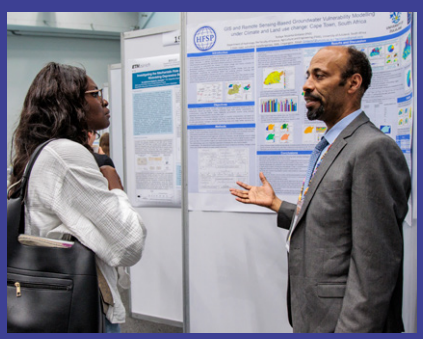
THE HUMAN FRONTIER SCIENCE PROGRAM
ANNOUNCES ITS

2024 Research Grant Awardees



35 years

International
Human Frontier
Science Program
Organization

The Human Frontier Science Program (HFSP) is unique in supporting international collaboration to undertake innovative, risky, basic research at the frontiers of the life sciences. Special emphasis is given to the support and training of independent young investigators, beginning at the postdoctoral level.

The Program is implemented by the International Human Frontier Science Program Organization (HFSPO), supported financially by Australia, Canada, the European Commission, France, Germany, India, Israel, Italy, Japan, New Zealand, Norway, the Republic of Korea, Singapore, South Africa, Switzerland, the United Kingdom of Great Britian and Northern Ireland, and the United States of America.

Since, 1990, more than 8,500 researchers from more than 70 countries have been supported. Of these, 29 HFSO awardees have gone on to receive the Nobel Prize.

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About HFSP's 2024 Grants
Message from the Director of Grants:

Almut Kelber,
Director HFSP Research Grant Program

I'm thrilled to announce this year's HFSP Research Grant Award Winners, who are among the world's most creative scientists pioneering the very frontiers of life science research today.

For 2024, HFSP has chosen to support 34 Research Grant project teams that include 108 scientists representing 23 nations. Their projects span 10 areas of the life sciences that range in focus from the most molecular science to cross-disciplinary investigations that span biomes. Each grant will last for three years and on average, each award is for $400,000 USD per year.

In this volume, our first HFSP Research Grant Awards Booklet, you will find the abstracts that impressed the review committee. They felt these proposals offered the promise of truly expanding the frontiers of life science research and may well lead to unimaginable findings! The research projects fall into two categories: Research Grant – Program and Research Grant – Early Career.

Our Program Grants are awarded to teams with two to four members at any stage of their careers who embark upon a new collaborative project. Our Early Career Grants require that all team members are within 5 years of obtaining an independent position and that it has been no more than 10 years since they earned their Ph.D. Among all of our awardees we seek scientists who form internationally, preferably intercontinentally collaborative teams, who have not worked together before, and who are engaging in work for which they have no preliminary data. In these ways, HFSP fosters frontier research and science diplomacy. To take a look at the Research Grants we have funded in the past, please visit our website at www.hfsp.org.

Congratulations are in order to all of our winners as they begin their investigations this year. Please know, we're all looking forward to see what you discover!

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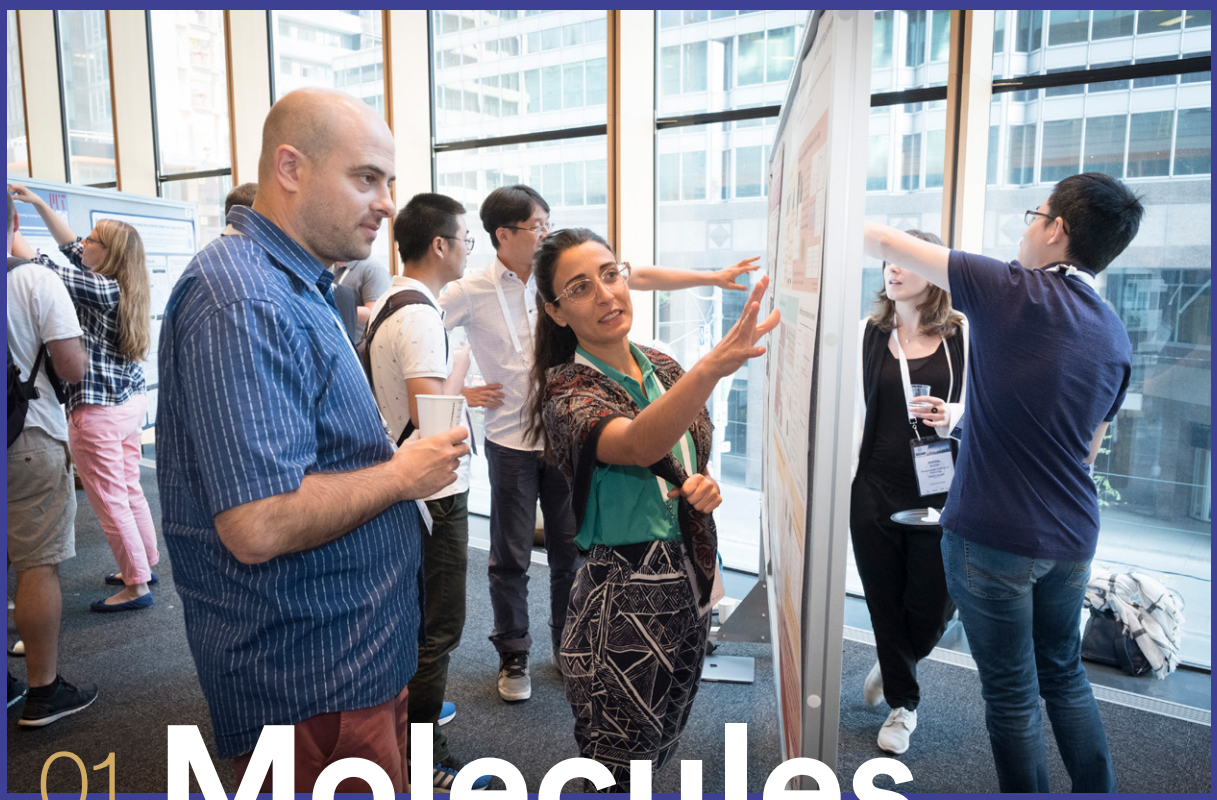

01 Molecules and Their Effects on Physiology

Discovering the Chemical Space of Bioactive Modified Nucleotides and Their Enzymatic Repertoire

HFSP Research Grant - Program
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Nucleotides are essentially the 'building blocks' of life, forming the backbone of DNA and RNA, the molecules that carry our genetic information. Aside from their role in genetics, these nucleotides exist in many modified forms, undertaking vital roles such as influencing gene activity. Moreover, these modified nucleotides can exhibit a wide range of fascinating and sometimes surprising properties. For instance, they can self-repair DNA and even facilitate the effectiveness of chemotherapy in cancer treatment. Despite their importance, we have only scratched the surface of understanding these modified nucleotides.

Their variety across different species and their powerful biological activities mean they could provide opportunities for new scientific understanding and medical treatments. However, they also carry risks, as some can induce harmful mutations or cause toxic reactions in the body. Fortunately, many organisms have natural enzymes that can "detoxify" harmful nucleotides to mitigate these risks, but we have yet to fully grasp how these enzymes function and evolve.

In our project, we will leverage a multidisciplinary approach pulling together advanced chemistry, computational modeling, and cellular biology techniques to explore this little-understood field of science. Our research aims to identify and understand these modified nucleotides in a systematic way, analyzing samples from both human and microbial sources. We are also keen on predicting and studying the enzymes that modify or detoxify these nucleotides, examining how they have evolved, and what roles they play in different organisms. We anticipate that this investigation will broaden our understanding of life on a fundamental level. By tracing the origins, impacts, and interactions of these nucleotides across different species, we will not only unlock new scientific knowledge, but potentially pave the way for innovations in medical therapy. We also hope to offer new insights into evolutionary biology, understanding the 'chemical conversations' that occur between different life forms at the molecular level, and thereby, enriching our comprehension of the intricate web of life on our planet.

Mechanoradicals as a Novel Form of Mechanosensing: from Protein Stretching to Animal Aging

HFSP Research Grant - Program
Ronen Zaidel-Bar, Dept of Cell and Developmental Biology, Tel Aviv University, Israel
Alexander Dunn, Dept of Chemical Engineering, Stanford University, USA
Frauke Gräter, Dept of Molecular Biomechanics, Heidelberger Institut für Theoretische Studien, Germany

As we move around in the world, our body is often exposed to forces such as squeezing and stretching. This is true also at the cellular level, and the field of mechanobiology involves the study of how cells can sense and respond to mechanical forces. A major challenge in this field is to elucidate the molecular mechanisms that allow cells to sense forces, and attention so far has been focused on proteins and structures within cells, such as the cytoskeleton and cell adhesions. The novel idea behind this proposal is that proteins outside of the cell, in what is called the extracellular matrix, can also be affected by force and generate diffusible chemical signals that can reach nearby cells and influence their function.

