will use mutagenesis-based forward genetics in reporter mice combined with gene profiling of motor neurons and endothelial cells to screen for novel regulators of neurovascular interactions and pathfinding. Candidate genes will be further characterized using in vivo mouse and chick models, in addition to in vitro studies to uncover the mechanisms of action. Through this multi-disciplinary approach, the proposal will address these fundamental questions: (i) Do neurovascular interactions instruct the assembly of neural and vascular networks? (ii) What signaling pathways connect region-specific vascularization of the CNS to the local metabolic and functional demand of neuronal tissues? (iii) What mechanisms account for specificity, spatiotemporal control and integration of guidance signaling? In addition, this research plan will generate comprehensive transcriptional/proteomic datasets and novel mouse mutants for future studies of neurovascular communication and patterning.

Keywords of the ERC project: Neurobiology of axon guidance and development; Neurovascular Crosstalk, Motor Neuron Disease

Keywords that characterize the scientific profile of the potential visiting researcher/s: cellular/molecular neurobiology; axon guidance and signaling; vascular biology; motor system disorders; ES models of disease
Understanding of the normal and diseased brain crucially depends on reliable knowledge of its microstructure. Important functions are mediated by small cortical units (columns) and even small changes in the microstructure can cause debilitating diseases. So far, this microstructure can only be determined using invasive methods such as, e.g., ex-vivo histology. This limits neuroscience, clinical research and diagnosis. My research vision is to develop novel methods for high-resolution magnetic resonance imaging (MRI) at 3T-9.4T to reliably characterize and quantify the detailed microstructure of the human cortex. This MRI-based histology will be used to investigate the cortical microstructure in health and focal cortical degeneration. Structure-function relationships in visual cortex will be elucidated in-vivo, particularly, ocular dominance columns and stripes. Specific microstructural changes in focal cortical degeneration due to Alzheimer’s disease and monocular blindness will be determined, including amyloid plaque imaging. To resolve the subtle structures and disease related changes, which have not previously been delineated in-vivo by anatomical MRI, unprecedented isotropic imaging resolution of up to 250 µm is essential. Methods for high-resolution myelin and iron mapping will be developed from novel quantitative MRI approaches that I have previously established. Super-resolution diffusion and susceptibility imaging will be developed to capture the neuropil microstructure. Anatomical imaging will be complemented by advanced high-resolution functional MRI. The multi-modal MRI data will be integrated into a unified model of MRI contrasts, cortical anatomy and tissue microstructure. My ambitious goal of developing in vivo MRI-based histology can only be achieved by an integrative approach combining innovations in MR physics, modelling and tailored (clinical) neuroscience experiments. If successful, the project will transform research and clinical imaging.

**Keywords of the ERC project:** Quantitative magnetic resonance imaging (MRI); in-vivo histology using MRI

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** Expert in MR physics, or ultra-high resolution fMRI, or advanced diffusion imaging, or multi-modal image processing
An intracellular approach to spatial coding in the hippocampus

The hippocampus is an important structure for spatial memory in rodents and episodic memory in humans. The hippocampus uses a sparse coding scheme where a given environment is represented by the place selective firing of a small group of cells, (called place cells) among a larger population of silent neurons. Thus a given environment is not only coded by the firing rate and timing of active cells but also by the very identity of these cells that fire or stay silent in that environment. Similarly, in humans, specific items or episodes are coded by the selective firing of particular cells in the temporal lobe among a larger population of silent neurons. Thus understanding the mechanisms involved in the selection of which cells will be active in a particular environment is one of the most important to understand the formation of spatial memories in rodents and episodic memories in humans. This question is at the core of our research project. Place cells have been extensively studied at the system level using extracellular recording which can only record the spiking output of neurons but not the intracellular mechanisms leading to that spiking. This is why I recently contributed to the development of a new technique allowing intracellular recordings in freely behaving animals. Using this technique we found an important role for intrinsic neuronal properties in the distinction between place and silent cells. Intriguingly, these differences were observed even before the new exploration began. Based on these findings we will address three objectives: 1) determine the role of intrinsic excitability in the initial selection of place cells, 2) test whether a similar coding scheme are valid for the other major hippocampal area for spatial coding: the CA3 area and last 3) determine whether these intrinsic mechanisms play a role in another major function of the hippocampus the remapping.

Keywords of the ERC project: spatial coding; hippocampus; spatial coding and memory; patch-clamp recordings; virtual reality; place cells

Keywords that characterize the scientific profile of the potential visiting researcher/s: computational models, virus tracing, optogenetics, pharmacogenetics
Smell and taste are the least studied of all senses. Very little is known about chemosensory information processing beyond the level of receptor neurons. Every morning we enjoy our coffee thanks to our brains ability to combine and process multiple sensory modalities. Meanwhile, we can still review a document on our desk by adjusting the weights of numerous sensory inputs that constantly bombard our brains. Yet, the smell of our coffee may remind us that pleasant weekend breakfast through associative learning and memory. In the proposed project we will explore the function and the architecture of neural circuits that are involved in olfactory and gustatory information processing, namely habenula and brainstem. Moreover we will investigate the fundamental principles underlying multimodal sensory integration and the neural basis of behavior in these highly conserved brain areas. To achieve these goals we will take an innovative approach by combining two-photon calcium imaging, optogenetics and electrophysiology with the expanding genetic toolbox of a small vertebrate, the zebrafish. This pioneering approach will enable us to design new types of experiments that were unthinkable only a few years ago. Using this unique combination of methods, we will monitor and perturb the activity of functionally distinct elements of habenular and brainstem circuits, in vivo. The habenula and brainstem are important in mediating stress/anxiety and eating habits respectively. Therefore, understanding the neural computations in these brain regions is important for comprehending the neural mechanisms underlying psychological conditions related to anxiety and eating disorders. We anticipate that our results will go beyond chemical senses and contribute new insights to the understanding of how brain circuits work and interact with the sensory world to shape neural activity and behavioral outputs of animals.

**Keywords of the ERC project:** zebrafish, neural circuits, systems neuroscience, neural computations, stress, learning, olfaction, habenula

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** computational, theoretical, optics, physics, engineering, neural circuits, neurophysiology
Zebrafish vision in its natural context: from natural scenes through retinal and central processing to behaviour.

All visual systems are specialised to best serve an animal’s sensory niche, yet how such specialisations are achieved through phylogenetic and developmental adaptations of the ‘common vertebrate visual system blueprint’ are poorly understood. I will study these adaptations in the visual system of zebrafish. I will use two-photon functional imaging and computational modelling to investigate how the visual system of zebrafish samples and processes behaviourally meaningful stimuli in the natural world. I will then use optogenetic manipulations while zebrafish navigate a virtual reality environment to directly probe the role of visual circuits in driving behaviour. Specifically, I will pursue four Aims: 1. What is the zebrafish eye designed to see? 2. How does the fish retina form feature selective output channels? 3. What does the fish’s eye tell the fish’s brain? 4. How does visual input to the brain lead to behaviour? Visual specialisations begin in the optics and movements of the eyes, and are subsequently deeply rooted in every step of neuronal computation. Therefore, I will study visual processing at these different organisational levels. Here, the highly ‘visual’ zebrafish present a powerful model. They (i) offer exquisite genetic tools to record and manipulate neurons, (ii) have transparent larval stages permitting optical access to the entire nervous system and (iii) there is a large array of well-studied and easily quantifiable visual behaviours. In addition, zebrafish undergo two distinct life-stages, from larva to adult - with distinct lifestyles in different visual environments and hence different feature-detection requirements. Comparison of processing strategies employed by the (a) larval and (b) adult zebrafish visual system with that of other species, including a complementary database already recorded in mice (c), will lead to an increasingly generalised understanding of biological vision.

Keywords of the ERC project: vision, retina, 2-photon imaging, zebrafish, visual ecology
Keywords that characterize the scientific profile of the potential visiting researcher/s: optical imaging, statistical modeling, genetics
The origins of dendritic computation within mammalian neural circuits

This proposal aims to address a simple question: what is the fundamental unit of computation in the brain? Answering this question is crucial not only for understanding how the brain works, but also if we are to build accurate models of brain function, which require abstraction based on identification of the essential elements for carrying out computations relevant to behaviour. In this proposal, we will build on recent work demonstrating that dendrites are highly electrically excitable to test the possibility that single dendritic branches may act as individual computational units during behaviour, challenging the classical view that the neuron is the fundamental unit of computation. We will address this question using a combination of electrophysiological, anatomical, imaging, molecular, and modeling approaches to probe dendritic integration in pyramidal cells and Purkinje cells in mouse cortex and cerebellum. We will first define the computational rules for integration of synaptic input in single and multiple dendrites by examining the somatic and dendritic responses to different spatiotemporal patterns of excitatory and inhibitory inputs in brain slices. Next, we will determine how these rules are engaged by patterns of sensory stimulation in vivo, by using various strategies to map the spatiotemporal patterns of synaptic inputs onto single dendrites. To understand how physiological patterns of activity in the circuit engage these dendritic computations, we will use anatomical approaches to map the wiring diagram of synaptic inputs to individual dendrites. Finally, we will perturb the dendritic computational rules by manipulating dendritic function using molecular and optogenetic tools, in order to provide causal links between specific dendritic computations and sensory processing relevant to behaviour. These experiments will provide us with deeper insights into how single neurons act as computing devices.

Keywords of the ERC project: dendrites, neural computation, cortex, synaptic transmission, pyramidal cell, computational neuroscience

Keywords that characterize the scientific profile of the potential visiting researcher/s: optics, electrophysiology, imaging, multiphoton, microscopy
Alzheimer’s disease is the most common form of dementia affecting more than 35 million people worldwide and its prevalence is projected to nearly double every 20 years with tremendous social and economical impact on the society. There is no cure for Alzheimer’s disease and current drugs only temporarily improve disease symptoms.

Alzheimer’s disease is characterized by a progressive deterioration of cognitive functions, and the neuropathological features include amyloid beta deposition, aggregates of hyperphosphorylated tau protein, and the loss of neurons in the central nervous system (CNS). Research efforts in the past decades have been focused on neurons and other CNS resident cells, but this “neurocentric” view has not resulted in disease-modifying therapies.

Growing evidence suggests that inflammation mechanisms are involved in Alzheimer’s disease and our team has recently shown an unexpected role for neutrophils in Alzheimer’s disease, supporting the innovative idea that circulating leukocytes contribute to disease pathogenesis.

The main goal of this project is to study the role of immune cells in animal models of Alzheimer’s disease focusing on neutrophils and T cells. We will first study leukocyte-endothelial interactions in CNS microcirculation in intravital microscopy experiments. Leukocyte trafficking will be then studied inside the brain parenchyma by using two-photon microscopy, which will allow us to characterize leukocyte dynamic behaviour and the crosstalk between migrating leukocytes and CNS cells. The effect of therapeutic blockade of leukocyte-dependent inflammation mechanisms will be determined in animal models of Alzheimer’s disease. Finally, the presence of immune cells will be studied on brain samples from Alzheimer’s disease patients. Overall, IMMUNOALZHEIMER will generate fundamental knowledge to the understanding of the role of immune cells in neurodegeneration and will unveil novel therapeutic strategies to address Alzheimer’s disease.

Keywords of the ERC project: Alzheimer’s disease, neuroinflammation, neuroimmunology, leukocyte trafficking, multi-photon microscopy

Keywords that characterize the scientific profile of the potential visiting researcher/s: immunologist, neuroscientist, neuroimmunologist, neuroimmunology, neuroscience, neuroinflammation, cell biology, immunology, imaging

BACKGROUND: Mosquitoes and other blood-feeding arthropods transmit important human and animal viruses (arthropod-borne viruses, arboviruses). With the increasing global threat of arboviruses, it is essential to understand the virus-vector interactions that determine virus transmission. The mosquito antiviral immune response is a key determinant of virus replication and transmission. We recently showed that arboviruses are targeted by a poorly-understood RNA silencing pathway in the major vector mosquito Aedes aegypti: the Piwi-interacting RNA (piRNA) pathway. Our (published and unpublished) observations imply that the piRNA pathway contributes to antiviral defense against different classes of viruses in somatic tissues of mosquitoes. Moreover, we identified a novel class of endogenous gene-derived piRNAs in mosquitoes that may form a new paradigm for piRNA-based regulation of cellular gene expression. AIM: This proposal has a three-fold aim: i) to delineate the biogenesis and function of the novel classes of virus- and gene-derived piRNAs, ii) to characterize mechanisms by which (arbo)viruses suppress or evade antiviral RNA silencing pathways, and by doing so, iii) to establish mosquitoes as an experimental model to characterize the complex piRNA machinery. APPROACH: We will use Aedes cell lines that recapitulate all aspects of piRNA biogenesis. This allows us to use a unique, powerful approach of genomic, cell biological, biochemical, and proteomic methodologies to study piRNA biogenesis and function. IMPORTANCE AND INNOVATION: This is the first study to comprehensively characterize viral and cellular piRNA biogenesis and function in mosquitoes. This proposal provides novel insights into the antiviral response in mosquitoes and may uncover novel regulatory functions of endogenous piRNAs. Moreover, it establishes a platform for functional and biochemical dissection of the complex biogenesis of piRNAs - the most enigmatic class of small silencing RNAs.

Keywords of the ERC project: Aedes aegypti, mosquito, RNA silencing, siRNA, piRNA, virus, arbovirus

Keywords that characterize the scientific profile of the potential visiting researcher/s: Postdoc or PI in one (or more) of the following fields: virology, small RNA biology, molecular entomology, or bio-informatics and insect genomics.
**Index:** -32 -

<table>
<thead>
<tr>
<th>Principal Investigator:</th>
<th>Dr George Kollias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Host Institution:</td>
<td>Biomedical Sciences Research Center Alexander Fleming - EL</td>
</tr>
</tbody>
</table>

**Mesenchymal Cells of the Lamina Propria in Intestinal Epithelial and Immunological Homeostasis.**

Mesenchymal cells (MCs) of the intestinal lamina propria refer to a variety of cell types, most commonly intestinal myofibroblasts, fibroblasts, pericytes, and mesenchymal stromal cells, which show many similarities in terms of origin, function and molecular markers. Understanding the physiological significance of MCs in epithelial and immunological homeostasis and the pathophysiology of chronic intestinal inflammatory and neoplastic disease remains a great challenge.

In this proposal, we put forward the challenging hypothesis that, especially during acute or chronic inflammatory and tumorigenic conditions, MCs play important physiological roles in intestinal homeostasis regulating key processes such as epithelial damage, regeneration and tumorigenesis, intestinal inflammation and lymphoid tissue formation. We further posit that a unifying principle underlying such functions would be the innate character of MCs, which we hypothesize are capable of directly sensing and metabolizing innate signals from microbiota or cytokines in order to exert homeostatic epithelial and immunological regulatory functions in the intestine.

We will be using genetic approaches to target innate pathways in MCs and state of the art phenotyping to discover the physiologically important signals orchestrating intestinal homeostasis in various animal models of intestinal pathophysiology. We will also study MC lineage relations and plasticity during disease and develop ways to interfere therapeutically with MC physiology to achieve translational added value for intestinal diseases, as well as for a range of other pathologies sharing similar characteristics.

---

**Keywords of the ERC project:** Chronic inflammation, tumorigenesis, intestinal homeostasis, animal models, mesenchymal cells

**Keywords that characterize the scientific profile of the potential visiting researcher/s:**
A combined evolutionary and proteomics approach to the discovery, induction and application of antiviral immunity factors

Humans are equipped with a variety of intrinsic immunity or host restriction factors. These evolved under positive selection pressure for diversification and represent a first line of defence against invading viruses. Unfortunately, however, many pathogens have evolved effective antagonists against our defences. For example, the capability of HIV-1 to counteract human restriction factors that interfere with reverse transcription, uncoating and virion release has been a prerequisite for the global spread of AIDS. We are just beginning to understand the diversity and induction of antiretroviral factors and how pandemic HIV-1 group M (major) strains evolved to counteract all of them. Here, I propose to use a genetics, proteomics and evolutionary approach to discover and define as-yet-unknown antiviral effectors and their inducers. To identify novel antiviral factors, we will examine the capability of all primate genes that are under strong positive selection pressure to inhibit HIV and its simian (SIV) precursors. This examination from the evolutionary perspective of the invading pathogen will also reveal which adaptations allowed HIV-1 to cause the AIDS pandemic. Furthermore, complex peptide-protein libraries representing essentially the entire human peptidome, will be utilized to identify novel specific inducers of antiviral restriction factors. My ultimate aim is to unravel the network of inducers and effectors of antiviral immunity - the "Anti-Virome" - and to use this knowledge to develop novel effective preventive and therapeutic approaches based on the induction of combinations of antiviral factors targeting different steps of the viral life cycle. The results of this innovative and interdisciplinary program will provide fundamental new insights into intrinsic immunity and may offer alternatives to conventional vaccine and therapeutic approaches because most restriction factors have broad antiviral activity and are thus effective against various pathogens.

Keywords of the ERC project: HIV, AIDS, restriction factors, human peptidome, viral evolution

Keywords that characterize the scientific profile of the potential visiting researcher/s: Creative, ambitious, molecular virology, cell biology
Inflammatory diseases affect over 80 million people worldwide and accompany many diseases of industrialized countries, being the majority of them infection-free conditions. There are few efficient anti-inflammatory drugs to treat chronic inflammation and thus, there is an urgent need to validate novel targets. We now know that innate immunity is the main coordinator and driver of inflammation. Recently, we and others have shown that the activation of purinergic P2X7 receptors (P2X7R) in immune cells is a novel and increasingly validated pathway to initiate inflammation through the activation of the NLRP3 inflammasome and the release of IL-1β and IL-18 cytokines. However, how NLRP3 sense P2X7R activation is not fully understood. Furthermore, extracellular ATP, the physiological P2X7R agonist, is a crucial danger signal released by injured cells, and one of the most important mediators of infection-free inflammation. We have also identified novel signalling roles for P2X7R independent on the NLRP3 inflammasome, including the release of proteases or inflammatory lipids. Therefore, P2X7R has generated increasing interest as a therapeutic target in inflammatory diseases, being drug like P2X7R antagonist in clinical trials to treat inflammatory diseases. However, it is often questioned the functionality of P2X7R in vivo, where it is thought that extracellular ATP levels are below the threshold to activate P2X7R. The overall significance of this proposal relays to elucidate how extracellular ATP controls host-defence in vivo, ultimately depicting P2X7R signalling through and beyond inflammasome activation. We foresee that our results will generate a leading innovative knowledge about in vivo extracellular ATP signalling during the host response to infection and sterile danger.

Keywords of the ERC project: Inflammation, NLRP3, inflammasome, P2X7, macrophage, cytokines, IL-1

Keywords that characterize the scientific profile of the potential visiting researcher/s:
Interplay between influenza viruses and host SUMO pathways

Influenza viruses cause a significant seasonal disease burden and continually threaten to initiate human pandemics. Antivirals are available for treatment of influenza, however drug-resistant viruses often emerge. Thus, there is urgent need to develop new antivirals with lower chances of selecting resistance. As viruses rely extensively on cellular functions, one way to minimise resistance is to target new antivirals against host factors. This concept requires a fundamental understanding of mechanisms underpinning the interplay between influenza viruses and their hosts. In this project, we will investigate the role that host SUMO pathways play during influenza virus replication. SUMO proteins are important regulators of cell signalling, and are covalently linked to other proteins in order to alter structure, localization or function. As such, SUMO conjugation regulates many diverse aspects of biology. Our own work shows that global cellular SUMOylation increases during influenza virus infection, and that virus replication is severely impaired when cells are depleted of key enzymes and components required for general SUMO conjugation. Here, we will determine what viral components trigger SUMOylation, and which specific cellular enzymes are involved. We will characterize where in the cell SUMO conjugates accumulate, and for the first time apply large-scale affinity-based quantitative proteomics to the identification of proteins that become SUMO modified during infection. A key aim will be to correlate changes to the SUMO sub-proteome with the function of specific host SUMO-modifying enzymes, thereby establishing the mechanistic role of these modifications during virus replication. Understanding basic mechanisms underlying SUMOylation during influenza virus infection will provide new insights into the fundamental biology of these important pathogens. The work could also lead to identification of key cellular pathways that can be exploited as novel therapeutic targets.

**Keywords of the ERC project:** influenza, virus, SUMO, ubiquitin, interferon, immunity, RNA, virus-host interaction, proteomics

**Keywords that characterize the scientific profile of the potential visiting researcher/s:**
Deciphering the molecular language orchestrating host-microbiome interactions and their effects on health and disease

The gastrointestinal tract hosts the microbiome, one of the highest microbial densities on earth. Diverse host-microbiome interactions influence a multitude of physiological and pathological processes, yet the basic mechanisms regulating host-microbiome interactions remain unknown. Deciphering the codes comprising the host-microbiome communication network and factors initiating loss of homeostasis (termed dysbiosis) will enable the recognition of pathways and signals critically important to initiation and progression of common immune and metabolic disorders. We recently identified the NLRP6 inflammasome as a critical innate immune regulator of colonic microbial ecology, with its disruption resulting in auto-inflammation and tumorigenesis. We will use this unique system, coupled with innovative robotic high-throughput modalities, gnotobiotics, metagenomics and multiple genetically altered mouse models to generalize our studies and decipher the critical principles governing host-microbiome interactions. We will elucidate the host-derived microbiome recognition signaling pathway at its entirety, from its upstream activators to the downstream effector molecules controlling microbial ecology; uncover the principles generating a stable microbiota composition; and develop and apply computational modelling to dissect the general mechanisms disrupting microbiome stability leading to dysbiosis. Using this innovative experimental and computational toolbox we will study the impact of dysbiosis on key components of the metabolic syndrome, and apply our findings to devise the first rational proof-of-concept approach for individualized microbiome-based treatment for these common disorders. At the basic science level, unraveling the principles of host-microbiota interactions will lead to a conceptual leap forward in our understanding of physiology and disease. Concomitantly, it may generate a platform for microbiome-based personalized therapy against common idiopathic illnesses.

Keywords of the ERC project: microbiome; microbiota; innate immunity; metabolic syndrome

Keywords that characterize the scientific profile of the potential visiting researcher/s:
Strengthening adaptive immunity via innate immunity: enhancing the CD8 T cell response by using the NKG2D ligand expressed in a herpesvirus vector

CD8+ T cells play a key role in the control of infections by intracellular pathogens. Recently, several top-notch studies provided ample evidence that NK cells are important in the regulation of CD8+ T cell response. NKG2D is an activating NK cell receptor which plays a role in the adaptive immune response by co-stimulating CD8+ T cells. Due to unique pattern of immune response, live attenuated CMVs are attractive candidates as vaccine vectors for a number of clinically relevant infections. The main idea behind this project stems from our preliminary data which suggest that a recombinant CMV vector expressing NKG2D ligand has a tremendous potential for subverting viral immunoevasion and boosting the efficiency of CD8 T cell response.

During the project we plan to systematically investigate the impact of all major innate immunity players on the CD8+ T cell response. A special focus will be given in obtaining new knowledge on the maintenance of memory CD8+ T cells during latent infection. This study will also provide novel insights on the role of NKG2D in both NK and T cell immunity. In order to test our hypothesis in vivo, we will employ state-of-the-art technology used in herpesvirus genetics coupled with high-end immune monitoring. Ultimately, we will translate our results to a human CMV vector, in order to gauge the impact of NKG2D signaling on immune response in a humanized mouse model.

We believe that the significance of the proposed study is enormous since stimulating CD8+ T cells has been widely recognized as a method of choice for vaccine development. There are relatively large number of pathogens for which the immunity acquired post-infection does not fully shelter against re-infection and disease. Therefore, we are in a desperate need for vaccines which offer superior protection compared to the one following natural infection. This study will provide groundbreaking information which will set the stage for the development of new vaccines and vaccine vectors.

Keywords of the ERC project: NK cells, CD8 T cells, NKG2D, protective immunity

Keywords that characterize the scientific profile of the potential visiting researcher/s: immunology, virology, biotechnology; NK cells, CD8 T cells, NKG2D, protective immunity
Fungal diseases represent a significant and growing threat to human health, particularly since the AIDS pandemic and increasing use of immunosuppressive drugs has produced a massive population of people with impaired immunity who are vulnerable to fungal infections. A great challenge in medical mycology is to understand how fungal virulence evolves. The vast majority of fungal species are not human pathogens and, for those that are, virulence appears to have evolved independently on many different occasions. Identifying the step(s) that convert an environmental fungus into a human pathogen, as well as subsequent changes in virulence within a pathogenic lineage, is therefore of fundamental importance. Based on a number of lines of evidence, I hypothesise that a critical regulator of fungal virulence in animal hosts is the activity of the fungal mitochondrion, an energy-generating organelle present in almost all eukaryotes. I propose to test this hypothesis comprehensively by combining genetic and cell biological approaches with high-resolution imaging methods.

Keywords of the ERC project: pathogen, innate immunity, macrophage, Cryptococcus, fungi

Keywords that characterize the scientific profile of the potential visiting researcher/s: Immunologist, microbiologist, cell biologist, fungal geneticist
Novel etiology of autoimmune disorders: the role of acquired somatic mutations in lymphoid cells

Molecular pathogenesis of most immune-mediated disorders, such as of autoimmune diseases, is poorly understood. These common maladies carry a heavy burden both on patients and on society. Current therapy is non-targeted and results in significant short- and long-term adverse effects. Large granular lymphocyte (LGL) leukemia is characterized by expansion of cytotoxic T- or NK-cells and represents an intriguing clinical continuum between a neoplastic and an autoimmune disorder. Patients suffer from autoimmune cytopenias and rheumatoid arthritis (RA), which are thought to be mediated by LGL cells targeting host tissues. My group recently discovered that 40-50% of LGL leukemia patients carry in their lymphoid cells acquired, activating mutations in the STAT3 gene – a key regulator of immune and oncogenic processes (Koskela et al, N Engl J Med, 2012). This breakthrough discovery gives insight to the pathogenesis of autoimmune disorders at large. I present here a hypothesis that a strong antigen-induced proliferation is a mutational driver, which causes somatic mutations in lymphoid cells. When mutations hit key activating pathways, autoreactive cells acquire functional advantage and expand. The target antigen of the expanded clone determines the clinical characteristics of the autoimmune disease induced. To prove this hypothesis, we will separate small lymphocyte clones from patients with autoimmune diseases and use sensitive next-generation sequencing methods to characterize the spectrum of somatic mutations in lymphoid cells. Further, we will study the function of mutated lymphocytes and examine the mechanisms of autocytotoxicity and end-organ/tissue damage. Finally, we aim to understand factors, which induce somatic mutations in lymphoid cells, such as the role of viral infections. The results will transform our understanding of molecular pathogenesis of autoimmune diseases and lead to accurate diagnostics and discovery of novel drug targets.

Keywords of the ERC project: autoimmune disease, genetics, T-cell clonality

Keywords that characterize the scientific profile of the potential visiting researcher/s: immunology, bioinformatics, next-generation sequencing, autoimmune diseases, genetics
Small and large non-coding RNAs are essential components at the heart of gene expression regulation. The past fifteen years have witnessed the emergence of a new field of research impacting diverse domains of biology. Among these, virology is no exception and discoveries such as the antiviral role of RNA silencing, virus-encoded microRNAs (miRNAs), or miRNA-based regulation of viruses have notably shifted our views of host-virus interactions. Although we know a lot about the mechanisms of action of ncRNAs, and their role in the context of viral infections, we know much less regarding the control of the regulatory RNAs themselves. In other words, how are the regulators regulated? To provide answers to this burning question, we propose to use different viruses as models to investigate the various levels where modulation of regulatory RNA can occur. Thus, we will study the importance of RNA secondary and tertiary structure as well as accessory proteins in the regulation of miRNA primary transcript processing. In a second axis, we propose to investigate how the functional, mature miRNAs can be controlled. To this end, we will focus on the mechanisms of target-mediated miRNA decay and the role of competing endogenous RNAs. We will finally turn to the regulation of antiviral RNA silencing. Although it seems that this kind of defence mechanism exist in mammalian cells, it is not yet clear how physiologically relevant it is and how it interfaces with other innate immune mechanisms. In this multidisciplinary project, we will use a combination of techniques ranging from bioinformatics to cellular biology to achieve our goal to get a comprehensive view of how RNA silencing processes are regulated during virus infection.

**Keywords of the ERC project:** RNA silencing; microRNA; virus; innate immunity; Gene regulation

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** Molecular biology, virology, RNA, high-throughput techniques, bioinformatics
This proposal aims to investigate the role of cytosolic DNA sensing pathways in CD4 T cell differentiation. Cellular host defense to pathogens relies on the detection of pathogen-associated molecular patterns including deoxyribonucleic acid (DNA), which can be recognized by host myeloid cells through Toll-like receptor (TLR) 9 binding. Recent evidence however suggests that innate immune cells can also perceive cytoplasmic DNA from infectious or autologous origin through cytosolic DNA sensors triggering TLR9-independent signaling. Activation of cytosolic DNA sensor-dependent signaling pathways has been clearly shown to trigger innate immune responses to microbial and host DNA, but the contribution of cytosolic DNA sensors to the differentiation of CD4 T cells, an essential event for shaping adaptive immune responses, has not been documented. This proposal aims to fill this current knowledge gap.

We aim to decipher the molecular series of transcriptional events triggered by DNA in CD4 T cells that ultimately result in altered T cell differentiation. This aim will be addressed by combining in vitro and in vivo approaches such as advanced gene expression analysis of CD4 T cells and use of transgenic and gene-deficient mice. Structure activity relationship and biophysical studies will also be performed to unravel novel immunomodulators able to affect CD4 T cell differentiation.

**Keywords of the ERC project:**

*Keywords that characterize the scientific profile of the potential visiting researcher/s:*
Novel approaches to determining the function of tissue-specific regulatory T cells

Regulatory T cells (Tregs) are formed through the expression of the transcription factor Foxp3 in T cells, resulting in the rewiring of the cell function into an immunosuppressive phenotype. Recently, it has been proposed that Tregs also have additional tissue-specific physiological roles when resident in different tissues. For example, tissue-specific Tregs residing in the muscle and adipose tissue possess immunological and non-immunological functions in these tissues, distinct from the generic Tregs in circulation. Currently, research into tissue-specific functions of Tregs, or any other migratory cell type, is limited by the available research tools. A vital part of immunological studies is cell depletion, yet a major limitation of all available methods is that they deplete target cells across the entire organism. This makes it extremely difficult to ascertain the function of tissue-resident Tregs, as systemic deletion results in severe autoimmunity, confounding the study of tissue-specific subsets. In order to assess these tissue-resident subsets new research tools are required to deplete the target cells in a specific anatomical region while leaving the same cell type unaffected in other organs. This project proposes to generate new synthetic biology tools for depleting tissue-resident cells and then to apply these tools to the study of tissue-resident Tregs in the brain, lung, liver, kidney and pancreas, thus creating a comprehensive atlas of tissue-specific functions. These studies will be extended by systematic molecular, cellular and kinetic analysis using existing innovative methods established in the laboratory. Finally, our tissue-specific deletion system will have a profound impact on immunology beyond the direct scope of the project, as the tools will be developed to allow flexible application to any cell type. In essence, this is a field of research currently held back by the absence of appropriate tools, waiting for the generation of a new toolkit.

Keywords of the ERC project: Tregs, immune, synthetic biology, immunology

Keywords that characterize the scientific profile of the potential visiting researcher/s: molecular biology, immunology
From longitudinal proteomics to dynamic individualized diagnostics

Longitudinal omics data hold great promise to improve biomarker detection and enable dynamic individualized predictions. Recent technological advances have made proteomics an increasingly attractive option but clinical longitudinal proteomic datasets are still rare and computational tools for their analysis underdeveloped. The objective of this proposal is to create a roadmap to detect clinically feasible protein markers using longitudinal data and effective computational tools. A biomedical focus is on early detection of Type 1 diabetes (T1D). Specific objectives are: 1) Novel biomarker detector using longitudinal data. DynaOmics introduces novel types of multi-level dynamic markers that are undetectable in conventional single-time cross-sectional studies (e.g. within-individual changes in abundance or associations), develops optimization methods for their robust and reproducible detection within and across individuals, and validates their utility in well-defined samples.

2) Individualized disease risk prediction dynamically. DynaOmics develops dynamic individualized predictive models using the multi-level longitudinal proteome features and novel statistical and machine learning methods that have previously not been used in this context, including joint models of longitudinal and time-to-event data, and one-class classification type techniques.

3) Dynamic prediction of T1D. DynaOmics builds a predictive model of dynamic T1D risk to assist early detection of the disease, which is crucial for developing future therapeutic and preventive strategies. T1D typically involves a relatively long symptom-free period before clinical diagnosis but current tools to predict early T1D risk have restricted power. The objectives involve innovative and unconventional approaches and address major unmet challenges in the field, having high potential to open new avenues for diagnosis and treatment of complex diseases and fundamentally novel insights towards precision medicine.

Keywords of the ERC project: computational biomedicine, bioinformatics, statistical data mining, machine learning, longitudinal data analysis, biomarkers,

Keywords that characterize the scientific profile of the potential visiting researcher/s:
Unravelling respiratory microflows in silico and in vitro: novel paths for targeted pulmonary delivery in infants and young children

Fundamental research on respiratory transport phenomena, quantifying momentum and mass transfer in the lung depths, is overwhelmingly focused on adults. Yet, children are not just miniature adults; their distinct lung structures and heterogeneous ventilation patterns set them aside from their parents. In RespMicroFlows, we will break this cycle and unravel the complex microflows characterizing alveolar airflows in the developing pulmonary acini. Our discoveries will foster ground-breaking transport strategies to tackle two urgent clinical needs that burden infants and young children. The first challenge relates to radically enhancing the delivery and deposition of therapeutics using inhalation aerosols; the second involves targeting liquid bolus installations in deep airways for surfactant replacement therapy. By developing advanced in silico numerical simulations together with microfluidic in vitro platforms mimicking the pulmonary acinar environment, our efforts will not only deliver a gateway to reliably assess the outcomes of inhaling aerosols and predict deposition patterns in young populations, we will furthermore unravel the fundamentals of liquid bolus transport to achieve optimal surfactant delivery strategies in premature neonates. By recreating cellular alveolar environments that capture underlying physiological functions, our advanced acinus-on-chips will deliver both at true scale and in real time the first robust and reliable in vitro screening platforms of exogenous therapeutic materials in the context of inhaled aerosols and surfactant-laden installations. Combining advanced engineering-driven flow visualization solutions with strong foundations in transport phenomena, fluid dynamics and respiratory physiology, RespMicroFlows will pave the way to a new and unprecedented level in our understanding and quantitative mapping of respiratory flow phenomena and act as catalyst for novel targeted pulmonary drug delivery strategies in young children.

Keywords of the ERC project: Lungs, aerosols, children, therapy, flows, Drug delivery, Lungs, Inhalation Therapy, Particle Transport, Flows

Keywords that characterize the scientific profile of the potential visiting researcher/s: Nanotechnology, particles, theragnostics, drug delivery, Drug Delivery, Nanotechnology, Functionalized Particles
Radical Medicine: Redefining Oxidative Stress

Oxidative stress, an excess of radical and other reactive oxygen species (ROS), has been suggested as a major disease mechanism. However, the major clinical trials using anti-oxidants have been failures, even suggesting serious side effects. Here, I propose completely different approaches: First, instead of letting radicals form and then scavenge them we will identify their diseases-relevant sources and prevent their formation or specifically repair the damage caused by ROS. Second, we will differentiate beneficial signalling roles of ROS. In combination, this will result in unprecedented precision and molecular specificity. In 2010, I submitted a somewhat related proposal to the ERC and received a comment as being “too focused on essential hypertension”. This proposal has a much broader focus and impact beyond cardiovascular diseases. In the past months we achieved major breakthroughs by identifying a radical/ROS source (NOX4) as fundamental mechanism in stroke, the fastest growing and soon no 1 cause of death. We are also developing in phase II a radical formation inhibitor for neurotrauma. Moreover, our basic research facilitated the development of drug classes re-activating an oxidatively damaged signalling receptor, now in phase III. Further, we identified angiogenesis as a radical/ROS-dependent and protective (!) signalling event. This proposal is just the beginning: our basic science will open up new fields and leap forward in personalized medicine with groundbreaking technologies and approaches. We will contribute to the diagnosis and early identification of patients at risk and to monitor their successful treatment (in vitro/blood-based); to the localization of disease processes (in vivo/molecular imaging) before the onset of symptoms; and to a new generation of more effective, predictable, and mechanism-based drugs. We also expect to later apply our findings and tools to neurobiology and oncology, where ROS also play physiological and pathological roles.

Keywords of the ERC project: oxidative stress, drug discovery, stroke, diabetic complications, reactive oxygen species, diabetes, oxidative stress, cyclic GMP

Keywords that characterize the scientific profile of the potential visiting researcher/s: phage display, antibodies, in vivo pharmacology, stroke models, drug discovery, stroke, diabetes, oxidative stress, cyclic GMP
Hairy Cell Leukemia (HCL), a chronic B-cell neoplasm, is initially sensitive to chemotherapy with purine analogs, but ~40% of patients eventually relapses and becomes less responsive to these drugs. Furthermore, purine analogs may cause myelotoxicity, immune-suppression and severe opportunistic infections. Therefore, molecularly-targeted less toxic drugs are highly desirable in HCL. However, its low incidence and the initial efficacy of purine analogs has made HCL an orphan in the world of cancer research and has spoiled the academic and industrial interest in developing better treatments for this disease. But recently we identified the V600E activating mutation in the BRAF kinase as the key genetic lesion of HCL (similar to BCR-ABL1 in chronic myeloid leukemia). Orally available specific BRAF inhibitors (e.g., Vemurafenib) have in the meantime showed remarkable efficacy in melanoma patients harboring the BRAF-V600E mutation, although resistance to such drugs eventually develops in this malignancy through reactivation of MEK (the downstream target of BRAF). The ground-breaking objective of this project is to introduce for the first time in HCL, by means of phase-2 investigator-driven pilot clinical trials, the concept of BRAF and/or MEK inhibition as an oral, non chemotherapy-based, entirely out-patient, genetics-driven and rationally designed treatment strategy, first in patients with active disease despite (or severe toxicity from) previous chemotherapy with purine analogs, and then, potentially, in the frontline setting. In comparison to melanoma, deeper and longer effect of BRAF inhibition may be expected in HCL, due to its much lower genetic complexity and proliferation rate. Anyway, potential mechanisms of resistance will be searched for to identify other genes recurrently mutated or aberrantly expressed in HCL patients developing resistance to BRAF inhibition (if any), and the clinical feasibility of combined BRAF and MEK inhibition will be addressed.

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:
Modeling Disease through Cell Reprogramming: a Translational Approach to the Pathogenesis of Syndromes Caused by Symmetrical Gene Dosage Imbalances

The fundamental limitation in our ability to dissect human diseases is the scarce availability of human tissues at relevant disease stages, which is particularly salient for neural disorders. Somatic cell reprogramming is overcoming this limitation through the derivation of patient-specific induced pluripotent stem cells (iPSC) that can be differentiated into disease-relevant cell-types. Despite these tantalizing possibilities, there are critical issues to be addressed in order to secure iPSC-modeling as a robust platform for the interrogation of disease aetiology and the development of new therapies. These concern the taming of human genetic variation, the identification of differentiation stages in which to uncover and validate phenotypes, and finally their translational into drug discovery assays. This project confronts these challenges focusing on the paradigmatic case of two rare but uniquely informative disorders caused by symmetric gene dosage imbalances at 7q11.23: Williams Beuren Syndrome and the subset of autism spectrum disorders associated to 7q11.23 microduplication. The hallmark of WBS is a unique behavioral-cognitive profile characterized by hypersociability and intellectual disability in the face of comparatively well-preserved language abilities. Hence, the striking symmetry in genotype and phenotype between WBS and 7dupASD points to the 7q11.23 cluster as a surprisingly small subset of dosage-sensitive genes affecting social behaviour and cognition. We build on a large panel of iPSC lines that we already reprogrammed from a unique cohort of WBS and 7dupASD patients and whose characterization points to specific derangements at the level of transcriptional/epigenetic control, protein synthesis and synaptic dysfunction. Through the integration of transcriptomic and epigenomic profiling with targeted mass spectrometry and gene network prediction we propose an innovative drug discovery pipeline for the identification of new therapeutic leads.

Keywords of the ERC project: disease modeling; stem cells; epigenetics; transcriptomics; iPSC; autism spectrum disorder; bioinformatics

Keywords that characterize the scientific profile of the potential visiting researcher/s: graduate degree in bioinformatics / computational biology / informatics; PhD in molecular biology / neurobiology; experience in the analysis of -omics data; excellent track record
Nature-inspired theranostic nanodevices for tumor imaging, early diagnosis and targeted drug-release

Late diagnosis and difficult treatment represent major obstacles in the fight against cancer. I propose here the development of self-regulated theranostic nanodevices supporting both early cancer diagnosis and targeted, tumor-cell-specific drug-release. Specifically, I will exploit the “designability” of nucleic acids to design and optimize molecular nanodevices that undergo binding-induced conformational changes upon target binding and, in doing so, signal the presence of a specific tumor marker or release a toxic therapeutic cargo. The inspiration behind my approach is derived from nature, which employs similar nanometer-scale protein and nucleic-acid-based “switches” as devices to detect –and respond to- specific molecules even against the complex background “noise” of the physiological environment. Furthering on this “nature-inspired” synthetic biology view I will also exploit naturally occurring regulatory mechanisms (e.g., allostery, cooperativity, etc.) to tune and edit the dose-response curve of these nanodevices, improve their analytical sensitivity, and optimize drug-release efficiency. In summary, I will use biomimetic “tricks’ taken directly from nature to move beyond the state-of-the-art of sensor design, with the goal being improved diagnostics and “smarter,” more effective drug delivery. Achieving these goals will require multidisciplinary expertise in the field of analytical chemistry, biophysics, electrochemistry, bioengineering, computational chemistry and synthetic biology. In my career I have demonstrated skills and expertise in similarly complex projects and in each of these challenging fields. Finally, the development of the proposed nanodevices will significantly impact the safety, compliance and efficacy of therapies and medical procedures bringing to scientific, technological and socio-economic benefits.

**Keywords of the ERC project:** DNA nanotechnology, synthetic biology, biosensors, nanodevices, nanomachines, supramolecular chemistry, bioengineering, Aptamers, Conformation switching probes, Smart drug-release, Electrochemical sensors.

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** DNA nanotechnology, synthetic biology, biosensors, nanodevices, nanomachines, supramolecular chemistry, bioengineering, Aptamers, Conformation switching probes, Smart drug-release, Electrochemical sensors.
Determination of Orphan Receptor Physiological Agonists and sigNals

G protein-coupled receptors make up both the largest membrane protein and drug target families. DE-ORPHAN aims to determine the close functional context; specifically physiological agonists and signaling pathways; and provide the first research tool compounds, of orphan peptide receptors.

Determination of physiological agonists (aka de-orphanization), by high-throughput screening has largely failed. We will introduce a new research strategy: 1) developing highly innovative bioinformatics methods for handpicking of all orphan receptor targets and candidate ligand screening libraries; and 2) employing a screening technique that can measure all signaling pathways simultaneously. The first potent and selective pharmacological tool compounds will be identified by chemoinformatic design of focused screening libraries. We will establish the ligands’ structure-activity relationships important for biological activity and further optimization towards drugs. The first potent and selective Gs- and G12/13 protein inhibitors will be designed by structure-based re-optimization from a recent crystal structure of a Gq-inhibitor complex, and applied to determine orphan receptor signaling pathways and ligand pathway-bias. They will open up for efficient dissection of important signaling networks and development of drugs with fewer side effects. DE-ORPHANs design hypotheses are based on unique computational methods to analyze protein and ligand similarities and are founded on genomic and protein sequences, structural data and ligands. The interdisciplinary research strategy applies multiple ligands acting independently but in concert to provide complementary receptor characterization. The results will allow the research field to advance into studies of receptor functions and exploitation of druggable targets, ligands and mechanisms. Which physiological insights and therapeutic breakthroughs will we witness when these receptors find their place in human pharmacology and medicine?

Keywords of the ERC project: GPCR, drug design, computational chemistry, pharmacology, medicinal chemistry, virtual screening, database development, programming, receptor function

Keywords that characterize the scientific profile of the potential visiting researcher/s: GPCR, drug design, computational chemistry, pharmacology, medicinal chemistry, virtual screening, database development, programming, receptor function
Clinical ultrasound platform for the quantitative and longitudinal imaging of theranostics and cellular therapy

The success of modern medical treatments such as cellular therapy and targeted treatments requires appropriate tools for in vivo monitoring. Imaging modalities, such as magnetic resonance imaging (MRI), single photon emission computed tomography (SPECT) and positron emission tomography (PET) are key candidates due to their noninvasive nature. However, these imaging techniques are extremely expensive and can involve radiation, both of which hinder their longitudinal and repetitive use. Ultrasound has so far been unsuitable due to the absence of a label to differentiate regions of interest from tissue background, the main problem being that current ultrasound contrast agents (CAs) have active lifetimes in the order of minutes. The CoNQUeST platform (Clinical Nanoparticles for Quantitative Ultrasound with high Stability) proposed here is an entirely new type of ultrasound CA that is extremely stable (lifetime of a year) and is not affected by insonation. This mechanism of contrast generation appears completely novel: The polymeric particles are under 200nm in diameter and must contain a soluble metal (M. Srinivas et al., patent pending, filed 09/2012). Based on the current state of the art, these particles are too small and do not contain the requisite gaseous component for ultrasound contrast. CoNQUeST particles are applicable to longitudinal and repeated imaging, as is necessary for cell tracking, due to their stability. Furthermore, these particles can be chemically bound to targeting agents, dyes and drugs, and are suitable for multimodal imaging, including MRI (both 1H and 19F), fluorescence and SPECT. Finally, the CoNQUeST agents are suitable for clinical use. I propose the application of the CoNQUeST agents to a clinical trial for tracking dendritic cell therapy in melanoma patients, longitudinal theranostic imaging in preclinical models and thorough characterisation of this novel mechanism of ultrasound contrast generation.

Keywords of the ERC project: imaging, nanoparticles, MRI, ultrasound, cell tracking

Keywords that characterize the scientific profile of the potential visiting researcher/s: nanoparticles, ultrasound, photoacoustics, nanotechnology
Common Oncogenic Mechanisms in Multi-Partner Translocation Families in Acute Myeloid Leukemia

Acute Myeloid Leukemia (AML) is the most frequent cancer of the blood system, with >80% mortality within 5 years of diagnosis. Straightforward clinical decisions are complicated by the genetic complexity of AML. In particular, fusion proteins arising from chromosomal aberrations are recurrently found in AML and often act as strong driver oncogenes. In “Multi-Partner Translocation” (MPT) families, one specific gene is fused to many recipient loci. Due to this modular architecture, MPT families are of particular interest to comparative studies of oncogenic mechanisms. The three most common MPT families in AML represent translocations of the MLL, RUNX1 and NUP98 genes. Despite their clinical significance, the molecular mechanism of transformation remains unknown for the majority of fusion proteins and it is unclear if transforming mechanisms are conserved within and across different MPT families. We hypothesize that common oncogenic mechanisms of fusion proteins are encoded in physical and genetic cellular interaction networks that are specific to MPT families. We propose to delineate critical common effectors of oncogenic mechanisms in AML driven by MPT families through a comprehensive, comparative, functional analysis of 20 clinically representative MLL-, RUNX1- and NUP98-fusion proteins using a unique experimental pipeline. Characterization of protein interactomes and their effects on gene expression will identify common cellular denominators of MPT families, whose functional contribution will be assessed through pooled shRNA screens in clinically relevant model systems. High-confidence hits will be validated in mouse models and primary cells from AML patients. This project will generate large informative datasets and novel experimental systems that are of relevance for basic and clinical cancer research. It will contribute to improved understanding of oncogenic mechanisms, which may directly impact on diagnostic and therapeutic strategies in the management of AML.

Keywords of the ERC project: Leukemia, Fusion proteins, functional genomics

Keywords that characterize the scientific profile of the potential visiting researcher/s: Leukemia, Fusion proteins, functional genomics
Exploring brain intracellular space using diffusion-weighted NMR spectroscopy in vivo

Alterations of the intracellular space, including intracellular protein accumulation, organelle and cytoskeleton dislocation, and modifications in cell shape, are an early hallmark of many neurodegenerative processes. The ability to assess and quantify these alterations non-invasively would be of tremendous interest, not only in a clinical context, but also for preclinical research. However, no tool currently exists allowing such measurements.

Diffusion-weighted magnetic resonance spectroscopy (DW-MRS) gives access to the apparent diffusion coefficient (ADC) of brain metabolites in vivo, which is related to their average quadratic displacement. Since metabolites are purely intracellular, their ADC is solely governed by the properties of the intracellular space. The dependency of the ADC on the delay during which displacement is measured (the “diffusion time” Td) tells how metabolite motion deviates from free diffusion, which can in theory help untangle and quantify the different factors governing motion.

So far, DW-MRS has only been performed in a limited number of studies, for Td ranging from ~10 to ~100 milliseconds, and has not yet demonstrated its ability to quantitatively assess the intracellular space. In the present work, we will develop cutting-edge DW-MRS methods to probe brain metabolite motion for Td varying over several orders of magnitude (from ~0.1 milliseconds to ~10 seconds). The dependency of the ADC over Td will provide unique insights about the mechanisms governing metabolite motion at very different scales. Data will be modeled to quantitatively extract parameters such as the intracellular viscosity, the size of intracellular structures, and cell shape and size. Estimated parameter values will be compared to values derived from other techniques, such as microscopy. Finally, developed methods will be used to investigate early alterations of the intracellular space in animal models of neurodegeneration.

**Keywords of the ERC project:** Magnetic resonance; spectroscopy; brain; diffusion; cell morphology; modeling

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** modeling; magnetic resonance; spectroscopy; diffusion; singlet state; long-lived state; carbon 13; 13C; chemical shift imaging; spectroscopic imaging; CSI
Cancer is a devastating disease affecting 1 in 3 people in their lifetime. The incidence is rising because of our aging population and causes a huge economic impact on our society because of hospitalization and lost productivity. Radiotherapy alone or in combination with surgery and/or chemotherapy is used in ~50% of all patients and uses ionizing radiation to induce DNA breaks that are lethal to cells. While significant progress has been made, radiotherapy is often limited because of side-effects in normal tissues and tumor control often fails because of resistance and metastases. Novel treatment paradigms are urgently needed. Among the key classical biological factors that determine radiation response in normal and tumor cells are the 4R; Reoxygenation, Repopulation, Redistribution and Repair. They are determined by intrinsic (genetic) as well as extrinsic factors from the tumor microenvironment and underlie tumor heterogeneity a hallmark of cancers and a decisive factor in clinical response. Yet, standard cancer treatments are largely based on the flawed assumption that tumors are homogenous within and between patients. We hypothesized that NOTCH signaling and tumor hypoxia cause tumor heterogeneity and are tumor selective therapeutic targets. First we will study key biological mechanisms that determine intra tumor heterogeneity, second we will establish their role in therapy response and third we will exploit this knowledge to enhance radiotherapy and provide proof of concept of a highly innovative approach to selectively activate cancer therapeutics targeting the NOTCH stem cell pathway in therapy resistant tumor cells without adverse effects in normal tissues.

DIRECT interrogates the molecular details of key cancer therapy response parameters providing opportunities for the next generation of tumor cell specific treatments that improve disease outcome.

**Keywords of the ERC project:** NOTCH, HYPOXIA, CANCER, STEM CELL, RESISTANCE, PRODRUGS, SECRETASE INHIBITOR, METABOLISM

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** BIOCHEMISTRY, ENZYMES, TUMOR METABOLISM, HIGH RESOLUTION IMAGING
Cataract is the opacification of the crystalline lens of the human eye. It is usually related with age and is one of the leading causes of blindness. The increase in light scatter in the lens reduces the contrast in the retinal images severely degrading vision. The current solution is to perform surgery to remove the natural lens that is substituted by an artificial intraocular lens. This is a successful procedure restoring good quality of vision in most patients. However, in many situations it would be incredible advantageous to actually “see” through a cataractous eye. The optics of the eye is affected by two factors: aberrations and scatter. In the last decade, correcting optical aberrations in the eye was accomplished by using adaptive optics techniques. This permitted to obtain high resolution images of the retina and also to improve vision. However, the possibility of correcting scatter in the eye was never considered before. We propose here the use of spatial and temporal advanced photonics techniques for imaging through the turbid media of the cataractous lens. We envision two direct applications of this technology: a dedicated fundus camera to register images of the retina in patients affected by cataracts and a novel type of opto-electronics spectacles restoring some vision in cataract patients. The fundus camera would offer clinicians the unique opportunity to determine if there is any retinal pathology underneath the cataractous eye. The scatter-correcting goggles would be useful in those cases where surgery were not possible for any reason or as a temporarily relieve until the surgery is performed. The same type of technology could be applied in the case of normal eyes with lower levels of scatter but desiring to achieve a better than normal vision for some specific tasks. This proposal presents a completely new and disruptive idea, which if successful would render immediate and significant benefits to patients worldwide.

Keywords of the ERC project: Optics, Photonics, Biomedicine, Cataracts

Keywords that characterize the scientific profile of the potential visiting researcher/s: Applied physics, Optics, Photonics, Biomedical engineering, Electrical engineering
Mechanotransduction in Cell-to-Cell Communication

Cell-to-cell communication pathways coordinate cellular functions in multicellular organisms. Cells that are nearest neighbours can communicate through specific interactions between ligand and receptor proteins present in their respective cell membranes. The objective of this research program is to address the hypothesis that the physical context of the ligand/receptor interaction contributes to defining the fundamental mechanisms of action of cell-to-cell communication pathways and their cellular outcomes.

