CIC biomaGUNE

SEMINAR

Tuesday, 26th January, 12.00 pm, Seminar Room

Host: Prof. Luis M. Liz-Marzán

Understanding Language in the Brain: from the lab to the actual world

Manuel Carreiras

BCBL. Basque Center on Cognition, Brain and Language, Donostia-San Sebastián, Spain
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Most of people acquire a first language without effort, but some have difficulties speaking and understanding it, and others learning to read. Most people either learn more than one language from birth or invest quite a lot of time and effort learning a second language. Finally, some people loose part of their linguistic abilities with age or after some brain damage. In this talk I will review the different research lines we are carrying out in the BCBL to understand how we acquire language, how we process language (comprehension and production) and reading in monolingual and bilingual settings, in children with typical and atypical developmental trajectories, in the elderly and in patients with brain damage.

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SEMINAR

Tuesday, 9th February, 11.00 pm, Seminar Room

Host: Prof. Luis Liz-Marzán

Gold Nanostars: Synthesis, Stabilization and Applications as Surface-enhanced Raman Scattering Tags

Ana Belén Serrano-Montes
BioNanoPlasmonics Group

Surface enhanced Raman scattering (SERS) nanotags are appealing contrast agents that offer important advantages over classical (bio)labeling methods. They present high photostability, sensitivity and superior multiplexed capacity due to the small line width of vibrational Raman bands. In addition, the enhanced optical contrast and tissue penetration achieved by using NIR light render them excellent candidates for in vivo Raman imaging. The synthesis of new SERS-tags suitable for biological applications requires the use of metal nanoparticles with high plasmonic enhancing efficiency. In this regard, anisotropic nanostructures such as gold nanostars, which present optical responses in the tissue optical transparency window as well as extremely high electromagnetic field enhacements at their tips, are attractive nanoplatforms for the design of SERS-encoded nanoparticles. This PhD thesis focuses on the preparation and stabilization of gold nanostars and their use as novel multifunctional nanoprobes for SERS applications. The results presented here are expected to have enormous implications towards the engineering of new SERS-based nanoplatforms for biomedical applications.

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SEMINAR

Tuesday, 9th February, 12.00 pm, Seminar Room

Host: Prof. Luis Liz-Marzán

Rational Synthesis and Self-Assembly of Anisotropic Plasmonic Nanoparticles

Leonardo Scarabelli
BioNanoPlasmonics Group

This thesis presents significant advancement in both synthesis and self-assembly of different anisotropic plasmonic nanoparticles. The final goal is the development of novel nanostructured plasmonic materials based on crystalline assemblies of anisotropic nanoparticles, to be used as optical enhancers for the surface enhanced Raman scattering detection of bacterial Quorum Sensing signaling molecules. More specifically, the thesis was oriented toward the design of such nanostructures, and on the characterization of their optical properties by means of various experimental techniques. The first of the experimental work was dedicated to the optimization of various synthetic procedures; subsequently, the self-assembly of the synthesized building blocks was optimized to control the formation of ordered nanostructures with different sizes and shapes over large areas (centimeters squared). The presented results could have important applications in several fields, such as nanomedicine, biosensing or catalysis.

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SEMINAR

Friday, 12th February, 12.00 pm, Seminar Room

Host: Prof. Luis M. Liz-Marzán

Self-assembling Cyclic Peptide Nanotubes: Modulation of Internal and External Properties

Juan R. Granja
Professor
Department of Organic Chemistry and Center for Research in Biological Chemistry and Molecular Materials (CIQUS)
University of Santiago de Compostela

In the last few year our group has been working on the design of self-assembling peptides to obtain new functional material. Especially we were interested in the preparation of nano tubular structure and for that purpose we have prepared cyclic peptides that allow the modulation of both external and internal properties. This control allowed us to design cyclic peptides that interact with biological membranes and transport across the membrane different hydrophilic components. In this talk, the new research achievements in this topic will be presented.

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SEMINAR

Tuesday, 16th February, 11.00 pm, Seminar Room

Host: Prof. Luis Liz-Marzán

Engineering the Morphology and Organization of Gold Nanostructures for SERS Detection

Andrea La Porta
BioNanoPlasmonics Group

Since its discovery, Surface-enhanced Raman Scattering (SERS) has become one of the most powerful and intensively studied spectroscopic analytical techniques. The electric near-field enhancement created by illumination of metallic nanostructures provides SERS with the ability to overcome the main drawback of standard Raman scattering spectroscopy, namely its low sensitivity. Many efforts are therefore currently devoted toward the fabrication of high-performance, homogeneous and reproducible SERS substrates by means of the most advanced methods, both top-down and bottom-up. Metallic nanoparticles represent an attractive route to the design of SERS supports with suitable properties.

In this work, different approaches in the fabrication of SERS substrates have been studied. Among all the available metals and related alloys, gold and silver are the principal materials of choice because of their special interaction with light. Applications of SERS spectroscopy are foreseen in a wide variety of fields like medicine, biology, forensic science, archaeology, pharmacy and others.

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SEMINAR

Tuesday, 16th February, 12.00 pm, Seminar Room

Host: Prof. Luis Liz-Marzán

Biosensing using metal nanoparticles

Marc Coronado
BioNanoPlasmonics Group

Metal nanoparticles display fascinating nanoplasmonic features that are essential for the development of new plasmonic biosensors. In this sense, suitable nanostructures with improved plasmonic properties were successfully obtained and implemented for the biodetection of relevant molecules for biology and human health. In a first batch of experiments we have developed highly sensitive, selective and inexpensive colorimetric biosensors for biological molecules (such as glucose and nerve gases) by combining enzymes and gold nanorods. The introduction of biocatalytic molecular species significantly improved the efficiency and biocompatibility of the system, thus opening new possibilities in biosensing using metal nanoparticles (NP). In a second set of experiments, The SERS performance of highly monodisperse gold nanotriangles was explored and the combination of this nanostructure with mesoporous silica gated NP allowed us to detect pathogenic DNA (Mycobacterium spp.) and cocaine. Altogether, the NP synthetic methods developed in this work along with the use of biological catalysts and mesoporous silica NP allowed us to easily detect different biomolecules without complicated and expensive instrumentation. Indeed, some sensors can be even read out by the naked eye.

