The winter school

GDR Groupement de recherche B2i Bio-ingénierie des interfaces

SNOSCELLS

Surfaces and New Original Strategies for CELL Studies

Explore the properties of surfaces and their action on eukaryotic or prokaryotic cell behaviour

Course Booklet

January 22-27, 2023

Les Houches (Haute-Savoie, France)

Partners and sponsors

GDR Biomim - 2088

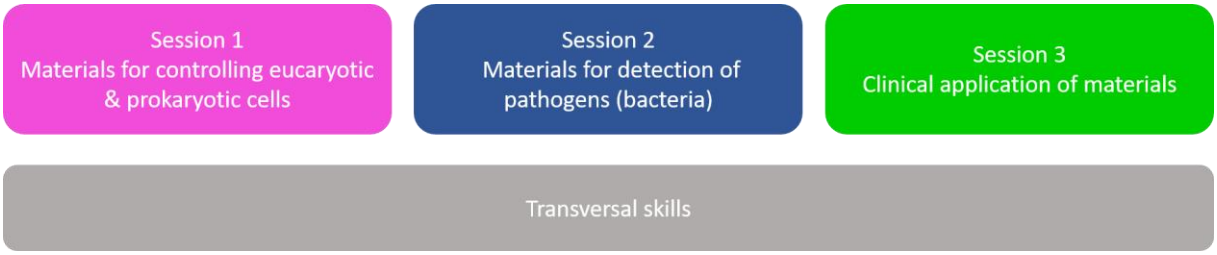
Hierarchical & Functional Materials for health, environment & energy | HiFunMat

The Interdisciplinary thematic institutes of the University of Strasbourg & cnrs & Inserm funded under the Excellence Initiative program

Presentation of winter school

Physical interactions between living cells and surfaces are a key process in several domains such as biosensing, tissue engineering, drug delivery, development of medical devices, etc. The aim of the workshop is thus to explore the interface between physics, chemistry and biology to better understand and control cell behaviour onto solid surfaces of new highly-defined materials and biomaterials. In this context, SNOSCELLS workshop provides an overview of the recent developments achieved on materials and surfaces to better control cell-surface interactions in order to tune and exploit biological processes. This five-day-long event is organized in 3 main sessions, as illustrated in the scheme below.

The following topics compose the program:



Main topical sessions

A. Active surfaces to control cell behaviour (session 1). Focus on how to design a bioactive material surface to act on cellular events for applications in cell-based assays, bio-sensing, development of medical devices and regenerative medicine.

B. Bactericidal or bacteriostatic surfaces (session 1). Focus on the engineering of materials to repel, avoid or control bacterial adhesion and biofilm formation.

C. Design of microsystems for the fast and sensitive detection of pathogens (session 2). Focus on microfluidic-based and other miniaturized devices dedicated to the fast and easy-to-operate detection of pathogens for biomedical or food applications.

D. Biomaterial engineering for tissue and bone healing (session 3). Focus on the design of scaffolds enabling a fast and safe tissue regeneration.

These topics highlight how different scientific communities are developing original and cross-disciplinary strategies to address common issues, namely the modelling, design, fabrication and processing of materials dedicated to better control living cell-surface interactions. This approach is a key feature in the novelty and originality of this workshop in regard to what has been proposed so far in a similar format. In parallel to these topics, we propose (after dinner) lectures and round table discussions on cross-cutting themes.

Main transversal sessions

A. The management of bio-ethical issues in research for Health. The aim is to raise concerns on the ethical aspects to be considered when developing science and designing devices and applications at the interface between inert materials and living cells. This topic will be presented and discussed by **Prof Nicolas Aumonier**.

B. The (un)ability of the international scientific community to correct itself in a highly competitive and comparative world. In the context of an increasing pressure to publish a large number of papers, in high index journals, the publication of (deliberately or not) wrong results is getting a dangerous concern. This topic will be presented and discussed by **Prof Raphaël Levy**, who coordinates the ERC Synergy NanoBubbles project (see https://erc.europa.eu/news-events/magazine/erc-2020-synergy-grants-examples).

C. Moving from scientific result production to an industrial valorisation. We wish to share the industrialization experience of academic researchers in the scientific scope of the school. Such feedbacks are particularly valuable as a such transfer requires specific skills and knowledge only poorly taught to young researchers. **Dr Max Piffoux** will present the EVerZom company as a perfect example to illustrate a successful translation of academic research into industrial application.

Program

(details of interventions are listed above)

	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday
7:45-8:25		Breakfast				Breakfast and check-out
8:30-9:40		Workshop introduction (20') **Pr. Gautrot (1/3)** ***Design of soft polymer biointerfaces for regenerative medicine***	**Pr. Gautrot (2/3)** ***Design of soft polymer biointerfaces for regenerative medicine***	**Pr. Gautrot (3/3)** ***Design of soft polymer biointerfaces for regenerative medicine***	**Pr. Weiss (2/3)** ***Biomaterials dedicated to bone regeneration***	**Dr. Boulmedais (3/3)** ***Polyelectrolyte layer-by-layer films to explore mammalian and bacterial cell control***
9:40-10:50		**Pr. Barthélémy (1/2)** ***Supramolecular materials for bioengineering***	**Dr. Boulmedais (1/3)** ***Polyelectrolyte layer-by-layer films to explore mammalian and bacterial cell control***	**Pr. Barthélémy (2/2)** ***Supramolecular materials for bioengineering***	**Dr. Boulmedais (2/3)** ***Polyelectrolyte layer-by-layer films to explore mammalian and bacterial cell control***	**Pr. Leblois (2/2)** ***Sensors for biomedical applications***
10:50-11:05		Break				
11:05-12:15		**Pr. Weiss (1/3)** ***Biomaterials dedicated to bone regeneration***	**Pr. Leblois (1/2)** ***Sensors for biomedical applications***	**Dr. Laurenceau (2/3)** ***Functionalized surfaces for the detection of rare cells and pathogens***	**Dr. Laurenceau (3/3)** ***Functionalized surfaces for the detection of rare cells and pathogens***	**Pr. Weiss (3/3)** ***Biomaterials dedicated to bone regeneration***
12:30-13:30		Lunch - take away				
14:00-17:30		*FREE TIME*				*DEPARTURE*
17:30-18:40	ARRIVAL AND REGISTRATION	**Dr. Durrieu & Pr. Laroche (1/2)** ***Micro- nano-patterns for cell biology***	**Dr. Laurenceau (1/3)** ***Functionalized surfaces for the detection of rare cells and pathogens***	**Dr. Durrieu & Pr. Laroche (2/2)** ***Micro- nano-patterns for cell biology***	Poster session	
18:40-19:30	*FREE TIME*	*FREE TIME*				
19:30	Dinner	Dinner			Dinner and farewell party	
20:30		**Pr. Aumonier** ***Ethics at the interface of Life and materials***	**Dr. Piffoux** ***Testimonies on the industrial valorization of biomedical engineering method***	**Pr. Levy** ***Is it somebody else's problem to correct errors in the scientific literature?***		

Each slot will last 50 minutes then followed by a 15 minutes long discussion with the audience.

Speakers' presentations and course summaries

SESSION 1: Materials for controlling eukaryotic & prokaryotic cells

- **Julien Gautrot (Professor, Queen Mary University of London, UK)**

The expertise of Professor Julien Gautrot focuses on the design of novel biomaterials and methodologies that allow the study of bio-interfaces and their control for applications in cell-based assays, bio-sensors and regenerative medicine. His approach to design new biomaterials is directly inspired by Nature's strategies to generate complexity and control biomaterial function and properties such as mechanical, chemical and biological properties.

https://www.sems.qmul.ac.uk/staff/research/j.gautrot

Lecture: ***Design of soft polymer biointerfaces for regenerative medicine (3 parts)***

*1. Design of polymer brushes for the biomedical field - from biosensing to regenerative medicine applications (**Monday 23th January 2023**)*

Polymer brushes are polymer chains that are tethered by one end to a substrate and can be grown to very high densities using controlled radical polymerisation techniques. Their inherent confinement confers to these coatings unique physico-chemical properties. For example, some polymer brushes display ultra-high protein resistance, enabling them to resist the adsorption of proteins and other biomacromolecules present in biological fluids such as blood or plasma, or cell culture medium. This property, combined to suitable biofunctionalisation and microfabrication strategies, has paved the way to the engineering of new generations of biosensors, cell-based assays and coatings for tissue engineering applications. On the other hand, polyelectrolyte brushes, based on charged repeat units, display unique responsive and structural properties for the capture of biomacromolecules. This property has been harnessed not only for the design of protein-based biosensors, but also for the design of gene delivery vectors. This lecture will give an overview of the design of polymer brushes for applications in the biomedical field, with emphasis on protein resistant and polycationic brushes.

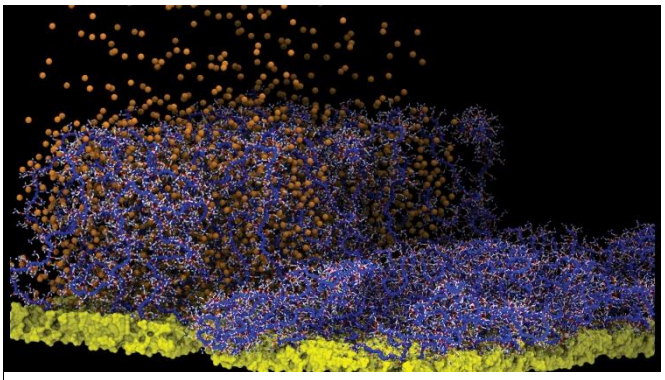


Figure 1: Atomistic model of cationic polymer brushes responding to their environment.

*2. Microengineered biomaterials to regulate cell phenotypes and tissue formation at different length scales (**Tuesday 24th January 2023**)*

Cells can sense a range of physical properties in their microenvironment. The geometry of the cell-matrix and cell-adhesive landscape is a major regulator of tissue development, homeostasis and repair. Strategies aiming to reproduce or control such adhesive cues have important applications for the control of stem cell phenotype and tissue formation or regeneration. Such sensing can take place at multiple length scales, from the nanoscale, at which cell-matrix adhesions are typically regulated, to the micro-to millimetre scale, at which tissue structure and function are regulated. Nano- to microfabrication platforms are essential to control the geometry of the adhesive landscape. This lecture will present some approaches to engineer biomaterials at multiple length scales and microfabricate 3D tissue models that reproduce some of the structure and functions of tissues. This ranges from the regulation of stem cell adhesion and fate decision by the nanoscale geometry of extra-cellular matrix, to the formation of vascularised tissue models in microflulidic chips.

Figure 2: Cardiac spheroid embedded in a microvascularised microfluidic chip for use as advanced in vitro model.