The research program relies on the development of tools that provide well-defined physical inputs to cells, not confounded by simultaneous changes in chemical inputs. Therefore, beyond state-of-the-art developments in nanotechnology are here integrated with cell biology. In particular, DNA origami technology is applied to the development of ligand nanoclusters with customized spatial organization and mechanical properties. These ligand nanoclusters are used to probe the roles of physical properties of the ligand presentation on the activation of intracellular signalling pathways.

We will focus on the ephrin/Eph cell-to-cell communication pathway, which regulates embryonic development and the homeostasis of adult organs. ephrin/Eph signalling is commonly disrupted in cancer, showing tumour suppressing or tumour promoting character. The mechanisms that generate the diversity of outcomes of the ephrin/Eph pathway are largely unknown. We will use DNA origami/ephrin ligand nanoclusters to investigate whether the spatial organization and mechanical properties of ephrin ligand assemblies impact Eph receptor function and contribute to generating diversity in the pathway. Our novel approach is readily transferrable to the study of other signalling pathways. We aim to generate a knowledge foundation for the roles of mechanotransduction, the conversion of physical to biochemical signals, in cell-to-cell communication mediated by membrane-bound ligands and receptors.

Keywords of the ERC project: receptor, clustering, nanotechnology, omics, membrane biophysics

Keywords that characterize the scientific profile of the potential visiting researcher/s: biophysics, cell signalling, nanotechnology, omics, superresolution
Study on Environmental and Genome-Wide predictors of early structural brain Alterations in Young students

Mounting evidence suggests that early life factors have an important impact on the occurrence of late-life neurological diseases. From a public health perspective this is of particular relevance for dementia, the prevalence of which is increasing drastically, with no available preventive treatment, and epidemiological data suggesting that pathological processes may begin many years before clinical diagnosis. MRI-defined structural brain phenotypes are powerful intermediate markers for dementia, and can already show measurable alterations in young and middle-aged adults. These include global and regional brain volumes, gray matter volume and cortical thickness, and markers of white matter integrity. The SEGWAY project aims to: (i) explore the heritability and genetic determinants of structural brain phenotypes in young adults in their early twenties participating in the i-Share study, the largest ongoing student cohort; (ii) take a lifetime perspective by examining the shared genetic contribution to structural brain alterations in young adulthood (i-Share) and late-life, among participants of a large French population-based study (3C-Dijon); (iii) explore the interaction between genetic variants and vascular risk factors with established impact on structural brain phenotypes, in both age groups; (iv) examine the clinical significance of genetic risk variants for structural brain alterations by testing their association with cognitive performance in young and older adults. Replication and of our findings will be sought in the multigenerational Framingham Heart Study and other independent samples. Identifying common biological mechanisms underlying both early and late-life structural brain changes would provide important information on the mechanisms and timecourse of brain aging throughout a lifetime and could be of major importance for identifying of molecular drug targets and characterizing high risk populations most likely to benefit from early interventions.

Keywords of the ERC project: brain imaging genomics; lifetime approach; next generation sequencing; cutting-edge MRI markers; large scale genomic studies in population-based setting; meta-analyses of genomic studies in context of international consortia

Keywords that characterize the scientific profile of the potential visiting researcher/s: statistical genetics; genetic epidemiology; brain imaging genomics; bioinformatics
Project ID: 647426  
Project Acronym: 3D-JOINT  
Evaluation Panel: LS7 - Diagnostic Tools, Therapies and Public Health

Principal Investigator: Dr Jos Malda
Host Institution: Universitair Medisch Centrum Utrecht - NL

**3D Bioprinting of JOINT Replacements**

The world has a significant medical challenge in repairing injured or diseased joints. Joint degeneration and its related pain is a major socio-economic burden that will increase over the next decade and is currently addressed by implanting a metal prosthesis. For the long term, the ideal solution to joint injury is to successfully regenerate rather than replace the damaged cartilage with synthetic implants. Recent advances in key technologies are now bringing this “holy grail” within reach; regenerative approaches, based on cell therapy, are already clinically available albeit only for smaller focal cartilage defects. One of these key technologies is three-dimensional (3D) bio-printing, which provides a greatly controlled placement and organization of living constructs through the layer-by-layer deposition of materials and cells. These tissue constructs can be applied as tissue models for research and screening. However, the lack of biomechanical properties of these tissue constructs has hampered their application to the regeneration of damaged, degenerated or diseased tissue. Having established a cartilage-focused research laboratory in the University Medical Center Utrecht, I have addressed this biomechanical limitation of hydrogels through the use of hydrogel composites. Specifically, I have pioneered a 3D bio-printing technology that combines accurately printed small diameter thermoplastic filaments with cell invasive hydrogels to form strong fibre-reinforced constructs. This, in combination with bioreactor technology, is the key to the generation of larger, complex tissue constructs with cartilage-like biomechanical resilience. With 3D-JOINT I will use my in-depth bio-printing and bioreactor knowledge and experience to develop a multi-phasic 3D-printed biological replacement of the joint.

**Keywords of the ERC project:** cartilage, regenerative medicine, 3D printing, biofabrication, electrospinning

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** biology, tissue engineering, robotics, bioreactors
Nodding Syndrome: a trans-disciplinary approach to identify the cause and decrease the incidence of river epilepsy

Nodding syndrome (NS) is a neurological, incurable syndrome, currently affecting mainly children between 5 and 15 years of age in South Sudan, Uganda and Tanzania. Since 1950, when NS was first described, its cause has remained a mystery. NS is characterized by head-nodding (an atonic form of epilepsy), often followed by clonic-tonic seizures, developmental retardation and faltering growth. In the affected regions, NS is a major public health problem associated with severe socio-economic consequences. After exploratory missions to South Sudan, Uganda and the Democratic Republic of the Congo (DRC), we gathered epidemiological evidence that supports the hypothesis that NS is a disease caused by a pathogen transmitted by blackflies, the vectors that transmit the parasitic worm that causes onchocerciasis. This pathogen could be an unknown neurotropic virus or another pathogen that is transmitted either independently or as a symbiont of the worm. We postulate that this pathogen is able to cause typical NS, but also other forms of epidemic epilepsy. We hypothesise that the same disease is also endemic in other onchocerciasis hyper-endemic regions e.g. in the Mbam valley, Cameroon and the Orientale Province, DRC (where it is referred to as “river epilepsy”). In this project we aim to investigate our hypotheses in South Sudan, Uganda, Tanzania, Cameroon and the DRC with a trans-disciplinary approach including clinical-epidemiological, post-mortem, eco-entomological, and metagenomic studies. We will study the effect of vector control methods and ivermectin distribution on the incidence of river epilepsy. So far a multi-country study on NS was never done and nearly all previous studies were cross-sectional, carried out during short country visits. With this long term research plan we hope to finally discover the cause of NS and detect effective control strategies to decrease the incidence of epilepsy in onchocerciasis endemic areas.

Keywords of the ERC project: nodding syndrome, epilepsy, onchocerciasis, burden of disease, etiology

Keywords that characterize the scientific profile of the potential visiting researcher/s: epidemiology, mathematical modeling, neurology, tropical diseases, parasitology
Hybrid immune-eluding nanocrystals as smart and active theranostic weapons against cancer

Nanomedicine tools for cancer treatment comprise many nanosized systems, so far developed with smart functions such as efficient drug delivery and cell targeting abilities. However they remain still undercharacterized in terms of immunogenicity, potential toxicity due to the materials itself or the unwanted release of drugs. To overcome these challenges this project aims to develop a new generation of multifunctional therapeutic and diagnostic (thus theranostics) nanosystems displaying non-immunogenicity, improved cancer treatment, cell imaging, and high safety for the hosting organism. The innovative concept behind this approach relies on a core-shell nanosystem with a therapeutically active core, i.e. a TrojaNanoHorse (TNH), here validated against leukaemia. The injectable TNH have a lipid bilayer shell derived from autologous cancer cell membrane, naturally non-immunogenic. The hemocompatibility, antithrombogenicity, and targeting ability with antibodies toward malignant blood cells will be proved during this project. Studies will show the zinc oxide nanocrystal core activation developing toxic reactive oxygen species (ROS) for cancer killing, and its green fluorescence emission. The whole TNH would go beyond the state-of-the-art due to its nature-derived biomimetic shell, absence of drugs, its safety and biodegrading fate, and green luminescent emissions for diagnosis. This project will also develop novel set-up for non-immunogenic therapy and diagnosis, impacting on future technology, new standardized protocols for nanomaterial safety assessment, and study chemical and biological mechanism of ROS development effects on cancer cell. Achieving the ultimate goal of a multifunctional TNH will require multidisciplinary expertise in chemistry, material science, biology, medicine and engineering, opening new horizons as nanomedicine tools for efficient cancer therapy with strong scientific, technological and socio-economic benefits.

Keywords of the ERC project: Zinc Oxide Nanocrystals, Exosome, Reactive Oxygen Species, Cancer Cell Targeting, Leukemia, Ultrasound activated Therapy, Sonoluminescence imaging

Keywords that characterize the scientific profile of the potential visiting researcher/s: fluorescence live-cell imaging for cell targeting and apoptosis, exosome separation and engineering, lipid bilayers and liposomes, electron paramagnetic spectroscopy, preparation of colloidal suspensions, ultrasound-mediated processes and imaging, microb
This grant application proposes to develop a novel, customizable and personalized anti-cancer vaccine: peptide-coated conditionally replicating adenovirus (PeptiCrad). Anti-cancer vaccines represent a promising approach for cancer treatment because they elicit durable and specific immune response that destroys primary tumors and distant metastases. Oncolytic viruses (OVs) are of significant interest because in addition to cytolysis they stimulate anti-tumor immune responses, thereby functioning as anti-tumor vaccines. However, their efficacy among cancer patients has been modest. One reason for this shortcoming is that the immune responses generated by virus infection primarily target the virus rather than the tumor. In addition, tumors differ across patients. Specific and personalized approaches (rather than generic virus infection strategies) are required to optimize therapy. To this end we propose to develop a novel vaccine platform that combines the strengths of OVs with the specificity of vaccines. Our technology is called PeptiCrad. PeptiCrad is a virus “dressed as a tumor”. It directly kills cancer cells (i.e., oncolytic viruses) and expresses immunomodulatory molecules (i.e., cytokines or the immune checkpoint inhibitors anti-CTLA4 or anti-PDL1); most importantly, it diverts immunity toward the tumor (i.e., the capsid becomes covered with MHC-I-restricted tumor-specific peptides).

The method that we have developed to cover the virus with tumor peptides is novel and exceeds current state-of-the-art. Importantly, it is fast and does not require genetic or chemical manipulation of the virus; this feature has a significant impact on the translational capability of the project.

Our preliminary results show great potential but significant questions regarding the development and the personalization of PeptiCrad remain to be studied. In this grant I propose two lines of research, one focused on the development and the other one on the personalization of PeptiCrad.

**Keywords of the ERC project:** Immunotherapy, virotherapy, oncolytic adenovirus, peptides, tumour-specific peptides, Ligandome analysis

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** Ligandome analysis, peptides discovery, neoantigens, oncolytic herpes virus, oncolytic vaccinia virus,
In Europe, around two million individuals die from cancer each year. Cancer is a genetic disease and each patient's tumour contains several genetic lesions which are identified by next generation sequencing (NGS) and influence patient's outcome. A global current challenge lies in translating NGS data into benefit of cancer patients.

As attractive novel therapeutic concept, precision medicine addresses genetic lesions using targeted therapies. A large number of targeted drugs and compounds exist and are currently developed such as kinase inhibitors; unfortunately, numerous clinical trials on targeted therapies failed.

In order to better exploit NGS data, it is important to discriminate between genetic lesions that are required and maintain patients' tumours in vivo and others that do not – an impossible mission so far. My proposal aims at solving this key question.

Using acute leukaemia as model tumour disease, we propagate primary tumour cells from patients in immunodeficient mice. We recently pioneered a worldwide unique technique which allows the distinct genetic manipulation of individual patients' tumour cells while they grow in vivo.

We will molecularly target tumour-specific genetic lesions one by one; if tumour load is reduced, the lesion fulfils an essential function; essential lesions represent attractive therapeutic targets. Using our cutting edge technology, we will identify genetic lesions with essential, tumour-relevant function (i) in established tumour disease and (ii) in the clinically challenging situations of minimal residual disease and relapse.

Our approach implements a new paradigm for target selection in oncology. Our work introduces molecular target validation as important step into the value chain of precision medicine which will tailor drug development by industry and academia. Our approach will improve patient care and the success rate of clinical trials for the benefit of patients suffering acute leukaemia and putatively other cancers.
Mumps VIrus EXploitation of the human adhesion receptor GPR125

Mumps virus is a re-emerging pathogen that causes painful inflammatory symptoms, such as parotitis (salivary gland infection) and orchitis (testis infection). It is highly neurotropic with evidence of brain infection in half of cases and clinical evidence in up to 10%. It is a small RNA virus belonging to the family of paramyxoviridae that includes e.g. viruses for measles and pneumonia, all having a huge impact on global economics and human health. Current vaccine programs have not managed to eliminate mumps and infections occur also in vaccinated individuals.

Seven transmembrane (7TM) receptors are important drug targets. Large DNA viruses (herpes- and pox-) assign large parts of their genomes to exploit 7TM receptors. No such mechanism has however yet been described for small viruses.

Based on strong preliminary data, I will in this interdisciplinary project test the groundbreaking hypothesis that the adhesion 7TM receptor GPR125 is central for the organ damage caused by mumps virus via an interaction with the mumps virus-encoded short-hydrophobic (SH)-protein. I will do so by determining:

1 - The functional consequences of GPR125-SH-interaction at a single cell, organ and whole body level within the context of mumps virus infection
2 - The structural requirements for the GPR125-mumps virus interaction using NMR and resolution of crystal structure in preparation for future drug design

The project is high risk and high gain, yet the gain clearly exceeds the risk. On account of my past expertise in pharmacology and virology, and that of several expert collaborators, the project is indeed feasible. It has tremendous perspectives as SH-proteins are present also in other viruses. The SH-GPR125 complex might thus represent a general principle for organ damage and a mode of action more generally amenable to therapeutic interference. In fact, novel approaches, mechanism-based, might be seen as more appealing to those who fear current vaccination 'modes'.

Keywords of the ERC project: G protein-coupled receptors (GPCRs), adhesion GPCRs, blood brain barrier, virus infections

Keywords that characterize the scientific profile of the potential visiting researcher/s: G protein-coupled receptors (GPCRs), drug development, mouse models for infection and metabolism, novel antiviral therapy
An Integrative Approach to Understanding Convergent Evolution in Ant-eating Mammals

Despite its widespread occurrence across the tree of life, many questions still remain unanswered concerning the fascinating phenomenon of convergent evolution. Ant-eating mammals constitute a textbook example of morphological convergence with at least five independent origins in placentals (armadillos, anteaters, aardvarks, pangolins, and aardwolves). The large extent of convergent morphological evolution, the importance of molecular convergence, and the role of the host microbiome in diet adaptation are currently gaining acceptance. However, large-scale comparative studies combining morphology, host genomics, and metagenomics of the associated microbiome are still lacking. In the ConvergeAnt project, we propose taking advantage of the unique set of convergently evolved characters associated with the ant-eating diet to investigate the molecular mechanisms underlying phenotypical adaptation. By using state-of-the-art phenotyping methods based on X-ray micro-computed tomography and Illumina sequencing technologies we will combine morphometric, genomic, and metagenomic approaches to evaluate the extent of convergent evolution in the skull of myrmecophagous placentals, in their genomes, and in their associated oral and gut microbiomes. With this ambitious research proposal, we aim at providing answers to longstanding but fundamental evolutionary questions pertaining to the mechanisms of convergent evolution. The ConvergeAnt project will be the first of its kind to apply such an integrative approach to investigate the complex interplay between the mammalian genome and its associated microbiome in a classical case of adaptive convergence driven by a highly specialized diet.

Keywords of the ERC project: Evolutionary genomics - Convergent molecular evolution - Microbiomes - Phylogenomics - Mammals , Evolutionary genomics

Keywords that characterize the scientific profile of the potential visiting researcher/s: Mammalian comparative genomics - Microbiome evolution , Comparative genomics - Molecular evolution
Phylogeography and somatic evolution of cancer tumor cells

By far, most evolutionary research has focused on the changes that occur in the germline of individuals across generations, within and between species. For different reasons, much less attention has been given to the process of change within the somatic line of a multicellular individual. The formation of cancer tumors due to uncontrolled cell proliferation is one of the most prominent forms of somatic evolution. The evolution of cancer tumors in a body can be likened with the evolution of populations in more or less fragmented habitats. The tumor is usually an expanding population of clonal cells, which may differentiate to a bigger or lesser extent (population structure) and disperse to contiguous (range expansion) or more distant tissues (long distance colonization). During tumor progression, this population of cells is subject to distinct somatic evolutionary processes like mutation, drift, selection or migration, which can act at different points in time and geographical space. Very recently, the discovery of extensive intratumor heterogeneity, together with the rise of single cell genomics, has created an unique opportunity to study the phylogeography of cancer tumor cells. So far evolutionary inferences drawn from cancer genomes have been mostly qualitative. Here we propose to study a thousand single cell genomes from different regions in primary tumors and matched metastases. We will develop and apply state-of-the-art statistical and computational techniques from phylogenetics, phylogeography and population genomics to understand the tempo and mode of evolution of cell lineages within and between cancer tumors. By doing so we aim to construct a robust theoretical and methodological evolutionary framework that can contribute to a better understanding of the process of somatic evolution and shed light into the biology of cancer.

Keywords of the ERC project: cancer evolution, cancer genomics, CRC, CLL

Keywords that characterize the scientific profile of the potential visiting researcher/s: computational biologist, cancer genomicist, oncologist
Project ID: 339347  
Project Acronym: SpaceRadarPollinator  
Evaluation Panel: LS8 - Evolutionary, Population and Environmental Biology

Principal Investigator: Dr Lars Chittka  
Host Institution: Queen Mary University Of London - UK

Space use by bees– radar tracking of spatial movement patterns of key pollinators

Current radar tracking technology to monitor insect movements in space allows us to catch only glimpses of their spatial movements – it is severely constrained by the restricted range that can be covered, the fact that individuals can only be tracked one at a time, and the lack of a height dimension. Here we propose groundbreaking technology advances to make insect telemetry fit for the 21st century, to answer multiple fundamental questions in pollinator space use and its implications for the plants they pollinate. We will work towards transponder miniaturisation to make application to a large number of insect species viable; we will develop radar technology to allow coverage of areas of up to 10km² and the exploration of the 3rd dimension of insect flight, and we will adapt the equipment so that multiple individuals can be traced simultaneously. We will identify the rules of bee movements at the landscape scale, and the extent to which they use familiar landmarks and learnt vectors to link multiple locations. We will explore whether speed-accuracy tradeoffs are relevant in landmark navigation. Natural resource exploration and exploitation will be monitored over the entire foraging career of select individuals, and we will quantify individual differences in space use. Tracking bees in three dimensions will allow us to ask whether looking at the landscape from above aids efficient navigation. The tracking of multiple bees simultaneously will allow us to monitor competitive interactions as well as the possibility of social learning in space use. For the first time we will also track the spatial movement strategies of queens and males to see how they interface the search for mates with the need to forage efficiently. Our findings will have wide-ranging applications not just for the understanding of pollinator space use, but also for the conservation, management, and the understanding of mating patterns in the plants they pollinate.

Keywords of the ERC project: entomology, behavior, navigation, sensory systems, insects, pollination, flowers, networks

Keywords that characterize the scientific profile of the potential visiting researcher/s: behavior, navigation, sensory systems, insects, pollination, flowers, networks, neuroscience, cognition
Understanding the origin of the remarkable biodiversity in nature is an important goal in biological studies. Despite recent advances in evolutionary developmental biology, our understanding of the interaction between developmental genetic processes and the ecological environment in shaping the phenotype remains largely fragmented. This is mainly because of the difficulty to transfer molecular genetic tools to natural systems where we have a good understanding of the ecology. In this proposal, we combine original natural systems, water-walking insects, with state-of-the-art tools of functional and developmental genetics, to study the interplay between developmental genetic pathways and the ecological environment, and how this interaction can shape adaptive phenotypic change. About 200 million years ago, the common ancestor of water-walking insects (Heteroptera, Gerromorpha) invaded water surface and radiated into a diverse array of niches, from shorelines to open oceans. This ecological transition and specialization is associated with an array of adaptive changes that enabled these insects to support their body weight and generate efficient propulsion on the water surface.

In this project, we aim to develop a multilevel functional approach that combines developmental and evolutionary genetics, ecology, and comparative genomics and transcriptomics, to study a set of key morphological traits directly associated with the initial event of transition to water surface life, and the diversification that followed. To achieve this, we chose three water-walking insects, along with a terrestrial and under-water outgroups, based on their morphology, ecology, and amenability for laboratory culturing and functional experiments. We will identify the genes and genetic changes responsible for the development and evolution of the hydrophobic bristles—a key trait that was instrumental in the transition from terrestrial to water surface life. In addition, we will identify the geneti

Keywords of the ERC project: Evo-Devo, Adaptation, Evolution, Hemiptera, Genetics, Development

Keywords that characterize the scientific profile of the potential visiting researcher/s: Evolution, Genomics, Bioinformatics, development
Haploid selection in animals: investigating the importance of genetic and epigenetic effects in sperm

An inescapable consequence of sex in eukaryotes is the evolution of a biphasic life cycle with alternating diploid and haploid phases. The occurrence of selection during both phases has far reaching consequences for fundamental evolutionary processes including the rate of adaptation, the extent of inbreeding depression and the load of deleterious mutations, as well as for applied research into assisted fertilization. It has been a long-standing dogma that, unlike in plants, selection at the haploid gametic level in animals is of no great importance. However, empirical evidence for postmeiotic haploid gene expression is increasing and with the recent recognition of the importance of epigenetic effects for evolutionary mechanisms it is paramount to revisit haploid selection in animals. The aim of the proposed project is to reconsider haploid selection in animals and to investigate the relative importance of genetic and epigenetic effects in sperm for the subsequent generation. The project consists of three logically connected parts, which tackle the question from different angles using the zebrafish Danio rerio as the main model system. In Part I, I will disentangle genetic from epigenetic effects and identify epigenetic effects that affect sperm and offspring performance by combining experimental evolution with next-generation sequencing data. In Part II, I will pinpoint genes that are expressed at the postmeiotic haploid stage of spermatogenesis and determine which of these genes may be under haploid selection. In Part III, I will get to the core of the question and perform single-cell genotyping to explore possible links between sperm phenotype and the underlying sperm genotype. By combining aspects from evolutionary biology, mathematical modeling, genomics and developmental biology this project will advance our understanding of how epigenetic and genetic differences among gametes shape phenotypes and mediate evolutionary change in animals.

Keywords of the ERC project: evolution, genetics, genomics, epigenetics, zebrafish

Keywords that characterize the scientific profile of the potential visiting researcher/s: evolution, genetics, genomics, epigenetics
Discovering the genetic changes underlying species differences is a central goal in evolutionary genetics. Most evolutionarily important traits affecting fitness are complex or quantitative traits, whose genetic bases are elusive. In mammals, dissecting the genetic basis of complex trait variation is particularly challenging, because efficient genetic mapping requires enormous pedigrees or specialized genetic panels that are typically beyond the resources of individual groups. Using a radically novel method to circumvent breeding limitations by “breeding” mice in vitro, I propose to dissect the genetic basis of evolutionary developmental variation. This ground-breaking approach will allow me to create large genetic mapping panels of potentially any size from mouse interspecific hybrids of increasing evolutionary divergence. In vitro crosses promise a breakthrough in evolutionary biology: by bypassing hybrid sterility and inviability, we will ask which genetic changes underlie species differences. The proposed experiments address how genetic changes accumulate during evolution of new species to shape gene regulatory networks and cause phenotypic changes at the gene expression, fitness and organismal level. This research has the potential to revolutionize genetic mapping. If realized, its impact on personalized medicine, agricultural science and evolutionary research cannot be understated.

**Keywords of the ERC project:** Evolutionary Genetics, Mouse, Stem Cell, Genetic mapping

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** Tissue engineer; Evolutionary Geneticist; System biologist; Quantitative Geneticist
Physiological Reaction to Predation - A General Way to Link Individuals to Ecosystems

This proposal aims to advance a new general theory that links plasticity in prey responses to predation and biogeochemical processes to explain context-dependent variations in ecosystem functioning. The physiological reaction of prey to predation involves allocating resources from production to support emergency functions. An example of such a reaction is an increase in maintenance respiration concomitant with higher carbohydrate and lower N demand. Such changes in prey energy and elemental budget should alter the role prey play in regulating the quality of detrital inputs to soils. Nutrient content of detritus is an important determinant of the way soil communities regulate ecosystem processes. Thus, the physiological reaction of prey to predation can potentially explicate changes in ecosystem functioning. My first empirical examination of a few selected mechanisms of this theory has yielded very promising insights.

The main objectives of this proposal are: (1) To systematically test whether prey reactions to predation are consistent with the proposed theory's predictions across species and ecosystems; (2) to examine the interface between stress physiology and anti-predatory behaviors in explaining predator induced diet shift, and (3) to evaluate how predator induced responses at the individual level regulate ecosystem processes. To address these objectives, I propose combining manipulative field experiments, highly controlled laboratory and garden experiments, and stable-isotopes pulse chase approaches. I will examine individual prey responses and the emerging patterns across five food-chains that represent phylogenetically distant taxa and disparate ecosystems. The proposed study is expected to revolutionize our understanding of the mechanisms by which aboveground predators regulate ecosystem processes. Promoting such a mechanistic understanding is crucial to predict how human-induced changes in biodiversity will affect life-supporting ecosystem services.

Keywords of the ERC project: food-web, inducible defenses, ecosystem functioning, nutritional ecology, predation risk

Keywords that characterize the scientific profile of the potential visiting researcher/s: ecosystem modelling, soil ecology, microbial ecology, nutritional ecology, predator-prey interactions
Animal coloration through deep time: evolutionary novelty, homology and taphonomy

What does the fossil record tell us about the evolution of colour in animals through deep time? Evidence of colour in fossils can inform on the visual signalling strategies used by ancient animals. Research to date often has a narrow focus, lacks a broad phylogenetic and temporal context, and rarely incorporates information on taphonomy. This proposal represents a bold new holistic approach to the study of fossil colour: it will couple powerful imaging- and chemical analytical techniques with a rigorous programme of fossilisation experiments simulating decay, burial, and transport, and analysis of fossils and their sedimentary context, to construct the first robust models for the evolution of colour in animals through deep time. The research will resolve the original integumentary colours of fossil higher vertebrates, and the original colours of fossil hair; the fossil record of non-melanin pigments in feathers and insects; the biological significance of monotonal patterning in fossil insects; and the evolutionary history of scales and 3D photonic crystals in insects. Critically, the research will test, for the first time, whether evidence of fossil colour can solve broader evolutionary questions, e.g. the true affinities of enigmatic Cambrian chordate-like metazoans, and feather-like integumentary filaments in dinosaurs. The proposal entails construction of a dedicated experimental maturation laboratory for simulating the impact of burial on tissues. This laboratory will form the core of the world’s first integrated ‘experimental fossilisation facility’, consolidating the PI’s team as the global hub for fossil colour research. The research team comprises the PI, three postdoctoral researchers, and three PhD students, and will form an extensive research network via collaborations with 13 researchers from Europe and beyond. The project will reach out to diverse scientists and will inspire a positive attitude to science among the general public and policymakers alike.

**Keywords of the ERC project:** fossil colour, taphonomy, fossil insects, fossil feathers, pigments, structural colour
**Keywords that characterize the scientific profile of the potential visiting researcher/s:** fossil colour, taphonomy, fossil insects, fossil feathers, pigments, structural colour, phylogenetics, morphometrics, SAXS, biomarkers, organic geochemistry, inorganic geochemistry, palaeomics
Vegetation forms a key interface between Earth surface and atmosphere. The important role of vegetation carbon, water and energy exchanges is well established, but the overall impact of plant trace gas (VOC) emission for large-scale Earth processes is poorly understood. Although it is widely accepted that VOCs play major roles in the formation of ozone, secondary organic aerosols (SOA) and cloud condensation nuclei (CNN) with potentially profound impacts on air quality and Earth radiative balance, the research has so far focused only on constitutive emissions from species considered “emitters”. However, differently from constitutive VOCs emitted only by certain species, all plant species can be triggered to emit induced VOCs under abiotic and biotic stress. So far, induced high-reactivity VOCs are not considered in global VOC budget, and thus, this proposal tests the key assumption that VOC emissions worldwide have been vastly underestimated. As global change is resulting in higher level of stress in Earth ecosystems, the relevance of induced emissions is further expected to gain in importance. The current project has the overall objective to evaluate the effect of plant-generated VOC emissions on air composition and environment under global change, with particular emphasis on the role of VOCs induced in response to environmental stress. The study first quantifies the VOC production vs. stress severity relationships across species with differing stress tolerance and advances and parameterizes the qualitative induced VOC model developed by PI. The novel quantitative model is further verified by flux measurements and scaled up to regional and global scales to assess the contribution of induced emissions to overall VOC budget, and study the feedbacks between stress, ozone, SOA and CNN formation and the Earth climate using an hierarchy of available models. This highly cross-disciplinary project is expected to result in key contributions in two research fields of major significance: plant stress tolerance from molecules to globe and the role of vegetation component in atmospheric reactivity and Earth climate. The first part of the study provides fundamental insight into the stress responsiveness of plants with differing tolerance to environmental limitations, extending “leaf economics spectrum”, a hotspot of current plant ecology research. The second part provides quantitative information on large-scale importance of plant VOCs in globally changing climates with major relevance for understanding the role of plants in the Earth’s large scale processes.

Keywords of the ERC project: stress volatiles, biogenic volatiles, plant trace gases, climate change, secondary organic aerosols, biosphere-atmosphere feedbacks, ozone, climate modelling, global change

Keywords that characterize the scientific profile of the potential visiting researcher/s: GC-MS, plant stress physiology, volatile emissions, climate modelling, cloud modelling, aerosol modelling, trace gas eddy flux measurements, global change
Modelling lianas as key drivers of tropical forest responses to climate change

Tropical forests are essential components of the earth system. Yet, much uncertainty exists about the exact role of this biome in the global carbon cycle. Our limited understanding of tropical forest functioning is reflected in uncertain global vegetation model projections. A large source of uncertainty in these models is their representation of ecosystem demographic processes. Interestingly, fieldwork has revealed lianas as important components of tropical forests, which are apparently increasing in abundance. Liana proliferation might be a key adaptation mechanism of tropical forests to climate change, which has potentially large impacts on the long term tropical forest biome carbon balance. Nevertheless, no single terrestrial ecosystem model currently includes lianas. TREECLIMBERS will generate important insights into the mechanisms by which lianas influence the carbon balance of tropical forests, by building the first vegetation model that includes lianas. We will make the first integrative study of (1) the contribution of lianas to instantaneous carbon and water fluxes, (2) liana contribution and influence on canopy structure, (3) their role for long term demographic processes, and (4) of their role in forest responses to drought events. TREECLIMBERS will develop the first liana plant functional type (PFT) by combining a unique global meta-analysis of existing data with innovative terrestrial LiDAR 3D measurements of the canopy to study the contribution of lianas to the canopy structure. New and available data will be integrated in the Ecosystem Demography (ED) model, a forerunner of the next generation of vegetation models. By using model-data fusion we will, for the first time, integrate the large amount of available and emerging liana data, leading to an integrated insight into the role of lianas in tropical forest functioning. This project aims to show that shifts in floristic composition due to global change may have important impacts in tropical forests.

Keywords of the ERC project: vegetation modelling, lianas, tropical forest, lidar, carbon cycle

Keywords that characterize the scientific profile of the potential visiting researcher/s: modelling, programming, lidar scanning, ecology, biogeochemistry
Local adaptation, whereby individuals of a population exhibit higher fitness in their local environment compared to that experienced by other populations, has the potential to shape the distribution of genetic diversity and influence speciation. However, detecting and quantifying the extent of local adaptation is challenging, since neutral demographic processes can leave signatures which are hard to distinguish from those of local selection. In this project, I propose to quantify the extent of local adaptation in Anatomically Modern Humans by using climate-informed spatial genetic models (CISGeM) to reconstruct past population sizes, local movements, and range expansions, and thus provide a null model against which the signature of geographically-localised selection can be detected. In CISGeM, demography is affected by local resource availability, which in turn is defined by paleoclimate and paleovegetation reconstructions. By using these additional lines of evidence, it is possible to generate accurate demographic reconstructions for any number of populations, as well as integrating information from both modern and ancient genomes. Such spatially-explicit reconstructions are key for defining the expected neutral patterns due to complex demography, and thus allow us to isolate the signals of selection from this noisy background with high fidelity. The availability of paleoclimate reconstructions also enables formally testing hypotheses about the drivers of selection, integrating the changes in the strength of selection through space and time. While this project will be focused on Anatomically Modern Humans, the framework that I will develop will be applicable to the investigation of local adaptation from genomic data in any species. Such tools are very timely, given the ever-increasing availability of large genetic datasets thanks to the decreasing cost of genotyping and sequencing in both model and non-model organisms.

Keywords of the ERC project: Human demography, population genetics, natural selection, climate models

Keywords that characterize the scientific profile of the potential visiting researcher/s: Population genetics, computation modelling, climate modelling, vegetation modelling
Sex-limited experimental evolution of natural and novel sex chromosomes: the role of sex in shaping complex traits

The origin and evolution of sexual reproduction and sex differences represents one of the major unsolved problems in evolutionary biology, and although much progress had been made both via theory and empirical research, recent data suggest that sex chromosome evolution may be more complex than previously thought. The concept of sexual antagonism (when there is a positive intersexual genetic correlation in trait expression but opposite fitness effects of the trait(s) in males and females) has become essential to our understanding of sex chromosome evolution. The goal of this proposal is to understand how the interacting effects of sexual antagonism, sex-linked genetic variation, and sex-specific selection shape the genetic architecture of complex traits. I will test the hypotheses that: 1) individual sexually antagonistic loci are common in the genome, both in separate-sexed species and in hermaphrodites, and drive patterns of sexual antagonism often seen on the trait level. 2) That the response to sex-specific selection in sex-linked loci is usually due to standing sexually antagonistic genetic variation. 3) That sexually antagonistic variation is primarily non-additive in nature. To accomplish this, I will use a combination of approaches, including sex-limited experimental evolution of the X chromosome and reciprocal sex chromosome introgression among distantly related populations of Drosophila, quantitative genetic analysis and experimental evolution mimicking the creation of a novel sex chromosome in the hermaphroditic flatworm Macrostomum, and analytical and simulation modeling. This project will serve to confirm or refute the assumption that trait-level sexual antagonism reflects the contributions of many individual sexually antagonistic loci, increase our understanding of the contribution of coevolution of the sex chromosomes to population divergence, and help provide us with a better general understanding of how genotype maps to phenotype.

Keywords of the ERC project: evolutionary genetics, sexual conflict, sexual antagonism, experimental evolution, drosophila, macrostomum

Keywords that characterize the scientific profile of the potential visiting researcher/s:
Antimicrobial resistant bacteria are a global threat spreading at an alarming pace. They cause over 25,000 annual deaths in the EU, and represent an economic burden exceeding €1.5 billion a year. Current methods for microbial detection in clinical settings take about 24-36 h, but for slow-growing bacteria, as those causing tuberculosis, it can take more than a week. Early-detection and confinement of the infected individuals are the only ways to provide adequate therapy and control infection spread. Thus, tools for rapid identification of bacterial infections are greatly needed. The analysis of microbial volatile metabolites is an area of increasing interest in diagnostics. Recent works demonstrate that fast microbial identification is possible with chemical nose sensors. These sensors usually present limited stability and selectivity, and require aggressive conditions during processing and operation. Bioinspired nose sensors employing biological olfactory receptors are an alternative. Unfortunately, their complexity and low stability are a limitation. My group recently discovered a new class of stimulus-responsive gels which tackle these key challenges. Our gels are customisable and have a low environmental footprint associated. I intend to further explore their potential to advance the field of odour detection, while providing new tools for the scientific community. I will focus specifically in fast microbial detection. To accomplish this, I propose to 1) build libraries of hybrid gels with semi-selective and selective properties, 2) generate odorant specific peptides mimicking olfactory receptors, 3) fully characterise the gels, 4) assemble artificial noses for analysis of microbial volatiles, 5) create databases with organism-specific signal signatures, 6) identify pathogenic bacteria, including those with acquired antimicrobial resistances. This project is a timely approach which will place Europe in the forefront of infectious disease control.
An artificial water-soluble photosystem by protein design

This project aims at producing a fully functional light energy conversion system that is inspired by, but does not necessarily mimic, the fundamental solar energy conversion unit of natural photosynthesis – the photosystem. This is a formidable challenge that can be met with thorough understanding of biological energy and electron transfer processes, and the growing capabilities of computational protein design. Here, this knowledge and capabilities will be further developed and utilized for the design and construction of multi-cofactor, multi-subunit protein complexes with photosystem functionality. These will be designed to efficiently capture light in the visible and near infrared range, exploit it for driving the oxidation of a molecular redox carrier at one end, and providing highly reducing electrons at the other end.

Our general goal will be achieved by designing protein-cofactor complexes that will facilitate light-driven electron- and excitation energy-transfer that will make up the reaction center, and light harvesting modules, respectively. Constructing protein scaffolds that will assemble and organize arrays of multiple pigments, and chains of redox cofactors are significant challenges at the forefront of the field of protein de novo design, and current theories of biological energy and electron transfer.

Success will set a new standard, well beyond the current state of the art, for our ability to use computational protein design methods for assembling functional protein-cofactor complexes. These can be used as benchmarks to test and validate the engineering principles of biological energy conversion systems, as well as new ideas about their evolution. Practically, it will open new and exciting technological possibilities for constructing artificial solar energy conversion systems from biological building blocks, which may enable their introduction into living systems and the construction of novel bioreactors for light driven fuel production.

Keywords of the ERC project: artificial photosynthesis; protein design; light harvesting; electron transport

Keywords that characterize the scientific profile of the potential visiting researcher/s: protein chemistry; protein expression and purification; biophysical methods;
The Power of Maternal Microbes on Infant Health

Recent reports suggest that early microbial colonization has an important role for in promoting health. This may contribute to reduce the risk of chronic diseases such as obesity, allergies and inflammatory conditions. Advances in understanding host-microbe interactions imply that maternal microbiota plays a crucial role on health programming. This process begins in utero and it is modulated by mode of delivery and diet. My research has shown that i) specific shifts in milk microbial composition are associated with lactation time and mode of delivery, ii) milk microbes drive the infant microbiota composition; iii) maternal microbiota dysbiosis may be transferred to the infant. However, factors defining maternal microbiota and its biological role upon infant’s health are not yet fully understood. Hence, this project aims to characterize maternal microbes to be transferred to neonates and determine their function in infant health programming. The specific aims are: (1) understanding how the maternal microbiome is influenced by host and environmental factors; (2) characterizing the microbial core and bioactive compounds transmitted to the offspring mainly via breastfeeding and their key roles in the microbial modulation and host response; (3) understanding the interactions among breast milk bioactive compounds and their role in infant health; (4) shedding light on how maternal microbes influence the infant immune system & (5) development of new dietary strategies and therapies based on microbial replacement and modulation. To achieve these objectives, a systems biology approach by means of state-of-the-art techniques and new methodologies based on subpopulation enrichment by flow cytometer-sorter to study host–microbe interactions will be used. Results obtained will demonstrate the interaction between infant nutrition, microbes and host response in early life and its key role in health programming, enabling new applications in the field of personalized nutrition & medicine.

Keywords of the ERC project: food, nutrition, diet, microbiome, health, mother-infant, early life, lactation

Keywords that characterize the scientific profile of the potential visiting researcher/s: metagenome, microbiome, metabolome, transcriptomics, bioinformatics, biostatistics
Development trajectories of temperate forest plant communities under global change: combining hindsight and forecasting (PASTFORWARD)

The last decades are characterized by an upsurge of research on the impacts of global environmental changes on forests. Climate warming, atmospheric deposition of acidifying and eutrophying pollutants and land-use change are three of the most important threats to biodiversity in temperate forests. However, most studies focused on the effects of single factors over short time periods, such that our ability to predict the combined effects of multiple global change drivers over longer time periods remains rudimentary. The lack of knowledge on effects of global change drivers on forest herb layer communities is particularly striking, since the herb layer contains the largest part of vascular plant diversity in temperate forests and provides key ecosystem services. Therefore PASTFORWARD will build an integrative understanding of the interactive effects of land-use change, atmospheric deposition and climate warming on forest herb layer communities, starting from the insight that changes in herb layer communities are driven primarily by past land use, but can be modulated by atmospheric deposition, climate warming and forest management. Indeed, it is still largely ignored that sensible predictions of herb layer development trajectories under global change can only be made by taking the forest’s land-use history into account, as legacies of past land use can leave century-long imprints on forest herb layer communities. Three complementary data sources (a database with resurveyed vegetation plots, field measurements in a pan-European network of resurvey plots, and a multi-factor experiment) combined with an ecosystem model will be used. Furthermore, concepts and tools from different disciplines, ranging from history over sylviculture to community and ecosystem ecology will be applied. The results of PASTFORWARD will help forest managers and policy makers in taking more informed decisions on how to combine resource extraction with biodiversity conservation.

Keywords of the ERC project: global change, forest ecosystems, long-term community dynamics, ecosystem functioning

Keywords that characterize the scientific profile of the potential visiting researcher/s: community ecologist, ecosystem modeller, forest ecologist, historical ecologist
Understanding how organisms regulate size is one of the most fascinating open questions in biology. The aim of the AMAIZE project is to unravel how growth of maize leaves is controlled. Maize leaf development offers great opportunities to study the dynamics of growth regulatory networks, essentially because leaf development is a linear system with cell division at the leaf basis followed by cell expansion and maturation. Furthermore, the growth zone is relatively large allowing easy access of tissues at different positions. Four different perturbations of maize leaf size will be analyzed with cellular resolution: wild-type and plants having larger leaves (as a consequence of GA20OX1 overexpression), both grown under either well-watered or mild drought conditions. Firstly, a 3D cellular map of the growth zone of the fourth leaf will be made. RNA-SEQ of three different tissues (adaxial- and abaxial epidermis; mesophyll) obtained by laser dissection with an interval of 2.5 mm along the growth zone will allow for the analysis of the transcriptome with high resolution. Additionally, the composition of fifty selected growth regulatory protein complexes and DNA targets of transcription factors will be determined with an interval of 5 mm along the growth zone. Computational methods will be used to construct comprehensive integrative maps of the cellular and molecular processes occurring along the growth zone. Finally, selected regulatory nodes of the growth regulatory networks will be further functionally analyzed using a transactivation system in maize.

AMAIZE opens up new perspectives for the identification of optimal growth regulatory networks that can be selected for by advanced breeding or for which more robust variants (e.g. reduced susceptibility to drought) can be obtained through genetic engineering. The ability to improve the growth of maize and in analogy other cereals could have a high impact in providing food security.

Keywords of the ERC project: Plant growth - maize

Keywords that characterize the scientific profile of the potential visiting researcher/s: Leaf growth - maize - Regulatory networks
Focal Adhesion Kinetics In nanosurface Recognition

The provision of advanced functional materials in the area of regenerative medicine and discovery applications depends on many different factors to provide the appropriate targeted function. As adherent cells also read their environment through substrate interactions there is a great interest in developing such substrates in a predictable manner. Their first point of contact is through their focal adhesions and it is also through them that forces are applied allowing the cell to migrate and establish cytoskeletal tension which in turn regulates cell function. The objective of this project is to investigate the cell-substrate interaction at the nanoscale and correlate that to the surface topography for predictable biomaterials. Through the application of state-of-the-art nanofabrication we will fabricate precise surface topographies with length scales comparable to the structural units found in the focal adhesions. The aim is to map and understand the topographical influence in the architectural arrangement of the proteins in the adhesions. Aided by high resolution microscopy we will classify cell types on different nanotopographies. Combining that information with machine learning, we will be able to gain information about cell characteristics from the rule set. That information can also be used in reverse to identify cell types with the previously defined characteristic. This approach is similar to face recognition seen on cameras and mobile phones. The proposed research project will not only provide insight to an area of biomaterials not previously explored, yet aim to provide a blueprint for future design of biomaterials.

Keywords of the ERC project: Nanofabrication, topography, focal adhesions, stem cells, super resolution microscopy, machine learning

Keywords that characterize the scientific profile of the potential visiting researcher/s: Machine learning, super resolution microscopy, design of fluorescent proteins
Transcription Factor-mediated Neuronal Cell Fate Programming in Human Stem Cells

The discovery of pluripotent stem cells has expanded the working modes in biology towards the reverse engineering of specific cell types. Unlike studying developmental phenomena in vivo, we are now theoretically able to mimic some of these processes in a dish. The use of human induced pluripotent stem (iPS) cells facilitates studying the genesis of human cell types in an ethically approved setting. However, exploiting the full potency of stem cells is only possible with very few differentiated cell types. In particular, the generation of neurons is in its infancy: of the many neuronal types present in the brain, only a few types have been generated in vitro. So far, neuronal differentiation protocols are multifaceted and tailored to individual cell types. The molecular events that occur during reprogramming remain enigmatic. Hence, we cannot confer these protocols easily on producing different neurons of interest. Therefore, we plan to induce transcription factors as differentiation control buttons in human iPS cells in order to explore in vitro neurogenesis systematically. First, we will apply a human transcription factor library to conditional fluorescent iPS reporter lines, facilitating high-throughput isolation and analysis of induced neurons. Second, the underlying gene regulatory networks will be revealed using RNA-sequencing over the entire differentiation period to identify the biological rules of in vitro neuronal differentiation. We will combine these in-depth transcriptomic analyses with morphological, anatomical, and functional characterizations. Finally, based on our discoveries, we will engineer human photoreceptors that can be applied to cell transplantation experiments in retinal degeneration diseases. Conceptually, our approach paves the way for targeted “forward” programming of human iPS cells to neurons.

Keywords of the ERC project: Transcription Factor-mediated Neuronal Cell Fate Programming in Human Stem Cells

Keywords that characterize the scientific profile of the potential visiting researcher/s: Neuroscience, stem cell research, systems biology, bioengineering
Plants are continuously exposed to a wide variety of pathogenic attackers that cause major crop losses to agriculture worldwide. Unlike vertebrates that use specialized immune cells to detect non-self, each individual plant cell is thought to be capable of launching an effective immune response. Plant immune responses are largely orchestrated by the immune hormone, salicylic acid (SA), which accumulates upon infection and establishes both local and broad-spectrum systemic immunity. SA induces the reprogramming of thousands of genes to prioritize immune responses over normal cellular growth functions. Consequently, commercial SA mimics have been developed and applied as crop protection agents worldwide. Nonetheless, how SA reprograms the transcriptome remains poorly understood yet is critical for the design of improved crop protection strategies that avoid plant growth and yield penalties.

SA-induced transcription reprogramming is largely mediated by NPR1, a master coactivator of gene expression. We recently reported that direct perception of SA by a Cullin3-RING ubiquitin ligase (CRL3) in the nucleus regulates the transcriptional activity of NPR1 by targeting it for degradation via the ubiquitin proteasome system (UPS). Our latest data suggest that ubiquitination by CRL3 and other ubiquitin chain modifying enzymes may be processive and establishes a transcriptional timer for NPR1 activity. This proposal aims to understand the flexibility and necessity of this transcriptional ubiquitin timer in meeting cellular demands for dynamic gene expression during SA-mediated plant immune responses. Moreover, we will uncover the full substrate ranges of SA-induced ubiquitin ligases and their post-translational regulation to precisely chart the intimate roles the UPS plays in coordinating plant immune gene expression. Importantly, these findings will provide novel chemical and genetic targets that can be harnessed in future crop improvement strategies.

**Keywords of the ERC project:** ubiquitin, proteasome, plant immunity, transcription

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** ubiquitin, proteasome, plant immunity, transcription, post-translational modifications
The aim of this project is to understand the causal factors contributing to the cognitive decline during senescence and to develop sensitive and standardized behaviour tests for early detection in order to increase the welfare of affected species. With the rapidly ageing population of Europe, related research is a priority in the European Union.

We will focus both on characterising the ageing phenotype and the underlying biological processes in dogs as a well-established natural animal model. We develop a reliable and valid test battery applying innovative multidisciplinary methods (e.g. eye-tracking, motion path analysis, identification of behaviour using inertial sensors, EEG, fMRI, candidate gene, and epigenetics) in both longitudinal and cross-sectional studies. We expect to reveal specific environmental risk factors which hasten ageing and also protective factors which may postpone it. We aim to provide objective criteria (behavioural, physiological and genetic biomarkers) to assess and predict the ageing trajectory for specific individual dogs. This would help veterinarians to recognise the symptoms early, and initiate necessary counter actions.

This approach establishes the framework for answering the broad question that how we can extend the healthy life of ageing dogs which indirectly also contributes to the welfare of the owner and decreases veterinary expenses. The detailed description of the ageing phenotype may also facilitate the use of dogs as a natural model for human senescence, including the development and application of pharmaceutical interventions.

We expect that our approach offers the scientific foundation to delay the onset of cognitive ageing in dog populations by 1-2 years, and also increase the proportion of dogs that enjoy healthy ageing.

**Keywords of the ERC project:** cognition, social behaviour, genetics, neuroscience, aging, dog

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** bioinformatics, theoretical and practical background in animal behaviour/cognition
Peptide building blocks serve as very attractive bio-inspired elements in nanotechnology owing to their controlled self-assembly, inherent biocompatibility, chemical versatility, biological recognition abilities and facile synthesis. We have demonstrated the ability of remarkably simple aromatic peptides to form well-ordered nanostructures of exceptional physical properties. By taking inspiration from the minimal recognition modules used by nature to mediate coordinated processes of self-assembly, we have developed building blocks that form well-ordered nanostructures. The compact design of the building blocks, and therefore, the unique structural organization, resulted in metallic-like Young's modulus, blue luminescence due to quantum confinement, and notable piezoelectric properties. The goal of this proposal is to develop two new fronts for bio-inspired building block repertoire along with co-assembly to provide new avenues for organic nanotechnology. This will combine our vast experience in the assembly of aromatic peptides together with additional structural modules from nature. The new entities will be developed by exploiting the design principles of small aromatic building blocks to arrive at the smallest possible module that form super helical assembly based on the coiled coil motifs and establishing peptide nucleic acids based systems to combine the worlds of peptide and DNA nanotechnologies. The proposed research will combine extensive design and synthesis effort to provide a very diverse collection of novel buildings blocks and determination of their self-assembly process, followed by broad chemical, physical, and biological characterization of the nanostructures. Furthermore, effort will be made to establish supramolecular co-polymer systems to extend the morphological control of the assembly process. The result of the project will be a large and defined collection of novel chemical entities that will help reshape the field of bioorganic nanotechnology.

Keywords of the ERC project: Nanotechnology, molecular self-assembly, peptides, peptide nucleic acids, biotechnology, bio-inspired materials

Keywords that characterize the scientific profile of the potential visiting researcher/s: organic chemistry, supramolecular chemistry, biochemistry, biophysics, protein and peptide chemistry
EFSA recently prohibited 75% of insecticides to account for their toxicity and ecotoxicity. Moreover, the spread of insecticide resistance and invasion of Europe by new tropical vectors and pests require the development of alternative biological techniques.

Recently, we hypothesized that shifting the vision of the sterile male from a sexual competitor only to a specific transporter of active biocides to the targeted female might boost the impact of the sterile insect technique (SIT). Here we want to demonstrate this concept using three biocides: Pyriproxifen, Bacillus thuringiensis and a Densovirus against the Tiger mosquito (Aedes albopictus). Pyriproxifen will also be tested against tsetse and fruit flies.

We will test the technology both in the laboratory and at an operational scale and model the relative impacts of SIT and boosted-SIT on the dynamics of the targeted population. Moreover, we will compare the evolutionary response of the target population to these different control pressures (multiple lethal mutations, multiple lethal mutations + biocides), for three different biocides and three demographic strategies. This will generate breakthrough knowledge on the transmission of biocides and pathogens in insects and the sustainability of genetic control, provide a new control technique for mosquitoes, and improve the cost-effectiveness of SIT in tsetse and fruit flies.

We will have to address technical issues associated to mass rearing, sterilization, sex separation and aerial release of mosquitoes as well as regulatory issues required for releasing sterile males coated with biocides.

**Keywords of the ERC project:** Insect control, genetic control, sterile insect technique, densovirus, mosquitoes, fruit flies, tsetse

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** Post docs, PhD, researchers
We will use modern techniques in algebraic geometry, originating from string theory and mirror symmetry, to study fundamental problems of classical flavour. More concretely, we apply wall-crossing in the derived category to the birational geometry of moduli spaces. Bridgeland stability is a notion of stability for complexes in the derived category. Wall-crossing describes how moduli spaces of stable complexes change under deformation of the stability condition, often via a birational surgery occurring in its minimal model program (MMP). This relates wall-crossing to the most basic question of algebraic geometry, the classification of algebraic varieties. Our previous results additionally provide a very direct connection between Bridgeland stability conditions and positivity of divisors, the main tool of modern birational geometry. This makes the above link significantly more effective, precise and useful. We will exploit this in the following long-term projects: 1. Prove a Bogomolov-Gieseker type inequality for threefolds that we conjectured previously. This would provide a solution in dimension three to well-known open problems of seemingly completely different nature: the existence of Bridgeland stability conditions, Fujita's conjecture on very ampleness of adjoint line bundles, and projective normality of toric varieties. 2. Study the birational geometry of moduli space of sheaves via wall-crossing, adding more geometric meaning to their MMP. 3. Prove that the MMP for local Calabi-Yau threefolds is completely induced by deformation of Bridgeland stability conditions. The motivation is a derived version of the Kawamata-Morrison cone conjecture, classical questions on Chern classes of stable bundles, and mirror symmetry. 4. Answer major open questions on the birational geometry of the moduli space of genus zero curves (for example, the F-conjecture) using exceptional collections in the derived category and wall-crossing.