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SEMINAR

Tuesday, 23rd February, 12.00 pm, Seminar Room

Host: Prof. Luis M. Liz-Marzán

Hybrid organic-inorganic materials for optoelectronic devices

Rubén D. Costa
Department of Chemistry and Pharmacy & Interdisciplinary Center for Engineering of Advanced Materials (EAM), Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU), Egerlandstr. 3, 91058 Erlangen, Germany
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Hybrid organic-inorganic optoelectronics are heralded as the next generation of lighting and photovoltaic technologies.[1] In this context, our efforts encompass three main actions, namely the development of suitable third generation of electroluminescent materials for ionic-based lighting devices, the application of nanocarbon-based hybrids in solar cells and lighting devices, and the development of bio-inspired components for lighting, energy conversion, and diagnostic applications.

Herein, the implementation of the third generation of materials – *i.e.*, lighting perovskite nanoparticles, small molecules, and copper(I) complexes – for light-emitting electrochemical cells (LECs) will be presented as new approaches to develop deep-red, blue, and white lighting sources.[2] Next, carbon nanohorns will be shown as new integrative components for preparing new nanocarbon-hybrid dye-sensitized solar cells (DSSCs), resulting in several breakthroughs, namely i) the enhancement of charge transport and collection in the electrodes, ii) the development of iodine-free, solid-state electrolytes, and iii) the fabrication of platinum-free counter electrodes.[3] Finally, a new strategy to stabilize any type of bio-components – *i.e.*, enzymes, fluorescent proteins, *etc*. - in a rubber-like material was developed. As an example, the latter was applied to fabricate the first bio-inspired hybrid light-emitting diodes featuring a bottom-up energy transfer protein-based cascade coatings. The synergy between the excellent features of fluorescent proteins and the easily processed rubber produces bio-HLEDs with less than 10% loss in luminous efficiency over 100 hours.[4] Currently, other applications like bio-reactors and ready-to-go-kits are under development in our laboratory.[4]

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SEMINAR

Friday, 4th March, 12.00 pm, Seminar Room

Host: Prof. Luis M. Liz-Marzán

Plasmonic Supraparticles for Biosensing and Nanomedicine

Dr. Roberto de la Rica
University of Strathclyde

In this talk I will show several approaches aiming at assembling gold supraparticles with improved plasmonic properties. For example I will explain a bio-inspired method for assembling citrate-stabilized gold nanoparticles into superstructures containing crystallographically aligned nano-building blocks. I will also show that anisotropic Au superstructures with tunable LSPR can be assembled on highly magnetic nanoparticle cores. The resulting magnetic and plasmonic nanoparticles can be used to manipulate cells, detect analytes with SERS spectroscopy, and generate heat in photothermal therapy.

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SEMINAR

Thursday, 10th March, 12.00 pm, Seminar Room

Host: Dr. Niels C. Reichardt

Exploring new frontiers, role of tumor-secreted exosomes in metastasis

Héctor Peinado Selgas, PhD.
Head of Microenvironment and Metastasis Group Molecular Oncology Program Spanish National Cancer Research Centre (CNIO), Madrid

Cancer is a systemic disease, while most of the research effort has been focused on analyzing the primary tumor, there is a lack of information on how the tumor microenvironment influences metastasis. The importance of the microenvironment in metastasis is now fully acknowledged. Prominent roles for stromal cells, such as fibroblasts, endothelial cells, lymphatic endothelial cells, bone marrow-derived cells, soluble factors and secreted vesicles have been established. Exosomes are secreted vesicles carrying lipids, proteins, RNA and DNA molecules. By carrying these molecules, and facilitating their cell-to-cell transfer, exosomes can modulate the behavior of resident cells that can impact disease progression. Exosomes can serve as vehicles for horizontal transfer of proteins, RNA and DNA to the surrounding cells, thus promoting additional modifications in the tumor and metastatic microenvironments. Our studies in metastatic melanoma demonstrated that tumor exosomes are a major tumor-derived factor that acts systemically to promote bone marrow-derived cells (BMDCs) recruitment to the tumor and metastatic microenvironments. We showed that exosome secretion by melanoma cells influences BMDC mobilization and recruitment to pre-metastatic and metastatic niches, thus promoting metastasis in a process that we have termed “education”. Our novel studies suggest that tumor exosomes can fuse specifically to stromal cells within the metastatic microenvironments. We have analyzed the role of tumor-secreted factors in lymph node and distant metastasis. Our data suggest that tumor-secreted exosomes define the metastatic tropism preparing metastatic niches.

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SEMINAR

Friday, 11th March, 12.00 pm, Seminar Room

Host: Dr. Sergio Moya

Design, Physico- Chemical Characterization and Bioactivity Studies of Hybrid Nanostructured Titanium Surfaces for Enhanced Osseointegration

Danijela Gregurec

Titanium, a material with excellent biocompatibility and widely used as dental or orthopaedic implant, still displays a poor osseointegration, the implant fixation in the bone. Bone- implant binding starts at the interface between bone forming cells and the implant surface, thus ossointegration may be improved with optimization of the surface properties.

In this thesis hybrid titanium –based surfaces are designed with aim to enhance its bioactivity.

An inorganic modification of the titanium is based on the niobium doped carbon coating that introduced a surface topography analogous to the natural one in the bone environment and enhanced surface mechanical properties, thus influencing positively osteoblast cell activity.

A stable biopolymer coating achieved with the collagen and alginate has enhanced osteoblast functions due to close mimic of extracellular matrix in regards of its topographical and biomechanical properties.

A design based on polyacrylic acid brush on titanium additionally enabled controlled complexation of osseoactive strontium that resulted in rapid biomineralization and superior activity of the osteoblast cells.