Our project builds on our recent observation that in controlled lab conditions, stretching extracellular protein collagen causes rupture of chemical bonds that release free radicals, which we call mechanoradicals. Our goal is to prove that this process happens also in living tissues under normal physiological forces and to study the impact of mechanoradicals on the health of the tissue and the entire organism. For this, we are going to use two model systems: a tendon taken from a mouse and the worm *Caenorhabditis elegans*.

Tendons are highly collagenous tissue that connects muscles to bones and can be cultured outside of the animal for several days. *C. elegans* is a powerful genetic model system and its exoskeleton (cuticle) is made nearly entirely of collagen. We will employ a combination of cutting-edge techniques, including minute fluorescent molecules, which report on forces present in the tissues, molecular dynamics simulations of the detailed structure of the collagens at hand, and genetic engineering, in order to visualize and manipulate the consequences of mechanoradicals in tendons and *C. elegans*. Those capabilities will allow us to go further and measure, for the first time, the effect of mechanoradicals on the integrity of the tissue and the well-being of the organism, including its fertility, resilience to stress, and lifespan. Thus, our project will uncover mechanoradicals as a previously unrecognized molecular species in life that converts tension into physiological responses with implications for health, disease, and aging.

02 Organelles, Cells, Tissues and Organs

Vibrational Information Transfer Between Living Cells in the Extracellular Matrix

HFSP Research Grant - Program
Ayelet Lesman, School of Mechanical Engineering, Tel Aviv University, Israel
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Ramon Zaera Polo, Continuum Mechanics and Structural Analysis, University of Carlos III Madrid, Spain
Beth Mortimer, Dept of Biology, University of Oxford, UK

Can cells use small motions to transmit information among themselves? We will focus on fibroblasts, specialized cells that are important components of connective tissue and are essential for wound healing, tissue repair and growth, and other functions. Fibroblast cells live within a bed of fibers and liquid known as a matrix, which has the potential to transmit motions through its network to other cells, similar to vibrations within a spiders' web. We know that fibroblast cells can generate forces, but we don't know if they transmit information through oscillations that vary over time.

Our project aims to study the generation of these dynamic motions, how they move through the matrix where the cells are embedded, and how the cells respond to these tiny motions. We will do this by drawing together expertise from across biology and engineering, combining cutting-edge experimental techniques to measure cell-driven motions, and using computer modeling to understand how cells generate and interact with these tiny motions.

Together, the project will give important insights into whether fibroblasts make use of motions for information. This is important for understanding how fibroblasts can influence and coordinate each other during important processes such as wound healing, inflammation, regulating the heartbeat, and other important medical applications.

Optogenetic Control of Organelle “Chatter” and Effects on Calcium Dynamics in Human Cardiomyocytes

HFSP Research Grant - Program

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Michael Colman, Dept of Biomedical Sciences, The University of Leeds, UK
Moritoshi Sato, Dept of Life Sciences, The University of Tokyo, Japan

Complexity in biological function is borne out of intricate subcellular and multicellular organization and coordinated communication between specialized partitions/organelles. In the case of heart muscle cells, the orchestration of events linking the electrical messages to the mechanical action of each beat must be smooth and fault-proof. Subcellular calcium stores are accessed and refilled in a precise manner to support the heart’s normal operation. Proximity, by way of nanoscale interfaces between the compartments, allows small variations in ions to quickly and significantly alter the local concentration to respond to the demands of mechanical work. In some cardiac pathologies, these processes get disrupted and lead to life-threatening rhythm abnormalities, called arrhythmias. Contributors to the disruption can come from improper communication between the main calcium store and other calcium storage organelles, i.e., from disruptions in the subcellular arrangement.

To gain better understanding of the biology behind these interactions, we will use new genetic tools to bring various subcellular organelles together in a precise, quick, and reversible manner by using light pulses. These engineered light-responsive structures, known as photoswitches, come in polarized pairs that attract each other like magnets, and when expressed in various cellular compartments in the presence of light, they can help move organelles closer together and increase their communication. As a result of this light-controlled action we can alter the way electrical signals are translated into mechanical heart contractions to mimic disease conditions, or to boost muscle performance.

Our studies will permit – for the first time – the ability to assess how various secondary calcium storages, such as the energy-generating organelles (mitochondria), or the waste clearing organelles (lysosomes) shape heart activity. Using the experimental data, we will create predictive computational models of how these various compartments may talk to each other via critical calcium release events for both health and disease. We project this research will advance fundamental understanding of critical events during the heart beat and lead to new approaches to control these events and generate new therapeutic solutions.

Deciphering the Role of Ion Distribution in Mitochondria for Long-term Memory Formation

HFSP Research Grant - Program
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Elizabeth Jonas, Dept of Internal Medicine, Yale University, USA
Nicholas Tomkinson, Dept of Pure and Applied Chemistry, University of Strathclyde, UK

How the brain works is a key question of our time. In particular, our understanding of how memory is formed is still in its infancy. We know that nerve cells are stimulated and that certain synapses are strengthened. These processes are energy intensive. The brain relies primarily on oxidative phosphorylation to produce ATP, a molecule that serves as the energy currency in the cell to pay for energy-consuming processes.

Oxidative phosphorylation is a process that takes place in the mitochondria. It involves the coupling of reactions to generate proton and ion gradients across the inner mitochondrial membrane. As ions and protons are electrically charged, the chemical gradient across the membrane also generates an electrical voltage difference, referred to as membrane potential, which is used for ATP synthesis by an enzyme called ATP synthase. During memory formation, the efficiency of ATP supply appears to increase. We hypothesize that memory formation involves changes in membrane potential not only at the plasma membrane of neurons, but also within the mitochondria, leading to increased ATP production.

Based on this assumption, we will look more closely at ion fluxes across the inner mitochondrial membrane in neurons after neuronal stimulation to test whether the mitochondrial membrane potential also changes. We suspect that better use of the mitochondrial membrane potential will lead to increased ATP synthesis, and thus, increased energy supply for synaptogenesis and memory formation. To do this, we will visualize the processes using fluorescent biosensors imaged with state-of-the-art microscopes, including super-resolution microscopy. Our project will be a collaborative effort involving an international team, including a Scottish chemical biologist, a German cell biologist with expertise in super-resolution microscopy, and an American neurobiologist.

From Nano to Organismal Scale: Structural Regulation of Regenerating Jellyfish

HFSP Research Grant - Program
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Regeneration is a phenomenon observed across the natural world that allows many organisms to replace or repair injured body parts. Intriguingly, the ability to regenerate organs or tissues varies greatly among different species. While some organisms can complete minor tissue repairs, others can achieve complete regrowth of organs or missing body parts. Yet, why do only some injuries lead to regeneration?

Our research team addresses this fundamental, unresolved question from the original standpoint of the marine jellyfish *Clytia hemisphaerica*. Clytia jellyfish are lesser known, but powerful laboratory animals. Small, transparent animals they have exceptional capacities for body repair and organ regeneration, which makes them an ideal regenerative model. As fundamental cellular mechanisms and tissues behaviours are shared across many living organisms, the jellyfish provides a simplified platform for understanding complex regenerative processes and the emerging properties of real, living tissues.

We aim, through the synergy of our expertise – biomaterial science, biophysics, and regenerative and marine biology – to create a flexible and integrative “in vivo-vitro-silico” model system to probe the self-organising and regenerative capacities of living matter. This research will help build a new experimental and theoretical framework for both regenerative medicine and the properties of self-healing materials. Our vision requires three interacting branches of study feeding back on each other, and can thus, only succeed through a collaborative approach; parallel projects would fail. Quantitative jellyfish data will inform the analytical model and the generation of synthetic matrices. In silico and in vitro results will then guide in vivo experiments. Collectively, these three intertwined branches will create a continuous loop of investigation and discovery and open the door to a novel and integrative understanding of biological repair and regeneration.

