

7th Plenary Days of GDR B2i

July 3rd-4th, 2024

Mulhouse (Haut-Rhin, France)



The Booklet



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Understanding Interfaces



Seeing beyond

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I. About the conference

This year, the GDR Bioingénierie des Interfaces organizes the plenary meeting from 3rd to 4th July 2024 in Mulhouse in the heart of the Alsace region (<https://gdr-b2i-2024.sciencesconf.org/>).

The GDR Bioingénierie des interfaces (B2i) focuses on the interface between materials and biological environments in the broadest sense. The scientific scope of this GDR includes the development, characterization, and modeling of biointerfaces for applications in the fields of tissue engineering, antifouling, biosensors, but also for the study of biological mechanisms or specific interactions. Due to its interdisciplinary nature, the GDR B2i brings together teams working in the fields of (bio) physical chemistry of materials and interfaces, and biology. To know more about the GDR B2i, please see https://events.femto-st.fr/GdR_B2i/fr.

The aim of these days is to stimulate new collaborations and create synergies among the GDR member teams by sharing the latest research advances with the community. The scientific program includes invited lectures, oral and poster presentations, and best oral and poster awards for young researchers.



Three special sessions

Cancer: treatment and detection.

Invited talk by Elena Ishow (Nantes Université)

“Photoactive organic nanoparticles as tunable actors for theranostics”

Materials and Light.

Invited talk by Christophe Moser (EPFL)

“Volumetric Bioprinting: a new tool for producing artificial tissue models”

Bacteria/Material Interactions.

Invited talk by Régis Grimaud (Université de Pau et des Pays de l’Adour)

“Biofilm formation: a microbial strategy to assimilate particular substrates”

II. Program

Invited and other oral presentations will last 40 and 20 minutes each, respectively, including discussion with the audience.

Wednesday, July 3rd

8:30-9:00	<i>Registration</i>
9:00-9:20	<i>Welcome address</i>
	Session 1 Cancer: treatment and detection.
9:20-10:00	Invited talk by Elena Ishow (Nantes Université) “Photoactive organic nanoparticles as tunable actors for theranostics”
10:00-10:20	Axelle AUBERT “Towards a development of electro-apta-sensors to detect biomarkers of inflammation”
10:20-10:40	Wilfrid BOIREAU “Multiplex characterization and quantification of extracellular vesicles in multiple myeloma”
10:40-11:00	<i>Coffee break & posters</i>
	Session 2 Cell & protein / material interactions
11:00-11:20	Eve RANDRIANARIDERA “Development of an in vitro foreign body reaction model to evaluate silicone influence on fibrinogen conformation and macrophage polarization”
11:20-11:40	Guillaume LEKS “Evaluation of a new pediatric prosthesis made of thermoplastic elastomeric poly(urethane) (TPU) functionalized with polydopamine and type I collagen”
11:40-12:00	Marie-Ly CHAPON “Role of substrate curvature in cell migration and tissue morphogenesis”
12:00-12:20	Charlotte VENDRELY “Interactions of a protein inspired from a barnacle adhesive cement with different material surfaces”
12:20-12:30	Erik NILEBÄCK (Quantum Design) “Introducing QSense Omni – a new era for QCM-D analysis”
12:30-14:30	<i>Lunch & posters & demo</i>

	Session 3 Materials and Light
14:30-15:10	Invited talk by Christophe Moser (EPFL) “Volumetric Bioprinting: a new tool for producing artificial tissue models”
15:10-15:30	Guillaume NONGLATON “Development of an integrated biofunctionalized silicon photonic platform for allergen immuno-detection in food matrices”
15:30-15:50	Angélique SIMON-MASSERON “Zeolite-based composites for biomedical applications”
15:50-16:00	Grégory MICHEL (ZEISS) “3D Imaging Technology: what & why?”
16:00-16:20	<i>Coffee break & posters</i>
	Session 4 Nano-objects & nano-structuration
16:20-16:40	Laurent VONNA “Macrophage internalization dynamics of adsorbed submicron and nanoscale silica particles: insights for biomedical coatings”
16:40-17:00	Dahlia SAAD “1D and 3D-AFM characterization of liquid/polymer brushes (PAA, PEO)/gold interfaces”
17:00-17:20	Jilong LI “Lysozyme-responsive core-shell nanoparticles formed by pH-drive and transglutaminase cross-linking and their properties”
17:20-17:40	Milan TOLEDO NAUTO “Non-covalent nanobody biofunctionalization of organic electrochemical transistor (OECT) for the specific detection of chlordecone”
17:40-18:00	Philippe STEMPFLE “Optimization of a new venous stenosis treatment self- expanding nitinol stent using a multi-scale tribological approach from catheter to the veins”
18:00-18:10	Véronique SCHLOUPT (DATAPHYSICS INSTRUMENTS) “How to analyse surfaces in regard to their electrical charge in a liquid solution: Zeta potential measurements in practice”
18:10-19:30	<i>Social event</i>
19:30	<i>Evening at Lerchenberg</i>

Thursday, July 4th

	Session 5 Bacteria/material interactions
9:00-9:40	Invited talk by Régis Grimaud (UPPA) “Biofilm formation: a microbial strategy to assimilate particular substrate”
9:40-10:00	Thibaut ZWINGELSTEIN “Development of a specific microfluidic bio-interface for the detection of pathogenic bacteria in the agro-food industry”
10:00-10:20	Capucine LOTH “Ion triggered self-assembly of antibacterial Fmoc-based tripeptide: physical chemistry and MD simulation”
10:20-10:50	<i>Coffee break & posters</i>
10:50-11:10	Marie CHAMPION “Hydrophilic antiadhesive coating to prevent marine organisms' colonization”
11:10-11:30	Lylia FELLAH “Study of the antibacterial impact of photocatalytic surfaces in the marine environment”
11:30-11:50	Corinne NARDIN “Polymer coatings to prevent microbially influenced corrosion”
11:50-12:10	Gwenaël CORBEL “Water disinfection with Cu(OH) ₂ nanorods”
12:10-12:30	Lydie VIAU “Antibacterial surfaces prepared by electropolymerization of pyrrole-tailed imidazolium ionic liquids”
12:30-12:50	Ahmed HAMRAOUI “Challenges in modulating surface energy to optimize axonal growth”
12:50-13:00	<i>Awards & Conclusion</i>
13:00	Lunch (box)

III. Biographies and abstracts

1. Invited speakers' presentations and talk summaries

Elena ISHOW

Full Professor

Laboratoire Chimie et Interdisciplinarité, Synthèse, Analyse, Modélisation (CEISAM)

Nantes Université (France)



Eléna Ishow entered the Ecole Normale Supérieure de Cachan in 1990 in the Chemistry Department and prepared her Ph.D. in the group of Nanosciences at CEMES laboratory (Toulouse) under the supervision of A. Gourdon onto the elaboration of molecular wires (1997). She worked as a postdoctoral in the group of Prof. V. Balzani in Bologna (Italy) on photoinduced molecular machines fellow (1997-1998). In 1998, she was appointed assistant professor at ENS Cachan (nowadays ENS Paris Saclay) at PPSM laboratory in the group led by Prof. K. Nakatani and spent meanwhile a one-year sabbatical in T. Swager's lab at MIT (2003-04). She was promoted full professor at Nantes University in 2010, while joining CEISAM laboratory to carry out her research activities.

She has been developing light-responsive molecules and molecular materials (especially photoswitchable) for more than 25 years to address issues for second-harmonic generation and optical data storage, OLEDs, and hybrid magneto-fluorescent nanoassemblies for dual imaging and on-command theranostics. These various research axes have prompted her to initiate and participate in strongly interdisciplinary research programs at the interface of functional organics, materials science, photonics, biology, clinical psychology, and nanomechanics where light-matter interactions remain the common thread to either conceive the targeted systems or unravel collective phenomena.

Abstract

Photoactive organic nanoparticles as tunable actors for theranostics

The strong development of theranostic nanomaterials, advantageously combining therapeutics and diagnostics, has brought to the forefront fluorescent organic nanoparticles (FONs), made out of self-assembled -conjugated species. Their "smart" properties actually rely on the high payload of active units, the extensive interactions between the dyes, their ability to self-assemble with hydrophobic drugs, and eventually their large surface-to-volume ratio. There is nowadays no area left unexplored by such functional nanomaterials, amenable to multimodal bioimaging, drug delivery, biochemical sensing, or photodynamic therapy to cite only a few. Whatever the area, the first step relies on the mutual interactions developed between nanoparticles and their surrounding biological media. After a brief survey of the main classes of emissive nanoparticles and their potential pros and cons, we will show through selected examples how photoactive organic nanoparticles have been designed and harnessed to inform on their cellular internalization and fate, and offer dynamic follow-up of drug release as well as selective and minute-like diagnostics.

Christophe MOSER

Full Professor

Institute of Electrical and Micro Engineering (IEM)

École Polytechnique Fédérale de Lausanne (EPFL, Switzerland)



Christophe Moser is Full Professor of Optics in the department of Electric and MicroEngineering (IEM) at EPFL. He obtained his PhD at the California Institute of Technology in optical information processing in 2000. He co-founded and was the CEO of Ondax Inc (now Coherent Inc.), Monrovia California for 10 years before joining EPFL in 2010. His interests are Volumetric 3D printing, ultra-compact endoscopy through multimode fibers, retinal imaging and optical computing. He co-founded Composyt light lab in the field of head worn displays in 2014 (acquired by Intel Corporation in 2015). He is the co-founder of EarlySight SA (2019), Readily3D SA (2020) and Modendo (2021). He is a fellow of the European Optica Society. He is the author and co-author of over 100 peer reviewed publications and over 60 patents.

Abstract

Volumetric Bioprinting: a new tool for producing artificial tissue models

3D printing has revolutionized the manufacturing of volumetric components and structures in many areas. Several fully volumetric light-based techniques have been recently developed thanks to the advent of photocurable resins, promising to reach unprecedented short print time (down to a few tens of seconds) while keeping a good resolution (around 100 microns). However, these new approaches only work with homogeneous and relatively transparent resins so that the light patterns used for photo-polymerization are not scrambled along with their propagation. We will illustrate a method that considers light scattering in the resin prior to computing projection patterns. Light scattering in resins having a high cell density (> 4 million cells /mL) is severe and we will show that scattering correction method allows to print high-resolution structures.

We will show several examples of complex 3D tissue models including bone, liver and a pancreatic cancer tissue. This scattering correction extends the capabilities of conventional light-based volumetric printing which opens up promising perspectives for bioprinting cell-laden constructs.

Régis GRIMAUD

Full Professor

Institut Pluridisciplinaire de Recherche en Environnement et Matériaux (IPREM)

Université de Pau et des Pays de l'Adour (UPPA, France)



Régis Grimaud is Full Professor in the group Chemistry and Microbiology of Environment of IPREM at UPPA (France). He prepared his PhD at both the Université Libre de Bruxelles (Belgium) and Joseph Fourier University in Grenoble (France) in cell and molecular biology in 1995. Before joining the Université de Pau et des Pays de l'Adour (UPPA) in 2001, he conducted research at the Université Libre de Bruxelles (Belgium) and National Institutes of Health (Bethesda Maryland, USA) as a post-doctoral fellow. His interests are the molecular aspects of biofilms degrading hydrophobic organic compounds, and iron assimilation in marine bacteria. He is a fellow of the board of Société Française de Microbiologie (SFM) and is the author of over 60 peer reviewed publications.

Abstract

Biofilm formation: a microbial strategy to assimilate particular substrates

Heterotrophic bacteria are dependent on organic compounds to sustain their growth, but they can only absorb low molecular weight compounds dissolved in water. In natural habitats, a substantial part of the organic carbon is represented by polymeric substances (proteins, polysaccharides, lipids...) that are poorly soluble in water and occur as particles or adsorbed on surfaces and are therefore not directly assimilable by bacteria. Biofilm formation appears to be a strategy to overcome the low accessibility of nearly water-insoluble substrates and is therefore a critical process in the assimilation of organic matter. Since these biofilms develop on a nutritive interface that serves as both physical support and growth substrate, they also represent an original facet of biofilm biology. This presentation will focus on biofilm formation as a mechanism to exploit water-insoluble nutrients such as chitin, cellulose, or hydrocarbons that are inaccessible to planktonic bacteria. The most prominent mechanisms of biofilm formation on organic particles as revealed by studies on model strains will be reviewed, with particular emphasis on biofilm formation on lipids and hydrocarbons by *Marinobacter nauticus*.