Keywords of the ERC project: Wall-crossing, birational geometry, stability conditions, derived categories

Keywords that characterize the scientific profile of the potential visiting researcher/s:
Spectral theory of random operators

The theme of this proposal is the study of random operators associated with some geometric structure, and the influence of the geometry on the spectral properties of the operator. Such operators appear in problems from theoretical physics, and lead to new and interesting mathematical structures. One circle of questions is related to random operators, which describe the motion of a quantum particle in a disordered medium, such as random band matrices. The behaviour of the particle is influenced by the underlying geometry, as quantified by the (non-rigorous) Thouless criterion for localisation in terms of the mixing time of the classical random walk; in the context of random band matrices, the predictions of the Thouless criterion are supported by additional (non-rigorous) arguments. These predictions have so far not been rigorously justified; an exception is my own result, validating it at the spectral edges. One of our goals is to develop new methods, which would be applicable in the bulk of the spectrum, for random band matrices and other operators with geometric structure. Another circle of questions is given by random processes taking values in large random matrices. The spectral properties of the random matrix at every point of the underlying space are described by the random matrix theory; but how does the spectrum evolve along the underlying space? The richness of this question is apparent from the one-dimensional case of Dyson Brownian motion. We intend to study the local eigenvalue statistics of general matrix-valued random processes with multi-dimensional underlying space; to give a complete description of the random processes which appear in the limit, first for the spectral edges and then for the bulk of the spectrum, and to explore the appearance of these processes in a variety of basic questions of mathematical physics.

Keywords of the ERC project: random operators, random matrices, spectral theory,

Keywords that characterize the scientific profile of the potential visiting researcher/s: mathematical physics, analysis, probability,
Harmonic Analysis, Partial Differential Equations and Geometric Measure Theory

The origin of Harmonic Analysis goes back to the study of the heat diffusion, modeled by a differential equation, and the claim made by Fourier that every periodic function can be represented as a series of sines and cosines. In this statement we can find the motivation to many of the advances that have been made in this field. Partial Differential Equations model many phenomena from the natural, economic and social sciences. Existence, uniqueness, convergence to the boundary data, regularity of solutions, a priori estimates, etc., can be studied for a given PDE. Often, Harmonic Analysis plays an important role in such problems and, when the scenarios are not very friendly, Harmonic Analysis turns out to be fundamental. Not very friendly scenarios are those where one lacks of smoothness either in the coefficients of the PDE and/or in the domains where the PDE is solved. Some of these problems lead to obtain the boundedness of certain singular integral operators and this drives one to the classical and modern Calderón-Zygmund theory, the paradigm of Harmonic Analysis. When studying the behavior of the solutions of the given PDE near the boundary, one needs to understand the geometrical features of the domains and then Geometric Measure Theory jumps into the picture. This ambitious project lies between the interface of three areas: Harmonic Analysis, PDE and Geometric Measure theory. It seeks deep results motivated by elliptic PDE using techniques from Harmonic Analysis and Geometric Measure Theory. This project is built upon results obtained by the applicant in these three areas. Some of them are very recent and have gone significantly beyond the state of the art. The methods to be used have been shown to be very robust and therefore they might be useful towards its applicability in other regimes. Crucial to this project is the use of Harmonic Analysis where the applicant has already obtained important contributions.

Keywords of the ERC project: Harmonic Analysis, Partial Differential Equations, Geometric Measure Theory

Keywords that characterize the scientific profile of the potential visiting researcher/s:
This proposal deals with a collection of problems in PDE arising from fluid mechanics. The primary motivation is the understanding of the evolution of isolated vortex lines for 3D Euler. The importance of the evolution of vorticity in incompressible fluid mechanics is very well known. To date, only nonrigorous approaches are known to try to obtain an evolution equation for isolated vortex lines. Two desingularization procedures are carried out (including a time renormalization) to obtain an evolution equation (the binormal equation). While an isolated vortex line does not fit any known concept of solution (given the singularity of the velocity), and there has been significant recent activity on the nonuniqueness of solutions of Euler (De Lellis & Szekelyhidi, and recently Isett) it is expected that the geometric assumptions made about the solution will still make it possible to find a suitable concept of solution. In the proposal I describe an approach that should help to rigorously understand vortex lines. It is motivated by a programme developed for the Surface Quasi-Geostrophic (SQG) equation with C. Fefferman and for some related desingularized models with my student Zoe Atkins (Nov 2012 PhD). SQG has been of great interest in the PDE community due to the striking similarities it exhibits with 3D Euler. In particular, the evolution of sharp fronts for SQG corresponds to the evolution of vortex lines. In recent years I have developed an approach that overcomes the divergences known to exist for the velocity field (as in 3D Euler). The positive results obtained for SQG motivate the methodology and tools described in the proposal, including the construction of solutions with very large gradients and simple geometry and the use of a measure-theoretic approach to identify fundamental curves within these objects. Surprising connections with other equations motivate some other directions and linked projects, for example with Prandtl and boundary layer theory.

Keywords of the ERC project: PDE, Euler Equations, vortex dynamics

Keywords that characterize the scientific profile of the potential visiting researcher/s: PDE, Euler Equations, vortex dynamics
The symplectic geometry of anti-self-dual Einstein metrics

This project is founded on a new formulation of Einstein's equations in dimension 4, which I developed together with my co-authors. This new approach reveals a surprising link between four-dimensional Einstein manifolds and six-dimensional symplectic geometry. My project will exploit this interplay in both directions: using Riemannian geometry to prove results about symplectic manifolds and using symplectic geometry to prove results about Riemannian manifolds. Our new idea is to rewrite Einstein's equations using the language of gauge theory. The fundamental objects are no longer Riemannian metrics, but instead certain connections over a 4-manifold $M$. A connection $A$ defines a metric $g_A$ via its curvature, analogous to the relationship between the electromagnetic potential and field in Maxwell's theory. The total volume of $(M, g_A)$ is an action $S(A)$ for the theory, whose critical points give Einstein metrics. At the same time, the connection $A$ also determines a symplectic structure $\omega_A$ on an associated 6-manifold $Z$ which fibres over $M$. My project has two main goals. The first is to classify the symplectic manifolds which arise this way. Classification of general symplectic 6-manifolds is beyond current techniques of symplectic geometry, making my aims here very ambitious. My second goal is to provide an existence theory both for anti-self-dual Poincaré--Einstein metrics and for minimal surfaces in such manifolds. Again, my aims here go decisively beyond the state of the art. In all of these situations, a fundamental problem is the formation of singularities in degenerating families. What makes new progress possible is the fresh input coming from the symplectic manifold $Z$. I will combine this with techniques from Riemannian geometry and gauge theory to control the singularities which can occur.

**Keywords of the ERC project:** Differential geometry, Riemannian geometry, symplectic geometry, Einstein manifolds, gauge theory, holomorphic curves, asymptotically hyperbolic manifolds

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** Any of the following: Riemannian geometry, symplectic geometry, Einstein manifolds, gauge theory, holomorphic curves, asymptotically hyperbolic manifolds
Large Discrete Structures

The proposed project seeks to introduce novel methods to analyze and approximate large graphs and other discrete structures and to apply the developed methods to solve specific open problems. A need for such methods comes from computer science where the sizes of input structures are often enormous. Specifically, the project will advance the recently emerged theory of combinatorial limits by developing new insights in the structure of limit objects and by proposing a robust theory bridging the sparse and dense cases. The analytic methods from the theory of combinatorial limits will be used to analyze possible asymptotic behavior of large graphs and they will be applied in conjunction with structural arguments to provide solutions to specific problems in extremal combinatorics. The obtained insights will also be combined with methods from discrete optimization and logic to provide new algorithmic frameworks.

Keywords of the ERC project: graph limits, combinatorial limits, extremal combinatorics, graph theory, discrete mathematics

Keywords that characterize the scientific profile of the potential visiting researcher/s: extremal combinatorics, probabilistic method, graph theory, discrete mathematics
Rigidity of groups and higher index theory

The Atiyah-Singer index theorem was one of the most spectacular achievements of mathematics in the XXth century, connecting the analytic and topological properties of manifolds. The Baum-Connes conjecture is a hugely successful approach to generalizing the index theorem to a much broader setting. It has remarkable applications in topology and analysis. For instance, it implies the Novikov conjecture on the homotopy invariance of higher signatures of a closed manifold and the Kaplansky-Kadison conjecture on the existence of non-trivial idempotents in the reduced group C*-algebra of a torsion-free group. At present, the Baum-Connes conjecture is known to hold for a large class of groups, including groups admitting metrically proper isometric actions on Hilbert spaces and Gromov hyperbolic groups. The Baum-Connes conjecture with certain coefficients is known to fail for a class of groups, whose Cayley graphs contain coarsely embedded expander graphs. Nevertheless, the conjecture in full generality remains open and there is a growing need for new examples of groups and group actions, that would be counterexamples to the Baum-Connes conjecture. The main objective of this project is to exhibit such examples. Our approach relies on strengthening Kazhdan’s property (T), a prominent cohomological rigidity property, from its original setting of Hilbert spaces to much larger classes of Banach spaces. Such properties are an emerging direction in the study of cohomological rigidity and are not yet well-understood. They lie at the intersection of geometric group theory, non-commutative geometry and index theory. In their study we will implement novel approaches, combining geometric and analytic techniques with variety of new cohomological constructions.

Keywords of the ERC project: index theory; geometric group theory; property (T);

Keywords that characterize the scientific profile of the potential visiting researcher/s: index theory; geometric group theory; property (T);
Mathematical aspects of three-dimensional water waves with vorticity

The goal of this project is to develop a mathematical theory for steady three-dimensional water waves with vorticity. The mathematical model consists of the incompressible Euler equations with a free surface, and vorticity is important for modelling the interaction of surface waves with non-uniform currents. In the two-dimensional case, there has been a lot of progress on water waves with vorticity in the last decade. This progress has mainly been based on the stream function formulation, in which the problem is reformulated as a nonlinear elliptic free boundary problem. An analogue of this formulation is not available in three dimensions, and the theory has therefore so far been restricted to irrotational flow. In this project we seek to go beyond this restriction using two different approaches. In the first approach we will adapt methods which have been used to construct three-dimensional ideal flows with vorticity in domains with a fixed boundary to the free boundary context (for example Beltrami flows). In the second approach we will develop methods which are new even in the case of a fixed boundary, by performing a detailed study of the structure of the equations close to a given shear flow using ideas from infinite-dimensional bifurcation theory. This involves handling infinitely many resonances.

Keywords of the ERC project: mathematical analysis, nonlinear partial differential equations, fluid mechanics, free boundaries, nonlinear waves

Keywords that characterize the scientific profile of the potential visiting researcher/s:
New frontiers in numerical general relativity

In recent years general relativity (GR) has become an increasingly important new tool in areas of physics beyond its traditional playground in astrophysics. The main motivation for this comes from the AdS/CFT correspondence which conjectures an equivalence between gravity in anti-de Sitter (AdS) spaces and certain conformal field theories (CFT’s). Via this correspondence, GR now plays a key role in improving our understanding of non-gravitational physics at strong coupling. The AdS/CFT correspondence naturally leads to the study of GR in dimensions greater than four and/or in AdS spaces. Our current understanding of GR in these new settings is rather limited but it has been realized that the physics of gravity can be significantly different than in the 4d asymptotically flat case. Moreover, to access these new gravitational phenomena numerical methods have been and will be essential. However, the use of numerical GR beyond the traditional 4d asymptotically flat case is still in its infancy. The goal of this project is to improve our understanding of GR in higher dimensions and/or AdS spaces using numerical techniques. To achieve this goal, we will focus on the study of the following topics: 1. Develop stable codes for doing numerical GR in AdS and higher dimensions. We will use numerical GR and the AdS/CFT correspondence to study out of equilibrium phenomena in strongly coupled CFT’s. We will also use numerical GR to understand the endpoint of the various black hole instabilities and thereby address long standing conjectures in GR. 2. New types of stationary black holes. We will use numerical GR to numerically construct new types of black holes in higher dimensions and in AdS, with novel topologies and fewer symmetries than the known ones. We shall apply them to the study of equilibrium configurations in strongly coupled gauge theories at finite temperature.

Keywords of the ERC project: numerical general relativity, black holes, AdS/CFT, numerical relativity, higher dimensions

Keywords that characterize the scientific profile of the potential visiting researcher/s: numerical general relativity, black holes, AdS/CFT, numerical relativity
With QITBOX we aim to develop a novel device-independent framework for quantum information processing. In this framework, devices are seen as black boxes that only receive inputs and produce outputs. Our main objective is to understand what can and cannot be done for information processing using only the observed correlations among the devices. We will structure our effort along three main research lines: (i) Characterization of quantum correlations: the general objective will be to characterize those correlations that are possible among quantum devices; (ii) Protocols based on correlations: the general objective will be to understand how quantum correlations can be exploited in order to construct relevant information protocols and (iii) Applications to physical setups: here the previous results to concrete physical setups will be applied, such as the quantum-optical realizations of the protocols or the study of the non-local properties of many-body systems. The expected results of QITBOX are: (i) Novel methods for the characterization of quantum correlations, (ii) Improved or novel device-independent protocols, (iii) Proposals for feasible experimental implementations of these protocols and (iv) Novel methods for the study of many-body systems based on correlations. QITBOX is a highly-interdisciplinary project with implications in Physics, Mathematics, Computer Science and Engineering. The execution of the planned research work will provide a unifying framework for a Quantum Information Theory with black BOXes (hence the acronym). Such a framework will bring quantum information processing to an unprecedented level of abstraction, in which information protocols and primitives are defined without any reference to the internal physical working of the devices. This, in turn, will lead to much more robust practical implementations of quantum information protocols, closing the mismatch between theoretical requirements and experimental realisations.

Keywords of the ERC project: quantum information theory, quantum cryptography, quantum foundations, Bell's theorem, quantum physics

Keywords that characterize the scientific profile of the potential visiting researcher/s: quantum information theory, quantum cryptography, quantum physics,
Principal Investigator:  Dr Konstantin Zarembo
Host Institution:  Stockholms Universitet - SE

Integrable Systems in Gauge and String Theory

The project is aimed at uncovering new links between integrable systems, string theory and quantum field theory. The goal is to study non-perturbative phenomena in strongly-coupled field theories, and to understand relationship between gauge fields and strings at a deeper level.

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:
### Physics of Atoms with Attosecond Light Pulses

The field of attosecond science is now entering the second decade of its existence, with good prospects for breakthroughs in a number of areas. We want to take the next step in this development: from mastering the generation and control of attosecond pulses to breaking new marks starting with the simplest systems, atoms. The aim of the present application is to advance the emerging new research field "Ultrafast Atomic Physics", where one- or two-electron wave packets are created by absorption of attosecond pulse(s) and analyzed or controlled by another short pulse. Our project can be divided into three parts: 1. Interferometric measurements using tunable attosecond pulses

**How long time does it take for an electron to escape its potential?**

We will measure photoemission time delays for several atomic systems, using a tunable attosecond pulse source. This type of measurements will be extended to multiple ionization and excitation processes, using coincidence measurements to disentangle the different channels and infrared ionization for analysis. 2. XUV pump/XUV probe experiments using intense attosecond pulses

**How long does it take for an atom to become an ion once a hole has been created?**

Using intense attosecond pulses and the possibility to do XUV pump/ XUV probe experiments, we will study the transition between nonsequential double ionization, where the photons are absorbed simultaneously and all electrons emitted at the same time and sequential ionization where electrons are emitted one at a time. 3. "Complete" attosecond experiments using high-repetition rate attosecond pulses

**We foresee a paradigm shift in attosecond science with the new high repetition rate systems based on optical parametric chirped pulse amplification which are coming to age.** We want to combine coincidence measurement with angular detection, allowing us to characterize (two-particle) electronic wave packets both in time and in momentum and to study their quantum-mechanical properties.

---

**Keywords of the ERC project:** attosecond physics, ultrafast optics, lasers, atomic physics, high-order harmonic generation

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** atomic physics, spectroscopy, nonlinear optics, high order harmonic generation
Crystal channeling to extract a high energy hadron beam from an accelerator

A new generation of parasitic beam extraction of high energy particles from an accelerator is proposed in CRYSBEAM. Instead of massive magnetic kickers, bent thin crystals trapping particles within the crystal lattice planes are used. This type of beam manipulation opens new fields of investigation of fundamental interactions between particles and of coherent interactions between particles and matter. An experiment in connection to Ultra High Energy Cosmic Rays study in Earth’s high atmosphere can be conducted.

Several TeV energy protons or ions are deflected towards a chosen target by the bent lattice planes only when the lattice planes are parallel to the incoming particles direction.

The three key ingredients of CRYSBEAM are:
- a goniometer based on piezoelectric devices that orients a bent finely-polished low-miscut silicon crystal with a high resolution and repeatability, monitoring its position with synthetic diamond sensors. Novel procedures in crystal manufacturing & testing and cutting-edge mechanical solutions for motion technology in vacuum are developed;
- a silica screen that measures the deflected particles via Cherenkov radiation emission in micrometric optical waveguides. These are obtained with an ultra-short laser micro-machining technique as for photonic devices used in quantum optics and quantum computing. The screen is a direct beam-imaging detector for a high radiation dose environment;
- a smart absorber, which simulates the Earth’s atmosphere, where particles are smashed and secondary showers are initiated. This sets the path to measure hadronic cross sections at an energy relevant for cosmic rays investigation.

The R&D for the various components of such a system are carried out within this project and direct tests at CERN Super Proton Synchrotron to be performed prior to the final installation in the Large Hadron Collider at CERN are proposed. A new concept of particle accelerator operations will be finally set in place.

Keywords of the ERC project: crystal channeling, cosmic rays, accelerator beam steering

Keywords that characterize the scientific profile of the potential visiting researcher/s:
SpecMAT aims at providing crucial experimental information to answer key questions about the structure of atomic nuclei:

- What are the forces driving the shell structure in nuclei and how do they change in nuclei far from stability?
- What remains of the $Z = 28$ and $N = 50$ “magic numbers” in $^{78}\text{Ni}$?
- Do we understand shape coexistence in nuclei, and what are the mechanisms controlling its appearance? The position of natural and “intruder” shells will be mapped in two critical regions, the neutron-rich nuclei around $Z = 28$ and the neutron-deficient nuclei around $Z = 82$. The centroids of the shell strength are derived from the complete spectroscopy of those systems in nucleon-transfer measurements. This method will be applied for the first time in the region of neutron-deficient $^{208}\text{Pb}$ nuclei. In SpecMAT (Spectroscopy of exotic nuclei in a Magnetic Active Target) a novel instrument will overcome the present challenges in performing such measurements with very weak beams of unstable nuclei. It combines high luminosity, high efficiency and a very large dynamic range and allows detection of both charged-particle and gamma-ray radiation. The instrument owns its remarkable performances to a number of advanced technologies concerning the use of electronics, gaseous detectors and gamma-ray detectors in a magnetic field. The SpecMAT detector will be coupled to the HIE-ISOLDE facility for the production and post-acceleration of radioactive ion beams in construction at CERN in Geneva. HIE-ISOLDE will provide world-unique beams thanks to the use of the proton injector of the CERN complex. If successful, SpecMAT at HIE-ISOLDE will produce specific results in nuclear structure which cannot be reached by other programmes elsewhere. Such results will have a significant impact on the present theories and models of the atomic nucleus.

**Keywords of the ERC project:** experimental nuclear structure

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** nuclear structure, nuclear reactions, radiation detection
Project ID: 335739  
Project Acronym: Fields-Knots  
Evaluation Panel: PE2 - Fundamental Constituents of Matter

<table>
<thead>
<tr>
<th>Principal Investigator:</th>
<th>Dr Piotr Sulkowski</th>
</tr>
</thead>
<tbody>
<tr>
<td>Host Institution:</td>
<td>Uniwersytet Warszawski - PL</td>
</tr>
</tbody>
</table>

**Quantum fields and knot homologies**

This project is concerned with fundamental problems arising at the interface of quantum field theory, knot theory, and the theory of random matrices. The main aim of the project is to understand two of the most profound phenomena in physics and mathematics, namely quantization and categorification, and to establish an explicit and rigorous framework where they come into play in an interrelated fashion. The project and its aims focus on the following areas:  
- Knot homologies and superpolynomials. The aim of the project in this area is to determine homological knot invariants and to derive an explicit form of colored superpolynomials for a large class of knots and links.  
- Super-A-polynomial. The aim of the project in this area is to develop a theory of the super-A-polynomial, to find an explicit form of the super-A-polynomial for a large class of knots, and to understand its properties.  
- Three-dimensional supersymmetric N=2 theories. This project aims to find and understand dualities between theories in this class, in particular theories related to knots by 3d-3d duality, and to generalize this duality to the level of homological knot invariants.  
- Topological recursion and quantization. The project aims to develop a quantization procedure based on the topological recursion, to demonstrate its consistency with knot-theoretic quantization of A-polynomials, and to generalize this quantization scheme to super-A-polynomials. All these research areas are connected via remarkable dualities unraveled very recently by physicists and mathematicians. The project is interdisciplinary and aims to reach the above goals by taking advantage of these dualities, and through simultaneous and complementary development in quantum field theory, knot theory, and random matrix theory, in collaboration with renowned experts in each of those fields.

**Keywords of the ERC project:** high energy physics, quantum field theory, topological field theory, exact results in gauge and string theories, matrix models, topological recursion, knot theory

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** high energy physics, quantum field theory, topological field theory, exact results in gauge and string theories, matrix models, topological recursion, knot theory
Towards the NEXT generation of bb0nu experiments

Neutrinoless double beta decay is a hypothetical, very slow radioactive process whose observation would establish unambiguously that massive neutrinos are Majorana particles --- that is to say, identical to their antiparticles ---, which implies that a new physics scale beyond the Standard Model must exist. Furthermore, it would prove that total lepton number is not a conserved quantity, suggesting that this new physics could also be the origin of the observed asymmetry between matter and antimatter in the Universe. In recent years, many innovative ideas have been put forward to improve the sensitivity of bb0nu experiments. In general, these propositions have sought to increase the number of experimental signatures available to reject backgrounds while attempting to use isotopes and detector techniques which can be more easily scaled to large masses. The objective of this project is to realize the NEXT experiment, an innovative detector based on a high-pressure xenon gas (HPXe) TPC that will run at the Laboratorio Subterráneo de Canfranc (LSC), in Spain. Our primary goal is to complete the construction and commissioning of a 150 kg HPXe TPC (NEXT-100) by 2014, and start a physics run in 2015 that can improve the present bound set by the EXO experiment and perhaps discover the Majorana nature of neutrinos. In addition, we will carry out an R&D program focused in demonstrating the scalability of the technology to the ton scale.

Keywords of the ERC project: high pressure xenon TPC, neutrinoless double beta decay

Keywords that characterize the scientific profile of the potential visiting researcher/s: instrumentation, time projection chambers, low background, deep neural networks
Our proposal addresses theoretical and phenomenological properties of large distance ("Infra-Red", IR in the following) modifications of the gravitational interaction. Such modifications are motivated by two main reasons: firstly, to find alternative explanations to the presence of dark matter or dark energy in cosmology; secondly, to better understand the currently well accepted cosmological model, disentangling there what does from what does not depend on the large distance dynamics of gravity and extracting as much as possible new information on gravity from the latest cosmological observations. For the second goal, it matters to have at hand alternatives to the standard cosmological model based on general relativity, to serve as benchmarks. Very recently, new ideas have been proposed to modified gravity in the IR. First, a large class of scalar-tensor theories featuring the “k-mouflaging” of the scalar has been proposed and partly classified. Second, new kinds of massive gravities which might be devoid of the standard pathologies of those models have been discovered. Third, models of non local gravity have been proposed with many interesting features. In this proposal, we intend to better understand those constructions, in which the works of the applicant played a major role, and whose properties are largely unexplored. As transversal goals, we also intend to propose new ways to modify gravity in the IR, as well as to develop schemes to tests IR modifications of gravity against cosmological and gravitational data. The project will be lead by the applicant, four postdocs and two students.

Keywords of the ERC project: Modified gravity, cosmology

Keywords that characterize the scientific profile of the potential visiting researcher/s: Modified and Einstein Gravity, Cosmology, Relativistic Field Theories
Open SYstems RevISited: From Brownian motion to quantum simulators

This proposal concerns open systems, i.e. systems interacting with the environment, and their fundamental role in natural sciences. The main objectives are: i) to develop theory of Brownian motion for molecules in biological environments; ii) to adapt classical many-body open systems such as kinetic or/and diffusion-aggregation models to the quantum domain; iii) to develop theory of open systems as quantum simulators; finally iv) to develop theory of quantum Brownian motion in inhomogeneous media. Although all these objectives may seem to be quite unrelated, our main goal will be to connect them in order to unambiguously assess the relevance of open systems in specific areas of physics, biology and beyond. Accordingly, objective i) will be explored in close collaboration with experimentalists in which the diffusion of biomolecules on cell membranes requires a description in terms of Brownian motion in correlated disordered potentials. In ii) we will search for many-body kinetic and growth models that provide the configurations that may serve as samples of random potentials desired in i). These models can be regarded as quantum models with non-Hermitian generators of evolution; in some situations they can be generalized to genuine quantum ones, described by a quantum master equation, linking ii) and iii). In iii) we will look for applications of quantum open systems as quantum simulators of condensed matter/high energy physics. We will also look at single particle interactions with quantum many body environment, linking the objectives iii) with iv) and i). Expected results are: a) understanding the relationship between biological function and the spatiotemporal dynamics of single molecules in living cells; b) understanding of the structure of classical many body stochastic models and their relation to quantum ones; c) concrete proposals for open systems quantum simulators; and d) development of tools to characterize and observe quantum Brownian motion.

Keywords of the ERC project: open systems, anomalous diffusion, Brownian motion, quantum Brownian motion, classical many body stochastic processes, quantum many body stochastic processes, quantum simulators, quantum annealers

Keywords that characterize the scientific profile of the potential visiting researcher/s: classical stochastic processes, quantum stochastic processes, statistical physics, non-equilibrium classical and quantum dynamics, quantum simulation, quantum annealers
Genuine Quantumness in Cooperative Phenomena

The proposed research programme addresses issues of fundamental and technological importance in quantum information science and its interplay with complexity. The main aim of this project is to provide a new paradigmatic foundation for the characterisation of quantumness in cooperative phenomena and to develop novel platforms for its practical utilisation in quantum technology applications. To reach its main goal, this programme will target five specific objectives:

01. Constructing a quantitative theory of quantumness in composite systems;
02. Benchmarking genuine quantumness in information and communication protocols;
03. Devising practical solutions for quantum-enhanced metrology in noisy conditions;
04. Developing quantum thermal engineering for refrigerators and heat engines;
05. Establishing a cybernetics framework for regulative phenomena in the quantum domain.

This project is deeply driven by the scientific curiosity to explore the ultimate range of applicability of quantum mechanics. Along the route to satisfying such curiosity, this project will fulfill a crucial two-fold mission. On the fundamental side, it will lead to a radically new level of understanding of quantumness, in its various manifestations, and the functional role it plays for natural and artificial complex systems traditionally confined to a classical domain of investigation. On the practical side, it will deliver novel concrete recipes for communication, sensing and cooling technologies in realistic conditions, rigorously assessing in which ways and to which extent these can be enhanced by engineering and harnessing quantumness. Along with a skillful team which this grant will allow to assemble, benefitting from the vivid research environment at Nottingham, and mainly thanks to his creativity, broad mathematical and physical preparation and relevant inter-disciplinary expertise, the applicant is in a unique position to accomplish this timely and ambitious mission.

Keywords of the ERC project: Quantum information, quantum foundations, quantum correlations, quantumness, complex systems, entanglement, quantum communication, quantum metrology, quantum technologies, mathematical physics, quantum computing, quantum algorithms

Keywords that characterize the scientific profile of the potential visiting researcher/s: Quantum information, quantum foundations, quantum correlations, quantumness, complex systems, entanglement, quantum communication, quantum metrology, quantum technologies, mathematical physics, quantum computing, quantum algorithms
Gauge theories play a central role in particle and condensed matter physics. Heavy-ion collisions explore the strong dynamics of quarks and gluons, which also governs the deep interior of neutron stars, while strongly correlated electrons determine the physics of high-temperature superconductors and spin liquids. Numerical simulations of such systems are often hindered by sign problems. In quantum link models - an alternative formulation of gauge theories developed by the applicant - gauge fields emerge from discrete quantum variables. In the past year, in close collaboration with atomic physicists, we have established quantum link models as a framework for the atomic quantum simulation of dynamical gauge fields. Abelian gauge theories can be realized with Bose-Fermi mixtures of ultracold atoms in an optical lattice, while non-Abelian gauge fields arise from fermionic constituents embodied by alkaline-earth atoms. Quantum simulators, which do not suffer from the sign problem, shall be constructed to address non-trivial dynamics, including quantum phase transitions in spin liquids, the real-time dynamics of confining strings as well as of chiral symmetry restoration at finite temperature and baryon density, baryon superfluidity, or color-flavor locking. New classical simulation algorithms shall be developed in order to solve severe sign problems, to investigate confining gauge theories, and to validate the proposed quantum simulators. Starting from U(1) and SU(2) gauge theories, an atomic physics tool box shall be developed for quantum simulation of gauge theories of increasing complexity, ultimately aiming at 4-d Quantum Chromodynamics (QCD). This project is based on innovative ideas from particle, condensed matter, and computational physics, and requires an interdisciplinary team of researchers. It has the potential to drastically increase the power of simulations and to address very challenging problems that cannot be solved with classical simulation methods.

Keywords of the ERC project: Quantum simulation of gauge theories, sign problem, strongly correlated systems

Keywords that characterize the scientific profile of the potential visiting researcher/s: computational condensed matter physics, strongly correlated systems, quantum simulators
The Higgs: A colored View from the Top at ATLAS

With the ground-breaking discovery of a new, Higgs-like boson on July 4th, 2012, by the CMS and ATLAS collaborations at CERN, a new era of particle physics has begun. The discovery is the first step in answering an unsolved problem in particle physics, the question how fundamental bosons and fermions acquire their mass. One of the major goals in collider physics in the next few years will be the deeper insight into the nature of the new particle, its connection to the known fundamental particles and possible extensions beyond the standard model (SM) of particle physics. My project aims at a particular interesting field to study, the relation of the new particle with the heaviest known elementary particle, the top quark. I aim to develop new, innovative techniques and beyond state-of-the-art methods to extract the Yukawa coupling between the top quark and the Higgs boson, which is expected to be of the order of one - much higher than that of any other quark. I will analyse the only process where the top-Higgs Yukawa coupling can be measured, in associated production of top quark pairs and a Higgs boson. The Higgs boson mainly decays into a pair of b-quarks. This is one of the most challenging channels at the LHC, as huge background processes from gluon splitting contribute. In particular, I will develop and study color flow variables, which provide a unique, powerful technique to distinguish color singlet Higgs bosons from the main background, color octet gluons. The ultimate goal of the project is the first measurement of the top-Higgs Yukawa coupling and its confrontation with SM and beyond SM Higgs boson models, resulting in an unprecedented insight into the fundamental laws of nature. The LHC will soon reach a new energy frontier of 13 TeV starting in 2014. This new environment will provide never seen opportunities to study hints of new physics and precisely measure properties of the newly found particle. This sets the stage for the project.

Keywords of the ERC project: top, Higgs, Yukawa, colour, QCD
Keywords that characterize the scientific profile of the potential visiting researcher/s: top, Higgs, BSM
The nuclear magnetic resonance spectroscopy (NMR) is a versatile and powerful tool, especially in chemistry and in biology. However, its limited sensitivity and small amount of suitable probe nuclei pose severe constraints on the systems that may be explored. This project aims at overcoming the above limitations by giving NMR an ultra-high sensitivity and by enlarging the NMR "toolbox" to dozens of nuclei across the periodic table. This will be achieved by applying the β-NMR method to the soft matter samples. The method relies on anisotropic emission of β particles in the decay of highly spin-polarized nuclei. This feature results in 10 orders of magnitude more sensitivity compared to conventional NMR and makes it applicable to elements which are otherwise difficult to investigate spectroscopically. β-NMR has been successfully applied in nuclear physics and material science in solid samples and high-vacuum environments, but never before to liquid samples placed in atmospheric pressure. With this novel approach I want to create a new universal and extremely sensitive tool to study various problems in biochemistry. The first questions which I envisage addressing with this ground-breaking and versatile method concern the interaction of essential metal ions, which are spectroscopically silent in most techniques, Mg2+, Cu+, and Zn2+, with proteins and nucleic acids. The importance of these studies is well motivated by the fact that half of the proteins in our human body contain metal ions, but their interaction mechanism and factors influencing it are still not fully understood. In this respect NMR spectroscopy is of great help: it provides information on the structure, dynamics, and chemical properties of the metal complexes, by revealing the coordination number, oxidation state, bonding situation and electronic configuration of the interacting metal. My long-term aim is to establish a firm basis for β-NMR in soft matter studies in biology, chemistry and physics.

Keywords of the ERC project: ultrasensitive NMR on metal ions, liquid NMR, metal ion interaction with biomolecules, chemical shift and relaxation time calculations, laser spin polarization, radioactive ion beams,

Keywords that characterize the scientific profile of the potential visiting researcher/s: physical chemist, bio-physicist or bio-chemist with expertise in experimental or theoretical NMR studies; familiar or interested with liquid NMR of metal ions; NMR expert interested in new NMR methods; laser spectroscopist working with optical pumping
The discovery of cosmic neutrinos is one of the major breakthroughs in science in the year 2013. These neutrinos are expected to point back to the origin of the cosmic rays, which are produced in the most powerful accelerators in the universe. In order to solve the puzzle where the highest energetic neutrinos and cosmic rays come from, the key information could be the composition of the observed cosmic ray flux. The question critical for the future development of high-energy astrophysics is especially how heavier nuclei can be accelerated and escape from the sources, such as gamma-ray bursts or active galactic nuclei, without disintegration, or what the consequences for the neutrino fluxes and cosmic ray compositions at the sources are. Neutrinos, on the other hand, may be good for surprises, such as new physics only detectable at extreme energies, distances, or densities. In addition, the possibility to measure neutrino properties in neutrino telescopes has been emerging, either using astrophysical or atmospheric neutrino fluxes, which means that the border line between neutrino physics and astrophysics applications in these experiments fades. The key idea of this proposal is therefore to combine the expertise from astrophysics and particle physics in a multi-disciplinary working group 1) to study the effect of heavy nuclei on the source fluxes from multiple messengers, such as a neutrinos, cosmic rays, and gamma-rays, using efficient descriptions for the radiation processes and particle interactions, and 2) to optimize future experiment infrastructure in ice and sea water for both astro- and particle physics applications. The key goals are to eventually identify the origin of the cosmic rays and cosmic neutrinos, and to solve the open questions in particle physics, such as neutrino mass hierarchy and leptonic CP violation.

Keywords of the ERC project: Neutrinos, cosmic rays

Keywords that characterize the scientific profile of the potential visiting researcher/s: Neutrinos, cosmic rays
Direct Visualization of Light-Driven Atomic-Scale Carrier Dynamics in Space and Time

Electronics is rapidly speeding up. Ultimately, miniaturization will reach atomic dimensions and the switching speed will reach optical frequencies. This ultimate regime of lightwave electronics, where atomic-scale charges are controlled by few-cycle laser fields, holds promise to advance information processing technology from today’s microwave frequencies to the thousand times faster regime of optical light fields. All materials, including dielectrics, semiconductors and molecular crystals, react to such field oscillations with an intricate interplay between atomic-scale charge displacements (polarizations) and collective carrier motion on the nanometer scale (currents). This entanglement provides a rich set of potential mechanisms for switching and control. However, our ability to eventually realize lightwave electronics, or even to make first steps, will critically depend on our ability to actually measure electronic motion in the relevant environment: within/around atoms. The most fundamental approach would be a direct visualization in space and time. This project, if realized, will offer that: a spatiotemporal recording of electronic motion with sub-atomic spatial resolution and sub-optical-cycle time resolution, i.e. picometers and few-femtoseconds/attoseconds. Drawing on our unique combination of expertise covering electron diffraction and few-cycle laser optics likewise, we will replace the photon pulses of conventional attosecond spectroscopy with freely propagating single-electron pulses at picometer de Broglie wavelength, compressed in time by sculpted laser fields. Stroboscopic diffraction/microscopy will provide, after playback of the image sequence, a direct visualization of fundamental electronic activity in space and time. Profound study of atomic-scale light-matter interaction in simple and complex materials will provide a comprehensive picture of the fundamental physics allowing or limiting the high-speed electronics of the future.

Keywords of the ERC project: ultrafast electron microscopy, attosecond physics

Keywords that characterize the scientific profile of the potential visiting researcher/s: ultrafast electron microscopy, attosecond physics
Very fast Imaging by Broadband coherent RAman

The VIBRA project aims at developing an innovative microscope for real-time non-invasive imaging of cells and tissues, which promises to have a revolutionary impact on several fields of biology and medicine. Chemically specific vibrational signatures of molecules enable their direct structural characterization. Reliable and quantitative endogenous bio-markers can be established, e.g., to follow cell differentiation and to identify crucial properties of tissues (malignant vs benign phenotype of a tumour). In this way neoplasms can be located and their borders with normal tissue traced for surgery. Spontaneous Raman spectroscopy demonstrated this capability, but it is intrinsically too slow for imaging. Coherent Raman microscopy, on the other hand, can reach extremely high speed (up to the video rate) but at the expense of poor chemical selectivity, being limited to a single vibrational frequency. The ground-breaking goal of VIBRA is to combine the most detailed molecular information over the entire vibrational spectrum with the highest acquisition speed. The PI will develop a complete coherent Raman microscope for near-video-rate broadband vibrational imaging. This high risk/high gain goal will be achieved by the combination of four key developments: improved pulsed laser source; optimized non-linear interaction, enhancing the signal; increase in acquisition speed, thanks to innovative spectrometers; parallel on-board data processing. In the final application phase, the VIBRA project will validate the performances of the novel vibrational imaging system studying two important biomedical problems: cancerous cell differentiation and detection of neuronal tumours. This will pave the way towards future “virtual histopathology”: intraoperative non-invasive evaluation of cancerous tissue. My vision is to allow researchers and doctors without a specific knowledge in lasers and optics to routinely visualize functional properties of cells and tissues in vivo.

Keywords of the ERC project: Coherent Raman Sectroscopy and Microscopy, CARS, SRS (Stimulated Raman Scattering), ultrafast lasers

Keywords that characterize the scientific profile of the potential visiting researcher/s: Biologist with expertise in linear and non-linear microscopy. Laser scientist. Spectroscopist.
Strongly interacting Rydberg slow light polaritons

A fundamental property of optical photons is their extremely weak interactions, which can be ignored for all practical purposes and applications. This phenomena forms the basis for our understanding of light and is at the heart for the rich variety of tools available to manipulate and control optical beams. On the other hand, a controlled and strong interaction between individual photons would be ideal to generate non-classical states of light, prepare correlated quantum states of photons, and harvest quantum mechanics as a new resource for future technology. Rydberg slow light polaritons have recently emerged as a promising candidate towards this goal, and first experiments have demonstrated a strong interaction between individual photons. The aim of this project is to develop and advance the research field of Rydberg slow light polaritons with the ultimate goal to generate strongly interacting quantum many-body states with photons. The theoretical analysis is based on a microscopic description of the Rydberg polaritons in an atomic ensemble, and combines well established tools from condensed matter physics for solving quantum many-body systems, as well as the inclusion of dissipation in this non-equilibrium problem. The goals of the present project addresses questions on the optimal generation of non-classical states of light such as deterministic single photon sources and Schrödinger cat states of photons, as well as assess their potential for application in quantum information and quantum technology. In addition, we will shed light on the role of dissipation in this quantum many-body system, and analyze potential problems and fundamental limitations of Rydberg polaritons, as well as address questions on equilibration and non-equilibrium dynamics. A special focus will be on the generation of quantum many-body states of photons with topological properties, and explore novel applications of photonic states with topological properties.

Keywords of the ERC project: quantum many body systems, quantum optics, strongly interacting photons, novel phases of quantum matter

Keywords that characterize the scientific profile of the potential visiting researcher/s: quantum many body systems, quantum optics, strongly interacting photons, novel phases of quantum matter
Quantum Black Holes: A macroscopic window into the microstructure of gravity

The thermodynamic behavior of black holes is a precious clue in unravelling the microscopic structure of quantum gravity. High precision computations of quantum black hole entropy provide a new window into the fundamental microscopic theory of gravity and its deviations from classical general relativity. Traditional methods of quantum field theory have proved to be not well-suited to perform these computations. Two breakthroughs in my recent work establish new ground for progress. On one front, a new method to sum up all perturbative quantum contributions to the entropy of a large class of black holes has been developed. This gives rise to the first exactly solvable model of a quantum black hole. On a second front, a longstanding theoretical obstacle called the wall-crossing problem has been cleared in my recent work on the microscopic description of black holes in string theory. The newly-developed field of mock modular forms is shown to be the correct framework to address questions of exact black hole entropy. This makes a large class of microscopic models amenable to analytic control, many of which were previously beyond reach. These developments open up a new line of research that I propose to pursue along two intersecting avenues. First, I aim to extend the computations of exact quantum black hole entropy towards models of realistic black holes. Second, I aim to advance the theoretical understanding of quantum black holes by investigating the deeper origins of mock modular symmetry. As a concrete application, I aim to establish that newfound group-theoretical structures called “moonshine” symmetries are physically realized in quantum black holes, thus opening up connections between two exciting fields of research previously thought to be distinct. Together, the broad goal is to explain black hole microstructure through systematic computations of exact quantum entropy, and to investigate its consequences on the fundamental microscopic theory of gravity.

Keywords of the ERC project: String theory, black holes, modular forms
Keywords that characterize the scientific profile of the potential visiting researcher/s:
Temporal Quantum Correlations

Correlations are central for our modern view on the foundations of quantum theory and applications like quantum information processing. So far, research concentrated on correlations between two or more particles. Indeed, for this situation it is well established that spatial quantum correlations are a useful resource for tasks like quantum cryptography and quantum metrology. There are, however, other types of correlations in quantum mechanics, which arise if a sequence of measurements on a single quantum system is made. These temporal quantum correlations have recently attracted attention, because they are central for the understanding of some differences between the quantum and the classical world. Moreover, due to experimental progress their observation has become feasible with trapped ions, polarized photons, or other quantum optical systems. This project aims at a full understanding and characterization of temporal quantum correlations. For that, we will derive criteria and measures for temporal quantum correlations and investigate their connection to information theory. Then, we will elucidate to which extent temporal correlations can be used to prove that a system is quantum and not classical. Finally, we consider implementations of temporal quantum correlations using continuous variable systems like nanomechanical oscillators and applications in quantum information processing.

Keywords of the ERC project: quantum optics, quantum information theory, temporal correlations

Keywords that characterize the scientific profile of the potential visiting researcher/s: quantum optics, quantum information theory
The objective of the proposed project is to pioneer a magnetometry-based experimental framework for the detection of time-varying signatures of the ‘dark sector’. This novel approach will enable systematic searches for particles contributing to the dark matter and for dark-energy components. The nature of dark matter and that of dark energy are among the central open problems in modern physics. There are only few experimental bounds and so far no conclusive observations of dark-sector particles or fields. Experiments enabling a direct coupling to the dark sector and thus a systematic search for and study of the contributing particles and fields would open up new vistas for areas ranging from particle physics to astrophysics and cosmology, and would in particular provide insights into the physics beyond the Standard Model. Here, we propose a framework for such experimental searches based on high-precision magnetometers, and networks thereof. Our approach is distinct from existing efforts in two ways. First, it will enable searches for so-far unexplored couplings to ultra-light bosonic particles present in the Universe that could be components of dark matter and/or dark energy, in particular axions and axion-like particles (ALPs). Second, we will develop and use devices and methods tailored to search for oscillating and transient, rather than time-independent, effects. Specifically, we will use nuclear magnetic resonance (NMR) techniques for detecting spin precession caused by background axion and ALP dark matter, and geographically separated magnetometers for identify transient effects, such as crossing domain walls of ALP fields, which have been proposed as a possible dark-energy component. The devices and methods developed in the framework of this project will provide the essential components for unique searches for a broad class of dark-matter and dark-energy candidates and might enable the key experiments to understanding the dark sector.

Keywords of the ERC project: Ultralight dark matter, axions, axion-like particles, NMR, atomic magnetometers

Keywords that characterize the scientific profile of the potential visiting researcher/s:
<table>
<thead>
<tr>
<th>Principal Investigator:</th>
<th>Dr Georgios Katsaros</th>
</tr>
</thead>
<tbody>
<tr>
<td>Host Institution:</td>
<td>Institute Of Science And Technology Austria - AT</td>
</tr>
</tbody>
</table>

**Towards spin qubits and Majorana fermions in Germanium self-assembled hut-wires**

A renewed interest in Ge has been sparked by the prospects of exploiting its lower effective mass and higher hole mobility to improve the performance of transistors. Ge emerges also as a promising material in the field of spin qubits, as its coherence times are expected to be very long. Finally, it has been proposed that strained Ge nanowires show an unusually large spin orbit interaction, making them thus suitable for the realization of Majorana fermions. In view of these facts, one is able to envision a new era of Ge in information technology.

The growth of Ge nanocrystals on Si was reported for the first time in 1990. This created great expectations that such structures could provide a valid route towards innovative, scalable and CMOS-compatible nanodevices. Two decades later the PI was able to realize the first devices based on such structures. His results show that Ge self-assembled quantum dots display a unique combination of electronic properties, i.e. low hyperfine interaction, strong and tunable spin-orbit coupling and spin selective tunneling. In 2012, the PI’s group went a step further and realized for the first time Ge nanowires monolithically integrated on Si substrates, which will allow the PI to move towards double quantum dots and Majorana fermions. In view of their exceptionally small cross section, these Ge wires hold promise for the realization of hole systems with exotic properties.

Within this project, these new wires will be investigated, both as spin as well as topological qubits. The objective of the present proposal is mainly to: a) study spin-injection by means of normal and superconducting contacts, b) study the characteristic time scales for spin dynamics and move towards electrical spin manipulation of holes, c) observe Majorana fermions in a p-type system. The PI’s vision is to couple spin and topological qubits in one “technological platform” enabling thus the coherent transfer of quantum information between them.

**Keywords of the ERC project:** low temperature electronic transport, quantum dots, hybrid superconductor-semiconductor devices

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** low temperature physics, semiconductor nanodevices, superconductivity, high frequency electronics
**Biological Membranes in Action: A Unified Approach to Complexation, Scaffolding and Active Transport**

In recent breakthrough publications, the effect of fluctuations on the affinity of membrane-confined molecules has been evaluated, and a quantitative model for the time evolution of small adhesion domains has been developed under my leadership. Now I propose to bring my research to a new level by tackling the problem of active and passive organisation of proteins into macromolecular structures on fluctuating fluid membranes, using a physicist’s approach across established disciplinary boundaries. The formation and transport of supramolecular complexes in membranes is ubiquitous to nearly all functions of biological cells. Today, there is a variety of experiments suggesting that macromolecular complexes act as scaffolds for free proteins, overall yielding obstructed diffusion, counterbalanced by active transport by molecular motors. However, an integrative view connecting complexation and transport is largely missing. Furthermore, the effects of membrane mediated interactions and (non)-thermal fluctuations were so far overlooked. Gaining a quantitative insight into these processes is key to understanding the fundamental functioning of cells. Together with my carefully selected team, I will address these intrinsically biological problems, by means of theoretical physics. Phenomena such as active and anomalous transport, as well as complexation are also currently subject to intense research in the statistical and soft matter physics communities. In this context, the aim of this proposal is to bridge the divide between the two worlds and significantly contribute to both physics and the life sciences by developing general principles that can be applied to processes in cells. Resolving these issues is of fundamental importance since it would identify how interactions on the cell surface arise, and may translate directly into pharmaceutical applications.

**Keywords of the ERC project:** modeling cell adhesion and tissue growth

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** experiments on tissue growth, modeling using stochastic dynamics methods

From cell biology to polymer photovoltaics, (self-)assembly processes that give rise to morphology and functionality result from non-equilibrium processes, which are driven by both, external forces, such as flow due to pressure gradients, inserting energy, or manipulation on a local molecular level, or internal forces, such as relaxation into a state of lower free energy. The resulting material is arrested in a metastable state. Most previous work has focused on the relationship between structure and properties, while insight into the guiding principles governing the formation of a (new) material, has been lacking. However, a comprehensive molecular level understanding of non-equilibrium assembly would allow for control and manipulation of material processes and their resulting properties. This lag of knowledge can be traced to the formidable challenge in obtaining a molecular picture of non-equilibrium assembly. Non-equilibrium processes have been studied extensively on a macroscopic level by non-equilibrium thermodynamics. We take a novel route approaching the challenge from a molecular point of view. Recent advances in experimental, but especially computational modeling, now allow to follow (supra-) molecular structural evolution across the range of length and time scales necessary to comprehend, and ultimately control and manipulate macroscopic functional properties of soft matter at the molecular level. Soft matter is particularly suited for that approach, as it is “slow” and easy to manipulate. We take the computational physics route, based on simulations on different levels of resolution (all atom, coarse grained, continuum) in combination with recent multiscale and adaptive resolution techniques. This work will initiate the way towards a paradigm change from conventional Structure Property Relations (SPR) to molecularly based Structure Process Property Relations (SPPR).

Keywords of the ERC project: Multiscale Modeling of Soft Matter, Non-Equilibrium Processes, Polymers, Formation of Functional Materials

Keywords that characterize the scientific profile of the potential visiting researcher/s: Computational Physics, Non-Equilibrium Physics, Soft Matter Materials Science
Interfacing quantum states in carbon nanotube devices

Coherent control and sensitive detection of quantum states in condensed matter are among the most topical challenges of modern physics. They drive the development of novel materials, theoretical concepts, and experimental methods to advance our understanding of fundamental laws of quantum mechanics and to create transformative technologies for future applications. During the past decades carbon has emerged as a new material platform to address these challenges: graphene and carbon nanotubes have been created as paradigm systems with exceptional physical properties. As atomically-thin cylinders carbon nanotubes combine ultra-low mass with extreme mechanical stiffness. This identifies them as perfect candidates for the realization of ultra-high quality mechanical resonators with applications in quantum metrology and sensing. Their crystalline lattice can be made free of nuclear spins by material engineering to ensure ultra-long electron spin coherence times for quantum information processing and coherent spintronics. In addition, semiconducting single-wall carbon nanotubes exhibit optical resonances with unprecedented tunability in color for quantum communication and cryptography. These outstanding material properties form the basis for our scientific research proposal. Our vision is to realize up-conversion schemes interfacing light with spin, mechanical, and spin-mechanical degrees of freedom in carbon nanotube devices. In particular, we will study spin dynamics in carbon nanotubes with an isotopically engineered nuclear spin lattice and we will suspend individual carbon nanotubes in high-fidelity optical micro-cavities to detect and control mechanical motion down to the quantum ground state. Ultimately, our devices will realize entirely novel regimes of quantum states by hybridizing light with magnetic or mechanical excitations and explore the foundations of emerging technologies at the quantum limit.

Keywords of the ERC project: optical spectroscopy, solid-state quantum optics, carbon nanotubes, transition metal dichalcogenides, layered semiconductors

Keywords that characterize the scientific profile of the potential visiting researcher/s: optical spectroscopy, solid-state quantum optics, carbon nanotubes, transition metal dichalcogenides, layered semiconductors
Plasmon-based Functional and Quantum Nanophotonics

Plasmon-based nanophotonics, an explosively growing research field concerned with surface-plasmon waveguides and circuitry, is oriented towards exploiting unique perspectives opened for radiation guiding along metal surfaces: extreme mode confinement (i.e., far beyond the diffraction limit) and seamless interfacing of electronic and photonic circuits (that both utilize the same metal circuitry). At the same time, unavoidable radiation absorption by metals results in the fundamental trade-off between the mode confinement and propagation loss, so that the problem of making the most of the above unique features becomes of paramount importance. The proposal encompasses two ground-breaking research directions in plasmonics that explore and utilize extremely confined plasmon-waveguide modes for functional and quantum nanophotonics. These directions of in-depth investigations concentrate within two interrelated and largely unexplored research areas within plasmonics: development of ultra-compact plasmonic configurations exhibiting unique functionalities and realization of strong coupling between extremely confined plasmonic modes and individual quantum emitters. Fundamental studies of ultimate mode confinement and coupling to quantum emitters would evolve into investigations carried out within forefront topics including (i) dynamic control of plasmon-waveguide modes using the same metal circuitry for both radiation guiding and its control with electrical signals; (ii) moulding the radiation flow by gradually varying waveguide cross sections in order to realize efficient nanofocusing of radiation, miniature ultra-dispersive wavelength-selective components and table-top models of plasmonic black holes, and (iii) quantum plasmonics with individual quantum emitters being strongly coupled to deep subwavelength surface plasmon modes, targeting the realization of a saturable waveguide mirror, single-photon transistor and long-distance entanglement of two remote quantum emitters.