03 Life and Evolution

Unambiguous Biosignatures for Life Detection

HFSP Research Grant - Program

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Sean McMahon, School of Physics and Astronomy, University of Edinburgh, UK
Mark Van Zuilen, Laboratoire Geo-Ocean, Institut National des Sciences de l'Univers, France

The search for evidence of life beyond Earth is widely recognized as one of the most profound challenges in modern science. Although organisms make and do things that inanimate matter simply cannot, it is difficult to identify what is distinctive about life in quantitative terms. Astrobiologists and paleontologists have attempted to define biosignatures and develop criteria to assess whether a material is of biological origin. However, ambiguity persists; both life-like self-organization in abiotic systems and universal quantifiable distinctions between life and non-life are underexplored.

Several national and collaborative space agencies are sending probes to solar system bodies where life could conceivably exist. Thus, there is strong interest in creating refined life detection methods, particularly an approach that could assess quantitatively whether a material is of biologic origin. Such an approach would avoid arbitrary qualitative descriptions, could be tailored to avoid false positives and minimize exclusion of false negatives, and above all could express life detection as a probability relative to a transparent decision procedure, rather than an absolute yes/no verdict (this is similar to how physicists express the detection of new particles probabilistically).

We will create a diagnostic workflow for assessing the biogenicity of planetary materials and in the process derive fundamental insights into the properties of biological materials. Our unique, data-driven approach will integrate quantifiable chemical and morphological parameters into a single multi-dimensional parameter space and then populate it with a broad range of biological and non-biological features. This multivariate approach will use machine learning to discriminate between life and non-life in concrete, quantitative terms and make it possible to test new hypotheses about what makes life "special."

Developing quantitative methods to discriminate biological and abiotic materials, patterns, and processes will provide fundamental methods for defining and detecting life in the universe. Our proposal will involve an astrobiologist with expertise in microbiology, a geobiologist, and a prebiotic chemist/organic geochemist. The three team members will combine their results to build a single multi-dimensional parameter space in which signals of known life and signals of "abiotic mimics" can be distinguished.

Functional Ecology of Flagellates Sheds New Light on Early Eukaryotic Evolution

HFSP Research Grant - Program

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Kirsty Wan, Living Systems Institute, University of Exeter, UK
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A flagellum is an organelle that allows cells of many types to move, such as sperm, bacteria, and fungal spores. Flagellates are organisms that move thanks to a flagellum, and the last common ancestor of eukaryotes was a flagellate. All other eukaryotes – from amoebae to animals and plants – have evolved from them. Flagellates are abundant today and are found in all the major branches of the eukaryotic tree of life. Understanding their history is key to understanding early eukaryotic evolution.

We aim to infer the morphology and ecology of the Last Common Eukaryotic Ancestor (LECA) that lived more than a billion years ago, and to trace its evolutionary history. Traditionally, scientists use DNA and morphology to solve this puzzle, but as genes are exchanged between species, features that look the same may not have a common origin. Our novel approach is to also analyze how these organisms live and behave, i.e., their functional ecology.

We will focus on flagellates from several distantly related groups that share morphological features. Some of these are proposed to be the living cells that are most similar to LECA. Understanding the functional ecology of these groups may help us separate morphological features that are the same (homologous) from features that just appear similar. Morphological features found in distant branches of the tree, that are homologous, are likely to be characteristic of LECA. The feature shared by most of these organisms is a groove on the cell surface in which a flagellum with a vane beats. We suspect that this feature is related to how they swim and feed. While the typical representative of this group of flagellates feeds on small bacteria, others feed on other larger flagellates; thus, similar structures may function differently.

We will use high-speed video microscopy to quantify prey capture and swimming and fluid physics to interpret the observations and advanced microscopy to compare details in the morphology of different species. We will develop models to compare distinct morphological features and behaviors to understand their functional significance. We will combine all this with genetic information to paint a comprehensive picture of LECA.

Deciphering the Evolution, Cellular Biology and Biogeochemistry of Symbioses in Anaerobic Eukaryotes

HFSP Research Grant – Early Career

Filip Husnik, Okinawa Institute of Science and Technology Graduate University, Japan
Roxanne Beinart, Graduate School of Oceanography, University of Rhode Island, USA
Courtney Stairs, Dept of Biology, Lund University, Sweden

Life on Earth can be classified into two categories: eukaryotes (plants, animals, fungi) and prokaryotes (bacteria and archaea). In addition to the multicellular eukaryotes that we see around us, there are single-celled eukaryotes (e.g., an amoeba). Under the microscope, a drop of pond water contains thousands of different prokaryotes and eukaryotes interacting together.

Sometimes this interaction is antagonistic, such as an amoeba eating a bacterium. But sometimes organisms work together to survive in their environment. For example, an amoeba and a bacterium may rely on each other to provide different nutrients for each other's survival, especially in environments that lack oxygen (e.g., animal guts and aquatic sediments). This type of cooperation is called symbiosis and is pervasive across nature.

Despite their small cell sizes, microbial symbionts are essential to life on our planet as they contribute to important processes, such as the cycling of carbon dioxide, nitrogen, and sulfur. In this research, we will examine the molecular nature of these symbioses in eukaryotic microorganisms to discover how cells interact physically and what nutrients are shared between cells.

How Predictable is Evolution? Eco-evolutionary Dynamics of Fungi Across Biological Scales

HFSP Research Grant – Early Career

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Daniel Charlebois, Dept of Physics, University of Alberta, Canada
Meike Wortel, Dept of Microbiology, University of Amsterdam, The Netherlands

The study of evolution has traditionally been more descriptive than predictive. However, the rapid evolution of many microorganisms, including pathogens that adapt to resist drugs has motivated the need for scientific investigations that reflect a more quantitative, predictive approach.

Evolution is a combination of the random process of mutation and the deterministic process of selection, which raises the question: Can we predict evolution? This is often studied by assessing the repeatability of evolution, stemming from the question famously posed by the evolutionary biologist Stephen Jay Gould: “If we replay the tape of life, do we get the same outcome?”

Previous studies on this topic have focused on bacteria and antibiotics, leaving it unknown as to how these results generalize to other domains of life. Compared to bacteria, yeasts have additional complexities, including their genetics that can affect evolution. Furthermore, all microbes exist in interacting, multispecies communities that alter their evolutionary properties. In this research, we will study evolutionary repeatability in fungal communities consisting of multiple species of Candida yeasts that infect humans and rapidly evolve resistance to antifungal drugs. Our project will determine whether species diversity and interactions increase or decrease the repeatability of evolution.

This study requires the integration of different scientific fields and tools, including fungal biology, mathematical models, and physics-inspired theory and analysis of evolutionary data. We will develop biophysics-based models of drug selection and ecological interactions in this system, which we will use to simulate antifungal resistance evolution. Using our modeling results, we will perform antifungal resistance evolution experiments with varying interspecies interactions. There is a high potential for our project to lead to fundamental advances on how diversity affects evolution due to the novel combination of models that consider multiple biological scales and eco-evolutionary dynamics together with evolution experiments on communities of fungi. We expect the techniques we develop will facilitate breakthroughs for other open questions, as many areas of the life sciences will benefit from our interdisciplinary, multiscale approach to studying evolution.

Mechanisms and Evolutionary Consequences of Stress-induced Mutagenesis

HFSP Research Grant – Program

Martin Kupiec, The Shmunis School of Biomedicine and Cancer Research, Tel Aviv University, Israel
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Mutations arise constantly among individuals in populations. They are the basis for evolution, since individuals carrying mutations that confer some advantage generally thrive better than others, and their genetic information is then spread in the population. Mutagenesis plays also a pivotal role in the development of cancer, in the emergence of pathogens (e.g., COVID) and in the emergence of antibiotic resistance and anti-drug therapies. Thus, understanding the mechanisms that generate mutations is of utmost importance.

While it is customary to think about evolutionary advantage at the individual level, the advantages are only apparent within the context of a population. In this project, we want to understand the control of variation at the population level. For example, are there intercellular signals that elicit variation in the population to help overcome stressful conditions? Can a population-level reaction to stress be evolutionarily advantageous, even when individual cells may be negatively affected?

Our proposal involves collaboration between molecular genetics, mathematics, and computation. We will use baker's yeast (the same used to brew beer) as a model, and carry out a combination of theoretical and experimental work to answer fundamental questions related to the induction of variation by stress. Yeast is a rapidly growing microorganism amenable to sophisticated molecular biology, biochemical, and genetics approaches. Most importantly, it is easy to set up evolution experiments in the lab. We expect to obtain from these studies a better understanding of the evolutionary mechanisms that operate in times of stress, and their molecular details.