2. Industrial sponsors

Quantum Design (Erik NILEBÄCK, Gauthier CABY)

Introducing QSense Omni – a new era for QCM-D analysis

Biolin Scientific are experts in surface science and we provide various analytical instrumentations based on widely adopted techniques for measuring surface properties and chemical interaction processes on surfaces. QSense is one of the product brands within Biolin Scientific and is world leader within QCM-D analysis and instrumentation.

QSense QCM-D is a surface sensitive technology that measures mass changes in real-time, i.e. time-resolved. It measures molecular interaction with surfaces, and you can follow these interactions as they happen by following the mass changes, i.e. mass uptake or mass loss. It also follows the viscoelastic properties of the layer, revealing if you have a rigid or soft structure.

During this presentation and live demo, the newly launched QSense Omni instrument will be introduced, and participants will have the possibility to see the instrument live.

An overview of the QCM-D technology will also be presented and technical experts from Biolin Scientific will be present to answer any questions regarding QCM-D or QSense products that the participants might have.

Carl ZEISS (Grégory MICHEL*, Michael GUE)

3D Imaging Technology: what & why?

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Since the arrival of confocal microscopy in the 1980s, microscopy has been enriched with numerous 3D microscopy techniques. Recently, Zeiss has developed new microscopy solutions in order to meet the challenges of modern microscopy resolutely focused on understanding dynamic mechanisms in the life sciences. The development of solutions such as Airyscan in confocal microscopy and more recently solutions based on Lattice illumination (Lattice Lightsheet & Lattice SIM) offer unprecedented compatibility with life imaging by protecting samples against the negative effects of the light [1]. Additionally, several solutions have been developed for electronic microscopy, such as Array tomography, FIB-SEM and serial block-face Imaging (Volutome). We will focus here on understanding which microscopy techniques are best suited to answer your biological questions.

[1] Sauer et al., Nature, 2015

Keywords: Imaging, Confocal microscopy, 3D microscopy, Electronic microscopy

DATAPHYSICS INSTRUMENTS (Véronique SCHLOUPT^{1*}, Michaela LAUPHEIMER², Dr. Sebastian SCHAUBACH²)

How to analyse surfaces in regard to their electrical charge in a liquid solution: Zeta potential measurements in practice

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The zeta potential ζ is a parameter for analysing the surface charge. More precisely, the zeta potential characterises the electrochemical properties near a solid surface in a liquid solution. If the zeta potential is known, it is possible to estimate whether attractive or repulsive forces occur between two surfaces. Depending on the size and shape of the samples, the zeta potential can be determined using different measurement techniques. For larger samples in the millimeter and centimeter range, the analysis of the streaming potential or the streaming current has proven to be advantageous. The ZPA 20 zeta potential analyzer from DataPhysics Instruments was developed especially for such samples. The device can be equipped with measuring cells for solid materials such as plates, membranes, or foils; a cell for fibers, powders, and granulates; as well as a cell for hollow tubes or fibers.

The ZPA 20 uses a patented measuring method to achieve results with high accuracy. It is the only device on the market measuring the streaming potential and current in a bidirectional and oscillating fashion. The electrolyte solution is pumped over or through the sample not only in one direction, but alternately in opposite directions. Additionally, the flow rate of the electrolyte liquid changes within every repeated cycle, resulting in pressure changes. Thus, results with excellent statistical quality are generated within a short time frame. The patented measuring method of the ZPA 20 does not only save time during the measurements, but also helps to reduce common sources of error, such as the polarization of device electrodes and asymmetries of the sample surface, due to inhomogeneous fiber or powder packages as well as insufficiently fixed flat samples.

Characterizing the zeta potential is important in many industries. This presentation highlights some use cases, in detail: how to determine the coating on a wafer surface [1], on a glass fiber fleece [2], on dialysis membranes, and on functionalized polyester fibers [3]. Additionally, the presentation analyses surfactant absorption processes while washing textiles [4], membrane fouling processes, and seawater desalination processes.

[1] Dr. Qiongjie Liu et al., 2023, <https://t.ly/H7xE7>

[2] Dr. Qiongjie Liu et al., 2023, <https://t.ly/hYNFw>

[3] Dr. Qiongjie Liu, et al., 2023, <https://t.ly/brsSa>

[4] M. Reischl et al., 2006, Materials Science Forum, 514–516, 1374–1378

Keywords: Zeta Potential, Surface Charge, Surface Analysis, Streaming Potential, Streaming Current

3. Oral contributions

SESSION 1: Cancer: treatment and detection

Towards a development of electro-apta-sensors to detect biomarkers of inflammation

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The aim of our work is to develop a system for real-time monitoring of the secretion of biomarkers of inflammation in an organoid-on-a-chip. The biosensor we intend to develop will be composed of a gold electrode coated with a conductive polymer onto which the selected aptamers, decorated with a redox probe, will be covalently attached. In the presence of their target, the aptamers will undergo a conformational change, inducing a variation in distance between the redox probe and the electrode, thereby altering the electrochemical signal for detection.

To produce this system, we divided the study into two parts. On the one hand, we have selected an aptamer targeting human interferon- γ (IFN- γ) which is one of the most important biomarker found in blood for inflammation. With this aptamer covalently modified at one end with methylene blue, which acts as a redox probe for electrochemical detection, we initially investigated the electrochemical detection of IFN- γ by grafting the aptamer onto a gold surface via a thiol bond.

On the other hand, we investigated the feasibility of depositing a conductive polymer onto electrodes using Dielectric Barrier Discharge Cold Atmospheric Plasma (DBD-CAP), which involves nebulizing a monomer at the center of a torch composed of two concentric electrodes (Fig. 1). The advantages of this deposition technique are that it is fast, solvent-free, and easy to industrialize.

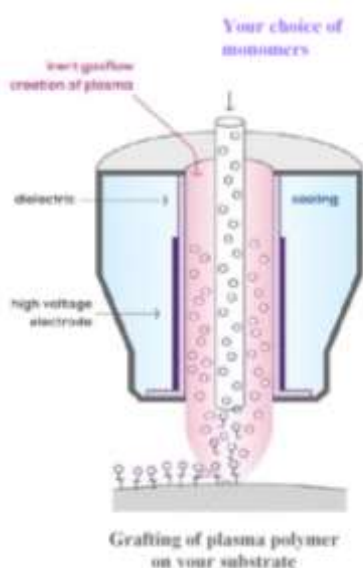


Figure 1. Scheme of the torch plasma (source: molecularplasmagroup.com)

The initial results of these studies will be presented, along with a future outlook, including the investigation of the electrical conductivity of the polymer deposit, the aptamer grafting onto this polymer deposit, and the exploration of aptamers targeting other cytokines such as Interleukin 6 (IL6) or Tumor Necrosis Factor- α (TNF- α).

Keywords: aptamers, biosensor, real-time monitoring

Multiplex characterization and quantification of extracellular vesicles in multiple myeloma

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Multiple myeloma (MM) is a haematological malignancy (HM) characterized by the proliferation of clonal plasma cells in the bone marrow and abnormal increase of monoclonal paraprotein, leading to specific end-organ damage, its pathophysiology, and the underlying mechanisms of its complications. Extracellular Vesicles (EVs) are lipid bilayer particles released by both healthy and malignant cells, raised attention in oncological research areas [1]. As liquid biopsy technologies and EVs detection evolve, their implementation in cancer clinical settings intensifies, heralding a new era in non-invasive, real-time oncological assessments. Laurenzana, et al. have previously demonstrated that higher concentrations of CD38 or CD138 positive EVs derived from plasma cells were found in the plasma of MM patients than in healthy subjects [2]. Another study conducted by Bergantim et al. highlights the potential of circulating EVs as a non-invasive biomarker, potentially reducing the need for bone marrow biopsies [3].

Despite these recent advances, the ongoing research into EVs in MM and other malignancies underscores the necessity of continued exploration and methodological refinement. The future of EV research lies in correlating changes in EV subpopulations with clinical outcomes. The aim of this study was to implement the use of a nano-bioanalytical platform to characterize and quantify extracellular vesicles in the plasma of MM patients, and to find/identify one or several EV subset bioindicators that could help in the diagnosis and therapeutic follow up.

[1] Boyiadzis M. et al., *Expert Rev Mol Diagn*, 2016;16(6):623-9

[2] Laurenzana I. et al., *Int J Nanomedicine*, 2021, 16, 3141-60

[3] Bergantim R. et al., *Int J Mol Sci*, 2022, 23(22), 13686

Keywords: extracellular vesicles, SPR biochip, AFM, Multiple Myeloma

SESSION 2: Cell & protein / material interactions

Development of an *in vitro* foreign body reaction model to evaluate silicone influence on fibrinogen conformation and macrophage polarization

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Despite an ongoing debate on implant biocompatibility, it is now widely accepted that silicone implants may cause a broad spectrum of chronic inflammatory diseases [1,2]. In fact, breast implants trigger a cascade of stereotype immune events so called Foreign Body Reaction (FBR). This process starts with fibrinogen adhering to the implant, triggering macrophage activation and results to the formation of a capsule around the implant, isolating it from the rest of body. Capsule and immune cells patrolling on it, then becomes the first recipient of silicone substances released by the implant (Fig. 1). We assume that silicone small molecules permanently leaking from the gel through the shell can pave the way to immune dysregulation and breast implant illnesses such as fibrosis.

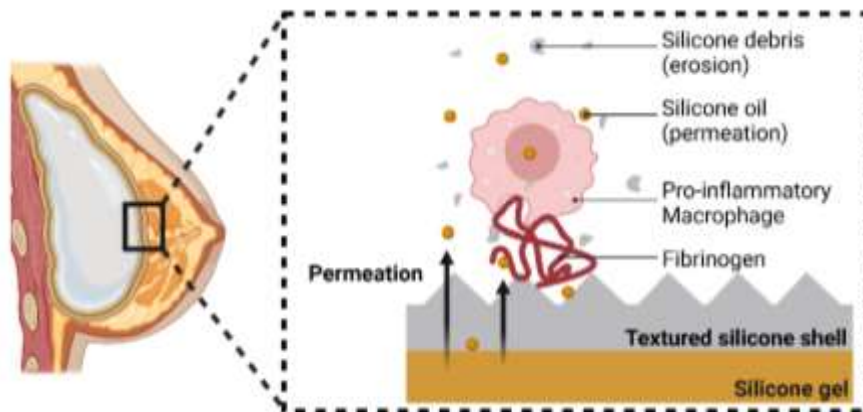


Figure 1. Immune cells patrolling in the capsular tissue can be exposed to different sources of silicone

We developed an *in vitro* model to study the Foreign Body Reaction (FBR) and support transition to safer implants, based on 3 axes:

- 1) Identification by Gel Permeation Chromatography and Mass Spectrometry of silicone species that could impact protein conformation and affect inflammatory response.
- 2) Analysis by Fourier-transform infrared spectroscopy (FTIR) of fibrinogen conformation after silicone exposure. Fibrinogen was chosen as a protein model for *in vitro* experiments since it is most abundant in plasma and known to activate macrophages.
- 3) Analysis of *in vitro* macrophage polarization after silicone exposure, using THP1 as model cell line. Macrophages lead the FBR using their ability to switch between a pro-inflammatory (M1) and a pro-healing (M2) state in a process known as polarization. Therefore, M0, M1 and M2 macrophages will be characterized upon their specific cytokine released signatures.

[1] Kaplan, J. & Rohrich, R., *Gland Surg.* 2021, vol. 10, 430–443

[2] Shoenfeld, Y. & Agmon-Levin, 2011, vol. 36, 4–8

Keywords: silicone breast implant, foreign body reaction, macrophage, fibrinogen

Evaluation of a new pediatric prosthesis made of thermoplastic elastomeric poly(urethane) (TPU) functionalized with polydopamine and type I collagen

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Congenital diaphragmatic hernia (CDH) is a rare malformation that occurs during fetal growth. It is defined by a posterolateral defect of the diaphragm which in 1 case out of 2 requires the use of a prosthesis, the most used being expanded polytetrafluoroethylene (e-PTFE) in 80% of large defect. However, this synthetic non-degradable biomaterial presents a significant recurrence due to insufficient colonization and mechanical properties not adapted to child's growth [1].

