PhD Course in Physics and Astronomy - XXXVIII cycle, a.y. 2022/2023

n.1 scholarship funded by Department linked to the project: *"Innovative methods of scintillation optimization for low radioactive background detectors for Double Beta Decay searches"*

Abstract

Conventional scintillators alone fail to meet the requirements for some of the state-of-the-art applications in ionizing radiation detection and a technological breakthrough is required for a significant performance improvement. In the Department of Physics, studies are carried out on two possible alternative approaches of possible application in the field of Double Beta Decay research: scintillating nano-compounds and scintillating cryo-detectors. This project will aim at the optimization of these two approaches. This ambitious goal will be achieved by making the most of the state of the art of the various technologies from different perspectives. In parallel, protocols for radioactivity screening and mitigation will be developed, given the extremely low background required in searches for rare events, which require careful selection of materials. Finally, a simulation framework will be implemented to model the behavior of the devices: following an iterative approach, this tool will take as input the data of the experimental measurements that will be carried out and will help to optimize the design of the devices developed in the research project.

n.1 scholarship funded by Eni S.p.a. linked to the project: *"Development of a diagnostic system for neutron spectroscopy for the high magnetic field fusion reactor SPARC"*

Absract

The recent development of high temperature superconducting magnets, that can produce magnetic fields up to 20 T at temperatures of 23 K, has opened a new research line on compact size, high magnetic field tokamaks such as, for instance, the SPARC project of Commonwealth Fusion System. The ambitious goal is to accelerate by, at least, 20 years the time required to develop a fusion reactor as compared to the timeline foreseen by the ITER research line, which is based on larger devices that operate at lower magnetic fields. In view of what may be a revolutionary development in the field of net energy production by nuclear fusion, we propose a research activity aimed at designing and developing a diagnostic system for neutron measurements in high field tokamaks that operate with a deuterium-tritium plasma mixture. The activity will encompass the calculation of the neutron emission in such devices, as well as the design of a detection system to enable spectral measurements of 14 MeV neutrons. The development and test of the system at nuclear laboratories or presently available tokamaks will also be part of the project.

Intellectual property clauses agreed with the Company apply to this scholarship.

n.1 scholarship funded by Eni S.p.a. linked to the project:" *Development of a diagnostic system of gamma-ray emissions for the high magnetic field fusion reactor SPARC"*

Abstract

The recent development of high temperature superconducting magnets, that can produce magnetic fields up to 20 T at temperatures of 23 K, has opened a new research line on compact size, high magnetic field tokamaks such as, for instance, the SPARC project of Commonwealth Fusion System. The ambitious goal is to accelerate by, at least, 20 years the time required to develop a fusion reactor as compared to the timeline foreseen by

the ITER research line, which is based on larger devices that operate at lower magnetic fields. In view of what may be a revolutionary development in the field of net energy production by nuclear fusion, we propose a research activity aimed at designing and developing a diagnostic system for gamma-ray measurements in high magnetic field tokamaks. The activity will encompass the calculation of the gamma-ray emission that can occur from the main nuclear reactions in such devices, as well as the design of a detection system to enable, in particular, the determination of the fusion power from such emission. The development and test of the system at nuclear laboratories or presently available tokamaks will also be part of the project.

Intellectual property clauses agreed with the Company apply to this scholarship

PhD Course in Computer Science - XXXVIII cycle, a.y. 2022/2023

n.1 scholarship funded by Ospedale San Raffaele S.r.l. linked to the project:" *Computational modeling of RNA transcription using scRNA and getSEQ data to infer trajectories in single cell maps and highlight coupled regulation between different layers of the RNA biology*"