Such an understanding is both scientifically interesting and important for public health. Medical problems such as bacterial infections and cancer can be understood in terms of evolution and antibiotic resistance, and cancer therapies that fail often occur due to the emergence of mutations. Our studies may present novel strategies to pre-empt such problems.

Resurrecting the Multiple Origins of Tyrosine Kinase Activity and Phosphotyrosine Recognition

HFSP Research Grant – Early Career

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Understanding how life originated and has evolved is one of the most fundamental questions in life science, one which can be explored by using molecular systems thanks to their experimental tractability. In fact, our understanding of evolutionary relationships among species and how gene and protein sequences change and evolve has improved so much in recent decades that we can now "resurrect" extinct, ancestral proteins and study their functions.

While we can now study evolution for theoretically any molecular function, most molecular functions have only emerged once in evolution. This prevents us from "replaying the tape of life" and evaluating whether "functional solutions" other than the one taken by nature were possible.

One of the few molecular systems that has emerged multiple times in evolution is phosphotyrosine signaling. Phosphotyrosine signaling involves two key components: phosphotyrosine "writers," which catalyze the formation of phosphorylated tyrosine residues (or phosphotyrosines for short) on other proteins, and phosphotyrosine "readers," which recognize phosphotyrosines. While these "writers" and "readers" function as a combined signaling set, both the absolute and relative evolutionary time when these molecular components initially emerged and later evolved is unclear.

We plan to computationally reconstruct these evolutionary origins and test the ancestral molecular components to determine when these events occurred and which individual molecular steps were involved. Taking advantage of the fact that phosphotyrosine "writers" have evolved multiple times in history, we will determine when and how each of these independent events occurred and experimentally determine whether these different "solutions" to evolving the same function could substitute for one another. Our goal is to address a long-standing question in biology as to whether the evolution of new molecular functions is dictated by biophysical constraints that are contingent on evolutionary origins, or whether there were many possible evolutionary solutions.

A Tale of Tails – Reconstructing Evolutionary Transition Between Archaeal and Eukaryotic Chromatin

HFSP Research Grant – Early Career
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Svetlana Dodonova, Structural and Computational Biology Unit, EMBL-Heidelberg, Germany

All eukaryotic genomes are packaged into a DNA-protein complex called chromatin. The fundamental unit of chromatin is the nucleosome, and it consists of 147 bp of DNA wrapped around histone proteins. DNA accessibility in chromatin can vary depending on the linear spacing between nucleosomes and on their 3D arrangement, thus, enabling regulation of chromatin-based processes such as transcription.

Eukaryotic chromatin regulation strongly depends on the disordered N-terminal regions of the histones. These flexible regions, called histone tails, serve as hubs for post-translational modifications, mediate interactions between nucleosomes, and recruit various proteins that modulate nucleosomal arrays and higher-order chromatin structure. Histones are also widely found in the prokaryotic domain Archaea, from which eukaryotes arose. Archaeal histones can form nucleosomes and regulate gene expression, suggesting that the primitive histone-based chromatin structure and its role in gene regulation predated the emergence of eukaryotes from the archaeal domain. However, the vast majority of archaeal histones do not have tails, which are crucial for eukaryotes.

This raises key questions in the chromatin-evolution field: How did eukaryotes evolve histone tails and tail-based regulatory mechanisms from an archaeal ancestor, and what role could the tails play in proto-eukaryotic chromatin? In this project, we aim to answer these questions by creating the first synthetic model of proto-eukaryotic chromatin. We will merge eukaryotic histone tails with an archaeal tail-less histone, and test how this affects the molecular properties of the histone, its interactions with the DNA, and how it influences chromatin architecture both in the test tube and inside archaeal cells. By employing biochemistry, biophysics, genetic engineering, and state-of-the-art DNA sequencing and electron microscopy technologies, we will investigate the structural and functional effects of tail acquisition by an archaeal histone on both genomic and molecular scales. Our study will provide insight into how the emergence of histone tails impacted proto-eukaryotic chromatin, and how it led to the subsequent evolution of tail-based regulatory mechanisms in the eukaryotic lineage.

04 Embryo Development

Physical Forces and Mechanotransduction During Mouse Embryo Implantation

HFSP Research Grant - Program
Xavier Trepat, Dept of Integrative Cell and Tissue Dynamics, Fundacio Institut de Bioenginyeria de Catalunya, Spain
Takashi Hiiragi, Dept of Multi-cellular Coordination, Hubrecht Institute, The Netherlands

In this project, we aim to quantify the mechanical interaction between the embryo and the uterus to understand how physical forces affect embryo development.

We will focus on the interactions between cells composing the embryo and the implantation surface of the uterus; how the embryo adjusts its orientation after attachment; and how the spherical embryo develops into an egg cylinder.

Implantation is a critical early stage in pregnancy when the embryo first contacts the maternal uterine tissue to initiate pregnancy and embryo development. During implantation, the embryo undergoes significant changes, not only increasing in size and cell count, but also transforming into a cylindrical structure. Most importantly, it is at this stage that the fate of cells within the embryo is decided as to which will become embryonic cells that compose the embryo's body and which will contribute to the formation of extra-embryonic tissues such as the placenta and umbilical vesicle. The complex dynamic interactions between the embryo and uterus during implantation support successful embryo development.

While most of the research on the embryo-uterine interaction during implantation has focused on biochemical and genetic mechanisms, recent studies have indicated that mechanical forces also act as strong cues to guide embryo development. We will study the mechanics of mouse embryo implantation in vitro. We will directly measure forces between cells in the embryo as well as between cells and different materials that mimic the uterus surface. We will then study whether and how the embryo translates these mechanical cues into biomolecular signals to drive peri-implantation development.

Finally, we will measure mechanical interactions inside the pregnant mouse by combining advanced tools for imaging and force mapping. To achieve these goals, this project brings together an embryologist and a tissue biophysicist. Our results will provide an understanding of how mechanical, biochemical, and genetic processes combine to drive mammalian embryo implantation.

Mechanical Control of Hidden Embryonic Boundaries

HFSP Research Grant – Early Career

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Maria Almuedo-Castillo, Dept of Gene Regulation and Morphogenesis, Centro Andaluz de Biología del Desarrollo, Spain
Mattia Serra, Dept of Physics, University of California, San Diego, USA

During embryogenesis, a single cell gives rise to a multicellular, functional body. But how cells make decisions during this transformation — at the proper position and time — remains largely unknown. The complexity of this problem is increased by the highly dynamic nature of embryo development, implying that cells acquire their identity (e.g., muscle vs. neuron) while they navigate through ever-changing environments.

Importantly, cells receive information from their surroundings and use it to change their behaviors and decide which type of cell they want to become. Thus, understanding how different cell types arise requires following individual cells and recording the mechanical stimuli that they are sensing while migrating. Elucidating this fundamental mechanism has critical implications for understanding human development, detecting birth defects, and designing self-remodeling biomaterials. Using novel methods, we will measure the mechanical properties of this changing environment, that is, how soft and fluid the embryo is at any given point in time and space.

Like inert materials, tissues behave as either fluids or solids, and can even switch quickly from one state to the other in a process known as phase transition. Unraveling the role of mechanics during in vivo early embryogenesis is notoriously difficult because cells undergo large-scale, intricate motions, and only a few tools exist to measure mechanical properties in developing tissues. The analysis of these characteristic mechanical environments requires first the identification of novel regions in the embryo which organize the movements of all the cells. These regions, which behave very differently compared to the rest of the embryo, are known as repellers and attractors, and are similar to the repellers and attractors that control ocean currents.

We will develop a novel strategy for discovering repellers and attractors, which cannot be identified using standard techniques, and thus unveil the dynamic environment to which cells are exposed. This knowledge will allow us to understand how early cells decide to differentiate based on external inputs.

05

Microbes and Their Hosts

3D-bioprinting Meets Machine Learning: a Novel Tool to Decipher the Determinants of Viral Tropism

HFSP Research Grant – Program

Gabriel Castrillo, School of Biosciences, University of Nottingham, UK
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Just like humans, plants can be infected with a wide variety of viruses. Plant virus infections account for astounding global economic losses and are responsible for a high percentage of plant diseases worldwide, which compromises global food security. The main determinant of a viral infection is the ability of the virus to infect a cell type, a tissue or a species. This virus characteristic is called viral tropism and is determined by the virus' interaction with the plant's immune system, the site of entry, and the type of cell, tissue, or infected host species. Thus, knowing the determinants of viral tropism is vital for the development of antiviral strategies.