To tackle this issue, our colleague from ICPEES developed a bi-face thermoplastic elastomeric poly(urethane) (TPU) prosthesis having a fibrous side facing the thoracic compartment which should facilitate cell attachment and a smooth side to avoid adhesion with the abdominal viscera. First studies, performed on murine fibroblasts via MTS viability assay and immunostaining, has shown a colonization on the rough side being equivalent to the reference prosthesis e-PTFE and a smooth side being less adherent. In addition, looking at the inflammatory effect of materials, no activation of macrophages could be evidenced by nitric oxide production (Griess' test) after 24-hour culture leading to TPU being no pro-inflammatory.

Then, focusing on rough surface to improve further the colonization, functionalization was performed with a pro-adherent film made of polydopamine (PDA) obtained by an oxidative reaction of dopamine (DA) with sodium periodate (NaIO₄). Type I collagen was then added to the anchoring layer of PDA at different concentration. An improvement of the spreading and metabolic activity could be evidenced at a concentration of 100 µg/mL promoting early colonization after 2 and 4 days. After having selected the most effective formulation, new evaluations were done on myoblasts, as diaphragm muscles are the main players in its contractile function. The functionalized TPU permit to obtain a bigger significant difference than raw TPU compared to e-PTFE after 4 and 7 days.

This material expressing good mechanical properties and greater colonization permit to move on *in vivo* testing on rats. Firsts results have shown a cellular covering and integration in the rough surface of the material being more important on the new TPU material, independently of the functionalization, than e-PTFE.

[1] Schneider A. et al., Eur J Pediatr Surg, 2017

Keywords: Polyurethane-Based Biomaterials, Congenital Diaphragmatic Hernia, Polydopamine, Type I Collagen

Role of substrate curvature in cell migration and tissue morphogenesis

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Tissues and organs establishment require some complex cell migration processes at the individual cell and collective cells level. Knowledge about mechanisms behind control of these processes are crucial to understand fundamental concepts in developmental biology as well as regenerative medicine. Recent works carried out in the biointerface lab showed that substrate curvature affects cell migration and epithelium growth but mechanisms behind are poorly understood. As demonstrated, microgrooves made surfaces oriente the epithelium growth by inducing cell migration and cell division along concave lines (Fig. 1A) [1]. During my project, experiments show that parallels and perpendiculars microgrooves can oriente the epithelium growth and change epithelium growth speed without changing individual cell migration speed (fig. 1B). Now focus will be on biological mechanisms, intracellular remodeling and signalling pathway behind. Objectives are to finely control the epithelium growth with more complex curvature networks based on some prior works and modeling (fig. 1C) [2]. These advances could be useful to understand embryonic sheets rearrangement during development or to develop new surfaces for tissue engineering application.

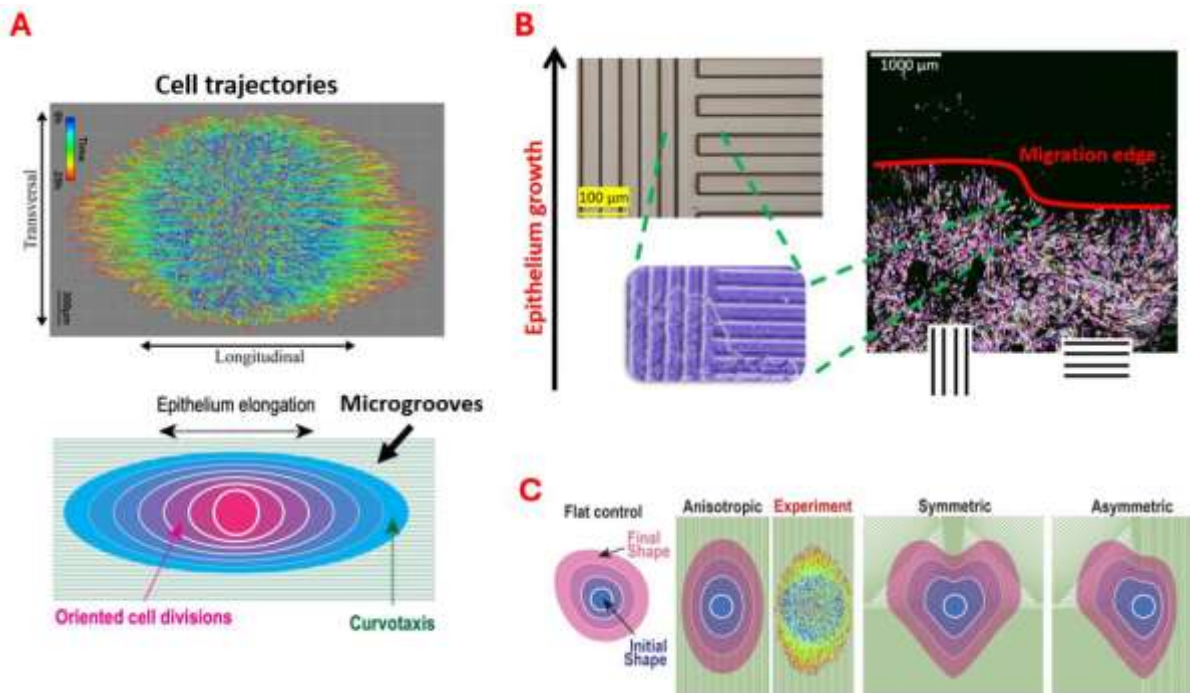


Figure 1. Epithelium growth control by curvature. A-Epithelium elongation on parallel microgrooves, B-Epithelium growth control by parallel and perpendicular microgrooves, C-Epithelium growth control by complex curvatures networks.

[1] Rougerie, P. et al., Sci Rep, 2020, 10, 14784, doi: 10.1038/s41598-020-70907-0

[2] Vassaux, M. et al., Biophys. J., 2019, 117, 1136-1144, doi: 10.1016/j.bpj.2019.07.022

Keywords: curvature, cell migration, epithelium morphogenesis

Interactions of a protein inspired from a barnacle adhesive cement with different material surfaces

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Among the main animals responsible for marine biofouling, barnacles are crustaceans able to adhere to various materials thanks to a protein complex named cement. The adhesion mechanism seems to be linked to the self-assembly of proteins secreted by the animal, forming a network of fibers on surfaces. The interaction of these proteins with the materials is a key step in the animal's adhesion. To investigate this process, we produced and purified with high purity a recombinant protein inspired from a protein composing the cement of *Megabalanus rosa* barnacle. As the variety of materials encountered in the natural environment is large (boats, rocks, animal skin and shells...), we have analyzed and compared the adsorption of this protein on a wide range of model surfaces with varying physico-chemical properties. To this end, we have combined different approaches based on enzyme linked immunoassay (ELISA) and surface plasmon resonance imaging (SPRi) experiments. The results obtained are linked with those from studies of protein self-assembly. Depending on surface properties and the conditions such as pH and ionic force, the protein behavior can be modified. The detailed analysis of protein interactions with various surfaces provides a better understanding of the early stages of barnacle cement formation, helping to decipher the natural adhesion as well as to suggest anti-fouling strategies.

Keywords: Barnacle, adhesion, proteins, surfaces

SESSION 3: Materials and Light

Development of an integrated biofunctionalized silicon photonic platform for allergen immuno-detection in food matrices

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Food allergens monitoring is an increasing demand from worldwide public health authorities since food allergy occurrence is on the rise. Highly processed food consumption in developed countries can explain part of the phenomenon, along with genetics [1]. Nowadays, the food processing industry mainly relies on complex, time-consuming outsourced analysis of their products. In order to meet the continuous evolution of the regulations regarding allergens tolerance level, next-generation allergens detection platforms development is key [2]. The challenges are numerous: portable, rapid, quantitative, multiplexed and user-friendly are some of the keywords that best describe researchers' ambitions. CEA-Leti produces silicon-based transducer that holds great potential for biosensor development [3]. Among them, Mach Zehnder Interferometer (MZI) chips built with silicon nitride waveguides are investigated for several biosensing applications, including allergens detection in food matrices. These transducers gather hundreds of individual MZIs in a compact centimeter-large chip, allowing for high throughput and multiplexed targets detection. For that purpose, a specific surface biochemical modification is required to turn the silicon chip into a sensitive and specific biological sensor. The functionalization procedure will be detailed during this talk, along with preliminary results of gliadin detection, the main protein of gluten, in model solutions and real food matrices samples, down to the ppm range, the current regulation tolerance levels. Finally, an overview of microfluidic integration of the biofunctionalized MZI chip will be presented.

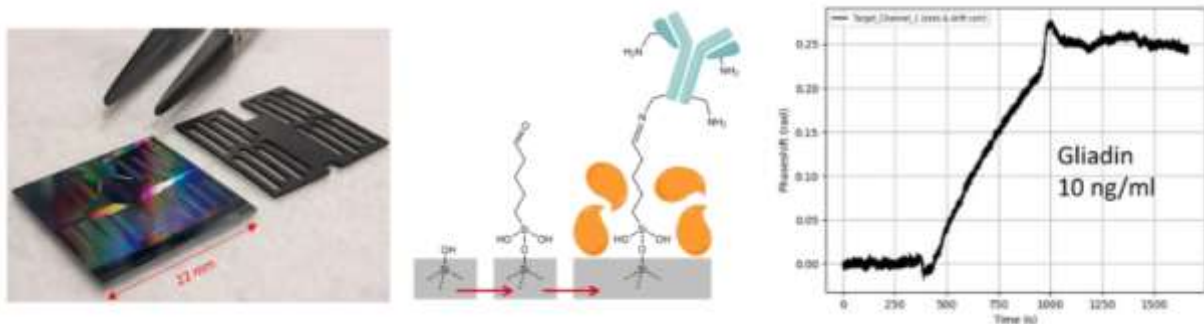


Figure 1. From left to right: a picture of the 512 MZI photonic chip, chemical procedure for antibody grafting and results of 10 ng/mL gliadin detection

[1] M. Lesage, 2018, agreste.agriculture.gouv.fr/agreste-web/download/publication/publie/Ana130/Analyse_1301811.pdf

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[3] L. Laplatine et al., *Opt Express*, 2022, 30(19), 33955–33968, doi: 10.1364/OE.461858

Zeolite-based composites for biomedical applications

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Zeolites are a set of crystallized aluminosilicates with a high specific surface area. Thanks to their microporous structures and their properties (cationic exchange, acidity, (selective) adsorption), these molecular sieves have various applications in the fields of adsorption and separation, catalysis, water treatment, medical engineering and optics. In the recent years, several works incorporating zeolites as fillers to prepare polymer/zeolite composites via photopolymerization under near UV/visible light have been realized especially in our laboratory [1-4]. Zeolite is utilized to enhance the mechanical properties of the polymer and transfer its properties to the composite.

Zeolite/polymer-based composites we prepared were cured by LED irradiation (405 nm). We tested a variety of zeolite, studied the influence of different monomers and zeolite crystal size, the interaction zeolite-photoinitiator. Some cured composites, whether or not heat-treated to decompose polymer and produce a zeolitic monolith, retained the cationic exchange property of zeolite in aqueous medium (Fig.1). We obtained composites with different shapes (Fig.1), and the zeolite content can increase up to 95 wt%. The growing interest in zeolites-based composites will be illustrated by examples from literature in dentistry.