Titanium alloys etched with the sodium hydroxide exhibit controlled nano and micro roughness mimicking topography of the bone extracellular matrix. This approach enabled an elegant way to control the topography and achieve ability to bind strontium to the titanium alloy

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SEMINAR

Friday, 18th March, 12.00 pm, Seminar Room

Host: Dr. Ralf Richter

Biomaterial physical properties in tissue regeneration and disease

Dr. Amaia Cipitria
Charité - Universitätsmedizin Berlin

Cells respond not only to biochemical but also to physical cues, such as stiffness, geometry and matrix degradability. In-vitro studies showed that hydrogel elasticity or degradation properties alone can direct cell differentiation, while scaffold geometry can control tissue growth rate. However, little is known about how these findings translate to an in-vivo scenario. Bone defect healing experiments were used to investigate how the architecture of a semi-rigid scaffold may pattern the organization of collagen fibers and subsequent mineralization in-vivo, using a 30 mm critical-sized defect in sheep tibia as model system. The hierarchical material structure and properties of regenerated tissue were investigated using a multi-scale and multi-modal approach. Next, alginate hydrogels with varying stiffness were used for in-vivo host cell recruitment and osteogenic differentiation in a rat femoral 5 mm critical-sized defect. Current activities focus on tailoring the spatio-temporal degradation properties of novel click-crosslinked alginate hydrogels to direct cell migration and proliferation, guide spatial distribution and directionality of extracellular matrix deposition, and pattern in-vivo tissue formation. Possible extension of tissue engineering approaches to create physiologically relevant 3D in-vitro models to investigate cell-cell and cell-matrix interactions in tumor progression will be discussed.

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SEMINAR

Wednesday, 13th April, 12.00 pm, Seminar Room

Host: Dr. Niels C. Reichardt

Imaging Degradation

Sander van Kasteren, Faculty of Science
Leiden Institute of Chemistry, Bio-organic Synthesis

Degradation of antigen into short MHC-loadable polypeptides by antigen presenting cells presents a Heisenbergian conundrum: reporter strategies for imaging these processes affect the processes themselves; often to such an extent that the information obtained from reporter antigen strategies may not be representative of the process itself.

For example genetic fusion constructs of antigens are only imagable until the point they are degraded or separated from the antigen. As processing into MHC-loadable antigens is an essential part of antigen presentation, it means these reporters are of limited use for imaging later aspects of processing. These approaches can also result in "imaging bias": only those sections of the pathway during which reporters remain intact are seen. Complications can also arise from the fact that reporter-constructs can alter the rate of proteolysis and routing by virtue of changing overall physiochemical properties of the antigens.

I will present our perceived methods to address some of these issues, namely ´bioorthgonal antigens´: these are antigens that carry chemical groups of 2 or 3 atoms in size in some amino acid sidechains (e.g. only in a non-MHC-binding position in the epitope) that can be visualised using 'click'-chemistry. This approach has two key advantages, namely the diminuitive size and exceptional stability of the groups. The fact that they are not degraded by proteolysis, are uncharged and small means that their altering effect on antigen processing can be minimal.

We are using these bioorthogonal antigens, for example, to determine the spread of degrading antigen inside an APC or the determination of the rate of epitope appearance on the cell surface without the need for peptide-MHC-specific antibodies, as the handles are so small, that the peptides are presented with their detectable groups intact.

We believe this approach offers the first opportunity to get a glimpse into the late events of presentation and cross-presentation, an area that has been notoriously difficult to study to date.

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SEMINAR

Friday, 15th April, 12.00 pm, Seminar Room

Host: Prof. Manuel Martín-Lomas

The Fight against Scientific Misconduct: Research Integrity and Good Scientific Practices

Pilar Goya
Instituto de Química Médica, CSIC. Madrid

Research integrity is vital for the development and advance of science. Scientific misconduct such as fabrication, falsification and plagiarism is detrimental for research, undermines trust among scientists and damages the public image of science. The stakeholders involved, researchers, institutions and financing agencies should promote scientific integrity by means of developing and implementing guidelines and codes of conduct. This talk will deal with scientific misconduct, its frequency, causes and impact, and with the initiatives carried out at the institutional and international levels to promote research integrity.

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SEMINAR

Monday, 18th April, 12.00 pm, Seminar Room

Host: Prof. Luis M. Liz-Marzán

Synthesis of Functional Materials by Atomic Layer Deposition

Mato Knez[1,2]
[1]*CIC nanoGUNE, Donostia – San Sebastián, Spain*
[2]*IKERBASQUE, Basque Foundation for Science, Bilbao, Spain*
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Atomic layer deposition (ALD) is a thin film deposition technique that was developed in the 1970s to meet the needs for processing thin film electroluminescent displays (TFEL). Technically and chemically it is similar to chemical vapor deposition (CVD). However, in contrast to CVD, ALD incorporates as a specific feature the separation of the chemical reaction into two half-reactions. The exposure of the substrate to separate precursor vapors allows for chemical saturation of the substrate surface with a monolayer of the precursors and thus for a precise sub-Å growth control in a cycle-by-cycle manner. In addition, being a non-line-of-sight deposition technique, ALD allows for good coating conformality even with 3D nanostructured substrates or structures with a high aspect ratio together with a good capability for up scaling.

This presentation will show a variety of approaches towards (multi)functional materials that were enabled by ALD. This process does not only allow deposition of compact thin films, but also area-selective and defect-sensitive deposition of clusters and nanoparticles, the bottom-up growth of porous thin films, and a top-down hybridization of inorganic and organic materials triggered by the diffusion of molecules. The resulting materials may serve as platform for the development of future advanced functional materials for use in energy storage, catalysis, plasmonics, and so on.

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SEMINAR

Tuesday, 19th April, 12.00 pm, Seminar Room

Host: Prof. Luis M. Liz-Marzán

Scientific Publishing From the Inside Out

Dr. Phillip Szuromi
Science Senior Editor
Knoxville, Tennessee. USA

I will present a brief overview of how papers get published at *Science*. The *Science* editors not only direct the peer review process but also stay informed about their fields and identify emerging fields. I will make some general comments on the changing scientific publishing landscape, and recap some of our recent initiatives to uphold high standards of author and referee conduct. As part of the American Association for the Advancement of Science (AAAS), a nonprofit organization, our goal is not just to publish papers but to ensure that the impact of research we publish has benefit to society. We also try to advance a general appreciation for the value of thinking scientifically about the many challenges our world now faces.