In the past decade, in humans, this has been possible as there has been a revolution in organ and cell models with the development of human organoids, which are similar to actual human organs. Using organoids it was possible to rapidly determine which cells, tissues, or organs were infected by the SARS-CoV-2 virus and design effective therapies against it. Unfortunately, in plants, similar technology has not yet been developed, slowing down the progress of research on plant virus infections.

We propose to address this urgent need, by creating plant organ models to deliver this knowledge using relevant plant cells and tissues. This is now possible thanks to the contribution of a multidisciplinary and international team with experts in plant sciences, biomaterials, virology, and machine learning methods.

In this project, we aim to design and create the main tissue layers of plant organs with their characteristic molecular and structural properties from key macromolecules and living cells. We will then 3D-print several artificial "organs" containing tuneable numbers of tissue layers to study key aspects of viral tropism of main families of viruses that infect plants. We will determine which tissues viruses affect and how. We will use this information to understand and predict, through computational modelling, what controls viral spread in intact plants. This will allow us to understand viral infection at a single tissue resolution and assist the design of strategies to tackle viral spreading.

Mechanisms and Origins of Glycosylation in Giant Viruses

HFSP Research Grant – Program
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Generally, viruses are viewed as harmful entities that pose a serious risk to public health, a perspective that has been largely reinforced by the recent SARS-CoV2 pandemic. However, viruses are extremely varied and only a tiny fraction of them are potentially dangerous to humans, while many others go unnoticed, such as those that infect microscopic organisms like microalgae, amoebae, and other single-celled eukaryotes.

Nevertheless, these viruses are extremely interesting in many aspects. First, they play an important role in the ecosystem by maintaining the balance between different species, for instance by terminating algal blooms. Second, when compared to human pathogenic viruses, these “environmental” viruses are utterly different. Their particle sizes often exceed those of human viruses and compete with small bacteria. However, the real surprise is found in their genomes: these viruses have the tools to produce an incredibly rich repertoire of proteins, many with unknown functions and others dedicated to tasks never found in human pathogenic viruses. Some viruses are therefore «giants» when compared to human viruses, and one of the most striking differences is that these viruses have the ability to manipulate sugars like cellular lifeforms. Although viruses are not considered to be alive, inside their host cells they unfold a complex machinery consisting of various enzymatic functions, which raises the question about their location in the evolutionary tree of life.

With this proposal, we aim to better understand the biological properties of some of the largest and most complex viruses by studying the ways they produce and use sugars during their infection cycles. We will investigate which sugar structures are present on the capsids of giant viruses, which tools the viruses use to make them, and where the viruses acquired these tools. Specifically, these tools are enzymes that manipulate sugars in various ways and are found in all life forms. Thus, from an evolutionary perspective, we will study the origins of the genes that encode these enzymes. Overall, this proposal will greatly enrich our knowledge about the world of viruses, in which we all live in, by highlighting some specific, but currently unknown properties, that viruses use to ensure their survival.

Elucidating Physico-chemical Forces Setting the Limit of Bacterial Growth

HFSP Research Grant – Program

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Vibrio natriegens is one of the fastest-growing organisms ever known, as it can double in about 10 minutes. That said, if we look simply at its protein sequences, it is more than 97% similar to another Vibrio species, *V. campbellii*, which takes twice as long to double. Therefore, it is unlikely that *V. natriegens* simply adopted its proteome for faster growth. Intrigued by this puzzle of supercharged growth, we recently compared the speed of enzymes found in *V. natriegens* with those of *V. campbellii*, and of the bacteria Escherichia coli, and Bacillus subtilis, which are much slower growing. We would like to find out why there are such substantial differences.

It seems that the biological environment created in the cytoplasm of *V. natriegens* has unique physico-chemical properties that effectively raise the temperature – and thus speed up – the rate at which reactions occur. Our team will characterise these factors: pH, osmolytes, crowding, and membrane potential, in a range of conditions that could influence them and further validate the effect of a limited set of candidate variables in vitro. In parallel, we will pursue a complementary approach, to look for additional pairs of closely-related Vibrio species with vastly different growth rates, apply comparative genomic analysis to identify potential genetic drivers, and test their effects in vivo and in vitro.

With the knowledge gained from all our measurements aided by mathematical models, we will move the identified genetic driver(s) from *V. natriegens* to the slower-growing *V. campbellii*, to make it grow faster. As a complement, we will randomly replace long segments of the *V. campbellii* chromosome with those of *V. natriegens* and select for fast growth. Our proposal will shed light on this little-explored, yet fundamental relationship between the intracellular physico-chemical environments and the overall rate of cell growth. Currently growth is primarily investigated in the context of molecular processes, such as signaling and regulation, we will now investigate the contribution and control of the cytoplasmic environment on cell growth.

06

Microbes Interacting with the Nervous System

Deciphering the Impact of Viral Infections on Human Neurocognitive Functions ex vivo

HFSP Research Grant – Program
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The human brain is a remarkably complex system that controls our thinking, learning, and memory through intricate networks of connections. Exposure to viruses poses a significant risk to the development and functioning of the brain, with the potential to lead to neurodevelopmental disorders, neurodegenerative diseases, and intellectual disabilities in children. However, the precise mechanisms behind these effects remain a mystery.

Studying these issues in humans is challenging because we lack suitable models that replicate the brain's complexity and adaptability in a lab setting. To address this gap, we have assembled a diverse team of experts to embark on an ambitious project. Our goal is to create a unique method for connecting artificial, brain-like structures grown in the laboratory with a small piece of brain tissue harvested from a deceased patient.

This innovative approach will allow us to investigate how infections affect the reshaping of the neural connections. To mimic real-world environmental interactions, we will employ a sophisticated system involving robotic technology and tiny fluidic channels. In essence, we are working towards constructing a miniature version of the brain components in the laboratory, in order to study its function, while developing new models that can replace animal-based experimentation. This novel approach will provide us with invaluable insights into how viruses interact with the complex circuitry of the brain. Ultimately, our research aims to establish the fundamental molecular foundations that underlie neural plasticity and cognition, both in health and in the face of disease.

Cross-talk Between the Skin Microbiome, Immunity and Sensory Innervation in Neurophysiology

HFSP Research Grant – Program
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Investigating the cellular and molecular communication between the skin microbiome, the immune system, and the peripheral nervous system can offer important clues as to how these systems are regulated and optimized to promote health.

Our research project will also explore how aging contributes to disrupting the communication between these three systems and identify mechanisms to promote youth for the benefit of human health. We will carry out experiments both in pre-clinical animal models and by using patient skin and microbiome material, allowing for in-depth mechanistic understanding and relevance to human translation.

The impact of this research is threefold. First, increase awareness of how the diversity of the skin microbiome affects peripheral and central nervous system activity and function, which might affect behavior to favor diversity of the skin microbiome and a healthy skin microenvironment. Second, evidence that the activity of peripheral nervous system might affect immunity in the skin and in turn the microbiome, might suggest that a healthy and active lifestyle could promote skin health and affect neuronal signalling, creating a virtuous cycle between the nervous system and the skin. Third, provide strategies to clarify and counteract aging-dependent changes that affect the cross-talk between skin microbiome, immunity, and the nervous system to support homeostatic physiological neurological function.

Hormone-like Bacterial Signaling Molecules as Mediators of Gut-Brain Dialogues

HFSP Research Grant – Program

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The gut of all mammals houses trillions of bacteria that are part of a diverse microbial community named the gut microbiota. Animals have a tight, bidirectional relationship with these passengers and communicate through chemical signals that impact the host's well-being, even influencing how the brain functions. However, the specific molecules responsible for this conversation and the sensors that receive these signals have largely remained unknown.

Recently, a new fascinating group of molecules called pyrazinones was discovered. These molecules were found in pathogens, where they act as signals between bacteria, influencing infection severity. Interestingly, these pyrazinones may also be produced by commensal microbes residing in healthy gut communities. Moreover, these bacterial signals share structural similarities with neurotransmitters produced by the mammalian host, and the bacterial pyrazinone receptors can sense host neurotransmitters. This suggests a crosstalk between these microbial molecules and host neurotransmitters potentially influencing not only the behavior of gut bacteria, but also the central nervous system and behaviors of the host.

