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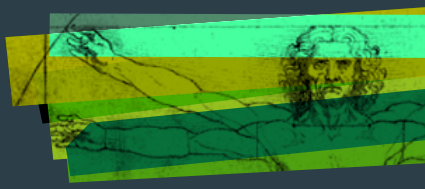
ABSTRACTS



7 - 9 September 2015

Bioinspired molecular assemblies as protective and delivery systems

LOCATION

Centre International Universitaire
pour la Recherche
1, rue Dupanloup
45000 Orléans

CONVENORS

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LE STUDIUM RESEARCH FELLOW
FROM Yerevan State University - Armenia

IN RESIDENCE AT
Interfaces, Confinement, Matériaux et Nanostructures (ICMN) -
UMR 7374 - CNRS, Université d'Orléans

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Bioinspired molecular assemblies as protective and delivery systems

Biological systems being complex entities bring to life elegant and efficient strategies to make materials that often outperform man-made materials of similar composition. One of the main goals of the interdisciplinary field of bioinspired materials is to unlock the secrets of these systems - the composition, processing, self-assembly, hierarchical organization and properties of biological materials - and use this information to synthesize and engineer novel functional materials for a variety of practical applications. Bioinspired concepts are becoming increasingly integrated into materials and devices intended for food safety, cosmetic formulation and drug delivery systems.

EDITO

Created in 1996 on the CNRS campus in Orleans La Source, LE STUDIUM has evolved to become a multidisciplinary Loire Valley Institute for Advanced Studies (IAS), operating in the region Centre-Val de Loire of France. In December 2013 LE STUDIUM moved to the city centre of Orleans and into a newly renovated 17th century building. These amazing facilities are shared with the University of Orleans. In 2014 new developments and programmes linked to the smart specialisation of the Centre-Val de Loire region came to strengthen existing IAS cooperative relationships with the local and the international community of researchers, developers and innovators.

LE STUDIUM IAS offers to internationally competitive senior research scientists the opportunity to discover and work in one of the IAS's affiliate laboratories from the University François-Rabelais of Tours, the University of Orleans, National Institute of Applied Sciences (INSA) Centre Val de Loire and ESAD Orléans, as well as of nationally accredited research institutions located in the region Centre (BRGM, CEA, CNRS, INSERM, INRA, IRSTEA). Our goal is to develop and nurture trans-disciplinary approaches as innovative tools for addressing some of the key scientific, socio-economic and cultural questions of the 21st century. We also encourage researchers' interactions with industry via the IAS's links with Poles of Competitiveness, Clusters, Technopoles, and Chambers of Commerce etc.

LE STUDIUM has attracted over one hundred and fifty LE STUDIUM RESEARCH FELLOWS, LE STUDIUM RESEARCH CHAIRS and LE STUDIUM RESEARCH PROFESSORS for periods of six months and up to two years. In addition to the contribution in their host laboratories, researchers are required to participate in the scientific life of the IAS through attendance at monthly interdisciplinary meetings called LE STUDIUM THURSDAYS and LE STUDIUM CLUB fora that involve participants from industry.

For the period 2015-2020, LE STUDIUM operates with an additional award from the European Commission in the framework of the Marie-Skłodowska Curie Actions (MSCA) with the programme MSCA-COFUND for the mobility of experienced researchers. This co-funding instrument increases the number of LE STUDIUM fellowships to be awarded each year.

Researchers are also invited and supported by the IAS to organise, during their residency and in collaboration with their host laboratory, a two-day LE STUDIUM CONFERENCE. It provides them with the opportunity to invite internationally renowned researchers to a cross-disciplinary conference, on a topical issue, to examine progress, discuss future studies and strategies to stimulate advances and practical applications in the chosen field. The invited participants are expected to attend for the duration of the conference and contribute to the intellectual exchange. Past experience has shown that these conditions facilitate the development or extension of existing collaborations and enable the creation of productive new research networks.

The present LE STUDIUM CONFERENCE devoted to Bioinspired molecular assemblies as protective and delivery systems is the 41st in a series started at the end of 2010 and listed at the end of this booklet.

We thank you for your participation and wish you an interesting and intellectually stimulating conference. Also, we hope that during these two days some of you will see an opportunity to start a productive professional relationship with LE STUDIUM Loire Valley Institute for Advanced Studies and laboratories in the region Centre-Val de Loire.

Professor Ary Bruand

Chairman
LE STUDIUM

SUMMARY

Dr Nóra Ábrahám

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Dr Nóra Ábrahám obtained her PhD degree at University of Szeged, Hungary in the group of Prof Imre Dékány. During her doctoral work she has been synthesized monodispersed ZnO nanoparticles and formed their ordered two-dimensional films (by means of Langmuir-Blodgett and wrinkle assisted confinement techniques) for their special optical and photoluminescence properties in sensor technology. Later her interest turned to phospholipid Langmuir and Langmuir-Blodgett films as model membrane surfaces. Her research focuses on the interaction of biofunctionalized nanoparticles with phospholipid Langmuir-films. Currently she is on maternity leave.