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SEMINAR

Thursday, 28th April, 12.00 pm, Seminar Room

Host: Dr. Fernando López-Gallego

Microscopic dynamics of proteins: from energy landscapes to enzyme engineering

Dr. David De Sancho
Ikerbasque Research Fellow
Nanobiomechanics Group, CIC nanoGUNE

Atomistic molecular dynamics (MD) simulations provide a uniquely detailed tool for understanding the dynamics of proteins, the workhorses of living organisms. Analyzing the results from these simulations is however an overwhelming task, as it involves making sense of gigabytes of data consisting of the coordinates of the protein and the surrounding solvent for the many snapshots in time. To help us solve this "big data" problem Markov state models have recently emerged as the method of choice for the analysis of MD simulations. They are able to provide information of the slow, and usually most relevant, transitions of the system (e.g. folding), but without loosing the resolution on the microscopic dynamics. One of their advantages is their fine-grained resolution, which allows for exquisite comparison of the simulation results with experiment.

In my talk I will introduce this approach using a very small peptide as example. Studying this system we have been able to calculate the rate of the most fundamental process in protein folding, helix nucleation[1]. Then we will gradually move up in complexity to show how these approaches can help us solve problems posed by experimentalists in the field protein folding, like the molecular origin of "internal friction" in proteins[2,3]. Finally I will present applications of this type of approaches to enzyme engineering in systems of industrial interest[4,5]

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SEMINAR

Friday, 13th May, 12.00 pm, Seminar Room

Host: Dr. Luca Salassa

Towards Near-Infrared Photoactivation of Anticancer Metal Complexes

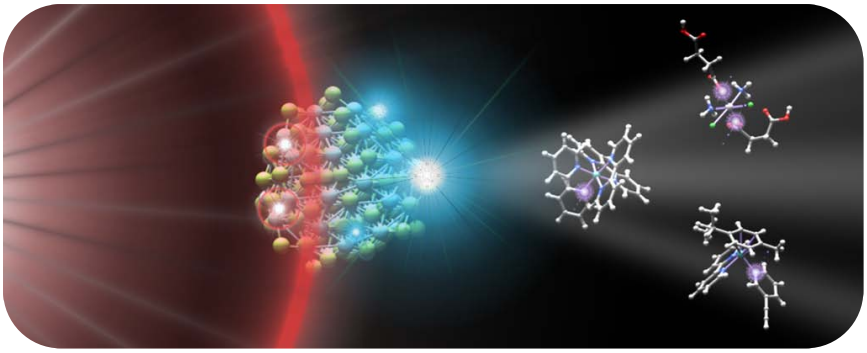
Emmanuel Ruggiero

Photoactivatable metal complexes are an attractive alternative to classic metal-based chemotherapeutic drugs. Light activation of prodrugs allows spatiotemporal control of cytotoxic effects, decreases systemic toxicity of treatments and limits unwanted side effects. Metal prodrugs for photochemotherapy obviously must be nontoxic and stable in the dark under physiological conditions, but at the same time, upon light irradiation, they should be capable of generating cytotoxic species. Importantly, the inorganic photochemotherapy approach merges the advantages of two clinical treatments: the selectivity of phototherapy (e.g. PDT) and the well consolidated clinical use of Pt chemotherapy. Anticancer Pt complexes such as cisplatin, carboplatin and oxaliplatin are administered globally almost to half of the patients undertaking cancer chemotherapy.

A key obstacle that hamper the progress of inorganic photochemotherapy towards preclinical and clinical stages are the modest light absorption properties and reactivity of metal complexes in the phototherapeutic window (650–1000 nm). Coordination and organometallic compounds typically require high-energy UV-blue light to induce their antineoplastic activity. UV-blue activation is not ideal for therapeutic applications due to its low tissue penetration and the cellular damage that occur at such wavelengths.

To address this issue, an innovative strategy is presented herein, where Ru and Pt anticancer prodrugs candidates are integrated with upconverting nanoparticles (UCNPs) in order to use near-infrared light (highly penetrating) for the *in situ* generation of metal-based bioactive species. UCNPs are lanthanide doped nanocrystals which convert near-infrared light (NIR, 980 nm) into UV-visible light, meeting the demand of metal complexes for high-energy UV-blue light excitation. UCNPs are generally $NaYF_4$ or $NaGdF_4$ nanocrystals doped with lanthanides such as Yb, Er and Tm.

The main aim of this Ph.D. work was to explore the combination of UCNPs and metal complexes as viable strategy to provide novel photochemotherapeutic approaches which rely on NIR light mechanisms of action. Furthermore, UCNPs have unique multimodal imaging capabilities (UCL/MRI/PET/SPECT) which make hybrid nanosystems (UCNP-metal complexes) encouraging candidates for theranostics (simultaneous therapy and diagnosis).



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SEMINAR

Wednesday, 18th May, 12.00 pm, Seminar Room

Host: Dr. Niels C. Reichardt

Exosomes: metabolic nano-machines encoding complex signals

Juan Manuel Falcón
Ikerbasque Research Professor
Exosomes Lab- CIC bioGUNE

For many years, cell biologists were focused on what was happening inside cells, without paying too much attention to the reactions and processes that were happening in the intercellular space. A revolution of this intracellular view followed the discovery of small biological vesicles observed outside cells and circulating in the bodily fluids. In the past decade, it has been shown that most of the cell-types forming the body synthesise and secrete small vesicles, exosomes, which interchange materials and signals with the adjacent and distal cells of the body. Dr. Falcon´s group was pioneer in the study of exosomes secreted by hepatocytes and showed that they carry active enzymes that had a significant impact in the serum metabolic composition suggesting that they could have important consequences in different pathophysiological processes including drug-induced liver injury and regeneration. Furthermore, his group has shown that exosomes can be useful in identifying minimally invasive markers and provided a repertoire of molecules that could aid in the development of novel diagnostic and prognostic tools. Finally, his group is also very active in studying novel strategies to isolate and quantify them as well as in the development of exosomes-based therapeutics tools.

