Abstract dei progetti FIS 2

Investigating the principles behind cell reciprocal reach out motion as a function of microenvironment space-time deformation
PI: Cacopardo Ludovica
Starting Grant
LS9

Cell migration is a hallmark of a wide variety of pathophysiological process such as morphogenesis, regeneration and cancer. Migration patterns are often related to physical and biochemical gradients in the extracellular matrix, which may be also modulated by the cells to coordinate the motion of distant cells. A fascinating and unexplored example of cell coordination along distance is represented by cell reach-out motion across specific space pathways, arising when cells from different cluster move reciprocally meeting halfway through. INTERCELLAR aims at investigating this behaviour under the light of space-time microenvironment deformation, decoupling it from chemo- and topo-taxis. The generation of not-symmetric in-plane components of the gravitational force and the time-evolving nature of substrate deformation on viscoelastic materials may modulate cell motility. The combination of these aspects has never been investigated and open the road for a further intriguing question, which is related to cell time perception in the presence of a mass altering the space continuum. To verify these concepts, cell reach out movements will be investigated engineering cell culture substrates which will be optimised using in-silico tools. Adhesion rates will be finally optimised on base of the experimental data obtained integrating advanced imaging strategies and atomic force microscopy, providing a prediction tool which accounts for altered cell time perception. As a proof of concept, a space-time maze will be fabricated combining gels with different τ and different masses altering both substrate space and cell perception time. Behind the understanding and characterisation of the mechanobiological process responsible for cell reciprocal motion, the project represents a pioneer work for predicting cell behaviour in pathologies and for defining novel approaches in tissue engineering, regenerative medicine and in-vitro modelling.

Sustainable and innOvative blUe food pRodCtion under one hEalth approach
PI: De Marchi Lucia
Starting Grant
LS9

The SOURCE project aims to promote more sustainable, safe and innovative aquaculture systems through the application of integrated nature-based strategies, in line with the *One Health* approach. This approach recognises the close interconnection between human health, animal health and ecosystem protection, which are now central aspects in the development of more responsible and resilient food systems. Aquaculture is one of the fastest-growing sectors in global food production. However, its intensification may contribute to the deterioration of water quality, the emergence of infections in farmed organisms and the consequent use of antibiotics. The extensive or inappropriate use of these compounds can contribute to the spread of antimicrobial resistance and generate potential risks for the environment, animal health and food safety. In this context, SOURCE focuses on the study of organic feed additives, particularly essential oils and related bioactive compounds, as potential sustainable alternatives to conventional antibiotic-based approaches. The project will assess the antibacterial potential, ecotoxicological profile and biological effects of these compounds in commercially relevant aquaculture species, including finfish and bivalve molluscs. This will be achieved by combining *in vitro* and *in vivo* approaches with microbiological, biochemical, histological, pharmacokinetic and metabolomic analyses. The final objective is to contribute to the development of responsible aquaculture models capable of improving the health and resilience of farmed organisms, reducing the environmental impact of production practices and supporting the transition towards safer and more sustainable blue food production systems. SOURCE also aims to foster dialogue among scientific research, the production sector, policymakers and civil society, promoting innovative solutions consistent with the Blue Growth Agenda and the Common Fisheries.

How new genes emerge: exploring a model of novel gene creation following the evolution of wheat

PI: Mascagni Flavia

Starting Grant

LS9

My project, NEXT-G, represents a pioneering investigation into transposon-derived genes in bread wheat.

Transposable elements (TEs) are autonomous repetitive DNA sequences responsible for rapid genome remodelling and new regulatory gene networks. One intriguing yet understudied aspect of transposon dynamics is their involvement in novel gene creation through a process known as exaptation. In exaptation, a TE with advantageous traits for the host is co-opted and assumes the characteristics of a conventional gene.

Using advanced bioinformatics and new genomics techniques, I will scrutinize the impact of TEs on gene innovation in wheat, one of the world's most vital crops. Wheat represents an ideal system to chase such a goal. Since its evolutionary history is well- characterized, it is possible to pinpoint the formation of new genes derived from transposons and reconstruct the evolutionary events leading to their emergence. Identifying exapted transposons in wheat and its relatives, I will yield insights into the timing and mechanisms of transposon exaptation and shed light on how transposons can drive the formation of new genes in response to selective pressures, including in the early stages of plant domestication.