Abstract

RNA molecules are produced by the cell to transfer information form the DNA to different parts of the cell. RNA molecules are inherently instable, and their lifespan is often related to their molecular function. For instance, structural and housekeeping genes are associated to long-living RNAs, while transcription factors or signaling genes are associated to shorter living ones. The RNA turnover determines the persistence upon transcriptional shutdown and defines RNA (and consequently protein) levels [1]. The direct measurement of RNA stability always proven challenging. In fact, computational tools have been developed in order to infer stability from indirect biological observations. Software tools that infer the transcription, splicing and degradation dynamics of RNAs have recently been used in tracing trajectories in single cells experiments and in inferring the directionality of the underlying process, thus enabling the prediction of a future state from the current [2,3]. Moreover, multimodal experiments that couple RNA levels with chromatin opening, mechanistically preceding transcription, have been developed and computational models that include this layer are under development [4]. The inclusion of additional layers in the experimental and computational design of the trajectories allows an increased resolution and precision in trajectory sketching and opens new horizons in the analysis of transcriptional regulation. So far, all the models developed assume that changing RNA levels depend solely upon changes in transcription, neglecting the role of processing and degradation rates. Even though transcription is predicted to be the rate with the highest impact on RNA levels, this assumption suffers from the limits in the fidelity of RNA processing and stability measurements [5]. Moreover, the step of RNA degradation is known to be fundamental in differentiation and exit from the pluripotent state, which are blocked in the absence of the degrading protein [6].

The aim of this project is to develop an innovative tool that using single-cell RNA data coupled with getSEQ [7], one of the most recent advances in chromatin profiling, will be able to identify key modulations of RNA processing and stability that occur in biological processes. getSEQ, developed in the Innovation Lab of our hospital [8], is an assay able to identify signal from both open and closed chromatin in single cells, thus increasing the resolution of assaying chromatin compared to canonical ATAC-seq. Thanks to the computational analysis of both open and closed chromatin signals, coupled with premature and mature RNA, the PhD candidate will develop a software tool that will be able to reconstruct cell-cell trajectories with higher fidelity compared to available methods and, most importantly, will be able to identify complex modes of RNA

regulation that are key for understating the dynamical process under studies. Such processes, which might involve the multiple and coordinated regulation of different rates, i.e. RNA transcription and processing, or RNA transcription and degradation, will shed new light on the mechanisms of transcriptional regulation during different biological processes, and will suggest novel mechanisms of coupling between the different layers of the RNA biology.

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Intellectual property clauses agreed with the Company apply to this scholarship.

PhD Course in Translational and Molecular Medicine - XXXVIII cycle, a.y. 2022/2023

n.1 scholarship funded by Istituto di Neuroscienze - Consiglio Nazionale delle Ricerche (CNR-IN) linked to the project:" *Deciphering inflammation pathways in Parkinson's disease and setting new gene therapy strategies to attenuate its progression*"

Abstract

We have generated new mouse models with strictly selective alpha-Synuclein (·Syn) accumulation in microglial and astroglial cells by inducible gene expression through lentiviral transduction in the nigral tissue. Surprisingly, these mice develop progressive and restricted degeneration of dopaminergic (DA) neurons. Thus, glial cells play a pivotal role in promoting neurodegeneration in Parkinson's diseases. This aim of this project is to decipher the pathophysiological mechanisms triggered by glial cells that contribute to undermine neuronal survival in these PD mouse models. Single-cell and bulk transcriptomics of freshly isolated neuronal and glial cell populations will be carried out to identify new molecular pathways in glial cells responsible for neuronal toxicity. Moreover, it will be explored a new gene therapy approach which restrict the expression of anti-inflammatory molecules to only microglial cells in order to curb neuroinflammation and ·Syn deposition in neurons.

n.1 scholarship funded by Fondazione Centro San Raffaele linked to research project:" *Identification and targeting of cellular and metabolic programs during hematopoietic stem cell aging"*