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SEMINAR

Thursday, 19th May, 12.00 pm, Seminar Room

Host: Dr. Luca Salassa

NMR chemosensing with self-organized nanoparticle-based receptors

Fabrizio Mancin
Dipartimento di Scienze Chimiche, Università di Padova, via Marzolo 1, 35131 Padova, Italy.
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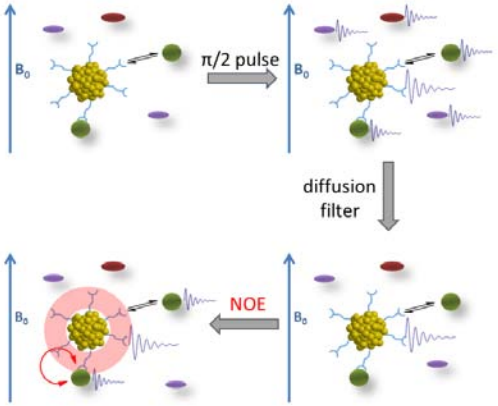

Gold nanoparticles protected by a monolayer of organic molecules offer a straightforward route to the realization of complex chemical systems. Our research interest mainly focus on the crowding of organic functional groups that can be obtained by assembling appropriate coating molecules in the monolayer.[1] Such spatial proximity can be exploited to obtain cooperative functions. In particular, self-organized binding sites can be realized by properly exploiting different supra-molecular interactions.

This recognition ability, conjugated with the nanoparticle (large) size, enable new detection protocols that conjugate the selectivity of chemosensors with the large structural information provided by NMR. The rationale of our recently reported "NMR chemosensing" method rests upon the slow diffusion rate of the 2-nm gold core nanoparticles with respect to small analytes, and on the intermolecular dipolar interactions as a pathway to transfer magnetization between two interacting species.[1] The NMR chemosensing experiment starts with a diffusion filter which dephases the magnetization of all the small, fast diffusing species in the sample while retaining that of the nanoparticles. This magnetization is then transferred via NOE to the small analytes interacting with the nanoparticles monolayer, and the resulting signals are detected. The main advantage in the use of such nanoparticles-assisted spectral editing is the fact that the signal produced by the sensing system is the full NMR spectrum of the analyte, and not just a variation of one sensor property. This allows not only a detection and quantification of the analyte, but also its unambiguous identification. Moreover, important insight on the structure of the nanoparticle coating monolayer and on the parameter that control its interaction with molecular species can be obtained.

Financial support by ERC-StG Project MOSAIC 259014 and ERC-PoC Project INSIGHT *640849*.

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SEMINAR

Monday, 30th May, 12.00 pm, Seminar Room

Host: Prof. Luis Liz-Marzan

Five dimensional optoacoustic imaging of small animals, humans and individual particles

Xosé Luis Deán Ben
Helmholtz Zentrum München - German Research Center for Environmental Health
IBMI Institute of Biological and Medical Imaging
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85764 Neuherberg, Germany

Optoacoustic (photoacoustic) imaging emerged in the early 2000s as a promising technique to bring high-resolution optical contrast at depths beyond the optical diffusion barrier limiting optical microscopy. In the last decade, optoacoustics has become the fastest growing biomedical imaging modality and is increasingly being used in biological research. Recently developed systems further enable the clinical translation of this technology. By using state-of-the art data acquisition technologies and fast-tunable lasers, it is possible to acquire three-dimensional images in real time with multispectral specificity, turning optoacoustics into a five dimensional imaging modality (three spatial dimensions + time + optical wavelength). We present the basic technological principles and biomedical applications of five dimensional optoacoustic tomography along with new methods based on dynamic imaging of individual absorbers that can take optoacoustics to a next level of imaging performance.

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SEMINAR

Friday, 3rd June, 12.00 pm, Seminar Room

Host: Dr. Niels Reichardt

Chemonezymatic synthesis and immunological studies of xylosylated n-glycans

Katarzyna Brzezicka
Glycotechnology Laboratory, CICbiomaGUNE

Glycosylation is one of the most common post-translational modifications in eukaryotic cells. It changes during cell development and differentiation and it is tissue and more importantly, species specific. While core α-1,6 fucose and/or terminal sialyl residues are typical mammalian features, most of the plant, insects and parasite derived N-glycans contain core α-1,3-fucose, β-1,2-xylose and other terminal motifs. In mammals, some of these glycan elements are believed to be at least partially involved in the stimulation or regulation of immune responses in parasite infected individuals and in the pathophysiology of food allergens.

In this Thesis, the chemoenzymatic synthesis of 39 core xylosylated N-glycans will be described. Using glycan microarray-assisted studies, the carbohydrate interaction with biologically relevant glycan binding proteins such as plant lectins and animal C-type lectin receptors will be evaluated. Additionally, glycan microarrays will be employed for the screening of anti-carbohydrate antibodies raise against S. mansoni parasite. The responses induced in patients from endemic areas will be compared and the potential biological role of different glycan families will be discussed.

Finally, based on the microarray-assisted screenings, novel ovalbumin based neoglycoconjugates and glycoprotein-stabilized gold nanoclusters will be prepared and explore their use as dendritic cells targeting molecules.