*3. How do cells sense the mechanical properties of their environment? Implications for tissue engineering and stem cell technologies (**Wednesday 25th January 2023**)*

The ability of cells to sense the mechanical properties of their environment has been extensively reported and studied. The mechanisms via which cells are able to do so, and how in turn this enables to regulate a range of cell phenotypes have recently become clearer. This lecture will present a brief overview of the molecular mechanisms enabling cells to sense the mechanical properties of their environment. In turn, how this impacts on stem cell phenotype and the implications of such knowledge for biomaterials design for regenerative medicine will be discussed. Finally, this lecture will present recent work demonstrating that cell adhesions most directly respond to the local, nanoscale, mechanical properties of their environment. These may significantly differ from bulk and overall macroscale mechanical properties of biomaterials. This has important implications for the design of novel generations of biomaterials for stem cell technologies.

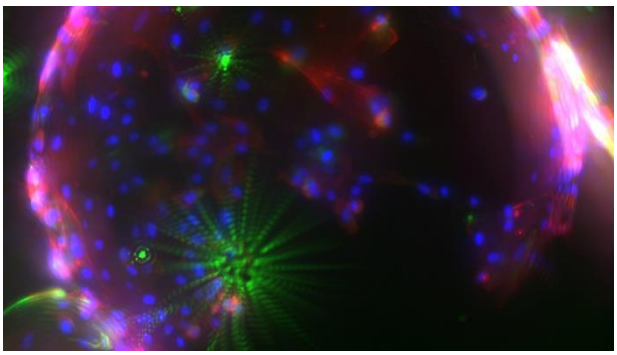


Figure 3: Mesenchymal stem cells respond to the nanoscale mechanics of their environment, enabling their culture at the surface of oil droplets without loss in stem cell phenotype.

- **Philippe Barthélémy (Professor, ARNA, INSERM, CNRS, Université de Bordeaux, France)**

Professor Philippe Barthélémy is an expert in designing and assembling nucleoside-based amphiphiles for various biological applications (drug delivery, bioimaging, cell culture). He will provide lectures in the field of supramolecular materials (gels…) suitable for stem cell cultures, tissue engineering and/or bioprinting.

http://chembiopharm.fr/portfolio_page/philippe-barthelemy/

Lecture: *Supramolecular materials for bioengineering (2 parts)* ***(Monday 23th January 2023)***

Amphiphilic biomolecules are emerging as promising supramolecular materials for biomedical and technological applications. In this presentation we will highlight the recent progresses in the field of nucleic acid based lipids with an emphasis on their molecular design, supramolecular properties, physicochemical behaviours, and applications in the field of health science. In a first part we will focus on the design and the study of nucleolipids and the glyconucleolipid family. Also, recent contributions of responsive materials involving nucleolipids and their use as smart drug delivery systems will be discussed. The supramolecular materials generated by nucleic acid-based lipids open new challenges for biomedical applications[1-7], including the fields of medicinal chemistry, biosensors, biomaterials for tissue engineering, drug delivery, and the decontamination.

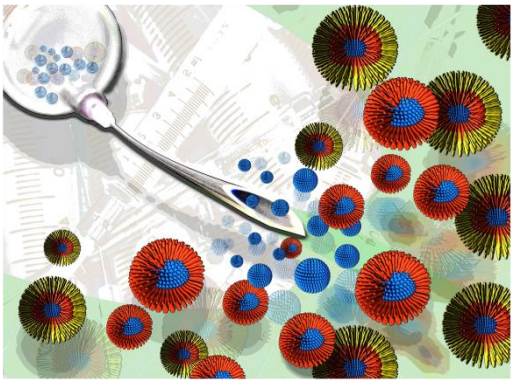


Figure. Illustration of supramolecular based nanomaterials for drug delivery applications

References

[1] Kassahun, G. S., Farias, E. D., Benizri, S., Mortier, C., Gaubert, A., Salinas, G., Garrigue, P., Kuhn, A., Zigah, D., and Barthélémy P. ACS Applied Materials & Interfaces (2022) DOI: 10.1021/acsami.2c02993.

[2] Benizri, S., Gaubert, A. Soulard, C., Gontier, E., Svhan, I., Rocchi, P., Vacher, G., and Barthélémy, P. Biomaterials Science, (2021) DOI: 10.1039/D1BM00273B.

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[4] Baillet, J., Desvergnes, V., Hamoud, A., Latxague, L., Barthélémy, P. Adv. Mater. (2018) DOI: 10.1002/adma.201705078.

[5] V. Brune, A. Gissot, R. Delzor and P. Barthelemy, Chem. Commun., (2017) DOI: 10.1039/C7CC05693A.

[6] Ramin MA, Latxague L, Sindhu KR, Chassande O, Barthélémy P, Biomaterials (2017) DOI: 10.1016/j.biomaterials.2017.08.034.

[7] M. A. Ramin, K. R. Sindhu, A. Appavoo, K. Oumzil, M. W. Grinstaff, O. Chassande, P. Barthélémy, Adv. Mater. (2017) DOI: 10.1002/adma.201605227.

- **Marie-Christine Durrieu (Ph.D., INSERM-CBMN CNRS UMR5248, Université de Bordeaux, France)**

Dr. Marie-Christine Durrieu is a senior INSERM researcher specialized in biomaterials and tissue engineering. She has been active in many biomaterials engineering fields. She carries out research in surface functionalization, micro-, nano-patterning of materials using mainly peptides in order to favour cell adhesion, migration and differentiation.

http://www.cbmn.u-bordeaux.fr/?fond=membre&id_dossier=54&client_bmail=marie-christine.durrieu@inserm.fr

& Gaëtan Laroche (Professor, Laval University, Québec, Canada)

Dr. Gaétan Laroche is a full professor in the Materials Engineering Department of the Faculty of Science and Engineering at Laval University. He is a member of the Centre de Recherche sur les Matériaux Avancés (CERMA) of Laval University. He is internationally recognised for his work on the surface modification of materials using gas plasmas. More specifically, he is developing strategies for the surface modification of vascular and orthopaedic biomaterials to improve their biocompatibility.

https://www.crchudequebec.ulaval.ca/recherche/chercheurs/gaetan-laroche/

Lecture: *Micro- nano-patterns for cell biology (2 parts)*

*1. Surface treatment of biomaterials for bone tissue engineering (**Monday 23th January 2023**)*

The treatment of bone traumas and fractures concerns a yearly market of about one million patients in the EU and the US. Bone is the most often transplanted tissue, with up to one million grafts realized each year in Europe only. Autografts (*tissue that is taken from one part of a person's body and transplanted to a different part of the same person*) are ideally suited to repair bones from an immunology standpoint; however, they require to harvest bone in the patient, which needs to perform a second operation with possible associated complications; in addition, large reconstructions remain difficult. Allografts (*a tissue graft from a donor genetically unrelated to the recipient*) are essentially obtained from decellularized bone scaffolds taken from human cadavers; although quite efficient regarding the scaffold structure itself, they may cause possible adverse immunologic reactions. In addition, their osteoinductive properties are limited. In native bone, osteoblasts (*bone cells*), osteogenic precursors and endothelial cells (*cells that lines the interior surface of blood vessels*) interact in a synergetic way towards the coordinated development of vasculature and mineralized tissue; therefore, close spatial relationships are established between the two tissues in the forming bone: the vascular network acts as a 'template' for the deposition of bone mineral (Figure).

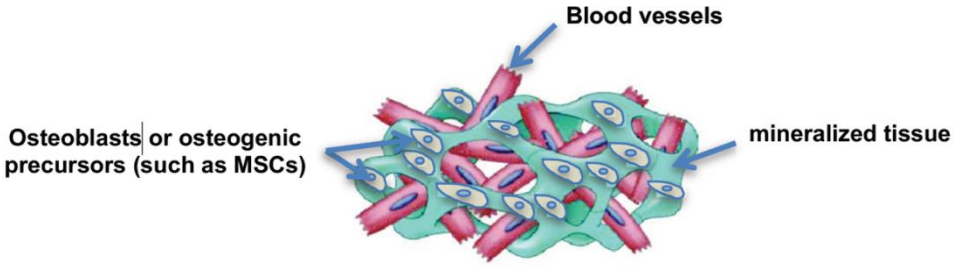

Figure.

The study of Mesenchymal Stem Cells (MSC, *stem cells able to generate osteoblast and then bone*) has raised the hope of a cell-based therapy for tissue engineering due to their high availability based on self-renewal and their high capability of differentiation into different kind of cells. Identification of factors that maintain their stemness properties, monitor and control MSC differentiation is crucial. *In vivo*, cells evolve following nanoscale physical and chemical signals they receive from ExtraCellular Matrix (ECM) surrounding cells. The challenge lies in synthesizing materials able to reproduce these processes. Such materials could be used for implantation, but also as physiologically relevant models in basic and translational studies of bone development, disease and drug discovery.

The objective today is to create new bioactive nano-, micro-structured surfaces able to maintain MSC in their stem state or to allow their selective differentiation.

The goals of the present course may be summarized as follows:

- *How to functionalize biomaterial surface using plasma treatment?*
In the first part of this lecture, we will show how plasma modification may be used to functionalize the surface of biomaterials that are otherwise not chemically reactive. An example will be provided for PTFE (Teflon®), which is known to be completely chemically inert, but can be successfully conjugated with biomolecules once modified with plasma. The presentation will put a particular emphasis on the characterization of plasma-modified surfaces and on the strategies that can be put forward to conjugate biological molecules, by taking advantage on the reactive chemical functionalities inherently present in their structure. Examples will also be provided to highlight the importance of selecting the appropriate surface conjugation strategy to preserve the bioactivity of biomolecules.

- *How to modify surface of biomaterial to favour adult human stem cell fate?*

In the second part of this lecture, we review the biomaterial platforms that have been engineered to control stem cell fate. We explore how altering immobilized biochemical cues and biophysical cues such as dimensionality, stiffness, and topography can enhance our control over stem cell fates.

*2. Synergy between biochemical and biophysical cues to promote cell differentiation (**Wednesday 25th January 2023**)*

It is becoming increasingly appreciated that the role of extracellular matrix (ECM) extends beyond acting as scaffolds to providing biochemical and biophysical cues, which are critically important in regulating stem cell self-renewal and differentiation. To date, more than 15 different extrinsic (environmental) factors, including the matrix spatial organization, topography, stiffness, porosity, biodegradability and chemistry have been identified as potent

regulators of stem cells specification into lineage-specific progenies. Thus, it is plausible that the behaviour of biomaterials inside the human body will depend to a large extent on their ability to mimic ECM properties of the tissue to be replaced. Recently, nano- and microengineering methods have emerged as an innovative tool to dissect the individual role of ECM features and understand how each element regulates stem cell fate. In addition, such tools are believed to be useful in reconstructing complex tissue-like structures resembling the native ECM to better predict and control cellular functions, such as stem cell differentiation. For example, it is now possible to tune the mechanical properties of biomaterials to closely match those of the tissues and organs that they are intended to replace. When interacting with mechanically tuned materials, stem cells were demonstrated to adapt their differentiation scheme to match their phenotype to the cells of the tissues that they are intended to replace of repair.