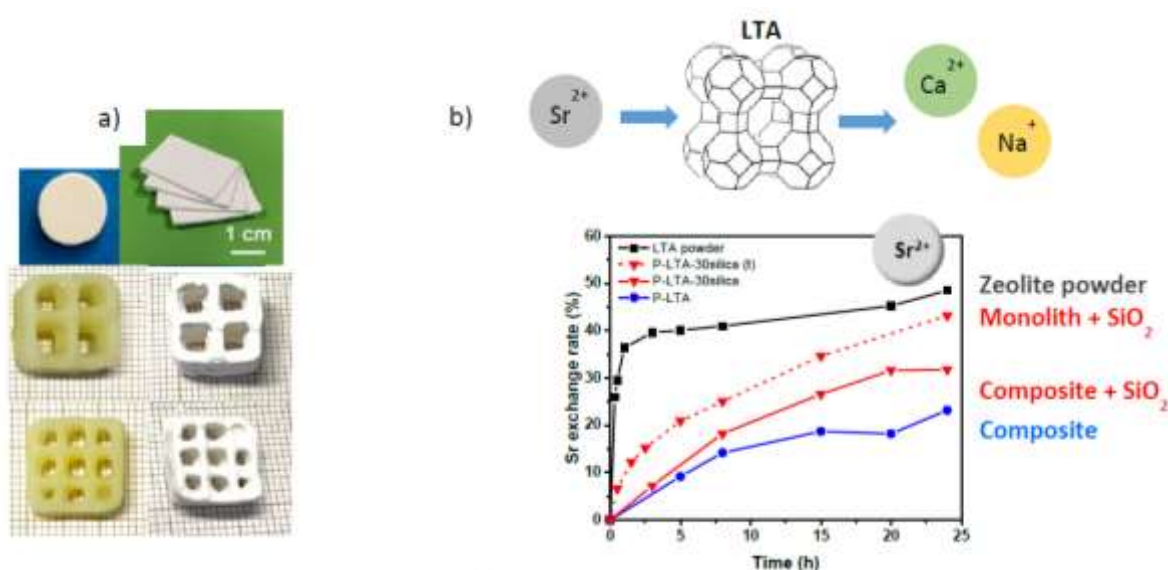


Figure 1. a) Different shapes of composite. b) Sr²⁺ exchange rate for composite prepared from LTA zeolite [4].

[1] Y. Gao, et al., ACS Appl. Nano Mater, 2023, 6, 10156

[2] Y. Gao, et al., Chem Eur J, 2024, sous presse, doi: 10.1002/chem.202302229

[3] Y. Gao, et al., ACS Appl Eng Mater, 2023, 1, 3323

[4] Y. Gao, et al., Mater Chem Phys, 2023, 293, 126853

Keywords: Zeolite, composite, photopolymerization, cationic exchange, adsorption

SESSION 4: Nano-objects & nano-structuration

Macrophage internalization dynamics of adsorbed submicron and nanoscale silica particles: insights for biomedical coatings

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In the field of biomedicine, functional coatings assembled from submicron and nanoscale particles have emerged for various applications. However, a significant challenge associated with these nanoparticle-based coatings is their vulnerability to internalization by macrophages, key players in the immune response. This study examined the efficiency with which RAW 264.7 murine macrophages internalize physisorbed silica nanoparticles across a range of particle sizes (35 nm to 450 nm) and incubation times (1 h to 12 h) [1].

Our results revealed two distinct internalization regimes dependent on particle size. Larger particles (450 nm and 300 nm) exhibited a high degree of removal by the macrophages, indicative of potential phagocytosis. Conversely, smaller particles (200 nm, 100 nm, and 50 nm) displayed a partial removal trend that decreased with particle size, suggesting a possible endocytic mechanism. Furthermore, the study identified a delay before the onset of internalization, which increased with decreasing particle size. This delay translates to a window of stability for the nanoparticle-based monolayers before macrophage interaction.

This investigation underscores the critical role of considering the adsorbed state of nanoparticles when evaluating cellular uptake. The findings elucidate the interplay between particle size, incubation time, and the governing internalization mechanisms. This novel approach paves the way for further exploration of fundamental cellular behaviors and interactions between cells and materials textured with particles, in the field of biomaterials, biosensor development, and drug delivery strategies.

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Keywords: nanoparticles, monolayers, physisorption, macrophages, internalization, endocytosis, phagocytosis

1D and 3D-AFM characterization of liquid/polymer brushes (PAA, PEO)/gold interfaces

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Self-assembled or grafted onto organic monolayers bound to a solid surface, like polymer brushes, have versatile uses. They serve as detection layers for specific biomolecules in biosensors or as protective coatings in tribological systems or lab-on-chip devices. Understanding how the unbound section of the polymer brush is structured and how it interacts with liquid surroundings is crucial for these applications, especially at the nanometric scale.

Our study aims to characterize this liquid/polymer brush interface using force spectroscopy, or 1D-AFM, as well as considering the 3D-AFM mode developed by T. Fukuma and R. Garcia [1]. In this mode, a 2D cross-sectional image (xz) representing the liquid organization at the interface is constructed from the recording of frequency variations Δf during scanning. We particularly focus on thiol-based interfaces deposited on a pure gold surface in a liquid medium, aiming for applications in biosensors and tribology [2]. Three samples were studied: ultra-flat pure gold, pure Poly(acrylic acid) PAA, and pure Poly(ethylene oxide) PEO.

The polymers were observed in liquids with different pH levels: after treatment with HCl to create an acidic solution (pH = 4), in pure water (pH = 5.5), and in PBS (pH = 7.4). We also tested them in salt-concentrated solutions achieved by including NaCl. The force curves obtained with 1D-AFM measurements show the effect of different liquid environments on the behavior of the polymer chain, manifested as changes in the chain length. 3D-AFM measurements complement the obtained results, and our initial experiments suggest that this method is well-suited for visualizing the organization of the liquid molecules and ions on the polymer brush layer, and its dependence on variations in pH and ionic concentration (Fig. 1).

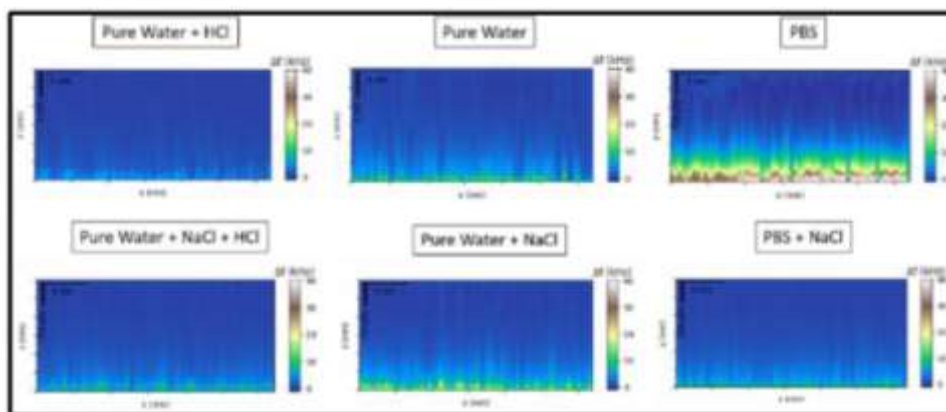


Figure 1. 2D (xz) cross-sectional images of the pure PAA sample characterized in different solutions by 3D-AFM.

[1] T. Fukuma et al., ACS Nano, 2018, 12, 11785

[2] M. F. Delcroix et al., Biomacromolecules, 2013, 14, 215

Keywords: 3D-AFM, force spectroscopy, organic monolayer, polymer brushes

Lysozyme-responsive core-shell nanoparticles formed by pH-drive and transglutaminase cross-linking and their properties

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As core-shell nanoparticles synthesized from gelatin and chitosan may be effective target delivery systems for curcumin, lysozyme-responsive nanoparticles were fabricated using a hydrophilic protein (gelatin type A) as the core and a hydrophobic polysaccharide (chitosan) as the shell. Curcumin was used as a model molecule for encapsulation and to promote the aggregation of gelatin nanoparticles. Transglutaminase catalyzed both intra-molecular cross-linking within gelatin and inter-molecular cross-linking between gelatin and chitosan. The formation mechanism of gelatin nanoparticles was investigated by molecular docking simulations, circular dichroism spectroscopy, UV-Vis spectroscopy, turbidity analysis, and dynamic light scattering. Results indicated that pH-driven processes induce molecular conformational changes of gelatin. However, these alone are insufficient to induce nanoparticle formation. Hydrogen bonding, Pi-alkyl interactions, Pi-Pi interactions, and van der Waals forces between gelatin and curcumin are crucial for the core formation. The coating mechanism of chitosan involved covalent bonds catalyzed by transglutaminase and electrostatic interactions, as verified by dynamic light scattering and Fourier transform infrared spectroscopy. Physicochemical properties characterization revealed that the core-shell nanoparticles exhibited a maximum encapsulation efficiency of $(97.2 \pm 0.3) \%$ and an average particle size of $(120 \pm 21) \text{ nm}$. Furthermore, the nanoparticles effectively retarded the thermal and pH degradation of the encapsulated curcumin. Additionally, they demonstrated significant lysozyme responsiveness.

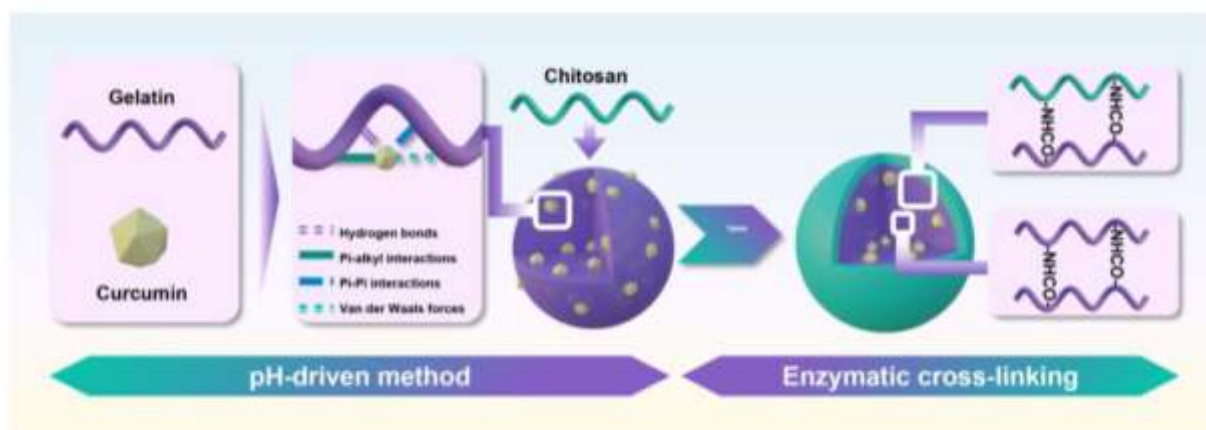


Figure 1. The scheme of pH-driven method and enzymatic cross-linking.

Keywords: curcumin, chitosan, gelatin, nanoparticle, lysozyme

Non-covalent nanobody biofunctionalization of organic electrochemical transistor (OECT) for the specific detection of chlordecone

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Chlordecone (CLD) is an eternal pollutant used as pesticide in intensive agriculture. When released into the environment, it persists, causing multiple diseases in global public health [1]. Therefore, it is urgent to develop new tools to monitor water and soil contamination. In this work, we present a non-covalent strategy to immobilize nanobody VHH-Glypoo102-His₆-Tag via coordination bonds thanks to the introduction of NTA-Ni²⁺ complex on the gold gate. This strategy allows to immobilize nanobody in an oriented manner thus improving the recognition properties of the nanobody towards its target [2]. Thanks to various techniques such as WCA, AFM, XPS, and FTIR, we have confirmed the immobilization of nanobody on a surface that functions as a top-gate electrode (G), which will specifically detect CLD in water. In addition, the specific interaction between nanobody and CLD was explored with XPS and cyclic voltammetry (CV) characterizations. The Fig. 1 displays the CV curves that correspond to signal changes between control (bare-Au) and SAM (NTA-Ni²⁺-VHH/Au) electrodes. These successful immobilization and specific recognition of the top-gate electrode results are crucial and validate the first step of the development of straightforward, inexpensive and easy-to-use OECT-type biosensors presenting good sensitivity and specificity for CLD detection [3].