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SEMINAR

Friday, 10th June, 12.00 pm, Seminar Room

Host: Prof. Luis Liz-Marzán

Artificial protein engineering for multimodal plasmonic colloid morphosynthesis and self-assembly

Erik DUJARDIN
Research Director, Head of the NanoSciences Group
CEMES CNRS UPR 8011, Toulouse, France

The optical properties of metallic colloidal nanostructures can be tuned by controlling the nanoparticle shape [1] and/or assembly. [2, 3] We first illustrate the potential of self-assembled colloidal plasmonic superstructures to reach ultimate lateral confinement, long-range delocalization and spectrally tunable propagation of surface plasmon modes and become extremely narrow waveguides.[3]
Yet, order and predictability of colloidal self-assembly pathways as well as non-trivial shape control still need to be improved.
In biology, engineered proteins with specific recognition for a chosen molecular target can be isolated and identified from a large library by phage display selection. We show that this standard biochemical technique rapidly yields antibody binders for an inorganic target, crystalline metallic gold. Twenty-one anti-gold antibody proteins were identified and sequenced. The statistical analysis of all the sequences reveals a strong occurrence of arginine in anti-gold antibodies. Once tethered to gold nanoparticles, the selected antibodies drive the self-assembly of the colloids onto the surface of single crystalline gold platelets, as a first step toward programmable protein-driven construction of complex plasmonic architectures. [4]
Next, we report on the design of fully artificial repeat protein having a rigid 3D architecture and well-placed random residues. Protein pairs selected from a library of 10^9 homologous proteins for their nM affinity constants are used to drive the massive but reversible assembly of Au nanoparticles. [5] Finally, we expand our approach to the morphosynthesis of gold colloids under the growth inhibition of repeat proteins selected ofr their affinity for chosen gold crystal facets.[6]

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SEMINAR

Tuesday, 21st June, 12.00 pm, Seminar Room

Host: Dr. Jordi Llop

In vivo imaging in (radio)pharmaceutical research: advantages and pitfalls

Sebastian Eigner
Center for Advanced Preclinical Imaging (CAPI)
1st Faculty of Medicine
Charles University in Prague
Czech Republic
sebik1109@gmail.com

Molecular imaging can allow the non-invasive assessment of biological and biochemical processes in living subjects. Molecular and functional imaging applied in the initial stages of drug development can provide evidence of biological activity, confirm on-target drug effects and identify patients who are more likely to benefit. Therefore implementation of imaging technologies has the potential to enhance our understanding of disease and drug activity during preclinical and clinical drug development and could aid decisions to select candidates that seem most likely to be successful or to halt the development of drugs that seem likely to ultimately fail.

However, successful implementation of the above mentioned technologies largely depends on the understanding of the working principles of the used technologies, biochemistry of the drugs and diseases involved and provides room for errors in each step of the characterization and validation process

Here, with an emphasis on radionuclide imaging (PET/SPECT) we review the applications of molecular imaging in drug development, highlighting successes and identifying key challenges that need to be addressed for successful integration of molecular imaging into the drug development process and additionally show the pitfalls of implementation of molecular imaging in drug development.

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SEMINAR

Wednesday, 22nd June, 12.00 pm, Seminar Room

Host: Dr. Aitziber L. Cortajarena

Designs for novel protein-based materials and supramolecular assemblies

Lynne Regan
Yale University Molecular - Biophysics & Biochemistry
322 Bass Center, New Haven CT. USA

Proteins perform myriad functions in all living organisms. These can be co-opted and modified to create novel and potentially useful new entities.

I will begin by talking about our recent work in which we investigate the extent to which simple hard-sphere models are sufficient to specify many elements of protein structure. Not only do these studies enhance our basic understanding of the underlying physics and chemistry that determine protein structure, but they also provide new strategies by which to engineer novel structures and functions. In the second part of my talk I will describe our latest designs for protein-base supra-molecular structures, assemblies and interfaces.

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SEMINAR

Friday, 1st July, 12.00 pm, Seminar Room

Host: Prof. Luis M. Liz-Marzán

Some Surprises and Open Questions in Soft and Particulate Matter

Steve Granick
Director, IBS Center for Soft and Living Matter, South Korea
www.softmatt.ibs.re.kr
Professor Emeritus, University of Illinois, USA
www.groups.mrl.uiuc.edu/granick

A fundamental challenge of modern soft matter science is to form structure that is not frozen in place but instead reconfigures internally driven by energy throughput and adapts to its environment robustly. Predicated on fluorescence imaging at the single-particle level, this talk describes quantitative studies of how this can happen. With Janus colloidal clusters, we show the powerful role of synchronized motion in self-assembly. In living cells, we find that transportation efficiency problems bear a provocative parallel with polymer chain trajectories with their spatial extent, and with jammed matter in their time evolution. A picture emerges in which simple experiments, performed at single-particle and single-molecule resolution, can dissect macroscopic phenomena in ways that surprise.

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SEMINAR

Friday, 8th July, 12.00 pm, Seminar Room

Host: Prof. Luis M. Liz-Marzán

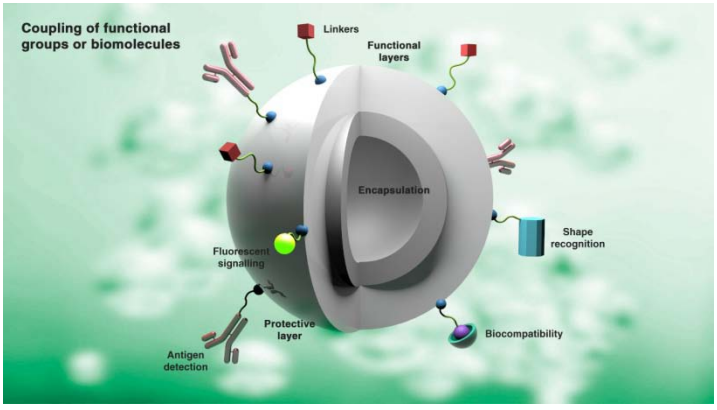
Novel (Coordination) Polymer Nanoparticles for Advanced Theranostics

F. Novio[1], J. Lorenzo[2], F. Nador[1], S. Suarez-García[1], D. Montpeyó[1], D. Ruiz-Molina[1]

[1] *Catalan Institute of Nanoscience and Nanotechnology (ICN2), CSIC and The Barcelona Institute of Science and Technology, Campus UAB, Bellaterra, 08193 Barcelona, Spain*

[2] *Institut de Biotecnologia i de Biomedicina. Universitat Autònoma de Barcelona, 08193 Bellaterra, Barcelona, Spain.*

Recently, nanoscale coordination polymer particles (CPPs) have emerged as an alternative platform to provide new opportunities for engineering multifunctional systems with applications in drug delivery and/or biomedical imaging. In general, CPPs exhibit high metal ion payloads content, high biocompatibility, low toxicity and offer the possibility to harbor additional functions. The pre-synthetic design strategies like judicious choice of metal ions and ligands can address the challenges of synthesizing such functional materials. Moreover, the ability to incorporate diverse metals useful for MRI nd/or fluorescence allows constructing novel contrast agents for biomedical imaging. In this communication we will revise the different approaches developed in the group with this aim.*



Key Words: drug delivery, imaging, coordination polymer, nanoparticles

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Correspondence: druiz@cin2.es

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SEMINAR

Friday, 15th July, 12.00 pm, Seminar Room

Host: Prof. Luis M. Liz-Marzán

Design of patchy polymers: biomimetic self-knotting chains

Ivan Coluzza
Department of Physics
University of Vienna. AUSTRIA

We present a novel theoretical framework within which we are able to design new experimentally realisable materials with tuneable self-assembling properties.