Application of phospholipid Langmuir monolayers as model membrane systems

N. Ábrahám, I. Dékány

Nanomedicine is currently a highly developing interdisciplinary area, which has provided a large number of new nanomaterials and methods for both medical diagnostics and therapy. For the application of nanoparticles/nanostructured systems it is important to discover how they interact with different biomolecules (proteins, lipids, etc.) and how they can be transported to the target tissue/cells. A possible way to study the interaction of nanomaterials with biological systems is to do model experiments. Such simplified experiments provide step-by-step understanding of a complex process.

Langmuir monolayers formed at the air water interface are excellent models of a biological membrane: there are a lot of parameters which can be varied easily such as the lipid composition, additional constituents (e. g. peptides), the subphase (composition, ionic strength, pH, etc.) and temperature to mimic the biological membranes. By transferring the floating monolayers onto solid substrates, lipid bilayers can be formed and used for further experiments.

In my lecture I will present how we have used Langmuir monolayer technique for the study of the interaction between gold nanoparticles and the lipid monolayer. We have synthesized spherical and rod-like gold nanoparticles and applied surface functionalization with different biomolecules. The interaction between the biofunctionalized gold nanoparticles and the model lipid membrane was followed by measuring the surface pressure of the floating monolayer.

Dr Véronique Aguie-Beghin

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Research engineer (biochemist and physic-chemist) at INRA, in UMR FARE INRA/URCA from 1995. Research in UMR FARE is focused on the study of the parameters related (1) to lignocellulose which govern their potential for transformation and (2) to integrate the different scales and properties of lignocellulose that control accessibility to transformation agents. Due to the high complexity of lignocellulosic plant cell wall, Dr. V. Aguié develops bioinspired assemblies (films, coatings) based of cellulose nanocrystals, hemicelluloses and lignins to study their structure and properties at molecular scale before and after chemical and biological transformation processes, depending on the application field.
Between 1995-2007, research of Dr V. Aguié, with Dr R. Douillard was focused on the structure and properties of biopolymers at interfaces (fluid, solid) – Applications: proteins, champagne macromolecules, polyphenols, lignins,...

Bioinspired molecular assemblies based of lignocellulosic polymers:Spectroscopic and physico-chemical properties

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Within the framework of research on the valorisation of by-products from 2nd generation biorefineries, we have designed novel nanocomposite materials made of cellulose nanocrystals, hemicelluloses and lignins. These materials were prepared without chemical modification or functionalization of the biopolymers either by spin-coating to carry out successive deposits of each polymer solutions to build a multilayer assembly [1] or by evaporation starting from a mixture of these polymers [2-3]. Both nanocomposites were in the form of thin transparent films with a thickness in the range of several nm to several µm, supported on glass slides or self-supported respectively. These films exhibit variable spectroscopic and physico-chemical properties [3-4] according to the process used. The modulation of the interactions between the lignin and the polysaccharide makes it possible to obtain either anti-reflective films or anti-UV films with low wettability and good resistance to water. The combination of the optical properties of films made from cellulose nanocrystals and the spectroscopic properties of lignins are of particular interest for surface coverings with protective properties (optical glass, filters, wood protection, etc.). Antioxidant [5], antibacterial and mechanical properties can be added to these properties.

[1] A. Hambardzumyan et al. (2011) CR Biol., 334, 839-850.

[2] A. Hambardzumyan et al. (2012) Biomacromolecules, 13, 4081-4088.

[3] A. Hambardzumyan et al. (2015) Chem. Engin. J., 264, 780-788

[4] L. Muraille et al. (2015) Europ. Polym. J., 64, 21-35.

[5] V. Aguié-Béghin et al. (submitted)

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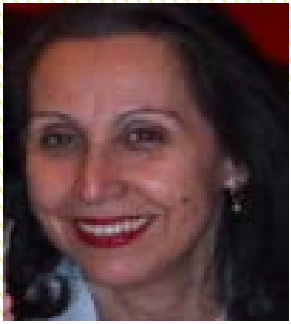
Sylvie Begin-Colin completed her PhD degree in Material Chemistry at University of Nancy (France) in 1992. She has then integrated the CNRS as Researcher at the Laboratory of Science and Engineering of Material and of Metallurgy at the Mining Engineering School of Nancy. Then she was appointed Professor in September 2003 at the European Engineering School in Chemistry, Material and Polymer (ECPM) of the University of Strasbourg and is currently Director of ECPM. She has developed a new research activity at IPCMS of Strasbourg on the synthesis, functionalization and organisation of oxide nanoparticles for biomedical, energy and spintronic applications. One great part of her research activity is devoted to the design of oxide nanoparticles as these nano-objects are highly sought after for their applications in the biomedical field and are also considered as the building blocks of the future nanotechnological devices in fields of spintronic or energy. Most of these studies are made in collaboration with organic chemists, biologists and physicists. Sylvie Bégin has obtained ANR, INCA, ARC grants and has participated and participates as partner to different European programs. Her work has been awarded by the "Jean-Rist" price of the French Society for Metallurgy and Materials. She is holder of 130 publications in peer-reviewed journals and 39 invited conferences.

Dendronized magnetic nanoparticles designed for targeting, MRI and hyperthermia

Some of the significant and most promising applications for inorganic nanoparticles (NPs) lie in the fields of biology and biomedicine. Due to their magnetic properties tuned by their shape and/or composition, superparamagnetic iron oxide NPs (SPIO) with appropriate surface chemistry can be used in numerous in vivo applications such as MRI contrast enhancement, hyperthermia treatment, cell sorting, drug delivery...