This course will focus on examples of such synergies between biochemical and biophysical cues that are possible to engineer on materials to exacerbate stem cell fate toward the desired lineage. First, it will be demonstrated that a mimetic peptide derived from the Bone Morphogenic Protein-2 (thereafter referred to as BMP-2 mimetic peptide) see its osteogenic differentiation potential increased toward mesenchymal stem cells (MSCs) while co-conjugated with an adhesion peptide. Second, it will also be shown that this osteogenic differentiation conferred by the simultaneous presence of both peptides may even be enhanced by patterning these biochemical cues on specific microdomains on the biomaterials surface. Finally, it will also be put in evidence that controlling the mechanical properties of hydrogels with further surface conjugation can promote the differentiation of MSCs into osteocytes.

SESSION 2: Materials for detection and control of pathogens

- **Thérèse Leblois (Professor, FEMTO-ST, UMR CNRS 6174, Besançon, France)**

Dr. Thérèse Leblois is a professor at the University of Bourgogne Franche-Comté since 2007. She is working on the design and the implementation of micro-sensors based on acousto-fluidic interactions for biomedical applications. She has expertise on resonant sensors with biofunctionalized surface for bacteria detection and quantification and for blood analysis.

https://www.femto-st.fr/fr/personnel-femto/thereseleblois

Lecture: ***Sensors for biomedical applications (2 parts)*** *(Tuesday 24th January 2023, Friday 27th January 2023)*

The development of microfluidics technology brings many advantages to health and food industries. In fact, microfluidic platforms allow many biochemical tests to be miniaturized, having the advantages to: reduce reagent volumes, have high analytical throughput, enhance sensitivity and improve analytical performance. This course will give a compilation of the current trends regarding the materials and the processes of microfabrication used in miniaturized platforms of tests. The topic includes both the materials used for all the components of the device, as well as the sensors used for the detection systems added for an end-use perspective of the devices. Examples illustrating these lectures emphasize on biomedical, environmental and food safety applications.

The first lecture will focus on biosensors, on the principles of transducers and their miniaturization, fabrication and performances (specificity, sensitivity, non-toxicity, small concentration detection, and cost-effectiveness). Examples will illustrate the topic.
The second lecture will be dedicated to the platforms of detection (Lab-on-chip) including microfluidics and integrated sensors.

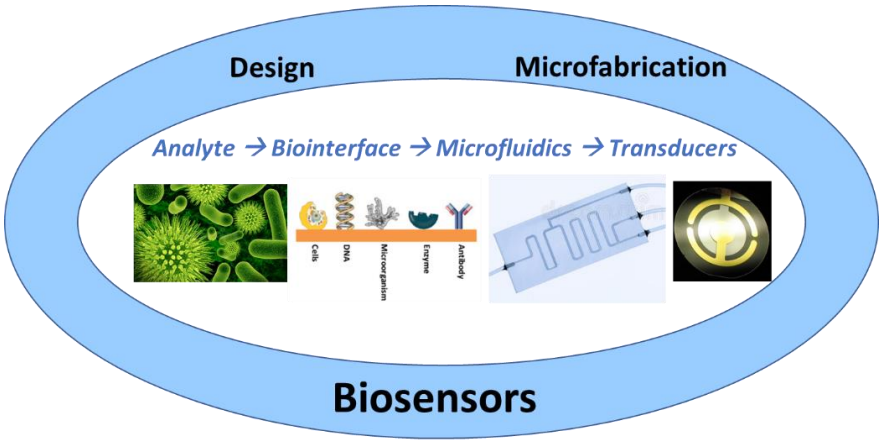

Figure: Components of a lab-on-chip detection platform.

- **Emmanuelle Laurenceau (Assistant Professor, Ecole Centrale de Lyon, CNRS, INSA Lyon, Université Claude Bernard Lyon 1, CPE Lyon, CNRS, INL, UMR5270, France).**

Dr. Emmanuelle Laurenceau is an expert on the development of miniaturized tools for cancer diagnosis and prognosis. She is also recognized for her work on the development of new surface chemistries to control cell adhesion to materials.

https://www.ec-lyon.fr/contacts/emmanuelle-laurenceau

Lecture: ***Functionalized surfaces for the detection of rare cells and pathogens (3 parts)*** ***(Tuesday 24th January 2023, Wednesday 25th January 2023, Thursday 26th January 2023)***

Cell separation and detection are of great importance in biomedical research including diagnosis and cell biology. For instance, some cells are found at extremely low number in the blood, such as circulating tumor cells (CTC), and their detection offer important guidance for the early diagnosis, personalized treatment and evaluation of tumor resistance. Moreover, pathogens detection, such as bacteria and viruses, is today an essential concern in the field of medicine as well as in that of the environment or the food industry. But conventional detection techniques are mainly based on cell culture, immuno-labelled detection, nucleic acid analysis which are often slow, very expensive, requiring specialized support and devices. Thus, there is a need for specific, rapid, on site, low cost and easy to handle techniques allowing the detection and separation of rare cells and pathogens. Biosensors and Lab-On-a-Chip (LOC) meet these specifications but it requires the ability to design, engineer and control biology/ materials interfaces at the molecular level. Various strategies have been developed to design and control such interfaces for the detection of cells and pathogens in various samples including surface functionalization.

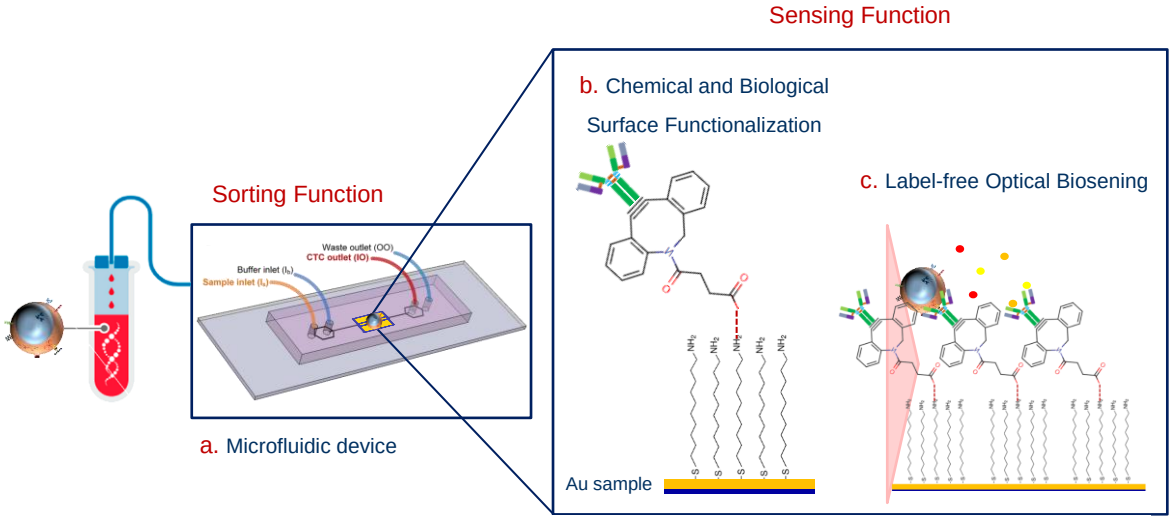

Figure: Schematic of microfluidic device for the sorting and analysis of circulating tumor cells (CTC).

In my first lecture, I will present the issues for the development of innovative technologies in the field of cell and pathogens detection and separation. In the second lecture, I will focus on CTC detection, separation and analysis (Figure 1). And in the third lecture, I will address pathogens detection through the state of the art.

SESSION 3: Tissue and bone engineering

- **Pierre Weiss (Professor, Université de Nantes, INSERM, CHU Nantes, UMR1229, France)**

Dr. Pierre Weiss is a senior INSERM researcher and medical doctor. He has a strong expertise in bone and cartilage tissue engineering with the design and development of synthetic extracellular matrices that will serve as biomaterials and as a support for differentiated cells or stem cells to be re-implanted in the body to regenerate bone tissue or cartilage.

https://rmes.univ-nantes.fr/pierre-weiss

Lecture: *Biomaterials dedicated to bone regeneration (3 parts)* ***(Monday 23th January 2023, Thursday 26th January 2023, Friday 27th January 2023)***

1. First is an introduction of bone and skeletal tissues before a reflexion on the 4R medicine: Replace, Repair, Regenerate and reprogram.

We will focus in this part more on the 2 first parts of the 4 R medicine concept, Replace end Repair. Surface and material/cells interaction are key issues of this approaches to allow biocompatibility and osteointegration.

2. The second part will be focused on Regenerative biomaterials for bone.

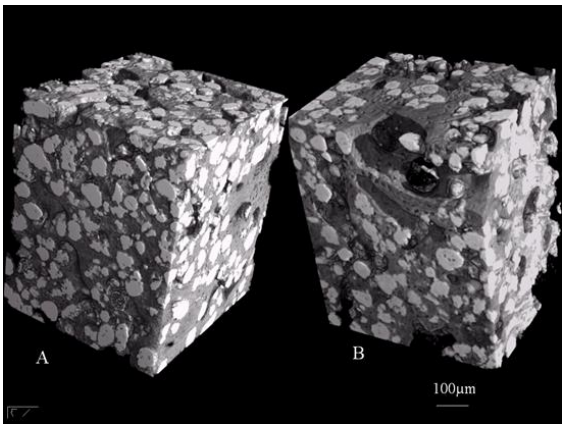

Figure 1: Synchroton 3D image of bone ingrowth in Injectable Bone substitute (from Weiss, P., et al. (2003). Synchrotron X-ray microtomography (on a micron scale) provides three-dimensional imaging representation of bone ingrowth in calcium phosphate biomaterials. Biomaterials, 24(25), reproduced with permission).

20 years ago, we designed injectable bioactive suspensions in water of calcium phosphate ceramics for bone and periodontal regenerations Because of leakage of these suspensions, we focused on injectable hydrogels before to set in situ by chemical crosslinking to form 3D scaffold. We set up a platform to develop a series of innovative hydrogels for bone, cartilages and periodontal tissue regeneration. We based our strategy on polysaccharides macromolecules because they are renewable materials, that originate from biological sources and generally are biocompatible, non-toxic and biodegradable. We developed a family of silated macromolecules able to react forming biocompatible hydrogels. The silated polymers are self-setting hydrogels able to covalently crosslink under pH variation, without addition of toxic crosslinking agent.