To explore this intriguing concept, we will employ advanced techniques to uncover the types of pyrazinones produced by the gut microbiota, and engineer gut bacteria to manipulate these pathways. We will investigate the effects in mice colonized with these engineered bacteria and create chemical tools to identify the host sensors that respond to these molecules and map their distribution using mice. We will also use mice that lack receptors for pyrazinones to confirm their roles. By synthetically producing pyrazinones and studying their impact on the behavior of both gut bacteria and mice, we aim to unravel a new dimension of communication between the animal host and their microbial symbionts. Our focus will be on understanding how these microbial signals can influence neurological functions. In summary, our research explores the possibility that these microbial signals, pyrazinones, can shape brain functions and behaviors. By shedding light on this novel form of communication, we hope to uncover new insights into the complex relationship between animal hosts and their microbial partners in the gut.

07 Neurobiology and Intelligence

Probing the Evolutionary Ecology of Cognition Through High-density Diffuse Optical Tomography

HFSP Research Grant – Program

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Have you ever wondered how animal brains evolved to be smart and to find behavioral solutions to life's many challenges? Scientists have been studying this question for a long time, but surprisingly in only just a few species. Recent developments in brain imaging technology are allowing us to look inside animals' heads to figure out how their brains are wired. However, the currently available tools for doing so are bulky, expensive, and often require sedation, which isn't great for studying brain function.

Our team wants to develop a better brain imaging tool that is smaller, cheaper, and can be used in awake animals. With this tool, we aim to study how brains are wired in different species and how those wiring patterns help individuals think, interact with others, and take full advantage of their environments. Imagine what we could do if we could look at the wiring diagrams of a lot of different types of animal brains. We could, for example, try to figure out how thoughts are formed and complex tasks are accomplished, or why some animals are better than others at certain things. We could also start asking whether certain types of wiring diagrams tend to occur in specific environments or in creatures with certain characteristics. The answers to these questions would take us closer to understanding why more powerful brains evolved and what these abilities mean for the lucky few that have them.

To achieve this vision, our team will undertake three main endeavors. Make a new tool to easily and cheaply map the wiring of bird brains and test it with pigeons, computer simulations, and other brain imaging tools. Develop computer programs that can help us better understand and compare brain wiring diagrams. Use our new tool to study the brains of four species with very different abilities to begin exploring how a brain's internal wiring ultimately determines what it is able to accomplish. From a technical standpoint, the tools we will develop are important because they will enable broader, cheaper and better studies of brain function. From a conceptual point of view, this exciting project will help us learn more about how brains work and how they are shaped by the habits and environments of the creatures that carry them. These are truly fundamental questions that can shine important light on abilities of critical importance to our own species.

Cognitive Convergence: Vertebrate Carnivore-like Predatory Planning Behaviors in Jumping Spiders

HFSP Research Grant – Program

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Portia jumping spiders live in tropical forests and often take long detours to stalk other spiders, many of which would otherwise pose deadly threats to *Portia* spiders. These detours allow *Portia* to approach unseen, rather than taking the direct route and confronting the prey head-on with the higher risk that the prey will either fight back or escape.

In this process, *Portia* spend long periods observing the prey and scanning the environment, reminiscent of lions on the African savanna peeking over tall grass while slowly approaching an antelope for a surprise attack. In both cases, the predator seems to be assessing and comparing the rewards and risks of alternative options and forming a plan before taking action. Notably, *Portia*'s vision is exceptionally good among invertebrates with visual acuity higher than a cheetah, despite being more than 100 times smaller.

Recent theoretical and computational models have shown that animals can gain a major advantage by planning ahead during predator-prey interactions given a particular combination of ecological conditions. Specifically, both the predator and prey have long-range vision that enables them to assess rewards and risks in real time from a far. In addition, the environment is partially open and partially cluttered, allowing animals to hide their movements. If these conditions are satisfied, planning may be possible not only in mammals and birds with large brains, but also in small animals with tiny brains, such as *Portia*, which has a brain with 1 million times fewer neurons than a human brain.

To test whether this theoretical prediction holds true for *Portia*, we will to develop tools and integrate field, lab, and model studies to carry out the first investigation of the detouring behavior of *Portia* as they hunt non-*Portia* jumping spiders, both of which have excellent vision, even in patchy environments. This research is a necessary, important first step towards a long-term vision to establish *Portia* as an exceptionally tractable invertebrate model system for teasing apart the neural basis of planning as a form of sophisticated cognition.

The Emergence of Collective Intelligence: Understanding Human Behavior Through AI Agents

HFSP Research Grant – Early Career

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Most of us would probably agree with the old adage that "two heads are better than one." Indeed, many heads are often even better, as evidenced by the fact that the greatest achievements in human history have almost always been accomplished by large teams of individuals working together. In groups, we have learned how to take care of the land we live on, built cities, developed mathematics, discovered how to extend our lives through medical innovations, and engineered global communications platforms.

When humans or other animals work in groups to collectively solve problems, what are optimal communication and collaboration strategies and how do they arise? What features of individuals enhance or suppress group ability? How do group diversity, group consistency, external competition, and the ability of group participants to anticipate each other's behavior influence the group's problem-solving capabilities? We hope to tackle these questions through the study of emergent collective intelligence and the factors that enhance it.

We will examine groups of humans completing game-based tasks and model their behavior using techniques from the intersecting disciplines of artificial intelligence, neuroscience, and complex systems. We will determine how individual cognitive function, coupled with patterns of interaction among individuals, gives rise to collective group intelligence. We will then study how collective intelligence is affected by the replacement and renewal of participants within each game, the addition of predators and other threatening factors, the overall diversity of the group in terms of participant ability, and participants' anticipation of each other's behavior. Our goal is to uncover the fundamental principles leading to the emergence of collective intelligence in groups of humans. We expect our findings may have additional implications for fields such as decision making in organizations, swarm robotics, and social behavior in animals.

08 Light, Time, and Transcription of Sensory Information

Decoding Invisibility: from Genome Evolution to Tissue Optical Properties in Transparent Fish

HFSP Research Grant – Program

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Some animals, especially those that live in open water, have developed the invisibility «superpower» to hide from both predators and prey. They've become as transparent as glass to avoid being seen. This transparency has evolved in fish, and they have lost their color to become see-through. But there's still an open question: How do their insides, like muscles and organs, also become transparent without absorbing or scattering light? Some research has shown that in certain animals, this transparency is actively controlled by their bodies and depends on their health status instead of being simply a passive property of their tissues and organs.

In this project, we want to understand how these animals become transparent. We're going to focus on a group of fish called Danionin fish, where many different species have independently developed body transparency. To do this, we'll use a common fish called *Danio rerio*, also known as zebrafish, which isn't transparent, and compare it to a highly transparent fish called *Danionella cerebrum*. First, we'll closely examine the tissues of both zebrafish and *D. cerebrum*, including how blood vessels and red blood cells are distributed, and we'll study the structure of skin cells and muscle fibers.

These findings will help us create models to understand how changes in these tissues affect transparency. At the same time, we'll look at the genes of additional Danionin fish species to find out which ones are linked to whole-body transparency. We'll also study where these genes are most active within the fish's bodies. Lastly, building upon the knowledge acquired from the previous objectives, we'll use advanced genetic techniques to make changes in the genes of both zebrafish and *D. cerebrum*. By the end of this project, we hope to gain a much deeper understanding of the differences in genes, body parts, and tissues that make these animals transparent. This knowledge will help us unlock the secrets of how some adult vertebrates can become nearly invisible in their underwater worlds.

Ultraviolet Opsin as the Sensor for Magneto-sensation in Animals

HFSP Research Grant – Program

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Migrating animals rely on celestial cues to navigate, much as sailors once used the sun and stars. Yet, unlike humans, birds and insects can also detect the magnetic field generated by Earth's magnetic core and use it to determine their position and direction relative to their destination. Despite more than 50 years of research into magneto-reception in animals, scientists have been unable to decipher the molecular mechanism for magneto-sensing and its use in navigation. Indeed, both the magnetic sensor itself and the mechanism that can sense such a weak magnetic field remain elusive – note: the Earth's magnetic field is 100-fold weaker than the magnetic field of a refrigerator.

Magnetic sensation has been proposed to be intimately coupled with visual sensation. Our preliminary results indicate that the visual pigment that responds to the ultraviolet range of the light spectrum possesses biophysical properties that are compatible with magnetic sensation upon light activation. This special magneto-sensitive state, known as a triplet state, is sensitive to the direction of the magnetic field due to a quantum interference effect between the three triplet components. Specifically, when in this state, the visual pigment accumulates a quantum "geometric phase" relative to the magnetic direction, yielding a true quantum biological effect. In this project, we aim to identify the molecular sensor and validate its role in magneto-sensation using synergistic in silico, in vitro, and in vivo approaches.