In that context, we propose a concept combining a dendritic coating of magnetic oxide nanoparticles with phosphonate anchors. Indeed, phosphonates ensure a strong anchoring at the NPs surface while preserving their magnetic properties, and dendritic shells, in addition to their small and easily controllable size (as a function of their generation), are promising building blocks simultaneously solving the problems of biocompatibility, large in vivo stability and specificity. Dendronized iron oxide nanoparticles were demonstrated to induce any cytotoxicity. In vivo and in vitro MRI measurements showed that the contrast enhancement properties of the dendronized NPs were higher than those obtained with commercial polymer-coated NPs. Moreover, both types of dendronized NPs were eliminated by urinary and hepatobiliary pathways without unspecific uptake especially in the RES organs and in the lungs. The design of dendronized NPs was further improved to obtain theranostic nano-objects (which can both identify disease states and simultaneously deliver therapy) by adjusting the morphology and the composition of the inorganic magnetic core and by designing multifonctionalized dendrons. These NPs were found suitable to combine imaging and therapy by hyperthermia. Finally these dendronized NPs bearing melanin vectors were demonstrated very suitable to specifically target in vivo tumoral cells.



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Faïza Annabi-Bergaya obtained a PhD in inorganic chemistry at Paris-La-Sorbonne in 1971 and a Doctorat d'Etat Es-Sciences Physiques at the University of Orleans in 1978. She is currently Emeritus Research Director at CNRS at the ICMN (Orleans).
Her research relates to physicochemical properties of clay minerals (surface/interface, structural/textural modifications of clay colloids).
She directed 20 PhD and has a track-record of more than 150 publications, 6 patents and several book chapters. She was Secretary of the European Clay Group Association (1999–2003), President of the French Clay Group (2003–2007) and is a member of the International Association for the Study of Clays (Nomenclature Committee). She is Editor-in Chief of Applied Clay Science, Series Editor of Developments in Clay Science, and co-editor of several multi-authors books (Handbook of Clay Science, 2006 & 2013; Nanosized Tubular Clay Minerals, for 2016).

Clay minerals as nano-objects Performance of tubular halloysite as drug carrier

Faïza ANNABI-BERGAYA[1] and Peng YUAN[2]

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Clay minerals, the oldest known nanomaterials, are naturally available in all the countries. Their diversity in morphology, structure, properties and their ability to be tailored for targeted unlimited applications, led to consider them as unique multidisciplinary nano-objects. They are widely considered for pharmaceutical and drug delivery purposes.

Halloysite (Hal) is a porous tubular material suitable for use as drugs carrier because of its unique mesoporous (2-50 nm) or even macroporous (>50 nm) lumen and its excellent biocompatibility. Drugs are normally anchored to the external and lumen surfaces via weak interactions. Organo-modifications of both Hal surfaces show a significant enhanced capacity of Hal for the loading of drugs. Two examples will be presented of the organo-modification effects on the controlled loading and release of drugs. The first modification is the grafting of 3-aminopropyltriethoxysilane (APTES) on the lumen surface. APTES Hal was used as carrier for a known anti-inflammatory drug, ibuprofen (IBU). A strong affinity between the IBU carboxyl groups and the aminopropyl groups of modified Hal enhanced the loading content of IBU compared to the unmodified Hal and retarded the *in vitro* release of IBU. The second modification is the grafting of methanol on the interlayer surface of Hal leading to an increased of d_{001} value at 1.27 nm. This intercalated Hal was used as carrier for an anti-cancer drug, 5-fluorouracil (5FU). The intercalated drug exhibited a slow release depending on the pH: it is prolonged in simulated colonic and intestinal fluids (pH > 5), but a faster release was observed in simulated gastric fluid (acidic pH).

Dr Eduardo Guzmán

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Born in Madrid, November 28, 1981. 2004. Master in Chemistry in Universidad Complutense de Madrid. 2006. Master in Science and Technology of Colloids and Interfaces in Universidad Complutense de Madrid. 2009. PhD in Science in Universidad Complutense de Madrid.
January 2010- June 2010. Postdoctoral Researcher in the Chemical Physics I Department- Universidad Complutense de Madrid. July 2010-June 2014. Postdoctoral Researcher in Istituto per l'Energetica e le Interfasi-Consiglio Nazionale delle Ricerche (Genoa, Italy) . From July 2014. Research Fellow in the Chemical Physics I Department-Universidad Complutense de Madrid. Coauthor of 31 JCR publications, 5 book chapters and more than 75 presentations in National and International Conference. H-index: 14

Assembly of Multilayers, Nanocapsules and Multicapsules by the Layer-by-Layer Method

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The Layer-by-Layer (LbL) assembly is a versatile technique for the fabrication of functional materials, allowing the building of supramolecular structures loaded with active compounds which can be delivered to the environment under specific conditions. The growing interest in the building and processing of LbL multilayers is the result of the simplicity and extraordinary versatility of these films. It is possible to use of a broad range of materials as building blocks, from synthetic polyelectrolytes to complex biological macromolecules. This makes possible to design systems with different size and shape, as well as chemical nature, which is very relevant for applications in the drug delivery field. The control of the assembly conditions allows a fine tuning of the building process and properties of the LbL films.