Altogether, NEXT-G will provide an unprecedented perspective on the evolution of large-sized plant genomes, specifically focusing on newly acquired genes via exaptation, proposing a unique investigation in wheat and for any plant. This work will enhance our understanding of the creation of new genes and help identify key sequences that can have contributed to speeding up evolution.

Structural Control of Supramolecular Chiral Organic Materials with Multispectroscopic and Computational Tools

PI: Zinna Francesco

Starting Grant

PE4

Chirality is broadening the horizons of organic materials in spintronics, photonics, and electronics. It has led to circularly polarized (CP) OLEDs, emitting CP light without passive components like polarizing filters, to CP-sensitive electronic devices, promising enhanced efficiency and compactness, and to chirality-induced spin selectivity (CISS).

Chiral conjugated organic molecules self-assemble in thin films, amplifying chirality at higher hierarchical levels and directly impacting the properties of the material. They offer the flexibility of plastic-like properties alongside chiral functionalities, rendering them valuable in chiral photonics, electronics, and spin control. However, several questions remain unanswered:

- How chiral information is transferred from the molecular level to different hierarchical levels.
- The structure-property relationships in terms of chiroptical properties and charge transport.

Currently, predicting supramolecular packing from molecular structures remains challenging, and the fundamental interactions underlying these assemblies remain elusive. This ultimately limits the progress of the field.

To address this challenge, we propose an integrated synthetic, spectroscopic, and computational approach to identify general rules for forming structures suitable for chiral electronics and photonics applications. Small conjugated chiral organic molecules will be prepared following a modular synthetic approach, allowing for a computation-guided exploration of chemical space. Thin films will be examined using various techniques to gain insight into the supramolecular structures at various hierarchical levels. Experimental data will inform molecular dynamics simulations; then, variations in molecular structures will be introduced computationally to explore their effects on supramolecular packing and (chiro)optical properties. The most promising structures will be prepared and studied to confirm the hypotheses. Finally, the compounds will be tested in CP-OLEDs and CP-photodetectors.

The project will provide fundamental knowledge to guide the development of chiral materials with enhanced chiroptical properties and conductivity for use in electronic devices, contributing to driving the field of chiral electronics to the next stage.

EPSILON: Endogenous Pseudo-Stochastic IntelLigence: unveiling the pivotal role of nondeterministic Oscillations in complex biological Networks
PI: Valenza Gaetano
Consolidator Grant
PE7

EPSILON represents a transformative endeavor in the realm of biomedical signal processing, departing from conventional methodologies for characterizing dynamical systems. In the non-trivial case of complex deterministic systems driven by dynamical noise, the system output at time t_n can be described as $x_n = T(x_{n-1}, x_{n-2},\ldots, x_0) + \varepsilon_n$, where the stochastic components ε_n recursively combine with a deterministic map T in the phase space. By modeling such components as a sequence of random variables ε_n defined on a probability space, quantifying their statistical properties, such as power, in the absence of specific knowledge or assumptions about T poses significant challenges. EPSILON introduces a new framework for closed-form estimation of dynamical noise statistics, independent of knowledge about the specific T function. The framework also enables the characterization of stochastic vectorial components driving multi-dimensional dynamical systems for any T map functions. Through the estimation of covariance matrices and directional indices of causal information transfer, EPSILON aims to elucidate the intricate dynamics of coupled, unknown complex systems. In turn, the characterisation of dynamical noise statistics will allow novel avenues in signal denoising.

The primary focus of EPSILON is the characterization of physiological dynamics and associated biological noise. By revealing intrinsic stochastic fluctuations that causally modulate neural and cardiovascular dynamics, we seek to identify new biodynamics sustaining physilogical and pathophysiological states. Leveraging existing research in computational physiology and neuroscience, we aim to re-evaluate previous findings in light of newfound insights into noise distribution across different brain regions and cardiovascular districts.