Keywords of the ERC project: plasmonics, plasmon-based nanophotonics, quantum plasmonics

Keywords that characterize the scientific profile of the potential visiting researcher/s: plasmonics, nano-optics, nanophotonics
Optical Quantum Control of Magnetic Molecules

A revolution is underway, as molecular magnets are establishing a fundamental link between spintronics, molecular electronics and quantum computation. On the other hand, we know almost nothing on how a magnetic molecule is affected by electrons flowing through it or by the excitation of a molecular group. OptoQMol will investigate these uncharted waters by developing innovative, ultra-clean methods that will provide information inaccessible to established procedures. This will allow an unprecedented study of the interplay of electronic and spin degrees of freedom in magnetic molecules and of its possible use for quantum logic. OptoQMol is a strongly multidisciplinary project, and makes use of an innovative mix of chemical and physical methods to overcome present experimental limitations, both in terms of time resolution and cleanliness. Instead of placing a magnetic molecule between bulk electrodes, we will directly grow photoactive groups on the molecule, so that electrons will flow through or close to the spin centers after a light pulse. This affords an ultra-clean system that can be studied in bulk, with a perfectly defined geometry of the magnetic and electronic elements. We will then combine optical and electron paramagnetic resonance techniques with ns time resolution, so as to observe the effect of electron flow on the spins in real time and measure the spin quantum coherence. Eventually we will use these innovative methods to control the interactions among spins and perform quantum logic operations. The success of OptoQMol will answer two fundamental questions: How do molecular spins interact with flowing electrons? How can we use electronic excitations to perform quantum logic operations between multiple electron spins? The results will open a totally new area of experimental and theoretical investigation. Moreover they will redefine the limits and possibilities of molecular spintronics and allow quantum logic operations among multiple electron spins.

Keywords of the ERC project: spintronics, molecular magnetism, electron spin resonance, time resolved experiments, donor-acceptor dyads

Keywords that characterize the scientific profile of the potential visiting researcher/s: spintronics, molecular magnetism, electron spin resonance, time resolved experiments, donor-acceptor dyads
Large Deviations and Non Equilibrium Phase Transitions for Turbulent Flows, Climate, and the Solar System

The aim of this project is to predict and compute extremely rare but essential trajectories in complex physical systems. We will compute rare transitions trajectories, first between two different turbulent attractors in models of planetary jet dynamics, and second between two configurations of ocean currents for a model of the thermohaline circulation. We will compute the dynamics and the probability for collisions between two planets in the solar system, on time scales of order of billions of years. We will evaluate rare events that lead to extremely large drags or torques on objects embedded in turbulent flows, directly from the dynamics. Because of the huge range of time scales, all those trajectories are not accessible through direct numerical simulations. The project’s unity stems from the methodology based on large-deviations theory. Large deviation rate functions generalize the concept of entropy or free energy in non-equilibrium extended systems: they provide a global characterization of their most probable state, their large fluctuations and their phase transitions. Impressive explicit computations of large deviation rate functions have been recently performed in simple non-equilibrium systems. The main aim of this project is to bridge the gap between those extremely interesting new concepts and algorithms, and complex dynamical systems such as turbulent flows, semi-realistic models of fluids related to climate dynamics, or the long time behavior of the solar system. In order to achieve this goal, we will use macroscopic fluctuation theory, instanton theory, and other analytical methods in order to compute explicitly large deviation rate functions for essential macroscopic quantities (the velocity or density fields). We will also develop and use algorithms specifically dedicated at computing the statistics of extremely rare trajectories, based on the generalization of importance sampling implemented through cloning or multilevel splitting methods.

Keywords of the ERC project: Statistical physics, Climate Dynamics, Large deviation theory, Turbulence, Rare event algorithms

Keywords that characterize the scientific profile of the potential visiting researcher/s: Theoretical physics /applied mathematics or climate scientist
Keywords of the ERC project: Topological insulators, Majorana fermions

Keywords that characterize the scientific profile of the potential visiting researcher/s: Quantum transport, superconductivity, topological insulators, Majorana fermions
In condensed matter physics there are several iconic predictions that have evaded experimental discovery for many decades. Well-known examples include the proposed fractionally-charged quasiparticles in one-dimension, the theorized quantum crystal of electrons, and the elusive Kondo cloud. These sought-after many-body states all share two key aspects underscoring why they are so hard to discover: They each involve a fragile quantum state of matter that is destroyed easily by disorder or elevated temperatures, and in each case the distinguishing fingerprint is encoded in their real-space structure, which is often difficult to probe directly. The discovery of such phases therefore requires two challenging experimental components: A superb material system in which these phases can be generated, and a novel real-space probe that can image their spatial structure, yet is minimally invasive as not to destroy them.

Recently, we have developed a radically new approach for creating the state-of-the-art in both material systems and scanning probes, based on carbon nanotube devices of unprecedented complexity and cleanliness. With these components in place, we are poised to make the next quantum leap in technology by building a conceptually new experimental platform in which fragile quantum states of matter can be realized and studied microscopically: We will use a nanotube single-electron-transistor as a high-resolution, ultrasensitive scanning charge detector to non-invasively image an exotic quantum state within a second pristine nanotube. With this new platform we will thus be able to address several foundational questions in condensed matter physics (including those mentioned above) and unravel their underlying physics.

Keywords of the ERC project: nanotube graphene scanning probe stm transport many-body

Keywords that characterize the scientific profile of the potential visiting researcher/s:
Interfacing spin waves with superconducting quantum circuits for single magnon creation and detection

The proposed project will experimentally interface ferromagnets with superconducting quantum circuits to study dynamics within the magnet. To this end, magnonic elements made up by thin, structured magnetic films will be strongly coupled to the qubit. Superconducting qubits are ideal detectors due to their quantum limited back-action on the measured object and energy resolution. Spectroscopy and coherence measurements on the hybrid system will be made in order to address fundamental aspects such as spin wave generation, detection, coherence, or wave propagation down to mK temperatures and at ultra-low power (atto-watts). Amplitude and phase noise of spin wave resonators will be determined. At the final stage of the project, the quantum limited resolution of qubits will facilitate single magnon creation and detection. Quantum states are swapped between qubit and magnon, and superpositioned and entangled states will be explored. Monitoring the qubit response to its magnetic environment the low and high-frequency flux noise spectrum of spin waves will be inferred. The research methodology employs junctions, resonators, and qubits as research objects and detectors. The samples will be characterized at cryogenic temperatures by transport, magnetometry, resonator and qubit setups. Magnetic materials will be deposited and structured beneath or on top the superconducting quantum circuits. Exploring spin wave dynamics in thin films by coupling to a superconducting qubit complements conventional measurement techniques based on photon, electron or neutron scattering methods, which require highly populated excitations. The project connects to and extends research objects of ground-breaking nature to open up new horizons for quantum, magnon and spin electronics. Magnetic material physics is enhanced by new research concepts such as quantum resolved spectroscopy and coherence measurements on intrinsic dynamic states.

Keywords of the ERC project: quantum technology, superconducting qubits, spin waves, ferromagnets

Keywords that characterize the scientific profile of the potential visiting researcher/s: cryogenic measurements, spectroscopy, time domain dependence, quantum manipulation
**INhomogenieties and fluctuations in quantum CohErent matter Phases by ultrafast optical Tomography**

Standard time domain experiments measure the time evolution of the reflected/transmitted mean number of photons in the probe pulses. The evolution of the response of a material is typically averaged over the illuminated area as well as over many pump and probe measurements repeated stroboscopically. The aim of this project is to extend time domain optical spectroscopy beyond mean photon number measurements by performing a full Time Resolved Quantum State Reconstruction (TRQSR) of the probe pulses as a function of the pump and probe delay. The nature of the light matter interaction and the transient light-induced states of matter will be imprinted into the probe quantum state after the interaction with the material and can be uncovered with unprecedented detail with this new approach to time domain studies. TRQSR will be implemented by combining pump and probe experiments resolving single light pulses with balanced homodyne detection quantum tomography in the pulsed regime. We will apply and exploit the unique capabilities of TRQSR to address two different unresolved problems in condensed matter. Firstly, we will investigate the coherent and squeezed nature of low energy photo-induced vibrational states. We will use TRQSR with probe pulses shorter than the phonon timescale to interrogate the time evolution of the vibrational state induced by the pump pulse. Secondly, we will address inhomogeneities in photo-induced phase transformations. With TRQSR we can perform time domain measurements with a very small photon number per pulse which will give information on the interaction between the material (as prepared by the pump pulse) and individual photons. In this limit, TRQSR will allow us to retrieve rich statistics. While the average will deliver the information of a standard pump and probe experiment, higher order moments will give information on the time evolution of spatial inhomogenieties in the transient state.

**Keywords of the ERC project:** non-equilibrium properties, complex material, quantum optics

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** quantum optics
Biological motion and forces originate from mechanically active proteins operating at the nanometer scale. These individual active elements interact through the surrounding cellular medium, collectively generating structures spanning tens of micrometers whose mechanical properties are perfectly tuned to their fundamentally out-of-equilibrium biological function. While both individual proteins and the resulting cellular behaviors are well characterized, understanding the relationship between these two scales remains a major challenge in both physics and cell biology. We will bridge this gap through multiscale models of the emergence of active material properties in the experimentally well-characterized actin cytoskeleton. We will thus investigate unexplored, strongly interacting nonequilibrium regimes. We will develop a complete framework for cytoskeletal activity by separately studying all three fundamental processes driving it out of equilibrium: actin filament assembly and disassembly, force exertion by branched actin networks, and the action of molecular motors. We will then recombine these approaches into a unified understanding of complex cell motility processes. To tackle the cytoskeleton’s disordered geometry and many-body interactions, we will design new nonequilibrium self-consistent methods in statistical mechanics and elasticity theory. Our findings will be validated through simulations and close experimental collaborations. Our work will break new ground in both biology and physics. In the context of biology, it will establish a new framework to understand how the cell controls its architecture and mechanics through biochemical regulation. On the physics side, it will set up new paradigms for the emergence of original out-of-equilibrium collective behaviors in an experimentally well-characterized system, addressing the foundations of existing macroscopic “active matter” approaches.

Keywords of the ERC project: theory; active matter; cytoskeleton; actin

Keywords that characterize the scientific profile of the potential visiting researcher/s: Physics; Theory; Soft Matter; Biophysics; Statistical Mechanics
Dynamical magnetic excitations with spin-orbit interaction in realistic nanostructures

Nano-spin-orbitronics is an emerging and fast growing field that aims at combining three degrees of freedom – spin, charge and spin-orbit interaction – to explore new nanotechnologies stemming from fundamental physics. New magnetic phases of matter are investigated using, in particular, atomic design to tailor beneficial physical properties down to the atomic level. Storage, transport and manipulation of magnetic information within a small set of atoms does not only require a fundamental understanding of their ground-state properties from the perspective of quantum mechanics, but crucially also their dynamical excited states. We propose to go beyond the state of the art by investigating from first-principles the dynamical properties of chiral spin textures in nanostructures from 2-dimensions to 0-dimension with these nanostructures being deposited on different substrates where spin-orbit interaction plays a major role. Understanding their response to external dynamical fields (electric/magnetic) or currents will impact on the burgeoning field of nano-spin-orbitronics. Indeed, to achieve efficient manipulation of nano-sized functional spin textures, it is imperative to exploit and understand their resonant motion, analogous to the role of ferromagnetic resonance in spintronics. A magnetic skyrmion is an example of a spin-swirling texture characterized by a topological number that will be explored. This spin state has huge potential in nanotechnologies thanks to the low spin currents needed to manipulate it.

Based on time-dependent density functional theory and many-body perturbation theory, our innovative scheme will deliver a paradigm shift with respect to existing theoretical methodologies and will provide a fundamental understanding of: (i) the occurrence of chiral spin textures in reduced dimensions, (ii) their dynamical spin-excitation spectra and the coupling of the different excitation degrees of freedom and (iii) their impact on the electronic structure.

Keywords of the ERC project: Chiral low-dimensional magnets; Dynamical magnetic excitations; Spin-orbit interaction; Time-dependent density functional theory; Many-body perturbation theory; Magnetic nanodevices; Skyrmions

Keywords that characterize the scientific profile of the potential visiting researcher(s): ab-initio; supercomputing; method development; magnetism; dynamics
The rise in bacterial infections that are resistant to antibiotic treatment poses a major global health challenge. Addressing this challenge is not just a clinical issue: understanding bacterial resistance evolution calls for an interdisciplinary approach, in which the development of new physics, in coordination with biology, chemistry and engineering, has a central role to play. In particular, statistical physics, to predict the stochastic emergence of drug-resistant mutants, must be integrated with soft matter and chemical physics, to understand the spatial organization of the bacterial populations within which this happens. Bacterial infections are very often spatially heterogeneous. This is known to influence the outcome of antibiotic treatment – for example bacterial biofilms, which form on the surfaces of medical implants, are notoriously hard to remove. However, much less attention has been paid to the role of spatial structure in the evolution of drug resistance, i.e. the emergence and spread of genetically drug-resistant bacterial strains. I will lead a research programme which will for the first time uncover the two-way link between the emergence of spatial structure in bacterial multicellular assemblies and the evolution of drug resistance. The programme builds on my current theoretical, simulation and experimental work. I will first determine the basic principles of evolution in drug gradients using theoretical models, combined with experiments in a controlled, 1D geometry. I will then explore how these principles translate to the more realistic scenario of bacterial biofilms, where spatial structure and drug gradients are emergent properties, using advanced computer simulation methods and both confocal microscopy and evolution experiments. In the final part of the programme, I will use these insights to reveal optimization principles for the design of evolution-resistant surface coatings for applications in medical devices.

Keywords of the ERC project: antibiotic resistance, biofilms, spatial structure

Keywords that characterize the scientific profile of the potential visiting researcher/s: Biological physics, microbiology, evolutionary biology, computer simulations, statistical physics
Electron-lattice-spin correlations and many-body phenomena in 2D semiconductors and related heterostructures

Two-dimensional crystalline materials exhibit exceptional physical properties and offer fascinating potential as fundamental building blocks for future two-dimensional electronic and optoelectronic devices. Transition metal dichalcogenides (TMDCs) are of particular interest as they show a variety of many-body phenomena and correlation effects. Key properties are: i) additional internal degrees of freedom of the electrons, described as valley pseudospin and layer pseudospin, ii) electronic many-body effects like strongly-bound excitons and trions, and iii) electron-lattice correlations like polarons. While these phenomena represent intriguing fundamental solid state physics problems, they are of great practical importance in view of the envisioned nanoscopic devices based on two-dimensional materials. The experimental research project FLATLAND will address the exotic spin-valley-layer correlations in few-layer thick TMDC crystals and TMDC-based heterostructures. The latter comprise other 2D materials, organic crystals, metals and phase change materials as second constituent. Microscopic coupling and correlation effects, both within pure materials as well as across the interface of heterostructures, will be accessed by time- and angle-resolved extreme ultraviolet-photoelectron spectroscopy, femtosecond electron diffraction, and time-resolved optical spectroscopies. The project promises unprecedented insight into the microscopic coupling mechanisms governing the performance of van der Waals-bonded devices.

Keywords of the ERC project: 2D materials, heterostructures, ultrafast dynamics, structural dynamics

Keywords that characterize the scientific profile of the potential visiting researcher/s: time-resolved spectroscopy, photoemission spectroscopy, time-resolved diffraction, 2D heterostructures
Mitochondria are cell organelles that provide the energetic requirements of the body. The majority of cellular ATP is produced by the membrane protein ATP synthase through a proton gradient across the mitochondrial inner membrane. Alterations in ATP synthase biogenesis can result in severe mitochondrial diseases affecting tissues with high energy requirements as brain and muscles. Mitochondrial diseases affect approximately 20 million people in the EU, causing 35% of deaths during the first year of life of newborns. However, the available therapeutic approaches, are still extremely limited and there is no specific treatment for ATP synthase deficiencies. To improve the treatments currently available for mitochondrial diseases, the project will focus on the realization of artificial mitochondria (AM). Based on artificial lipid vesicles, AM will be fabricated by means of microfluidics methods, a powerful tool able to produce identical replicas of a given bio-inspired membrane-object. ATP synthase will be expressed and assembled within the lipid bilayer by encapsulating cell-free protein expression systems. To test the ability of AM as in-situ energy fabrication systems, targeting-AM will be endocytosed inside cultured cells and ATP synthesis will be triggered by taking advantage of the proton gradient provided by endosomes. Finally, by enclosing other plasmids encoding for diverse proteins, AM can be used as energy-factoring pockets to elicit protein expression just when internalized within cells. This novel approach may constitute an advanced new concept in gene therapy to more effectively create breakthroughs in improving human health.

**Keywords of the ERC project:** Artificial organelles, membrane protein reconstitution, ATP synthase, mitochondrial diseases

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** molecular mitochondrial physiology
Controlling the Motion of Complex Molecules and Particles

The main objective of COMOTION is to enable novel experiments for the investigation of the intrinsic properties of large molecules, including biological samples like proteins, viruses, and small cells. X-ray free-electron lasers have enabled the observation of near-atomic-resolution structures in diffraction-before-destruction experiments, for instance, of isolated mimiviruses and of proteins from microscopic crystals. The goal to record molecular movies with spatial and temporal atomic-resolution (femtoseconds and picometers) of individual molecules is near.

The investigation of ultrafast, sub-femtosecond electron dynamics in small molecules is providing first results. Its extension to large molecules promises the unraveling of charge migration and energy transport in complex (bio)molecules.

Matter-wave experiments of large molecules, with currently up to some hundred atoms, are testing the limits of quantum mechanics, particle-wave duality, and coherence. These metrology experiments also allow the precise measurement of molecular properties.

The principal obstacle for these and similar experiments in molecular sciences is the controlled production of samples of identical molecules in the gas phase. We will develop novel concepts and technologies for the manipulation of complex molecules, ranging from amino acids to proteins, viruses, nano-objects, and small cells: We will implement new methods to inject complex molecules into vacuum, to rapidly cool them, and to manipulate the motion of these cold gas-phase samples using combinations of external electric and electromagnetic fields. These external-field handles enable the spatial separation of molecules according to size, shape, and isomer.

The generated controlled samples are ideally suited for the envisioned precision experiments. We will exploit them to record atomic-resolution molecular movies using the European XFEL, as well as to investigate the limits of quantum mechanics using matter-wave interferometry.

Keywords of the ERC project: control; biomolecule; nanoparticle; laser control; cooling; imaging; diffraction; atomic resolution ultrafast; cryogenic; buffer gas

Keywords that characterize the scientific profile of the potential visiting researcher/s: biophysics; molecular physics; physical chemistry; laser physics; computer science; computational physics
Nanostructuring graphene and graphitic substrates for controlled and reproducible functionalization

Graphene is a new class of promising material with exceptional properties and thus warrants a plethora of potential applications in various domains of science and technology. However, due to intrinsic zero bandgap and inherently low solubility, a prerequisite for the use of graphene in several applications is its controlled and reproducible functionalization in a nanostructured fashion. Being a ‘surface-only’ nanomaterial, its properties are extremely sensitive not only to chemical modification but also to noncovalent interactions with simple organic molecules. A systematic knowledge base for targeted functionalization of graphene still eludes the scientific community. The present experimental protocols suffer from important shortcomings. Firstly, graphene functionalization occurs randomly in solution based methods and there is scarcity of methods that can exert precise control over how and where the reactions/interactions occur. Secondly, due to random functionalization, producing reproducible samples of structurally uniform graphene and graphitic materials remains a major challenge. Lastly, a molecular level understanding of the functionalization process is still lacking which precludes systematic strategies for manipulation of graphene and graphitic materials.

NANOGRAPH@LSI aims to develop systematic experimental protocols for controlled and reproducible (covalent, non-covalent as well as the combination of both) functionalization of graphene and graphitic materials in a nanostructured fashion at the liquid-solid interface (LSI), along with the implementation of new nanoscale characterisation tools, targeting a broad range of applications in the fields of electronics, i.e. graphene bandgap engineering, sensing, and separation. Supramolecular self-assembly of organic building blocks at the liquid-solid interface will be employed as a basic strategy. In view of the above mentioned applications, also upscaling protocols will be developed and implemented.

Keywords of the ERC project: graphene, graphite, self-assembly, device
Keywords that characterize the scientific profile of the potential visiting researcher/s:
Beyond structure: integrated computational and experimental approach to Ensemble-Based Drug Design.

Although protein dynamics plays an essential role in function, it is rarely considered explicitly in current structure-based approaches to drug design. Here I propose the computer-aided design of ligands by modulation of protein dynamics, or equivalently, protein structural ensembles. The detailed understanding of ligand-induced perturbations of protein dynamics that will result from this study is crucial not just to accurately predicting binding affinities and tackling "undruggable" targets, but also to understanding protein allostery. Three major aims will be pursued during this project. First, I will combine concepts from chemoinformatics and non-equilibrium thermodynamics to detect cryptic "druggable" small molecule binding sites in computed structural ensembles. New computational methods will be developed to predict how binding at these putative sites is likely to influence protein function. This will enable rational approaches to allosteric control of protein function. Second, new classes of non-equilibrium sampling algorithms will be developed to improve by 2-3 orders of magnitude the speed of computation of protein/ligand structural ensembles by molecular simulations. This will enable routine consideration of protein flexibility in ligand optimisation problems. Third, I will address with the above methods a frontier problem in molecular recognition: the rational design of protein isoform-specific ligands. To achieve this goal, I will integrate computation with experiments and focus efforts on the therapeutically relevant cyclophilin protein family. Experimental work will involve the use of purchased or custom-synthesized competitive and allosteric ligands in enzymatic assays, calorimetry and crystal structure analyses. Overall, this project proposes fundamental advances in our ability to quantify and engineer protein-ligand interactions, therefore expanding opportunities for the development of future small molecule therapeutics.

Keywords of the ERC project: molecular simulations, protein dynamics, drug design, free energy

Keywords that characterize the scientific profile of the potential visiting researcher/s: computational chemist, biophysical chemist, bioNMR spectroscopist
Functional materials from on-surface linkage of molecular precursors

With the advent of self-assembly, increasingly high hopes are being placed on supramolecular materials as future active components of a variety of devices. The main challenge remains the design and assembly of supramolecular structures with emerging functionalities tailored according to our needs. In this respect, the extensive research over the last decades has led to impressive progress in the self-assembly of molecular structures. However, self-assembly typically relies on non-covalent interactions, which are relatively weak and limit the structure’s stability and often even their functionality. Only recently the first covalently bonded organic networks were synthesized directly on substrate surfaces under ultra-high-vacuum, whose structure could be defined by appropriate design of the molecular precursors. The potential of this approach was immediately recognized and has attracted great attention. However, the field is still in its infancy, and the aim of this project is to lift this new concept to higher levels of sophistication reaching real functionality. For optimum tunability of the material’s properties, its structure must be controlled to the atomic level and allow great levels of complexity and perfection. Complexity can be reached e.g. with hybrid structures combining different types of precursors. In this project, this hardly explored approach will be applied to three families of materials of utmost timeliness and relevance: graphene nanoribbons, porous frameworks, and donor-acceptor networks. Along the pursuit of these objectives, side challenges that will be addressed are the extension of our currently available chemistry-on-surfaces toolbox by identification of new reactions, optimized reaction conditions, surfaces, and ultimately their combination strategies. A battery of tools, with special emphasis on scanning probe microscopies, will be used to visualize and characterize the reactions and physical-chemical properties of the resulting materials.

Keywords of the ERC project: on-surface synthesis, surface-supported chemistry, graphene nanoribbons, covalent organic frameworks, scanning probe microscopy

Keywords that characterize the scientific profile of the potential visiting researcher/s: scanning probe microscopy, physical chemistry, surface science
**3D Model Catalysts to explore new routes to sustainable fuels**

Currently fuels, plastics, and drugs are predominantly manufactured from oil. A transition towards renewable resources critically depends on new catalysts, for instance to convert small molecules (such as solar or biomass derived hydrogen, carbon monoxide, water and carbon dioxide) into more complex ones (such as oxygenates, containing oxygen atoms in their structure). Catalyst development now often depends on trial and error rather than rational design, as the heterogeneity of these composite systems hampers detailed understanding of the role of each of the components. I propose 3D model catalysts as a novel enabling tool to overcome this problem. Their well-defined nature allows unprecedented precision in the variation of structural parameters (morphology, spatial distribution) of the individual components, while at the same time they mimic real catalysts closely enough to allow testing under industrially relevant conditions. Using this approach I will address fundamental questions, such as:* What are the mechanisms (structural, electronic, chemical) by which non-metal promoters influence the functionality of copper-based catalysts?* Which nanoalloys can be formed, how does their composition influence the surface active sites and catalytic functionality under reaction conditions?* Which size and interface effects occur, and how can we use them to tune the activity and selectivity towards desired products?Our 3D model catalysts will be assembled from ordered mesoporous silica and carbon support materials and Cu-based promoted and bimetallic nanoparticles. The combination with high resolution characterization and testing under realistic conditions allows detailed insight into the role of the different components; critical for the rational design of novel catalysts for a future more sustainable production of chemicals and fuels from renewable resources.

**Keywords of the ERC project:** particle size effects, electrocatalysis, synthesis gas conversion, Cu nanoparticles, bimetallics, promoters

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** particle size effects, electrocatalysis, synthesis gas conversion, Cu nanoparticles, bimetallics, promoters
To understand and modulate biological processes, we need their spatiotemporal molecular models. In this project we propose to build these models by a holistic approach. The recent methodological and technical advances in fluorescence spectroscopy and microscopy as well as in multi-scale modelling of complex biochemical systems set the stage to tackle cross-fertilizing challenges in biophysics, biochemistry and cell biology. The applicant proposes to develop a novel integrative platform for a Molecular Fluorescence Microscope (MFM) to achieve ultimate resolution in space (sub-nanometer) and time (picoseconds) for characterizing structure and dynamics of proteins. MFM will combine Multi-parameter Fluorescence Detection with Computational Microscopy (molecular dynamics and coarse grained simulations) in a hybrid approach, first, to derive a complete molecular description of all fluorescence properties of the tailored dyes in proteins (objectives 1 and 2) and, second, to utilize this information in simulations to report on the protein properties (objective 3). In this hybrid approach high precision FRET measurements are the core experimental technique (hybridFRET). The MFM will allow us to tackle the central biophysical question of how intra- and intermolecular domain interactions modulate proteins' overall structure, dynamics, and thus ultimately function (objective 4). In this proposal we will apply MFM to two prototypic proteins of significant medical relevance. The combination with Multi-parameter Fluorescence Image Spectroscopy will exploit the ultimate resolution of the MFM for molecular protein imaging in live cells. To follow and ultimately understand biological processes, we need their spatiotemporal models of the integrative fluorescence spectroscopy platform. Until now, no holistic use of fluorescence spectroscopy for structural modelling of proteins has been reported.

Keywords of the ERC project: Resolving the structure and dynamics of biomolecular systems by fluorescence spectroscopy and imaging with multi-parameter detection and super-resolution (STED). In vitro and live cell studies combined with computer simulations (coarse grained and all-atom MD simulations). Integrative structural modeling of structural ensembles using also other biophysical techniques such as EPR, NMR and SAXS. Molecules of interest: multi-domain proteins and nucleic acids.

Keywords that characterize the scientific profile of the potential visiting researcher/s: Super-resolution fluorescence microscopy, integrative modeling, computer simulations, structural promiscuous biomolecular systems, expression of proteins with unnatural amino acids that can be used for labeling.
Biocompatible and Interactive Artificial Micro- and Nanoswimmers and Their Applications

Microswimmers, i.e., biological and artificial microscopic objects capable of self-propulsion, have been attracting a growing interest from the biological and physical communities. From the fundamental side, their study can shed light on the far-from-equilibrium physics underlying the adaptive and collective behavior of biological entities such as chemotactic bacteria and eukaryotic cells. From the more applied side, they provide tantalizing options to perform tasks not easily achievable with other available techniques, such as the targeted localization, pick-up and delivery of microscopic and nanoscopic cargoes, e.g., in drug delivery, bioremediation and chemical sensing.

However, there are still several open challenges that need to be tackled in order to achieve the full scientific and technological potential of microswimmers in real-life settings. The main challenges are: (1) to identify a biocompatible propulsion mechanism and energy supply capable of lasting for the whole particle life-cycle; (2) to understand their behavior in complex and crowded environments; (3) to learn how to engineer emergent behaviors; and (4) to scale down their dimensions towards the nanoscale.

This project aims at tackling these challenges by developing biocompatible microswimmers capable of elaborate behaviors, by engineering their performance when interacting with other particles and with a complex environment, and by developing working nanoswimmers.

To achieve these goals, we have laid out a roadmap that will lead us to push the frontiers of the current understanding of active matter both at the mesoscopic and at the nanoscopic scale, and will permit us to develop some technologically disruptive techniques, namely, targeted delivery of cargoes within complex environments, which is of interest for drug delivery and bioremediation, and efficient sorting of chiral nanoparticles, which is of interest for biomedical and pharmaceutical applications.

**Keywords of the ERC project:** microswimmers, experimental, active brownian motion, soft matter, stochastic phenomena, optical manipulation

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** statistical physics, microswimmers, active brownian motion, soft matter, stochastic phenomena, optical manipulation
A molecular interface science approach: Decoding single molecular reactions and interactions at dynamic solid/liquid interfaces

After decades of truly transformative advancements in single molecule (bio)physics and surface science, it is still no more than a vision to predict and control macroscopic phenomena such as adhesion or electrochemical reaction rates at solid/liquid interfaces based on well-characterized single molecular interactions. How exactly do inherently dynamic and simultaneous interactions of a countless number of interacting “crowded” molecules lead to a concerted outcome/property on a macroscopic scale?

Here, I propose a unique approach that will allow us to unravel the scaling of single molecule interactions towards macroscopic properties at adhesive and redox-active solid/liquid interfaces. Combining Atomic Force Microscopy (AFM) based single molecule force spectroscopy and macroscopic Surface Forces Apparatus (SFA) experiments CSI.interface will (1) derive rules for describing nonlinearities observed in complex, crowded (water and ions) and chemically diverse adhesive solid/liquid interfaces; (2) uniquely characterize all relevant kinetic parameters (interaction free energy and transition states) of electrochemical and adhesive reactions/interactions of single molecules at chemically defined surfaces as well as electrified single crystal facets and step edges. Complementary, (3) my team and I will build a novel molecular force apparatus in order to measure single-molecule steady-state dynamics of both redox cycles as well as binding unbinding cycles of specific interactions, and how these react to environmental triggers.

CSI.interface goes well beyond present applications of AFM and SFA and has the long-term potential to revolutionize our understanding of interfacial interaction under steady state, responsive and dynamic conditions. This work will pave the road for knowledge based designing of next-generation technologies in gluing, coating, bio-adhesion, materials design and much beyond.

**Keywords of the ERC project:** interface science, single molecule physics, force probe experiments, solid/liquid interfaces

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** solid/liquid interface simulations, ambient pressure XPS, single molecule physics, interface science, peptide materials
Rational Design of Photoreceptor Mutants with Desired Photochemical Properties

From a technological viewpoint photoreceptor proteins, the light-sensitive proteins involved in the sensing and response to light in a variety of organisms, represent biological light converters. Hence they are successfully utilized in a number of technological applications, e.g. the green-fluorescent protein used to visualize spatial and temporal information in cells. However, despite the ground-breaking nature of this utilization in life science and other disciplines, the attempts to design a photoreceptor for a particular application by protein mutation remains an open challenge. This is exactly the scope of my research proposal: the application of multi-scale modelling for the systematic design of biological photoreceptor mutants. With this target in mind I will study representatives of two prominent photoreceptor proteins subfamilies which are of towering interest to experimentalists: proteorhodopsins and cyanobacteriochromes. Computer models of these proteins will be constructed using accurate multi-scale modeling. Their excitation energies and other properties (e.g. excited-state reactivity and efficiency) will be calculated using multireference methods that were shown to have an accuracy of <3 kcal/mol. The insights gained from simulations of the wild-type proteins will provide the basis for proposing mutations with altered photochemical properties: in essence to predict absorption and emission spectra, excited-state lifetime and quantum yields. This research requires interactions across the disciplines, as the best candidates will be synthesized and characterized experimentally by collaborators. The outcome of these experiments will provide feedback to improve both the properties of the mutants and the simulation methodology. Ultimately this high-risk/high gain project should derive a comprehensive understanding that would result in novel biotechnological applications, e.g. optogenetic tools, fluorescent probes and biosensors.

Keywords of the ERC project: Photoreceptor, Rhodopsin, Retinal, Cyanobacteriochrome, Computational Photochemistry

Keywords that characterize the scientific profile of the potential visiting researcher/s: Spectroscopy, Photoreceptor, Rhodopsin, Phytochrome, Retinal, Mutant, Extremophiles, Photolyase, Cryptochrome, UV, Bacteria
Ultrafast spectroscopy is a powerful tool able to disclose the atomistic real-time motion picture of the basic chemical events behind technology and Life, such as catalytic reactions or photosynthetic light harvesting. Nowadays, by cleverly harnessing the interaction of the studied molecules with plasmons (collective electron excitations supported, e.g., by metal nanoparticles) it is becoming possible to focus these investigations on specific nanoscopic regions, such as a portion of a catalytic surface or of a photosynthetic membrane. This coupling can also produce new quantum effects such as molecule-plasmon hybrid excitations. On the other hand, it makes the real-time molecular evolution and its perturbation by light more complex, and thus calls for new theoretical treatments. The available ones are unable to tackle this complexity, because they consist of phenomenological models focused on field enhancements or on generic features of the various plasmon-molecule coupling regimes. The goal of TAME-Plasmons is to develop a theoretical chemistry approach to directly simulate the real time evolution of molecules interacting with plasmons and light. Our approach lifts the current theoretical limitations by coupling a real-time quantum chemical description of the molecules with a time-dependent electromagnetic description of plasmons, rooted in our previous work on steady-state molecular plasmonics. We will implement this approach in an open-source software, accessible also to non-specialists. We will address current open issues such as the controversial nature of plasmon-aided frequency up-conversion by noble gases and the interpretation of sub-molecularly resolved photoemission induced by scanning tunneling microscopy. We will also anticipate questions that may arise along with progress in the field, for example how to engineer energy transfer paths in photosynthetic light harvesting proteins by exploiting the coupling to plasmons.

Keywords of the ERC project: molecular plasmonics, quantum chemistry, theory of ultrafast optical spectroscopy

Keywords that characterize the scientific profile of the potential visiting researcher/s: quantum chemistry, computational chemistry or physics, classical electromagnetic theory
Coherent multidimensional spectroscopy of controlled isolated systems

Fundamental quantum mechanical processes determine the properties of matter and their functionality. In order to understand complex processes such as light harvesting in photosynthesis and photovoltaics, a detailed knowledge of coherent effects in excitation and charge transfer processes and related dynamics is required. To a large extent, the complexity of the systems induces too many interactions and perturbations of the processes to isolate and understand individual mechanisms. Advanced experimental methods, capable of detecting quantum coherences, so far are not applicable to quantum state controlled molecular complexes isolated from the perturbing environment, due to the low density of such targets. In this project we will for the first time employ coherent femtosecond multidimensional spectroscopy to dilute isolated molecular complexes. For a specific heterogeneous synthesis we will use aggregation in superfluid helium at millikelvin temperatures. In order to reach the needed sensitivity we will setup a novel phase modulation technique including lock-in demodulation in combination with mass-resolved ionization and photoelectron detection. Advanced mathematical methods will furthermore be developed and applied, boosting efficient collection of multidimensional datasets. We will be able to (a) identify processes and coherent dynamics of excitation and charge transfer in fundamental heterogeneous complexes, in particular van der Waals bound donor acceptor complexes (b) elucidate coherence and dissipation effects in contact with tailored external baths, (c) investigate microsolvation, i.e. measure the evolution of dynamic properties as a function of attached solvent molecules, (d) determine collective effects like autoionization in dilute atomic gases or exciton annihilation in semiconductor systems, (e) implement compressed sensing in multidimensional data acquisition, (f) implement largely parallelized phase-cycling into real-time data acquisition.

Keywords of the ERC project: 2-dimensional coherent spectroscopy

Keywords that characterize the scientific profile of the potential visiting researcher/s: experimental femtosecond spectroscopy, molecular and cluster beams
Dynamic Penetrating Peptide Adaptamers

The aim of this proposal is to identify, at the molecular level, the minimal topological and structural motifs that govern the membrane translocation of short peptides. A covalent reversible bond strategy will be developed for the synthesis of self-adaptive penetrating peptides (adaptamers) for targeted delivery. It is known that the recently developed therapeutic technologies (i.e. gene therapy, chemotherapy, hyperthermia, etc.) cannot reach their expected potential due to limitations in the current delivery strategies, which hinder the efficient targeting of the appropriate tissues, cells and organelles. Despite the enormous therapeutic potential of short penetrating peptides, these molecules suffer from drawbacks such as toxicity, instability to protease digestion and lack of specificity. Dynamic covalent chemistry has significant synthetic advantages. In the proposed research, peptide scaffolds with clickable reversible groups (e.g. hydrazide) will be conjugated with collections of aldehydes to afford self-adaptive biomimetic transporters, whose secondary structure and penetrating properties will be systematically characterized by biophysical, cell-biology and pattern recognition techniques. The versatility of dynamic supramolecular “peptide adaptamers” with precisely positioned protein ligands will be explored for multivalent specific recognition, protein transport, cell targeting of drugs and probes and membrane epitoping. Additionally, we propose to synthesise dynamic and environmentally sensitive fluorescent probes for biocompatible membrane labelling and uptake signalling. The resulting discoveries of this research will allow the formulation of novel transfecting reagents for gene therapy, selective platforms for drug-delivery and the development of dynamic fluorescent membrane probes. The potential results of this proposal will shake the fields of drug-delivery and non-viral gene transfection and will resolve the limitations of the current approaches.

**Keywords of the ERC project:** Supramolecular chemistry, Organic chemistry, Peptide Chemistry, Cell Transport, Membrane Chemistry, Fluorescent Probes, Imaging,

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** Supramolecular chemistry, Organic chemistry, Peptide Chemistry, Cell Transport, Membrane Chemistry, Fluorescent Probes, Imaging,
Entangled pincer ligand architectures and their application in the transition-metal-mediated activation of alkanes

The selective transformation of alkanes is an area of contemporary importance with wide-ranging implications for organic synthesis and the effective use of petroleum resources. While homogeneous transition metal catalysis is a potentially powerful means for achieving this objective, the fundamental organometallic chemistry of alkane activation reactions has proven to be exceedingly difficult to investigate due to the weakly interacting nature of alkanes. To address this knowledge gap and provide the foundation for future advancement of the field, ENTANGLED-TM-ALKANE outlines a systematic approach for the study of pivotal sigma–alkane complex intermediates; nominally transient and extremely reactive metal–alkane adducts formed through coordination of an intact C–H bond to the metal centre. Inspired from supramolecular chemistry, the approach involves the innovative use of systems containing alkane substrates held in close proximity to reactive metal centres through mechanical entanglement within supporting tridentate macrocyclic ‘pincer’ ligands (i.e. alkane based [2]rotaxanes and [2]catenanes). Through the interwoven topology of these systems, problematic dissociation reactions of sigma–alkane complexes will be circumvented, facilitating isolation and ultimately enabling their structure and reaction chemistry to be probed in much greater detail than has been previously possible. The project objectives are to: (a) develop and use new synthetic (supramolecular) methodologies for the preparation of these mechanically interlocked metal–alkane assemblies; (b) systematically investigate the organometallic chemistry of the metal centre and its interaction with the entangled alkane; and through variation of the macromolecules’ components (macrocycle donors and geometry, alkane, metal), (c) compile a definitive and unprecedented body of qualitative and quantitative structure-activity relationships for the activation alkanes using transition metals.

Keywords of the ERC project: Alkane, C-H bond activation, late transition metal, organometallic chemistry, supramolecular chemistry

Keywords that characterize the scientific profile of the potential visiting researcher/s: Alkane, C-H bond activation, late transition metal, organometallic chemistry, supramolecular chemistry
Ice-binding proteins: from antifreeze mechanism to resistant soft materials

Crystallization of water into ice is lethal to most organisms and detrimental to many soft materials. Freeze-tolerant fish living in polar seas evolved to tackle this problem with an unusual coping strategy. They produce ‘antifreeze’ proteins that block the growth of nascent ice crystals within a narrow temperature range known as the ‘thermal hysteresis gap’ enabling survival under extreme conditions. Encoding this functionality into synthetic polymers would open up new avenues in biomedicine, agrifood and materials science for e.g. cryopreservation, crop hardiness, ice-templating, dispersion stability, and advanced coatings. Progress requires a profound understanding of the mechanism of non-colligative freezing point depression at the molecular level and allows for efficient strategies for the design and preparation of powerful macromolecular antifreezes.

I propose to unravel how antifreeze proteins work and to build upon these insights to explore effective routes towards ice-binding polymers aiming to make sensitive soft materials freeze-resistant. Within this challenge we first focus on single-molecule experiments to visualize bound proteins and study the strength of the non-covalent interaction with ice. We will study if and when adsorption on ‘foreign’ interfaces and solution assembly impact activity. These fundamental insights will guide our research towards synthetic antifreeze agents with superior functionality to achieve record supercooling in complex environments. This knowledge-based design of polymers with high affinity for crystalline interfaces holds great promise for many areas of science and technology in which crystallization plays a decisive role.

Keywords of the ERC project: antifreeze; biophysics; ice; microfluidics; single molecule localization microscopy; single molecule force spectroscopy

Keywords that characterize the scientific profile of the potential visiting researcher/s: biophysicist; soft matter physicist
Selective Carbon-Carbon Bond Activation: A Wellspring of Untapped Reactivity

The creation of new molecular entities and subsequent exploitation of their properties is central to a broad spectrum of research disciplines from medicine to materials. Most—if not all—of the efforts of organic chemists were directed to the development of creative strategies to build carbon-carbon and carbon-heteroatom bonds in a predictable and efficient manner. But is the creation of new bonds the only approach that organic chemistry should follow? Could we design the synthesis of challenging molecular skeleton no more through the construction of carbon-carbon bonds but rather through selective cleavage of carbon-carbon bonds (C-C bond activation)? The goal of this work is to develop powerful synthetic approaches for the selective C-C bond activation and demonstrate that it has the potential to be a general principle in organic synthesis for the regio-, diastereo- and even enantiomerically enriched preparation of adducts despite that C-C single bonds belong among the least reactive functional groups in chemistry. The realization of this synthetic potential requires the ability to functionalize selectively one C-C bond in compounds containing many such bonds and an array of functional groups. This site selective C-C bond activation is one of the greatest challenges that must be met to be used widely in complex molecular synthesis. To emphasize the practicality of C-C bond activation, we will prepare in a single-pot operation challenging molecular framework possessing various stereogenic centers from very simple starting materials through selective C-C bond activation. Ideally, alkenes will be in-situ transformed into alkanes that will subsequently undergo the C-C activation even in the presence of functional group. This work will lead to ground-breaking advances when non-strained cycloalkanes (cyclopentane, cyclohexane) will undergo this smooth C-C bond activation with friendly and non toxic organometallic species.

Keywords of the ERC project: C-C bond cleavage, organic synthesis, stereoselectivity,

Keywords that characterize the scientific profile of the potential visiting researcher/s: Synthetic organic chemist
Exploiting Synergistic Properties of Mesoionic Carbone Complexes: Teaching Rusty Metals Challenging Catalysis

The non-innocence of specific ligands in transition metal complexes is well-documented. For example, mesoionic carbenes engage in bond activation processes via reversible hydrogen capture. Such cooperativity between the metal center and the ligand flattens the potential energy surface of a catalytic reaction and hence rises the competence of the catalyst, thus entailing higher turnover numbers as well as the conversion of more challenging substrates. Likewise, such cooperativity is expected to enhance the catalytic activity of metal centers that are typically not considered to be catalytically very active, such as the ‘rusty’ first row transition metals (Mn, Fe, Ni). Surprisingly, however, this concept has largely been overlooked when designing catalytic transformations based on these earth-abundant and low-cost transition metals. This project will exploit the synergistic potential of mesoionic carbenes as synthetically highly versatile and actively supporting ligands to access a new generation of sustainable high-performance catalysts based on Me, Fe, and Ni for challenging redox transformations such as dehydrogenative oxidations. Specifically, 1,2,3-triazolylidenes, which support ligand-metal cooperativity through their mesoionic character, will be utilized for (transient) storage/release of protons and electrons. Apart from enabling challenging transformations — with obvious impact on synthetic methodology, energy conversion, and molecular electronics — this project will break into new grounds in catalyst design that will be widely applicable as a new paradigm. Furthermore, this project will capitalize on the unique synthetic versatility of triazolylidine precursors and the opportunity to combine different functional entities such as carbohydrates, surfactants, or dyes with an organometallic entity, thus providing a straightforward approach to new classes of multifunctional materials for application in therapeutics and diagnostics, or as smart surfaces.

Keywords of the ERC project: homogeneous catalysis; base metals; n-heterocyclic carbene; iron; nickel

Keywords that characterize the scientific profile of the potential visiting researcher/s: functional group transformation; small molecule activation; bond activation; computational chemistry; EPR spectroscopy
Colloidal inorganic nanocrystals (NCs) are among the most investigated nanomaterials in Nanoscience due to their high versatility. Research on NCs went through much advancement lately, especially on synthesis, assembly and on the study of their transformations, most notably via cation exchange (all fields in which the PI has contributed already). However, the integration of NCs with fabrication tools that employ conditions such as irradiation, etching and annealing is at a very early stage since we do not have a systematic knowledge of what transformations are triggered in the NCs under those conditions. Also, an issue related to the incorporation of NCs in materials/devices is whether, over time, the NCs will remain as they are, or they will transform into other structures. Plus, these transformations in NCs are poorly studied as they require fast recording techniques. This proposal will embark on an ambitious investigation of post-synthetic transformations in solution-grown NCs: by advancing the understanding of various aspects of chemical, structural and surface transformation of NCs, we will uncover new fabrication techniques that will employ such nanostructures as the key ingredients. This in turn will have a strong impact in opto-electronics, as several electronic components entirely made of NCs will be delivered. Four objectives are targeted: i) developing radically new sets of experimental tools for the investigation of chemical transformations in NCs, above all the ability to monitor in real time these transformations; ii) developing solution-grown nanostructures able to undergo programmed transformations under a defined stimulus; iii) understanding the role of irradiation on the fate of surface ligands and on cation exchange reactions in NCs; iv) combining chemical, structural and surface transformations towards NC-based opto-electronics. The success of the proposal hinges on the proven capabilities of the PI, with ample support from the host Institution.

**Keywords of the ERC project:** nanocrystals, nanoparticles, transformations, electron microscopy, optoelectronics, synthesis

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** synthesis, materials science, device fabrication, optoelectronics
Imagine a world, in which countless embedded microelectronic components continuously monitor our health and allow us to seamlessly interact with our digital environment. One particularly promising platform for the realisation of this concept is based on wearable electronic textiles. In order for this technology to become truly pervasive, a myriad of devices will have to operate autonomously over an extended period of time without the need for additional maintenance, repair or battery replacement. The goal of this research programme is to realise textile-based thermoelectric generators that without additional cost can power built-in electronics by harvesting one of the most ubiquitous energy sources available to us: our body heat. Current thermoelectric technologies rely on toxic inorganic materials that are both expensive to produce and fragile by design, which renders them unsuitable especially for wearable applications. Instead, in this programme we will use polymer semiconductors and nanocomposites. Initially, we will focus on the preparation of materials with a thermoelectric performance significantly beyond the state-of-the-art. Then, we will exploit the ease of shaping polymers into light-weight and flexible articles such as fibres, yarns and fabrics. We will explore both, traditional weaving methods as well as emerging 3D-printing techniques, in order to realise low-cost thermoelectric textiles. Finally, within the scope of this programme we will demonstrate the ability of prototype thermoelectric textiles to harvest a small fraction of the wearer’s body heat under realistic conditions. We will achieve this through integration into clothing to power off-the-shelf sensors for health care and security applications. Eventually, it can be anticipated that the here interrogated thermoelectric design paradigms will be of significant benefit to the European textile and health care sector as well as society in general.

Keywords of the ERC project: organic thermoelectrics, 3D printing, textile, plastic, polymer

Keywords that characterize the scientific profile of the potential visiting researcher/s: thermoelectrics, electrical engineering, graphene, carbon nanotube, polymer, 3D printing, fiber
Chemotherapy is, after surgery, the second most efficient therapy against cancer. However, it has many side effects for cancer patients because anticancer drugs kill cancer cells but also healthy ones. My project aims at synthesizing new metal-containing compounds that 1) are poorly toxic in the dark; 2) can be attached via a light-sensitive bond to liposomes that will carry them into cancer cells; and 3) detach from their carriers and become toxic upon light irradiation, thus killing cancer cells. These new compounds contain ruthenium, a metal combining photochemical and anticancer properties. I will replace the weakly bound chloride ligands of known cytotoxic ruthenium compounds by strongly bound sulfur ligands. By doing so, the DNA- and protein-binding ability of the ruthenium compounds will be lowered, which will lower their toxicity in the dark. Thioether-lipid conjugates will be used to attach the ruthenium prodrugs to liposomes carriers that are well taken up by cancer cells. Techniques to irradiate tumors in vivo are nowadays available in the clinics. By shining light onto the ruthenium-enriched cancer cells photochemical cleavage of the Ru-S bond will take place, thus detaching the metal complex from its carrier and allowing it for binding to biological molecules. Thus, the ruthenium prodrug will be transformed inside cancer cells into a highly toxic molecule that will kill the cells. I will study mononuclear compounds and molecules containing several ruthenium centres; visible light activation and near infrared light activation. The final aim is to obtain ruthenium-functionalized liposomes that are poorly toxic in the dark, preferentially go into cancer cells, and become toxic at the place of irradiation, using light that penetrates well into biological tissues. Because of this unique combination of properties my new light-activatable ruthenium prodrugs will ultimately lead to selective anticancer treatment showing low side effects for cancer patients.

**Light-activatable ruthenium-based anticancer prodrugs**

**Keywords of the ERC project:** phototherapy, photodynamic, metallodrugs, bioinorganic chemistry, photochemistry, hypoxic tumours, PACT, chemotherapy

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** tumour spheroids, cancer biology, hypoxic tumours, tumour targeting
iPes project aims to provide adequate support to Dr. David Mecerreyes (DM) who is at the stage of consolidating an independent research team. During his scientific career, DM has demonstrated creative thinking and excellent capacity to carry out research and going beyond the state of the art. His meritorious record of research, scientific publications (128 ISI articles, h index = 33), project conception, private sector experience, networking ability (participated in 10 European collaborative projects) and capacity for supervising and coordinating a research team are presented in detail in the initial part of the proposal. He recently moved from the private sector to create a new research group at the University of the Basque Country. He is now in an excellent academic position and research environment to commit and be devoted to an ERC frontier research project. DM’s proposal passed to the second stage in the ERC starting grant call of last year. This year the research project has been re-built taking into account his group directions and the detected weak points of last year’s proposal. This is his last opportunity for participating to the ERC starting-grant call. iPes proposes an innovative research programme at the forefront of polymer chemistry. The proposal goes in depth into the topic of energetic polymers. iPes activities will fully develop the field of polymers for energy storage by using an innovative macromolecular engineering approach generating the ground for future innovations. The main S&T goal is to obtain new polymeric materials, to get an insight into their unique electronic properties, to model the new energetic polymers and to investigate their application in innovative battery prototypes. These technologies are currently dominated by inorganic electrode materials. iPes aims at bringing polymer chemistry to a next level and developing basic knowledge about innovative polymeric materials which may open up new opportunities for Energy Storage.

Keywords of the ERC project: polymers, batteries, ionic liquids

Keywords that characterize the scientific profile of the potential visiting researcher/s: polymer scientist, materials scientist, electrochemist, battery technology
Towards a Self-Amplifying Carbon-Fixing Anabolic Cycle

How can simple molecules self-organize into a growing synthetic reaction network like biochemical metabolism? This proposal takes a novel synthesis-driven approach to the question by mimicking a central self-amplifying CO2-fixing biochemical reaction cycle known as the reductive tricarboxylic acid cycle. The intermediates of this cycle are the synthetic precursors to all major classes of biomolecules and are built from CO2, an anhydride and electrons from simple reducing agents. Based on the nature of the reactions in the cycle and the specific structural features of the intermediates that comprise it, we propose that the entire cycle may be enabled in a single reaction vessel with a surprisingly small number of simple, mutually compatible catalysts from the recent synthetic organic literature. However, since one of the required reactions does not yet have an efficient synthetic equivalent in the literature and since those that do have not yet been carried out sequentially in a single reaction vessel, we will first independently develop the new reaction and sequences before attempting to combine them into the entire cycle. The new reaction and sequences will be useful green synthetic methods in their own right. Most significantly, this endeavour could provide the first experimental evidence of an exciting new alternative model for early biochemical evolution that finally illuminates the origins and necessity of biochemistry’s core reactions.