Abstract

Human Hematopoietic Stem and Progenitor Cells (HSPC) serve as a lifelong reservoir for mature blood cells. Accumulation of DNA damage in HSPC is a contributing factor to aging and bone marrow failure syndromes of inherited diseases characterized by telomeric shortening. We recently discovered that repeated activation of human aged bone-marrow derived HSPC out of their quiescence state elicits the DNA damage response (DDR)

as a consequence of DNA replication stress. Yet, we have just scratched the surface of a plethora of still unexplored molecular mechanisms governing the biology of HSPC during aging. The candidate will assess whether DNA replication stress triggers HSPC senescence in vivo and affects the reconstitution upon transplantation of aged HSPC. He/She will undertake an imaging-based quantitative evaluation of several senescence markers (including SA-β-Gal, DDR, heterochromatin foci, micronuclei) in progenitors and primitive HSPC subsets by ImageStreamX, a technology that combines high content imaging with the quantitative power of flow cytometry. The candidate will then perform a metabolomic analyses of young and aged HSPCs upon activation ex-vivo and during the early and late phases of hematopoietic reconstitution. Mechanistically, the candidate will assess the contribution of telomeric DNA damage to age-related dysfunctions of HSPCs and define by single cell RNA sequencing and chromatin accessibility analysis the molecular interplay between metabolism and chromatin alterations in young and aged HSPCs. Lastly, he/she will attempt to mitigate cellular barriers by specifically dampening DDR at telomeres and/or by targeting identified downstream metabolic pathways with the final goal to improve hematopoietic reconstitution of aged HSPCs. This set of investigations will identify innovative strategies to counteract age-associated dysfunctions of the hematopoietic lineage.

Intellectual property clauses agreed with the Company apply to this scholarship

n.1 scholarship funded by Istituto Auxologico linked to research project: *"SGKJ inhibition as a nove! therapeutic approach in Long QT syndrome (SILENCE-LQTS)"*

Abstract

The fellowship funds the PhD program in Translational Medicine (DIMET) for a master graduate in Biology whose research activity will bridge the laboratory of Cardiac Cell Physiology (Department of Biotechnology and Bioscience UNIMIB) and the Cardiovascular Physiology Unit (Research and Biomedical Technologies, IRCCS Istituto Auxologico Italiano; Dr Luca Sala as IRCCS Researcher) coordinated by Prof. Antonio Zaza. The two laboratories provide equipment and expertise ideally complementary for the study of molecular/cellular pathogenesis of genetic cardiomyopathies , with particular reference to arrhythmogenic ones. The PhD student's activity will therefore be focussed on the study of disease mechanisms and pharmacological approaches through functional (patch-clamp, dynamic fluorimetry, potential mapping in isolated tissues, cellular respiration etc.) and biomolecular approaches (transcript analysis, protein expression, immunolocalization, etc.) in multiple cellular models (cell lines, primary myocyte cultures, hiPS-derived human cardiomyocytes etc.). The specific project on which the PhD student will begin his/her activity will be the evaluation of SGK1 inhibitors in the correction of functional abnormalities of LQT syndromes (SILENCE-LQTS project).

PhD Course in Material Science - XXXVIII cycle, a.y. 2022/2023

n.1 scholarship funded by Department linked to research project:" *Electroactive Materials for Rechargeable Batteries with Super-Concentrated Electrolyte*"

University Supervisor: Prof. Riccardo Ruffo (riccardo.ruffo@unimib.it)

Abstract

The research activities are part of a collaborative exploratory project between ENI and the Electrochemical Energy Storage group of the Department of Materials Science regarding the possible development of aqueous batteries with super-concentrated electrolyte. These devices could find important applications in systems where cost and power density are more important parameters than energy density. In addition, the use of aqueous electrolytes makes the devices intrinsically safer and less environmentally impactful.
The research work is divided into two parts: the characterization of electrolytes and the design of electrode interfaces. In the first case, high concentrated solutions (> 10 mol per kg of solvent) based on acetates or other polyanions (TFSI, FSI, etc.) of alkali metals (Li, Na, Cs) will be considered, determining their rheological (viscosity), thermal (phase diagram), electrical (conductivity) and electrochemical (anodic and cathodic decomposition) properties. The best electrolytes will be coupled to electrode materials that will be properly designed, synthesized, and characterized. An important part of the study will concern the stability of the electrode/electrolyte interface, which will be optimized by surface treatments of the active materials or by the addition of additives in the electrolyte. Small prototypes of full devices will be fabricated and evaluated.