Understanding the Molecular Basis of Animal Cold Thermosensation

HFSP Research Grant – Program

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One of the major determinants of life on Earth is environmental temperature. Changes in the intensity and distribution of solar radiation reaching the Earth's surface and oceans result in geographical variations in climate, including daily and seasonal cycles. Temperature changes play a key role in the survival of animals and plants, and their response through behavioral and morphological adaptation largely dictates their geographical distribution. While animals' biological adaptations are well documented, how they sense changes in the temperature of their environment at a molecular level — and how this subsequently influences their physiology — are unresolved questions.

Regulating body temperature is one of the most critical functions of the nervous system. Research over the past two decades has identified thermoreceptors, specialized proteins in the nervous system and skin cells of mammals and birds, that are activated by cold conditions, and other thermoreceptors that are activated by heat. We will explore the molecular mechanisms by which animals sense changes of cold temperature that trigger many different physiological responses. We will analyze genes that code for thermosensitive proteins from species adapted over millions of years to different thermal environments, including extinct woolly mammoths and their living relatives, Asian elephants. Genomic and functional studies will be complemented with advanced structural analysis to obtain atomic level structures of these proteins.

We hypothesize that the thermal sensitivity of unique thermoreceptors will be very different according to the preferred thermal environment of each species, and understanding the thermoregulatory systems at the molecular level is central to understanding our own physiology. Our investigation into how animals have evolved to sense and respond to low temperature changes will provide clues as to how specific species responded changes in climate over extensive time scales. This is important research for our times, as organisms living on Earth are currently uniquely adapted to their specific natural habitats, but will likely need to undergo drastic biological and physiological adaptation to protect themselves against pressing climate change.

Temporal Structures in Complex Deep-sea Versus Surface Marine Life: from Molecules to Communities

HFSP Research Grant – Program
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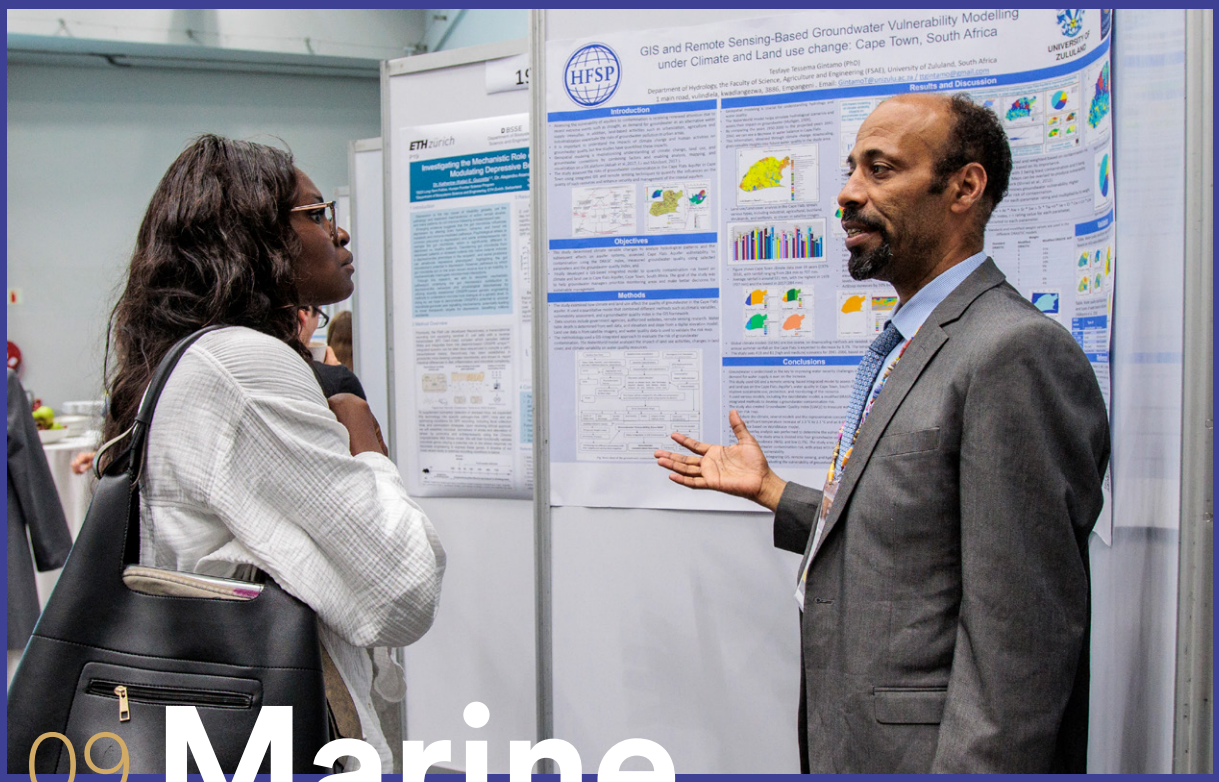
On terrestrial environments it is the sun that dominates the rhythms of life, but in the ocean the moon plays decisive roles. Through its tidal forces, the moon even causes rhythmicity in deep-sea environments that are out of reach of sun- and moonlight.

Hydrothermal vents are likely influenced by tidal forces that cause changes in temperature, chemical composition, and pressure, to name a few. Recent work even shows that deep-sea tides can have profound influences on sessile benthic communities. The vent mussel *Bathymodiolus azoricus*, a deep-sea mollusk, exhibits these rhythms and can make up more than half of the biomass at hydrothermal vents.

We will delve into the mysteries behind these rhythms: What purpose do they serve in such extreme environments? How dark is the deep-sea really and could radiation (within or beyond the visible spectrum) emitted by the vents and/or light-producing creatures influence deep-sea rhythms? Can artificial light, for instance from deep-sea mining, perturb them? How do the rhythms originate and stabilize on population and molecular scales? What role do rhythms and inner oscillators play on the fitness and health of individuals and populations? How do they compare to rhythms present in shallow water mollusks and what can that tell us about how rhythms evolve?

Hydrothermal vents are also areas of important geochemical and thermal exchanges, and deep sea tides can influence the direction of hydrothermal fluids, i.e., hot liquids emitted from vents with sulfide, hydrogen, methane and iron ion concentrations >1000 fold higher than surrounding seawater. Animal communities that populate vent fields must be highly adapted to such dynamics.

We will conduct our research at the “Lucky Strike” vent at -1700m as it offers a large record of chemical, oceanographic, physical and eukaryote species documentation data. Our interdisciplinary team includes a deep-sea ecologist, a molecular chronobiologist, an evolutionist, and a biophysicist.



09

Marine and Wetland Ecology

Trapped in Ice

HFSP Research Grant - Program

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Sea ice is a major, at times ubiquitous, feature of the biosphere, where bacteria, archaea and eukaryota can survive and thrive despite freezing and deep freezing temperatures. Even single-celled algae manage to survive under these conditions; yet, spinach or lettuce, in a garden during an early frost, or in a refrigerator and too close to outflow vent, will burst its cells.

Surprisingly, living organisms can colonize sea ice while concentrating up to 20,000 times in this natural bioreactor, and adapt to drastic phase shifts while ice forms. These are fundamental topics in understanding the origins of life on Earth and its occurrence elsewhere in the universe, yet scientists have not extensively explored these areas —they remain mysterious.

Our highly interdisciplinary project involves biology, glaciology, bioengineering, biochemistry, and optics. We will use ice-dwelling microalgae as models to characterize the physical and biochemical processes that lead to colonization of growing sea ice, and the physiological and genetic controls underpinning the survival and plasticity of biota during phase changes.

Purpose-built sea ice chambers will allow the growth of various types of sea ice and monitor interactions with microalgae during key phases, including: nucleation of ice crystals, scavenging of cells by ice crystals, and colonization of this porous medium filled with brine inclusions. To specifically address the possible role of nucleation in the colonization of sea ice by microorganisms, experiments will also be conducted using a novel microfluidic approach where individual diatom cells will be injected in pressure-controlled supercooled seawater.

The climate of our planet is changing dramatically with the fastest change occurring in the polar regions; understanding these long-standing questions is now urgent. Our timely collaboration will bring insights into fundamental questions of how life trapped in ice has evolved to thrive in this freezing environment. We expect the research will offer insight on the implications given Earth's dramatically changing climate and possible existence of life in other frozen worlds.