Keywords of the ERC project: prebiotic chemistry; metabolism; reaction networks

Keywords that characterize the scientific profile of the potential visiting researcher/s: analytical chemistry; reaction networks; geology
Insect-inspired capillary nanostamping

Aim of the proposed project is a) development and establishment of insect-inspired capillary nanostamping (IICN) as next-generation contact nanolithography, b) replacing state-of-the-art lithographic and synthesis protocols requiring use of sacrificial templates or time-consuming self-assembly steps by IICN and c) significant IICN-driven acceleration and upscaling of the production of extended nanostructured systems. To meet these aims, IICN stamp design will be inspired by insect feet depositing small secretion droplets through arrays of hairy contact elements on counterpart surfaces. Monolithic IICN stamps extending cm² will consist of spongy ink-filled substrates connected to extended arrays of spongy nanoscale dispensing elements with diameters in the 100 nm range (density up to ~130 dispensing elements per square micron). Ink supplied through the spongy pore systems forms capillary bridges between each dispensing element and counterpart surfaces, thus enabling massively parallel capillary bridge-guided nanorod synthesis. Capillary bridge rupture during stamp retraction leads to massively parallel lithographic deposition of ink nanodroplet arrays (target nanodroplet volume: a few 10 zeptolitres). IICN model applications include production of a) ultrathin nanoporous membranes for separation; b) ordered silicon nanostructures by IICN-supported metal-assisted etching; c) nearly-ergodic arrays of encapsulated liquid nanocontainers for massively parallel ensemble nanochemistry or ensemble tracing of single molecules; d) nearly-ergodic biochips for massively parallel analyte detection with single-molecule resolution. As example for substitution of time-consuming self-assembly in nanomaterial synthesis by IICN, IICN-accelerated production of ordered nanoporous alumina will be studied. To pave the way for upscaling and potential commercialization of IICN, high-throughput IICN devices for automated operation in batch and continuous roller modes will be constructed.

Keywords of the ERC project: Capillary nanostamping, nanostructures, lithography, nanodroplet arrays, nanoporous materials

Keywords that characterize the scientific profile of the potential visiting researcher/s:
Tubular Supramolecular Polymers: A new class of therapeutic polymers

This research programme will establish a new class of materials and develop them into functional devices for biomedical applications. We will design tubular supramolecular polymers, supramolecular polymer brushes (SPBs), based on the self-assembly of cyclic peptide – polymer conjugates. The synergy between the cyclic peptide, which directs the formation of the SPBs and the polymer conjugate, which provides functionality, will open the route to a wealth of new functional structures. We will build on our initial work and expand our research to generate new synthetic routes for the ligation of polymers to peptides, develop new protocols for the characterisation of the materials, and establish the mechanism of supramolecular polymerisation. This research programme will open new horizons in the fundamental understanding and production of supramolecular polymers. In particular, beyond the generation of new materials, the functionality of these systems may allow the development of supramolecular living polymers, a long-standing goal in polymer chemistry that is still elusive. The functionality and versatility of the SPBs obtained in this work open the route to a wealth of applications, and we will focus on one specific target: the fabrication of drug delivery vectors. We will exploit the unique combination of features presented by this new class of polymer therapeutics, such as multiple attachment points for one or more drug(s) / targeting ligands / markers, the ability to self-disassemble into smaller and easy-to-excrete components, and an elongated shape that enables diffusion and interaction with cells more efficiently than traditional globular delivery systems. We will study the pharmacology properties of the SPBs, including their stability, toxicity, mode of cell penetration and ability to deliver a single or a combination of bioactive agent(s) (in the case of concerted mechanisms).

Keywords of the ERC project: supramolecular, nano materials, nanotechnology, materials

Keywords that characterize the scientific profile of the potential visiting researcher/s: supramolecular, nano materials, nanotechnology, materials
A preparative approach to geometric effects in innovative solar cell types based on a nanocylindrical structure

The ERC Consolidator Grant project SOLACYLIN aims at providing experimental insight into the function of 'third-generation' photovoltaic systems by generating materials stacks structured in a well-defined, accurately tunable, nanocylindrical geometry.

To this goal, we will develop and exploit advanced preparative methods based on two fundamental ingredients: (a) ordered 'anodic' porous oxides and (b) atomic layer deposition (ALD). The former solids will be generated as templates providing ordered arrays of straight, cylindrical pores, the diameter and length of which can be varied between 20 nm and 300 nm and between 0.5 microns and 50 microns, respectively. The latter method will be used to coat the inner pore walls with one or several layers of the photovoltaic stack, each with a thickness set to values chosen between 1 nm and 30 nm.

We will invent and characterize novel surface reaction schemes for the deposition in ALD mode (from the gas phase and from solutions) of functional materials (doped semiconductors and intrinsic light absorbers) with tailored chemical and physical properties. We will investigate the experimental conditions in which they can be combined in a way that optimizes the quality of their interfaces.

Finally, we will quantify the electrical and photovoltaic performance of p-i-n junctions prepared with our methods. We will have the unique capability of describing in a systematic, accurate manner how the experimental photovoltaic parameters depend on the individual thicknesses of the individual layers and on the length of the cylinders. This direct experimental handle on the amount of light absorbed, on the one hand, and the charge carrier transport distances to the electrical contacts, on the other hand, will be correlated with the relevant material parameters (absorption coefficients, carrier mobilities). This information will unveil the phenomena limiting the efficiency of each type of solar cell, and suggest avenues to remedy them.

Keywords of the ERC project: photovoltaics, atomic layer deposition, 3D nanomaterials, porous materials

Keywords that characterize the scientific profile of the potential visiting researcher/s: photovoltaics, semiconductors
A Chemical Approach to Molecular Spin Qubits: Decoherence and Organisation of Rare Earth Single Ion Magnets

Coordination Chemistry and Molecular Magnetism are in an ideal position for the rational design of Single-Molecule Magnets which can be used as molecular spin qubits, the irreducible components of any quantum technology. Indeed, a major advantage of molecular spin qubits over other candidates stems from the power of Chemistry for a tailored and inexpensive synthesis of systems for their experimental study. In particular, the so-called Lanthanoid-based Single-Ion Magnets, which are currently the hottest topic in Molecular Magnetism, have the potential to be chemically designed, tuning both their single-molecule properties and their crystalline environment. This will allow the independent study of the different quantum processes that cause the loss of quantum information, collectively known as decoherence. The study of quantum decoherence processes in the solid state is necessary both to lay the foundations for next-generation quantum technologies and to answer some fundamental questions. The goals of this project are:

1. To unravel the mechanistic details of decoherence in molecular spin qubits based on mononuclear lanthanoid complexes. This study will establish criteria for the rational design of single spin qubits.
2. To extend this study to the coupling between two or more spin qubits. This will allow us to explore the use of polynuclear lanthanoid complexes to achieve quantum gates or simple algorithms.
3. To extrapolate to infinite systems formed by the complex organization of spin qubits. This exploratory goal will permit us to move beyond zero-dimensional systems, thus facilitating the advance towards complex quantum functions.

Keywords of the ERC project: Molecular Spin Qubits, Quantum Decoherence, Pulsed EPR, http://www.uv.es/gaita/decresim.html

Keywords that characterize the scientific profile of the potential visiting researcher/s: Solid-state physicist, Theoretical physicist, Open quantum systems
Unconventional Bifunctional Catalysts

The development of sustainable chemical processes is one of the most important features in modern chemistry. It has become a key research area worldwide providing solutions to important societal demands by optimizing the use of natural resources and minimizing waste and environmental impact. Among the relevant methods for achieving this goal, catalysis represents a key and central approach. Both Organocatalysis and Metal Catalysis have emerged as solutions to the problems in this context. In this field, the progress of a novel bifunctional organocatalyst that could increase the number of different activations, and therefore the synthesis of valuable enantio-enriched molecules, would be highly desirable. Especially important, but still unknown, are the bifunctional-catalysts based on a Neutral Coordinate Organocatalyst and Photo-Organocatalysts. This proposal aims to develop two new unconventional approaches for the synthesis of bifunctional organocatalysts.

The first one is based on the development of new Bifunctional Neutral Coordinate Organocatalyst and their application to the synthesis of biologically relevant compounds. I propose to use these bifunctional catalysts to promote the dual activation of silyl reagents and suitable electrophiles. This approach constitutes an unconventional way to synthesize asymmetric molecules and has no precedent in the literature.

The second section of this proposal explores the photo-activation-bifunctional organocatalyst. I propose the design and application of new metal-free Bifunctional Photo-Organocatalysts which are able to chemically and photo-activate the substrate simultaneously in an asymmetric manner.

This project has the potential to change the general view of asymmetric Neutral Coordinate Organocatalyst and Photo-catalysis as we know it today. These unconventional bifunctional would be incorporated into the privileged catalyst library for its applications in new asymmetric transformations.

Keywords of the ERC project: Organocatalysis, Photocatalysis

Keywords that characterize the scientific profile of the potential visiting researcher/s: photocatalysis, catalytic-materials
Towards the design of Personalised Polymer-based Combination Nanomedicines for Advanced Stage Breast Cancer Patients

Research on anticancer therapies has provided little progress towards improved survival rates for patients with metastatic disease. The intrinsic advantages of polymer conjugates can be optimised to rationally design targeted combination therapies, concept I pioneered that allows enhanced therapeutic efficiency. Early clinical trials involving conjugates showed activity in chemotherapy refractory patients and reduced drug-related toxicity. However, there is a growing concern on patient variability regarding tumor patho-physiology that underlie successful therapeutic outcome. Specific biomarkers are required to select those patients most likely to show good clinical response to these therapies. The objective of MyNano is to engineer polymer-based combination therapies designed to treat metastatic breast cancer in a patient personalised manner. Therefore, novel multicomponent polymer conjugates with precise control over size, shape, solution conformation, multifunctionality and bioresponsiveness will be obtained while in parallel their structure activity relationships to underlying proposed mechanisms of action in clinically relevant models will be studied. Polyglutamates obtained by controlled polymerisation and self-assembly strategies will be the carriers. Primary breast cancer patient tissue will be used to generate cell and in vivo models representing different clinical molecular subtypes. MyNano will also investigate new combination strategies using current treatments together with inhibitors of tumor-derived exosome release pathways, phenomenon related to metastasis and resistance mechanisms. The aim is to provide a novel methodological approach that would allow by reiterative design to optimise the design of the next generation nanoconjugates for the treatment of specific metastatic cancer clinical subtypes. MyNano will be a breakthrough as it introduces a paradigm shift in the strategy to design nanomedicines in areas of unmet clinical need.

**Keywords of the ERC project:** Biological chemistry; New materials; Intelligent materials; Polymer Chemistry; Polymer Therapeutics; Nanomedicine; Targeted drug delivery; Advanced Breast Cancer; Exosomes; Metastasis

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** Exosomes; Patient Derived xenografts; organoids; Metastasis; Biomarkers; Predictors
Artificial-Intelligence Driven Discovery and Synthesis of Polyoxometalate Clusters

We outline a 5 year programme that introduces a new platform for the preparation, understanding, and exploitation of precisely defined nano-molecules / materials based upon the assembly of molecular metal oxide precursors (polyoxometalates) under non-equilibrium conditions with well-defined physical properties using automated intelligent feedback. We will elucidate the mechanism of assembly of these gigantic molecules and devise a set of rules similar to the magic numbers found in gold nanoclusters, using these to break the 10 nm size barrier for a single molecule. Targeted properties include photochemical and electrochemical sensors, bistable molecules, doped traditional oxides with polyoxometalates, and new catalysts including water oxidation via a Universal Building Block (UBB) approach that links properties of the building blocks with emergent properties of the resulting clusters and materials for the first time. The new approach includes the conversion of batch to flow synthesis not only for automation, but to understand fundamental mechanistic aspects, and to use artificial intelligence algorithms to help move through the myriad of possible combinations (without needing to synthesise every possible molecule). The SMART-POM approach is therefore not merely automation of one-pot chemistry, but an entirely new paradigm building on our recent developments and will allow us to move through a vast combinatorial space effectively only locating areas of novelty via feedback control. This feedback will be used to discover, design, and develop complex, adaptive and functional metal oxide-based materials based upon sensory feedback from the physical properties measurements. Thus SMART-POM will open up a whole new synthetic space, give mechanistic understanding, and allow the discovery of molecules with potential real-world applications. Finally, we will aim to extend the SMART-POM paradigm to other areas of chemistry which will benefit from the search for novelty.

Keywords of the ERC project: inorganic chemistry; artificial intelligence; self-assembly; self-organisation; deep learning; big data; supramolecular echemistry

Keywords that characterize the scientific profile of the potential visiting researcher/s: inorganic chemist; computer scientist; robotics; computer vision; synthetic chemistry; interdisciplinary;
Efficient, Flexible Synthesis of Molecules with Tailored Shapes: from Photo-switchable Helices to anti-Cancer Compounds

The creation of new molecular entities and subsequent exploitation of their properties is central to a broad spectrum of research disciplines from medicine to materials but progress has been limited by the difficulties associated with chemical synthesis. We are now proposing a fundamentally new strategy, which has the potential to revolutionise how we conduct complex organic synthesis. The basic C–C bond-forming step involves the reaction of a lithiated carbamate with a boronic ester to give a homologated boronic ester with complete stereocontrol. Furthermore, the reaction shows >98% efficiency in most cases and can be conducted iteratively and in one pot (up to 9 iterations has been demonstrated with full stereocontrol). We will now extend this methodology to more functionalised carbamates as this will enable the rapid synthesis of polypropionates, which are amongst the most important classes of biologically active molecules. The robust methodology is now ripe for transfer to the solid phase as this will enable the preparation of libraries of these molecules. Through applying our assembly-line-synthesis methodology to complex molecules with diverse structures, we will demonstrate its scope, robustness, and full potential. The methodology enables stereochemistry to be ‘dialed in’ to a carbon chain, which in turn controls the conformation and we will exploit this feature in the shape-selective synthesis of molecules. We will explore how the sense of helical chirality of these molecules can be switched (M to P) just with light. We will target helical molecules with specific groups at specific places for optimum binding to disrupt protein–protein interactions involved in cancer. Finally, our methodology provides ready access to a family of building blocks that represent common repeat units found in polyketides. By combining these building blocks iteratively using lithiation-borylation, we should be able to rapidly and reliably prepare complex natural products.

Keywords of the ERC project: organic synthesis, boron, stereoselective, coupling, catalysis, natural products,

Keywords that characterize the scientific profile of the potential visiting researcher/s: organic synthesis, catalysis, natural products
MONACAT proposes a novel approach to address the challenge of intermittent energy storage. Specifically, the purpose is to conceive and synthesize novel complex nano-objects displaying both physical and chemical properties that enable catalytic transformations with a fast and optimum energy conversion. It follows over 20 years of research on "organometallic nanoparticles", an approach of nanoparticles (NPs) synthesis where the first goal is to control the surface of the particles as in molecular organometallic species. Two families of NPs will be studied: 1) magnetic NPs that can be heated by excitation with an alternating magnetic field and 2) plasmonic NPs that absorb visible light and transform it into heat. In all cases, deposition of additional materials as islands or thin layers will improve the NPs catalytic activity. Iron carbides NPs have recently been shown to heat efficiently upon magnetic excitation and to catalyse CO hydrogenation into hydrocarbons. In order to transform this observation into a viable process, MONACAT will address the following challenges: determination and control of surface temperature using fluorophores or quantum dots, optimization of heating capacity (size, anisotropy of the material, crystallinity, phases: FeCo, FeNi, chemical order), optimization of catalytic properties (islands vs core-shell structures; Ru, Ni for methane, Cu/Zn for methanol), stability and optimization of energy efficiency. A similar approach will be used for direct light conversion using as first proofs of concept Au or Ag NPs coated with Ru. Catalytic tests will be performed on two heterogeneous reactions after deposition of the NPs onto a support: CO2 hydrogenation into methane and methanol synthesis. In addition, the potential of catalysis making use of self-heated and magnetically recoverable NPs will be studied in solution (reduction of arenes or oxygenated functions, hydrogenation and hydrogenolysis of biomass platform molecules, Fischer-Tropsch).

Keywords of the ERC project: nanoparticles, magnetism, catalysis, hyperthermia, carbon oxides hydrogenation

Keywords that characterize the scientific profile of the potential visiting researcher/s: catalysis, magnetism, Fischer-Tropsch
Taming non convexity?

In many important areas and applications of science one has to solve non convex optimization problems and ideally and ultimately one would like to find the global optimum. However in most cases one is faced with NP-hard problems and therefore in practice one has been often satisfied with only a local optimum obtained with some ad-hoc (local) optimization algorithm. TAMING intends to provide a systematic methodology for solving hard non convex polynomial optimization problems in all areas of science. Indeed the last decade has witnessed the emergence of Polynomial Optimization as a new field in which powerful positivity certificates from real algebraic geometry have permitted to develop an original and systematic approach to solve (at global optimality) optimization problems with polynomial (and even semi-algebraic) data. The backbone of this powerful methodology is the « moment-SOS » approach also known as « Lasserre hierarchy » which has attracted a lot of attention in many areas (e.g., optimization, applied mathematics, quantum computing, engineering, theoretical computer science) with important potential applications. It is now a basic tool for analyzing hardness of approximation in combinatorial optimization and the best candidate algorithm to prove/disprove the famous Unique Games Conjecture. Recently it has also become a promising new method for solving the important Optimal Power Flow Problem in the strategic domain of Energy Networks (as the only method that could solve to optimality certain types of such problems). However in its present form this promising methodology inherits a high computational cost and a (too) severe problem size limitation which precludes from its application many important real life problems of significant size. Proving that indeed this methodology can fulfill its promises and solve important practical problems in various areas poses major theoretical & practical challenges.

Keywords of the ERC project: Applied Mathematics - Optimization, Scientific computing

Keywords that characterize the scientific profile of the potential visiting researcher/s: Applied Mathematics; Optimization & Computer Scientist
Synthesis Technologies for Reactive Systems Software Engineers

The design and development of open reactive systems, which compute by reacting to ongoing stimuli from their environment, and include, for example, mobile applications running on smart phone devices, web-based applications, industrial robotic systems, embedded software running on chips inside cars and aircraft, etc., is a complex and challenging task. Despite advancement from low-level assembly languages to higher-level languages with powerful abstraction mechanisms, and the use of automated testing and formal verification, reactive systems software development is still a mostly manual and error-prone iterative activity of coding and debugging. A fundamentally different alternative approach to reactive systems development is synthesis, the automatic creation of correct-by-construction software from its specification. Synthesis has the potential to transform the way open reactive systems software is developed, making the process more effective and productive, and making its results more reliable and usable. However, while important advancements have been recently made on the algorithmic aspects of synthesis, no work has yet taken advantage of these achievements to change software engineering practices from “program centric” to “specification centric”. No effective end-to-end means to use synthesis are available to engineers, and the potential revolutionary impact of synthesis on the engineering of reactive systems software is far from being fully explored. The proposal targets four objectives: a new, rich specification language, tailored for synthesis and for use by software engineers; a set of new methods for specification centric development; tool implementations in ‘killer app’ application domains; and systematic evaluation with engineers. The research aims to unleash and evaluate the potential of synthesis to revolutionize reactive systems software development and to open the way for new directions in software engineering research and practice.

Keywords of the ERC project: Software engineering, reactive synthesis, modeling, Formal Methods

Keywords that characterize the scientific profile of the potential visiting researcher/s: software engineering, formal methods, Modeling
Algorithms for Complex Collective Decisions on Structured Domains

The aim of this proposal is to substantially advance the field of Computational Social Choice, by developing new tools and methodologies that can be used for making complex group decisions in rich and structured environments. We consider settings where each member of a decision-making body has preferences over a finite set of alternatives, and the goal is to synthesise a collective preference over these alternatives, which may take the form of a partial order over the set of alternatives with a predefined structure: examples include selecting a fixed-size set of alternatives, a ranking of the alternatives, a winner and up to two runner-ups, etc. We will formulate desiderata that apply to such preference aggregation procedures, design specific procedures that satisfy as many of these desiderata as possible, and develop efficient algorithms for computing them. As the latter step may be infeasible on general preference domains, we will focus on identifying the least restrictive domains that enable efficient computation, and use real-life preference data to verify whether the associated restrictions are likely to be satisfied in realistic preference aggregation scenarios. Also, we will determine whether our preference aggregation procedures are computationally resistant to malicious behavior. To lower the cognitive burden on the decision-makers, we will extend our procedures to accept partial rankings as inputs. Finally, to further contribute towards bridging the gap between theory and practice of collective decision making, we will provide open-source software implementations of our procedures, and reach out to the potential users to obtain feedback on their practical applicability.

Keywords of the ERC project: computational social choice

Keywords that characterize the scientific profile of the potential visiting researcher/s: algorithms, preferences, voting, game theory
Leveraging Binary Analysis to Secure the Internet of Things

We are in the midst of the shift towards the Internet of Things (IoT), where more and more (legacy) devices are connected to the Internet and communicate with each other. This paradigm shift brings new security challenges and unfortunately many current security solutions are not applicable anymore, e.g., because of a lack of clear network boundaries or resource-constrained devices. However, security plays a central role: In addition to its classical function in protecting against manipulation and fraud, it also enables novel applications and innovative business models. We propose a research program that leverages binary analysis techniques to improve the security within the IoT. We concentrate on the software level since this enables us to both analyze a given device for potential security vulnerabilities and add security features to harden the device against future attacks. More specifically, we concentrate on the firmware (i.e., the combination of persistent memory together with program code and data that powers such devices) and develop novel mechanism for binary analysis of such software. We design an intermediate language to abstract away from the concrete assembly level and this enables an analysis of many different platforms within a unified analysis framework. We transfer and extend program analysis techniques such as control-/data-flow analysis or symbolic execution and apply them to our IL. Given this novel toolset, we can analyze security properties of a given firmware image (e.g., uncovering undocumented functionality and detecting memory corruption or logical vulnerabilities.). We also explore how to harden a firmware by retrofitting security mechanisms (e.g., adding control-flow integrity or automatically eliminating unnecessary functionality). This research will deepen our fundamental understanding of binary analysis methods and apply it to a novel area as it lays the foundations of performing this analysis on the level of intermediate languages.

Keywords of the ERC project: computer security

Keywords that characterize the scientific profile of the potential visiting researcher/s: computer security; binary analysis; Internet of Things;
Formalizing Subjective Interestingness in Exploratory Data Mining

The rate at which research labs, enterprises and governments accumulate data is high and fast increasing. Often, these data are collected for no specific purpose, or they turn out to be useful for unanticipated purposes: Companies constantly look for new ways to monetize their customer databases; Governments mine various databases to detect tax fraud; Security agencies mine and cross-associate numerous heterogeneous information streams from publicly accessible and classified databases to understand and detect security threats. The objective in such Exploratory Data Mining (EDM) tasks is typically ill-defined, i.e. it is unclear how to formalize how interesting a pattern extracted from the data is. As a result, EDM is often a slow process of trial and error. During this fellowship we aim to develop the mathematical principles of what makes a pattern interesting in a very subjective sense. Crucial in this endeavour will be research into automatic mechanisms to model and duly consider the prior beliefs and expectations of the user for whom the EDM patterns are intended, thus relieving the users of the complex task to attempt to formalize themselves what makes a pattern interesting to them. This project will represent a radical change in how EDM research is done. Currently, researchers typically imagine a specific purpose for the patterns, try to formalize interestingness of such patterns given that purpose, and design an algorithm to mine them. However, given the variety of users, this strategy has led to a multitude of algorithms. As a result, users need to be data mining experts to understand which algorithm applies to their situation. To resolve this, we will develop a theoretically solid framework for the design of EDM systems that model the user’s beliefs and expectations as much as the data itself, so as to maximize the amount of useful information transmitted to the user. This will ultimately bring the power of EDM within reach of the non-expert.

Keywords of the ERC project: Data science, data mining, exploratory data analysis, information theory

Keywords that characterize the scientific profile of the potential visiting researcher/s: Data science, data mining, algorithms, machine learning, probabilistic graphical models, information theory
Formal lexically informed logics for searching the web

Semantic search engines use structured knowledge to improve traditional web search, e.g. by directly answering questions from users. Current approaches to semantic search rely on the unrealistic assumption that all true facts about a given domain are explicitly stated in their knowledge base or on the web. To reach their full potential, semantic search engines need the ability to reason about known facts. However, existing logics cannot adequately deal with the imperfect nature of knowledge from the web. One problem is that relevant information tends to be distributed over several heterogeneous knowledge bases that are inconsistent with each other. Moreover, domain theories are seldom complete, which means that a form of so-called plausible reasoning is needed. Finally, as relevant logical theories do not exist for many domains, reasoning may need to rely on imperfect probabilistic theories that have been learned from the web. To overcome these challenges, FLEXILOG will introduce a family of logics for robust reasoning with messy real-world knowledge, based on vector-space representations of natural language terms (i.e. of lexical knowledge). In particular, we will use lexical knowledge to estimate the plausibility of logical models, using conceptual simplicity as a proxy for plausibility (i.e. Occam’s razor). This will enable us to implement various forms of commonsense reasoning, equipping classical logic with the ability to draw plausible conclusions based on regularities that are observed in a knowledge base. We will then generalise our approach to probabilistic logics, and show how we can use the resulting lexically informed probabilistic logics to learn accurate and comprehensive domain theories from the web. This project will enable a robust data-driven approach to logic-based semantic search, and more generally lead to fundamental progress in a variety of knowledge-intensive applications for which logical inference has traditionally been too brittle.

Keywords of the ERC project: entity embeddings, interpretable machine learning, knowledge representation and reasoning, description logics

Keywords that characterize the scientific profile of the potential visiting researcher/s:
Despite over 50 years of research in robotics, most existing robots are far from being as resilient as the simplest animals: they are fragile machines that easily stop functioning in difficult conditions. The goal of this proposal is to radically change this situation by providing the algorithmic foundations for low-cost robots that can autonomously recover from unforeseen damages in a few minutes. The current approach to fault tolerance is inherited from safety-critical systems (e.g. spaceships or nuclear plants). It is inappropriate for low-cost autonomous robots because it relies on diagnostic procedures, which require expensive proprioceptive sensors, and contingency plans, which cannot cover all the possible situations that an autonomous robot can encounter. It is here contended that trial-and-error learning algorithms provide an alternate approach that does not require diagnostic, nor pre-defined contingency plans. In this project, we will develop and study a novel family of such learning algorithms that make it possible for autonomous robots to quickly discover compensatory behaviors. We will thus shed a new light on one of the most fundamental questions of robotics: how can a robot be as adaptive as an animal? The techniques developed in this project will substantially increase the lifespan of robots without increasing their cost and open new research avenues for adaptive machines.

Keywords of the ERC project: robotics, machine-learning

Keywords that characterize the scientific profile of the potential visiting researcher/s:
Significant parts of our cultural heritage are produced on the Web, yet only insufficient opportunities exist for accessing and exploring the past of the Web. The ALEXANDRIA project aims to develop models, tools and techniques necessary to archive and index relevant parts of the Web, and to retrieve and explore this information in a meaningful way. While the easy accessibility to the current Web is a good baseline, optimal access to Web archives requires new models and algorithms for retrieval, exploration, and analytics which go far beyond what is needed to access the current state of the Web. This includes taking into account the unique temporal dimension of Web archives, structured semantic information already available on the Web, as well as social media and network information. Within ALEXANDRIA, we will significantly advance semantic and time-based indexing for Web archives using human-compiled knowledge available on the Web, to efficiently index, retrieve and explore information about entities and events from the past. In doing so, we will focus on the concurrent evolution of this knowledge and the Web content to be indexed, and take into account diversity and incompleteness of this knowledge. We will further investigate mixed crowd- and machine-based Web analytics to support long-running and collaborative retrieval and analysis processes on Web archives. Usage of implicit human feedback will be essential to provide better indexing through insights during the analysis process and to better focus harvesting of content. The ALEXANDRIA Testbed will provide an important context for research, exploration and evaluation of the concepts, methods and algorithms developed in this project, and will provide both relevant collections and algorithms that enable further research on and practical application of our research results to existing archives like the Internet Archive, the Internet Memory Foundation and Web archives maintained by European national libraries.

**Keywords of the ERC project:** temporal retrieval, exploration and analytics in web archives

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** information retrieval, social networks, scalable algorithms
Allocation Made Practical

The AMPLify project will lay the foundations of a new field, computational behavioural game theory that brings a computational perspective, computational implementation, and behavioural insights to game theory. These foundations will be laid by tackling a pressing problem facing society today: the efficient and fair allocation of resources and costs. Research in allocation has previously considered simple, abstract models like cake cutting. We propose to develop richer models that capture important new features like asynchronicity which occur in many markets being developed in our highly connected and online world. The mechanisms currently used to allocate resources and costs are limited to these simple, abstract models and also do not take into account how people actually behave in practice. We will therefore design new mechanisms for these richer allocation problems that exploit insights gained from behavioural game theory like loss aversion. We will also tackle the complexity of these rich models and mechanisms with computational tools. Finally, we will use computation to increase both the efficiency and fairness of allocations. As a result, we will be able to do more with fewer resources and greater fairness. Our initial case studies in resource and cost allocation demonstrate that we can improve efficiency greatly, offering one company alone savings of up to 10% (which is worth tens of millions of dollars every year). We predict even greater impact with the more sophisticated mechanisms to be developed during the course of this project.

Keywords of the ERC project: social choice, fair division, resource allocation, optimisation, game theory

Keywords that characterize the scientific profile of the potential visiting researcher/s: social choice, fair division, resource allocation, optimisation, game theory
Science is increasingly data-driven. Scientific research funders now routinely mandate open publication of publicly-funded research data. Safely reusing such data currently requires labour-intensive curation. Provenance recording the history and derivation of the data is critical to reaping the benefits and avoiding the pitfalls of data sharing. There are hundreds of curated scientific databases in biomedicine that need fine-grained provenance; one important example is GtoPdb, a pharmacological database developed by colleagues in Edinburgh. Currently there are no reusable methodologies or practical tools that support provenance for curated databases, forcing each project to start from scratch. Research on provenance for scientific databases is still at an early stage, and prototypes have so far proven challenging to deploy or evaluate in the field. Also, most techniques to date focus on provenance within a single database, but this is only part of the problem: real solutions will have to integrate database provenance with the multiple tiers of web applications, and no-one has begun to address this challenge. I propose research on how to build support for curation into the programming language itself, building on my recent research on the Links Web programming language and on data curation. Links is a strongly-typed language that provides state-of-the-art support for language-integrated query and Web programming. I propose to build on Links and other recent language designs for heterogeneous meta-programming to develop a new language, called Skye, that can express modular, reusable curation and provenance techniques. To keep focus on the real needs of scientific databases, Skye will be evaluated in the context of GtoPdb and other scientific database projects. Bridging the gap between curation research and the practices of scientific database curators will catalyse a virtuous cycle that will increase the pace of breakthrough results from data-driven science.

Keywords of the ERC project: programming languages; databases; web programming; curation

Keywords that characterize the scientific profile of the potential visiting researcher/s: programming languages; databases; query languages; scientific data management
Synthesising Inductive Data Models

Inspired by recent successes towards automating highly complex jobs like programming and scientific experimentation, the ultimate goal of this project is to automate the task of the data scientist when developing intelligent systems, which is to extract knowledge from data in the form of models. More specifically, this project wants to develop the foundations of a theory and methodology for automatically synthesising inductive data models. An inductive data model (IDM) consists of 1) a data model (DM) that specifies an adequate data structure for the dataset (just like a database), and 2) a set of inductive models (IMs), that is, a set of patterns and models that have been discovered in the data. While the DM can be used to retrieve information about the dataset and to answer questions about specific data points, the IMs can be used to make predictions, propose values for missing data, find inconsistencies and redundancies, etc. The task addressed in this project is to automatically synthesise such IMs from past data and to use these to support the user when making decisions. It will be assumed that the data set consists of a set of tables, that the end-user interacts with the IDM via a visual interface, and the data scientist via a unifying IDM language offering a number of core IMs and learning algorithms. The key challenges to be tackled in SYNTH are: 1) the synthesis system must "learn the learning task", that is, it should identify the right learning tasks and learn appropriate IMs for each of these; 2) the system may need to restructure the data set before IM synthesis can start; and 3) a unifying IDM language for a set of core patterns and models must be developed. The approach will be implemented in open source software and evaluated on two challenging application areas: rostering and sports analytics.

Keywords of the ERC project: artificial intelligence, data science, automating data science, data mining, constraints, probabilistic programming, inductive programming

Keywords that characterize the scientific profile of the potential visiting researcher/s: artificial intelligence researchers working on symbolic methods in data mining / data science / machine learning
Distributed Optimization Methods for Smart Cyber-Physical Networks

The combination of embedded electronics and communication capability in almost any mobile or portable device has turned this century into the age of cyber-physical networks. Smart communicating devices with their sensing, computing and control capabilities promise to make our cities, transportation systems, factories and living environments more intelligent, energy-efficient, safe and secure. This extremely complex system has raised a number of new challenges involving ICT disciplines. In particular, a novel peer-to-peer distributed computational model is appearing as a new opportunity in which a service is built-up cooperatively by peers, rather than by a unique provider that knows and owns all data. The interdisciplinary “Optimization Community” is facing this revolution sharing a common need: to find new theories, methodologies and tools to optimize over this complex network system. With this in mind, OPT4SMART has a twofold objective. First, to provide a comprehensive theoretical framework to solve distributed optimization problems over peer-to-peer networks. Second, to develop effective numerical tools, based on this framework, to solve estimation, learning, decision and control problems in cyber-physical networks. To achieve this twofold objective, we will take a systems-theory perspective. Specific problems from these four areas will be abstracted to a common mathematical set-up, and addressed by means of interdisciplinary methodologies arising from a synergic combination of optimization, controls, and graph theories. In particular, OPT4SMART will face the challenge of solving optimization problems under severe communication limitations, very-large-scale problem and data size, and real-time computational constraints. The expected result will be a combination of strong theoretical methods and effective numerical toolboxes available to people in Engineering, Computer Science, Mathematics and other areas, who are facing optimization in cyber-physical networks.

Keywords of the ERC project: Distributed optimization, distributed control, multi-agent systems, optimal control

Keywords that characterize the scientific profile of the potential visiting researcher/s: Optimization, Control Theory, Signal Processing, distributed control
BetterSense aims to solve the two main problems in current gas sensor technologies: the high power consumption and the poor selectivity. For the former, we propose a radically new approach: to integrate the sensing components and the energy sources intimately, at the nanoscale, in order to achieve a new kind of sensor concept featuring zero power consumption. For the latter, we will mimic the biological receptors designing a kit of gas-specific molecular organic functionalizations to reach ultra-high gas selectivity figures, comparable to those of biological processes. Both cutting-edge concepts will be developed in parallel and integrated together to render a totally new gas sensing technology that surpasses the state-of-the-art.

As a matter of fact, the project will enable, for the first time, the integration of gas detectors in energetically autonomous sensors networks. Additionally, BetterSense will provide an integral solution to the gas sensing challenge by producing a full set of gas-specific sensors over the same platform to ease their integration in multi-analyte systems. Moreover, the project approach will certainly open opportunities in adjacent fields in which power consumption, specificity and nano/micro integration are a concern, such as liquid chemical and biological sensing.

In spite of the promising evidences that demonstrate the feasibility of this proposal, there are still many scientific and technological issues to solve, most of them in the edge of what is known and what is possible today in nano-fabrication and nano/micro integration. For this reason, BetterSense also aims to contribute to the global challenge of making nanodevices compatible with scalable, cost-effective, microelectronic technologies.

For all this, addressing this challenging proposal in full requires a funding scheme compatible with a high-risk/high-gain vision to finance the full dedication of a highly motivated research team with multidisciplinary skill.

**Keywords of the ERC project:** low power devices, sensors, gas sensors, chemical sensors

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** electrical characterization, device test
A key challenge for the 21st century is, therefore to provide billions of people with the means to access, move and manipulate, what has become, huge volumes of information. The environmental and economic implications becoming serious, making energy efficient data communications key to the operation of today’s society. In this project, the Principal Investigator will develop a new framework for optical interconnects and provide a common platform that spans Fibre-to-the-home to chip-to-chip links, even as far as global on-chip interconnects. The project is based on the efficient coupling of the Photonic Crystal resonators with the outside world. These provide the ultimate confinement of light in both space and time allowing orders of magnitude improvements in performance relative to the state of the art, yet in a simpler simple system- the innovator’s dream. New versions of the key components of optical links- light sources, modulators and photo-detectors- will be realised in this new framework providing a new paradigm for energy efficient communication.

Keywords of the ERC project: nanophotonics, photonic crystal, silicon photonics, optical interconnects

Keywords that characterize the scientific profile of the potential visiting researcher/s: nanophotonics, photonic crystal, silicon photonics, optical interconnects
Nanophotonic Nanomechanical Mass Spectrometry for Biology and Health

“Mass Spectrometry has become a routine analytical tool in modern biological research, and has gained in recent years a foothold in the realm of clinical diagnostic and screening. However, it is still costly, complex and because its principle relies on ionization, it is incapable of analyzing biomolecules with masses greater than a few MDa. Averaging more than 100 million particles per measurement, it is also incapable of characterizing the diversity of such heavy entities. ENLIGHTENED aims at demonstrating a breakthrough concept based on Photonic Nano-Mechanical Mass Spectrometry, able to perform analysis of bioparticles of high biomedical significance, of ultra-high mass, never so far characterized, with single-molecule sensitivity and unprecedented resolution. The long-term vision beyond the current proposal is to provide the biologists with a tool which will be transformative for fundamental knowledge, and to make possible cheap, handheld devices for personalized medicine.

ENLIGHTENED proposes to use photons to shed light on unexplored species at the individual level, which is of high biomedical significance and will expand our understanding of simple life forms.”

Keywords of the ERC project: NEMS ; optomechanics ; mass sensing ; mass spectrometry ; nanoresonators ; frequency fluctuations ; decoherence ; biology applications

Keywords that characterize the scientific profile of the potential visiting researcher/s: NEMS ; optomechanics ; vacuum techniques ; mass spectrometry ; low noise instrumentation ; biology analysis
**MICROMACHINED OPTOMECHANICAL DEVICES:** looking at cells, tissues, and organs ... with a gentle touch.

Every time we grab an object to look at its geometrical details or to feel if it is hard or soft, we are ineluctably confronted with the limits of our senses. Behind its appearances, the object may still hide information that, encrypted in its microscopic features, remains undetected to our macroscopic assessment. In life sciences, those limits are more than just frustrating: they are an obstacle to study and detect life threatening conditions.

Many different instruments may overcome those limits, but the vast majority of them rely either on “sight” (optics) or “touch” (mechanics) separately. On the contrary, I believe that it is from the combination of those two “senses” that we have more chances to tackle the future challenges of cell biology, tissue engineering, and medical diagnosis. Inspired by this tantalizing perspective, and supported by a technology that I have brought from blackboard to market, I have now designed a scientific program to breach into the microscopic scale via an unbeaten path. The program develops along three projects addressing the three most relevant scales in life sciences: cells, tissues, and organs. In the first project, I will design and test a new optomechanical probe to investigate how a prolonged mechanical load on a brain cell of a living animal may trigger alterations in its Central Nervous System. With the second project, I will develop an optomechanical tactile instrument that can assess how subsurface tissues deform in response to a mechanical stroke – a study that may change the way physicians look at tissue classification. For the third project, I will deliver an acousto-optical gas trace sensors so compact that can penetrate inside the lungs of an adult patient, where it could be used for early detection of pulmonary life threatening diseases. Each project represents an opportunity to open an entire new field, where optics and micromechanics are combined to extend our senses well beyond their natural limits.

**Keywords of the ERC project:** Optical fiber sensors, Mechanobiology, Neuroscience, Instrument development

**Keywords that characterize the scientific profile of the potential visiting researcher/s:**
The Highly Efficient And Reliable smart Transformer (HEART), a new Heart for the Electric Distribution System

In the last 10 years, power electronics has moved significantly towards the electric grid, making it more flexible and decentralized. Still important challenges remain. One of the most thrilling is re-inventing the distribution transformer after more than 125 years since its first use in the electrification of a city. In fact, actual distribution transformers can no longer fulfill the requirements of a modern electric grid highly dominated by distributed sources and new sizable loads, like heat pumps and electric vehicles.

This project proposes the invention of a novel “Smart Transformer” (ST), based on a modular architecture of units made by power electronics converters, that will be able to manage the energy and the information flows among sources and loads in the distribution area with the goal of decoupling it from the rest of the bulk power system. Actual proposals of Smart Transformers cannot compete in terms of cost, efficiency and reliability with traditional transformers.

This project has decided to take this challenge with a paradigm shift in how to approach it and a new set of methodologies. The breakthrough results of this research will be obtained taking the following high-risk high-gain bet: significantly influence the efficiency and the reliability of the Smart Transformer by routing the energy flows among its power converter units. A new understanding of how the energy flows are managed by the modular connection of power converter units will guide the design of new architectures for the ST allowing different routes for the energy. Graph theory will be used to find optimal paths for the energy flows with the goal of maximizing efficiency and reliability. The energy flows will be managed by relying on information coming from the electric distribution system sensors (requirements) and from the power module sensors (constraints).

The holy grail of this research is to provide a new durable heart to the electric distribution system.

Keywords of the ERC project: power electronics, power system, WBG semiconductors, reliability

Keywords that characterize the scientific profile of the potential visiting researcher/s: power electronics, power system, WBG semiconductors, reliability
Control of contact interactions for robots acting in the world

What are the algorithmic principles that would allow a robot to run through a rocky terrain, lift a couch while reaching for an object that rolled under it or manipulate a screwdriver while balancing on top of a ladder? Answering this seemingly naïve question resorts to understanding the fundamental principles for robot locomotion and manipulation, which is very challenging. However, it is a necessary step towards ubiquitous robots capable of helping humans in an uncountable number of tasks. The fundamental aspect of both locomotion and manipulation is that the dynamic interaction of the robot with its environment through the creation of physical contacts is at the heart of the tasks. The planning of such interactions in a general manner is an unsolved problem. Moreover, it is not clear how sensory information (e.g. tactile and force sensors) can be included to improve the robustness of robot behaviors. Most of the time, it is simply discarded. CONT-ACT has the ambition to develop a consistent theoretical framework for motion generation and control where contact interaction is at the core of the approach and an efficient use of sensory information drives the development of high performance, adaptive and robust planning and control methods. CONT-ACT develops an architecture based on real-time predictive controllers that fully exploit contact interactions. In addition, the structure of sensory information during contact interactions is experimentally analyzed to create sensor representations adapted for control. It is then possible to learn predictive models in sensor space that are used to create very reactive controllers. The robot constantly improves its performance as it learns better sensory models. It is a step towards a general theory for robot movement that can be used to control any robot with legs and arms for both manipulation and locomotion tasks and that allows robots to constantly improve their performances as they experience the world.

Keywords of the ERC project: robotics, optimal control, contact interaction, learning

Keywords that characterize the scientific profile of the potential visiting researcher/s: learning control, reinforcement learning, optimal control
Policy Learning of Motor Skills for Humanoid Robots

The goal of SKILLS4ROBOTS is to develop an autonomous skill learning system that enables humanoid robots to acquire and improve a rich set of motor skills. This robot skill learning system will allow scaling of motor abilities up to fully anthropomorphic robots while overcoming the current limitations of skill learning systems to only few degrees of freedom. To achieve this goal, it will decompose complex motor skills into simpler elemental movements – called movement primitives – that serve as building blocks for the higher-level movement strategy and the resulting architecture will be able to address arbitrary, highly complex tasks – up to robot table tennis for a humanoid robot. Learned primitives will be superimposed, sequenced and blended.

Four recent breakthroughs in the PI’s research will make this project possible due to successes on the representation of the parametric probabilistic representations of the elementary movements, on probabilistic imitation learning, on relative entropy policy search-based reinforcement learning and on the modular organization of the representation. These breakthroughs will allow creating a general, autonomous skill learning system that can learn many different skills in the exact same framework without changing a single line of programmed code. To accomplish this goal, our skill learning system will autonomously extract the necessary movement primitives out of observed trajectories, learn to generalize these primitives to different situations and select, sequence or combine them such that complex behavior can be synthesized out of the primitive building blocks. We will evaluate our autonomous learning framework on a real humanoid robot platform with 60 degrees of freedom and show that it can learn a large variety of new skills.

Keywords of the ERC project: Robotics, Machine Learning

Keywords that characterize the scientific profile of the potential visiting researcher/s: Robotics, Machine Learning
Deep brain stimulation (DBS) is an effective therapy for treating the symptoms of Parkinson’s disease (PD). Despite its success, the mechanisms of DBS are not understood and there is a need to improve DBS to improve long-term stimulation in a wider patient population, limit side-effects, and extend battery life. Currently DBS operates in ‘open-loop’, with stimulus parameters empirically set. Closed-loop DBS, which adjusts parameters based on the state of the system, has the potential to overcome current limitations to increase therapeutic efficacy while reducing side-effects, costs and energy. Several key questions need to be addressed before closed loop DBS can be implemented clinically. This research will develop a new multiscale model of the neuromuscular system for closed-loop DBS. The model will simulate neural sensing and stimulation on a scale not previously considered, encompassing the electric field around the electrode, the effect on individual neurons and neural networks, and generation of muscle force. This will involve integration across multiple temporal and spatial scales, in a complex system with incomplete knowledge of system variables. Experiments will be conducted to validate the model, and identify new biomarkers of neural activity that can used with signals from the brain to enable continuous symptom monitoring. The model will be used to design a new control strategy for closed-loop DBS that can accommodate the nonlinear nature of the system, and short- and long-term changes in system behavior. Though challenging, this research will provide new insights into the changes that take place in PD and the mechanisms by which DBS exerts its therapeutic influence. This knowledge will be used to design a new strategy for closed-loop DBS, ready for testing in patients, with the potential to significantly improve patient outcomes in PD and fundamentally change the way in which implanted devices utilise electrical stimulation to modulate neural activity.

Keywords of the ERC project: Neural Engineering, deep brain stimulation, computational neuroscience, neural modelling, parkinson’s disease, electromyography

Keywords that characterize the scientific profile of the potential visiting researcher/s: electrophysiology, parkinson’s disease, deep brain stimulation, neuromodulation, neural prostheses
WireLess LOWband communications: massive and ultra-reliable access

The overall objective of WILLOW is to make wireless communication a true commodity by enabling lowband communications: low-rate links for massive number of devices and ultra-reliable connectivity. This research effort is a major endeavour in the area of wireless communications, taking a different path from the mainstream research that aims at “4G, but faster”. Lowband communication is the key to enabling new applications, such as massive sensing, ultra-reliable vehicular links and wireless cloud connectivity with guaranteed minimal rate. The research in WILLOW is centred on two fundamental issues. First, it is the efficient communication with short packets, in which the data size is comparable to the size of the metadata, i.e. control information, which is not the case in broadband communication. Communication of short packets that come from a massive number of devices and/or need to meet a latency constraint requires fundamental rethinking of the packet structure and the associated communication protocols. Second is the system architecture in which graceful rate degradation, low latency and massive access can exist simultaneously with the broadband services. The principles from WILLOW will be applied to: (a) clean-slate wireless systems; (b) reengineer existing wireless systems. Option (b) is unique to lowband communication that does not require high physical-layer speed, but can reuse the physical layer of an existing system and redefine the metadata/data relationship to achieve massive/ultra-reliable communication. WILLOW carries high risk by conjecturing that it is possible to support an unprecedented number of connected devices and wireless reliability levels. Considering the timeliness and the relevance, the strong track record of the PI and the rich wireless research environment at Aalborg University, WILLOW is poised to make a breakthrough towards lowband communications and create the technology that will enable a plethora of new wireless usage modes.

Keywords of the ERC project: wireless communications, machine-to-machine communication, ultra-reliable wireless

Keywords that characterize the scientific profile of the potential visiting researcher/s: Internet of Things, data mining, UAV, blockchain, wireless
Plasmonic-Silicon-Organic Hybrid – a Universal Platform for THz Communications

The PLASILOR project aims at combining the best of three worlds by bringing silicon, organic and plasmonic technologies onto one common platform. Within PLASILOR, we will develop novel devices that outperform the current state-of-the-art in terms of functionality, speed and size thanks to unique characteristics only offered by organics and plasmonics. The focus of the device activities will be on novel transmitters and receivers and their subcomponents. Key to the project will be high-speed plasmonic-organic hybrid modulators with 200 GHz bandwidth and novel plasmonic detectors with a similar bandwidth. The project will also pursue the development of novel waveguide and coupler concepts for optical, THz and plasmonic modes but also work actively towards the development of new organic sources and make them accessible to the communications community by benefiting from recent developments in the field of organic lighting. Finally, the potential of the new platform will be put at test by demonstrating a 240 GHz beam-steering link on a chip - an undertaking that would be difficult – if not impossible to realize by other means. This radio-over fiber link will be based on a cointegration of both high-speed photonics and RF elements such as antennas. The demonstrator will benefit from the unique large scale integration capabilities offered by silicon CMOS, the strong linear-electro-optic effect of tailored organic compounds and the ultra-fast and compact size offered by plasmonics. The project is disruptive and challenging but it builds on the device and system expertise of the applicant. For instance, Juerg Leuthold and his group have only recently demonstrated the first ultra-compact high speed plasmonic modulator and they introduced the first wireless 100 Gbit/s link. The new platform will not only be a solution for THz communications – but also for the wider field of THz applications.

Keywords of the ERC project: optical communications, integrated optics, plasmonics, radio-over fiber

Keywords that characterize the scientific profile of the potential visiting researcher/s: Communications theory, communications systems, integrated optics, nonlinear optics, fabrication technology
The ambition of PLASMIC is to address the bottleneck caused by electrical interconnects and develop on-chip optical interconnect solutions based on plasmonically-enhanced nanoscale emitters. Nanoscale photonic components are desirable for on-chip communications because of density, speed and because reducing the size of the cavity might reduce the lasing threshold. Conventional photonics are limited in scale by the diffraction-limit to dimensions of half of the wavelength of light in the material. This limit does not apply to plasmonics, an optical mode that exists at the interface between a metal and a dielectric. Thus, they have a great potential for applications where down-scaling and confinement are primordial.

One of the barriers for applying plasmonics is the large losses associated with the metals. Thus in PLASMIC alternative plasmonic metals will be investigated based on their potential for tuning, VLSI compatibility, deposition methods and achieving lower optical losses in the near-IR. I will focus on highly doped semiconductors, metal nitrides, as well as multi-layers and compounds to form new plasmonic materials. Specifically, I will evaluate the use of the field-effect to achieve the semiconductor-metal transition to tune the plasma frequency.

New pioneering device concepts for plasmonic-photonic emitters on a silicon platform integrated with passive silicon photonic waveguides will be developed. To implement the gain medium for the lasers, I will exploit a novel nanowire (NW) integration approach: Template-Assisted Epitaxy. The unique advantages make it possible to grow III-V NWs on any orientation of silicon and aligned to lithographic features.

The devices will be based on a hybrid cavity formed between the NW and a Si waveguide with gratings to provide feedback. My team and I will explore dimensional scaling potential as well as the energy efficiency of plasmonic and photonic devices operating both in a lasing as well as in a subthreshold operation mode.

Keywords of the ERC project: III'V materials, photonics, plasmonics, semiconductor technology

Keywords that characterize the scientific profile of the potential visiting researcher/s: Laser physics, cleanroom skills, III-V materials, sentaurus simulation, min 6 months.
Information-age microscopy for deep vision imaging of biological tissue

Modern biology could not exist without the optical microscope. Hundreds of years of research have seemingly developed microscopes to perfection, with one essential limitation: in turbid biological tissue, not even the most advanced microscope can penetrate deeper than a fraction of a millimetre. At larger depths light scattering prevents the formation of an image. DEEP VISION takes a radically new approach to microscopy in order to lift this final limitation.

Microscopes are based on the idea that light propagates along a straight line. In biological tissue, however, this picture is naïve: light is scattered by every structure in the specimen. Since the amount of ‘non-scattered’ light decreases exponentially with depth, a significant improvement of the imaging depth is fundamentally impossible, unless scattered light itself is used for imaging.

In 2007, Allard Mosk and I pioneered the field of wavefront shaping. The game-changing message of wavefront shaping is that scattering is not a fundamental limitation for imaging: using a spatial light modulator, light can be focused even inside the most turbid materials, if ‘only’ the correct wavefront is known.

DEEP VISION aims to initiate a fundamental change in how we think about microscopy: to use scattered light rather than straight rays for imaging. The microscope of the future is no longer based on Newtonian optics. Instead, it combines new insights in scattering physics, wavefront shaping, and compressed sensing to extract all useful information from a specimen.

Whereas existing microscopes are ignorant to the nature of the specimen, DEEP VISION is inspired by information theory; imaging revolves around a model that integrates observations with statistical a-priori information about the tissue. This model is used to calculate the wavefronts for focusing deeper into the specimen. Simulations indicate that my approach will penetrate at least four times deeper than existing microscopes, without loss of resolution.

Keywords of the ERC project: nonlinear microscopy, wavefront shaping, light scattering, computational imaging

Keywords that characterize the scientific profile of the potential visiting researcher/s: nonlinear microscopy, wavefront shaping, light scattering, computational imaging
Energy efficiency offers a vast and low-cost resource to address future energy demand while reducing carbon dioxide emissions. The unique properties of III-Nitride semiconductors make them the ideal material for future energy challenges. Their outstanding optical properties are revolutionizing the world with efficient LED light bulbs. Even greater impact is anticipated for power electronics. The much larger Baliga’s figure of merit of GaN compared to SiC and Si enables drastically more efficient power switches, which are at the heart of any energy generation/management system. However, current III-Nitride device performance is far from the fundamental materials capabilities, and severe thermal management and reliability limitations hinder their full potential for energy-efficiency.

The In-Need proposes a unique approach to address concurrently all current challenges based on advanced nanostructures designed to optimally exploit the superior properties of the new bulk GaN materials. Nanostructuring distinct regions of the device will allow a precise control over their intrinsic characteristics. To address reliability issues and yield unprecedented device performance, these nanostructures will be combined to the excellent properties of bulk GaN. This will open opportunities for new vertical devices, enabling smaller structures with larger voltages and higher efficiencies. Efficient thermal management will be achieved with ultra-near junction cooling. Nano/micro-channels filled with high thermal conductivity materials or coolants will be embedded inside the device.