In this lecture, the current state and trends on the study of polyelectrolyte assemblies and their applications will be discussed. These applications are closely correlated to the building process and properties of the films. As a consequence it is essential to control the different aspects that can modify the functionality of the films. In addition, for the specific applications, different morphological requirements must be considered, which can be easily achieved by the LbL method. These complex objects can be loaded with drug molecules, and can be functionalized to make them sensitive to external stimuli. In this way it is possible to obtain a controlled delivery of the active compounds.

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Jurriaan Huskens (1968) studied chemical engineering at the Eindhoven University of Technology, and obtained his PhD (1994) at the Delft University of Technology with Herman van Bekkum. After postdoctoral stays with Dean Sherry (UT Dallas) and Manfred Reetz (MPI Kohlenforschung), he became assistant professor (1998) with David Reinhoudt at the University of Twente, where he became full professor "Molecular Nanofabrication" in 2005. He received the Unilever Research Award 1990, a Marie Curie fellowship (1997), and the Gold Medal 2007 of the Royal Netherlands Chemical Society. Major research interests are supramolecular chemistry at interfaces, multivalency, bottom-up nanofabrication, and nanotechnology.

Multivalent interactions: from molecular design to biological function

Multivalency is the phenomenon that describes the interaction between multivalent receptors and multivalent ligands. It is well known to play a pivotal role in biochemistry, particularly in protein-carbohydrate interactions, both in solution and at interfaces (e.g. for the infection of cells by viruses).

Supramolecular host-guest chemistry at interfaces has remained limited to for example sensor development for specific guest compounds. In order to build assemblies at surfaces through supramolecular interactions for nanotechnological applications, other demands have to be met, such as larger thermodynamic and kinetic stabilities of the assemblies. For many supramolecular motifs, this inevitably leads to the use of multivalent interactions.

In recent years, we have developed the concept of molecular printboards, which are self-assembled monolayers functionalized with receptor groups suitable for nanofabrication. The design of guest molecules allows precise control over the number of interacting sites and, therefore, over their (un) binding strength and kinetics.

A key point of the current presentation will be the transition area between weak and strong multivalent interactions, and their influence on binding affinity, stoichiometry of binding and (super)selectivity. Examples will be shown of multivalent peptides and derivatives thereof with hydrophobic residues and their interaction with cyclodextrin molecular printboards. Another key point will be the control over the size and stability of supramolecular materials. Examples will be shown of supramolecular nanoparticle systems employing cyclodextrin or cucurbituril host-guest recognition.

Dr Gohar Khachatryan

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I was born in 14.12.1969 in Gyumri, Armenia. I received high school education an School Number 14 of S. Ordżonikidze in Gyumri. I graduated from Erevan State University in Armenia with a master degree of chemistry. After graduation, I moved to Poland where I completed my PhD at Faculty of Chemical Technology and Engineering at West Pomeranian University of Technology Szczecin. From 1996 to 2006 I had been employed as university teacher at the Department of Chemistry, University of Agriculture in Krakow and since 01.11.2006 I have worked as an Assistant Professor at the same university, Department of Chemistry and Physics.

Formation and properties hyaluronan/nano Ag and hyaluronan-lecitin/nano Ag films

Gohar Khachatryan, Karen Khachatryan

A facile and environmentally friendly method of the preparation of silver nanoparticles embedded in hyaluronan (Hyal/Ag) and hyaluronan-lecitin(HyalLec/Ag) matrix was developed. Thin, elastic foils were prepared by an in situ synthesis of Ag in an aqueous solution of sodium hyaluronate (Hyal), using D(+)Xyloze aqueous solution as a reducing agent. The obtained gels were applied to a clean, smooth, defatted Teflon surface and left for drying in the air. The dry foils were stored in closed container.

UVVIS spectroscopy, transmission electron microscopy (TEM) and Fourier transform infrared (FTIR) spectra confirmed formation of about 10 nm ball-shaped Ag nanoparticles situated within the polysaccharide template. Thermal properties of the composites were characterized involving differential scanning calorimetry (DSC) and thermogravimetric (TGA) analyses, whereas molecular weights of polysaccharide chains of the matrix were estimated with the size exclusion chromatography coupled with multiangle laser light scattering and refractometric detectors (HPSEC-MALLS- RI). Size exclusion chromatography showed a decrease in the molecular weight of the hyaluronate after generation of Ag nanoparticles, particularly in the lower molecular fraction of the hyaluronate. Differential scanning calorimetry (DSC) and thermogravimetric (TGA) analyses also revealed unique thermal behaviour confirming other specific properties of the foil.

The study confirmed that silver nanoparticles can be successfully prepared with environmentally friendly method, using hyaluronian as a stabilizing template. Hyaluronian and hyaluronan-lecitin matrices, which allow to obtain nanocrystals uniform in size and shape, are excellent for silver nanoparticles.

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Activities: Thin molecular films at interfaces, thermotropic liquid crystal materials for applications in optoelectronics, optical spectroscopy of ultrathin layers and construction of advanced laboratory equipments
Honours and memberships: Minister of Education Awards (1980, 1983); Secretary of Polish Academy of Sciences Award (1981); Rector Awards (several times); Medal of the National Education Commission (1995); Polish Physical Society and Polish Liquid Crystal Society – Member
Hobbies: books, classical music, tenis.