Illuminating Microbial Communication Networks: the Phycosphere Lab

HFSP Research Grant – Program

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It has long been assumed that chemical signaling is the language of life for planktonic microorganisms at sea and the best way for microorganisms to interact. Less effort has been made, however, to understand whether microbes might also use light to communicate, which might open new insights into symbiotic and parasitic behaviors among microbes. Most planktonic microorganisms (including phototrophs and parasites) are light-responsive, and can alter the local light seascape by scattering, absorption, and remission of light, or even through bioluminescence.

Our proposed work will determine whether microorganisms use light to communicate. To the best of our knowledge, we will conduct the first experiments to assess the role of light communication among and between marine microbial species in a controlled way using novel light-emitting nanoparticles. If microorganisms use light in addition to chemical signaling, this will be important for several broad areas of research.

Our research will benefit ecologists and biologists; provide new insight to microbiologists and modelers, considering the key role of inter-microbial interactions in controlling ocean biogeochemistry; and offer new solutions in the applied sciences, as specific light signals may be harnessed to attract and concentrate specific microorganisms.

Scaling the Impact of Viruses from Single Cells to the Global Methane Cycle

HFSP Research Grant – Program

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Virus infections impact all living organisms by killing cells, controlling population sizes, releasing nutrients from lysed cells, and regulating cell metabolism. From the largest elephants to microscopic bacteria and archaea, all living organisms are at risk of viral infections. While the impacts to people and animals have been studied extensively, we are only beginning to recognize the scale of virus diversity and the potential for impact to terrestrial ecosystems as a whole, particularly impact of viral infections on microbial hosts and the consequences of these interactions on global biogeochemical cycling. Microorganisms play fundamental roles in the biogeochemical cycling of carbon, oxygen, methane, nitrogen, among other elements essential to life on Earth.

Our project will investigate the impact of viruses on single-cell organisms and characterize the host-virus dynamics in space and time, virus-driven microbial turnover, and the impact on biogeochemical cycling to effectively understand the impacts to terrestrial ecosystems. Specifically, we will focus on the process of microbially mediated methane cycling in peatlands. These ecosystems are crucial for global carbon storage, and hold half of the planet's soil carbon, but they are also major sources of methane, a greenhouse gas that is more potent than carbon dioxide. Microorganisms control rates of degradation, consumption, and production of carbon sources and changes in water table depth and peat exposure to oxygen is a key regulator of methane production. Increasing temperatures and decreasing water table depth due to climate change, while increasing methane production caused by peatland degradation is a global concern. Our project will further investigate how viruses impact microbial communities and influence methane emissions under changing environmental conditions, which is completely unknown.

We will study peatlands on different continents, ranging from pristine locations to anthropogenically disturbed and fully restored sites. We will determine the impact of virus control on methane-cycling in peatlands at different stages of vulnerability to climate change and other anthropogenic impacts. State-of-the-art methodologies in microfluidics and microscopic imaging will uncover the frequency of viral-host encounters. Novel isotopic approaches will be developed to quantify rates of carbon transfer from microbial hosts to viruses. Novel omics technologies and computational tools will be developed to identify hosts of viruses and unknown viral protein functions to reveal their ecological roles. A population dynamics model will then be used to scale up to the ecosystem level, providing a global view of viral-mediated biogeochemical cycling.

10 Terrestrial Ecology

Quantifying the 4-Dimensional Microenvironment to Explain the Coexistence of Social Insects

HFSP Research Grant - Early Career

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Imagine your favourite location in nature. It could be a forest, a grassland, or shoreline. Regardless of where your imagination takes you, we can be sure of one thing: there will be many different species coexisting there. You will find a range of birds in the forest, many different spiders in the grassland, and a diversity of crabs within the rocky shore. Across nearly all landscapes of planet Earth species coexist. Why is this?

Traditionally, scientists have tried to explain species coexistence by focusing on the differences among species. For instance, different species eat different things, or they may nest in slightly different parts of the environment. These differences prevent species from directly competing with each other for resources, and this lack of competition means that they can coexist peacefully. This way of thinking has dominated the way that scientists view species coexistence. Species difference, however, cannot always explain coexistence patterns.

Repeatedly, we find examples where many species coexist despite their overlapping food, nesting or foraging requirements. How can this be? We propose a new, simple idea for these difficult-to-explain coexistence cases. Most organisms are small, and from their perspective, their environments are dynamic “mazes” of micro-environments. These mazes of micro-environments vary in four dimensions: left, right, up, down, and through time. Crucially, species may become isolated from each other in their own corner of these mazes. As this happens, the chances of competition decrease, while the chances of coexistence across the landscape as a whole increase.

Our project seeks to test this maze hypothesis. To do so we need a range of different research skills. Ultimately, we need to be able to measure micro-scale variation in the environment and relate this to the environmental, nesting, and feeding differences that coexisting species may (or may not) have. Our team will deploy micro-sensors, drones, specialized infrared detectors, and traditional field surveys. We will focus on the many coexisting ant species that live within the South African Karoo ecosystem. Overall, we want to understand whether 4-dimensional micro-environments play a role in causing the beauty and intrigue of species coexistence across the landscapes of planet Earth.

Securing Shifting Sands – from Genes to Geoengineering

HFSP Research Grant – Early Career

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Some species are called 'ecosystem engineers' as they can drive the formation of novel landscapes. Coastal sand dunes are one such landscape, and they are shaped by the interaction of sand being moved by wind and water and the specialised species of grasses that lock sand into place. While we know that different grass species produce different dune morphologies, our understanding of how sand dunes and the species responsible for their bioengineering have co-evolved is incomplete.

Our project combines expertise in evolutionary genetics, coastal ecology, and sediment transport with the ultimate aim of understanding how variation in grass species at the molecular level translates into whole landscape changes in terms of topography and resilience. Our molecular approaches will identify the genetic basis of key dune building traits (e.g., rhizome architecture and lignin content) and generate heritability and evolutionary rate estimates for these phenotypes using genome-wide data. We will conduct field measurements, manipulative experiments, and wind tunnel experiments to determine how plant phenotypic variation impacts wind flow dynamics, the ecological limits of the dune grasses, and how this is linked to sediment dynamics. Finally, we will combine our experimental and molecular results with geomorphological models to determine the effect this variation has on coastal morphodynamics.

Our project will advance fundamental knowledge of evolution and also has important applied outcomes. Coastal dunes protect a third of all shorelines from flooding, and our results will enable us to determine the adaptive potential this system has in mitigating the effects of climate change, including sea level rise and the impact of storm surges. If our results show that dune grasses lack the capacity to adapt to changing conditions, we may need to rapidly adopt mitigation strategies to avoid the collapse of our coastal defenses in the future.

A Novel Approach to Tropical Dendroclimatology Using Hyperspectral Imaging and Deep Learning

HFSP Research Grant – Early Career

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Dendroclimatology, the science of extracting past climate records from annual growth rings of trees (i.e., studying tree rings) plays a critical role in climate research. The science has been extensively applied in the temperate and boreal regions, where environmental factors induce annual ring formation that show clear, quite predictable seasonal patterns. In the tropical latitudes, however, such investigations have been limited as tree ring formation can be more complex. In this middle latitudes, seasons are not as clearly demarcated than in the polar and boreal regions, and during any given year there can be wide climate fluctuation if there are strong influences from El Niño, droughts, large hurricanes, or similar factors.

Thus, past climate records in tropical countries, particularly in Africa, are scarce and the continent's climate science is, to date, the least advanced in the world. Yet, tree-rings offer widely available climate-proxy data sources in Africa, indicating a need for improved tree-ring detecting and characterizing technologies.

Hyperspectral imaging (HSI) provides an efficient method for characterizing features in objects such as the tree rings, by collecting information from across the electromagnetic spectrum. HSI systems capture detailed spectral data and provide rich information about the composition and characteristics of objects in an image. On the other hand, deep learning (DL) provides an effective HIS data processing technique owing to its ability to automatically learn and extract complex patterns and features from images.

The project aims to test a novel approach to dendroclimatology using a combination of these cutting-edge analytical technologies on two selected tropical tree species. We will collaborate between a fully equipped HIS lab in Norway and an emerging tropical dendroclimatology lab in Ethiopia. The project will involve research in both HSI and DL techniques. Different HSI systems, sample preparation and instrumental setup techniques, and light conditions appropriate for detecting and characterizing tree rings from different sample types will be explored in the laboratory environment. Subsequently, advanced DL data processing algorithms will be explored to obtain good spectral signals from the tree samples and quality data for robust prediction models. Finally, a hyperspectral camera with relevant wavelength bands will be applied outdoors for field analysis of wooden samples.

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