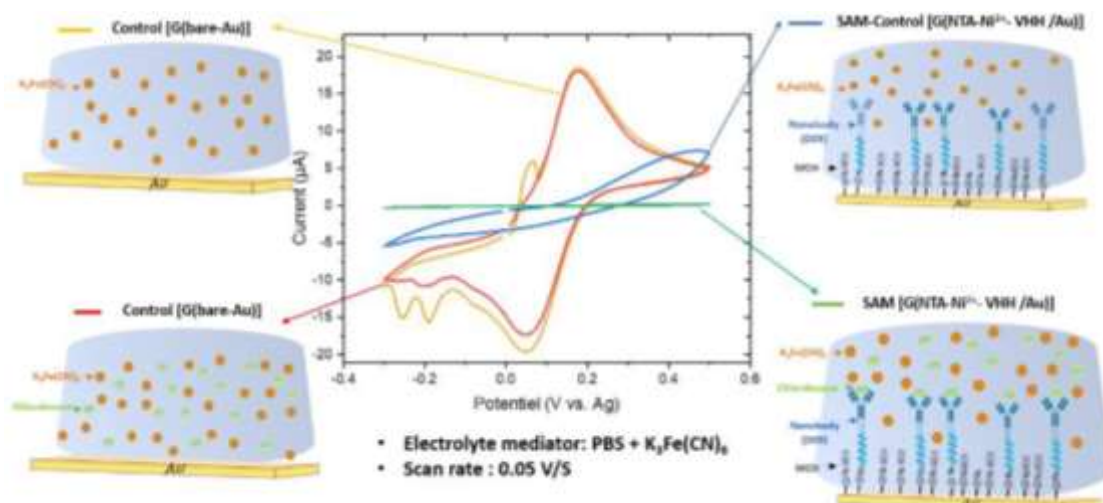


Figure 1. Representative scheme of nanobody immobilization (top-gate electrode) and recognition of CLD by CV, with yellow and red, curves corresponding to bare gold surface, before and after its incubation with CLD while blue and green curves correspond to VHH modified gold electrode in absence and in presence of CLD, respectively.

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[2] Y. Coffinier et al., Analyst, 2012, 137, 5527–5532, 2012

[3] S. Pecqueur et al., Sensors, 2017, 17

Optimization of a new venous stenosis treatment self-expanding nitinol stent using a multi-scale tribological approach from catheter to the veins

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Ni-Ti alloys, common shape memory alloys (SMAs) so-called nitinol [1], are known to have the ability to recover their original shapes, even after significant externally loads are applied, owing to the existence of an austenite-to-martensite reversible phase transformation allowed by a simple unloading. This super-elastic behaviour (SE), combined with its bio-compatibility, naturally leads nitinol to be an interesting candidate for various applications in medicine [2].

The present work focuses on a new patented one-piece double cross-sectional stent used in the treatment of venous stenosis, affecting vena cava, iliac veins and their bifurcations [2,3]. Owing to the diameters of the targeted veins, this unique stent displays two sections of different diameters once deployed, which are connected together by a compliant area. Since the SE nitinol stent is placed in veins by catheterization their sections are first reduced into a wire form to be inserted within a polytetrafluoroethylene (PTFE) catheter displaying both a low friction and a good biocompatibility. Once positioned in the diseased vein, stent then returns to its shape on its own, taking advantage of its SE behaviour to expand the diseased vein. However, numerous antagonistic tribological challenges arise during this release because the stent: (i) first needs to slide easily along the guide-wire (catheter), in order to avoid any stick-slip occurrence leading to PTFE abrasion wear [3], and (ii) should not be enabled to slide any more once located within the veins [4].

The first issue has been recently studied by using an original multi-scale approach [3]. The latter combines X-ray tomography, optical topography with the Persson's contact theory in both static and dynamic cases in order to track the evolution of the real contact area during the sliding process. Various stent designs have been then deduced and optimized to reduce friction through the catheter.

The present work actually addresses the second tribological issue by extrapolating the above approach in order to follow the evolution of the static real contact area during stent deployment within both the iliac and cave veins. The ultimate local normal contact pressures can be evaluated as function of the stent topography to both (i) insure the non-sliding conditions of stent within the veins [4] and, (ii) avoid any vein lesions by limiting the normal pressure exerted by the stent on the veins [5].

As these results directly influence the design and the surface treatment of each stent's part, this work will describe the optimized double structure displaying in the same time: (i) a very low rigidity in the catheter in order to promote sliding [2,3] and, (ii) a maximum contact area in the vein limiting both the radial pressure and the risk of slipping once deployed [4,5].

[1] W.J. Buehler et al., J. Appl Phys., 1963, 34(5), 1475-77

[2] A. Sallami et al., X ECCOMAS SMART, 2023, D.A. Saravanos et al (Eds)

[3] A. Sallami et al., submitted to Tribology International, May 2024

[4] K. Gibson, MEDTRONICS Medical Affairs Corner, 2021

[5] A.C. Dunn et al., Tribology Letters 2007, 27, 233-238

Keywords: self-expanding nitinol stent, frictional law, real contact area, Persson's contact theory

SESSION 5: Bacteria/Material Interactions

Development of a specific microfluidic bio-interface for the detection of pathogenic bacteria in the agro-food industry

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The detection of pathogenic bacteria has become a major issue in the agro-food and health industry. In 2019, 23 million people in Europe were falling ill from unsafe food each year [1]. To prevent those contamination, it became necessary to identify them as soon as possible to stop the production before commercialization. The actual method to detect those contamination take around 48h to 72h. A lot of new detection tools have been developed for a more sensitive, specific detection and to reduce those detection time. One of the ways is to use piezoelectric transducers

For the acoustic transduction, the Quartz Crystal Microbalance (QCM) is widely used for its sensitivity and reliability. With this microbalance, it is possible to measure very low mass variation. The Limit of detection (LOD) for the commercial QCM is 17.7 ng/(cm².Hz) at a resonant frequency of 5 MHz and 4.4 ng/(cm².Hz) at 10 MHz. Other acoustic bio-sensors have been developed with AsGa and ZnO in order to increase the sensitivity and multiplexed measures [2]. Considering the piezoelectric coefficients for Lithium Niobate (LN), we will have the opportunity to reach a lower LOD compared to QCM.

The first objective is to develop a bio-interface on LN for the specific sensing of our targeted bacteria *Listeria*. LN is an oxide that's why the silane functionalization is used. In this case, we are using 3-Aminopropyltriethoxysilane (APTES). The next step is to graft a linker, here PDITC, an antibody and performing a BSA passivation step. Different surface analyses were done to assess the proper grafting of each molecules. For the APTES grafting, different protocols have been developed but they all require a heating stage [3]. Using LN can be challenging due to its intrinsic pyroelectric properties. In order to optimize the grafting process, we used Titanium as a model material. In this study, we manage to graft APTES in chloroform without any heating step during the process. This method was successfully transposed on different cuts of LN.

The second part consists in static detection to assess the right orientation of our antibody and the antibody specificity. In order to do that, we incubate our sensors in different solutions with bacteria (*E. coli*, *L. innocua*) at a high concentration. After that, we are coloring them with Crystal Violet and count the number of bacteria using an optical microscope. The images are post processed with the ImageJ software. Preliminary data show on Ti a specificity of capture towards *Listeria* of 0.27%.

Concerning LN, a fluidic chamber is being designed for an in-flux detection together with specific electrodes for transduction. The different chamber designs simulated to avoid any turbulence in the fluid will be presented.

[1] World Health Organisation, 2019

[2] J. Chawich

[3] M. Sypabekova et al.

Ion triggered self-assembly of antibacterial Fmoc-based tripeptide: physical chemistry and MD simulation

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Hydrogels are materials with a high-water content, which makes them similar to natural tissues. They can be used as an injectable matrix directly on the infected site, making them suitable as drug delivery platforms. Small peptides as hydrogelators are of interest due to their high biocompatibility, degradability and ease of synthesis. They are formed upon solubility decrease induced by an external stimulus such as a change of solvent, pH switch or enzymatic modification [1,2,3]. Our group already demonstrated the formation of a hydrogel based on the self-assembly of Fmoc-FFpY (Fmoc: fluorenylmethoxycarbonyl, F: phenylalanine; pY: tyrosine phosphate) with a polycation (PAH) through π - π stacking and electrostatic interactions [4]. The study presented here aims to investigate the use of simple cations such as Fe^{3+} as counterions. This work was investigated through four major aspects: (i) structural characterization of the gel, (ii) study of its mechanical properties, (iii) molecular dynamic simulation and (iv) antibacterial assays. Spectroscopic analysis was carried out to highlight the secondary structure, and fiber structure. Rheological properties with self-healing tests showed a mechanical stiffness close to extra-cellular matrices, making it promising for cytotoxicity assays. The hydrogels showed an antibacterial activity against *S. aureus* probably due to the enhanced production of ROS induced by the presence of high concentration of $FeCl_3$.

[1] Reches, M. & Gazit, E. Israel Journal of Chemistry, 2005, 45, 363-371

[2] A. M. Smith, R. et al., Adv. Mater. 2008, 20, 37-41

[3] Z. M. Yang, et al, Adv. Mater. 2007, 19, 3152-3156

[4] Criado-Gonzalez, M. et al. Chemistry of Materials 2020, 32, 1946-1956

Keywords: peptide-based hydrogels, electrostatic assemblies, antibacterial hydrogels, Fmoc-FF

Hydrophilic antiadhesive coating to prevent marine organisms' colonization

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The development of biofouling on submerged surfaces leads to numerous operational, economic, health and environmental issues. The increasingly stringent European regulations on biocidal products are encouraging the study and understanding of the mechanisms of action of new systems, without toxicity. Current strategies tend to develop passive surfaces, free of biocides, limiting colonization solely through their physical, mechanical and chemical properties [1,2].

The marine environment is full of many polymers with interesting film-forming properties. In this work, chitosan, a biosourced polymer with modulable mechanical properties, is chosen as a good candidate for the design of coatings. Chitosan is already known for the design of hydrophilic cross-linked networks [3]. The ability of chitosan to be cross-linked will allow the mechanical properties and thus us to establish different formulations, thus varying the cross-linking. Modification of cross-linking will impact swelling, stiffness and surface hydrophilicity of coatings.

The objective of this study is to design different types of hydrophilic coatings in order to mask the surfaces to the organisms thanks to a hydration layer. The modulation of the physical and mechanical properties, characterized in a hydrated state, will allow us to understand the impact of hydrophilic coatings on the adhesion of organisms (bacteria, diatoms and oyster larvae). These modifications will enable us to determine the discriminating parameters inhibiting the colonization of marine organisms on the surface of cross-linked hydrophilic coatings. Thus, to propose new alternatives to coatings containing biocides.

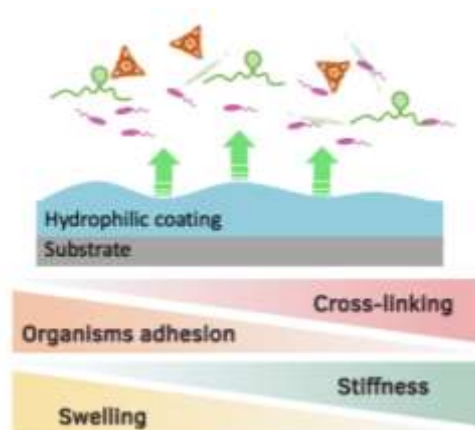


Figure 1. Relationship between modulation of the physical and mechanical properties of a hydrophilic coating and adhesion of marine organisms

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[2] A, Yapar EA., Universal Journal of Pharmaceutical Research, 2019, 4, 5

[3] Priyadarshi R, et al., Carbohydrate Polymers, 2018, 195, 329.

Keywords: Antiadhesive coating, marine environment, biofouling, hydrogels, hydrophilic coatings.

Study of the antibacterial impact of photocatalytic surfaces in the marine environment

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Marine biological fouling is an undesirable phenomenon that results in the spontaneous attachment of molecules, micro-organisms, plants and animals to all infrastructures immersed in the marine environment [1]. This has serious economic and environmental consequences [2]. Current antifouling measures are mainly based on the more or less controlled release of biocides. These have significant drawbacks. The most worrying of these is their ecotoxicity. [3]. They are harmful to non-target organisms [4]. The development of light-induced catalytic coatings is a promising alternative. It is more environmentally friendly. TiO₂ films are deposited by aerosol-assisted metal organic chemical vapour deposition (MOCVD). The surface topography of these films is characterized by forming microflower-like structures with nanometric petals. The study focused on the effect of these films on the adhesion and maturation of a biofilm of a biological model representing marine bacterial adhesion, *Vibrio harveyi* (DSM19623). The results show a biocidal effect of the lighted TiO₂ films on adherent bacteria. The percentage of damaged bacteria ranged from 69 to 82%. The surface topography of the films induces a high specific surface area for photocatalysis. An 85% inhibition of biofilm formation was also demonstrated. These results indicate that the photocatalytic activity of TiO₂ films succeeds in damaging bacteria and disrupting biofilm development.

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[3] Eduok, U. et al., Prog. Org. Coat., 2017, 111, 124–163

[4] Amara, I. et al., Environ. Toxicol. Pharmacol., 2018, 57, 115–130

Keywords: Antifouling, TiO₂ films, photocatalysis, coating.

