Suggestions for RESEARCH PROJECTS starting November 1st, 2018

Research Topic: Investigation of the electronic and vibrational properties of hybrid organic 2D materials as single-metal atom model catalysts for the synthesis of energy vectors

Supervison: Erik Vesselli

Physics Department

Nature often performs energy harvesting and funneling, as well as catalytic activity, by means of reaction centers based on few or even single metal atoms, embedded in organic matrices. By exploiting state-of-the art theoretical and experimental approaches, the project aims at the development and characterization of model systems to mimic nature's behavior in a controlled way. Hybrid-organic 2D materials will be investigated by means of non-linear laser spectroscopy methods in situ and operando at near-ambient pressure, together with complementary experimental tools (both microscopies and spectroscopies), and a thorough ab initio modeling. The research will be part of the activities of the Sum-frequency generation vibronic spectroscopy laboratory of the Physics Department at the University of Trieste, within the framework of an extended international scientific collaboration network. Both experimental and theoretical positions are available.

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Research Topic: APPLICATIONS FOR THE DELIVERY OF NUCLEIC ACIDS IN CANCER B CELLS

Supervison: Paolo Macor (pmacor@units.it)

B-cells malignancies are an heterogeneous group of diseases, for whom treatment options include both chemotherapeutics and immunotherapy. Despite the recent characterization of new drugs, most of patients develop resistances or do not respond to therapies. For these reasons new therapeutic approaches have to be developed.
The aim of this project is the characterization of a new therapeutic tools, which involves different polymeric nanoparticles (NPs) for the selective delivery of nucleic acids in cancer B-cells. Targeting antibodies will be employed to specifically target NPs to B-cells in vivo.
miRNA-17 is a molecule upregulated in several B-cells malignancies and it is associated to the development of drugs resistance mechanisms. AntagomiR17 is capable to pair and defeats miRNA-17. This project starts characterizing, both in vitro and in vivo, polymeric nanoparticles loaded with antagomiR17 and joined with tumor B-cells targeting antibodies. Moreover, the project plan to develop targeted nanosystems for the selective delivery of DNA vector for the local production of proteins, with the specific aim to cause cancer B-cells killing or to induce an immune response against cancer B-cells.
The best nanosystem for nucleic acid has to be study to allow their selective delivery in cancer cells.

Cell lines and cells from patients have to be used in vitro for an initial characterization while animal models of B-cell leukemia and lymphoma will be requested to understand particles distribution and the efficacy of the proposed therapeutic approach

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Research Topic: **Smart nanostructured catalysts for sustainable development**

Supervision: Prof. Paolo Fornasiero

The activity and selectivity of heterogeneous catalysts is dependent on their surface composition, surface electronic structure, and crystallite size and morphology, and a fundamental understanding of these structure-activity relationships is required for the rational design of catalysts that are highly active and selective for specific molecular transformations. Unfortunately, the inherent inhomogeneity of most catalysts presents challenges when trying to develop such correlations. This has motivated studies in which well-defined model catalysts, such as single crystals, coupled with modern surface-sensitive spectroscopic techniques, have been used to provide for more direct comparison between surface structure, electronic properties and reactivity. Indeed, much of what know about how structure affects the reactivity of supported metal catalysts can be attributed to these so called surface science studies, which have been carried out over the last forty years. This is also the case for metal oxide catalysts, although the lack of availability of single crystals for many oxides has limited the impact somewhat. While this approach to catalytic surface science has provided many useful insights, such studies still cannot capture all the intricacies of the high surface area catalysts that are used industrially.

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Research Topic: ELECTROSPUN NANOSTRUCTURED SCAFFOLDS FOR TISSUE ENGINEERING APPLICATIONS

Supervision: Prof. Roberto Di Lenarda

Tutor: Dr. Gianluca Turco

The success of an implantable tissue engineered graft relies, among other factors, on the development of a scaffold that mimics the native tissue extracellular matrix (ECM) [1]. This matrix could be seen as a three-dimensional network made of proteins and polysaccharides fibers with diameters in the 50-500nm range [2]. Electrospinning (ELS) emerged as a technique for the fabrication of nano-fibered scaffolds in this size range [3, 4]. ELS allows the production of fibers from a broad range of polymers, including purely natural, to synthetic, to composite mixtures of ECM analogs and constituents from organ-specific extracts. These nano-structured matrices with large surface area could be used as catalysts, filtration systems, protective clothing, drug delivery depots, optical wave guides, electronics and tissue engineering scaffolds. In this latter context, our interest is focused on the development of electrospun scaffolds with several applications as bone and vascular grafts, to name some. Several bio-polymer based mixtures will be considered and their effects on the structural and biological features of the produced scaffolds will be investigated by means of different analytic techniques. Particular attention will be paid to the release of bioactive molecules from the scaffolds and their effects on the differentiation of mesenchymal stem cells.