n.1 scholarship funded by Società Ricerca sul Sistema Energetico - RSE S.p.A. linked to research project:" *Materials for alkaline ion batteries based on MAX phase and related compounds towards a pre-industrial scale up*"

University Supervisor: Prof. Riccardo Ruffo (riccardo.ruffo@unimib.it)

Abstract

The research is part of a collaboration between the RSE Batteries group and the Electrochemical Energy Storage laboratory of the Department of Materials Science. The collaboration has produced important results in the study and applications of MXenes, a family of 2D materials based on titanium and carbon. These materials are obtained from MAX phases (M= Ti, A= Al, X=C or N) through etching processes involving the use of hazardous chemicals. In this frame, the new step of the collaboration aims to explore the possibility of preparing active materials for secondary batteries (i.e. Li+ or Na+ ion batteries) while avoiding the use of etching procedures or minimizing their environmental impact.
The candidate will design, develop and optimize thermal or chemical procedures to prepare active materials for secondary batteries starting from the MAX phases obtained by Spark Plasma Sintering (SPS) or traditional ceramic solid state reactions. All materials obtained will be characterized with respect to the chemical, structural and morphological features. The materials will be then formulated to produce thick film electrodes on metallic foil or as free-standing membranes. The electrochemical functional properties of the materials will be evaluated in half cells equipped with metallic foils as counter-electrodes. Finally, precommercial small prototypes of full cells will be fabricated and evaluated. Part of the activities (SPS, some characterizations, long cycles) will be carried out directly at RSE laboratories to which the user will have access.

Intellectual property clauses agreed with the Company apply to this scholarship

n.1 scholarship funded by Vishay Semiconductor GmbH linkd to research rpoject:"*Study of reliability behavior of MOCVD grown GaAs structures for low power IR emitting devices"*

University Supervisor: Prof. Stefano Sanguinetti (stefano.sanguinetti@unimib.it)

Abstarct

This joint PhD project between Vishay Semiconductor GmbH, Germany, and the Department of Materials Science of the University of Milano-Bicocca, focuses on the research and development of infrared emitting devices (IR-LEDs) based on GaAs, and will be carried out at both locations. In this case, low power IR-LEDs and their long-term reliability are of particular interest. Devices which perform stable and reliable at low currents are challenging with regard to their processing as well as their electrical characterization. The project includes the simulation of the electronic and mechanical properties of GaAs epitaxial structures, MOCVD growth thereof, characterization of the grown layers, establishment of low power testing techniques and the analysis and optimization of their reliability. This includes, for example, the analysis of failed devices and optimization of epistructures based on these findings. Up to 50% of the project take place at Vishay Heilbronn, Germany, at a state-of-the art GaAs fab.
The project covers a broad range of interesting practical, theoretical and analytical tasks in semiconductor processing and characterization, and enables the student to gain direct international industry experience.
For these purposes, this PhD project includes an obligatory stay at Vishay in Heilbronn, Germany, of up to 18 months. Moreover, in addition to good technical knowledge and interest in Materials Science, Solid State Physics or Microfabrication, the applicant needs to have an excellent command of English (equivalent to level B2 or higher) and should be highly motivated to both independent and team work. These activities require the additional signature upon enrolment and compliance with Vishay's and UNIMIB's confidentiality, intellectual property, health, safety, and ethics regulations

Intellectual property clauses agreed with the Company apply to this scholarship

The applicant needs to have an excellent command of English (equivalent to level B2 or higher)

n.2 scholarships funded by Eni S.p.a. linked to research project

1) **"*Rethinking Perovskite Solar Cells From A Circular Economy Perspective*"**

University Supervisor: Prof. Luca Beverina (luca.beverina@unimib.it)
Supervisor ENI: Dr. Paolo Biagini