We believe our judicious nano-scale design of new high-performing materials will result in state-of-the-art devices, leading to a large-scale impact in energy efficiency. The miniaturization and large power density enabled by our approach will allow future integration of power devices into single power microchips. This will revolutionize energy use much like Silicon microchips did for information processing.

**Keywords of the ERC project:** GaN, power electronics, ballistic devices, semiconductor physics, quantum devices

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** GaN, power electronics, ballistic devices, semiconductor physics, quantum devices
A Bidirectional MyoKinetic Implanted Interface for Natural Control of Artificial Limbs

MYKI aims at developing and clinically evaluating a dexterous hand prosthesis with tactile sensing which is naturally controlled and perceived by the amputee. This will be possible by overcoming the conventional approaches based on recording electrical signals from the peripheral nervous system (nerves or skeletal muscles) through the development of a radically new Human-Machine Interface (HMI) based on magnetic field principles, both able to decode voluntary motor commands and to convey sensory feedback to the individual. Core of this system is a multitude of magnets implanted in independent muscles and external magnetic readers/drivers (MRDs) able to (i) continuously localize the movements of the magnets and, at specific times, (ii) induce subtle movements in specific magnets. In fact, as a magnet is implanted it will travel with the muscle it is located in, and its localization will provide a direct measure of the contraction/elongation of that muscle, which is voluntarily controlled by the central nervous system. In this way it will be possible to decode the efferent signals sent by the brain by observing a by-product of the muscle fibres recruitment. On the other hand, a movement induced in the implanted magnet by the external MRD, could provide a perceivable stimulus, conveyed to the brain by means of the peripheral sensory receptors present in the muscle (e.g. muscle spindles or Golgi tendon organ) or in the neighbouring skin (tactile mechanoreceptors). In this way we aim to provide tactile and/or proprioceptive sensory information to the brain, thus restoring the physiological sensorimotor control loop. Remarkably, with passive magnetic tags (that do not require to be powered-on) and wearable readers/drivers, it will be possible to implement a wireless, bidirectional HMI with dramatically enhanced capabilities with respect to the state of the art interfaces, as illustrated in this proposal.

Keywords of the ERC project: Upper limb prostheses, artificial hand, grasping, manipulation, human machine interfaces, sensory feedback, myoelectric control, emg, Artificial sensors, bioengineering

Keywords that characterize the scientific profile of the potential visiting researcher/s: Upper limb prostheses, artificial hand, grasping, manipulation, human machine interfaces, sensory feedback, myoelectric control, emg, Artificial sensors, bioengineering, biomechanics, hand surgery
Hierarchical Carbon Nanomaterials

Over the past years, carbon nanomaterial such as graphene and carbon nanotubes (CNTs) have attracted the interest of scientists, because some of their properties are unlike any other engineering material. Individual graphene sheets and CNTs have shown a Youngs Modulus of 1 TPa and a tensile strength of 100 GPa, hereby exceeding steel at only a fraction of its weight. Further, they offer high currents carrying capacities of $10^9$ A/cm², and thermal conductivities up to 3500 W/mK, exceeding diamond. Importantly, these off-the-chart properties are only valid for high quality individualized nanotubes or sheets. However, most engineering applications require the assembly of tens to millions of these nanoparticles into one device. Unfortunately, the mechanical and electronic figures of merit of such assembled materials typically drop by at least an order of magnitude in comparison to the constituent nanoparticles. In this ERC project, we aim at the development of new techniques to create structured assemblies of carbon nanoparticles. Herein we emphasize the importance of controlling hierarchical arrangement at different length scales in order to engineer the properties of the final device. The project will follow a methodical approach, bringing together different fields of expertise ranging from macro- and microscale manufacturing, to nanoscale material synthesis and mesoscale chemical surface modification. For instance, we will pursue combined top-down microfabrication and bottom-up self-assembly, accompanied with surface modification through hydrothermal processing. This research will impact scientific understanding of how nanotubes and nanosheets interact, and will create new hierarchical assembly techniques for nanomaterials. Further, this ERC project pursues applications with high societal impact, including energy storage and water filtration. Finally, HIENA will tie relations with EU’s rich CNT industry to disseminate its technologic achievements.

Keywords of the ERC project: carbon nanotubes, hierarchical materials, energy storage, water filtration, CNT, graphene, battery, biomimetic

Keywords that characterize the scientific profile of the potential visiting researcher/s: CNT, carbon nanotubes, graphene, battery, hierarchical, biomimetic, water filtration
MULTIAX: Multiaxial and Multiscale Plasticity in Metals

Our ambition is to probe the influence of non-proportional multiaxial straining on the multiscale aspects of metal plasticity with focus on three deformation mechanisms: dislocation plasticity in bcc metals, mechanical twinning in fcc metals and the martensitic phase transformation. These mechanisms play a key role in modern TWIP and TRIP steels, yet about their response to multiaxial loading not much is known.

The underlying hypothesis of this research project is that by performing biaxial deformation tests at the micro-, meso- and macro-scale meanwhile following the microstructure in situ, ground-breaking insight can be obtained on how a second strain path, a change in strain path with or without prior unloading affects the operation of the deformation mechanism, the defect accumulation and as a consequence, the evolving microstructure.

The expected outcome of the research will help the formulation of criteria to be implemented in micromechanical models, for which constitutive equations are now relying solely on a knowledgebase derived from uniaxial testing.

Operationally, the project contains a development phase and a research phase. First a micro- and meso-scale biaxial test rig will be developed, allowing deforming small samples in two orthogonal directions independently, compatible to be installed at various Xray beamlines of synchrotron facilities in Europe and in SEMs. The research phase will be multiscale: the response of each deformation mechanism will be investigated at the level of the mechanism itself, at the level of an oligocrystal focusing on transmission of strain across grain boundaries and at the macrosopic level focussing on the evolution of the microstructure. Experimental research will be accompanied by synergetic computational simulations.

**Keywords of the ERC project:** multiaxial, deformation, alloys, microstructure, mechanical

**Keywords that characterize the scientific profile of the potential visiting researcher/s:**
Design, manufacturing and control of INterfaces in THERMally conductive polymer nanocomposites

This proposal addresses the design, manufacturing and control of interfaces in thermally conductive polymer/graphene nanocomposites.

In particular, the strong reduction of thermal resistance associated to the contacts between conductive particles in a percolating network throughout the polymer matrix is targeted, to overcome the present bottleneck for heat transfer in nanocomposites.

The project includes the investigation of novel chemical modifications of nanoparticles to behave as thermal bridges between adjacent particles, advanced characterization methods for particle/particle interfaces and controlled processing methods for the preparations of nanocomposites with superior thermal conductivity.

The results of this project will contribute to the fundamental understanding of heat transfer in complex solids, while success in mastering interfacial properties would open the way to a new generation of advanced materials coupling high thermal conductivity with low density, ease of processing, toughness and corrosion resistance.

Keywords of the ERC project: Thermal conductivity of polymer nanocomposites, graphene functionalization,

Keywords that characterize the scientific profile of the potential visiting researcher/s: graphene functionalization, phonon spectra, molecular dynamics, DFTB, SThM,
Innovative Catalyst Design for Large-Scale, Sustainable Processes

A systematic and novel, multi-scale model based catalyst design methodology will be developed. The fundamental nature of the models used is unprecedented and will represent a breakthrough compared to the more commonly applied statistical, correlative relationships. The methodology will focus on the intrinsic kinetics of (potentially) large-scale processes for the conversion of renewable feeds into fuels and chemicals. Non-ideal behaviour, caused by mass and heat transfer limitations or particular reactor hydrodynamics, will be explicitly accounted for when simulating or optimizing industrial-scale applications. The selected model reactions are situated in the area of biomass upgrading to fuels and chemicals: fast pyrolysis oil stabilization, glycerol hydrogenolysis and selective oxidation of (bio)ethanol to acetaldehyde. For the first time, a systematic microkinetic modelling methodology will be developed for oxygenates conversion. In particular, stereochemistry in catalysis will be assessed. Two types of descriptors will be quantified: kinetic descriptors that are catalyst independent and catalyst descriptors that specifically account for the effect of the catalyst properties on the reaction kinetics. The latter will be optimized in terms of reactant conversion, product yield or selectivity. Fundamental relationships will be established between the catalyst descriptors as determined by microkinetic modelling and independently measured catalyst properties or synthesis parameters. These innovative relationships allow providing the desired, rational feedback in from optimal descriptor values towards synthesis parameters for a new catalyst generation. Their fundamental character will guarantee adequate extrapolative properties that can be exploited for the identification of a groundbreaking next catalyst generation.

Keywords of the ERC project: catalysis, reaction engineering, rational design

Keywords that characterize the scientific profile of the potential visiting researcher/s: catalyst synthesis and characterization, high throughput testing
DropletMicroarrays: Ultra High-Throughput Screening of Cells in 3D Microenvironments

High-throughput (HT) screening of live cells is crucial to accelerate both fundamental biological research and discovery of new drugs. Current methods for HT cell screenings, however, either require a large number of microplates, are prone to cross-contaminations and are limited to adherent cells (cell microarrays), or are not compatible with adherent cells as well as with spatial indexing (droplet microfluidics). We recently demonstrated the use of superhydrophobic-superhydrophilic microarrays to create high-density arrays of microdroplets or hydrogel micropads. We propose here to develop a new platform for HT cell screening experiments using the unique properties of the superhydrophilic microarrays separated by superhydrophobic thin barriers. The new technology will allow us to perform up to 300K cell experiments in parallel using a single chip. Individual cell experiments will be performed in thousands of completely isolated microdroplet at defined locations on the chip. This will enable spatial indexing, time-lapse measurements and screening of either adherent or non-adherent cells. Parallel manipulations within individual microreservoirs, such as washing, addition of chemical libraries, or staining will be developed to open new possibilities in the field of live cell studies. Superhydrophobic barriers will allow complete isolation of the microreservoirs, thus preventing cross-contamination and cell migration. We will also develop a technology for the HT screening of cells in 3D hydrogel micropads. We will use these methods to gain better understanding of how different parameters of the 3D cell microenvironment influence various aspects of cell behavior. The project will require the development of new technological tools which can later be applied to a wide range of cell screening experiments and biological problems. Our long term aim is to replace the outdated microplate technology with a more powerful and convenient method for cell screening experiments.

Keywords of the ERC project: cell screening, droplet microarray, HTS, microfluidics

Keywords that characterize the scientific profile of the potential visiting researcher/s:
Non classical rarefaction shock-waves in molecularly complex vapours

The expansion of a dilute gas through a gasdynamics convergent-divergent nozzle can occur in three different regimes, depending on the inlet and discharge conditions and on the gas: via a fully subsonic expansion, via a subsonic-supersonic or via a subsonic-supersonic-subsonic expansion embedding a compression shock wave within the divergent portion of the nozzle. I devised an exact solution procedure for computing nozzle flows of real gases, which allowed me to discover that in molecularly complex fluids eighteen additional different flow configurations are possible, each including multiple compression classical shocks as well as non classical rarefaction ones. Modern thermodynamic models indicate that these exotic regimes can possibly occur in nozzle flows of molecularly complex fluids such as hydrocarbons, siloxanes or perfluorocarbons operating close to the liquid-vapour saturation curve and critical point. The experimental observation of one only of these eighteen flow configurations would be sufficient to prove for the first time that non classical gasdynamics phenomena are indeed possible in the vapour region of a fluid with high molecular complexity.

To this purpose, a modification to the blow-down wind tunnel for dense gases at Politecnico di Milano is proposed to use mixtures of siloxane fluids. Measurements are complemented by numerical simulations of the expected flow field and by state-of-the-art uncertainty quantification techniques. The distinctive feature of the proposed experiment is the adoption of mixture of siloxanes as working fluids. Mixtures of siloxanes are well known to exhibit a higher stability limit than their pure components, due to the redistribution process occurring at high temperature.

The increased understanding of real-gas dynamics will enable to improve the design of Organic Rankine Cycle Engines, to be used in small scale energy production from biomasses, binary geothermal systems and concentrating solar thermal power plants.

Keywords of the ERC project: Fluid mechanics, Non-ideal compressible-fluid flows, non-classical flows, thermodynamics, binary mixtures, siloxane fluids, turbomachinery

Keywords that characterize the scientific profile of the potential visiting researcher/s: Fluid mechanics, Non-ideal compressible-fluid flows, non-classical flows, thermodynamics, binary mixtures, siloxane fluids, turbomachinery
Transport, mixing and reaction of solutes and particles in natural media are of central importance in many fields of science and engineering, ranging from contaminant dispersion in geophysical flows to diffusion in living cells. Transport in these intrinsically heterogeneous media is characterized by early and late solute and particle arrivals, tailed spatial distributions, and scale effects in measured parameters. These behaviors cannot be explained by available models based on Fick’s law and are called anomalous despite their ubiquity. The origin of such phenomena lies in heterogeneity-induced mixing processes that lead to fluctuations in chemical concentration, or, in other words, to physical non-equilibrium. Current transport formulations based on the advection-dispersion-reaction equation or phenomenological non-equilibrium models lack the relation to the heterogeneity controls, fail to describe mixing and concentration variability and thus are not suited for the quantification of chemical reactions. The main objective of this proposal is to establish a global predictive framework that quantifies mixing across scales, anomalous transport and reaction, and dynamic uncertainty for heterogeneous media. We propose an integrated approach that links the interrelated phenomena of mixing, anomalous transport and chemical reaction. In short, the idea consists in quantifying microscale heterogeneity-induced mixing in terms of the flow kinematics and heterogeneity structure and linking it to transport through its relation to Lagrangian particle dynamics. These dynamics will be quantified stochastically by a novel generalized continuous time random walk approach and used to model chemical reactions under physical non-equilibrium in order to obtain a new solid approach for simulating reactive and conservative transport through natural media.

Keywords of the ERC project: mixing, dispersion, reaction, flow, groundwater, heterogenous media, anomalous transport, upscaling

Keywords that characterize the scientific profile of the potential visiting researcher/s:
Plasma-assisted development and functionalization of electrospun mats for tissue engineering purposes

In this project, I will explore the unique combination of two fascinating research themes: electrospinning and plasma technology. Electrospun nanofibrous matrices (so-called mats) are an exciting class of materials with a wide range of possible applications. Nevertheless, the development and functionalization of these electrospun materials remain very challenging tasks. Atmospheric pressure plasma technology will be utilized by my research group to create advanced biodegradable electrospun mats with unprecedented functionality and performance. To realise such a major breakthrough, plasma technology will be implemented in different steps of the manufacturing process: pre-electrospinning and post-electrospinning. My group will focus on four cornerstone research lines, which have been carefully chosen so that all critical issues one could encounter in creating advanced biodegradable electrospun mats are tackled. Research cornerstone A aims to develop biodegradable electrospun mats with appropriate bulk properties, while in research cornerstone B pre-electrospinning polymer solutions will be exposed to non-thermal atmospheric plasmas. This will be realized by probing unexplored concepts such as discharges created inside polymer solutions. In a third cornerstone C, an in-depth study of the interactions between an atmospheric pressure plasma and an electrospun mat will be carried out. Finally, the last cornerstone D will focus on plasma-assisted surface modification of biodegradable electrospun mats for tissue engineering purposes. Realization of these four cornerstones would result in a major breakthrough in their specific field which makes this proposal inherently a relatively high risk/very high gain proposal. I therefore strongly believe that this research program will open a whole new window of opportunities for electrospun materials with a large impact on science and society.

Keywords of the ERC project: non-thermal plasma, electrospinning, surface modification, biomaterials

Keywords that characterize the scientific profile of the potential visiting researcher/s: electrospinning, surface modification, biomaterials
The meaning of solar energy for future decentralized power supply will largely depend on both efficiency and cost of solar to electrical power conversion. All kinds of conversion strategies including photovoltaics, concentrated solar power, solar to fuel and others would benefit from efficiently collecting solar power on large areas. For this reason luminescent solar concentrators have been developed for over thirty years, but due to waveguide losses their maximum size is still limited to a few centimeters. The proposed project suggests the exploitation of a new type of electromagnetic waveguide in order to realize passive planar concentrators of unsurpassed collection efficiency, size, concentration, lifetime and costs. A dielectric TE1-mode shows a node, a position in the waveguide where no intensity is found. A thin film placed in this node remains largely “invisible” for the propagating mode. Such dielectric node modes (DNMs) have been investigated by the applicant in previous work, but only recently a silver island film (SIF) was for the first time placed in such a node. The resulting extremely low waveguide losses cannot be explained by our current understanding of waveguide modes and hint to a hybridization between the SIF-bound long-range surface plasmon polaritons (LRSPPs) and the DNMs into what we call hybrid node modes (HNMs). The SIFs strongly interact with incident light. An appropriate nanopatterning of SIFs enables efficient excitation of low-loss HNMs modes collecting solar power over square meters and concentrating it. To achieve this goal new technological methods are used that enable patterning on the nanometer scale and low cost roll-to-roll processing at the same time. New measurement techniques and numerical simulation tools will be developed to investigate the HNMs – a novel kind of electromagnetic modes – and their exploitation in the passive solar concentrators.

Keywords of the ERC project: optics, plasmonics, thin films, light concentrators

Keywords that characterize the scientific profile of the potential visiting researcher/s: optics, plasmonics, thin film technology
The aim of this project is to forge a physical understanding of the transitions and of the turbulent flow of semi-dilute/dense non-colloidal suspensions, for different particle features and suspending fluids. It is estimated that 10% of the world energy consumption is due to the transport and handling of granular materials of which particle suspensions are an important part. A deep understanding of the mechanisms underlying the flow of particle suspensions, the transition to turbulence and the turbulence characteristics is crucial for many important practical applications involving engineered complex fluids, such as pastes and paper pulp. A better prediction and control of the flow of suspensions will therefore have a huge impact.

Complex fluids are multiscale by nature where the physics at the microscale affects the macroscopic behaviour of the flow and vice versa giving rise to surprising and spectacular phenomena as well as making this one of the most important practical problem still to solve. Investigating the mechanisms by which the system microstructure determines the macroscopic flow properties and vice versa will not only give valuable insights into the nature of flowing suspensions but also will also lead to new ways to model and control it. Future generations of engineering CFD tools will have to contain models for complex suspensions. The fundamental approach proposed here, combined with challenging scientific and engineering examples backed up by experimental evidence, will make this possible and demonstrate it to a wider engineering community. The proposed project is based on highly accurate simulations of multiphase flow systems and state-of-the-art experiments. Such a holistic approach will enable us to understand the underlying mechanisms of instabilities and suspension turbulence and to develop accurate criteria for their prediction far in advance of what we could achieve with either approach separately.

Keywords of the ERC project: particle-laden flows, multiphase turbulent flows, numerical simulations, heat transfer in suspensions

Keywords that characterize the scientific profile of the potential visiting researcher/s: particle-laden flows, experimental particle-laden flows, computational algorithms for multiphase flows
Stability Islands: Performance Revolution in Machining

Cutting went through a revolution in the 1990s when high-speed milling (HSM) was introduced: the sculpture-like workpieces produced with high precision and efficiency resulted in one order of magnitude less parts in cars/aircrafts, which kept this traditional technology competitive at the turn of the century. This has been followed by an incremental development when not just the cutting speeds, but depths of cut and feed rates are pushed to limits, too.

The limits are where harmful vibrations occur. Cutting is subject to a special one called chatter, which is originated in a time delay: the cutting edge interferes with its own past oscillation recorded on the wavy surface cut of the workpiece. In 1907, the 3rd president of ASME, Taylor wrote: “Chatter is the most obscure and delicate of all problems facing the machinist”.

In spite of the development of the theory of delay-differential equations and nonlinear dynamics, Taylor’s statement remained valid 100 years later when HSM appeared together with a new kind of chatter. The applicant has been among those leading researchers who predicted these phenomena; the experimental/numerical techniques developed in his group are widely used to find parameters, e.g. where milling tools with serrated edges and/or with varying helix angles are advantageous.

The SIREN project aims to find isolated parameter islands with 3-5 times increased cutting efficiency. The work-packages correspond to points of high risk: (1) validated, delay-based nonlinear modelling of the dynamic contact problem between chip and tool; (2) fixation of the tool that is compatible with a dynamically reliable mathematical model of the contact between tool and tool-holder; (3) up-to-date dynamic modelling of the spindle at varying speeds.

High risk originates in the attempt of using distributed delay models, but high gain is expected with robust use of parameter islands where technology reaches a breakthrough in cutting efficiency for the 21st century.

**Keywords of the ERC project:** Time delayed mechanical systems, chatter, modelling of cutting, modelling of dynamic contacts, damping, friction

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** chip-formation, finite element modelling, dissipation, friction, contact force distribution, electric resistance, rotating spindle, bearing stiffness and damping, contactless measurement, semi-virtual machining, hardware-in-the-loop
Advances in transportation, energy harvesting, chemical processing, climatology, atmospheric and marine pollution are obstructed by the lack of understanding of turbulence. The turbulent energy transfer toward small-scales is characterized by highly non-Gaussian and out-of-equilibrium fluctuations that cannot be described by mean-field theories or traditional closure approximations. State-of-the-art computers and algorithms do not allow to perform brute-force direct numerical simulations of any realistic turbulent configuration: modelling is mandatory. On the other hand, turbulence models are often strongly limited by our lack of understanding of fundamental mechanisms. As a result, we have a deadlock: turbulence is thought of as ‘unsolvable’ theoretically and computationally ‘intensive’. Indeed, progress by using conventional methods has been slow. Last year, however, something new happened. Two unconventional conceptual and numerical methodologies to study Navier-Stokes equations appeared based on: (i) a surgery of nonlinear interactions with different Energy and Helicity contents, (ii) a fractal-Fourier decimation. These unexplored tools are potential breakthroughs to unravel the basic mechanisms governing the turbulent transfer in isotropic, anisotropic and bounded flows, e.g. the mechanism behind the growth of small-scales vorticity and formation/stability of coherent structures, a challenge that has defeated all numerical and theoretical attempts, up to now. The ultimate goal of NewTURB is to integrate the fresh knowledge achieved by using these novel numerical instruments to push forward the frontiers of turbulence modelling, exploiting the possibility to reduce the number-of-degrees-of-freedom in an innovative way to deliver alternative frontier ‘multiscale eddy-simulations’ methodologies for both unbounded and bounded flows with smooth walls or with heterogeneous landscapes, e.g. flows over a rough surface.

**Keywords of the ERC project:** turbulence, direct numerical simulations, large eddy simulations, atmospheric flows

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** turbulence, direct numerical simulations, large eddy simulations, dynamical systems, atmospheric flows, magnetohydrodynamics, out-of-equilibrium statistical mechanics, turbulent diffusion
I will develop an all new type of reactor for pharmaceutical and chemical process applications – the ‘tuneable membrane reactor’. These contain ground-breaking conducting polymer composite membranes that will allow in-situ tuning of the molecular selectivity for both neutral and charged species through them. This is revolutionary: current state-of-the-art membranes can be electrically tuned for charged species only. The project is timely, developing a new technology that can give the EU a competitive advantage for our declining pharmaceutical and (petro)chemical manufacturing base and builds on my recent research innovations. To do this, my team of 3 PDRAs, 3 PhDs and I will develop unique stable polymer-polymer acid-nanoparticle composite membranes that can be externally electrically tuned to different pore sizes and/or molecular selectivity, uniquely tuning for neutral and charged species. We will characterise the chemical, physical and transport mechanisms responsible for the membrane tuneability and relate these to transport models. We will then determine the feasibility of applying these unique tuneable membranes into membrane reactors, to allow in-situ external control of two key reactor parameters currently not possible: (1) Membrane fouling - membrane pore size/free volume and charge will be changed by applied potential allowing the fouling layer to be pushed off/through the membrane. (2) Precise external control of the reactant and product spectrum in the reactor by modifying species retention. By doing this, these tuneable membranes can be used to control the reaction rate, emissions and catalyst retention to maximise reaction rate and selectivity. This increases energy efficiency and emission control, helping the EU 20-20-20 environmental targets to be met. The overall impact applies beyond the project – we will be able to increase the control of membrane separations used worldwide, helping industries including food, water, healthcare and chemicals.

**Keywords of the ERC project:** membrane reactor, stimuli responsive materials, homogeneous catalysis, pharma synthesis, membrane separations, nanofiltration, smart materials

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** membrane reactor, stimuli responsive materials, homogeneous catalysis, pharma synthesis, membrane separations, nanofiltration, smart materials
Many therapeutic applications of stem cells require accurate control of their differentiation. To this purpose there is a major ongoing effort in the development of advanced culture substrates to be used as “synthetic niches” for the cells, mimicking the native ones. The goal of this project is to use a synthetic niche cell culture model to test my revolutionary hypothesis that in stem cell differentiation, nuclear import of gene-regulating transcription factors is controlled by the stretch of the nuclear pore complexes. If verified, this idea could lead to a breakthrough in biomimetic approaches to engineering stem cell differentiation. I investigate this question specifically in mesenchymal stem cells (MSC), because they are adherent and highly mechano-sensitive to architectural cues of the microenvironment. To verify my hypothesis I will use a combined experimental-computational model of mechanotransduction. I will a) scale-up an existing three-dimensional synthetic niche culture substrate, fabricated by two-photon laser polymerization, b) characterize the effect of tridimensionality on the differentiation fate of MSC cultured in the niches, c) develop a multiphysics/multiscale computational model of nuclear import of transcription factors within differentially-spread cultured cells, and d) integrate the numerical predictions with experimentally-measured import of fluorescently-labelled transcription factors. This project requires the synergic combination of several advanced bioengineering technologies, including micro/nano fabrication and biomimetics. The use of two-photon laser polymerization for controlling the geometry of the synthetic cell niches is very innovative and will highly impact the fields of bioengineering and biomaterial technology. A successful outcome will lead to a deeper understanding of bioengineering methods to direct stem cell fate and have therefore a significant impact in tissue repair technologies and regenerative medicine.

Keywords of the ERC project: mechanobiology, two-photon polymerization, nanofabrication, stem cell, bioengineering, biomechanics

Keywords that characterize the scientific profile of the potential visiting researcher/s: live imaging, confocal, molecular biology, biotechnology
Localization in biomechanics and mechanobiology of aneurysms: Towards personalized medicine

Rupture of Aortic Aneurysms (AA), which kills more than 30,000 persons every year in Europe and the USA, is a complex phenomenon that occurs when the wall stress exceeds the local strength of the aorta due to degraded properties of the tissue. The state of the art in AA biomechanics and mechanobiology reveals that major scientific challenges still have to be addressed to permit patient-specific computational predictions of AA rupture and enable localized repair of the structure with targeted pharmacologic treatment. A first challenge relates to ensuring an objective prediction of localized mechanisms preceding rupture. A second challenge relates to modelling the patient-specific evolutions of material properties leading to the localized mechanisms preceding rupture. Addressing these challenges is the aim of the BIOLOCHANICS proposal. We will take into account internal length-scales controlling localization mechanisms preceding AA rupture by implementing an enriched, also named nonlocal, continuum damage theory in the computational models of AA biomechanics and mechanobiology. We will also develop very advanced experiments, based on full-field optical measurements, aimed at characterizing localization mechanisms occurring in aortic tissues and at identifying local distributions of material properties at different stages of AA progression. A first in vivo application will be performed on genetic and pharmacological models of mice and rat AA. Eventually, a retrospective clinical study involving more than 100 patients at the Saint-Etienne University hospital will permit calibrating estimations of AA rupture risk thanks to our novel approaches and infuse them into future clinical practice. Through the achievements of BIOLOCHANICS, nonlocal mechanics will be possibly extended to other soft tissues for applications in orthopaedics, oncology, sport biomechanics, interventional surgery, human safety, cell biology, etc.

Keywords of the ERC project: mechanobiology, aneurysms, computational modelling, predictive/personnalized medicine,

Keywords that characterize the scientific profile of the potential visiting researcher/s: bioengineering
In-situ produced nanoparticles for enhanced oil recovery

The era of finding “easy oil” is coming to an end, and future supply will become more reliant on fossil fuels produced from enhanced oil recovery (EOR) process. Many EoR methods have been used, including mechanical, chemical, thermal and biological approaches, but there are still 50~70% of the original oil trapped in reservoir rocks after the primary and secondary recovery. NanoEOR, i.e, injecting nanoparticles (NPs) together with flooding fluids, is an emerging field. However all proposed applications are based on pre-fabricated NPs, which encountered enormous problems in NP stabilization and transport under reservoir conditions. This project proposes a revolutionary concept, iNanoEOR: in-situ production of NPs inside the reservoir for enhanced oil recovery. Rather than pre-manufacturing, dispersing and stabilizing NPs in advance, NPs will be produced in the reservoir by controlled hydrothermal reactions, acting as sensors to improve reservoir characterisation, or as property modifiers to effectively mobilize the trapped oil. This project will validate the innovative iNanoEOR concept by answering three questions: i) how the concept works? ii) what kind of NPs should be produced that can effectively mobilize trapped oil? iii) what are desired NP properties to allow them flow through a reservoir? Three work programs are designed, and a number of breakthroughs beyond state-of-art research are expected, which include i) proof-of-concept of the innovative iNanoEOR, ii) developing a new methodology for temperature measurement inside a reservoir, iii) revelation of the influence of NPs on EOR under reservoir-like conditions, iv) understanding the controlling factors in NP transport at different scales. The project will not only contribute directly to iNanoEOR, but also transfers the PI’s expertise in nanomaterials and multiphase flow into oil and gas sector and underpin many NP-related subsurface applications, which currently is non-existing in the Europe.

Keywords of the ERC project: nanotechnology, oil and gas, nanoparticle synthesis, controlled delivery

Keywords that characterize the scientific profile of the potential visiting researcher/s: nanomaterials, oil and gas, chemical engineering
The Materials Genome in Action

It is now possible to make an enormous spectrum of different, novel nanoporous materials simply by changing the building blocks in the synthesis of Metal Organic Frameworks (MOF) or related materials. This unique chemical tunability allows us to tailor-make materials that are optimal for a given application. The promise of finding just the right material seems remote however: because of practical limitations we can only ever synthesize, characterize, and test a tiny fraction of all possible materials. To take full advantage of this development, therefore, we need to develop alternative techniques, collectively referred to as Materials Genomics, to rapidly screen large numbers of materials and obtain fundamental insights into the chemical nature of the ideal material for a given application. The PI will tackle the challenge and promise posed by this unprecedented chemical tunability through the development of a multi-scale computational approach, which aims to reliably predict the performance of novel materials before synthesis. We will develop methodologies to generate libraries of representative sets of synthesizable hypothetical materials and perform large-scale screening of these libraries. These studies should give us fundamental insights into the common molecular features of the top-performing materials. The methods developed will be combined into an open access infrastructure in which our hypothetical materials are publicly accessible for data mining and big-data analysis.

The project is organized in three Work Packages, each centered around finding better materials for carbon capture: (1) screen materials for gas separations and develop the tools to predict the best materials for carbon capture; (2) gain insights into and develop a computational methodology for screening the mechanical properties of nanoporous materials; (3) achieve an understanding of the amine-CO2 chemistry in diamine-appended MOFs and use this to predict their performance.

Keywords of the ERC project: Molecular simulations, metal organic frameworks, materials genome

Keywords that characterize the scientific profile of the potential visiting researcher/s: molecular dynamics, monte carlo simulations, materials genome
The development of science and technology provides the availability of sophisticated products but concurrently, increases the use of combustible materials, in particular organic materials. Those materials are easily flammable and must be flame retarded to make them safer. In case of fire, people must be protected by materials confining and stopping fire. It is one of the goals of the FireBar-Concept project to design materials and assembly of materials exhibiting low flammability, protecting substrates and limiting fire spread. The objective of FireBar-Concept is to make a fire barrier formed at the right time, at the right location and reacting accordingly against thermal constraint (fire scenario). This fire barrier can be developed in several ways according to the chemical nature of the material and/or of its formulation: - Heat barrier formed by inherently flame retarded materials (e.g. mineral fibers, ceramic ...) and exhibiting low thermal conductivity (note the assembly of those materials can also provide low thermal conductivity controlling porosity and its distribution)- Evolution of reactive radicals poisoning the flame and forming a protective ‘umbrella’ avoiding the combustion of the material- Additives promoting charring of the materials and forming an expanding carbonaceous protective coating or barrier (intumescence)- Additives forming a physical barrier limiting mass transfer of the degradation products to the flameThe FireBar-Concept project is multidisciplinary and it requires expertise in material science, chemical engineering, chemistry, thermal science and physics. The approach is to make 5 actions linked together by transverse developments (3) according to this scheme: (i) fundamentals of fire barrier, (ii) multi-material and combination of concepts, (iii) modeling and numerical simulation, (iv) design and development of experimental protocols and (v) optimization of the systems.

**Keywords of the ERC project:** fire protection, reaction to fire, flame retardant, flame retard polymer

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** flame retardant, thermo-optical properties, numerical modeling, geopolymer, organic synthesis, biomimetics
Control for Orbit Manoeuvring through Perturbations for Application to Space Systems

Space benefits mankind through the services it provides to Earth. Future space activities progress thanks to space transfer and are safeguarded by space situation awareness. Natural orbit perturbations are responsible for the trajectory divergence from the nominal two-body problem, increasing the requirements for orbit control; whereas, in space situation awareness, they influence the orbit evolution of space debris that could cause hazard to operational spacecraft and near Earth objects that may intersect the Earth. However, this project proposes to leverage the dynamics of natural orbit perturbations to significantly reduce current extreme high mission cost and create new opportunities for space exploration and exploitation.

The COMPASS project will bridge over the disciplines of orbital dynamics, dynamical systems theory, optimisation and space mission design by developing novel techniques for orbit manoeuvring by “surfing” through orbit perturbations. The use of semi-analytical techniques and tools of dynamical systems theory will lay the foundation for a new understanding of the dynamics of orbit perturbations. We will develop an optimiser that progressively explores the phase space and, though spacecraft parameters and propulsion manoeuvres, governs the effect of perturbations to reach the desired orbit. It is the ambition of COMPASS to radically change the current space mission design philosophy: from counteracting disturbances, to exploiting natural and artificial perturbations.

COMPASS will benefit from the extensive international network of the PI, including the ESA, NASA, JAXA, CNES, and the UK space agency. Indeed, the proposed idea of optimal navigation through orbit perturbations will address various major engineering challenges in space situation awareness, for application to space debris evolution and mitigation, missions to asteroids for their detection, exploration and deflection, and in space transfers, for perturbation-enhanced trajectory design.

Keywords of the ERC project: Orbit perturbations, space trajectory design, optimisation, spacecraft dynamics, space debris, asteroids, astrodynamics, manifold dynamics, dynamical system theory in astrodynamics, semi-analytical methods, space missions

Keywords that characterize the scientific profile of the potential visiting researcher/s: applied mathematics, dynamical system theory, computer science, space engineer, physics, astronomy
Smart Monitoring, Inspection and Life-Cycle Assessment of Wind Turbines

The excessive energy consumption that Europe is faced with, calls for sustainable resource management and policy-making. Amongst renewable sources of the global energy pool, wind energy holds the lead. Nonetheless, wind turbine (WT) facilities are conjoined with a number of shortcomings relating to their short life-span and the lack of efficient management schemes. With a number of WTs currently reaching their design span, stakeholders and policy makers are convinced of the necessity for reliable life-cycle assessment methodologies. However, existing tools have not yet caught up with the maturity of the WT technology, leaving visual inspection and offline non-destructive evaluation methods as the norm. This proposal aims to establish a smart framework for the monitoring, inspection and life-cycle assessment of WTs, able to guide WT operators in the management of these assets from cradle-to-grave. Our project is founded on a minimal intervention principle, coupling easily deployed and affordable sensor technology with state-of-the-art numerical modeling and data processing tools. An integrated approach is proposed comprising: (i) a new monitoring paradigm for WTs relying on fusion of structural response information, (ii) simulation of influential, yet little explored, factors affecting structural response, such as structure-foundation-soil interaction and fatigue (ii) a stochastic framework for detecting anomalies in both a short- (damage) and long-term (deterioration) scale. Our end goal is to deliver a “protection-suit” for WTs comprising a hardware (sensor) solution and a modular readily implementable software package, titled ETH-WINDMIL. The suggested kit aims to completely redefine the status quo in current Supervisory Control And Data Acquisition systems. This pursuit is well founded on background work of the PI within the area of structural monitoring, with a focus in translating the value of information into quantifiable terms and engineering practice.

Keywords of the ERC project: wind turbines, sustainability, life cycle assessment, structural health monitoring, structural identification, multi fidelity modeling, decision support tools, infrastructure management

Keywords that characterize the scientific profile of the potential visiting researcher/s: wind turbines, life cycle assessment, structural health monitoring, structural identification, multi fidelity modeling, decision support tools
Intelligent functional glazing with self-cleaning properties to improve the energy efficiency of the built environment

The latest forecast by the International Energy Agency predicts that the CO2 emissions from the built environment will reach 15.2Gt in 2050, double their 2007 levels. Buildings consume 40% of the primary energy in developed countries with heating and cooling alone accounting for 63% of the energy spent indoors. These trends are on an ascending trajectory - e.g. the average energy demand for air-conditioning has been growing by ~17% per year in the EU. Counterbalancing actions are urgently required to reverse them.

The objective of this proposal is to develop intelligent window insulation technologies from sustainable materials. The developed technologies will adjust the amount of radiation escaping or entering a window depending upon the ambient environmental conditions and will be capable of delivering unprecedented reductions to the energy needed for regulating the temperature in commercial and residential buildings.

Recognising the distinct requirements between newly built and existing infrastructure, two parallel concepts will be developed: i) A new class of intelligent glazing for new window installations, and, ii) a flexible, intelligent, polymer film to retrofit existing window installations. Both solutions will be enhanced with unique self-cleaning properties, bringing about additional economic benefits through a substantial reduction in maintenance costs.

Overall, we aim to develop intelligent glazing technologies that combine: i) power savings of >250 W/m² of glazing capable of delivering >25% of energy savings and efficiency improvements >50% compared with existing static solutions; ii) visible transparency of >60% to comply with the EU standards for windows ,and, iii) self-cleaning properties that introduce a cost balance.

A number of technological breakthroughs are required to satisfy such ambitious targets which are delivered in this project by the seamless integration of nanotechnology engineering, novel photonics and advanced material synthesis.

Keywords of the ERC project: transition metal oxides, vanadium dioxide, tuneable plasmonics, thermochromic windows, smart windows, smart materials, superhydrophobic surfaces, antireflection coatings, nanotechnology, nanophotonics

Keywords that characterize the scientific profile of the potential visiting researcher/s: nanotechnology, nanophotonics, metamaterials, plasmonics, nanofabrication, finite difference time domain, heat transport, radiative cooling, thermochromic materials, transition metal oxides, superhydrophobic surfaces, thermodynamics
Breaking the temperature limits of Solid Oxide Fuel Cells: Towards a new family of ultra-thin portable power sources

Solid Oxide Fuel Cells (SOFCs) are one of the most efficient and fuel flexible power generators. However, a great limitation on their applicability arises from temperature restrictions. Operation approaching room temperature (RT) is forbidden by the limited performance of known electrolytes and cathodes while typical high temperatures (HT) avoid their implementation in portable applications where quick start ups with low energy consumption are required. The ULTRASOFC project aims breaking these historical limits by taking advantage of the tremendous opportunities arising from novel fields in the domain of the nanoscale (nanoionics or nano photochemistry) and recent advances in the marriage between micro and nanotechnologies. From the required interdisciplinary approach, the ULTRASOFC project addresses materials challenges to (i) reduce the operation to RT and (ii) technological gaps to develop ultra-low-thermal mass structures able to reach high T with extremely low consumption and immediate start up.

A unique μSOFC technology fully integrated in ultrathin silicon will be developed to allow operation with hydrogen at room temperature and based on hydrocarbons at high temperature. Stacking these μSOFCs will bring a new family of ultrathin power sources able to provide 100 mW at RT and 5W at high T in a size of a one-cent coin. A stand-alone device fuelled with methane at HT will be fabricated in the size of a dice. Apart from breaking the state-of-the-art of power portable generation, the ULTRASOFC project will cover the gap of knowledge existing for the migration of high T electrochemical devices to room temperature and MEMS to high T. Therefore, one should expect that ULTRASOFC will open up new horizons and opportunities for research in adjacent fields like electrochemical transducers or chemical sensors. Furthermore, new technological perspectives of integration of unconventional materials will allow exploring unknown devices and practical applications.

Keywords of the ERC project:
Keywords that characterize the scientific profile of the potential visiting researcher/s:
Glasses have traditionally been enabling materials to major societal challenges. Significant breakthroughs on many areas of technological progress have been very closely linked to the exploitation of glassy materials. It is strong consensus that this key role will persist in the emerging solutions to major global challenges in living, energy, health, transport and information processing, provided that the fundamental limitations of the presently available empirical or semi-empirical approaches to glass processing can be overcome.

In the coming decade, it is therefore a major task to take the step towards ab initio exploitation of disordered materials through highly-adapted processing strategies. This requires pioneering work and in-depth conceptual developments which combine compositional design, structural evolution and the thermo-kinetics of material deposition into holistic tools. Only those would significantly contribute to solving some of the most urgent materials needs for glass applications in functional devices, be it in the form of thin films, particles or bulk materials.

The present project challenges today’s engineering concepts towards the conception of such tools. For that, melt deposition, isothermal deposition from liquid phases, and gas-phase deposition of non-crystalline materials will be treated - within the class of inorganic glasses - in a generalist approach, unified by the understanding that glass formation represents the only strict deviation from self-organization, and that, hence, the evolution of structural complexity in glassy materials can be tailored on any length-scale through adequate processing. Providing a topological scheme for the quantification and chemical tailoring of structural complexity, UTOPES will answer to the challenge of finding order in disorder, and will thus break the grounds for the third generation of glasses with properties beyond what is presently thought as the limits of physical engineering.

Keywords of the ERC project: glass; photonics; optical materials; energy

Keywords that characterize the scientific profile of the potential visiting researcher/s: glass; photonics; optical materials; energy
Microscale Processes Governing Global Sustainability

Reactive transport modelling is a key tool in understanding the extremely complex interplay of flow, transport and reactions occurring over various temporal and spatial scales in the subsurface. The most difficult challenge in reactive transport is the capture of scale dependence, and upscaling reactive transport will ultimately only be successful if there is a detailed understanding of fundamental mechanisms at the pore level and the supporting data are available. State-of-the-art tools (e.g. X-ray microtomography and on-chip porous media) are not sufficient to understand reactive flow, as they do not provide real-time mapping of propagation of fronts (e.g. temperature, pressure, concentration) that are critical to refine and validate simulations. The ambition is to progress beyond the state of the art via additive manufacturing tools to print 3D replicas of porous cores that enable monitoring the properties within the pores. Our unique approach is to develop for the first time three-dimensional instrumented replicas of porous structures, so we can gain much needed dynamic data at the pore scale that can be incorporated into validated simulations coupling flow and reactive transport processes. We combine expertise and integrating ground-breaking work in: (i) additive manufacturing to produce three dimensional replicas of porous structures; (ii) tools to embed sensors to determine in-vivo propagation of fronts (pressure, temperature, pH) within complex structures; and (iii) novel high-fidelity in-silico pore models coupling relative permeability functions and critical saturations with compositional changes and validated using virtual reality tools. The ERC MILEPOST project will transform our ability to analyse and predict the behaviour of a wide range of pore-scale processes governing the macroscopic behaviour of complex subsurface systems and open up new horizons for science in other areas, e.g porosity controlled in polymers and bioprinting.

Keywords of the ERC project: Reactive transport, Porous media, Chemical rates, Pore modelling, 3D micromodels

Keywords that characterize the scientific profile of the potential visiting researcher/s: flow in porous media, 3D printing, embedding sensors
Combustion is an extremely important field for our society. The development of new, step-change technologies is essential and greatly benefits from computational design. However, turbulent combustion physics are complex, highly non-linear, of multi-scale and multi-physics nature, and involve interactions at many time-scales. This makes modeling quite challenging such that accurate predictive models, especially for the formation of pollutants, are not available. Today, the two major challenges for developing predictive simulations of turbulent combustion are first to account for its multi-scale nature by considering the non-universal behavior of small-scale turbulence, which is known to be critically important for turbulence-chemistry interactions, and second, to provide data in sufficient detail for rigorous analysis of model deficiencies and unambiguous model development. These two issues are addressed in the proposed work. The main overall objectives are: 1) Establish a new multi-scale framework to analyze and model turbulent combustion phenomena based on a new way to describe turbulence using so-called dissipation elements, which are space-filling regions in a scalar field allowing to capture its small-scale morphology and non-universality. 2) Create new unprecedented datasets using direct numerical simulations (DNS) and provide new analysis methods to develop and validate combustion models; this will include automatically reducing and optimizing chemical kinetic mechanisms for use in DNS and developing an on-the-fly chemistry reduction technique. 3) Apply new modeling approaches to complex and highly non-linear modeling questions, such as pollutant formation in turbulent spray combustion. The successful outcome of the project will provide new and unprecedented datasets, a quantitative description of the impact of non-universality in small-scale turbulence on different aspects of turbulent combustion, and the basis for an entirely new multi-scale closure.

Keywords of the ERC project: Turbulent Combustion, Dissipation Elements, Direct Numerical Simulation, Large Eddy Simulation

Keywords that characterize the scientific profile of the potential visiting researcher/s:
Monitoring bone healing around endosseous implants: from multiscale modeling to the patient’s bed

Implants are often employed in orthopaedic and dental surgeries. However, risks of failure, which are difficult to anticipate, are still experienced and may have dramatic consequences. Failures are due to degraded bone remodeling at the bone-implant interface, a multiscale phenomenon of an interdisciplinary nature which remains poorly understood. The objective of BoneImplant is to provide a better understanding of the multiscale and multitime mechanisms at work at the bone-implant interface. To do so, BoneImplant aims at studying the evolution of the biomechanical properties of bone tissue around an implant during the remodeling process. A methodology involving combined in vivo, in vitro and in silico approaches is proposed. New modeling approaches will be developed in close synergy with the experiments. Molecular dynamic computations will be used to understand fluid flow in nanoscopic cavities, a phenomenon determining bone healing process. Generalized continuum theories will be necessary to model bone tissue due to the important strain field around implants. Isogeometric mortar formulation will allow to simulate the bone-implant interface in a stable and efficient manner.

In vivo experiments realized under standardized conditions will be realized on the basis of feasibility studies. A multimodality and multi-physical experimental approach will be carried out to assess the biomechanical properties of newly formed bone tissue as a function of the implant environment. The experimental approach aims at estimating the effective adhesion energy and the potentiality of quantitative ultrasound imaging to assess different biomechanical properties of the interface.

Results will be used to design effective loading clinical procedures of implants and to optimize implant conception, leading to the development of therapeutic and diagnostic techniques. The development of quantitative ultrasonic techniques to monitor implant stability has a potential for industrial transfer.

Keywords of the ERC project: Bone, Implant, Biomechanics, ultrasound, modeling, simulation, osseointegration, acoustics, mechanical engineering, Medical engineering and technology, mechanical engineering, signal processing, mechanotransduction, micromechanics, orthopedic surgery, dental surgery, implantology, material characterization, biorheology

Keywords that characterize the scientific profile of the potential visiting researcher/s: Bone, Implant, Biomechanics, ultrasound, modeling, simulation, osseointegration, acoustics, mechanical engineering, Medical engineering and technology, mechanical engineering, signal processing, mechanotransduction, micromechanics, orthopedic surgery, den
Exploring the Plurality of New Worlds: Their Origins, Climate and Habitability

Recent surveys have revealed an amazing, and yet unexplained, diversity of planets orbiting other stars. The key to understanding and exploiting this diversity is to study their atmospheres. This is because exoplanets’ atmospheres are unique laboratories that hold the potential to transform our understanding of planet formation, physics, and habitability. This is a new opportunity to place the Solar System and the Earth’s ecosystem in a broader context; one of the main goals of modern astrophysics. The aim of this proposal is to leverage exoplanet detections, as well as observational capabilities and theoretical frameworks, to deepen and broaden our understanding of planetary physics. This project will transform the field of exoplanet atmospheres by contributing to three major advances. We will: i) push exoplanet characterization new frontiers by providing the largest in-depth study of atmospheres through the measurements of precise spectra, and the retrieval of their composition, in order to constrain their origins; ii) reveal for the first time global exo-climate through a novel method to probe atmospheric structure and dynamics; and iii) pioneer an innovative approach that uses robotic small telescopes to estimate the impact of stellar radiation on atmospheres, with a particular focus on their habitability. Theses objectives will be achieved via an ambitious portfolio of cutting-edge observations, combined with state-of-the-art modelling for their interpretation. Their accomplishment would be a major breakthrough, culminating in a comprehensive comparative exoplanetology, which in turn will open up new key discoveries in planetary formation and evolution. Our expertise will also enable predictions on conditions for habitability and direct the search atmospheric biosignatures with upcoming capabilities. The impact of our discoveries will go well beyond the scientific community since the quest of our origins is of interest to mankind.

Keywords of the ERC project: Astronomy, Planetary Systems Sciences, Exoplanets, Exoplanets atmospheres, Observations, exoplanets, exoplanet atmospheres, bio-signatures, planets, stars

Keywords that characterize the scientific profile of the potential visiting researcher/s: Exoplanets, planet atmospheres, exoplanet characterization, stellar astrophysics, astrobiology, biosignatures, exoplanets, exoplanet atmospheres, bio-signatures, planets, stars
Supernovae: Physics and Cosmology in the Next Decade

Exploding stars, or supernovae, impact upon many diverse areas of astrophysics, from galaxy formation, to stellar evolution, to cosmology and studies of dark energy. I am playing a leading role in new, wide-field, high-cadence optical surveys that are revolutionising the study of supernovae, searching vast volumes of space, locating hundreds of events to study their demographics in detail, and uncovering new and bizarre types of explosions. In concert with a major European Southern Observatory public spectroscopic survey, PESSTO, these imaging surveys will provide an extraordinary dataset for understanding all facets of the supernova and explosive transient population. My work will perform several tests of the progenitors and physics of the classical type Ia supernovae in an attempt to understand how these crucial standard candles depend on their progenitor stellar populations. I will use these results to inform a new generation of models of type Ia supernovae. I will this distill these results to make a detailed measurement of the dark energy that powers the accelerating universe in which we live, greatly improving upon existing measurements of the variation of dark energy over the last ten billion years. A final aspect of my research is an innovative search for superluminous supernovae: a new class of supernova explosion a hundred times brighter than traditional supernovae, capable of being studied in the very distant universe. These objects may become cosmology’s new standard candle, visible far beyond the reach of type Ia supernovae. My new search will significantly increase both the quantity and quality of superluminous supernova observations, allowing us to further our understanding of these enigmatic objects and use them in a cosmological setting for the first time.

Keywords of the ERC project: astrophysics; cosmology; supernovae; dark energy; stellar evolution

Keywords that characterize the scientific profile of the potential visiting researcher/s:

Modern cosmology assumes that General Relativity (GR) is the correct description of gravity on large scales. With this assumption and according to current data, the cosmological model needs in addition the existence of a Dark Sector: Dark Matter (DM) and Dark Energy (DE). We know very little about the nature of DM and it is yet to be detected experimentally. The simplest form of DE compatible with the data, a cosmological constant, has a value incompatible with our understanding of Quantum Field Theory. Given that the extrapolation of GR to cosmological scales has not been tested it is possible that the inference of the Dark Sector also needs to be revised. I propose to (i) determine the nature of DM and DE to a level not achieved before, (ii) test gravity on cosmological scales and (iii) test the screening of new gravitational degrees of freedom in the solar system. The first two goals will require the use of my general framework to parameterize field equations [Skordis, PRD 79, 123527 (2008); Baker, Ferreira & Skordis, PRD 87, 024015 (2013)]. My team will use this framework to construct simple models and observations to place limits on their parameters. We will employ the Cosmic Microwave Background (CMB) observations from ESA’s Planck Surveyor and the Atacama Cosmology Telescope. We will determine the sensitivity of the CMB lensing to the properties of DM and theories of gravity. To break possible degeneracies these data will be supplemented with large-scale structure data, weak lensing and red-shift space distortions. We will also perform forecasting for ESA’s EUCLID mission which will give us a handle on how well we will constrain GR with cosmology in the future. For the final goal (iii) we will employ the method of [Padilla & Saffin, JHEP 1207, 122 (2012)] to construct a perturbative expansion of theories that exhibit screening, inside the screening radius. We will determine the compatibility of such theories with solar system and other strong-field data.

Keywords of the ERC project: dark energy, dark matter, gravity, cosmology, future cosmological surveys

Keywords that characterize the scientific profile of the potential visiting researcher/s: dark energy, dark matter, gravity, cosmology, future cosmological surveys
It is now accepted that exoplanets are ubiquitous. However little is known about those planets we have detected beyond the fact they exist and their location. For a minority, we know their weight, size and orbital parameters. For less than twenty, we have some clues about their atmospheric temperature and composition. How do we progress from here?

We are still far from a hypothetical Hertzsprung–Russell diagram for planets and we do not even know whether there ever will be such classification for planets. The planetary parameters mass, radius and temperature alone do not explain the diversity revealed by current observations. The chemical composition of these planets is needed to trace back their formation history and evolution, as was the case for the Solar System.

Pioneering results were obtained through transit spectroscopy with Hubble, Spitzer and ground-based facilities, enabling the detection of ionic, atomic and molecular species and of the planet’s thermal structure. With the arrival of improved or dedicated instruments in the coming decade, planetary science will expand beyond the narrow boundaries of our Solar System to encompass our whole Galaxy.

In the next five years, ExoLights will address the following fundamental questions:

– Why are exoplanets as they are?
– What are the causes for the observed diversity?
– Can their formation history be traced back from their current composition and evolution?