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Research Topic: Carbon nanostructures for bioimaging

Supervision:: Prof. T. Da Ros, Department of Chemical and Pharmaceutical Sciences

Carbon based nanostructures (CNSs) have been extensively explored so far for many applications, thanks to their unique physicochemical properties. Among CNSs, new promising nanomaterials as nanodiamonds (NDs) and graphene quantum dots (GQDs) are attracting the scientific community interest also for their possible applications in drug delivery, therapeutic and cancer therapy, and bioimaging.

The envisioned applications of these materials are mainly in imaging, thanks to their unique physical and chemical characteristics, their fluorescence with emission in the NIR, very high quantum yield and no photobleaching.

This project is aimed to explore NDs and GQDs use in bioimaging to map and detail cells and living tissues with an unprecedented precision. NDs and GQDs functionalized by means of targeting units, as tumor homing peptides, will be used to discriminate tumor cells from healthy ones. Moreover the nanocompounds will be studied by means of functional electrochemical imaging technique

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Research Topic: Structural and electronic characterization of molecular architectures at metal surfaces

Supervision: Giovanni Comelli

The ability to control the structural and electronic properties of (hetero)-organic assemblies on metal surfaces is the key issue for the design of efficient devices in organic electronics, which has triggered a significant effort in the recent years in this field.

We plan to characterize, mainly by means of low temperature scanning tunneling microscopy (LT-STM), homo- and hetero-organic architectures formed on a gold (111) surface. With STM it is possible to obtain sub-molecular resolution images of a surface and, when at low temperature (4−77 K), to manipulate single molecules as well as to perform single molecule spectroscopies. Therefore, STM is the ideal technique to study 2D supramolecular systems.

In order to reach a thorough description of the systems under exam, STM data could be coupled with synchrotron radiation X-ray spectroscopy experiments and ab initio calculations, performed in collaboration with theoretical groups. The aim is to identify the role of the molecule-molecule and molecule-substrate interactions in determining the electronic and structural properties of the investigated systems.

The activity will be carried out at the Surface and Reactivity Laboratory within the TASC-CNR-IOM laboratory in Basovizza.

Prior contact is advised (giovanni.comelli@elettra.eu).

Research Topic: **Study with SERS spectroscopy of the nano-bio interface between biofluids and metal nanostructures.**

Supervison: Prof. Alois Bonifacio - Prof. Valter Sergo

A better understanding of the interaction between metal nanostructures, such as nanoparticles, and biological fluids (e.g. serum, saliva) is a necessary step toward the application of nanotechnology to biological systems, and in particular to humans. Gold and silver nanoparticles and nanostructured surfaces could be used for a variety of applications, from photothermal therapy to drug delivery, from drug monitoring to diagnostics, as antibacterial agents or as sensors. Many of these applications require a direct contact between the nanostructured materials and the biofluid, so that a better insight on how the nano-objects interact with these complex biological samples is crucial.
However, while most studies presently available on the "nano-bio interface" are concerned with the role of proteins, especially in the formation of an adsorbed layer ("protein corona") on gold and silver nanoparticles, the interaction of small-molecules, such as metabolites, with the metal nanostructures ("non-protein corona") still needs to be examined and studied.
The reason of this delay has been the lack of experimental techniques capable to investigate small molecules adsorbed on metal surfaces in the context of complex samples, as biofluids are. Surface-Enhanced Raman Spectroscopy (SERS) is an analytical technique capable of detecting the vibrational spectra of species adsorbed on nanostructured metal surfaces, and thus it is a very promising tool to identify adsorbed metabolites.
PhD candidates will use SERS to study the interaction of different biofluids (starting from model solutions or proteins and metabolites) with gold and silver nanoparticles and nanostructured surfaces. Besides SERS, other techniques will be used to characterize the nanostructures and the nano-biointerface, also in collaboration with other centers, such as electron microscopy (TEM, SEM), Dynamic Light Scattering, and FT-IR among others. While studying the nano-bio interface and based on their findings, candidates will be also encouraged to explore possible bioanalytical or clinical applications.

Short Bibliography

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Research Topic: Characterization of polymeric nanoparticles anti-glypican-1 (GPC1) for targeted therapy strategies in glioma

Supervison: Giuseppe Toffoli (gtoffoli@cro.it)

Gliomas are primary brain tumors characterized by high morbidity and mortality given their localization and locally invasive growth.[1] Despite the use of advanced surgery, radiotherapy, chemotherapy with alkylating agents as canonical approaches for treatment of glioma, the prognosis of patients remains poor.[1,2] Recently, different immunotherapies have been investigated in patients with this disease.[2] In this context, new therapeutic strategies targeting specific tumor antigens may concur to improve the outcome of glioma patients.