Our work takes inspiration from the results obtained with our recently developed protein coarse graining procedure, namely the “Caterpillar” model [1,2]. Based on these results we postulated the “maximum valence principle" (MVP). According to the MVP in order for a generalised bead-spring system to be designable and foldable, it is sufficient for the chain to have a sequence of different isotropic interactions combined with directional interactions that further constrain the configurational space. Based on this principle we introduced an optimal set of modular sub-units, and the definition of a design procedure necessary to choose a string of the units that once bonded into a chain will spontaneously fold to a specific target structure [3-5].

We show that such structures can be highly non-symmetrical and posses interesting topological properties fully controllable by the sequence of beads along the chain.

Biomimetic patchy polymers represent a considerable step forward in the synthesis of novel materials, because they are based on a limited alphabet of particles that can be reused and assembled, practically, in an infinite number of combinations. Artificial modular self assembling systems such as this one are not available at the moment and the one we propose is the first of this kind.

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SEMINAR

Tuesday, 19th July, 12.00 pm, Seminar Room

Host: Dr. Ralf Richter

Physical principles underlying structure, mechanics and dynamic re-organization of hyaluronan-rich matrices — from tissues to supramolecular models in experiment and theory

Xinyue Chen
Biosurfaces Group. CIC biomaGUNE

The extracellular matrix (ECM) is the acellular structure of all tissues and essential for multicellular life. Next to biochemical signals, the physical properties of the ECM provide important signals to cells. The polysaccharide hyaluronan (HA) is ubiquitous in the extracellular space of vertebrates and an important structural component of the ECM. HA is a linear, unbranched and regular polymer of the glycosaminoglycan (GAG) family, and serves as a scaffold that responds dynamically to molecular stimuli such as HA-binding proteins, or changes in pH or ionic strength. The objective of this PhD research project is to elucidate physical principles underlying the structure, mechanics and dynamic re-organization of HA-rich matrices. To address this question, we have studied the mechanical properties and morphology of HA-rich matrices at distinct levels of complexity. On one hand, we have studied the cumulus cell-oocyte complex (COC) matrix as an example of complex, native HA-rich tissue. On the other hand, we have studied so-called HA brushes as a well-defined *in vitro* reconstituted model of HA-rich matrices.

The HA-rich matrix in the COC forms around oocytes just before ovulation and plays vital roles in oocyte biology. We have analyzed the micromechanical response of mouse COC matrix by colloidal probe atomic force microscopy (AFM). We found the COC matrix to be extremely soft yet elastic, suggesting a stable gel-like network structure with high porosity and a large mesh size. With a Young's modulus around 1 Pa, COC matrices are among the softest elastic biological materials known to date. In addition, the elastic modulus increased progressively with indentation. Furthermore, using optical microscopy to correlate these mechanical properties with ultra-structure, we discovered that the COC is surrounded by a thick matrix shell that is essentially devoid of cumulus cells. We propose that the pronounced non-linear elastic behaviour of COC matrix is a consequence of structural heterogeneity and serves important functions in biological processes, such as oocyte transport in the oviduct and sperm penetration.

To understand more comprehensively the response of HA polymers to changes in their aqueous environment, the thickness and viscoelastic properties of films of end-grafted HA (also called HA brushes) as a well defined *in vitro* model of HA-rich matrices were characterized by reflection interference contrast microscopy (RICM) and quartz crystal microbalance with dissipation monitoring (QCM-D) as a function of Ca^{2+} concentration and pH. Within the physiological range, the thickness of HA brushes decreased significantly with Ca^{2+} concentration but did not change with pH. By screening a large range of Ca^{2+} concentrations, we discovered that the effect of Ca^{2+} on HA brush thickness is virtually identical to the effect of Na^{+} at 10-fold higher concentrations. HA brushes responded only weakly to pH changes above pH 6.0, but showed a sharp collapse around pH 3. Our results provide insights into how HA matrices are affected by solution properties, which is relevant in biological systems and for the design of synthetic tissues.

Finally, using theoretical computations based on self-consistent mean field theory, we elucidated how the morphology of polymer brushes is influenced by the formation of physical cross-links between polymers, such as they would occur in the presence of cross-linking proteins. We find that cross-links promote a denser and more homogeneous brush morphology. The effect of cross-links is comparable to the effect of reduced solvent quality when the density of cross-links is low, but unique features including the retention of solvent even with strong cross-links emerge at high cross-linking densities.

This work provides novel insights into how the supramolecular structure and thus the mechanical properties of HA-rich matrices can be dynamically regulated by changes in microenvironmental conditions. This can be linked to different biological functions of native HA-rich extracellular matrices but is also of interest for the design of tailored, synthetic HA-based materials for applications in tissue engineering.

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SEMINAR

Thursday, 15th September, 12.00 pm, Seminar Room

Host: Dr. Jordi Llop

Multiplexed PET: Towards simultaneous dual tracer PET imaging

Eduardo Lage
Instituto de Investigaciones Biomédicas "Alberto Sols"
CSIC, UAM

The value of positron emission tomography (PET) lies on its unsurpassed sensitivity for tracking radiolabeled compounds (radiotracers) in vivo. However, PET lacks the ability of multiplexing signals from more than one tracer because the radiation they emit is undistinguishable for the scanner. This talk introduces a new method that enables simultaneous imaging of two radiotracers in a single PET scan by using the gamma rays that some PET isotopes emit together with positrons. Our evaluation shows that recovered images from a simultaneous dual-tracer PET acquisition are comparable to those obtained in sequential single tracer scans. The integration of this technology in clinical PET/CT and PET/MRI systems opens new perspectives in molecular imaging and holds the potential to advance towards personalized medicine, by enabling the measurement of a range of disease aspects in a single scan.