For mineral scaffolding, we realized composites of calcium phosphates particles or cements with hydrogel, increasing the ductility and creating macroporous scaffold to propose foam bone cements well adapted to bone biomaterials and Bone tissue engineering.

3. Last part of the presentation will be focused on biomaterial for regeneration in Tissue engineering strategies before to move to personalized medicine with specific construct adapted to one patient.

Tissue engineering is a promising approach to regenerate damaged skeletal tissues. In particular, the use of injectable hydrogels alleviates common issues of poor cell viability and engraftment. However, uncontrolled cell fate, resulting from un physiological environments and degradation rates, still remain a hurdle and impedes tissue healing. 10 years ago, we know the key role of hydrogels parameters for cell fate control as stiffness, relaxation and degradation properties. Hydrogels are three dimensional networks that have the ability to retain large amounts of water. More than 90 % of the body is composed of macromolecules physically or chemically crosslinked in high water content and soluble compounds. Hydrogels have structural similarities with extracellular matrices (ECMs) and versatility that make them the ideal candidates in tissue engineering, drug delivery systems, and specific medical devices.

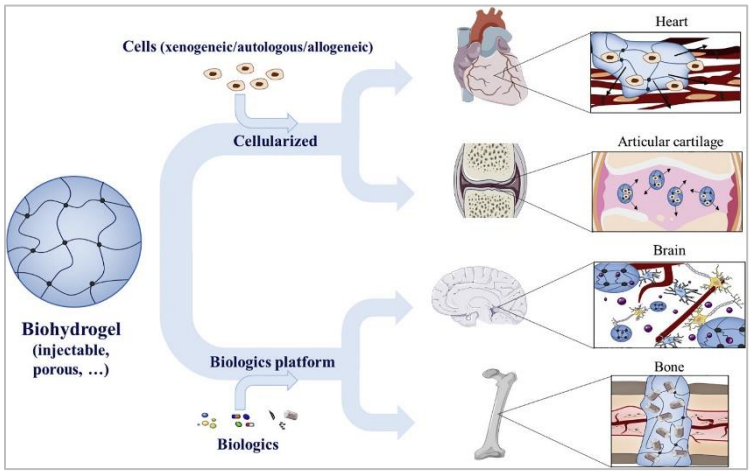

Figure 2: Main strategies used in regenerative medicine using cells and/or biologics to drive local tissue regeneration. (From Flégeau, K. et al. (2017) Toward the development of biomimetic injectable and macroporous biohydrogels for regenerative medicine. Adv Colloid Interfac 247, 589–609, reproduced with permission).

One of the challenges in bone tissue engineering with calcium phosphate cements is to create macroporous, degradable, injectable and bioactive materials. We propose to use a well-tailored tridimensional implant bioresorbable, biocompatible, with user friendling mechanical properties to perfectly fill the shape of bone defect in order to ensure a bone remodeling which will repair the bone defect. Cells or Bone marrow of biologics can be added to theses 3D constructs to improve the bone regeneration kinetic.

Collectively, these results suggest that these hydrogels associated with a large panel of calcium phosphate like nano particles, ceramic micro particles or ionic cements offer promising outcomes for skeletal tissue engineering for large bone tissue regeneration.

Perspectives are 3D printing and bio printing techniques. We will use our hydrogels platform to prepare tunable (bio)inks in skeletal medicine.

- **Fouzia Boulmedais (PhD, ICS, UPR22, CNRS, France)**

Dr. Fouzia Boulmedais is a CNRS Research Director, expert in material functionalization by polyelectrolyte layer-by-layer deposition. Her research deals with the control of polyelectrolyte multilayer constructions and the incorporation and release of bioactive molecules from these polymer matrices. Her work is especially applied to the development of new surfaces for bioengineering and control of eukaryotic and prokaryotic cells on biomaterials.

https://www.ics-cnrs.unistra.fr/member-209-Boulmedais%20Fouzia.html

Lecture: ***Polyelectrolyte layer-by-layer films to explore mammalian and bacterial cell control (3 parts)*** *(Tuesday 24th January 2023, Thursday 26th January 2023, Friday 27th January 2023)*

Implantable medical devices, called also biomaterials, are widely used in surgery not only to replace altered or lost tissues but also in critical care for fluid or gas administration using catheters or tracheal tubes, respectively. They are intended to be in contact with body fluids and/or tissues. Engineering the surface of such biomaterials is of vital importance for their successful (bio)integration by the body, i.e. colonization by the specific cell of the replaced tissue.

Among the surface modification techniques, the Layer-by-Layer (LbL) method is a versatile and a simple to implement process based on the alternated deposition of oppositely charged polyelectrolytes generally by dip coating (Figure). Performed at room temperature using aqueous solutions, the LbL method allows the development of biocompatible and bioactive nanofilms, for example with antimicrobial property or tissue regeneration. Since 1992 with the first paper of Gero Decher using polyelectrolytes (Decher, G. Science 1997, 277, 1232), a tremendous interest has been shown with thousands of annual publications with wide spectrum of applications in healthcare, environment or energy. A variety of materials (polymers, nanostructures, proteins or enzymes) have been used to develop LbL nanofilms over time.

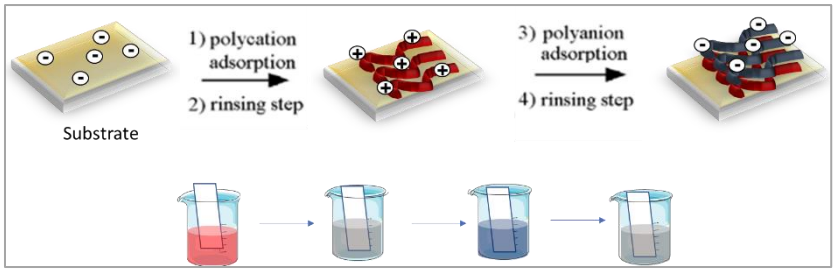

Figure: Build-up of polyelectrolyte layer-by-layer film by the dipping method.

During the courses, we will explore the physical-chemical properties of different types of LbL films based on electrostatic interactions, hydrogen bonding, or coordination bonds and the different techniques that are used to characterize them. Few examples will be given where the developed films were used as coatings to control the fate of mammalian cells or bacteria. The aim of the courses is to give few insights from the literature and especially the link between the physical chemistry properties of the films and cell adhesion/proliferation (Ren et al. Progress in Polymer Science 2019, 92, 1) or bacterial inhibition (Séon et al. Langmuir 2015, 31, 12856).

TRANSVERSAL SESSIONS

- **Nicolas Aumonier (Ph.D., Paris Sorbonne et Grenoble Alpes University, France)**

Dr. Nicolas Aumonier is a researcher of the Grenoble Alpes University. His research focuses on the notion of threshold, in philosophy of biology as well as in moral philosophy, understood as a limit-point to be crossed, or not, according to the representation of reality we choose to assume. In moral philosophy and in the field known as bioethics, his research focuses on the beginning and end of animal and human life, and on consensus in institutional dialogue.

https://iphig.univ-grenoble-alpes.fr/fr/presentation/membres/enseignants-chercheurs/aumonier-nicolas

Lecture: ***Quelques réflexions éthiques sur l'usage des biomatériaux*** *(**Monday 23th January 2023**)*

One of the goals of this thematic school is to use bioethical reflection as an underlying issue in research on biomaterials and devices related to the living.

Different ethical criteria allow us to question this research and to evaluate the possible risks or the promising perspectives. When we use a benefit/risk analysis grid, are we aware that we are relying on the Darwinian principle according to which the strongest prevails? But is the competing principle of respect for the human person not convenient in its very vagueness that does not prohibit much?

Today, supposedly anonymous blood samples, used for testing the best possible antibiotic response in a life-threatening emergency, can deliver bio-identifying information without the patient's awareness. Tomorrow, will a blood sample be used to reconstitute other cells, organs, or even an entire body, using a sort of elaborate PCR? Some fear it, others are working on it. Will our identities be weakened by this work and by the possibilities it opens? Are the usual ethical concepts adapted to these possible transformations?

These are some of the questions that will be addressed, before being completed and enriched by the participants' interventions and the common discussion.

- **Max Piffoux (Ph.D., EVerZom company, France)**

Dr. Max Piffoux is co-founder and scientific advisor of EVerZom. He has a master degree in Molecular Engineering from Art & Métiers ParisTech, a master degree in statistics and bioinformatics, and a Ph.D. in Sciences from Matter and Complex Systems Laboratory (CNRS, France). During his thesis, he developed the production process that are the origin of EVerZom creations (co-inventor of its core patents), he is therefore an expert in therapeutic applications and high-yield exosomes production. He is also member and co-founder of Evora Biosciences, a company specialized in the therapeutic use of EVs. He is currently a resident in oncology.

https://everzom.com/

Lecture: ***Testimonies on the industrial valorisation of biomedical engineering method: example of a drug loaded thermosensitive gel and bioreactors for the production of cell therapies*** ***(Tuesday 24th January 2023)***

This presentation aims at giving a few examples of ongoing industrial projects developed in start-ups that emerged from academic teams in the field of biomedical engineering and drug development from an academic "insider" point of view. The goal is to discuss these examples with the audience and give the first keys to people that may be interested in launching similar kinds of projects.

Apart from example to trigger the discussion, main topics that may be discussed depending on the audience interests: intellectual property, creating a company and a team, relations to the academia and technology transfer offices, choosing a project, the healthcare ecosystem and drug development, grant funding, private funding, public relations and networking, the relation between science and business.

- **Raphaël Levy (Ph.D., Univ. Paris Sorbonne, Nord Paris, France)**

Dr. Raphaël Levy leads an ERC Synergy project that aims at better understanding the mechanisms of correction of science and the obstacles to this correction, taking the field of nanoscience as an example. To achieve this goal, his work brings together researchers in France and the Netherlands, and combines scientific, historical, sociological and philosophical approaches.

https://www.univ-paris13.fr/raphael-levy-pilote-nanobubbles/

Lecture: ***Is it somebody else's problem to correct errors in the scientific literature?*** ***(Wednesday 25th January 2023)***

It is a common experience for a scientist reading a publication to disagree with the conclusions, to find errors, or more rarely, to discover features that are suggestive of scientific misconduct. It is also not uncommon to work for months or years on the basis of a publication only to find out that the results were not reproducible. It is often said that science is self-correcting but in practice there are many barriers to the correction of science. Furthermore, lack of, or delayed, correction has many negative consequences, e.g., on trust in science, waste of funding, patients' safety, research careers, etc. The speaker will summarise the difficulties he encountered in some of his attempts at correction of science in the field of bionanoscience and introduce the ongoing interdisciplinary project ERC Synergy NanoBubbles that aims to better understand how, when and why does science fails to correct itself, using the field of bionanosciences as one that we both study and contribute to. This will be a roundtable event so the speaker will particularly welcome questions and hope that the participants will also share their own experience to this important topic.