Perovskites based solar cells (PSC) revolutionized the scenario of third generation photovoltaic technologies. They combine solution processing fabrication techniques with power conversion efficiencies that reach those of silicon. They are intrinsically flexible and compatible with a variety of substrates including plastic, bioplastics and even paper.
State of the art performances require the careful optimization of all the components of the multistacked ensemble constituting the final device, with a particularly strategic roles played by the active hybrid semiconductor and the hole transporting interlayer (HTL). The research in the field is still mainly focused on the quest for higher lab-scale performances but increasingly relevant efforts are also dedicated to make PSC technology ready for large scale commercial exploitation. This goal requires PSC technology to overcome still

existing hurdles: long-term stability, industrial upscaling, and environmental sustainability.
Recent literature demonstrated substantial improvements on PSC operational stability thanks to the development of new strategies (i.e. dimensional engineering, encapsulation, passivation) that have the potential to push the lifespan of devices to a level compatible with practical applications in the near future. Yet much is still to be done to improve sustainability.

The PhD project will be aimed at developing printable inks of colloidal perovskite nanocrystals in benign solvents. The approach enables the decoupling of crystallization and deposition steps with benefits in use and recovery of lead precursor and does not require the use of toxic high boiling aprotic polar solvents. It is general and can be extended to materials other than cation lead halides. Recycling of critical/toxic materials will be also addressed.

2) "*Solar Cells and Tandem Minimodules for Building Integrated Photovoltaic or Vehicle Integrated Photovoltaic*"

University Supervisor: Prof. Simona Binetti (simona.binetti@unimib.it)
Supervisor ENI: Dr. Gianni Corso

The increasingly urgent need to abandon fossil fuels has prompted the search for solutions to power systems, that perform the most varied functions, with renewable sources. As a result, photovoltaic modules have been integrated into the buildings' constructive and decorative elements, becoming one with tiles, windows, roofs, and facade cladding. Lately, the automotive industry has also begun to integrate mini photovoltaic modules on the roof of electric cars to increase their mileage. In this scenario, the research project aims to develop photovoltaic devices and mini-modules in tandem configuration to maximize the efficiency, for applications in Building Integrated Photovoltaic (BIPV) or Vehicle Integrated Photovoltaic (VIPV) based on kesterite and perovskite solar cells. These materials can be deposited with low-cost technologies, even on flexible substrates, and for this reason, they are suitable for use in BIPV and VIPV. The PhD project is, therefore, focused on the design of tandem solar cells on flexible substrates (steel and polyimide), combining perovskite- and kesterite-based solar cells to produce "tailor made" mini-modules. Furthermore, the optical band gap of both compounds under study can be easily controlled by modifying the chemical composition. Therefore, the absorption range of the photoactive materials, as well as the stacking order, will be adjusted according to the efficiency and stability in working conditions of the final device. The project target efficiency is 10% on flexible substrates with low-cost deposition technologies, low energy payback time, and the use of abundant and non-toxic elements.

Intellectual property clauses agreed with the Company apply to this scholarships

PhD Course in Chemical, Geological and Enviromental Sciences- XXXVIII cycle, a.y. 2022/2023

n.1 scholarship funded by Department, Curriculum in Chemical Sciences linked to research project: "*Multiscale computational approaches to the modeling of lytic polysaccharide monooxygenases (LPMOs) and bacterial cytochromes P450 (CYP) variants*"

Abstract

This PhD research project is part of a multi-disciplinary ongoing effort aimed at the development of a platform

based on metal-dependent oxidative enzymes for the conversion of recalcitrant substrates from abundant marine waste biomass into low-carbon second generation biofuels. Achieving such goal would provide a long-lasting energy supply from a waste biomass thereby contributing to the transition to a smart and sustainable economic growth. In fact, second generation biofuels are made from non-edible biomasses, at variance with first generation biofuels that rely on starch and sugar, which are both food sources. The biomass made up of seafood waste materials, such as crustacean shells, fish bones and scales, is rich in the polysaccharide chitin, which can be depolymerized by bacterial lytic polysaccharide monooxygenases (LPMOs) to simple sugars, to be eventually fermented to alcohols. In parallel, the fatty acid component of this biomass can be converted into alkanes/alkenes through decarboxylation that is performed by a class of bacterial cytochromes P450 (CYP152).
Some of the key steps of this project will be the characterization, at a molecular level, of the substrate binding to the protein active site, the detailed kinetic studies and evaluation of the catalytic mechanism of the enzymes involved in the process, and the optimization of engineered and artificial enzymes in terms of stability and functionality under different working conditions. To reach these goals and complement the ongoing experimental investigations, several computational techniques and approaches will be used, including classical Molecular Dynamics simulations, docking simulations, quantum chemical calculations and QM/MM methods. Such an integrated approach, involving different levels of theory, will allow elucidating the molecular determinants responsible of the enzymatic activity of LPMOs, and for rationally tuning the catalytic properties, stability and substrate scope of CYPs.