Ultrathin organic films for application in electronics

Organic materials with semiconducting properties have been intensively investigated due to their potential application in commercial electronics devices like field effect transistors (OFETs), organic light-emitting diodes (LEDs), flexible photovoltaic cells (OPVs), and various sensors. A large class of organic semiconductor with p-conductivity character have properties that meet the requirements for use in molecular electronics but n-type are still rare and much less developed.

The results of optical and electrical characterization of two groups of highly fluorescent dyes, namely derivatives of perylene-3,4:9,10-tetracarboxylic acid, with and without four chlorine atoms attached in bay position to the perylene core are presented. Depending on substituents the dyes have n-type or p-type semiconductive character. The dyes have been used in the form of ultrathin layers created by spin-coating, Langmuir-Blodgett and thermal evaporation in a high vacuum techniques. As substrates for the films, quartz plates for spectroscopic characterization and glass with ITO electrodes for electrical measurements have been used. The spectroscopic parameters of the dye have been measured in strongly dilute chloroform solutions and in the polycrystalline powders as a reference. Electric conductivity and fluorescence quantum yield of the ultrathin dye layers and the dye powders are the most important parameters for applications. In order to do this, fluorescence intensity has been measured with high accuracy in the integrating sphere. The textures of the films deposited by all the techniques used were analyzed in nanoscale by means of an atomic force microscope working in tapping and c-AFM mode.

Acknowledgments

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Dr. Dorota Matyszewska is currently research assistant in the Biological and Chemical Research Centre, University of Warsaw. She received her MsC in analytical chemistry and PhD in inorganic chemistry from the University of Warsaw under the supervision of Prof. Renata Bilewicz. During her PhD studies she focused on the influence of perfluorinated compounds on model cell membranes. Recently, her research interests include interactions of drugs and drug delivery systems with model membranes.

Model Lipid Membranes And Their Interactions With Biologically Active Species.

Langmuir technique is a powerful tool to study the interactions of model biological membranes with various biologically active substances including drugs, toxins, proteins or enzymes. The formation and characteristics of biomimetic membranes of different composition will be reported. Langmuir studies of the monolayers composed of analogs of stearic acid, 1,2-dipalmitoyl-sn-glycero-3-phosphothioethanol (DPPTE), 1,2-dimyristoyl-sn-glycero-3-phosphocholine (DMPC) and DMPC:Cholesterol mixtures will be presented as examples of biomimetic systems. In addition to Langmuir monolayer studies at the air-water interface along with Brewster angle microscopy, the layers were transferred onto solid support by means of Langmuir-Blodgett and Langmuir-Schaeffer method and other techniques including microscopy, electrochemistry and spectroscopy were employed in order to characterize these systems in more detail. In the next step model membranes of different composition were employed to study the interactions of anticancer drugs daunorubicin and doxorubicin. Both monolayer studies at the air-water interface and electrochemical experiments performed with supported model membranes revealed that the composition of the monolayers and its order of organization determines the type of the prevailing driving forces responsible for the interactions: electrostatic or hydrophobic. Additionally, in the presence of cholesterol in the membrane the competition between the drugs and cholesterol molecules has to be also considered. The effect of free drugs on model membranes will be also compared with the interactions of drugs attached to carbon nanotubes, which are potential drug carriers.

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Gabriel currently works as Application Specialist at Biolin Scientific AB in Sweden. He has a PhD in Engineering Physics from Chalmers University of Technology, Göteborg, Sweden, (Prof. Bengt Kasemo and Prof. Fredrik Höök). The title of his PhD thesis was: "Small-Scale Sample Handling for Studies of Liquid Crystals and Lipid-Based Soft Matter".

Experimental methods to study viscoelastic properties and phase transitions of lipids and protein films

1) A quartz crystal microbalance with dissipation monitoring (QCM-D) device was used to study lipids and liquid crystals at interfaces. Phase-transition induced structural changes of DTPC lipid vesicles adsorbed on a TiO2 surface and of 5CB liquid crystal films confined between SiO2 surfaces were investigated. The frequency and energy dissipation responses obtained upon scanning the temperature across the phase-transition temperature were fitted to a Voigt-based viscoelastic model. The phase-transition induced changes of the effective viscosity and effective film thickness were used to define the phase transition temperature, explore hysteresis upon temperature sweeps with different rates and to unravel structural changes during the phase transition.

2) Some proteins are known to denature and form a two-dimensional network at air-liquid and liquid-liquid interfaces. The denaturation of proteins can be examined by measuring the area changing (dilatational) and constant area (shear) dynamic viscoelastic properties of these interfaces. In this work the viscoelastic properties and the adsorption and network formation of protein solutions to interfaces were studied. Time-dependent data shows how to determine the gel point of the systems and demonstrates how the interfacial rheology measurements are extended from, not only studying self-absorption of macromolecules, but also to study Langmuir monolayers of model natural systems like cell membranes.