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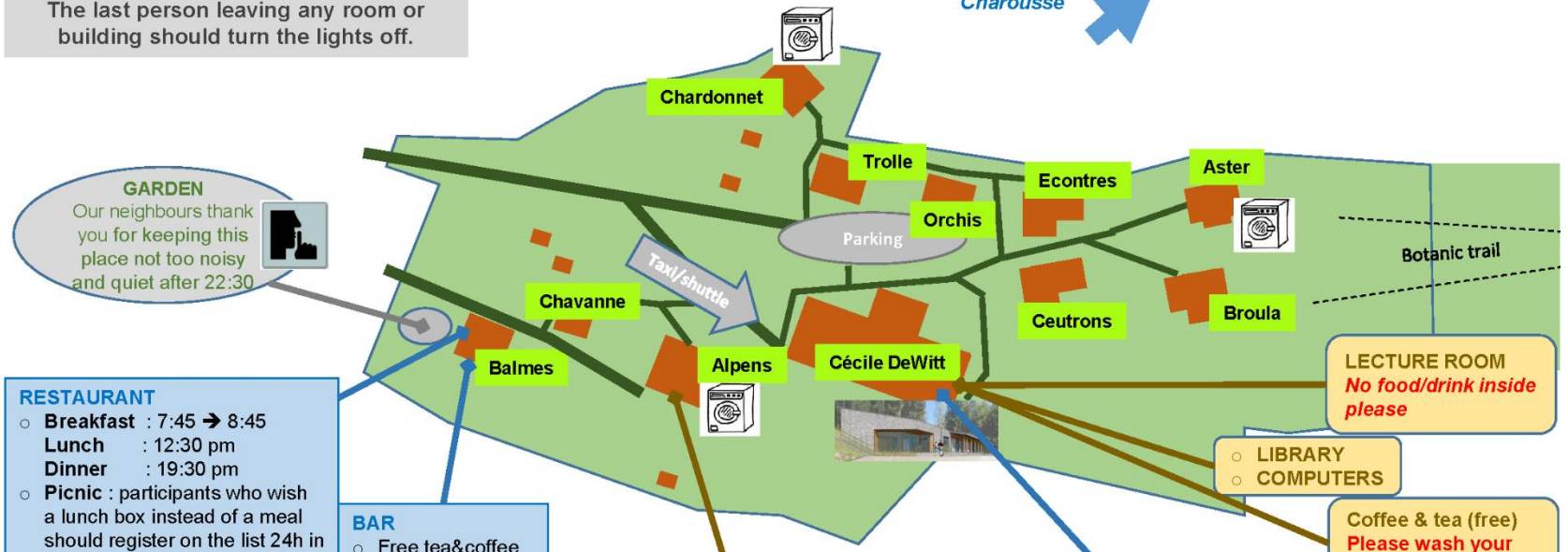
PRACTICAL INFORMATION

The school property is at your disposal for the session; please respect it and if possible improve it.
The last person leaving any room or building should turn the lights off.

Charousse

ÉCOLE DE PHYSIQUE DES HOUCHES



GARDEN
Our neighbours thank you for keeping this place not too noisy and quiet after 22:30

RESTAURANT
- **Breakfast** : 7:45 → 8:45
  Lunch : 12:30 pm
  Dinner : 19:30 pm
- **Picnic** : participants who wish a lunch box instead of a meal should register on the list 24h in advance
- **Drinks** (not included) can be bought on individual basis and paid here

BAR
- Free tea&coffee
  Table tennis, table football, piano, white boards

LECTURE ROOM
No food/drink inside please

- LIBRARY
- COMPUTERS

Coffee & tea (free)
Please wash your cups & glasses

CARETAKER
- Flat n°9 (3rd floor)
  Phone: **+33(0)6 78 98 52 40**
  (in case of emergency or serious problem only)

RECEPTION
- Information, taxi booking, help, requests, …
- To be paid : - school fee : 1st day
  - cold drink : last day

Direction of Mont Blanc

Mountain activities are at your own risk

Before any hike or climb, please put a note on the special book provided and include the name of the participants, approximate itinerary, schedule and phone number. We draw your attention to the fact we only hold a collective insurance for accidents occurring on the school campus.

Washing Machines & dryers Free use & washing powder

ÉCOLE DE PHYSIQUE DES HOUCHES

PRACTICAL INFORMATION

You are going to participate to a session at the Les Houches School of Physics. Website.

In order for you to have an enjoyable stay, please find below some practical information that we strongly recommend you read up to the end!

SITE / LOCATION

The Les Houches School of Physics is located in the Chamonix Valley, in a mountain area (altitude 1150 m).

In the winter (until April), appropriate outfit/equipment is essential:

- **Appropriate clothes and shoes for the snow.**
- **Snow tires and/or snow chains for vehicles.**

In the summer, temperatures can be very low, depending on the weather conditions. **Clothing suitable for the cold and rain**, and **comfortable shoes** are useful for walking along the school's paths.

ACCESS

By plane:
From Geneva airport, shuttle reservation (back and forth) for transportation and drop-off, right at the Les Houches School.

Click here for shuttle reservations!

As previously indicated, please plan to arrive at the school **after 15:00**.

By car:
On the main road **Le Fayet/Chamonix**, get off at the **exit "Le Prarion/Les Chavants"**. In front of the Bellevue cable car, turn right, **direction "Les Chavants"** and continue for 3 km. Follow the indications at the various crossings.
Compulsory Parking on the upper lot indicated on the map.

Note: special winter equipment required.

By train:
From the train station Saint-Gervais Les Bains/Le Fayet: take the train in the direction of Chamonix and get off at the **Les Houches Station**.

Note: there is no taxi station at the train station. It is essential to **reserve a taxi in advance** (NB: the School is over 3 km away from the station).

By taxi:
Participants from abroad can contact the secretariat, which will reserve a taxi for them. In this case, send an email to the secretariat **no later than Wednesday afternoon prior to your arrival,** indicating the date and time of your arrival at the station.
Beyond this date, your request cannot be processed! Click here to email the secretariat!

- Cham Taxi : +33/0 6.07.26.36.62
- Taxi Plus : +33/0 6.12.35.30.72



ARRIVAL

NOTE: **The School opens at 15:00 on the arrival day**; It is important not to arrive on the site any earlier, as the buildings are closed before this time.

The School is located far away from the village, in an isolated location. There is no service nearby (shops and restaurants are more than 3 km away).

BUILDING CÉCILE DEWITT

(ex Jacassière)

The **Cécile DeWitt building** is the main building, where you will find:

- **The accommodation plan**: this indicates the name of the chalet and the room number that you have been assigned. **Note**: the chalets' access codes sent by email must be saved in order to access the buildings/bedrooms (saved on a mobile phone but not printed out)
- **Nominative pigeonhole**, in the entrance hall: this contains information and a badge.

Attached is a "Practical information" sheet that summarizes the essential information on the campus. From the opening of the school, all buildings are accessible 24/24 and secured by access codes.

LODGINGS

Ensuite Bedrooms are individual, and distributed among eight buildings located on the school campus.

A safe is available in the closet of each bedroom.

Provided: bedsheets, towels, shower gel, shampoo, and hair-dryer.

On the last day of the conference, the bedrooms must be vacated by 9:00 am at the latest. **It is not possible to extend your stay before or after the dates and time indicated.**

CATERING

On the day of arrival, the first meal is dinner. On departure (Friday), the last meal is lunch, after the last lecture.

Any diet requirement must be indicated to the organizers.

Meal times:

- Breakfast from 7:45 to 8:45
- Lunch at 12:30
- Dinner at 19:30

We ask you to be on time.

It is useful to have some cash in euros on you to pay for your purchases at the bar located on the ground floor of the restaurant.

A telephone will be available in the restaurant hall, to receive calls (only) during meal times. Number: +33/0 4 57 04 10 49.

WI-FI

Wi-Fi is available in all buildings and accessible via EDUROAM, which is strongly recommended to use. Also, an individual Wi-Fi access code is provided, but this does not allow you to connect with multiple devices at the same time.

OTHER INFORMATION

- A headlamp or flashlight is useful for walking around the site in the evening and at night
- The School has only collective insurance
- Electricity: 220V AC
- Local time: GMT +2
- Animals are not admitted on the site.

Posters abstracts

New approach to glycoamphiphiles integrated in a liquid cristal-based biosensor for pathogen lectin detection

Aïcha Abdallah, Emilie Gillon, Anne Imberty, Sami Halila*

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Glycoconjugates present on membrane cell surfaces play critical roles in a wide variety of pathological processes acting as signaling, recognition, and bacterial adhesion. Consequently, major scientific and biotechnological interests in glycoconjugates derive from their use as probes for biological research, and lead compounds for diagnostic tools[1].

The project of this research aims at developing a modular access to GlycoAmphiphiles (GAs) for the liquid crystal-based optical detection[2] of carbohydrates interacting with lectins coming from opportunistic pathogens such as *Pseudomonas aeruginosa*[3].

This poster will discuss about the synthesis of GAs by *N*-aryl-glycosylation of unprotected carbohydrates. The recognition between the carbohydrates part of our GAs and their specific pathogenic lectins has been studied using isothermal titration calorimetry(ITC). The stability to chemical hydrolysis of the *N*-glycosidic bond was also analysed using HPLC.

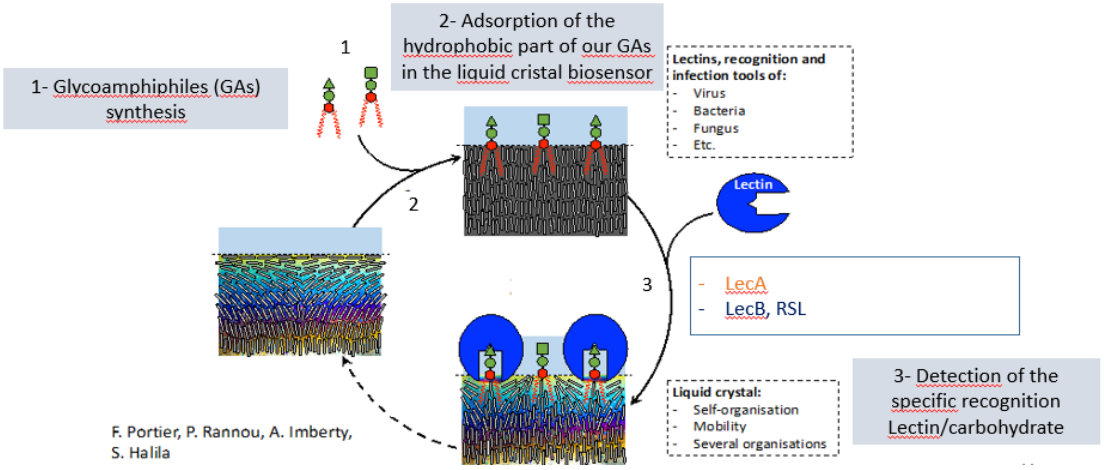

Figure 1: Simplified abstract schema.