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SEMINAR

Thursday, 22nd September, 12.00 pm, Seminar Room

Host: Dr. Luis Liz-Marzán

Monodisperse particles used as building blocks to control 3D location of materials in functional devices

Prof. Daisuke Nagao
Tohoku University, Japan

Monodisperse particles with precisely controlled shapes and sizes can be used as building blocks to be assembled for novel functional materials.
In our study, wet chemical processing techniques are employed to prepare monodisperse particles including composite particles with different materials.

To find new assembled structures of particles, applications of electric and/or magnetic field to the monodisperse particles have been explored .

In this talk, yolk/shell particles, which are composed of spherical shell incorporating a movable sphere in their hollow space, are introduced as building blocks promising for development of new-type switchable devices.

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SEMINAR

Thursday, 6th October, 12.00 pm, Seminar Room

Host: Dr. Luis Liz-Marzán

Strangely shaped plasmonic nanoparticles: stars and sponges

Prof. Dr. Thomas A. Klar
Johannes-Kepler-Universität Linz, Austria

Plasmonic nanoparticles of unusual shapes such as stars or sponges are investigated on a single nanoparticle level. We correlate the morphological and optical properties of single gold nanosponges, by comparing their SEM micrographs with dark-field optical scattering spectra. The nanosponges are three-dimensionally gold/air percolated nanoparticles comprising gold filaments with sizes well below 20 nm. FIB crosscuts prove their sponge like morphology. While nanosponges with a spherical outer circumference show scattering spectra with a high degree of polarization, the fluorescence from these sponges, originating from d-band hole recombination, is substantially less polarized.
Gold nanostars can be applied as single nanoparticle biosensors but also as scattering centres in random lasers. For the latter application, we empirically find that the nanostars actually outperform plasmonic nanoparticles of spherical or ellipsoidal shape. Star shaped plasmonic nanoparticles have also been found to improve the yield of electroluminescence in organic light emitting diodes.

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SEMINAR

Thursday, November 3rd 12.00 pm Seminar Room

Host: Dr. Jordi Llop

Targeted Polymeric Nanoparticles: Radiolabelling with Ga-67 and in vivo Evaluation in a Mouse Model of Pancreatic Adenocarcinoma using Single Photon Emission Computerized Tomography

Larraitz Gil Iceta
Nuclear Imaging Group

Nanoparticle (NP) based theranostics may play a pivotal role in oncology in the near future. However, determination of the pharmacokinetic (PK) properties of novel nanomedicines, which is essential for the determination of the effective dose and potential translation into the clinical setting, is extremely challenging. Radiolabelling of the NPs and subsequent imaging studies using nuclear imaging techniques can provide relevant information on the PK properties of novel nanomedicines, aiding in the selection of the most promising candidates while enabling the discontinuation of non-appropriate drugs at early stages in the process of drug development.

Within the frame of the EU-funded project “SaveMe”, NP-based theranostic agents for the early detection and treatment of Pancreatic Cancer (PaCa, the fourth deadliest cancer type), have been developed. Different polymeric and protein-based NPs were synthesised by different partners and decorated with targeting moieties with high affinity for somatostatin (SST) or galectin (Gal) receptors, both over-expressed in PaCa cells. The different particles have been radiolabelled with 67Ga via formation of chelator-radiometal complexes or by taking advantage of unspecific interactions between the radionuclide and the NP core. After assessing radiochemical integrity of the labelled NPs, Single Photon Emission Computerised Tomography (SPECT) studies were carried out in a subcutaneous mouse model of PaCa, which was implemented by subcutaneous injection of Panc-1 (human pancreatic adenocarcinoma) cells. The biodistribution of the labelled NPs and the accumulation of NPs in the tumour could be determined from SPECT images, which were combined with Computerized Tomography (CT) images for proper localization of the radioactive signal. Complementary studies were performed with Magnetic Resonance Imaging, which provided relevant information regarding tumour heterogeneity. Imaging studies enabled the selection of the most appropriate NP core and the investigation of the effect of the targeting moieties and other surface decorations on the accumulation of the NPs in the PaCa tumours.

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SEMINAR

Friday, December 16th 12.00 pm Seminar Room

Host: Dr. Sergio Moya

Engineered Interfaces with Polyelectrolyte Multilayers, Lipid Bilayer Membranes and Virosomes for Biomedical Applications

Eleftheria Diamanti
Soft Matter Nanotechnology Group

Different approaches for the surface engineering by means of polyelectrolyte multilayers (PEMs), alone or in combination with lipid bilayers and influenza virosomes, with potential biomedical applications will be presented.

Biopolymer PEM films based on poly-L-lysine and alginate are thermally annealed as an alternative method to cross-linking in order to enhance cellular adhesion, for applications in tissue engineering or for their use in antifouling applications. The impact of the annealing on the physicochemical properties of the PEMs is analyzed in detail.

The conditions for the assembly of a lipid bilayer membrane on top of PEM cushions and the interactions between lipids and polyelectrolytes are studied. Thus the influence of vesicles´ composition, top-layer chemistry, the presence of phosphate ions and the nature of polyanions are analyzed. Electrochemical impedance spectroscopy is applied to measure the conductivity of the supported lipid bilayer. Results show resistance values similar to that of a black lipid membrane, $1.89\ 10^7\ \Omega\ cm^2$, opening new perspectives on the use of lipid bilayers supported on polyelectrolyte cushions.

Finally, the fusion of immunostimulating reconstituted influenza virosomes, lacking any viral genetic material, is studied in terms of pH, temperature and hemagglutinin content, for the development of biocompatible surfaces, biosensors or drug delivery systems.