Polymer coatings to prevent microbially influenced corrosion

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Surface colonization by microorganisms is equally of concern for human and environmental health and for the energy sector with tremendous associated economic losses. If hospital acquired (nosocomial) infections are health threatening, microbially influenced corrosion (MIC) leads to medical devices and to industrial setting failures in both health and energy sectors. There is thus an urgent need to find antibiotic- and other biocides-free solutions to combat MIC, i. e. biocorrosion. To counteract this deleterious process, we recently initiated investigations using either natural, antimicrobial chitosan passive coating or redox responsive poly(ferrocenylsilane) (PFS) active coating on metal surfaces.

We combined adhesion tests, profilometry, electrochemical characterization and X-ray photoelectron spectroscopy (XPS) prior and subsequent to incubation with *Desulfovibrio vulgaris*. This bacterium, in anaerobic conditions, reduces sulphate, which produces corrosive hydrogen sulfide. Both approaches, passive and active coatings, were efficient in protecting the metal surface against both corrosion and biocorrosion. The main outcomes of these investigations demonstrate the preparation of adherent films of thickness in the μm range, which are stable even after five weeks of incubation with bacteria and which prevent both corrosion and biocorrosion.

Keywords: polymer, coating, redox active, natural, biocorrosion

Water disinfection with Cu(OH)₂ nanorods

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Large-scale production of fresh produce requires a lot of irrigation during the growing season. Enteric bacteria are present in freshwater used to irrigate crops due to faecal contamination. The use of wastewater is a growing practice for irrigation in areas where freshwater reserves are scarce but poses health risks if not treated. Recent outbreaks in the US, UK and Germany linked to the consumption of fruits and vegetables contaminated by irrigation water highlight the need to disinfect them. Due to its very low solubility in water and its stability at neutral pH, Cu(OH)₂ is a prime candidate for water disinfection. The aims of this study [1] were to evaluate the bactericidal activity of Cu(OH)₂ nanorods towards model bacteria suspended in water and then to determine the role played by released cupric ions in their toxicity. To address this issue, a substitution of cupric ions by Mg²⁺ was attempted in the crystal structure of Cu(OH)₂ nanorods to increase their solubility and measure its impact on the bactericidal activity. The remarkable bactericidal activity of Cu(OH)₂ nanorods (100% reductions of *E. coli* and *S. aureus* in 3 h) is not linked to cupric ions released in water since the mass concentration is several orders of magnitude lower than the minimal concentrations inhibiting the growth of bacteria (even for the Mg-substituted counterparts). The toxicity arises from the lethal amount of free oxygen radicals produce by the particles themselves in the presence of H₂O₂, a by-product of the normal metabolism of oxygen in aerobic bacteria.

[1] B. Clavier et al., , Journal of Materials Chemistry B, 2022, 10, 779

Keywords: Disinfection, *E. coli*, *S. aureus*, Reactive Oxygen Species, Copper

Antibacterial surfaces prepared by electropolymerization of pyrrole-tailed imidazolium ionic liquids

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Conductive polymers (CPs) have found a lot of applications especially in the microelectronic and optoelectronic fields. More recently, researchers are applying the knowledge gained in these areas toward biomedical applications. Especially, the biocompatible polypyrrole (PPy) CP is suitable for implantation into the body. At the same time, ionic liquids (ILs), especially those based on imidazolium cations showed promising application as novel antimicrobial agents. In particular, poly(ionic liquids) (PILs) present the advantages of combining antibacterial properties and a polymeric character that have been used to manufacture antibacterial membranes. PILs that possess an intrinsically conducting polymers (ICP) backbone like polypyrrole have been synthesized with the objective to combine ionic and electronic conducting properties in the same polymer. However, polypyrrole-based PILs have never been explored as antibacterial materials. In this study, we developed a strategy to prepare antibacterial surfaces by electropolymerization of a pyrrole-functionalized imidazolium ionic liquid bearing an halometallate anion. For this, imidazolium-based ILs bearing a pyrrole function with different alkyl chain lengths were synthesized and the antibacterial activities of these monomers were investigated by means of their MIC/MBC (MIC = Minimal Inhibitory Concentration; MBC = Minimal Bactericidal Concentration) determination against Gram-negative *E. coli* and Gram-positive *S. aureus*. Our polypyrrole-PILs were then obtained by electropolymerization on FTO substrate. The antibacterial activities of the polypyrrole-PIL membranes were determined both by disk diffusion method and by the colony forming units (CFU) counting method over time. Our results evidenced excellent antibacterial activity for our polypyrrole-based PILs that depends strongly both on the monomer concentration and the alkyl chain length [1].

[1] Ben Halima, H. et al., ACS Applied Mater. Interfaces, 2023, 28, 33383

Keywords: antibacterial, polypyrrole, ionic liquid, electropolymerization, zinc

Challenges in modulating surface energy to optimize axonal growth

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Neuronal differentiation is crucial for the regeneration of nervous tissues after injury, and adhesion to a substrate is essential for neurite extension. The formation and guidance of neurites occur in response to extracellular signals, such as adhesion energy (e.g., the surface tension of the substrate) and particularly local gradients. It is therefore important to study the characteristics of the substrates with which the growth cone (axon tip) interacts, translating into neurite extension in response to these physical signals. The ability to control the spatial distribution of adhesion energy is of particular interest for numerous applications in biomedical and tissue engineering.

Each year, millions of people suffer from peripheral nerve injuries. In the United States alone, approximately 20 million people are affected by nerve lesions, with over 600,000 new cases annually. The annual cost to the U.S. healthcare system exceeds 150 billion dollars, including medical care and lost productivity. In Europe, the nerve regeneration device market is valued at about 2 billion euros, while globally, it exceeds 5 billion dollars, with expected growth due to technological advancements and increasing demand for effective solutions.

Recent results (fig. 1) indicate that, in addition to the chemical nature and mechanical properties of the substrate, physical cues such as surface energy gradients also impact cellular functions, such as the differentiation of PC12 cells (a model for neurons) and NSC34 cells (a motor neuron line). However, it remains to be determined which surface effect is predominant in triggering neuronal cell differentiation.

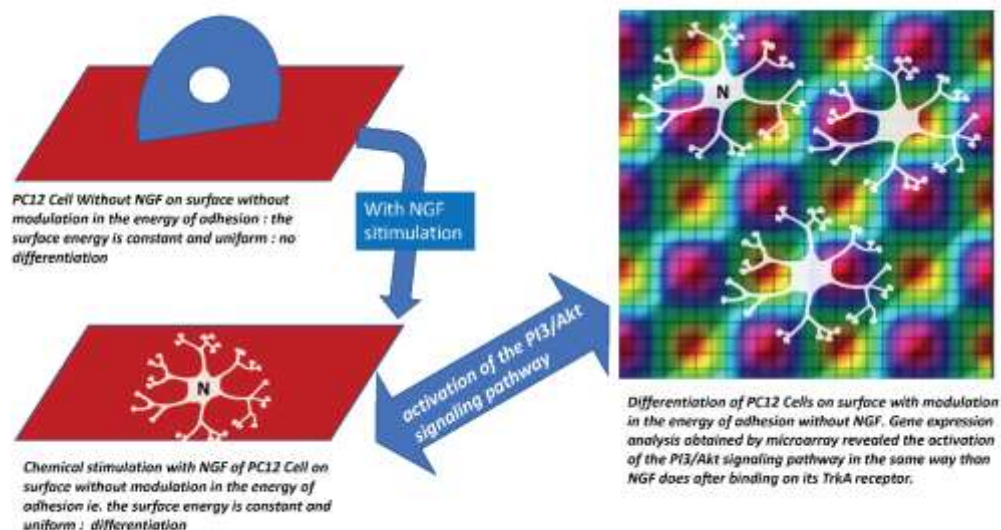


Figure 1.

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P18	Thérèse Leblois	Lab-on-chips & organ-on-chips at FEMTO-ST/MN2S/BIND
P19	Lydie Viau	Electropolymerization of pyrrole-based metal N-Heterocyclic carbenes for antibacterial applications

P1/ Pioneering new frontiers: the implication of graphene in dental applications

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In the realm of developing dental biomaterials incorporating graphene, it is imperative to address concerns regarding the safety of graphene-based materials used in dental applications. Understanding their interactions with biological systems holds paramount importance due to possible toxic effects that may arise. The nature of these interactions has been observed to be dependent upon the synthesis methodology and surface functionalization of graphene [1]. One approach to few-layer graphene (FLG) synthesis involves using graphite as the starting raw material, followed by liquid-phase exfoliation and in situ functionalization [2]. The use of surfactants to assist exfoliation of graphite in liquid medium, such as water, is recognized for enhancing dispersibility of carbon layers and, has been shown to attenuate toxicity [3]. In our *in vitro* study, a plant derived surfactant molecule (A), was employed. A liquid-phase exfoliation process was conducted, and the interaction of the composite (A-FLG) with human periodontal ligament stem cells (PDL) was examined. The evaluation focused on *in vitro* cytotoxic effects, including studying metabolic activity, alterations in cell morphology, and chromatin architecture following contact with the composite material. This study offers novel perspectives on the repercussions of graphene-based nanomaterials on dental cells.

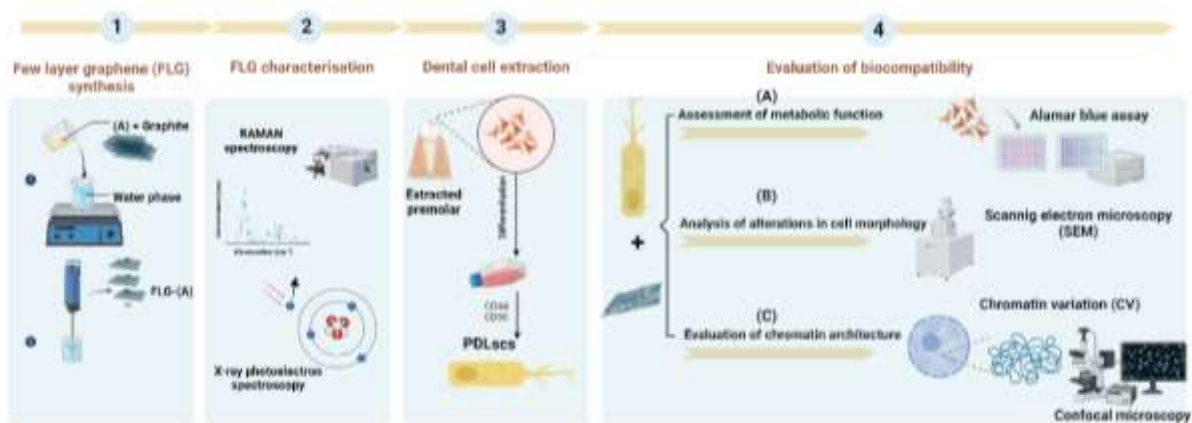


Figure 1. Schematic planning demonstrates the different steps including fabrication phase and *in vitro* cytotoxicity evaluation of the composite on PDL cells.

[1] Achawi S, et al., *Nanomaterials*, 2021, 11(11), 2963

[2] Lozano-Chico M, et al., *Sustain Mater Technol*, 2024, 40, e00956

[3] Li J, et al., *Toxicol Sci*, 2019, 167(1), 269-81

Keywords: few layer graphene (FLG), periodontal ligament cells (PDL), biocompatibility, chromatin architecture

P2/ Design of active microparticles in bioprinted organoids: controlled degradation and cellular metabolic monitoring

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3D bioprinting enables the development of complex biological models imitating the structure and properties of native tissues. This technology is based on the incorporation of living cells into a polymer matrix, called bioink, which reproduces the extracellular environment. In the extrusion bioprinting process, the bioink is deposited layer by layer by constant pneumatic pressure, in the form of a continuous filament. This pressure generates shear stresses that can damage cell membranes, leading to cell death.

This is why, porous poly(D,L-lactic-co-glycolic acid) (PLGA) polymer microparticles were incorporated into the bioink [1]. The role of these microscaffolds is twofold: to act as a support to improve cell adhesion and to protect cells against mechanical stress. In addition, after printing, the cells will initiate remodeling of the ink by partially degrading the microparticles. This degradation time can extend over several months, longer than the few days required for printed tissue to grow.