References :

(1) Varki, A. Biological Roles of Glycans. *Glycobiology* 2017, *27* (1), 3–49.

(2) Qu, R.; Li, G. Overview of Liquid Crystal Biosensors: From Basic Theory to Advanced Applications. *Biosensors* 2022, *12* (4)

(3) Imberty, A.; Wimmerová, M.; Mitchell, E. P.; Gilboa-Garber, N. Structures of the Lectins from Pseudomonas Aeruginosa: Insights into the Molecular Basis for Host Glycan Recognition. *Microbes and Infection* 2004, *6* (2), 221–228.

Keywords : carbohydrate chemistry, glycosylation, lectin, biosensor, pathogen.

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Development of integrated micro-electro-apta-sensors into a diabetes organoid-on-a-chip device

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In diabetic individuals, adipose tissue cells exhibit chronic low-grade inflammation(1), the mechanisms of which are not yet clearly established. In ordrer to better understanding those mechanisms and associated secretions, scientits are developing organoid-on-a-chip systems that mimic the biological functions of studied organs. However, there is a need to develop integrated miniaturized sensors to monitor chemical or biological markers secreted by organs. The aim is to develop a multiplexed miniaturized system for continuous, real-time and non-invasive monitoring of the secretion of blood markers for the inflammation in a organoid-on-a-chip device. To produce this system of electrochemical microsensors based on aptamers, we propose to study an innovative cold atmospheric plasma technology, which would allow to co-deposit conductive polymers and aptamers on the electrodes(2).

References :

(1) Fève, B. ; Bastard, J-P. ; Vidal, H., Les relations entre obésité, inflammation et insulinorésistance : acquisitions récentes. C. R. Biol. 2006, 329 (8), 587-597

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Keywords : Biosensors, Aptamers, Electrochemical, Atmospheric Plasma

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Surface-confined host/guest electrochemical switching

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Different systems based on host/guest interactions have been developed for analytical and biomedical applications. One of the strategies uses redox-sensitive interactions between guest ferrocene (Fc) and host β-cyclodextrin (β-CD) [(1)]. Using this approach, different molecules and nano-objects have been reversibly assembled on planar surfaces for the controlled binding of molecules and biological entities such as cells. Our objective is to extend this strategy to nanostructures such as nanoparticles (NPs) or patterned nanoarchitectures and to design fluorescence switches based on the tunable NP/fluorophore distance (Fig. 1A). Our recent study on thermosensitive polymers proved the possibility of such switching [(2)]. Our first results on model planar surfaces show successful co-immobilization of Fc and β-CD (Fig. 1B), while their complexation strongly depends on the surface chemistry (diluting thiol, β-CD/Fc ratio, linker nature, etc.).

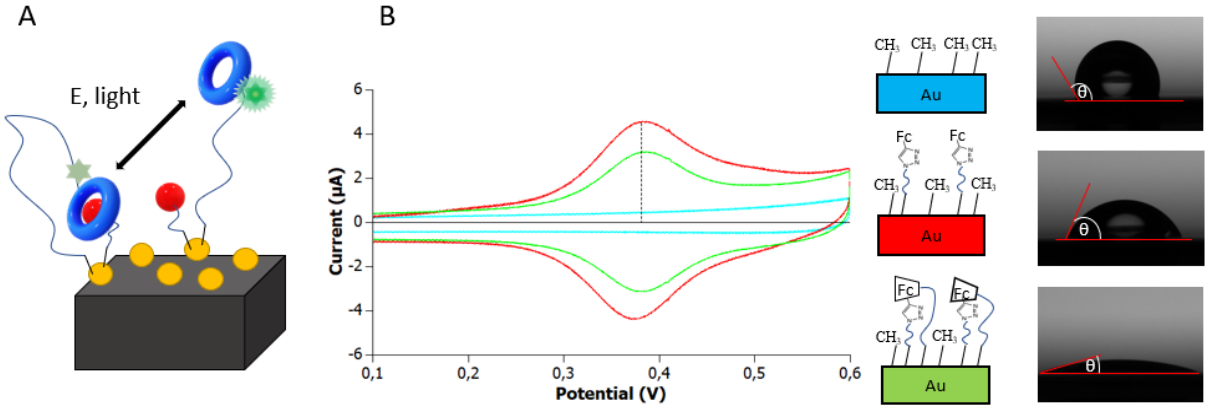

Figure 2: A. Host/guest system on nanostructured surfaces. B. Cyclic voltammetry showing Fc response with and without β-CD (left), supported by contact angle results (right).

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[(1)] G. Dubacheva et al., Langmuir 2010, 26, 13976-13986

[(2)] G. Dubacheva et al., Langmuir 2021, 37, 37, 10971–10978

Keywords : surface chemistry, supramolecular interactions, electrochemistry, fluorescence, nanostructures.

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Growth of intestinal cells under different levels of curvature varying over time

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The intestine is an organ with many levels of curvature, deformed by a combination of muscular, mainly related to digestion, and external movements produced for example by the passage of the food bolus. This complex architecture can be affected in case of severe pathologies(1) that are not yet fully understood and still require effective treatments. A promising approach, the Gut-on-Chip, consists in partially reproducing the intestine to study the influence of a treatment on its various structural, mechanical and chemical parameters(2,3). However, the movement and deformation of the intestinal epithelium remain poorly studied, although they are predominant in the gut. To develop this aspect, we grow several types of epithelial cells, such as intestinal organoids (Fig. 1a)(4), on different substrates reproducing the intestinal villi (Fig. 1b), and which can be deformed by a magnetic field (Fig. 1c).

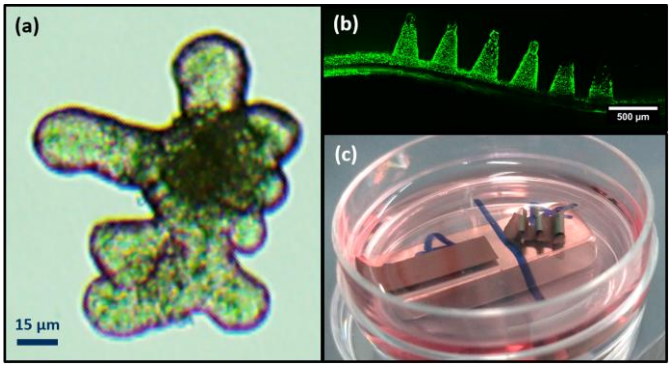

Fig. 1: Pictures of the cells and substrates employed. (a) Picture of a gut organoid cultured in 3D. (b) Villi replicas on a deformed membrane covered with MDCK (Madin-Darby Canine Kidney) cells (green represents nuclei, H2B-GFP). (c) Magnetic membranes covered with Caco-2 (Cancer Colon) cells in a 35mm petri dish on a permanent magnet.

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Keywords: Intestine, Organ-on-Chip, Magnetic composites, Tissue mechanics

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Toward a SPR imaging in situ system to detect domoic acid,

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Harmful Algal Blooms are increasingly recognized as impacting the coastal ecosystem and the economics of fisheries and shellfish farms. Blooms of Pseudo-nitzschia producing a neurotoxin known as Domoic Acid (DA) are of increasing concern as their frequency and intensity increase rapidly. Although these toxic algal blooms represent a serious public health and economic problems, no cost-effective device, allowing the detection of dissolved DA in seawater is not yet available on the market. Surface Plasmon Resonance (SPR) biosensors have demonstrated their ability to detect small molecules at very low concentrations in real-time. We recently reported a rapid SPR immunosensor inhibition assay to measure dissolved DA in the seawater matrix in-field deployment. However, this first prototype suffered from certain limitations. Multiplexing the assay increasing of the detection range, reproducibility and sample replicates are now required. Thus, a new biosensor based on SPR imaging (SPRi) technique is currently under development.

Keywords :

SPR, Immunosensor, Domoic acid, coastal monitoring

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Interaction of gold nanoclusters with membranes for labeling and encapsulation

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According to their high electron density and ultrasmall size, gold nanoclusters (AuNCs) have unique luminescence and photoelectrochemical properties that make them very attractive for various biomedical fields. These applications require a clear understanding of their interaction with biological membranes to enhance their biocompatibility and delivery efficiency.

We demonstrate the ability of the AuNCs as markers for lipidic bilayer structures such as synthetic liposomes and biological extracellular vesicles (EVs). The AuNCs can selectively interact with liposomes or EVs through an attractive electrostatic interaction as demonstrated by zetametry and fluorescence microscopy. The strong adsorption of AuNCs can result in the formation of a lamellar phase as demonstrated by cryo-transmission electron microscopy and small-angle X-ray scattering techniques.[1] In addition, the high colloidal stability of the C3E6D NC and their ultra-small size makes possible to encapsulate the C3E6D NC into synthetic liposomes (GUVs, LUVs, SUVs) with a high efficiency by preserving the bilayer integrity and the vesicle morphology.[2]

So these ultra-small and stable gold nanoclusters can serve as biomarkers of lipidic membranes such as EVs; furthermore liposomes encapsulation can serve as cargo to bring Au NCs into cells or EVs for in-situ biosensing or drug delivery.