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Born on 21 February 1940 in V.Tarnovo (Bulgaria). MSc, PhD, DSc and Full Professor of Physical Chemistry in the Sofia University. Founder of the Laboratory of Biophysical Chemistry. Vice-Dean of the Center of Biotechnology and Dean of the Faculty of Chemistry and Pharmacy (1999-2003). Invited professor in French universities in Paris (1974-75), Marseilles (1982-86) and Angers (1993-96).Member of the Chemical Society of France. President of the Bulgarian National Evaluation and Accreditation Agency (2004-2011). Author and co-author of more than 140 scientific publications in the field of Physical Chemistry of interfaces and disperse systems and Biophysical Chemistry cited more than 1000 times and of more than 15 publications devoted to the problems of the quality assurance of Higher education.

Interfacial reorganization of molecular assemblies used as drug delivery systems

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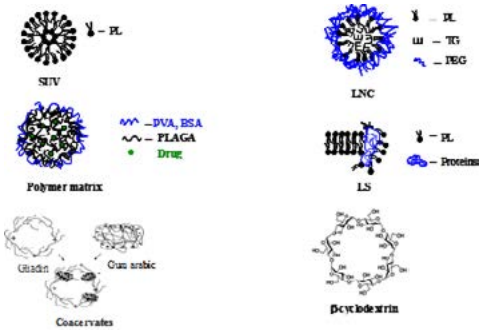
Nowadays a real revolution in galenics occurs. The traditional forms of drug administration give up one's place to the new drug delivery systems. During the last decades, an important progress has been made by tailoring various kinds of micro- and nanosized molecular assemblies used as drug carriers: the small unilamellar vesicles (SUV); the lipid nanocapsules (LNC) with a core of triglycerides (TG) covered by a soft layer of polyethylene glycol (PEG) and stabilized by phospholipids (PL); the biodegradable polyester matrix of poly (α-hydroxy acis)s - PLAGA; more complex structures of commercially available lung surfactant (LS), containing phospholipids (PL) and proteins (P); the coacervates containing plant proteins like α-gliadin and cage molecules like β-cyclodextrin.



From the physicochemical point of view, a better understanding of their behaviour in living environment seems indispensable. Despite the complexity of the living systems, it is possible to produce generic models of the reorganization at membrane interfaces of molecular assemblies by considering simple model systems.

Some experimental results and theoretical description of complex phenomena occurring during the reorganization of SUV, LNC, PLAGA matrix, LS and α-gliadin coacervates at model membrane interfaces will be briefly exposed. More attention will be paid to recently studied case of interaction between the Paclitaxel (Ptx)-loaded LNC and 2D and 3D mucous membrane models.

Pr Chantal Pichon

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Chantal Pichon has completed a Ph.D. in Cellular Biology and Microbiology in 1991 at the University of Aix-Marseille before working at the Babraham institute (Cambridge, UK) as post-doc fellow. She has been appointed as assistant professor in 1993 at the Orléans University.
Currently, Chantal Pichon is full Professor at the University of Orléans where she leads the Institute of Life Sciences and Chemistry for Life (6 research units and 8 masters). She is performing her research activities at the Center for Molecular Biophysics (CNRS- Orleans, France) where she coordinates the "Cell Biology and new therapeutic targets" department and co-supervises the team "Nucleic acids transfer by non-viral systems" with Dr Patrick Midoux (Deputy Director of CBM). The team has an outstanding expertise in delivery systems.
Chantal Pichon has a track-record of more than 100 publications and is the recipient of 20 grants (PI of 10 grants) including french national research grant, EEC Health innovation projects and Ambition and R&D 2020 of Région Centre Val de Loire. She is also involved in research projects with cosmetic industries of the Region Centre Val de Loire.

Bioinspired nanoassemblies for efficient delivery of nucleic acids therapeutics

Recent clinical trials of gene therapy unambiguously demonstrate the potentiality of this innovative therapy to cure diseases related to genetic disorders. Even though viral delivery systems remain the best vehicles to introduce genes into cells; there are some adverse events that raise serious safety concerns. Therefore, clinical developments still require the use of alternative approaches of high safety, low immunogenicity and easy manufacture. Efforts have been carried out to design chemical delivery systems that incorporate viral or bacterial-like features to gain efficient biological activity. The main stages are the protection of the nucleic acid from nucleases, the penetration into the cell, the transfer inside the cytosol and in the nucleus, and for some applications its integration into the genome of the host cells, all these steps being milestones. During this lecture, I will present how we and others have been inspired by examination of interactions between host cells and natural particulates including pathogens for the development of drug/gene delivery systems. Highly optimized devices were engineered and assembled with a specific order on molecular platform to overcome extracellular and intracellular barriers that nanoparticle based-therapeutics have to face upon their administration inside the body. The goal is to obtain smart nanoparticles that meet all requirements for successful biomedical applications.

Dr Marie-Hélène Ropers

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Marie-Hélène Ropers is researcher at INRA (French National Institute for Agricultural Research), in the research unit Biopolymers Interactions and Assembly (BIA) - located in Nantes. After obtaining her PhD in Physical Chemistry in 2000 (University of Nancy, France), she spent two years in the Max-Planck Institute for Colloids and Interfaces (Germany). Since 2002, she works in the research unit BIA where she applies her skills in the characterization of fluid interfaces to projects dealing with pectins at interfaces, proteins and fluorinated contaminants, interfaces in lipid oxidation and more recently nanoparticles. She passed her habilitation in 2013.