New spectroscopic observations of a select sample of exoplanets’ atmospheres (~20 out of the 150 observable today) will be analysed with state-of-the-art statistical techniques and interpreted through a comprehensive set of spectral retrieval models, developed by the PI and her team. This programme, together with the homogeneous re-analysis of archive observations of a larger sample of exoplanets, will allow us to use the chemical composition as a powerful diagnostic of the history, formation mechanisms and evolution of gaseous and rocky exoplanets.

**Keywords of the ERC project:** Exoplanets, atmospheric physics, spectroscopy, space missions

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** Exoplanets, big data analysis techniques, planetary science

Galactic stellar nuclei are very common in all types of galaxies and are marked by the presence of nuclear star clusters, the densest and most massive star clusters in the present-day Universe. Their formation is still an unresolved puzzle. The centre of the Milky Way contains a massive black hole and a stellar nucleus and is orders of magnitude closer than any comparable target. It is the only galactic nucleus and the most extreme astrophysical environment that we can examine on scales of milli-parsecs. It is therefore a crucial laboratory for studying galactic nuclei and their role in the context of galaxy evolution. Yet, suitable data that would allow us to examine the stellar component of the Galactic Centre exist for less than 1% of its projected area. Moreover, the well-explored regions are extraordinary, like the central parsec around the massive black hole, and therefore probably not representative for the overall environment. Fundamental questions on the stellar population, structure and assembly history of the Galactic Centre remain therefore unanswered. This project aims at addressing the open questions by obtaining accurate, high-angular resolution, multi-wavelength near-infrared photometry for an area of several 100 pc$^2$, a more than ten-fold increase compared to the current state of affairs. The Galactic Centre presents unique observational challenges because of a combination of high extinction and extreme stellar crowding. It is therefore not adequately covered by existing or upcoming imaging surveys. I present a project that is specifically tailored to overcome these observational challenges. In particular, I have developed a key technique to obtain the necessary sensitive, high-angular resolution images with a stable point spread function over large, crowded fields. It works with a range of existing ground-based instruments and will serve to complement existing data to provide a global and detailed picture of the stellar nucleus of the Milky Way.

Keywords of the ERC project: Near infrared observational astronomy; stellar populations, Galactic Center, high angular resolution

Keywords that characterize the scientific profile of the potential visiting researcher/s: Near infrared observational astronomy; stellar populations, Galactic Center, high angular resolution, image analysis
A new window on the Universe: The formation and evolution of galaxy clusters and proto-clusters

The formation and evolution of clusters and proto-clusters of galaxies will be studied using unique diagnostic tools provided by the new pan-European radio telescope LOFAR and the APERTIF phased arrays on WSRT radio telescope. Combined with new ultra low frequency antennas (an extension to LOFAR here proposed), these new facilities will for the first time enable sensitive observations from the lowest possible frequencies accessible from the ground (~15 MHz) up to 1400 MHz. The guaranteed time projects (PI HR) to carry out ultradeep pointed observations and to survey the entire northern sky will be unique in terms of angular resolution, depth, and extremely large frequency range. This enables a coherent study of clusters of galaxies over the entire history of the universe up to the formation of the first proto-clusters. Studies of the associated shock waves produced by cluster mergers and the magnetic field properties of the cluster gas will constrain models of the formation of galaxy clusters. The large field of views of both LOFAR will enable the detection of radio emission from millions of star-forming galaxies up to z=2-3, at the epoch at which the bulk of galaxy formation is believed to have occurred. In combination with infrared surveys, the first significant sample of proto-clusters of galaxies will be obtained. This will enable the first complete study of the overall properties of proto-clusters and their galaxy contents. With LOFAR’s ability to pinpoint radio sources with extremely steep radio spectra, we will detect radio galaxies at unprecedented distances. As our previous radio and optical investigations have established that distant radio galaxies are often located in proto-clusters, the most distant LOFAR radio galaxies would be excellent targets to locate and study the first proto-clusters close to or even at the epoch of reionisation.

Keywords of the ERC project: radio astronomy, merging clusters, protoclusters, distant radio galaxies, epoch of deionisation, radio feedback

Keywords that characterize the scientific profile of the potential visiting researcher/s: radio astronomy, merging clusters, protoclusters, distant radio galaxies, epoch of deionisation, radio feedback
Cosmological Tests of Gravity

Einstein’s theory of General Relativity (GR) is tested accurately within the local universe i.e., the solar system, but this leaves open the possibility that it is not a good description at the largest scales in the Universe. The standard model of cosmology assumes GR as a theory to describe gravity on all scales. In 1998, astronomers made a surprising discovery that the expansion of the Universe is accelerating, not slowing down. This late-time acceleration of the Universe has become the most challenging problem in theoretical physics. Within the framework of GR, the acceleration would originate from an unknown “dark energy.” Alternatively, it could be that there is no dark energy and GR itself is in error on cosmological scales. The standard model of cosmology is based on a huge extrapolation of our limited knowledge of gravity. This discovery of the late time acceleration of the Universe may require us to revise the theory of gravity and the standard model of cosmology based on GR. The main objective of my project is to develop cosmological tests of gravity and seek solutions to the origin of the observed accelerated expansion of the Universe by challenging conventional GR. Upcoming surveys will make cosmological tests of gravity a reality in the next five years. There are remaining issues in developing theoretical frameworks for probing gravitational physics on cosmological scales. We construct modified gravity theories as an alternative to dark energy and analyse “screening mechanisms” to restore GR on scales where it is well tested. We then develop better theoretical frameworks to perform cosmological tests of gravity that include non-linear scales by exploiting our theoretical knowledge of the models and our state-of-the-art simulations. This grant will exploit and develop the world-leading position of the group initiated by Kazuya Koyama at the University of Portsmouth funded by the ERC starting grant (2008-2013).

Keywords of the ERC project: cosmology, dark energy, modified gravity, large scale structure
Keywords that characterize the scientific profile of the potential visiting researcher/s: postdoctoral researcher, lecturer, professor
Do intermediate-mass black holes exist?

With this proposed project I will determine whether intermediate-mass black holes (IMBHs) exist. I propose to use ESA’s new Gaia mission, the rich Hubble Space Telescope data archive, and state-of-the-art techniques to investigate systems predicted to exist but not yet found hitherto, such as recoiled hyper-compact stellar systems, red-supergiant mass donors to ultra-luminous X-ray sources, and white dwarf tidal disruption events. The latter can only be detected if black holes with masses less than 1E5 Msun are involved. Using these systems and events we can probe the sphere of influence of the IMBH and determine the black hole mass dynamically. Currently, there are strong indications for the existence of IMBHs, but dynamical evidence, the irrefutable proof of their existence, is still lacking. Whereas the unequivocal detection of an IMBH will be a breakthrough discovery in itself, it has also important consequences for searches of dark matter annihilation signals, it will provide a baseline for the rate predictions of gravitational wave radiation events involving IMBHs, and the properties of a population of IMBHs provides important constraints on the growth of supermassive black holes and galaxies. Finally, if we discover IMBHs in hyper-compact star clusters it validates numerical relativity simulations that predict that merging black holes receive a recoil kick. My membership of Gaia’s Data Processing and Analysis Consortium gives me a distinct advantage in analysing and interpreting Gaia data that, through the superb angular resolution, immediate spectroscopic observations and all-sky coverage, provides unique capabilities ideally suited for answering the question whether IMBHs exist. My proposed project is the first to recognize the potential of Gaia (WP1&2) as well as the implications of having red supergiant mass donors in some ultra-luminous X-ray sources (WP3) for answering the question on the existence of IMBHs.

Keywords of the ERC project: Intermediate-mass black holes, super-massive black holes

Keywords that characterize the scientific profile of the potential visiting researcher/s: Astronomer, post-doc, researcher
Dust in the wind — a new paradigm for inflow and outflow structures around supermassive black holes

Active galactic nuclei (AGN) represent the active growing phases of supermassive black holes. For the first time, we are able to resolve the dusty gas on parsec scales and directly test our standard picture of these objects. While this “unification scheme” relates the parsec-scale IR emission with a geometrically-thick disk, I have recently found that the bulk of the dust emission comes from the polar region of the alleged disk where gas is blown out from the vicinity of the black hole. Along with these polar features, the compactness of the dust distribution seems to depend on the accretion state of the black hole. Neither of these findings have been predicted by current models and lack a physical explanation.

To explain the new observations, I proposed a revision to the AGN unification scheme that involves a dusty wind driven by radiation pressure. Depending on their masses, velocities, and frequency, such dusty winds might play a major role in self regulating AGN activity and, thus, impact the interplay between host and black hole evolution. However, as of now we do not know if these winds are ubiquitous in AGN and how they would work physically. Upon completion of the research program, I want to

- characterise the pc-scale mass distribution, its kinematics, and the connection to the accretion state of the AGN,
- have a physical explanation of the dusty wind features and constrain its impacts on the AGN environment, and
- have established dust parallax distances to several nearby AGN, as a multi-disciplinary application of the constraints on the dust distribution.

For that, I will combine the highest angular resolution observations in the IR and sub-mm to create the first pc-scale intensity, velocity, and density maps of a sample of 11 AGN. I will develop a new model that combines hydrodynamic simulations with an efficient treatment of radiative transfer to simulate dusty winds. Finally, direct distances to 12 AGN with a combined 3% precision will be measured.

**Keywords of the ERC project:** astronomy, astrophysics, active galactic nuclei, cosmology

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** astronomy, astrophysics, active galactic nuclei, cosmology
This project focuses on Sun-like stars, which possess convective envelopes and universally exhibit magnetic activity (in the mass range 0.1 to 1.3 MSun). The rotation of these stars influences their internal structure, energy and chemical transport, and magnetic field generation, as well as their external magnetic activity and environmental interactions. Due to the huge range of timescales, spatial scales, and physics involved, understanding how each of these processes relate to each other and to the long-term evolution remains an enormous challenge in astrophysics. To face this challenge, the AWESoMeStars project will develop a comprehensive, physical picture of the evolution of stellar rotation, magnetic activity, mass loss, and accretion.

In doing so, we will
(1) Discover how stars lose the vast majority of their angular momentum, which happens in the accretion phase
(2) Explain the observed rotation-activity relationship and saturation in terms of the evolution of magnetic properties & coronal physics
(3) Characterize coronal heating and mass loss across the full range of mass & age
(4) Explain the Skumanich (1972) relationship and distributions of spin rates observed in young clusters & old field stars
(5) Develop physics-based gyrochronology as a tool for using rotation rates to constrain stellar ages.

We will accomplish these goals using a fundamentally new and multi-faceted approach, which combines the power of multi-dimensional MHD simulations with long-timescale rotational-evolution models. Specifically, we will develop a next generation of MHD simulations of both star-disk interactions and stellar winds, to model stars over the full range of mass & age, and to characterize how magnetically active stars impact their environments. Simultaneously, we will create a new class of rotational-evolution models that include external torques derived from our simulations, compute the evolution of spin rates of entire star clusters, & compare with observations.

Keywords of the ERC project: low-mass stars, stellar rotation, stellar magnetic activity, stellar winds, accretion, stellar evolution, angular momentum, MHD, numerical simulations

Keywords that characterize the scientific profile of the potential visiting researcher/s:
Stardust to asteroids: Unravelling the formation and earliest evolution of a habitable solar system

As far as we know, our solar system is unique. It could, in principle, be the only planetary system in the Universe to harbor intelligent life or, indeed, life at all. As such, attempting to reconstruct its history is one of the most fundamental pursuits in the natural sciences. Whereas astronomical observations of star-forming regions provide a framework for understanding the formation of low-mass stars and the early evolution of planetary systems in general, direct information about the earliest solar system can only come from primitive meteorites and their components and some differentiated meteorites that record the birth of the solar system.

The main objective of this proposal is to investigate the timescales and processes — including the role of supernovas — leading to the formation of the solar system by measurement of isotopic variations in meteorites. To achieve our objectives, we will integrate long-lived and short-lived radioisotope chronometers with the presence/absence of nucleosynthetic anomalies in various meteorites and meteoritic components. Our isotopic measurements will be obtained using state-of-the-art technologies such as second-generation mass spectrometers housed in laboratories directed by the PI and fully dedicated to cosmochemistry. This will allow us to: 1) define the mechanism and timescale for the collapse of the protosolar molecular cloud and emergence of the protoplanetary disk, 2) constrain the source and locale of chondrule-forming event(s) as well as the nature of the mechanism(s) required to transport chondrules to the accretion regions of chondrites, and 3) provide robust estimates of the timing and mechanism of asteroidal differentiation. We aim to understand how the variable initial conditions imposed by the range of possible stellar environments and protoplanetary disk properties regulated the formation and assemblage of disk solids into asteroidal and planetary bodies comprising our solar system.

Keywords of the ERC project:

Keywords that characterize the scientific profile of the potential visiting researcher/s:
The ubiquity of arsenic resistant genes across all of life’s variety suggests a close intimacy between arsenic biogeochemistry and evolution, over geological time scales. However, the behaviour of arsenic in past environments where life originated and its impact on our evolution is essentially unknown. Arsenic is of particular importance because of its toxic properties, prevalence in tight association with ubiquitous iron and sulfide minerals and as a major component of sulfide-rich waters, all common features of Precambrian oceans. Arsenic obstructs the synthesis of the building blocks of life, exhibiting both chronic and acute toxicity at very low concentrations. These properties make arsenic an agent capable of exerting strong selective pressure on the distribution, success and diversity of life. This is exemplified by when the release of arsenic into groundwater following rock-weathering processes results in widespread poisoning. Using the state of the art stable isotopes tools, coupled to biomass production, bacterial iron, arsenic and sulfur cycling under ancient oceanic conditions, this project will open a new discussion on the much debated relationship between ocean chemistry and evolution, by introducing a new arsenic framework. This will be achieved under three majors themes: 1) Does there exist a biogeochemical connection between arsenic and the timing and transition from the iron-rich to the hypothesized sulfide-rich oceans that are linked to the rise of atmospheric oxygen? 2) Does arsenic and sulfide show concomitant cyclicity during the Precambrian? 3) Could arsenic thus serve as a proxy for the calibration of key transitional steps in the timing of biological innovation?

Keywords of the ERC project: arsenic, Precambrian oceans, marine biogeochemical cycles, evolution of life

Keywords that characterize the scientific profile of the potential visiting researcher/s: isotopic geochemist, sedimentologist, geochemist, biogeochemist, geomicrobiologist
Towards a new understanding of carbon processing in freshwaters: methane emission hot spots and carbon burial

In spite of their small areal extent, inland waters play a vital role in the carbon cycle of the continents, as they emit significant amounts of the greenhouse gases (GHG) carbon dioxide (CO2) and methane (CH4) to the atmosphere, and simultaneously bury more organic carbon (OC) in their sediments than the entire ocean. Particularly in tropical hydropower reservoirs, GHG emissions can be large, mainly owing to high CH4 emission. Moreover, the number of tropical hydropower reservoirs will continue to increase dramatically, due to an urgent need for economic growth and a vast unused hydropower potential in many tropical countries. However, the current understanding of the magnitude of GHG emission, and of the processes regulating it, is insufficient. Here I propose a research program on tropical reservoirs in Brazil that takes advantage of recent developments in both concepts and methodologies to provide unique evaluations of GHG emission and OC burial in tropical reservoirs. In particular, I will test the following hypotheses: 1) Current estimates of reservoir CH4 emission are at least one order of magnitude too low, since they have completely missed the recently discovered existence of gas bubble emission hot spots; 2) The burial of land-derived OC in reservoir sediments offsets a significant share of the GHG emissions; and 3) The sustained, long-term CH4 emission from reservoirs is to a large degree fuelled by primary production of new OC within the reservoir, and may therefore be reduced by management of nutrient supply. The new understanding and the cross-disciplinary methodological approach will constitute a major advance to aquatic science in general, and have strong impacts on the understanding of other aquatic systems at other latitudes as well. In addition, the results will be merged into an existing reservoir GHG risk assessment tool to improve planning, design, management and judgment of hydropower reservoirs.

Keywords of the ERC project: biogeochemistry, limnology, aquatic science, sedimentology, ecosystem ecology, carbon cycling, greenhouse gases

Keywords that characterize the scientific profile of the potential visiting researcher/s: biogeochemistry, sedimentology, modeling
Algal Lipids: the Key to Earth Now and aNcient Earth

Alkenones are algal lipids that have been used for decades to reconstruct quantitative past sea surface temperature. Although alkenones are being discovered in an increasing number of lake sites worldwide, only two terrestrial temperature records have been reconstructed so far. The development of this research field is limited by the lack of interdisciplinary research that combines modern biological and ecological algal research with the organic geochemical techniques needed to develop a quantitative biomarker (or molecular fossil) for past lake temperatures. More research is needed for alkenones to become a widely used tool for reconstructing past terrestrial temperature change. The early career Principal Investigator has discovered a new lake alkenone-producing species of haptophyte algae that produces alkenones in high abundances both in the environment and in laboratory cultures. This makes the new species an ideal organism for developing a culture-based temperature calibration and exploring other potential environmental controls. In this project, alkenone production will be manipulated, and monitored using state-of-the-art photobioreactors with real-time detectors for cell density, light, and temperature. The latest algal culture and isolation techniques that are used in microalgal biofuel development will be applied to developing the lake temperature proxy. The objectives will be achieved through the analysis of 90 new Canadian lakes to develop a core-top temperature calibration across a large latitudinal and temperature gradient (Δ latitude = 5°, Δ spring surface temperature = 9°C). The results will be used to assess how regional palaeo-temperature (Uk37), palaeo-moisture (δDwax) and palaeo-evaporation (δDalgal) respond during times of past global warmth (e.g., Medieval Warm Period, 900-1200 AD) to find an accurate analogue for assessing future drought risk in the interior of Canada.

Keywords of the ERC project: biomarkers, lakes, temperature, environment, algae, alkenone, lipids, paleoclimate

Keywords that characterize the scientific profile of the potential visiting researcher/s:
Despite intensive abatement efforts, airborne particulate matter remains a major public health issue with costs across the European Union estimated at 600 billion euros in 2005. Road traffic remains one of the major sources of particulate matter, and diesel emissions are by far the largest source of atmospheric nanoparticles in urban areas. Semi-volatile organic compounds emitted largely in the condensed matter phase are a major component of diesel emissions, and as primary particles are advected from their road traffic source, the semi-volatile compounds vaporise and are oxidised, forming a greater mass of secondary organic aerosol (SOA). However, the semi-volatile compounds are extremely poorly characterised as they are not resolved by traditional gas chromatographic methods, presenting an unresolved complex mixture (UCM). For this reason, despite being a major precursor of SOA, such compounds are often poorly represented or completely omitted from atmospheric chemistry-transport models. This proposal is concerned with applying new two dimensional gas chromatographic methods to characterisation of the UCM at a molecular level which will be followed by studies of the physico-chemical properties of representative components of the semi-volatile emissions. The very abundant nucleation nanoparticle mode of diesel emissions is comprised almost entirely of semi-volatile organic material and hence these particles are progressively lost from the atmosphere by evaporation. Until now, there has been insufficient knowledge of the properties of the semi-volatile components to model this behaviour reliably. Such processes will be quantified through both controlled laboratory studies and carefully designed field measurements. Numerical models on both a street canyon and a neighbourhood (5x5 km) scale will be developed to simulate the key processes, such that spatial patterns and size distributions will be predicted, and compared with independent measurements.

Keywords of the ERC project: Diesel exhaust; atmospheric aerosol; hydrocarbon analysis; atmospheric modelling; atmospheric measurements

Keywords that characterize the scientific profile of the potential visiting researcher/s: atmospheric scientist
Tracking the early traces of life preserved in very old rocks and reconstructing the major steps of its evolution is an exciting and most challenging domain of research. How amazing it is to have a cell that is 1.5 or 3.2 billion years old under a microscope! From these and other disseminated fragments of life preserved along the geological timescale, one can build the puzzle of biosphere evolution and rising biological complexity. The possibility that life may exist beyond Earth on other habitable planets lies yet at another scale of scientific debates and popular dreams. We have the chance now to live at a time when technology enable us to study in the finest details the very old record of life, or to land on planets with microscope and analytical tools, mimicking a geologist exploring extraterrestrial rocky outcrops to find traces of water and perhaps life. There is still a lot to be done however, to solve major questions of life evolution on Earth, and to look for unambiguous life traces, on Earth or beyond. The project ELiTE aims to provide key answers to some of these fundamental questions.

Astrobiology studies the origin, evolution and distribution of life in the Universe, starting with life on Earth, the only biological planet known so far. The ambitious objectives of the project ELiTE are the following: 1) The identification of Early traces of life and their preservation conditions, in Precambrian rocks of established age 2) The characterization of their biological affinities, using innovative approaches comprising micro to nanoscale morphological, ultrastructural and chemical analyses of fossil and recent analog material 3) The determination of the timing of major steps in evolution. In particular, the project ELiTE aims to decipher two major and inter-related steps in early life evolution and the rise of biological complexity: the evolution of cyanobacteria, responsible for Earth oxygenation and ancestor of the chloroplast, influencing drastically the evolution of life and the planet Earth, and the evolution of the domain Eucarya since LECA (Last Eucaryotic Universal Ancestor). 4) The determination of causes of observed pattern of evolution in relation with the environmental context (oxygenation, impacts, glaciations, tectonics, nutrient availability in changing ocean chemistry) and biological innovations and interactions (ecosystems evolution). Objective 1 has implications for the search for unambiguous traces of life on Earth and beyond Earth. Objectives 2 to 4 have implications for the understanding of causes and patterns of biological evolution and rise of complexity in Earth life. Providing answers to these most fundamental questions will have major impact on our understanding of early life evolution, with implications for the search for life beyond Earth.

Keywords of the ERC project: early life, evolution, microfossils, paleobiology, precambrian, eukaryotes, cyanobacteria, microanalyzes, astrobiology, biosignatures

Keywords that characterize the scientific profile of the potential visiting researcher/s: microspectroscopist, precambrian sedimentologist, geochemist, astrobiologist, micropaleontologist
Earthquakes represent one of the deadliest and costliest natural disasters affecting our planet – and one of the hardest to predict. To improve seismic hazard evaluation in earthquake-prone regions, an understanding of earthquake nucleation and of the underlying microphysical and chemical processes is crucial. A better understanding of the processes that control earthquake nucleation is also of rapidly growing importance for mitigation of induced seismicity, caused by activities such as gas and oil production, and geological storage of CO2 or gas. The SEISMIC project is a multi-scale study aimed at understanding the parameters that control slip (in)stability in experiments and models addressing earthquake nucleation. A central question to be tackled is what controls the velocity-dependence of fault friction and hence the potential for accelerating, seismogenic slip, and on what length scales the processes operate. A novel acoustic imaging technique will be developed and applied in experiments to obtain direct information on the internal microstructural evolution of fault slip zones during deformation, and on how this evolution leads to unstable slip. The SEISMIC project will link experiments with sophisticated numerical models of grain-scale frictional processes. Using both experiments and grain scale modelling, the SEISMIC project will in turn directly test boundary element models for large scale fault slip. The coupling of experiments with grain-scale numerical models, based on in-situ imaging, will provide the first, integrated, multiscale physical basis for extrapolation and upscaling of lab friction parameters to natural conditions. Ultimately, the SEISMIC project will test and validate the resulting models for fault slip by simulating and comparing patterns of seismicity for two natural-laboratory cases: a) for the l’Aquila region of Central Italy, and b) for a reservoir-scale case study involving induced seismicity in the Netherlands.

Keywords of the ERC project: friction, earthquakes, seismic cycle, faulting

Keywords that characterize the scientific profile of the potential visiting researcher/s: Faulting modeler, field geologist, seismologist
**Project ID:** 637483  
**Project Acronym:** TERRA  
**Evaluation Panel:** PE10 - Earth System Science

<table>
<thead>
<tr>
<th>Principal Investigator:</th>
<th>Dr Richard Butler</th>
</tr>
</thead>
<tbody>
<tr>
<td>Host Institution:</td>
<td>The University Of Birmingham - UK</td>
</tr>
</tbody>
</table>

**375 Million Years of the Diversification of Life on Land: Shifting the Paradigm?**

Life on land today is spectacularly diverse, representing 75–95% of all species on Earth. However, it remains unclear how this extraordinary diversity has been acquired across deep geological time. This research project will address this major knowledge gap by reassessing the dominant paradigm of terrestrial diversification, an exponential increase in diversity over the last 375 million years, using the rich and well-studied fossil record of tetrapods (four-limbed vertebrates) as an exemplar group. Previous analyses of tetrapod diversification have been based on an outdated and problematic dataset that is likely to artificially inflate apparent diversity towards the present day. A major new dataset will be assembled, detailing the spatial and temporal distribution of terrestrial tetrapods across their entire fossil record in unprecedented detail. These data will be analysed using the latest approaches to sampling-standardisation in order to generate completely novel, rigorous curves of diversification through time. These will be compared within a cutting-edge statistical framework to alternate diversification models, as well as to changes in rock record sampling, global environments (e.g. sea level and atmospheric composition) and marine diversity. These comparisons will allow us to address the following key questions: (i) Does terrestrial diversification follow an exponential pattern over the last 375 million years? (ii) Is the terrestrial fossil record as complete as the marine fossil record? (iii) Are long-term patterns of terrestrial diversification driven by physical changes in the Earth system such as climate change? (iv) Did marine and terrestrial biodiversity follow similar trajectories across geological time? (v) How severely did mass extinction events impact upon terrestrial tetrapod diversification? Our work will establish a new, rigorous paradigm for the long-term pattern of terrestrial diversification, and test and identify its drivers.

**Keywords of the ERC project:** Palaeontology, species richness, biodiversity, fossil record, terrestrial, Tetrapoda, Cenozoic, Mesozoic, databases

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** Biodiversity analysis, biogeography, species richness, fossil record
Synchronisation to enhance reliability of climate predictions

Climate prediction is the next frontier in climate research. Prediction of climate on timescales from a season to a decade has shown progress, but beyond the ocean skill remains low. And while the historical evolution of climate at global scales can be reasonably simulated, agreement at a regional level is limited and large uncertainties exist in future climate change. These large uncertainties pose a major challenge to those providing climate services and to informing policy makers. This proposal aims to investigate the potential of an innovative technique to reduce model systematic error, and hence to improve climate prediction skill and reduce uncertainties in future climate projections. The current practice to account for model systematic error, as for example adopted by the Intergovernmental Panel on Climate Change, is to perform simulations with ensembles of different models. This leads to more reliable predictions, and to a better representation of climate. Instead of running models independently, we propose to connect the different models in a manner that they synchronise and errors compensate, thus leading to a model superior to any of the individual models – a super model. The concept stems from theoretical non-dynamics and relies on advanced machine learning algorithms. Its application to climate modelling has been rudimentary. Nevertheless, our initial results show it holds great promise for improving climate prediction. To achieve even greater gains, we will extend the approach to allow greater connectivity among multiple complex climate models to create a true super climate model. We will assess the approach’s potential to enhance seasonal-to-decadal prediction, focusing on the Tropical Pacific and North Atlantic, and to reduce uncertainties in climate projections. Importantly, this work will improve our understanding of climate, as well as how systematic model errors impact prediction skill and contribute to climate change uncertainties.

Keywords of the ERC project: Climate prediction, Interactive Ensemble, Climate Change Projections, Model Systematic Error, Machine Learning, Dynamical System, Data assimilation, Multi-model ensembles

Keywords that characterize the scientific profile of the potential visiting researcher/s: Climate modeller, Climate dynamics, Seasonal to decadal prediction, Machine Learning, Data assimilation
Quantifying the evolution of Earth’s atmosphere with novel isotope systems and modelling

Atmospheric oxygen is fundamental to life as we know it, but its concentration has changed dramatically over Earth’s 4.5 billion year history. An amazing qualitative story has emerged, in which Earth’s atmosphere was devoid of free oxygen for the first 2 billion years of planetary history, with two significant increases in concentration at ~2.4 and ~0.55 billion years ago. Both oxygenation events were accompanied by extreme climatic effects – the “snowball earth” episodes – and paved the way for massive reorganization of biogeochemical cycles such as the Cambrian radiation of macroscopic life. Despite these profound influences on the Earth system, we currently lack fundamental quantitative constraints on Earth’s atmospheric evolution. I am poised to add substantial quantitative rigor to Earth’s atmospheric history, by constraining the concentrations of important gases (e.g., O2, O3, CO2, CH4, organic haze) in ancient atmospheres to unprecedented accuracy. I will accomplish this via an innovative interdisciplinary program focused on the unusual mass-independent isotope fractionations observed in sedimentary rocks containing sulfur and oxygen. These signals are direct remnants of ancient atmospheric chemistry, and contain far more information than can currently be interpreted. This project combines novel experimental and methodological approaches with state-of-the-art numerical modelling to significantly advance our ability to decipher the isotope records. A unique “early Earth” UV lamp coupled to a custom-built photocell will enable direct production of isotope signals under Earth-like conditions, with time-dependent sampling. Groundbreaking analytical methodologies will vastly increase the global geochemical database. The experimental results and data will provide ground-truth for next-generation atmospheric models that will constrain atmospheric composition and its feedbacks with the Earth-biosphere-climate system during key points in our planetary history.

Keywords of the ERC project: Earth System Science, atmospheric evolution, mass-independent isotope fractionation (MIF), oxygen, sulfur, early earth

Keywords that characterize the scientific profile of the potential visiting researcher/s: Numerical modelling, experimentalist, photochemistry, isotope geochemist, field geology
Observation and Modelling of Radiocarbon in Atmospheric Methane for Methane Source Identification

Observation and Modelling of Radiocarbon in Atmospheric Methane for Methane Source Identification

Greenhouse gas emissions are the primary cause of global climate change, and methane (CH4) is the second most important contributor after carbon dioxide (CO2). Major sources of methane are both natural (wetlands) and anthropogenic (agriculture, landfills and fossil fuels). Current efforts to assess the anthropogenic CH4 influence on climate change and the effectiveness of mitigation policies for CH4 are limited by large uncertainties in estimates of total methane emissions and their attribution to various sources by accounting-based techniques. This project will pioneer and apply innovative techniques for atmospheric observation and modelling of radiocarbon in CH4 that will enable unique quantification of fossil fuel vs. biogenic CH4 sources at regional and global scales, thereby improving the estimation and attribution of CH4 emissions of different types. The proposed work will significantly advance the frontier of current research on atmospheric methane and the characterization of anthropogenic sources on policy-relevant scales, and it has the potential to influence climate policy and industrial practices over the next 10-20 years.

Keywords of the ERC project: Atmospheric methane, Radiocarbon, Carbon cycle, Observations, Modelling, Emissions

Keywords that characterize the scientific profile of the potential visiting researcher/s: Atmospheric methane, Radiocarbon, Carbon cycle, Observations, Modelling, Emissions
Biogeochemical and ecosystem interactions with socio-economic activity in the global ocean

The global marine ecosystem is being deeply altered by human activity. On the one hand, rising concentrations of atmospheric greenhouse gases are changing the physical and chemical state of the ocean, exerting pressure from the bottom up. Meanwhile, the global fishery has provided large economic benefits, but in so doing has restructured ecosystems by removing most of the large animal biomass, a major top-down change. Although there has been a tremendous amount of research into isolated aspects of these impacts, the development of a holistic understanding of the full interactions between physics, chemistry, ecology and economic activity might appear impossible, given the myriad complexities. This proposal lays out a strategy to assemble a team of trans-disciplinary expertise, that will develop a unified, data-constrained, grid-based modeling framework to represent the most important interactions of the global human-ocean system. Building this framework requires solving a series of fundamental problems that currently hinder the development of the full model. If these problems can be solved, the resulting model will reveal novel emergent properties and open the doors to a range of previously unexplored questions of high impact across a range of disciplines. Key questions include the ways in which animals interact with oxygen minimum zones with implications for fisheries, the impacts fish harvesting may have on nutrient recycling, spatio-temporal interactions between managed and unmanaged fisheries, and fundamental questions about the relationships between fish price, fishing cost, and multiple markets in a changing world. Just as the first coupled ocean-atmosphere models revealed a wealth of new behaviours, the coupled human-ocean model proposed here has the potential to launch multiple new fields of enquiry. It is hoped that the novel approach will contribute to a paradigm shift that treats human activity as one component within the framework of the Earth System.

Keywords of the ERC project: ocean model biogeochemistry ecosystem fisheries

Keywords that characterize the scientific profile of the potential visiting researcher/s: model marine ecology economics behaviour governance
The terrestrial biosphere responds rapidly and sensitively to climate change and is important in mediating physical and biogeochemical feedbacks to climate. There are still enormous uncertainties in our understanding of how the terrestrial biosphere will respond to changes in climate in the 21st century, and large uncertainties in predictions of the climate feedbacks. Many issues that limit our ability to predict the future of the terrestrial biosphere can be addressed by examining what happened in the recent geologic past – where the drivers of climate change are relatively well known and there is abundant globally-distributed, quantitative, well-dated and unambiguous evidence of the biospheric response. The goal of this project is to unleash the power of the palaeo-record to understand the interactions of climate and the terrestrial biosphere, and to explain how terrestrial systems (vegetation, fire, hydrology, biogeochemical cycles including the carbon, trace gas and dust cycles) respond and contribute to long-term (millennial) and rapid (decadal to centennial) climate changes. I will use process-based models with global palaeodata syntheses to address four specific challenges to our understanding of past and future climate and environmental change: (1) How does vegetation respond to rapid climate change and what are the consequences of this response for climate? (2) To what extent does increasing CO2 enhance tree growth or competitive fitness, and how does this translate into changes in ecosystems and ecosystem services? (3) How does the terrestrial biosphere respond to changes in climate variability and the prevalence of extreme events? (4) How does the land surface affect regional climates, and why do models persistently fail to predict these effects accurately? In addressing these challenges, I will deliver public-access data sets, model outputs and comparison tools so the strengths of the palaeorecord can be exploited by the wider global change community.

Keywords of the ERC project: palaeoclimate; biosphere feedbacks; climate impacts on vegetation; vegetation modelling; abrupt climate change; PMIP

Keywords that characterize the scientific profile of the potential visiting researcher/s: palaeodata synthesis; climate reconstruction; climate modelling; environmental modelling; model evaluation
Information Aggregation in Elections

Elections are the foundation for democratic decision making. This research program will examine the effects of biased and privately informed entities—election organizers—on the ability of elections to aggregate information: Existing theory demonstrates that large electorates can reach correct decisions by aggregating information dispersed among many voters. However, existing theory does not account for the ubiquitous presence of biased organizers who intend to affect the election outcome. Examples of biased organizers may include a CEO holding a shareholder vote, a regional government holding a referendum, and political parties in general elections. This project will develop and analyze new models of voting that account for the effects of biased organizers on information aggregation. One of the examples I consider is an election organizer who can increase voter participation at some cost (e.g., through advertising). Preliminary work suggests that the presence of biased organizers has significant impact. As increasing participation becomes cheap, equilibria exist where the election organizer recruits a large number voters and yet the majority votes almost surely for the organizer’s favorite policy. This failure of information aggregation contrasts starkly with existing results for elections in which the number of voters is exogenously large. I will study the effectiveness of institutional safeguards against such manipulation, including supermajority rules, publicity requirements, and the regulation of communication to voters, and I will apply the theory in the context of shareholder voting and corporate control. Thus, this research program has important implications for the design of elections in realistic voting scenarios.

Keywords of the ERC project: economic theory, game theory, voting, Economic Theory, Auctions, Elections, Political Economy

Keywords that characterize the scientific profile of the potential visiting researcher/s: economic theorists,
Benefit-sharing for an equitable transition to the green economy - the role of law

Can benefit-sharing address the equity deficit within the green economy? This project aims to investigate benefit-sharing as an under-theorised and little-implemented regulatory approach to the equity concerns (disregard for the special circumstances of developing countries and of indigenous peoples and local communities) in transitioning to the green economy.

Although benefit-sharing is increasingly deployed in a variety of international environmental agreements and also in human rights and corporate accountability instruments, no comprehensive account exists of its conceptual and practical relevance to equitably address global environmental challenges. This project will be the first systematic evaluation of the conceptualisations and operationalisations of benefit-sharing as a tool for equitable change through the allocation among different stakeholders of economic and also socio-cultural and environmental advantages arising from natural resource use.

The project will combine a comparative study of international law with empirical legal research, and include an inter-disciplinary study integrating political sociology in a legal enquiry on the role of “biocultural community protocols” that articulate and implement benefit-sharing at the intersection of international, transnational, national and indigenous communities’ customary law (global environmental law).

The project aims to: 1. develop a comprehensive understanding of benefit-sharing in international law; 2. clarify whether and how benefit-sharing supports equity and the protection of human rights across key sectors of international environmental regulation (biodiversity, climate change, oceans, food and agriculture) that are seen as inter-related in the transition to the green economy; 3. understand the development of benefit-sharing in the context of global environmental law; and 4. clarify the role of transnational legal advisors (NGOs and bilateral cooperation partners) in the green economy.

Keywords of the ERC project: equity, international environmental law, human rights, climate change, agriculture

Keywords that characterize the scientific profile of the potential visiting researcher/s: Legal researcher, international environmental law, international human rights law, comparative environmental law
Prospects for International Migration Governance

Risk and uncertainty are inherent in any decision-making procedure, but while a substantial body of work on the governance of international migration focuses on challenges posed to governance systems, we know remarkably little about the impact of risk and uncertainty on: (i) the cognitive biases of actors within migration governance systems; (ii) the susceptibility of these biases to change; (iii) the relationship between cognitive bias and broader questions of systemic resilience, vulnerability and adaptation and (iv) the similarities and differences in migration governance between major world regions. Each of these is a significant gap in our knowledge of international migration governance. To address this gap this project will focus on the context of decision to ask: what are the causes and consequences of the cognitive biases concerning risk and uncertainty held by actors in migration governance systems? The project will: (i) test the causes and consequences of the ‘frames’ held by actors in migration governance systems, specify the scope for these frames to change and to analyse the likely systemic effects of change on migration governance systems in four major world regions. (ii) develop a comparative regional analysis of the micro-political foundations of migration governance and their implications for system adaptation and change. (iii) significantly advance conceptual and methodological understanding of international migration governance through the use of concepts of systemic adaptation, vulnerability and resilience that bridge behavioural theories of choice with theories of institutional and organisational change. (iv) disseminate the results effectively through a range of appropriate outlets and through engagement with a range of users of the results of this work in academia, policy-making communities, NGOs and the wider public.

Keywords of the ERC project: international migration, governance, politics, international relations, Asia-Pacific, South America, North America, Europe, regional integration.

Keywords that characterize the scientific profile of the potential visiting researcher/s: international migration, governance, politics, international relations, Asia-Pacific, South America, North America, Europe, regional integration.
Transforming Citizenship through Hybrid Governance: The Impacts of Public-Private Security Assemblages

This project is an anthropological study of how citizenship is being reconfigured through hybrid forms of governance. It will research these transformations by focusing on public-private ‘security assemblages’, with particular emphasis on the role of the private security industry. Much recent scholarly debate has focused on shifting modes of governance in a context of neoliberal globalization. Specific attention has focused on how governance is increasingly achieved through networks or assemblages of state, corporate and voluntary actors. Such assemblages of state and non-state actors blur the lines between public and private, and between local, national and transnational. This research will extend this debate by investigating the implications this form of governance has for how different groups enact and experience citizenship, concentrating on public-private security assemblages as hybrid, multi-scalar governance structures. It will examine how forms of ‘differentiated citizenship’ are produced, and how political subjectivities shift, as a result of these forms of security governance. These transformations in citizenship will be analyzed through a multi-sited, comparative analysis of security assemblages in Jerusalem (Israel), Kingston (Jamaica) and Nairobi (Kenya). The project will research the composition, operation and regulation of public-private security assemblages, with special attention to the global mobilities of security experts and expertise. In each setting, the project will study the practices and discourses that structure relations between state and non-state security providers, clients and those seen as threats. It will focus on the ‘security encounter’ between these different actors, in which new social relationships and subjectivities are produced. The project is expected to lead to the development of an anthropological theory of security governance with both theoretical and applied relevance.

Keywords of the ERC project: security, privatization, cities, citizenship, governance, neoliberalism, policing

Keywords that characterize the scientific profile of the potential visiting researcher/s: policing, security, assemblages, STS, materiality, cities, citizenship, infrastructure, urban, violence
A Comparative History of Insurance Law in Europe

The objective of the project is to work out interactions between the national developments of insurance law in Europe, to explore the possibility of common historical roots of European insurance law, and to reassess the history of insurance law in Europe. The project does, thereby, aim at creating a historical basis for a European legal scholarship in the field of insurance law. Today’s state of research in the field of the history of insurance law is unsatisfactory: with the exception of maritime insurance, modern research focuses on national developments and the history of insurance law is told differently in the European countries. Even though modern research suggests that there have been interactions between the national developments these interactions often appear to be only footnotes to a mainly national development. For the first time, the project takes these points of interactions as a starting point for an in depth research into the history of insurance law in Europe. It is, to take an example involving England and Germany, known that English life and fire insurers where present on the German market since the late 18th century and that those who, in the beginning of the 19th century, were involved in founding the first commercial life and fire insurers in Germany had been working for English insurers. What needs to be explored is what impact this had on the practice and standard contract terms of German insurers. On the basis of the research into this and other points of interactions it will, for the first time, be possible to research into the doctrinal history of insurance law on a European level. The project will help to reassess the history of insurance law in Europe and it will create a historical basis for a European scholarship in the field of insurance law: the harmonization of European insurance contract law is on the agenda. Comparative historical research will help to understand the existing differences between the insurance laws in Europe.

Keywords of the ERC project: Comparative History of Insurance Law in Europe
Keywords that characterize the scientific profile of the potential visiting researcher/s: Comparative Legal History; History of Business Law; History of Insurance Law
No Sword Bites So Fiercely as an Evil Tongue? Gossip Wrecks Reputation, but Enhances Cooperation

Social norms in general, and norms of cooperation in particular, are the cement of all human societies. For the difficult problems of the maintenance and enforcement of social norms and of cooperation, humans have developed surprisingly complex solutions. Reputation mechanisms and gossip are certainly among the compound informal solutions.

According to common wisdom, gossip channels mainly negative and often fictitious information. If it is so, how can dishonest gossip and the resulting biased reputations legitimize social order and promote cooperation? This is the main puzzle we tackle in the proposed project exploiting a wide scale of instruments. We use analytical modeling and agent-based simulation to derive hypotheses. We test simple hypotheses in small group experiments. We develop new methodological tools to appropriately analyze the triadic nature of gossip embedded in network flows of information. We utilize dynamic network datasets from primary and secondary school classes, and we gather qualitative and quantitative information from organizations to test conditional hypotheses about the role that gossip plays in reputation and cooperation in different developmental and social contexts of life. In addition, we apply new communication technologies currently under development to explore the hidden world of gossip and the dynamics of reputations in dormitories and organizations.

With the insights gained, we can overcome common stereotypes about gossip and highlight how gossip is related to credible reputational signals, cooperation, and social order. Expected results will help us to outline the conditions that can promote cooperativeness in work groups, and they will help to construct successful prevention strategies of social exclusion and other potentially harmful consequences of the evil tongue.

Keywords of the ERC project: gossip; reputation; cooperation; social norms; informal communication; social networks; status competition; honesty; indirect reciprocity; text analysis

Keywords that characterize the scientific profile of the potential visiting researcher/s: agent-based models; network dynamics; statistical models for networks; semantics; text analysis
Policy, practice and patient experience in the age of intensified data sourcing

The European healthcare services have begun collecting tissue samples and healthcare data from patients on an unprecedented scale. With POLICYAID we suggest the term 'intensified data sourcing' to describe these attempts at getting more data, on more people, of better quality while simultaneously making the data available for multiple uses. Data are used for research, for financial remuneration purposes, for quality assurance, to attract capital and even for police work. POLICYAID investigates how the diverse agendas interact in the making of a new infrastructure for healthcare.

POLICYAID ambitiously aims to understand the drivers for and implications of intensified data sourcing in the biomedical realm across three levels: 1) policymaking, 2) everyday clinical practices, and 3) citizen experiences of health, illness, rights and duties. To achieve this aim we compare four different forms of intensified data sourcing, and analyze the regulatory frameworks guiding the data procurement and use in Denmark, the EU and beyond. Based on PI’s strong inter-disciplinary background and experience, we fuse legal, sociological, anthropological and public health scholarship and develop new methodologies for policy analysis by combining document analysis, interviews, participant observation and register-based methodologies. Instead of simply assuming that data sourcing can be reduced to matters of surveillance, we open up the black box of data sourcing by describing how data are selected; financed; what they are used for; how data practices relate to the involved stakeholders' hopes and concerns, and; who gains which rights to the data. We can thereby explore how intensified data sourcing affects clinical routines and patient experience, as well as understand how Big Data for medical research emerges. POLICYAID thereby arrives at novel understandings of both policy making and what it means to be patient in the age of intensified data sourcing.

Keywords of the ERC project: Science and technology studies (STS), anthropology, Big Data, data politics, healthcare

Keywords that characterize the scientific profile of the potential visiting researcher/s: Science and technology studies (STS), anthropology, Big Data
The role of consumer behavior and heterogeneity in the integrated assessment of energy and climate policies

The objective of this project is to quantify the role of consumers’ behaviour on the design and assessment of policies aimed at enhancing energy efficiency and conservation and at promoting climate change mitigation. The project brings together different disciplines – namely energy policy, environmental and ecological economics, behavioral public finance, experimental economics, and technology policy - in an integrated fashion. COBHAM is designed to go beyond the standard analysis of energy and climate policies in the presence of environmental externalities, by accounting for the heterogeneity in consumers’ preferences, the role of social interactions, and the presence of behavioral tendencies and biases. The project seeks to: i) carry out innovative research in the theoretical understanding of the interplay between behavioral tendencies and environmental externalities; ii) generate new empirical data and research on individual preferences by means of original surveys and controlled experiments; iii) enhance integrated assessment models (IAMs) of economy, energy and climate with an advanced representation of consumers’ behavior. In doing so, the project will be able to provide a richer characterization of energy demand and of greenhouse gas emission scenarios, to better estimate consumers’ responsiveness to energy and climate policies, and to provide input to the design of new policy instruments aimed at influencing energy and environmental sustainable behavior. COBHAM is of high public policy relevance given Europe’s legislation on energy efficiency and CO2 emissions, and can provide important insights also outside the sphere of energy and climate policymaking.

Keywords of the ERC project: Behavioural economics. climate change. energy economics. Environmental science

Keywords that characterize the scientific profile of the potential visiting researcher/s: Behavioural economist. climate change economist. integrated assessment modeler.
Reshaping society and space: home-based self-employment and businesses

The aim of WORKANDHOME is to develop a new framework for understanding fundamental changes currently taking place to work that situates individuals as economic actors within the context of their wider life domains, household, home and neighbourhood. This will break new ground in how we understand and classify economic activity, the home, the firm, places of economic activity, labour markets and ‘residential’ neighbourhoods. Significant and rising numbers of people work from home as a self-employed worker or business owner throughout Europe. This will be the first study that explores social, economic and spatial aspects of homeworking by self-employed workers and business owners including the role of new technologies and social media in dissolving the home-work boundary. This is an important new area for social science research since home-based self-employment and businesses vividly manifest the interconnection of ‘home’ and ‘work’ and of the ‘economic’ and the ‘social’ as part of an increasingly complex society. WORKANDHOME will integrate theoretical perspectives from economic geography, entrepreneurship and small business research, sociology, economics, housing and neighbourhood studies. In order to investigate new realities of how people work and live, this study will integrate analytical methods across the social sciences and computer sciences and create a new fusion of primary, secondary and ‘big’ social media data from the UK, the Netherlands, Germany, Europe and the world. WORKANDHOME offers a major step forward in understanding how people live, work, do business and shape space. Its integrated and international approach will stimulate considerable interdisciplinary exchange across disciplines in the social sciences for better understanding and tackling contemporary societal and economic changes and challenges.

Keywords of the ERC project: business, homeworking, networks, commuting, coworking, neighbourhoods, cities, growth, inclusion, entrepreneurship, enterprise, GIS

Keywords that characterize the scientific profile of the potential visiting researcher/s: geography, geoinformatics, GIS
Unravelling the genetic influences of reproductive behaviour and gene-environment interaction

This project will be the first to engage in a comprehensive study of the role of genes and gene-environment (GxE) interaction on reproductive behaviour. Until now, social science research has focussed on socio-environmental explanations, largely neglecting the role of genes. Due to unprecedented advances in molecular genetics over the last two decades, for the first time in history we are able to examine whether there is a genetic component to reproductive outcomes, including age at first birth, number of children and infertility. Building on my substantive empirical research, I first develop a multifactor theoretical and measurement model isolating socio-environmental and lifestyle factors. Second, I apply the most cutting-edge techniques in genetics to examine the genetic architecture of reproductive behaviour, including: the first genome-wide association study (GWAS) of reproductive choice; polygenic risk scores; and, genome-wide complex trait analysis (GCTA). Third, I focus on gene-environment interactions (GxE) to test different mechanisms of how the environment moderates genetic influences. Fourth, I propose to use genetic markers as instrumental variables (IVs) in a bi-directional Mendelian randomization (MR) analysis to determine causality and address the endogeneity of lifestyle and education in reproductive outcomes. This transdisciplinary project will produce fundamentally different results, overturn established links and deliver major breakthroughs in fertility research and beyond. This project is not only ground breaking by setting a new research agenda, but due to the inclusion of new genetic variables and techniques to study the causal effects of genes and their interaction with environment, will yield major innovations useful within demography and beyond. Research builds on the proven expertise and existing collaboration with geneticists, and is carefully costed to include 2 postdocs and 2 PhDs.

Keywords of the ERC project: Fertility, genetics, life course, biosocial, assortative mating

Keywords that characterize the scientific profile of the potential visiting researcher/s: Combining social science and genetics, demography, life course, fertility, statistics, polygenic scores
<table>
<thead>
<tr>
<th>Principal Investigator:</th>
<th>Dr Michael Woods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Host Institution:</td>
<td>Aberystwyth University - UK</td>
</tr>
</tbody>
</table>

**The Global Countryside: Rural Change and Development in Globalization**

GLOBAL-RURAL aims to advance our understanding of the workings and impact of globalization in rural regions through the development and application of new conceptual and methodological approaches. Globalization has a pervasive influence in transforming rural economies and societies, with implications for the major societal challenges of environmental change and resource security. However, in comparison to studies of the global city, relatively little research has focused on the ‘global countryside’, and existing research lacks integration. GLOBAL-RURAL will develop an integrated perspective by drawing on relational analysis (and particularly the approaches of ‘assemblage theory’ and ‘countertopography’) to focus on the actual mechanics by which rural localities are ‘re-made’ through engagement with globalization processes, examining the mediating effect of national and regional context and the opportunity for local interventions. The research will be organized through five work packages. WP1 will develop the methodological application of assemblage theory to analysing the global countryside, informed by case studies in 6 countries. WP2 will combine GIS analysis of quantitative and qualitative data to produce new narratives and visualisations of globalization processes, impacts and responses. WP3 will focus on mundane, ‘everyday globalization’ in a Welsh small town, using a countertopographic methodology. WP4 will apply the assemblage methodology developed in WP1 to analysing the differential global engagement of rural localities in Brazil, China and Tanzania. WP5 will apply the methodology to examine conflicts around renewable energy schemes, mining and water projects and industrial agriculture in rural areas, and the implications for strategies to address global challenges. A sixth work package, WP6, will identify the policy applications of the research, and disseminate research findings to academic and non-academic users.

**Keywords of the ERC project:** Globalization, Rural, Assemblage Theory, Locality, Rural Development

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** Human Geography, Sociology, Anthropology
Responding to climate change has profound implications for behaviour; yet policies to achieve this change have met with limited success. A key challenge for environmental social scientists is the need to move forward in understanding how to bring about change in consumption, community and political behaviours, which is commensurate to the scale of the climate change challenge. One promising area is ‘behavioural spillover’, the notion that taking up a new behaviour (e.g., recycling) may lead to adoption of other, more environmentally beneficial, behaviours. Such a notion appears to hold the promise of changing a suite of behaviours in a cost-effective way. Yet despite robust theoretical principles (e.g., self-perception theory) underpinning behavioural spillover, there is little empirical research. The proposed research intends to produce a step-change in behavioural and sustainability science by undertaking a mixed-method, cross-cultural study of pro-environmental behavioural spillover in order to open up new ways of promoting sustainable lifestyle change and significantly broadening our understanding of behaviour within individuals and cultures. There are three objectives for the research:

1. To examine ways in which pro-environmental behaviour, lifestyles and spillover are understood and develop within different cultures;
2. To understand drivers of behavioural consistency and spillover effects across contexts, including home and work, and cultures; and
3. To develop a theoretical framework for behavioural spillover and test interventions to promote spillover across different contexts and cultures.