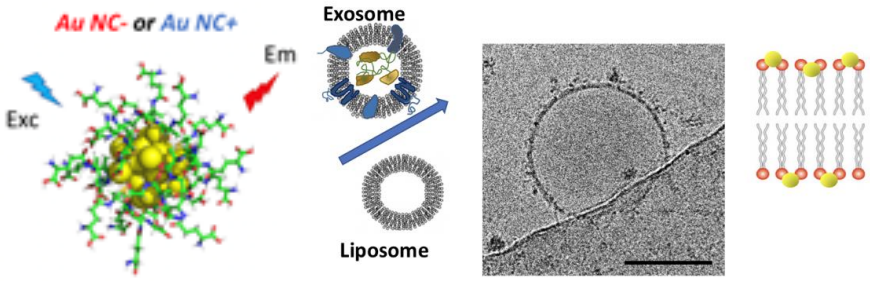

Figure 1: (a) Scheme of the gold nanoclusters, (b) Interaction with liposomes or exosomes

[1] Chiechio, R. M.; Ducarre, S.; Moulin, G.; Dupont, A.; Marets, C.; Even-Hernandez, P.; Artzner, F.; Musumeci, P.; Franzò, G.; Ravel, C.; LoFaro, M. J.; Marchi, V. Luminescent Gold Nanoclusters Interacting with Synthetic and Biological Vesicles. J. Phys. Chem. Lett. 2022, 13 (30), 6935–6943. https://doi.org/10.1021/acs.jpclett.2c01071.
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Screening of peptides by phage display for the development of biosensors

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Campylobacter jejuni and *Bacillus cereus* are two pathogenic agents that cause of millions of foodborne illnesses every year[1]. Thus, their rapid and sensitive detection is a key element for the efficient prevention of these diseases. This work focuses on the development of novel highly sensitive detection peptide probes through phage display. This technique is used to select highly specific peptides out of an initial pool of billions of candidates through a screening process[2]. Once the candidates have been selected, they will be tested using Surface Plasmon Resonance imaging (SPRi) in order to validate their affinity for the desired targets. Finally, we will select a small number (~5) of peptides with the highest affinity and focus on the fabrication of an electrochemical biosensor and an optoelectronic nose[4] for bacteria cell/spore recognition through the immobilization of these sensing molecules onto functionalized sensor surfaces.

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Keywords: Phage Display, peptide, biosensor, foodborne pathogen, detection, electronic nose.

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Brownian Motion as a Probe of Complex Surfaces

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In blood vessels, red blood cells flow further away from the vessels' walls than their white counterparts, the former being softer. Understanding and harvesting such elastohydrodynamic-related effects could lead to contactless ways to probe complex materials. To address this matter, a novel method based on Mie holography and stochastic inference was developed in the group(1). In a nutshell, the 3D trajectory of a Brownian sphere diffusing in salted water on top of a rigid glass surface is recorded and analyzed. Specifically, surface forces are measured down to a few femtonewtons, only limited by thermal noise (see Fig. 1). Also, fine deviations from the bulk Gaussian statistics of displacements are measured(2). This method, being contactless and relying only on a thermal excitation, is promising to cope with soft and fragile materials. Tests are now run on elastomeric ones.

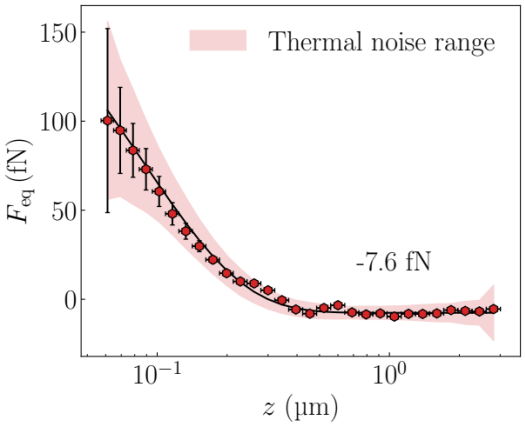

Fig. 1: Equilibrium force F_{eq} as a function of the separation distance z between a Brownian sphere diffusing in salted water and a glass wall. The force includes electrostatic repulsion and weight. The red dots correspond to experimental data, the solid line to the theoretical expectation, and the red-colored region to the theoretical thermal-noise limit.

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Keywords : Brownian motion, Mie holography, Stochastic inference, Contactless microrheology, Elastohydrodynamics.

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Inhibition of *Pseudomonas aeruginosa* by combining biosourced materials and *Staphylococcus epidermidis*

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In case of diabetes or burns, skin wounds are a gateway for bacteria to infect patients. Bacteria such as *Pseudomonas aeruginosa* (*P. aeruginosa*) are particularly harmful due to their facility to become resistant to therapeutic agents. In recent years, playing with skin microbiota[(1,2)] (especially *Staphylococcus epidermidis*[(3)] – *S. epidermidis* -) appeared as a novel way for anti-pathogen therapy. In this project, we study the antibacterial effect of *S. epidermidis* included in hydrogel containing a biosourced component A supplemented or not by a naturel extract B. The growth of *P. aeruginosa* is fully inhibited in the hydrogel composed of A, B and *S. epidermidis*, and a difference in Pseudomonas colony shape is observed. The next step will be to determine the risk of dispersion of *S. epidermidis* from the hydrogel and which substance(s) from *S. epidermidis* or/and natural extract B are responsible for *P. aeruginosa* inhibition.

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Keywords: Microbiota, *Pseudomonas aeruginosa*, *Staphylococcus epidermidis*, hydrogel, inhibition, bacteriotherapy.

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Agarose-based hydrogels: Effect of sucrose and glycerol on the antibacterial, physicochemical, and mechanical properties

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Agarose hydrogels are susceptible to microbial colonization yet have several uses in biomedicine due to their biocompatibility, self-gelling properties, water solubility, and tunable physicochemical and mechanical properties. Agarose hydrogels containing different concentrations of glycerol and sucrose as additives were synthesized in this study. The antibacterial efficiency of the hydrogels against *Staphylococcus epidermidis* and *Pseudomonas aeruginosa* in planktonic and biofilm states was investigated. Also, the surface elasticity and wettability, viscoelasticity (bulk), and hydration capacity of the hydrogels were analyzed. The addition of sucrose and glycerol decreased the hydration capacity and elasticity of the hydrogels but increased their antibacterial efficiency against *S. epidermidis* and *P. aeruginosa*, especially their biofilms. The hydrogels have the potential for use in wound dressing and bioprinting.

Keywords : agarose, antibacterial, hydrogel, sucrose, glycerol

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Investigation of the Antibacterial Properties of Silver-Doped Amorphous Carbon Coatings Produced by Low Pressure Magnetron Assisted Acetylene Discharges

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Hospital-acquired infections are responsible for a significant part of morbidity and mortality. Among the possible modes of transmission, this study focuses on environmental surfaces by developing innovative antibacterial coatings that can be applied on interior fittings in hospitals. This work aims to optimize a coating made of an amorphous carbon matrix doped with silver (a-C:H:Ag) produced by a hybrid PVD/PECVD process and to evaluate its antibacterial activity. We present a coating characterization (chemical composition and morphology) as well as its stability in an ageing process and after multiple exposures to bacteria. The antibacterial activity of the coatings is demonstrated against Escherichia coli (Gram-negative) and Staphylococcus aureus (Gram-positive) bacteria through several bioassays. Moreover, the data suggest a crucial role of silver diffusion towards the surface and nanoparticle formation to explain the very promising anti-bacterial activities reported in this work.

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Keywords : antibacterial coating; a-C:H; Ag; nanomaterials; diffusion

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Surface structuring at the nano and micrometric scale for stem cell differentiation

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Incorporating peptides within biomaterials surface mimics the native extracellular matrix, enhances cell recruitment, and induces cell signaling pathways[1]. Chemical stimuli and geometrical cues are crucial to modulate cellular physiological activities[2]. Our group has demonstrated that RGD/BMP-2 mimetic peptides enhance the osteogenic differentiation of MSCs (mesenchymal stem cells) when spatially distributed as specific micro-sized geometric cues[3]. Since it is well recognized that nano-scale structures have more significant effects on the adhesion and differentiation of cells[4], my thesis aims to investigate the impact of such engineered nanostructures on MSCs differentiation towards osteoblastic lineage.

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Keywords: patterning, mimetic peptides, BMP-2, stem cell differentiation, bone tissue engineering

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Engineering bioactive hydrogels with tunable mechanical properties for the control of stem cell differentiation

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**These authors contributed equally*

It is known that the *in vitro* differentiation of mesenchymal stem cells (MSCs) is affected by the stiffness [(1)] and viscoelasticity [(2, 3)] of the substrate in which they are cultured. However, it is necessary to further define the interplay between these mechanical characteristics and the presence of bioactive molecules. In this context, our research challenge is to develop a material that encompasses the optimal properties to obtain osteogenic differentiation of MSCs.

Hydrogels are fabricated by combining polymer chains of different lengths. The mechanical properties are evaluated at the macroscale and at the surface level. Two peptides are used for functionalization to enhance adhesion and differentiation. hMSCs are cultured on these materials and their differentiation towards the osteogenic lineage is evaluated via immunostaining.

Future work will focus on the multifunctionalization of the materials with different biomolecules and on the fabrication of 3D porous scaffolds.

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Keywords : hydrogels, mechanical properties, peptides, stem cells, osteogenic differentiation

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Screening of specific aptamers for *Bacillus cereus* by Surface Plasmon Resonance imaging (SPRi)

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Bacillus cereus is a food poisoning bacterium present in dairy products. To detect it, antibody based biosensors are efficient but antibodies are expensive and may cross-react with other *Bacillus* species. Aptamers are a good alternative to these issues. Herein, seven aptamer sequences derived from the literature[(1,2)] are compared and their specificity to *B. cereus* is assessed versus *Escherichia coli* and *Bacillus subtilis* by Surface Plasmon Resonance imaging. The grafting strategy was optimized to enhance aptamer density on the chip and avoid nonspecific adsorption. Bacteria were fragmented into nanosomes for better sensitivity. The results highlighted a better affinity of the aptamer SP15 for *B. cereus* nanosomes and the importance of the G-quadruplex form for the recognition. This has to be confirmed by NMR studies and the affinity constants of the best aptamer sequences will be calculated by ELISA.

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Keywords : *Bacillus cereus*, aptamer, SPRi, nanosomes, biosensor

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Gold nanoparticles with various morphologies and coatings for Physics, Chemistry, Biology and Health

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Our team specializes in the synthesis, interface control, and assembly of high quality gold nanoparticles for research in the fields of plasmonics, plasmon-driven chemistry, sensing and health. We develop ligand-exchange protocols and synthesize all kinds of monodisperse gold nanoparticles (NPs), including perfect spheres, cubes, nanodisks and microplates to provide suitable materials. The properties of these nanostructures are studied in collaboration with expert teams in various field. We have a 2 years postdoctoral position to develop a know-how in the preparation of 2D-metasurfaces by self-assembly of gold NPs at the liquid-liquid interface.

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Enhanced 2D cell adhesion on chitosan hydrogel through fibronectin coating and grafting

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Thermosensitive hydrogels based on chitosan (CS) and phosphate salts have been studied for decades[1] for biomedical applications. Recently, a cytocompatible formulation mixing two phosphate salts and CS has been developed[2], providing controlled gelation, physiological pH and osmolarity, and a macroporous structure for cell encapsulation. However, CS lacks binding sites for cell adhesion, and the metabolism of encapsulated cells declines over 24h. In this work, a glycoprotein involved in cellular processes[3], fibronectin (Fn), is grafted to CS (CS--Fn), still retaining the thermogelling properties of the system. Adhesion of MPNST cells on 2D substrates was evaluated by coating Tissue Culture Polystyrene (TCP) and CS hydrogel with free Fn, grafted CS--Fn or simply mixed CS+Fn (Figure). Improved adhesion found on grafted hydrogels will be translated to 3D encapsulation.