This thesis project aims to control the degradation of these porous microparticles. The approach is to modify the structure of PLGA microparticles to induce time-controlled degradation after bioprinting. The objective is to develop microparticles with active degradation, to facilitate the maturation of bioprinted tissues. Preliminary experiments were carried out to observe the behavior of fibroblast cells (NIH3T3) in the presence of PLGA microparticles under incubation over several weeks. Different coatings were tested to study cell adhesion and proliferation.

To monitor cell metabolism after printing, a second project consists of the integration of fluorescent poly(methylmethacrylate-co-methacrylic acid) (PMMA-MA) nanoparticles (NPs) into the microparticles, for use as oxygen nanosensors [2]. These NPs are based on the phenomenon of fluorescence resonance energy transfer (FRET). The signal intensity of the acceptor, an oxygen-sensitive molecule, is expected to increase with the consumption of oxygen by the cells. The integration of NPs into microparticles was tested and characterized by different characterization techniques, revealing a homogeneous distribution in mass and surface area.

The final aim is to combine these two projects to design microparticles capable of active degradation, with monitoring of their metabolism.

[1] Rousselle, A. et al., *Bioprinting*, 2022, 28, e00247

[2] Ashokkumar, P. et al., *Small*, 2020, 16(32), 2002494

Keywords: Bioprinting, microscaffolds, polymer, degradation, nanosensors

P3/ Functionalization of zirconia for enhanced osseointegration in dental implants

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This project is part of the Nomad European Project (Horizon Europe project 101091669) which aims to develop the next generation of dental implants with a focus on preventing peri-implantitis, consequently enhancing the long-term success of implants.

Zirconia is a promising material for dental implant due to its excellent aesthetic properties, such as opacity and white color. Zirconia has other advantages such as biocompatibility and very low inflammatory response when it comes in contact with tissues which again make it a possible alternative to titanium.

One specific strategy of the project is to stimulate bone tissue growth on zirconia implants. This may be achieved by functionalizing zirconia with extra cellular matrix (ECM) components. To do so, a first organic layer is attached to zirconia by chemical functionalization of the surface. This first layer aims to facilitate the grafting of biochemically active molecules (such as ECM components, growth factors and peptides) recognized by osteoblasts and promoting their growth. As we aim to enhance osseointegration, zirconia surface was sandblasted and etched with hydrofluoric acid to obtain a clean surface with a roughness (1-2 μm) that promotes adhesion and proliferation of osteoblasts while allowing functionalization. Zirconia surface preparation (sandblasting, surface cleaning, and surface activation) and its impact on the grafting of the first organic layer were studied. The surface roughness, composition, chemistry and the material crystallinity were characterized using surface analysis techniques including X-ray diffraction (XRD), water contact angle (WCA), scanning electron microscopy (SEM) and X-ray photoelectron spectroscopy (XPS). After deep characterization of the surface, two types of compounds were studied the first organic layer: organosilane and organophosphonic acids. This layer was characterized with XPS and colorimetric assays.

Keywords: zirconia, surface functionalization, dental implants, phosphonic acid, silane

This project would not have been possible without Anthogyr providing our samples, and without the NOMAD program (HORIZON-CL4-2022-RESILIENCE-01 program number 101091669).

P4/ Synthesis and characterization of an agarose-based hydrogel containing anti-biofilm molecules targeting amyloid fibrils

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Functional amyloids' prevalence and multifaceted roles in bacterial biofilms have made them attractive as promising targets for novel anti-biofilm molecules [1]. This approach could effectively inhibit the irreversible anchorage of bacteria onto surfaces and eventually disrupt biofilm formation, without bactericidal action [2]. This research focused on identifying anti-amyloid molecules (AAMs) capable of disassembling BAP and R5T, which are amyloid fibrils derived from *Staphylococcus aureus* and *Escherichia coli* respectively. Amongst the AAMs tested, two polyphenols – PP1 and PP2 – were found to have the highest activity in disaggregating BAP and R5T, based on Thioflavin T assays. These polyphenols reduced the β -sheets contents of BAP and R5T from an initial $\geq 60\%$ to $\leq 50\%$, at non-bacteriostatic concentrations. Subsequently, PP1 and PP2 were incorporated into an agarose hydrogel, and their release profiles and effects on the hydrogels' mechanical properties were evaluated. By identifying and characterizing molecules capable of disassembling bacterial amyloid fibrils, this study aims to contribute to developing antibiotics-free novel anti-biofilm approaches, addressing a critical unmet need in infectious diseases.

[1] Steadman, D., et al., Future Microbiology, 2014, 9, 887

[2] Matilla-Cuenca, L., et al., 2021, 10, 795

Keywords: anti-amyloid, biofilm, antibiotics-free, agarose, hydrogel

P5/ Towards omniphobic, eco-friendly and durable textiles for antifouling applications

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Omniphobic surfaces, renowned for their remarkable ability to repel both water and oil, have been extensively explored for their versatile applications across various industries. With notable advantages in cleanliness, contamination resistance and antifouling properties, these surfaces play a crucial role in critical sectors such as medical devices, outdoor textiles, marine equipment, and more [1].

The most effective treatments enabling the attainment of such properties involve the use of long-chain fluorinated substances (PFAS and PFOS). Nevertheless, their utilization is now restricted by regulatory constraints due to their adverse effects on both the environment and human health [2]. PFAS and PFOS are persistent organic pollutants that can bioaccumulate in living organisms, posing significant ecological and public health risks. Given these concerns, the development of alternative surface treatments becomes imperative.

In this context, our project aims to address this challenge by developing surface treatments specifically tailored for textiles, using innovative molecules and methods conducive to large-scale industrial production. By synergistically combining physical and chemical approaches, our goal is to achieve performance levels similar to perfluorinated derivatives in terms of durability and self-cleaning properties, while minimizing environmental and health concerns associated with PFAS and PFOS.

Our primary findings have demonstrated the effectiveness of combining surface activation techniques, such as UV ozone or plasma treatments, with the grafting of polymers and/or particles of interest to tune surface wettability and enhance repellent properties. These findings not only hold significance for the textile industry but also have profound implications for the development of sustainable and eco-friendly surface treatments in various industrial applications, including those related to antifouling and antibacterial properties.

[1] Huang, K.-W. et al., Prog. Org. Coat., 2022, 173, 107174

[2] Brennan, N. M., et al., Int. J. Environ. Res. Public Health, 2021, 18(20), 10900

Keywords: omniphobic surface, surface activation, polymer grafting, surface wettability, antifouling properties

P6/ Cartilage self-regeneration and 3D-bioprinted cartilage tissue engineering for osteoarthritis therapy

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Osteoarthritis is a pathology characterised by change of chondrocyte phenotype that differentiate into hypertrophic chondrocytes. This change is associated with an extra-cellular matrix remodeling leading to a mineralization an ossification process of the cartilage [1]. Chondrocytes originates from mesenchymal stroma cell (MSC) that are able to differentiate into chondrocytes, osteoblasts and adipocytes according mechanical and biochemical signals, such as mecanotransduction and growth factors. It has been shown that MSC contributes to damaged tissue reparation. This work proposes to study mechanisms involved in chondrogenic differentiation of stem cells and their capacity to colonise cartilage with help of bioprinted models. The first part consists in measuring migration capacity of MSC in 2D and 3D. A second part consists in the development of a 3D bioprinted model with a bioink containing cellularised porous microparticles [2]. Printing conditions such as cellularization methode, particles and bioink choice as well as culture and differentiation conditions will be optimized. Differentiation capacity will be assessed by histology, confocal imaging, western-blot and RTqPCR techniques. Finally, mechanotransduction mechanisms involved in chondrogenic differentiation will be study on these models.

[1] Pitsillides AA, and Beier F., Nat Rev Rheumatol., 2011, 7(11), 654-63

[2] A. Rousselle, et al., Bioprinting, 2022, 28, e00247

Keywords: osteoarthritis, MSCs, cartilage, microparticles, bioprinting

P7/ Development of a phase-contrast SPRi biosensor for the detection and counting of pathogens

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The rapid detection of pathogens, such as bacteria and viruses, is a significant challenge in the medical field, particularly in the context of the Covid-19 pandemic. This pandemic has highlighted the necessity for rapid, mobile, accurate and large-scale detection of pathogens. Biosensor-based technology is particularly promising for such applications. In this PhD thesis, we intend to develop a portable optical biosensor based on Surface Plasmon Resonance imaging (SPRi) systems, which are commonly used for the analysis of biomolecular interactions, in real-time without the need for labeling.

In this context, a new phase-contrast SPRi is being developed, which allows the detection and visualization of individual nano and microbiological objects (viruses, bacteria) with a greater spatial resolution. The specificity of the detection is obtained by functionalizing the SPRi prism with specific probes (such as antibodies, receptor-binding proteins and other specific receptors) for binding of the biological objects of interest.

Different bacterial strains were employed as models in this study, including *Escherichia coli* K12 and *Streptococcus pneumoniae*. These were successfully detected at concentrations as low as 10^3 cfu/mL. A microfluidic system is under development to further reduce the limit of detection and the detection time.

Keywords: biosensors, Surface Plasmon Resonance imaging (SPRi), bacterial pathogens, detection

P8/ Cell response and protein adsorption on amino-rich plasma polymer nanocoatings

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The rise in age-related conditions such as osteoporosis is leading to an increased need for bioactive orthopedic implants capable of integrating into osteoporotic bones. One approach to developing these implants involves coating materials with amino-rich polymers like trimethoxysilylpropyl modified poly(ethyleneimine) and poly(allylamine) [1-2].

In this research, we produced thin films of radio-frequency plasma polymerized allylamine (rf-PPAAm) on titanium substrates with different levels of amine content. We examined the MG-63 osteoblastic-like cells migration and their contact guidance behavior on these material surfaces. The thin films were created by plasma polymerization of allylamine on 1 x 1 cm titanium-coated flat and micro-grooved silicon wafer substrates using a specially designed radio frequency plasma apparatus with a vertical setup [2-3]. The plasma polymerization process was conducted at a controlled pressure of 0.2-0.4 mbar and power ranging from 20 W to 60 W, with a polymerization time of 10 minutes and duty cycle varying from 2% to 100%. We characterized the thin films using water contact angle measurement, Zeta potential measurement, profilometry, and X-ray photoelectron spectroscopy. Cell spreading, migration, and the disruption of cellular contact guidance were assessed using MG-63 osteoblastic-like cells and LSM780 and LSM800 confocal microscopes. The adsorption of bovine serum albumin (BSA) protein was also investigated.

Our findings demonstrate varying behaviors of osteoblast cells depending on the quantity and quality of amine groups present on the thin film surfaces. Cellular contact guidance abrogation and higher BSA adsorption were observed for rf-PPAAm surfaces with higher content of amine groups. The physico-chemical properties of the nanocoatings were correlated to explain the cell response mechanisms to the surfaces of these nanocoatings.

[1] S. Seemann, et al., *Molecules*, 2023, 28, 6505

[2] C. Mörke, et al., *ACS App. Mater. Interface.*, 2017, 9, 10461

[3] F. Bally-Le Gall, et al., *Plasma Process. Polym.*, 2019, 16, 1800134

Keywords: cell biology, protein adsorption, biointerface, plasma polymer, nanocoating

P9/ Influence of surface modification on iron oxide peroxidase-mimic activity for antibacterial application

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Concerns over microbial drug resistance drive extensive research for effective, stable, and broad-spectrum antimicrobial agents. Iron oxide nanoparticles (IONPs) have emerged as promising candidates owing to their intrinsic catalytic, magnetic properties, and biocompatibility [1]. These IONPs exhibit peroxidase (POD)-like activity, enabling the generation of reactive oxygen species (ROS) with potent antibacterial effects [2]. However, immediate radical quenching due to ultra-short halftimes hampers diffusion and bactericidal efficacy [3]. Our study aimed to investigate the POD-like activity of diverse IONP formulations and evaluate the impact of surface modification on their catalytic activity and antibacterial efficiency. Commercial NPs employed in our investigation included superparamagnetic iron oxide NPs (SPIONs), palladium-coated SPIONs (SPION-Pd), and polymer-coated γ -Fe₂O₃ NPs. Additionally, we have synthesized Fe₃O₄ NPs coated with oleic acid (OA-Fe₃O₄). Characterization of these IONPs was conducted using TEM, EDS, FTIR, and DLS techniques. Evaluation of POD-like activity and leached ions employed the TMB-H₂O₂ and ABTS-H₂O₂ assays, with absorbance measurements conducted at 650 nm and 405 nm, respectively. Notably, aptamer adsorption onto NPs induced significant alterations in the zeta potential of IONPs, corroborated by the presence of a phosphate peak in the FTIR spectra. Our preliminary findings unveiled distinctive responses to aptamer adsorption across various IONP formulations. Substrate-specific catalytic activity was observed, with OA-Fe₃O₄ and SPIONs exhibiting a notable increase in POD-like activity in the TMB-H₂O₂ assay upon aptamer adsorption. Conversely, in SPION-Pd and polymer-coated γ -Fe₂O₃, catalytic activity diminished in the TMB reaction following aptamer adsorption. In the ABTS-H₂O₂ assay, a decrease in POD-like activity was observed in OA-Fe₃O₄ and SPIONs upon aptamer adsorption. Our preliminary data indicate successful aptamer functionalization, and enhanced POD-like activity post-adsorption, suggesting potential for improved antibacterial efficacy. Future endeavors will focus on the identification of specific aptamers, antibodies, and nanobodies targeting pathogenic bacteria, alongside investigations into the capture and antibacterial activity of these nanoparticle formulations.