Three Work Packages will address these objectives:
1. Defining and understanding spillover: Focus groups with biographical questions and card sorts [Years 1-2]
2. Examining drivers of spillover: Cross-national survey with factor, correlation and regression analyses [Years 2-3]
3. Developing theory and testing interventions: Laboratory and field experiments [Years 3-5]

Keywords of the ERC project: Low-carbon, lifestyles, behaviour change, spillover, rebound effect, sustainable, cross-cultural

Keywords that characterize the scientific profile of the potential visiting researcher/s: Environmental psychologist, cross-cultural psychologist
RISk and uncertainty in developing and Implementing Climate change pOlicies

Uncertainty is pervasive in all aspects of climate change. Although this is beyond dispute, the vast majority of research assessing climate ignores uncertainty, in large part because of the technical complexities involved. The present project aims at advancing substantially the way we conceptualize, model and frame the climate change policy making process, focusing on the central role of uncertainty. The first step is that of applying state of the art techniques from operation research (stochastic dynamic and approximate dynamic programming) to the realm of integrated assessment models (the conventional tool used to perform climate change analysis). These techniques enable us to capture a wide range of stochastic phenomena in the decision process. However, to really move forward the research edge one needs to shift the focus on to the way we, as individuals, perceive these uncertain phenomena. Indeed, the literature on decision making under uncertainty spans way beyond economics, statistics and operations research: Notably psychology and philosophy. These disciplines have had a major role in extending what we know about the process of decision making under uncertainty, and this project aims at reconciling this strand of literature with that on climate change policy design and assessment. The three main research questions are:

1) What are key risk and uncertainty perception issues and “biases” when we face climate change and under what instances should they be included in normative analyses of climate change?
2) How can we map these “alternative” representations of uncertainty and risk perception into integrated assessment models and how will these affect the normative predicaments of these models?
3) How can we communicate and frame uncertainty itself, as well as results of stochastic analyses, in a way that help us reducing those biases that have no normative role, but arise from our limited attentional and information processing capacity?

Keywords of the ERC project: uncertainty perception; climate change uncertainty; science communication

Keywords that characterize the scientific profile of the potential visiting researcher/s: behavioral economics; decision science; climate cahnge
Size matters: scaling principles for the prediction of the ecological footprint of biofuels

There is a major scientific and societal challenge in quantifying and reducing ecological footprints of products. Ecological footprint calculations suffer severely from a limited availability of data, such as the amount of energy and materials associated with the production, use and disposal of products. Furthermore, ecological footprints pertaining to biodiversity are typically biased towards a limited number of well-known species with a focus on relative species richness, leaving out ecosystem service attributes of biodiversity. As it is virtually impossible to collect all the empirical data required for all species, there is an urgent need to develop an operational framework to derive representative ecological footprints with limited data requirements. I propose to develop a novel framework based on a set of unifying scaling principles related to the production size of products and the body size of species. These scaling principles will be developed to predict key characteristics of biofuel production, such as energy return of investment, agricultural land requirements and greenhouse gas emissions, as well as global impact indicators, such as species extinction risks. The focus of the research is on (1) liquid biofuel production (bioethanol and biodiesel) from various first and second generation feedstock as an important but controversial renewable energy source, (2) vascular plant diversity, as the common basis of all terrestrial ecosystems, and (3) habitat destruction and climate change, as important drivers of global change. Together with the PI, two PhD students, two Postdocs and a technical assistant will work on different components of the new predictive models, substantially enhancing the scientific understanding of how to provide reliable ecological footprints in practice.

Keywords of the ERC project: biodiversity impacts, biofuels, environmental footprints, global scale analysis, environmental scaling

Keywords that characterize the scientific profile of the potential visiting researcher/s: natural or technological science, environmental modeling,
Resolving conflicts between food security and biodiversity conservation under uncertainty

Resolving conflicts between food security and biodiversity conservation under uncertainty Conflicts between food security and biodiversity conservation are increasing in scale and intensity and have been shown to be damaging for both biodiversity and human livelihoods. Uncertainty, for example from climate change, decreases food security, puts further pressure on biodiversity and exacerbates conflicts. I propose to develop a novel model that predicts solutions to conflicts between biodiversity conservation and food security under uncertainty. ConFooBio will integrate game theory and social-ecological modelling to develop new theory to resolve conservation conflicts. ConFooBio will implement a three-tiered approach 1) characterise and analyse 7 real-world conservation conflicts impacted by uncertainty; 2) develop new game theory that explicitly incorporates uncertainty; and 3) produce and test a flexible social-ecological model, applicable to any real-world conflict where stakeholders operate under conditions of extreme uncertainty. The project has importance for society at large because ecosystems and their services are central to human wellbeing. Managing a specific natural resource often results in conflict between those stakeholders focussing on improving food security and those focussed on biodiversity conversation. ConFooBio will illuminate resolutions to such conflicts by showing how to achieve win-win scenarios that protect biodiversity and secure livelihoods. In this project, I will develop a practical, transparent and flexible model for the sustainable future of natural resources that is also robust to uncertainty (e.g., climate change); this model will be highly relevant for environmental negotiations among stakeholders with competing objectives, e.g., the negotiations to set the United Nations Sustainable Development Goals in September 2015.

Keywords of the ERC project: biodiversity, food security, conflict, ecosystem services, social-ecological systems

Keywords that characterize the scientific profile of the potential visiting researcher/s: biodiversity, food security, decision theory, game theory, behavioural games, environmental psychology, conflict, social-ecological systems
Project ID: 680176  
Project Acronym: SCALEFORES  
Evaluation Panel: SH3 - Environment, Space and Population

Principal Investigator: Dr Felix Eigenbrod  
Host Institution: University Of Southampton - UK

SCALEFORES: Scaling Rules For Ecosystem Service Mapping

It is now widely recognized that sustainably managing ecosystem services – the benefits humans obtain from nature – is essential for humanity’s prospects in the 21st century and beyond. However, at present there is little data on the distribution of most services in most places. To date, the discipline of ecosystem service mapping has tried overcome this lack of data by using proxies to map ecosystem services based on our perceived understanding of ecosystem services from small-scale studies. However, the most commonly used proxies have been shown to be inaccurate, particularly for understanding policy-relevant trade-offs and win-wins between ecosystem services. The challenge therefore remains - how do we reliably map such relationships between multiple ES, thereby enabling multifunctional, ES-based management of our landscapes? In the SCALEFORES project, I will address this challenge head-on by developing and testing a novel methodological framework that enables the use of existing data to produce accurate maps of the relationships between ES in previously unmapped regions. The overarching idea underpinning SCALEFORES is that we can use information on the scale-dependency of relationships between existing social and ecological datasets (e.g. land cover, soil type, human population density) to create maps of trade-offs and win-wins between ecosystem services. The SCALEFORES project will systematically examine the scale-dependency of relationships between ecosystem services and the social and ecological variables that underpin them. It will then use this knowledge to enable a step change increase in our ability to accurately map both relationships between ES and the distributions of ecosystem services themselves. The methodology developed in SCALEFORES will be validated against existing maps of ecosystem services in Europe, as this is the region with the best data on ecosystem services globally.

Keywords of the ERC project: ecosystem services, scale, landscape ecology, ecological modelling, macroecology

Keywords that characterize the scientific profile of the potential visiting researcher/s: DGVM modeller, land system modeller, earth systems modeller
**Cultural Evolution of Kinship Diversity: Variation in Language, Cognition, and Social Norms Regarding Family**

Why do human societies differ in whom they class as family? Why are cousins classed with siblings in some societies but not others? Accounting for the variable ways that cultures classify kin is an enduring puzzle. The VARIKIN project takes a cultural evolutionary approach to variety and unity and engages different fields—cultural phylogenetics, corpus linguistics, and cross-cultural child development. VARIKIN-Evolution asks how and why does kinship diversity evolve across cultures and over time? Using comparative phylogenetic modeling of cultural evolution we investigate the dynamics of how kinship terminologies and family norms change in eight language families. Are there “universal” patterns of change, or does local cultural history and context determine changes in family organisation? How do social norms drive change in kinship terminology? VARIKIN-Usage investigates how people use kinship language by using corpus linguistics, surveys, and interviews to quantify patterns of usage in spoken and written language. How frequently are kinship terms used in different contexts and what meanings are more prevalent? Do patterns vary between languages, and can the patterns of usage at the individual level be linked to historical processes of change? VARIKIN-Development investigates how children acquire and understand kinship across cultures. Using participant observation and elicitation tasks, we characterise children’s social learning of kinship in a small-scale, non-Western community. Are there cross-cultural patterns of acquisition? Can socialisation produce constraints on the kinds of kinship children can learn? These three research directions are united by a coherent framework for the integration of macro- and micro-evolutionary processes. With a highly multidisciplinary background, the Applicant is uniquely positioned to direct this vanguard project towards a comprehensive understanding of diversity in how we classify our social worlds.

**Keywords of the ERC project:** cultural phylogenetics, language diversity, corpus linguistics, cross-cultural child development, interdisciplinary approaches to kinship,

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** cognitive modelling, ethnography, anthropological fieldwork,
The retinae as windows to the brain: An oscillatory vision

Several sophisticated image processing circuits have been discovered in the animal retina, many of which manifest massive neural synchrony. A major insight is that this type of synchrony often translates to high-frequency activity on a macroscopic level, but electroretinography (ERG) has not been tapped to examine this potential in humans. Bolstered by our compelling results combining ERG with magnetoencephalography (MEG), this project will address several open questions with respect to human visual processing: 1) Could variable retinal timing be linked to intrinsic image properties and pass on phase variance downstream to visual cortex? Our data suggests the retina responds to moving gratings and natural imagery with non-phase-locked high gamma oscillations (>65 Hz) just like visual cortex, and that slower ERG potentials exhibit strong phase-locking within stimuli but large phase variance across stimuli. 2) Do such retinal gamma band responses, both evoked and induced, directly drive some cortical gamma responses? Pilot data suggests that it can, through retinocortical coherence, our novel ERG-MEG mapping technique. 3) Several kinds of motion have now been shown to elicit massive synchrony in mammalian retina circuits. Does this also result in macroscopic high-frequency activity? If so, our experiments will finally reveal and characterize motion detection by the human retina. 4) Do efferent pathways to the retina exist in humans? We discovered that the ERG exhibits eyes-closed alpha waves strikingly similar to the classic EEG phenomenon and, leveraging our retinocortical coherence technique, that this activity is likely driven by contralateral occipital cortex. Then, can retinal responses be influenced by ongoing cortical activity? Characterizing retinocortical interaction represents a complete paradigm shift that will be imperative for our understanding of neural synchrony in the human nervous system and enable several groundbreaking new avenues for research.

Keywords of the ERC project: retina, vision, cognitive neuroscience, magnetoencephalography, electroencephalography, retina, vision, neural oscillations

Keywords that characterize the scientific profile of the potential visiting researcher/s: retinal neurophysiology, vision, cognitive neuroscience, magnetoencephalography, electroencephalography, source localization, neural oscillations
Impact of Mental Training of Attention and Emotion Regulation on Brain and Behavior: Implications for Neuroplasticity, Well-Being and Mindfulness Psychotherapy Research.

Mindfulness-based therapy has become an increasingly popular treatment to reduce stress, increase well-being and prevent relapse in depression. A key component of these therapies includes mindfulness practice that intends to train attention to detect and regulate afflictive cognitive and emotional patterns. Beyond its therapeutic application, the empirical study of mindfulness practice also represents a promising tool to understand practices that intentionally cultivate present-centeredness and openness to experience. Despite its clinical efficacy, little remains known about its means of action. Antithetic to this mode of experiential self-focus are states akin to depression, that are conducive of biased attention toward negativity, biased thoughts and rumination, and dysfunctional self schemas. The proposed research aims at implementing an innovative framework to scientifically investigate the experiential, cognitive, and neural processes underlining mindfulness practice building on the current neurocognitive understanding of the functional and anatomical architecture of cognitive control, and depression. To identify these mechanisms, this project aims to use paradigms from cognitive, and affective neuroscience (MEG, intracortical EEG, fMRI) to measure the training and plasticity of emotion regulation and cognitive control, and their effect on automatic, self-related affective processes. Using a cross-sectional design, this project aims to compare participants with trait differences in experiential self-focus mode. Using a longitudinal design, this project aims to explore mindfulness practice training’s effect using a standard mindfulness-based intervention and an active control intervention. The PI has pioneered the neuroscientific investigation of mindfulness in the US and aspires to assemble a research team in France and a network of collaborators in Europe to pursue this research, which could lead to important outcomes for neuroscience, and mental health.

Keywords of the ERC project: mindfulness meditation, compassion meditation, emotion regulation, attention, consciousness, pain regulation, fMRI, EEG, MEG, predictive coding, meditation expertise, neurophenomenology

Keywords that characterize the scientific profile of the potential visiting researcher/s: ERP, fear conditioning, EEG, MEG, predictive coding, attention
### The human Parietal Lobe

We will use univariate and multivariate functional Magnetic Resonance Imaging (fMRI) techniques, surface and stereo EEG, and in depth single cell recording to investigate the role of human parietal lobe in the monocular or stereoscopic observation of actions performed by conspecifics either using their biological effectors or artificial implements (tools, spears, bicycle, microphone, etc). The fMRI techniques will provide evidence for segregated processing of different types of observed actions within the parietal cortex. The EEG techniques will provide the time course of the electric activity in the parietal regions in comparison to the events and dynamic changes in the video and the time course in other parts of the action observation network. The stereo EEG also provides a more precise localization than fMRI, serving as an important confirmation of the fMRI results. The single cell recordings are crucial to demonstrate the selectivity of the neuronal processes for actions observed, their postural or kinematic parameters or localization in the visual field. This selectivity is crucial to show the presence of mirror neurons for the different types of actions and the use of tools, to document the contribution of the parietal neurons to discrimination between actions, and to assess the benefits of stereoscopic viewing. This project should yield a comprehensive view of the role of parietal lobe in action planning and understanding, including using artificial implements, and pave the way for understanding how higher-order parietal cognitive processes are rooted in the simpler action planning and understanding capacities.

**Keywords of the ERC project:** action observation; parietal cortex, intra-cerebral recordings; fMRI

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** vision, electrophysiology, computational skills, human and non human primates
Many current theories implicate brain oscillations in perception, attention, consciousness or memory. However, has one critical implication that is often overlooked in cognitive sciences: if a perceptual function relies on an oscillatory basis, then it should operate periodically, as a sequence of successive episodes or ‘snapshots’, with more or less favourable moments recurring at a well-defined periodicity. The present project aims to explore the validity and the consequences of this groundbreaking notion of "rhythmic perception". Whereas current research links perceptual functions to relatively slow changes of oscillatory amplitude, we propose to investigate the perceptual consequences of brain rhythms at the rapid time scale of the oscillatory cycle – the notion of "perceptual cycles". In work-package (WP) 1, we will explore the range of perceptual and cognitive operations that depend on oscillatory neural implementations, and reveal their cyclic behaviour. In WP2, we will relate these perceptual and cognitive cycles to the underlying neural activities by means of brain imaging techniques (EEG, fMRI, TMS); a key innovation is a proposed novel fMRI method to visualize the spatio-temporal propagation of perceptual cycles. In WP3, we will utilize this knowledge to control the power, frequency and phase of perceptual rhythms and thus dynamically manipulate, improve or prevent perception. In WP4, we will bridge the gap between lower- and higher-frequency perceptual cycles (from ~2 to ~100Hz) by experimental studies of cross-frequency coupling and computational models of visual information multiplexing. The project as a whole will characterize the rhythmic dynamics of perception, their neural basis and their functional implications, bringing us closer to understanding perception itself. The idea that sensory perception and cognition might follow a succession of snapshots rather than a continuous stream could spark a major transformation in cognitive sciences.

Keywords of the ERC project: brain rhythms, perception, oscillations, awareness, perceptual framing, EEG, TMS, fMRI

Keywords that characterize the scientific profile of the potential visiting researcher/s: cognitive neuroscience, computational neuroscience, brain imaging, signal processing
The Radical Plasticity Thesis: How we learn to be conscious

RADICAL explores the idea that consciousness is something that the brain learns to do rather than a static property of certain neural states vs. others. Here, considering that consciousness is extended both in space and in time, I adopt a resolutely dynamical perspective that mandates an experimental approach focused on change, at different time scales. I suggest that consciousness arises as a result of the brain’s continuous attempts at predicting not only the consequences of its actions on the world and on other agents, but also the consequences of activity in one cerebral region on activity in other regions. By this account, the brain continuously and unconsciously learns to redescribe its own activity to itself, so developing systems of metarepresentations that characterise and qualify the target first order representations. Such learned redescriptions form the basis of conscious experience. Learning and plasticity are thus constitutive of consciousness. This is what I call the “Radical Plasticity Thesis”. In a sense, this is the enactive perspective, but turned both inwards and (further) outwards. Consciousness involves “signal detection on the mind”; the conscious mind is the brain’s (non-conceptual, implicit) theory about itself. Theoretically, RADICAL offers the possibility of unifying Global Workspace Theory with higher-order Thought Theory by showing how the former can be built through mechanisms that flesh out the latter. Empirically, RADICAL aims at testing these ideas in three domains: (1) the perception action loop, (2) the self-other loop, and (3) the inner loop. 20 experiments leveraging behavioural experimentation, brain imaging, and computational modeling are proposed to test and further develop RADICAL. The overarching goal of the project is to characterize the computational principles that differentiate conscious from unconscious cognition, based on a bold, original, and innovative theory in which learning and plasticity play central roles.

Keywords of the ERC project: consciousness, unconscious information processing, learning, neural plasticity

Keywords that characterize the scientific profile of the potential visiting researcher/s: computational modeling, cognitive neuroscience, philosophy of mind, experimental psychology, learning
Cooperation is essential for mitigating conflict between individual and collective interests in relationships and groups, such as providing public goods and conserving resources. Most research testing psychological and economic theory of cooperation has applied a highly specific lab method (e.g., the prisoner’s dilemma) that unnecessarily constrains the applicability of research findings. The discrepancies between cooperation observed in the lab and field can be due to variation in interdependence. Two limitations of lab studies to generalizing findings to the field are that (1) lab studies contain interdependence that differs from reality and (2) in the field people lack knowledge about their objective interdependence with others – and must infer their interdependence. I propose two inter-related research programs that test hypotheses derived from Functional Interdependence Theory on how objective and perceived interdependence affect cooperation. Project 1 applies meta-analysis to test hypotheses about how variation in objective interdependence across lab studies moderates the effectiveness of strategies to promote cooperation. Because Project 2 involves a pioneering effort to catalogue and analyze the 60 year history of research on cooperation, I will apply these efforts to develop an international, multidisciplinary institution and open access database for cataloguing studies in a way that facilitates scientific progress. Project 2 (a) develops a measure of perceived interdependence, (b) observes the interdependence people encounter in their daily lives, (c) tests two models of how people think about interdependence, and (d) innovates and applies a method to test hypotheses about factors that influence accuracy and bias in perceptions of interdependence. To maximize the ecological validity of research findings, I study cooperation in different samples (students, romantic couples, and employees) with the use of multiple methods (survey, experimental, and field).

Keywords of the ERC project: Cooperation, Social Dilemmas, Meta-analysis, Behavioral Economics, Social Psychology, Interdependence

Keywords that characterize the scientific profile of the potential visiting researcher/s: evolutionary dynamics, evolutionary psychology, economics, social psychology
For many years, human cooperation has been praised as beneficial in organizational and personal settings. Indeed, cooperation allows people to develop trust, build meaningful relationships, achieve mutually beneficial outcomes, and strengthen bonding with one’s group members. However, while the benefits of cooperation are clear, very little is known about its possible negative aspects. Such negative aspects include the potential emergence of unethical conduct among cooperating partners, or as termed here – corrupt collaboration. Such joint unethical efforts, benefiting (directly or indirectly) one or more of the involved parties, occur in business, sports, and even academia. Corrupt collaboration emerges when one party bends ethical rules (here: lie) to set the stage for another party to further bend ethical rules and get the job done, that is, secure personal profit based on joint unethical acts. We propose that corrupt collaborations most commonly occur when all involved parties gain from the corrupt behavior. The current proposal is aimed at unfolding the roots and nature of corrupt collaborations; their existence, the psychological and biological processes underlying them, and the settings most likely to make corrupt collaboration emerge and spread. Accordingly, the information gathered in the current proposal has the potential to change the commonly held conceptions regarding the unidimensional – positive – nature of cooperation. It will help create a comprehensive understanding of cooperation and, specifically, when it should be encouraged or, alternatively, monitored.

Keywords of the ERC project: Corruption; Decision Making; Ethics; Moral Psychology; Social Psychology; Behavioral Economics

Keywords that characterize the scientific profile of the potential visiting researcher/s: Decision Making; Behavioral Economics; Experimental Economics
Transdiagnostic views on eating disorders and obesity and new approaches for treatment

Eating disorders such as Anorexia Nervosa (AN), Bulimia Nervosa (BN), Binge Eating Disorder (BED) and overweight/obesity are highly prevalent in the EU and worldwide. They cause tremendous suffering, elevate suicide rates, and account for multiple organic effects that increase all-cause mortality. Etiological and maintenance factors are not well understood and transdiagnostic theoretical models across eating and weight disorders are largely missing. The present project aims to develop an integrated theoretical framework by studying psychological factors that contribute to non-homeostatic eating across the full spectrum of eating-related disorders. It is proposed that high levels on psychological traits such as restraint eating (i.e., chronic dieting behaviour), emotional eating (i.e., eating in response to negative emotional events rather than hunger), craving/food addiction (i.e., intense and chronic urge to consume palatable foods), impulsivity (i.e., inadequate food consumption planning and low self-control), and low self-esteem influence neural systems that balance appetitive (mostly bottom-up) with regulatory (mostly top-down) processes. This model is tested in the four patient groups and healthy controls utilizing an integrated set of assessment methods, involving psychometric testing, smartphone based ambulatory assessment, and neurocognitive laboratory measurement. Derived from this model, novel behavioural interventions such as smartphone based stimulus control and cognitive inhibition training will be developed.

Results will have implications for theoretical models of eating and weight disorders as well as for neuroaffective models of appetite regulation. Smartphone technology might usefully complement current interventions in supporting an effective transfer to daily life and help alleviate the burden for patients with eating-related mental and physical diseases.

Keywords of the ERC project: emotional eating, eating disorders, neuro-cognitive correlated of food image responses, ambulatory assessment, food choice

Keywords that characterize the scientific profile of the potential visiting researcher/s: Methodologically oriented researchers with expertise in statistical analysis of ambulatory monitoring data, EEG data analysis, food choice modelling
This study investigates the mechanistic bases of human freeze-fight-flight reactions. The ability to control our social behavior is essential for almost every social interaction. It frequently fails in challenging situations when people fall back on basic defensive “freeze-fight-flight” (FFF) reactions. It chronically fails in social motivational disorders, with social anxiety as one extreme, and aggression as another. Such disorders are notoriously resistant to therapy. Accordingly, it is essential that we obtain mechanistic insight into the psychological and neurobiological control of human FFF behavior.

Upon a social challenge, an automatic attentive immobility, the freeze reaction, serves fast risk-assessment, needed to optimize subsequent fight-or-flight responses. Precise temporal tuning of FFF responses is critical to adequate coping with social challenges. It is orchestrated by complex neuroendocrine systems, utilizing the steroid hormone testosterone. Imbalances in the temporal dynamics and associated neuroendocrine control of FFF behaviors are highly predictive of animal fear and aggression. Testing these mechanisms in humans is critical to advance mechanistic insight in human FFF control, but has as of yet been foreclosed in the absence of the requisite tools to objectively measure human FFF. Recent innovations have enabled us to demonstrate that human freeze reactions to social threat mimic animal freeze responses (bodily immobility and fear bradycardia). These findings open up paths toward investigating the role of FFF reactions in social motivational disorders.

The major aim of the proposed research program is to reveal the mechanistic basis of human FFF regulation through the use of three cutting-edge methods: First I intend to integrate body-postural and electroencephalographic measures to detect, for the first time, the temporal dynamics and neuroendocrine control of the full FFF sequence in healthy individuals and patients with social anxiety and aggressive disorders. Second, I will apply hormonal and neural interventions to directly manipulate human FFF control using testosterone administration and transcranial magnetic stimulation. Third, and most crucially, I will validate the predictive value of basic FFF tendencies prospectively in a large longitudinal study. I will test adolescents in a critical transition phase (age 14-17) when they are most vulnerable to social and hormonal influences and when most symptoms develop.

The projected findings will advance core theoretical knowledge of the mechanistic basis of human emotion regulation. Moreover they are of critical importance for clinical treatment and society, breaking the grounds for early symptom detection and (preventive) intervention into social anxiety and aggressive disorders that form an ever-growing burden for society.

Keywords of the ERC project: Neural circuits, steroid hormones, stress, defensive responses; Anxiety and aggression

Keywords that characterize the scientific profile of the potential visiting researcher/s: Cognitive Neuroscience; Computational modelling; Motivation and Emotion; Neuroendocrine mechanisms; Psychiatry
Episodic memory refers to the fascinating human ability to remember past events in a highly associative and information rich way. But how are these memories coded in human brains? Any mechanism accounting for episodic memory must accomplish at least two functions: to build novel associations, and to represent the information constituting the memory. Neural oscillations, regulating the synchrony of neural assemblies, are ideally suited to accomplish these two functions, but in opposing ways. On the one hand, neurophysiological work suggests that increased synchrony strengthens synaptic connections and thus forms the basis for associative memory. Neurocomputational work, on the other hand, suggests that decreased synchrony is necessary to flexibly express information rich patterns in a neural assembly. Therefore, a conundrum exists as to how oscillations code episodic memory. The aim of this project is to propose and test a new framework that has the potential to reconcile this conflict. The central idea is that synchronization and desynchronization cooperatively code episodic memories, with synchronized activity in the hippocampus in the theta (~4 Hz) and gamma (~40-60 Hz) frequency range mediating the building of associations, and neocortical desynchronization in the alpha (~10 Hz) and beta (~15 Hz) frequency range mediating the representation of mnemonic information. Importantly the two modules, with their respective synchronous/asynchronous behaviours, must interact during the formation and retrieval of episodic memories, but how and whether this is the case remains untested to date. I will test these fundamental questions using a multidisciplinary and multi-method approach, including human single cell recordings, neuroimaging, brain stimulation, and computational modelling. The results from these experiments have the potential to reveal the neural code that human episodic memory is based on, which is still one of the biggest mysteries of the human mind.

Keywords of the ERC project: Episodic memory, brain oscillations, human single unit recordings, combined EEG-fMRI, MEG

Keywords that characterize the scientific profile of the potential visiting researcher/s: memory, oscillations, EEG/MEG, intracranial EEG recordings, computational modelling of neural networks, hippocampus
Social Cognition in Adolescents: Brain Networks and Social Networks

The forming of social bonds is an evolutionary imperative, and a rich target for empirical research. Social scientists have scrutinized the structure of the elaborate social networks that characterize today’s society. Neuroscientists have elucidated the brain mechanisms underlying our ability to navigate this social world. Yet, these research lines have been largely separated. This proposal aims to integrate social network research and social brain research, focusing on adolescence as the most dynamic phase shaping the interplay between social networks and the social brain. Social development in adolescents is clearly driven by maturation of specific social-cognitive functions; yet these functions are manifest in, and moulded by, interpersonal relationships within social networks. I aim to clarify how changes in the social brain relate to changes in social network position and structure during adolescent development. This can be achieved by using the quantitative tools of social network analysis in conjunction with the experimental approach of social neuroscience. I plan to investigate a cohort of approximately 1000 adolescents nested in 50 classes in a longitudinal design with 6 measurements over 3 years; fMRI investigating task-related functional activation and connectivity is conducted yearly in a subsample of 100. The neural and behavioural correlates of social cognition are investigated using experimental tasks tapping i) understanding others and ii) interacting with others; social behaviour is charted through ecological momentary assessment techniques; social networks are mapped using surveys and digital information acquired routinely via mobile phones (mobile sensing). This approach clarifies how during a crucial developmental phase the social brain shapes the social environment, and vice versa, the social environment influences maturation of the social brain.

**Keywords of the ERC project:** social cognition, adolescence, social networks, functional neuroimaging

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** expertise in (social) cognitive neuroscience, interest in development during adolescence
How the Brain Learns to Forget - The Neural Signature of Fear Memory Erasure

Can fear memories be erased from the brain? While it sounds like science fiction, recent findings suggest that fear memories can be undone upon their retrieval, through either pharmacological or behavioural interventions. Still, whether such reconsolidation interference techniques genuinely result in permanent erasure of the original fear memory is a topic of considerable controversy. Purely behavioural work may never settle the debate, as it cannot be excluded that an apparent loss of fear memory reflects a long-lasting failure to retrieve the fear memory rather than its permanent erasure. We argue that a careful look at the brain memory circuits that control the reduced expression of fear after reconsolidation interference, through imaging studies in humans and inactivation studies in rats, does have the potential to resolve the controversy and decide between erasure and retrieval failure as mechanisms underlying reconsolidation interference [WP1]. To open up a memory trace for reconsolidation interference, it is important that retrieval of the memory is accompanied by surprise or prediction error (PE; a discrepancy between the memory and what actually happens), as we demonstrated in a break-through study in Science (Sevenster, Beckers, & Kindt, 2013). Here, we propose that subtle differences in the degree of PE generated during fear memory retrieval may be what demarcates memory erasure from impaired retrieval. To investigate that claim, we will pioneer an objective neural marker of PE in humans [WP2] and use optogenetics to directly trigger dopamine-based PE signals in the rat brain in order to establish the causal role of PE in enabling fear memory erasure. Along the way, we will investigate the generalization of fear to novel cues as both a problem and a potential target for fear memory modification [WP3] and test an innovative method to interfere with reconsolidation that circumvents limitations of current pharmacological and behavioural techniques [WP4].

Keywords of the ERC project: Emotional memory; fear learning; post-retrieval amnesia; reconsolidation

Keywords that characterize the scientific profile of the potential visiting researcher/s:
Developing and delivering neurocomputational models to bridge between brain and mind.

The promise of cognitive neuroscience is truly exciting – to link mind and brain in order to reveal the neural basis of higher cognitive functions. This is crucial, scientifically, if we are to understand the nature of mental processes and how they arise from neural machinery but also, clinically, if we are to establish the basis of neurological patients’ impairments, their clinical management and treatment. Cognitive clinical neuroscience depends on three ingredients: (a) investigating complex mental behaviours and the underlying cognitive processes; (b) mapping neural systems and their function; and (c) methods and tools that can bridge the gap between brain and mental behaviour. Experimental psychology and behavioural neurology has delivered the first component. In vivo neuroimaging and other allied technologies allow us to probe and map neural systems, their connectivity and neurobiological responses. The principal aim of this ERC Advanced grant is to secure, for the first time, the crucial third ingredient – the methods and tools for bridging systematically between cognitive science and systems neuroscience. The grant will be based on two main activities: (i) convergence of methods – instead of employing each neuroscience and cognitive method independently, they will be planned and executed simultaneously to force a convergence of results; and (ii) development of a new type of neurocomputational model - to provide a novel formalism for bridging between brain and cognition. Computational models are used in cognitive science to mimic normal and impaired behaviour. Such models also have an as-yet untapped potential to connect neuroanatomy and cognition: latent in every model is a kind of brain-mind duality – each model is based on a computational architecture which generates behaviour. We will retain the ability to simulate detailed cognitive behaviour but simultaneously make the models’ architecture reflect systems-level neuroanatomy and function.

Keywords of the ERC project: cognitive neuroscience; semantics and language; aphasia; computational modelling; fMRI; MR tractography

Keywords that characterize the scientific profile of the potential visiting researcher/s: cognitive neuroscience; imaging analyses; aphasiology
Major depression is among the most burdening health hazards. Its prevalence is 1-3%, an additional 8-16% have clinically significant symptoms, and prognosis is poor. Unfortunately, less than 20% of the cases are detected and treatment effectiveness is moderate. The Global Consortium for Depression Prevention stresses that our best chance to combat the global burden of depression is provide preventive intervention to identified people at risk. This project targets the strongest modifiable risk factor: insomnia. With prevalence estimates up to 40%, insomnia is among the most frequent disorders in the elderly population. Meta-analysis shows that no less than 13% of people with insomnia develop depression. This extreme risk and the very high prevalence of insomnia in the ageing population, shows the urgency and promise of: (1) early identification of these 13%, (2) finding mechanisms by quantification of how they differ from insomniacs that do not develop depression with respect to brain structure and function, psychological traits, behavioural habits and environmental exposures; and (3) enrolling them in intervention protocols aimed at sleep improvement and prevention of depression. The project extends recent findings emerging from the applicant’s pioneering, unconventional and innovative approach to insomnia; the proposal that distinct subtypes exist and can be discriminated data-driven by means of multivariate trait analysis and brain imaging. Ignorance of this heterogeneity has obstructed progress in mechanistic understanding and rational treatment. In an unprecedented interdisciplinary way the project (1) identifies the insomnia subtype that develops depression; (2) profiles mechanisms involved; and (3) optimizes effectiveness of internet-supported home-applicable interventions to improve sleep and prevent depression. This approach will identify risks and mechanisms, and facilitate immediate implementation of risk-based prevention strategies and policies.

**Keywords of the ERC project:** Insomnia, depression, mood, MRI, HD-EEG, RCT, multivariate analysis

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** multivariate analysis, MRI, HD-EEG
Calibration and integration of peripheral and foveal information in human vision

Human visual perception is one of the best-studied areas of research on the human mind. However, 99% of that research is concentrated on the central region making up less than 1% of our visual field. This is the region that gets mapped onto the fovea, where vision is best. However, information from the peripheral parts of a scene is highly important. Mediated by attention and eye movements, it is essential for guiding us through our environment. In the brain, the foveal and peripheral parts of the visual field undergo vastly different processing regimes. Since objects normally do not change their appearance, whether we view them foveally or peripherally, our visual system must integrate and calibrate peripheral information before an eye movement with foveal information after an eye movement.

We are planning to address these processes in four series of experiments. First, we will study the perception of basic visual features, such as orientation, numerosity and colour across the visual field and their integration in peripheral and foveal vision across eye movements. Second, we will investigate how this integration is supported by attention and memory resources. Third, since the integration requires learning and plasticity, we will track changes across the life span and study how healthy subjects can learn to compensate for artificial changes of peripheral and foveal vision. And fourth, we will explore whether we can manipulate the integration process for the optimal guidance of eye movements in complex natural search tasks.

The project will provide insights how the brain achieves a stable and homogeneous representation of the visual environment despite the ever changing sensory input and the inhomogeneity of processing across the visual field. We will reveal the basic learning mechanisms that allow a continuous calibration of peripheral and foveal vision, and that could be used in the long run for behavioural training of patients suffering from vision impairments.

**Keywords of the ERC project:** Visual perception; Neuroscience; Psychology;

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** Visual perception; Neuroscience; Psychology;
Visual perception in Context

Everything occurs in a context. We see a car in the context of a street scene and a stove in the context of a kitchen. Context greatly helps the processing of individual objects. Surprisingly however, context hardly plays a role in most models of visual perception, which treat perception as a largely bottom-up categorization process. In this research proposal, I will examine how context changes the cortical computations that give rise to visual perception, focusing on contextual modulations in space and time. Moreover, I will translate this research to a clinical condition that is marked by aberrant context modulations in perception.

Firstly, I will examine the influence of spatial context from the surround on cortical processing of individual elements. I aim to uncover the neural mechanisms responsible for the contextual facilitation of features and objects. I hypothesize that spatial context constrains sensory input by changing sensory representations at earlier stages in line with expectations at higher-order stages of perceptual analysis.

Secondly, I will examine the influence of temporal context from past history. I hypothesize that temporal contexts trigger cortical waves of neural ‘preplay’ activity, setting up time-varying templates of expected incoming visual input.

Thirdly, I will test the clinical significance of this framework to understand perceptual atypicalities in Autism Spectrum Disorder (ASD). I will empirically test the hypothesis that ASD is marked by deficient processing of contextual information, in both the spatial and temporal domain. This integrative approach has the potential to significantly advance theoretical models of perception, based on underlying neurobiology, and underline the importance of context for understanding perception. Moreover, the knowledge gleaned can have significant societal and clinical impact.

Keywords of the ERC project: Vision, perception, expectation, attention, context, fMRI, MEG, psychophysics

Keywords that characterize the scientific profile of the potential visiting researcher/s: top-down, attention, predictive coding, perception, neuroimaging, modeling
Cross-Linguistic Acquisition of Sentence Structure: Integrating Experimental and Computational Approaches

How children acquire their native language remains one of the key unsolved problems in Cognitive Science. This project will answer a question that lies at the heart of this problem: How do children acquire the abstract generalizations that allow them to produce novel sentences, while avoiding the ungrammatical utterances that result from across-the-board application of these generalizations (e.g., *The clown laughed the man)? Previous single-process theories (the entrenchment, preemption and verb semantics hypotheses) fail to explain all of the current English data, and do not begin to address the issue of how learners of other languages solve this learnability problem. The aim of the present project is to solve this problem by developing and testing a new unified cross-linguistic account of the development of sentence structure. In addition to the overarching theoretical question set out above, the research will address four key questions: (1) What do learners bring to the task in terms of cognitive-semantic universals?; (2) How do children form linguistic generalizations in the first place?; (3) Why are languages the way they are; would other types of systems be difficult or impossible to learn?; (4) What is the nature of development?. These questions will be addressed by means of four Work Packages (WPs). WP1 uses grammaticality judgment and elicited production paradigms developed by the PI to investigate the acquisition of basic transitive and intransitive sentence structure (e.g., The man broke the window/The window broke) across six typologically different languages: English, K’iche’ Mayan, Japanese, Hindi, Hebrew and Turkish (at ages 3-4, 5-6, 9-10 and 18+ years). WP2 uses the same paradigms to investigate idiosyncratic language-specific generalizations within three of these languages. WP3 uses Artificial Grammar Learning to focus on the issue of language evolution. WP4 uses computational modeling to investigate and simulate development.

Keywords of the ERC project: psychology; linguistics; language acquisition; language development

Keywords that characterize the scientific profile of the potential visiting researcher/s: psychology; linguistics; language acquisition; language development
This proposal proceeds from an anomaly. Apartheid routinely breached the separation that it names. Whereas the South African regime was deeply isolationist in international terms, new research links it to the Cold War and decolonization. Yet this trend does not consider sufficiently that the global contest over the meaning of apartheid and resistance to it occurs on the terrain of culture. My project argues that studying the global circulation of South African cultural formations in the apartheid era provides novel historiographic leverage over Western liberalism during the Cold War. It recasts apartheid as an apparatus of transnational cultural production, turning existing historiography inside out. This study seeks:

• To provide the first systematic account of the deterritorialization of “apartheid”—as political signifier and as apparatus generating circuits of transnational cultural production.
• To analyze these itinerant cultural formations across media and national borders, articulating new intersections.
• To map the itineraries of major South African exiles, where exile is taken to be a system of interlinked circuits of affiliation and cultural production.
• To revise the historiography of states other than South Africa through the lens of deterritorialized apartheid-era formations at their respective destinations.
• To show how apartheid reveals contradictions within Western liberalism during the Cold War, with special reference to racial inequality.

Methodologically, I introduce the model of thick convergence to analyze three periods:

Each explores a cultural dominant in the form of texts, soundscapes or photographs. My work stands at the frontier of transnational research, furnishing powerful new insights into why South Africa matters on the stage of global history.

Keywords of the ERC project: apartheid, Cold War, transnationalism, South African expressive culture, South African literature, South African music, liberalism, race, exile, decolonization, apartheid, political exile

Keywords that characterize the scientific profile of the potential visiting researcher/s: apartheid, South African literature, South African cultural studies, Cold War history, decolonization, expressive culture, political exile
Aristotle in the Italian Vernacular: Rethinking Renaissance and Early-Modern Intellectual History (c. 1400–c. 1650)

From the twelfth to the seventeenth century, Aristotle’s writings lay at the foundation of Western culture, providing a body of knowledge and a set of analytical tools applicable to all areas of human investigation. Scholars of the Renaissance have emphasized the remarkable longevity and versatility of Aristotelianism, but their attention has remained firmly, and almost exclusively, fixed on the transmission of Aristotle’s works in Latin. Scarce attention has gone to works in the vernacular. Nonetheless, several important Renaissance figures wished to make Aristotle’s works accessible and available outside the narrow circle of professional philosophers and university professors. They believed that his works could provide essential knowledge to a broad set of readers, and embarked on an intense programme of translation and commentary to see this happen. It is the argument of this project that vernacular Aristotelianism made fundamental contributions to the thought of the period, anticipating many of the features of early modern philosophy and contributing to a new encyclopaedia of knowledge. Our project aims to offer the first detailed and comprehensive study of the vernacular diffusion of Aristotle through a series of analyses of its main texts. We will thus study works that fall within the two main Renaissance divisions of speculative philosophy (metaphysics, natural philosophy, mathematics, and logic) and civil philosophy (ethics, politics, rhetoric, and poetics). We will give strong attention to the contextualization of the texts they examine, as is standard practice in the best kind of intellectual history, focusing on institutional contexts, reading publics, the value of the vernacular, new visions of knowledge and eclecticism. With the work of the PI, two professors, 5 post-docs and two PhD students we aim to make considerable advances in the understanding of both speculative and civil philosophy within vernacular Aristotelianism.

Keywords of the ERC project: renaissance, intellectual history, philosophy

Keywords that characterize the scientific profile of the potential visiting researcher/s: reseachers, teachers, professors, post-docs
Modern historiography produced in Asia belongs to the history-paradigm of the European humanities and it is from within these epistemological confines that Western as well as Eastern scholars of Asian studies view the Asian writing of the past. While source criticism and historicism have today become key parts of historical consciousness in Asia, Asian historical representations are nonetheless firmly embedded in pre-modern Asian literary traditions via specific uses in historical writing of traditional rhetorical structures of narrative, emplotment, tropes, and literary imagery.

Taking such linkage between present and past Asian traditions of historiography as its premise, project NAMO – with four team members consisting of the PI and three Postdocs – will examine the literary features of Asian historiography in India, China, and Tibet across the longue durée of the classical, medieval, and modern periods. First, a new method for the study of the literary forms that characterize historiography in Asia will be established by adapting basic analytical principles from Asian literary theories drawn from twelve classical Indian and Chinese works on poetics. Next, the team will determine the specific literary characteristics of narrative, plot, tropes, and historical explanation found in seventeen classical and medieval histories composed in China, India, and Tibet. Finally, it will be examined to which extent those traditional literary features still function as constitutive rhetorical elements in modern Asian history writing. This will be done by analyzing the literary forms used in a selection of twenty representative histories written in the People’s Republic of China and the Republic of India during the period 1980-2010.

The outcome will be a novel approach for the empirical study of Asian history that will open up a new level of comparative work in the theory of history across non-Western and Western traditions.

**Keywords of the ERC project:** The structures and use of narrative in Asian history writing with focus on China, India, Tibet, and Persia

**Keywords that characterize the scientific profile of the potential visiting researcher/s:** specialists of theory of history, Asian studies, and/or literary theory of narrative
Every single human is the product of a pregnancy: an approximately nine-month period during which a foetus develops within its mother’s body. Yet pregnancy has not been a traditional focus in philosophy. That is remarkable, for two reasons: First, because pregnancy presents fascinating philosophical problems: what, during the pregnancy, is the nature of the relationship between the foetus and the maternal organism? What is the relationship between the pregnant organism and the later baby? And when does one person or organism become two? Second, because so many topics immediately adjacent to or involved in pregnancy have taken centre stage in philosophical enquiry. Examples include questions about personhood, foetuses, personal identity and the self. This project launches the metaphysics of pregnancy as an important and fundamental area of philosophical research. The core aims of the project are:
(1) to develop a philosophically sophisticated account of human pregnancy and birth, and the entities involved in this, that is attentive to our best empirical understanding of human reproductive biology;
(2) to articulate the metaphysics of organisms, persons and selves in a way that acknowledges the details of how we come into existence; and
(3) to start the process of rewriting the legal, social and moral language we use to classify ourselves and our actions, so that it is compatible with and can accommodate the nature of pregnancy. The project will investigate these questions in the context of a range of philosophical sub disciplines, including analytic metaphysics, philosophy of biology and feminist philosophy, and in close dialogue with our best empirical understanding of the life sciences – most notably physiology.

Keywords of the ERC project: Philosophy, Pregnancy, Biology, Metaphysics

Keywords that characterize the scientific profile of the potential visiting researcher/s: Philosophy, Pregnancy, Biology, Metaphysics, Phenomenology
Epistemic Transitions in Islamic Philosophy, Theology and Science: From the 12th to the 19th Century

Not very long ago, it was still common to hold that little of interest took place in Islamic philosophy, theology and science after the death of the Peripatetic commentator Averroes in 1198. Recent research has produced increasing evidence against this view, and experts now commonly agree that texts from the so-called post-classical period merit serious analysis. That evidence, however, is still fragmentary, and we lack a clear understanding of the large scale and long run development in the various fields of Islamic intellectual culture after the twelfth century. This project will investigate debates concerning the nature and methods of knowledge in four of the most ambitious strands of Islamic theoretical thought, that is, philosophy, theology, natural science, and philosophically inclined Sufism. Its temporal scope extends from the end of the twelfth century to the beginning of the colonial era, and it focuses on foundational epistemological questions (how knowledge is defined, what criteria are used to distinguish it from less secure epistemic attitudes, what methods are identified as valid in the acquisition of knowledge) as well as questions concerning knowledge as the goal of our existence (in particular, whether perceptual experience is inherently valuable). Our study of the four strands is based on the hypothesis that the post-classical period is witness to a sophisticated discussion of knowledge, in which epistemic realism, intuitionism, phenomenalism, and subjectivism are pitted against each other in a nuanced manner. Hence, the project will result in a well-founded reassessment of the common view according to which post-classical Islamic intellectual culture is authoritarian and stuck to an epistemic paradigm that stifles insight and creativity. Thereby it will provide new ingredients for projects of endogenous reform and reorientation in Islam, and corroborate the view that our future histories of philosophy should incorporate the Islamic tradition.

Keywords of the ERC project: Islamic philosophy, Islamic theology, medieval philosophy, history of philosophy, history of science

Keywords that characterize the scientific profile of the potential visiting researcher/s: Islamic philosophy, Islamic theology, medieval philosophy, history of philosophy, history of science
This project explores the relationship between climate change and human behaviour. During the harshest conditions of the last ice age European human populations abandoned northern latitudes, with their range contracting to southern regions. By the time ice sheets retreated and large areas of land became available for resettlement there had been a hiatus of at least 7000 years. This project examines the recolonisation of these Northern regions which took place during a period of rapid climate change, the last major global warming event on earth. As people move eastwards and northwards increasing diversification is seen in their stone and bone tool industries which indicate human development. This project examines whether climate a) drove the human dispersal and development, b) played a more indirect role, or c) was of little significance to humans at this time. State-of-the-art scientific techniques (radiocarbon dating, DNA, stable isotope, clumped isotope and charcoal ring width analyses) will be used to create integrated chronological, palaeoclimatic and palaeoecological frameworks that are directly linked to the Late and Final Palaeolithic archaeological record. Temporal and spatial trends in climate change, prey abundance and behaviour, and technological development will be compared and considered in light of regional and global climate trends and archaeological evidence for hunting strategies, human mobility and landscape use. Such data will provide an insight into the conditions Palaeolithic people experienced and how this influenced their perceptions of the landscape they inhabited and the decisions they made.

Keywords of the ERC project: Archaeology, isotopes, ancient DNA, radiocarbon, environment, climate, colonisation, Palaeolithic, hunter gatherers, Palaeolithic, Archaeology, bioarchaeology, palaeoclimates, palaeoecology, climate change, colonization, demography, archaeological science, geochemistry

Keywords that characterize the scientific profile of the potential visiting researcher/s: archaeology, geochemistry, palaeoclimate, palaeoecology, palaeobiology, climate change, archaeological science, isotopes, ancient DNA,
Shadows of Slavery in West Africa and Beyond. A Historical Anthropology

Though the colonial abolition of West African slavery and slave trade is well researched, the aftermath of slavery still deserves attention. What does it mean to be of slave descent today? How does the legacy of slavery and the slave trade overlap with harsh contemporary forms of marginality and exploitation? Moreover, what do we see when these questions are raised in a much broader comparative perspective? This project looks at the follow up of the abolition of slavery and the slave trade, a global process that invested the world at different times with a rich and complex variety of outcomes. Most historical research has stopped at the early colonial period, a very well documented phase of world history. Here, the analysis expands up to the present, and beyond the boundaries West African studies. Four regions of the world, which are under scrutiny for trafficking and contemporary slavery, will be studied comparatively. These are Eastern Senegal (West-Africa), Libya (North Africa), Coastal Madagascar (Indian Ocean), and North Afghanistan (Central Asia). The ambition is to link the micro-study of lived experience, cultural meanings and practices with the analysis of linkages and broader historical processes. To get results, there is need of a dialogue with human rights, legal theory, studies of gender and racial discrimination as well as scholarly insights on globalization and neo-liberalism. The ultimate objective of the project is an analytically integrated study of the aftermath of slavery that captures both the variety of concrete case-studies and the larger history of linkages between different parts of Africa and the world, Europe included. Innovation stands at the crossroad of chronological, geographical and disciplinary boundaries.

Keywords of the ERC project: slavery, abolition, emancipation, Africa, free and unfree labor, meanings of freedom, slave descendants, contemporary slavery

Keywords that characterize the scientific profile of the potential visiting researcher/s: slavery, abolition, emancipation, Africa, Atlantic, Indian Ocean, free and unfree labor, meanings of freedom, slave descendants, contemporary slavery
Rethinking Disability: the Global Impact of the International Year of Disabled Persons (1981) in Historical Perspective

Approximately 10% of the world’s population is estimated to be disabled and this number is expected to rise in the next few decades. People in different cultural settings ascribe different meanings to disability; consequently, its repercussions are both culturally contingent and universal. This project brings together the local and global dimensions of disability and examines the interaction, tension and conflict between these two aspects by undertaking the first comprehensive study of the far-reaching political, societal and cultural implications of the International Year of Disabled Persons (IYDP) which was organized under the auspices of the United Nations in 1981. A landmark event which appears to have gone virtually unrecognized in scholarship; the IYDP was the first occasion to place disability into a global context by endorsing it authoritatively as a human rights issue and thereby raising the question as to how the concept may be understood in a multicultural world. There will be four closely-related objectives: 1. to examine the IYDP’s impact on human rights discourses and to scrutinize their applicability within global settings; 2. to document the IYDP’s contribution to emancipation and social change and to consider the different trajectories of emancipation in various parts of the world; 3. to assess the ways in which the IYDP influenced everyday life experiences, galvanized identity formation and inspired the emergence of a distinct subculture; 4. to analyze the transnational exchanges and knowledge transfer in conjunction with the IYDP and to examine how the Western oriented discourses penetrating the developing world interacted with the local environment. The project’s innovative contribution and academic impact lies in connecting the IYDP to broader political, social and cultural processes in the last quarter of the twentieth century and thereby bringing disability in a global context to the attention of mainstream historical scholarship.

Keywords of the ERC project: disability, welfare state, global health, development policies, social movements, human rights, vulnerability

Keywords that characterize the scientific profile of the potential visiting researcher/s: global health, human rights, disability, international organizations, global history, anthropology
Effects of phosphorus limitations on Life, Earth system and Society

P is an earthbound and finite element and the prospect of constrained access to mineable P resources has already triggered geopolitical disputes. In contrast to P, availabilities of carbon (C) and nitrogen (N) to ecosystems are rapidly increasing in most areas of the globe. The resulting imminent change in the stoichiometry of available elements will have no equivalent in the Earth’s history and will bear profound, yet, unknown consequences for life, the Earth System and human society. The ongoing shifts in C:N:P balances in ecosystems will necessarily affect the structure, function and diversity of the Earth system. P-market crises might put pressure on the global food system and create environmental ripple effects ranging from expansion of agricultural land to P-price-induced changes in land management exacerbating the stoichiometric resource imbalance. Yet, the impacts of this unprecedented human disturbance of elemental stoichiometry remain a research enigma. The IMBALANCE-P-team, that gathers four leading researchers in the fields of ecosystem diversity and ecology, biogeochemistry, Earth System modelling, and global agricultural and resource economics, is formidably positioned to address this Earth System management challenge by providing improved understanding and quantitative foresight needed to formulate a range of policy options that will contain the risks and mitigate the consequences of stoichiometric imbalances. IMBALANCE-P will integrate some of Europe’s leading integrated assessment and Earth system models, calibrated using ecosystem nutrient limitation data obtained from field experiments. The project will establish an international process of science-based P-diplomacy.

Keywords of the ERC project: phosphorus limitations, Earth System management

Keywords that characterize the scientific profile of the potential visiting researcher/s: ecosystem diversity and ecology, biogeochemistry, Earth System modelling, global agricultural and resource economics
Effects of phosphorus limitations on Life, Earth system and Society

P is an earthbound and finite element and the prospect of constrained access to mineable P resources has already triggered geopolitical disputes. In contrast to P, availabilities of carbon (C) and nitrogen (N) to ecosystems are rapidly increasing in most areas of the globe. The resulting imminent change in the stoichiometry of available elements will have no equivalent in the Earth’s history and will bear profound, yet, unknown consequences for life, the Earth System and human society. The ongoing shifts in C:N:P balances in ecosystems will necessarily affect the structure, function and diversity of the Earth system. P-market crises might put pressure on the global food system and create environmental ripple effects ranging from expansion of agricultural land to P-price-induced changes in land management exacerbating the stoichiometric resource imbalance. Yet, the impacts of this unprecedented human disturbance of elemental stoichiometry remain a research enigma. The IMBALANCE-P-team, that gathers four leading researchers in the fields of ecosystem diversity and ecology, biogeochemistry, Earth System modelling, and global agricultural and resource economics, is formidably positioned to address this Earth System management challenge by providing improved understanding and quantitative foresight needed to formulate a range of policy options that will contain the risks and mitigate the consequences of stoichiometric imbalances. IMBALANCE-P will integrate some of Europe’s leading integrated assessment and Earth system models, calibrated using ecosystem nutrient limitation data obtained from field experiments. The project will establish an international process of science-based P-diplomacy.

Keywords of the ERC project: phosphorus, nitrogen, nutrients, global change, ecology, earth system models, integrated assessment models

Keywords that characterize the scientific profile of the potential visiting researcher/s: dynamic, multidisciplinary, ecologist,