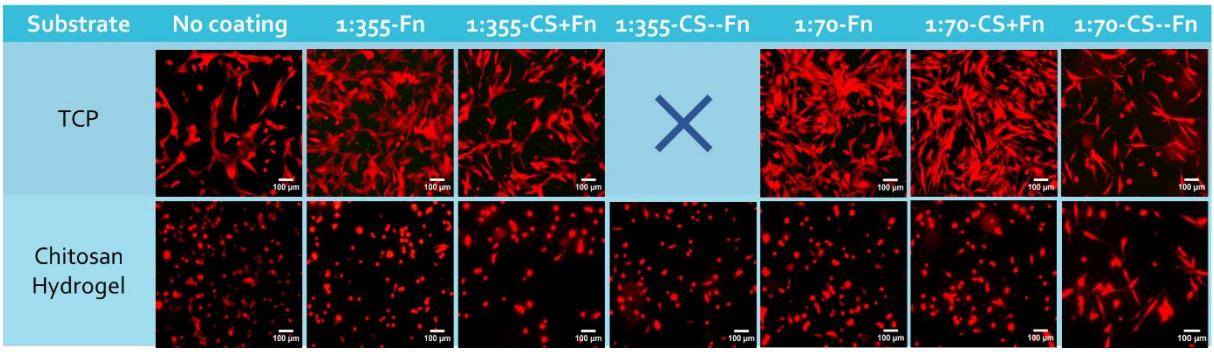

Figure: MPNST cells on coated TCP or CS hydrogel substrates after 48h incubation. 1:355 = 1 Fn for 355 CS chains; 1:70 = 1 Fn for 70 CS chains. Scale bar = 100 µm.

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Keywords: Thermosensitive chitosan hydrogel, Fibronectin coating, Fibronectin grafting, Cell adhesion

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Microscopic studies of luminescent carbon nanodots as myelin dopants

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Carbon nanodots (CNDs) are the nanostructures of multiple possible applications ranging from optoelectronics to bioimaging. In the frame of our studies we explore the non-linear optical properties of CNDs and their effective use in doping to the myelin structures.

Myelin sheath, exhibiting liquid crystalline properties, plays a crucial role in the propagation of action potential [1-2] . Many studies have focused on the importance of relevant model systems to better understand the behavior of biological membranes [3]. Therefore, the combination of luminescent nanomaterials with diverse biological components, such as phospholipids [4] , gains considerable attention for their potential applications in bioimaging.

In this work, we discuss the formation of synthetic myelin figures (MFs) made of phosphatidylcholines and doped with blue- and green-emitting carbon nanodots. To get insight into the details on the morphology of the multilamellar structures, we used the combination of polarized light and fluorescence microscopy techniques. Moreover, our studies indicate two-photon excited fluorescence microscopy (2PEFM) as a powerful method to study a three-dimensional view of the distribution of CNDs within MFs. Taking advantage of 2PEFM, we showed that the multilamellar tubes with dopants can be excited by wavelengths lying in the near-infrared region that corresponds to the first biological window, thereby providing deeper penetration depth and preventing strong photobleaching [5].

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Keywords : myline, carbon nanodots, two-photon microscopy, lyotropic liquid crystals, bioimaging

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Antimicrobial protections: combining chemical functionalization and nanostructuring to further explore cell/surface interactions.

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Microbial proliferation in human environments has been one major public health concern for years, especially due to recent pathogens growing antibiotic resistance. To effectively tackle infections, it is crucial to develop surfaces limiting pathogens adhesion and proliferation in their early stages. To provide antimicrobial properties to materials, two main approaches are explored: chemical functionalization using bioactive or anti-adhesive agents [(1)] and physical micro and nanostructuring, often inspired by natural surfaces such as cicada wings [(2)]. The main objective of this poster is to present the first results of the PhD exploring the potential synergy of these two methods, as it has been too little considered. The antibacterial effects of peptides coated surfaces, as well as gold electrodeposited nanostructured surfaces will be presented.

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Keywords : Cell-surface interaction, Antimicrobial surfaces, Peptides, Nanostructuring, Electrodeposition

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INVESTIGATION OF ELECTROFUNCTIONALIZATION AND ELECTROCHEMILUMINESCENCE ON SILICON

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The complexity and heterogeneity of the biochemical responses inside a population of immune cells is well known and underlines the need for single-cell analyses. Unfortunately, tools to kinetically achieve the measurement of cytokines at the cell level are not yet available. We propose the development of a microfluidic device, which allows single cell isolation, and detection of its secretory activity.

Our approach for secretion monitoring is to combine:

- The localized grafting of biomolecules in microfluidic restrictions on silicon using bipolar (BP) electropolymerization [(1)].
- The localized electrochemiluminescence (ECL) on the polymerized area.

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Keywords : electropolymerization, electrochemiluminescence, biosensor, microfluidics, cell secretions

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Studying and Imaging biofilm grown in porous media under flow

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Understanding the couplings between flow and bacterial growth in porous media is an important problem with applications ranging from soil bioremediation to groundwater contaminations, filter clogging or wastewater processing. In such systems, bacteria primarily develop within biofilms, dense colonies where cells are embedded in a self-produced matrix of extracellular polymeric substances that can substantially clog porous structures. Here we present a new bioreactor technology, combining 3D printing with a range of inline sensors and X-ray imaging relying on a newly developed functionalized gold contrast agent, that can be used to study the dynamics of biofilm clogging in porous media. We further present an experiment for the growth of Pseudomonas aeruginosa where we show a complex dynamic with no steady-state but rather a competition between growth and detachment.

Keywords: Biofilm, porous media, dynamic, 3D printing, imaging.

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Directing cell fate: biomimetic hydrogels for hMSC osteogenic differentiation

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Tissue engineering scaffolds that replicate, in a single material, the natural properties of the ECM required to fully control stem cell fate are quite rare. Following this attempt, we developed a biomaterial platform based on lysine dendrigrafts (DGLs) and polyethylene glycol (PEG) hydrogels for the differentiation of human mesenchymal stem cells (hMSCs) to the bone lineage. Nanoparticles composed only of lysine units, DGLs present surfaces rich in amine groups, making them biocompatible and highly versatile crosslinkers to form hydrogels of tunable stiffness, over a very broad range (fig. 1a-b). Rheological analysis also shows a viscoelastic behaviour in some cases (Fig. 1c). We modified the hydrogels surface with biomimetic peptides, to promote hMSCs adhesion and differentiation. After seeding, hMSCs adhere to the surface no signs of cytotoxicity. The osteoinductive bioactivity will be quantified by measuring the expression levels of key hMSCs markers by fluorescence microscopy and qPCR.

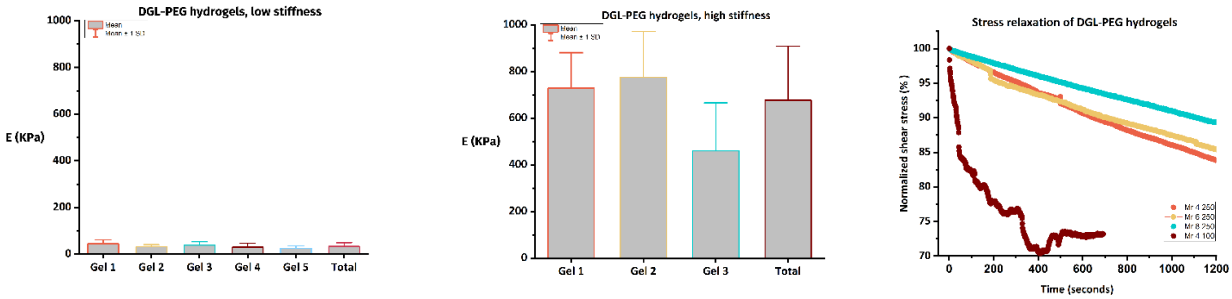

Fig. 1a (left and middle); 1c (right)

Keywords: scaffold, hydrogel, lysine dendrigrafts, stem cells, bone

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Developing hydrophobic poly(V3D3) surfaces to inhibit bacterial adhesion

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Biofilm is a major problem that affects many different fields from medical devices to the marine industry. The most direct way of combatting biofilm is killing the bacteria. However, concerns over biocide toxicity and antibioresistance have led scientists to question this strategy. Indeed, another way to fight biofilm development is to inhibit the initial adhesion of bacteria[1]. To do so, hydrophobic surfaces can be a solution, as an air barrier is created at the interface, limiting contact between the surface and the bacteria. In this study, V3D3 is deposited by two different techniques: Dielectric Barrier Discharge Cold Atmospheric Plasma (DBD-CAP)[2] and initiated Chemical Vapor Deposition (iCVD)[3,4]. These methods lead to the formation of thin films with different chemistries but both with hydrophobic properties. Fluorescence microscopy demonstrated lower adhesion of E.coli on poly(V3D3) surfaces than on SiO_2 after 6 and 48 h incubation in Mueller Hinton media.

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Keywords : surface fonctionnalisation, plasma deposition, initiated chemical vapor deposition, antibiofouling

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Exploiting disordered mimic peptide micropatterning for cell differentiation

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Stem cells display the ability to serve regenerative purposes by making choices for survival, self-renewal, and differentiation in a regulated manner.[1] The recent advances in tissue engineering and regenerative medicine have been promoted by several protocols inducing in vitro stem cell differentiation.[2] In vivo, the cellular microenvironment has a crucial impact on regulating cell behavior and functions.[3] We aim to create a smart microenvironment of mesenchymal stem cells (MSC)In this study, we investigate effects of density and distribution of adhesion and differentiation ligands grafted onto a polymer surface on osteoblastic differentiation of MSCs.

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Keywords : Spray; Chemical micropatterning; Surface modification

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Development of a fabrication process for a bio-based lab-on-a-chip

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Lab-on-a-chip (LoC) are microfluidic devices integrating miniaturized functions of a classical laboratory, allowing them to perform single-cell analysis. Currently, the fabrication of these microsystems is dependent on polymers derived from the petrochemical industry, such as PDMS or thermoplastics.(1) To reduce the impact of their extraction and disposal, the integration of bio-sourced and biodegradable materials in the fabrication is paramount. In this study, we focus on developing a fabrication process based on chitosan, a biodegradable and very abundant polysaccharide resulting from the valorization of seafood industry waste.(2) We have obtained rigid films of a few millimeters thickness, transparent, insoluble in water on which we patterned microfluidic channels and bounded to a glass slide. This study paves the way for the development of more complex and sustainable LoC integrating various functions.

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Keywords : chitosan, lab-on-a-chip, microstructuration

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