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n.1 scholarship funded by Department, Curriculum in Terrestrial and Marine Environmental Science linked to research project*:" Production and chemical functionalization of biochar for environmental applications*"

Abstract

The proposed project is in the frame of the Join Research Agreement between ENI and University of Milano Bicocca and aims at developing a new products to be applied in bioremediation of soil contaminated by hydrocarbons. Bioremediation technologies exploit the ability of natural microorganisms to efficiently remove organic pollutants. Biochar is a co-product of biomass pyrolysis. It is in fact a biological material produced in the absence of oxygen, at temperatures below 700 ° C, to generate more permeable, less dense and carbon-rich products. The presence of pores, the high surface area, the ability to bind and retain nutrients (N and P) as well as organic pollutants, make biochar a good support for persistence and microbial growth (bacteria and fungi), to be applied as a soil improver to maintain and increase the physical, chemical and biological properties/ activities of the soil. Recently, it has been suggested that applying biochar to contaminated soil helps plant-microorganism systems reduce hydrocarbon concentrations. Indeed, plant-microorganism

interaction can support the enzymatic ability of bacteria and fungi to degrade hydrocarbons. The aim of the project is to develop and validate a microbiologically activated biochar (Microbe-activated-Biochar (MaB)), to be applied to the biological treatment of soils contaminated by hydrocarbons. The planned activity for this project are: A) production of biochar from biomass through pyrolysis, followed by physical and chemical characterization of the biochar (proportion between the pyrolysis product and the original biomass, absorption capacity, specific surface, porosity, composition, etc.); B) functional activation of biochar in order to increase its chemical and biochemical compatibility with the strains of selected microorganisms. Functional modification of the biochar can be performed through physical or chemical activation; C) the effectiveness of the MaB obtained in WP3 will be evaluated in the bioremediation of soils contaminated by hydrocarbons by laboratory tests and pilot experiments in the field.

n.1 scholarship funded by Department, Curriculum in Terrestrial and Marine Environmental Science linked to research project: "*Phenotypic and genotypic characterisation of bacterial strains for biological functionalization of biochar*"

Abstract

The proposed project is in the frame of the Join Research Agreement between ENI and University of Milano Bicocca and aims at developing a new products to be applied in bioremediation of soil contaminated by hydrocarbons. Bioremediation technologies exploit the ability of natural microorganisms to efficiently remove organic pollutants. Biochar is a co-product of biomass pyrolysis. It is in fact a biological material produced in the absence of oxygen, at temperatures below 700 ° C, to generate more permeable, less dense and carbon-rich products. The presence of pores, the high surface area, the ability to bind and retain nutrients (N and P) as well as organic pollutants, make biochar a good support for persistence and microbial growth (bacteria and fungi), to be applied as a soil improver to maintain and increase the physical, chemical and biological properties/ activities of the soil. Recently, it has been suggested that applying biochar to contaminated soil helps plant-microorganism systems reduce hydrocarbon concentrations. Indeed, plant-microorganism interaction can support the enzymatic ability of bacteria and fungi to degrade hydrocarbons. The aim of the project is to develop and validate a microbiologically activated biochar (Microbe-activated-Biochar (MaB)), to be applied to the biological treatment of soils contaminated by hydrocarbons. The planned activity for this project are: A) selection of microorganism strains: bacteria and fungi will be found / isolated and monitored in order to obtain strains with the following metabolic characteristics: i) ease and low costs of cultivation, ii) biodegradation capacity of hydrocarbons, iii) promotion of plant growth (MaB + plant system). B) phenotypic and genotypic characterization of the selected strains: biodegradation tests will be performed on different hydrocarbons; for plant growth promoting microorganisms, metabolic capacities such as nitrogen fixation, phosphate solubilization and production of siderophores, phytohormones, 1-aminocyclopropane-1-carboxylate (ACC) deaminase and indole-3- acid will be investigated. acetic (IAA); determination and sequencing of the genetic determinants of the metabolic properties listed above; sequencing and annotation of complete genomes of selected strains