What was once an unwanted variable is now a measurable quantity, yielding a wealth of "noisy" but informative data and opportunities for the scientific and technical communities. In many pseudo-stochastic system equations, EPSILON will then emerge as the component of paramount interest, paving the way for novel conceptualizations of neurophysiological functions.

Next Generation Quantum Detectors for Low Energy Astroparticle Physics (QuLEAP)
PI: Federico Paolucci
Consolidator Grant
PE9

The challenges of modern fundamental physics lie in low energy phenomena, such as gravitational waves, cosmological inflation and dark matter. Indeed, different phenomena in astronomy (such as radio burst sources, cosmic microwave background, and GHz-peaked radio sources) need the development of sensitive bolometers operating in the GHz-THz bands. Furthermore, low energy particle physics requires single-photon detectors operating in the sub-visible bands down to a few GHz for the detection of dark photons, axions and weakly interacting massive particles. Indeed, state-of-the-art detectors for fundamental physics are mainly based on transition-edge sensors and kinetic inductance detectors. showing a noise-equivalent power (NEP) of $\sim 10^{-19}$ W/Hz$^{1/2}$ and an energy resolution of $\sim$500 GHz. Finally, the technologies nowadays in the R&D phase, such as superconducting qubits are limited to single-photon detection and extremely prone to the external environment.

QuLEAP aims at developing a new **cryogenic quantum detection platform** pushing the detection sensitivity towards unprecedented levels. To this scope, the project will exploit **innovative concepts** conceived by the PI for the charge and energy management in hybrid mesoscopic superconducting systems. First, the current control of critical temperature of fully superconducting Josephson junctions allows the Josephson escape sensor (JES) to show a record NEP $\sim 10^{-25}$ W/Hz$^{1/2}$ and energy resolution of $\sim$2 GHz. Second, the macroscopic phase coherence of superconductors will be exploited to realize a non-local superconducting detector (NLSD) with separated sensing and readout elements, thus able to reveal single-photons of frequency down to $\sim$10 GHz. Third, the bipolar thermoelectric response of fully superconducting tunnel junction will be employed to attain single-photon detection in a wide range of frequencies ranging from 10 GHz to 10 PHz.

Concluding, the set of unprecedentedly sensitive detectors developed within QuLEAP operates in synergy with current detection, cold electronics and room-temperature readout technologies, thus enabling new functionalities and filling the existing gaps between the requirements of fundamental physics experiments and the present sensing technologies.

Neurons Engineered with MagnEto-SwItches: a tool for Shaping the nervous system
PI: Raffa Vittoria
Advanced Grant
LS9

Our project aims to fulfil the dream of many neuroscientists: promoting axonal regeneration in living organisms, a challenge that remains unmet to this day. To achieve this, we will develop a new technology based on magneto-switches, small molecular devices activated by an external magnetic field that generates forces directly on axonal microtubules, triggering their growth and maturation. The goal is to demonstrate that this approach may promote axon regeneration in a living organism, for example promoting reinnervation from the brain to the spinal cord. If successful, the magneto-switch could become a new tool for promoting regeneration in the central nervous system.

Deep learning from Nature to design novel photoEnzymes

PI: Mennucci Benedetta

Advanced Grant

PE4

The emerging frontier of photobiocatalysis, a fusion of bio- and photo-catalysis, combines the selectivity of enzymes and the unique chemical transformations achieved through light-driven processes. Nature employs photobiocatalysis in photoenzymes, where light-absorbing cofactors drive catalytic reactions. Among the few natural photoenzymes which are known, the recently discovered fatty acid photodecarboxylases (FAP) represents a very intriguing system. An ambitious concept is to employ FAP as a template for designing novel photoenzymes that use its efficient mechanism to generate radical species, but enhancing their activity for synthetic applications, expanding substrate compatibility and generating novel products. The DeepEn project aims to tackle this challenge by combining the accuracy of multiscale modeling grounded in quantum chemistry with the formidable capabilities of deep learning. The conceptual novelty is to use the multiscale modeling to drive the deep learning-based design of the novel photoenzymes which will be finally validated in live cells.