The role of the interfacial film in the control of lipid oxidation in O/W emulsions

In many food formulations enriched in healthy n-3 fatty acids, polyunsaturated lipids are organized in the form of oil droplets that are dispersed in a more or less hydrated matrix. In these systems, often described as oil-in-water emulsions, the presence of a large excess of unadsorbed emulsifiers in the aqueous phase hindered the understanding of the role of emulsifiers located at interfaces on lipid oxidation. The design of O/W emulsions stabilized with emulsifiers mainly located at the oil-water interfaces allowed to unambiguously relate the kinetics and rate of lipid oxidation with the structure and the composition of the interfacial layer. The interfacial layers covered by surfactants were more efficient to protect lipids against oxidation than the interfacial layers stabilized with proteins, whereas the results of many previous studies, performed in excess of emulsifiers, claimed the opposite tendency. These results were explained by two facts. First, the reconstitution and characterization of the interfaces on planar air-water films proved the homogeneity of the interfacial layer to be a key factor in the development of lipid oxidation in emulsions. Second, proteins adsorbed at the interface were subjected to damages before lipid oxidation was detected. Finally these results led us to propose new concepts for the role of proteins in the development of oxidation in particular the lateral homogeneity of the interface.

Dr Charles Sennoga

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Charles SENNOGA is Chercheur Invité and LE STUDIUM RESEARCH FELLOW 2013 currently in residence at Inserm Unité 930 "Imagerie et Cerveau" in Faculté de Médecine, Université François Rabelais de Tours, France. He was educated in the United Kingdom where he took a BSc (Hons) and a PhD in Chemistry at Imperial College London. After his PhD, he undertook postdoctoral research at the MRC Clinical Sciences Centre which allowed him to discipline-hop from Chemistry to the Life sciences interface. Through this, he built-up expertise in the engineering of microbubbles, their use in noninvasive ultrasound-mediated diagnostic monitoring of disease progression (molecular imaging) and therapeutic drug/gene delivery. His current research interests are concerned with drug delivery to the brain and aneurysmal blood flow. He has authored >20 peer-reviewed journal publications, 2 patents, 2 book chapters and >12 conference proceedings. Under the aegis of LE STUDIUM he was co-organiser and host of a highly successful international conference, attracting >60 delates and 10 key-note speakers.

Microbubble Contrast Agents: From Laboratory Bench To Clinic

Contrast agents are widely used in imaging, but until recently they had no place in ultrasonography. This changed with the introduction of microbubbles—small (typically 3/1000 millimetres in diameter) gas filled bubbles that are usually injected intravenously. Injecting a gas into the circulation may seem potentially hazardous, but extensive clinical experience has shown that the tiny volume of air/gas administered (< 200 microlitres) is not dangerous, and the safety of microbubbles compares well to that of other conventional agents in radiography and magnetic resonance imaging. Although microbubbles were originally designed simply to improve conventional ultrasound scanning, recent advances have opened up powerful emerging applications. This presentation will give a short introduction on the stabilization of microbubbles and a description of their existing applications in radiology and cardiology, followed by the potential of emerging applications of microbubbles in targeted imaging and therapy.

Dr Nathalie Tarrat

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Nathalie Tarrat, PhD, CNRS researcher, is an expert in molecular modeling. During her PhD and her post-doctoral studies, she addressed, with simulation methods, different research themes ranging from biology (phosphate esters hydrolysis in solution) and chemistry (reactivity of very heavy metals in solution and proton transfer with ab initio molecular dynamics) to physics (core structure and mobility of dislocations in hcp metals and electronic structure and magnetism of nanoalloys). She joined the CNRS in 2010 to develop multi-scale approaches for protein design. Then she joined the Materials under stress (MC2) group of the CEMES laboratory in May 2013 where she puts in place a novel activity focused on the "Optimization of metallic nanoparticles devoted to biomedical applications".

Functionalized Gold Nanoparticles For Antimicrobial Therapy: From In Silico Modeling To Growth By Nano-Epitaxy

Nathalie Tarrat, Magali Benoit, Patrizio Benzo and Marie-José Casanove

In the fight against antibiotic resistance, gold nanoparticles (AuNP) with antibiotics grafted on their surfaces have been found to be potent agents. Ampicillin-conjugated AuNPs have been thus reported to prevent the growth of ampicillin-resistant bacteria. The first step towards rational engineering of such stable hybrid organic/metal functional systems is the understanding of the interaction between the antibiotic and the nanoparticle at the atomic scale. However, this interaction remains highly misunderstood.

To start to bridge the gap, the structure of the interface between an ampicillin molecule and three flat gold facets Au(111), Au(110) and Au(100) has been investigated in our group with numerical simulations (dispersion-corrected DFT). We show that all studied grafting modes exhibit the active site of the antibiotic outward, an orientation which is very favourable regarding the antibacterial activity of these nano-conjugates. The nano-conjugates stability is explained through large adsorption energies of the antibiotic, due to partial covalent bonding. Moreover, this computational study suggests that, to increase the stability of gold/antibiotics nanoconjugates, a strategy to explore is the synthesis of facet-controlled nanoparticles.