n.1 scholarship funded by Istituto per il Rilevamento Elettromagnetico dell'Ambiente del Consiglio Nazionale delle Ricerche linked to reserach project:" *Crop trait retrieval from Earth Observation multispectral and hyperspectral imagery for a sustainable agriculture*"

Abstract

The PhD project falls within the framework of remote sensing of environment. Space spectroscopy is

considered a fundamental technology for Earth Observation in order to extract quantitative value-added information of land surface properties. Thanks to national and international space agency initiatives, a new era for spaceborne hyperspectral remote sensing is occurring. Among these initiatives, the PRISMA (PRecursore IperSpettrale della Missione Applicativa) satellite, launched on March 22nd, 2019 by the Italian Space Agency (Agenzia Spaziale Italiana - ASI), represents the most advanced spaceborne sensor for Earth Observation, devoted to test the potentiality of new-generation hyperspectral sensors and products for environmental monitoring.
The PhD activities will be carried out within the project PRIS4VEG, funded by the Italian Space Agency. The project goal is to develop the fundamental knowledge to generate useful agronomic information related to crop bio-physical, biochemical and eco-physiological variables, starting from PRISMA data, to support precision farming activities for a sustainable agriculture. The availability of spaceborne hyperspectral data allows the development of new approaches for the operational mapping of important vegetation biophysical variables. Among these variables, chlorophyll and nitrogen content are of extreme interest given their importance in agricultural monitoring and specifically for the assessment of crop nutritional status. In particular, nitrogen (N) is the most important macro-nutrient for vegetation growth and productivity. Its management based on spatio-temporal information on actual crop status is fundamental for smart agriculture applications devoted to guarantee sustainable crop production and to reduce environmental impacts. Moreover, N estimation is considered important to assess final yield and crop quality such as grain protein content of cereals, fundamental to forecast crop production for the value chain of agroindustry. The candidate will develop methodological approaches and algorithms for the monitoring of vegetation compound with optical multispectral and hyperspectral data. In particular, the candidate will investigate machine learning techniques based on training data from ground measurements or simulations based on radiative transfer models, to estimate crop parameters of interest in the agro-sector as a contribution to a more sustainable agriculture. The candidate will conduct field campaigns contemporary to Earth Observation data acquisition to both i) collect spectro-radiometric measurements for CAL/VAL activities of PRISMA data and ii) estimate crop parameters to validate the retrieval approach. The final goal of the study is to provide a scenario for operational production of crop-parameter maps in the context of future downstream services for agro-monitoring.

n.1 scholarship funded by Eni S.p.a. linked to reserach project:" *Characterization and modelling of fracture networks with applications to the circulation and storage of geofluids*"

Abtract

Fracture networks (FNs) control the hydraulic properties of fractured geofluid reservoirs. Unfortunately, in the subsurface the distribution and characteristics of small-scale structures forming FNs is hardly characterized by direct or geophysical observations, impacting on reservoir modelling uncertainty.
The PhD candidate will participate in a Joint Research Project between the University of Milano Bicocca and Eni, aimed at the quantitative characterization and realistic modelling of fractured reservoirs important in the energy transition (Carbon Capture and Storage, Hydrogen Storage, geothermal energy, etc.). In this project, FNs will be characterized on large outcrops, analogues to subsurface reservoirs, using field techniques and photogrammetric Digital Outcrop Models. The ensuing quantitative analysis will allow defining the statistical distributions of FN parameters. Based on these datasets, innovative workflows will be developed to generate realistic stochastic models (Discrete Fracture Networks), which will be used for the upscaling of hydraulic properties with numerical methods. Improving this characterization and modelling workflow, and the geological realism of its results, is fundamental to successfully generalize structural observations and improve fluid flow simulations in reservoirs. The PhD candidate will work within a large multidisciplinary team, including researchers from the industry and the academy, and will spend one/two period(s) abroad in partner