Glypicans (GPCs) are membrane-bound heparan sulfate proteoglycans, linked to the cell surface by a glycosylphosphatidylinositol (GPI) anchor.[3] In mammals six members of the GPC family have been identified (GPC1 to GPC6), with similar size and structure. GPCs are overexpressed in several cancers and associated with tumor progression.[3] Of note, GPC1 has been found overexpressed in gliomas.[4,5,6] In particular, GPC1 overexpression has been associated with a disseminated pattern in glioblastoma (glioma classified as WHO grade IV).[6]

Our research work aims at the development of therapeutic approaches employing polymeric nanoparticles loaded with chemotherapeutic drugs or biological compounds, and conjugated with antibodies specific for GPC1, for glioma treatment. The project will be carried out in collaboration with the group of Dr Paolo Macor (Department of Life Sciences, University of Trieste) that has a recognized expertise in developing biodegradable nanoparticles (based on carboxylic acid terminated biodegradable polymers) conjugated with antibodies to target specific tumor antigens.[7,8] Experiments will be conducted to evaluate: i) the in-vitro killing efficacy of anti-GPC1 loaded nanoparticles in glioma cell line models; ii) in-vivo biodistribution; iii) in-vivo biodegradability and excretion; iv) in-vivo killing efficacy, in glioma xenograft and/ or syngenic mouse models, of anti-GPC1 loaded nanoparticles.

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Research Topic: Charge transfer processs in complex interfaces.

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Interface processes strongly affect the performances and efficiency of organic based devices. In general, the interposition of a 2D templating architecture between the electrode and the organic layer represents a powerful tool for the improvement of the overall device performances. Therefore, there is an increasing interest in the synthesis and characterization of possible 2D templates able to tailor the electronic properties of complex Metal/Template/Organic (MTO) architectures. Possible templates we are interested in range from functionalized 2D materials, to Covalent Organic Frameworks, to self-assembled monolayers of organic molecules. Major efforts have been made in last years to study the morphology of these systems, while their electronic properties are in most cases only partially described. There is a need therefore for a deeper understanding and control of processes like charge transfer at MTO interfaces. Charge injection across molecular junctions can occur at the femtosecond time scale or even shorter. We use X-ray spectroscopies to investigate charge injection in complex MTO hetero-structures. More specifically the Core hole clock implementation of the Resonant Photoemission spectroscopy (RESPES) allows us to determine charge dynamics in both directions (to/from the molecule) at these interfaces and can give clues on the interface parameters that can increase/decrease the charge transfer efficiency. The same type of processes will be studied with time resolved pump-probe spectroscopies using femtosecond lasers and Free Electron Lasers. Beside these time-resolved techniques, we adopt traditional X-ray spectroscopy measurements (XPS, UPS, NEXAFS) to characterize both the 2D template formation and the MTO static electronic properties.

Resarch Topic: Nanoresolved approaches for the study of Myocardial fibrosis

Supervision: Lisa Vaccari, Orfeo Sbaizero

Fibrotic diseases, which are caused by the formation of excessive scar tissue, account for up to **45% of deaths** in the industrialized world. They can affect any organ, producing a wide range of conditions including cardiovascular disease, pulmonary fibrosis, kidney disease, systemic sclerosis, liver cirrhosis and inflammatory bowel disease.

Fibrosis is a challenging therapeutic field given the great variability it can present among different organs and tissues.

In this project, we will tackle the myocardial fibrosis which is a significant global health problem associated with nearly all forms of heart disease. Cardiac fibroblasts comprise an essential cell type in the heart that is responsible for the homeostasis of the extracellular matrix; ***however, upon injury, these cells transform to a myofibroblast phenotype and contribute to cardiac fibrosis***. This remodeling involves pathological changes that include chamber dilation, cardiomyocyte hypertrophy and apoptosis, and ultimately leads to the progression to heart failure. Despite the critical importance of fibrosis in cardiovascular disease, our limited understanding of the cardiac fibroblast impedes the development of potential therapies that effectively target this cell type and its pathological contribution to disease progression. Our project will deal with the origins and roles of fibroblasts, mediators and signaling pathways known to influence fibroblast function after myocardial injury. In particular Fourier Transform Infrared (FTIR) microscopy and new-generation FTIR nanoscopy will be used to provide information on the chemical changes in the Extra Cellular Matrix (ECM) composition of co-cultures of cardiomyocyte and cardio fibroblasts to identify when and how fibroblasts become “activated fibroblasts - myofibroblasts” the key players in the fibrosis development. Chemical analysis through vibrational spectroscopy will be coupled with AFM force measurements on ECM of fibroblast and activated fibroblast at rest and under stress conditions. The aim is to get deeper insight on the cardiomyocytes mechanobiology, the emerging field of science at the interface of biology and engineering, by analyzing at the nanoscale the complexity of heart cells and their ECM.