In this framework, we present highly facetted Fe@Au core-shell nano-crystals which are synthesized in our group, aiming at enhancing the nano-conjugates stability while allowing the vectorization of the system thanks to the magnetic iron core. Numerical simulations on this system show that the adsorption energies can be controlled by the shell thickness.

Pr Maryam Tabrizian

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Maryam Tabrizian is full professor in the Biomedical Eng Dept at McGill University. She became Guggenheim Fellow (2010) and the Fellow of the Biomaterials Science & Engineering (FBSE) in 2011 for her contribution to the field of Biomedical Eng. & Biomedical Sci. She was the director of the Centre for Biorecognition and Biosensors for 10 years that she has founded in 2001. She is internationally known for her work in design of biointerface for promoting cell/protein-substrate interactions and for application in nanomedicine, regenerative medicine and Lab-on-a chip devices. She is the author of more than 170 peer-reviewed papers, 75 invited lectures, many book chapters, patents, and over 300 communications. She is currently the Editor–in-Chief of Materials, an Editorial Board Member of ACS-Bioconjugate Chemistry, an Associate Editor of the J. Biological Eng., and the International J. Biomaterials Res & Eng.

Rapidly Geling Injectable Sponges as a Potential Therapy to Target Remyelination Post-Spinal Cord Injuries

In the past decades, the main focus of investigators in the field of spinal cord injuries (SCI) has been to devise therapeutic measures, including the use of biomaterials that enhance neural regeneration. More recently, emphasis has been placed on enhancing remyelination and providing oligodendrocyte-protection after SCI. However, there are very few reports on biomaterials developed specifically to enhance remyelination post-SCI. Our laboratories have developed an injectable, rapidly-gelling, guanosine 5'-diphosphate (GDP)-crosslinked chitosan sponge to specifically target oligodendrocytes progenitor cells (OPCs) survival and differentiation. GDP is a natural anionic crosslinker that crosslinks the amine groups of chitosan and yields a highly porous sponge in less than 2 seconds. The sponge retains water up to 10 times of its weight and has mechanical properties close to those of soft tissues. It is cytocompatible with a variety of cell types including OPCs. Subcutaneous injections of the sponges in a rat model also confirmed their biocompatibility. Both rat-derived OPCs and human fetal OPCs adhered to the sponge and acquired physiological phenotypes. Moreover, neurotrophin-3 (NT-3) was successfully entrapped with high efficiency in the sponge and a sustained release for up to 30 days was achieved. OPCs cultured on the sponge for 8 days were shown to express myelin basic protein (MBP), a marker for mature oligodendrocytes. Currently, we examine the sponge in an animal model of SCI by administering the chitosan sponges containing neurotrophic factors either directly into the injury site or intrathecally on top of the injury. Preliminary results indicate that sponge is promising purine-based biomaterials that can be used as clinically-relevant therapies for enhancing remyelination post-SCI. v

Dr Roger Douillard

Né en 1946, Ingénieur agronome, Docteur ès science, Guide conférencier, il a fait sa carrière scientifique à l'INRA, en particulier sur les propriétés enzymatiques et technologiques de protéines. À Reims, dans l'UMR « Fractionnement des Agro-Ressources et Environnement », dont il a été le directeur, il a mis en évidence, en collaboration avec le CIVC le rôle des macromolécules dans la stabilité des bulles de la collerette du champagne.

Qualités et facteurs de qualité du champagne

Comme tous les produits, le champagne vise à satisfaire les besoins de ceux qui le consomment. Mais c'est un produit d'exception, adapté à des circonstances qui sortent le plus souvent de l'ordinaire. Ses qualités les plus recherchées sont ses qualités organoleptiques qui par l'intermédiaire de nos cinq sens suscitent du plaisir au cours de la dégustation. Ces qualités doivent être au niveau des attentes et conjuguer des modalités hors normes. Les qualités psycho-sociales du champagne ne doivent pas pour autant être négligées. On peut en résumer une partie importante au travers de la maxime : il n'est de champagne que de Champagne. C'est la renommée de l'appellation d'origine contrôlée, la tradition de prestige. Pour éviter toute ombre au tableau, les qualités environnementales du champagne doivent aussi se manifester à travers la mise en valeur des terroirs et des paysages de Champagne ainsi que des flux limités et raisonnés d'intrants et d'effluents. Pour ce vin d'exception, on ne peut se contenter de maintenir une qualité au cours des ans. Élaboré de façon maîtrisée depuis le XVIIIème siècle, le champagne ne cesse, depuis, d'accroître ses qualités. Pratiquement tous les facteurs intervenant dans la production du raisin, dans la protection de l'environnement, dans l'élaboration du vin calme, dans la deuxième fermentation conduisant à l'effervescence, dans le vieillissement du vin, dans le choix de la bouteille et de son emballage, dans les modalités de sa distribution, et dans la protection de l'appellation d'origine contrôlée interviennent sur les qualités du champagne. Pour conclure, rendons à César ce qui est à César. Ce travail permanent de promotion de la qualité est voulu et mis en place par l'ensemble des professions des viticulteurs et des maisons de champagne organisées au sein de leurs syndicats et associations et disposant d'un outil commun : le « Comité Champagne ».

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