universities and research centres

Intellectual property clauses agreed with the Company apply to this scholarship

PhD Course in Converging Technologies for Biomolecular Systems (TeCSBI)- XXXVIII cycle, a.y. 2022/2023

n.2 scholarship funded by Istituto di Ricerche Farmacologiche Mario Negri (IRCCS) linked to reserach project:

1) **"Desmoplastic response in pancreatic ductal adenocarcinoma (pdac): exploiting high throughput CRISPR screening to disrupt tumour-induced stromal reprogramming"**

Abstract

The tumor immune microenvironment and the biological mechanisms that lead to its reprogramming orchestrated by tumor cells have been in the spotlight for several years now. In contrast, fibroblasts and the mechanisms underlying their malicious recruitment to Cancer Associated Fibroblasts (CAFs) to support tumor spread and growth have remained largely in the shadows. As PDAC shows a unique desmoplastic response mediated by CAFs it represents the ideal disease to investigate their progressive engagement to sustain tumor cells. Single-cell RNA-Seq experiments have revealed that the CAFs-population is heterogeneous and is composed of multiple cell communities executing different tasks and functions. Indeed, killing off indistinctively the entire CAF population has the paradoxical effect of sensitizing the tumor cells to drugs but also facilitates their metastatic spread due to loosening of the extra-cellular matrix surrounding the tumor. We intend to continuously expose fibroblasts (i.e., stellate cells) to the PDAC's secretome, and through genome-wide CRISPR knock-out screens we aim at identifying which genes are exploited by the tumor to hijack healthy cells to become CAFs. The rationale behind, is that knocking out specific genes involved in the cross-talk between tumor cells and healthy fibroblast precursors could abolish the capability of malignant reprogramming into specific CAFs subtypes. By interfering with this signaling, we aim at preventing recruitment into CAFs and selectively eradicate individual subtypes, without affecting the entire CAF population. Druggable targets such as receptors will be prioritized, as their blockage by small molecules would better mimic the CRISPR knock-out. Hence, we aim at identifying pharmaceutical targets to reshape the tumor stroma and possibly alter the entire tumor microenvironment.

2) **"Contribution of brain's resident immune cells to neurological disorders in Wiskott-Aldrich syndrome"**

Abstract

Wiskott-Aldrich syndrome (WAS) is a rare genetic disorder caused by deficiency of the WAS protein, an important regulator of immune cell development. The most common clinical manifestations are autoimmune disorders and bleeding, but neurological manifestations can also occur. The mechanisms responsible for neurological events are poorly understood, but it is conceivable that non-neural cells resident in the brain are involved. The WAS gene is in fact constitutively expressed by microglia, the immune population residing in the brain. Microglia plays the physiological role of active surveillance of brain homeostasis and is activated in the case of brain pathologies. Furthermore, during brain development it participates in synaptic remodeling

through a phagocytic process that requires the recognition of complement system factors such as C3 and C1q. Considering that the WAS protein is involved in the modifications of the cytoskeleton that support the phagocytic activity of immune cells and that it is able to bind some complement receptors, it is conceivable that its deficiency alters the ability of the microglia to perform synaptic remodeling in development of the brain. On the basis of this hypothesis, the project aims to clarify: 1) whether WAS is involved in the physiological processes of brain development coordinated by resident immune cells; 2) whether WAS deficiency induces specific neurological consequences associated with behavioral alterations. The project involves in vitro models using reprogrammed pluripotent stem cells (IPSCs) and in vivo models using mouse models of the syndrome. The ultimate goal is to identify possible drug targets to limit the neurological consequences associated with the Wiskott-Aldrich syndrome and improve the life expectancy of affected patients.