[1] Asma Ghazzy, et al., *Nanoscale Advances*, 2024, 6(6)

[2] Sang, Y., et al., *Advanced Functional Materials*, 2019, 29(22)

[3] Gao, L., et al., *Nature Nanotechnology*, 2007, 2(9)

Keywords: iron oxide, aptamer, functionalization, peroxidase activity, antibacterial

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P10/ Surface modification of zirconia for bioactive dental implants to promote soft tissue integration and limit peri-implantitis

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Within the NOMAD project (Horizon Europe project 101091669), our primary mission is to contribute to the development of cutting-edge, resilient, and highly effective dental implants. Traditionally, Titanium (Ti) has been a widely employed dental implant material due to its robust osseointegration capabilities and cost-effectiveness. However, the emergence of high-performance ceramic materials, such as zirconia (ZrO₂), has gained prominence. Zirconia, distinguished by its tooth-like color, high mechanical strength and excellent soft tissue integration, has spurred an exploration of bioactive and osteogenic surface modifications [1]. Our overarching goal is to ensure the sustained clinical success of dental implants by improving zirconia dental implant osseointegration [2], while simultaneously mitigating the incidence of peri-implant diseases.

The prevalence of peri-implant mucositis and peri-implantitis, affecting 43% and 22% of treated individuals, respectively, underscores the importance of our research. In the present contribution, we focus on preventing peri-implantitis by enhancing the effective and fast sealing of soft tissue around the abutment as a result of the surface modifications of ZrO₂ implant with bioactive molecules [3].

Our team is functionalizing the ZrO₂ surface through the covalent bonding of specific peptides, utilizing an intermediate layer of organo-silanes or organo-phosphonic acids bearing a chemically active functional group at the ω- position.

The covalent biofunctionalization process unfolds in two steps. First, a covalent bonding of an intermediate layer of organosilanes or phosphonic acids with a carboxylic acid, amine or iodine at the ω- position is established. Subsequently, since grafting peptides directly on the material is challenging, peptide grafting occurs on this first layer, with coupling performed through click chemistry, NHS ester/EDC chemistry or direct nucleophilic substitution. In the present contribution, to minimize surface contamination and activate the oxide's surface, samples underwent pre-treatment techniques, including polishing and ozone treatment under UV exposure. The resulting surfaces were characterized using Water Contact Angle (WCA) measurements, X-ray Photoelectron Spectroscopy (XPS) and Scanning Electron Microscopy (SEM). Next, the grafting of organo-phosphonic acid and organo-silane molecules were optimized. The efficacy of the grafting was ascertain using WCA, colorimetric assays (Toluidine blue, ADECA titration) and XPS. The zirconia surface pre-treatment and functionalization will be discussed.

[1] S. K. Hsu et al., Elsevier B.V., 2014, 572, 91–98, doi: 10.1016/j.tsf.2014.07.068

[2] G. Hong et al., Applied Surface Science, 2021, 570, doi: 10.1016/j.apsusc.2021.151144

[3] A. L. Palkowitz et al., Advanced Healthcare Materials, 2021, 10, doi: 10.1002/adhm.202100132

Keywords: zirconia, covalent biofunctionalization, peptide grafting

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P11/ Development of copper free click chemistry active surfaces for bacteria trapping on porous silicon: gas phase silanisation and molecular dynamics simulations studies

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Sepsis is a blood bacterial infection that can lead to death in few hours in the most severe cases. In sepsis patients, bacteria are difficult to identify because of their low blood concentration (1 CFU/ml). Today, sepsis diagnosis requires blood culture for several days before mass spectrometry (MS) analysis of bacteria. Our aim is to develop chemically functionalized porous silicon surfaces (pSi) to enhance the selective trapping of bacteria from blood and allow their identification by infrared desorption-ionization on silicon (IR-DIOS)-MS in few minutes at the bedside of the patient. Compared to UV lasers classically used in DIOS-MS (detection of metabolites), IR will broaden the range of masses detected, which should be more suitable for the analysis of bacteria. pSi surfaces (pore diameters around 1 μ m) are expected to act as a blood filter, to increase the specific surface, and to improve bacteria desorption thanks to nanophotonic effects. Bacteria will be specifically trapped on the pSi surface thanks to the immobilization through copper free click reaction of azide modified nanobodies with dibenzocyclooctyne (DBCO) modified surfaces.

Our first objective is to functionalize the pSi surface with DBCO-PEG-silane molecules in vapour-phase [1]. This method enables the high aspect ratio surfaces to be functionalised homogeneously, without any solvent, and to mix silane molecules with different chain lengths and with/without DBCO terminal groups. A home-made reactor was built and the impact of process parameters on propyldimethylmethoxysilane was first investigated (pSi surface temperature, silane molecule injection modes, silanization duration). The functionalized surfaces were characterized by FTIR-ATR. The process is being implemented for DBCO-PEG₃₄-silanes molecules.

The availability of DBCO groups, as well as the conservation of their structure, are essential to allow the subsequent grafting of a nanobody. In addition, the nanobody must maintain its bioactivity with respect to antigens. Therefore, its structure must not be modified through interaction with the surface. Consequently, molecular dynamics (MD) simulations were performed to predict the optimal (i) surface coverage of DBCO-PEG-silane molecules, (ii) PEG chain length, (iii) the "DBCO-PEG-silane: PEG-silane" ratio, and (iv) the PEG chain length of the DBCO-PEG-silane molecules in a mix self-assembled monolayer. The availability of DBCO was found to be optimal under the following conditions: 0.3 molecule per nm² and a ratio "DBCO-PEG₃₄-silane: PEG₃₄-silane" equal to 1:1. We are now studying by MD simulations the conformational changes of the grafted nanobody under such conditions.

Future work will focus on establishing the proof of concept of our device by grafting Listeria nanobodies on the DBCO-PEG-silane modified pSi surfaces to trap Internalin B in model solution and then in plasma for IR-DIOS-MS analysis.

[1] Pujari, S. P. et al., *Angew Chem Int Ed*, 2014, 53(25), 6322

Keywords: chemical functionalization of porous silicon surfaces, molecular dynamics simulation, Listeria nanobody, surface characterization by FTIR-ATR, IR-DIOS Mass Spectrometry

P12/ Selective anchorage of tailored DNA origami on SiO₂ and TiO₂ substrates: characterization by fluorescence imaging and Atomic Force Microscopy

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DNA origami method [1] consists in folding a long DNA strand into a desired shape. It provides an elegant approach for elaborating nanoobjects with predefined shapes with a theoretical spatial resolution of 2 nm. DNA origami is currently explored as a strategy for bottom-up nanofabrication [2]. In this perspective, one of the challenges with DNA origami is to address them adequately on precise locations. Chemical deterministic positioning on multi-material substrates can be a strategy for achieving this goal. Herein, an interplay between specific interaction and electrostatic forces were explored. Phosphonic acids are known to bind on oxidized titanium surfaces [3]. Triangular fluorescent DNA origami with 40 nm of characteristic size and 7 nm height were modified with fluorescent oligonucleotides bearing terminal phosphonates moieties according to different geometries [4]. The resulting tailored DNA origami were left to interact with TiO₂ and SiO₂ substrates with different physico-chemical conditions and washing steps. Surfaces were analyzed by fluorescence imaging and Atomic Force Microscopy (Fig. 1). Semi-automatic analysis enabled to quantify the surface coverage fraction for different ionic composition. Buffer composition, presence or absence of phosphonate terminal moieties and substrate type enabled to anchor DNA origami triangles with different yields.

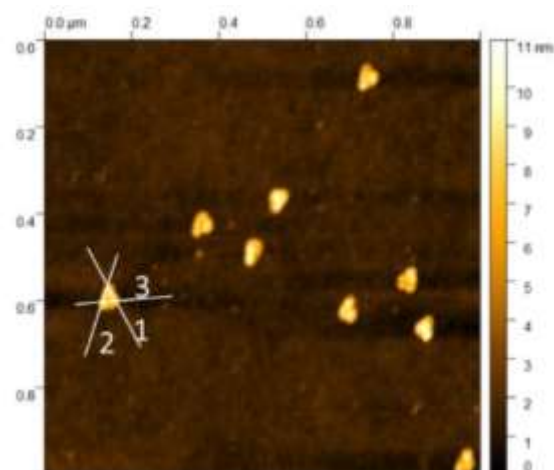


Figure 1. AFM image of DNA origami deposited on SiO₂/Si substrate and washed with buffer solution (TBE) containing 5.5 mM of magnesium chloride

[1] The first 3D DNA origami paper, doi: 10.1038/nature08016

[2] G.Thomas, et al., ACS Appl. Mater. Interfaces, 2020 12, 36799

[3] J.Zhang, et al., Langmuir, 2019, 35, 9554

[4] B.Gerland, et al., Org. Chem., 2012 77, 7620

Keywords: DNA origami, modified oligonucleotides, surface interactions

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P13/ Pathogens dairy contamination detection by QCM

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Food industry is increasingly affected by pathogen contamination [1]. The time required for accurate detection of products potentially contaminated by pathogens is long, ranging from one to several days depending on the case. In the dairy industry, pathogenic bacteria are present in very low concentrations and can only be detected after 20 to 36 hours best. In addition, European standards stipulate that 25 g of milk or cheese must be free from bacteria before it can be marketed. To enable suppliers to act in time to stop the production and marketing of these potentially contaminated products, it is necessary to considerably reduce the analysis time, by a factor of at least 2, and to lower the detection limit.

The aim of the project is to optimize the two main steps in the analytical process: to significantly reduce the time taken to obtain the first negative result (absence of bacteria), and to lower the detection limit (LOD50) of the target in order to detect bacteria in the sample quickly and efficiently.

With this in mind, we have chosen to use magnetic nanoparticles functionalized with specific antibodies. Their role will be multiple: on one hand, to enable “artificial” enrichment by magnetic separation and elution, followed by recovery in a smaller volume [2]. On the other hand, the capture of a bacterium by one or more nanoparticles around 50 times heavier will enhance detection by quartz crystal microbalance (QCM).

The chosen detection method is thus based on gravimetric analysis, using a QCM, of *Listeria* and *E. coli* bacteria, weighed down with functionalized magnetic $\text{Fe}_3\text{O}_4@SiO_2$ nanoparticles (creation of bacteria-nanoparticle complexes, B-NP). The quartz surfaces used in the QCM and the nanoparticles will be functionalized with specific antibodies against the target bacteria, to create a “sandwich” type device for trapping bacteria. (Fig. 1) Surface functionalization protocols have been validated with *E. coli* and *Listeria innocua* captures. Tests of dynamic and static capture of bacteria alone via QCM have been carried out, and preliminary results show specific capture of the targeted pathogen.

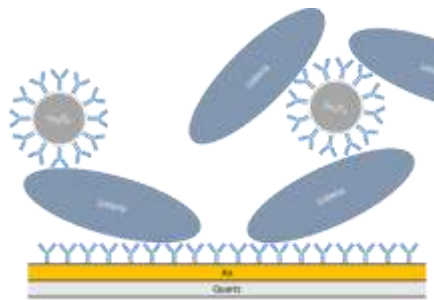


Figure 1. “Sandwich” type device for trapping bacteria

[1] <https://www.who.int/news/item/05-06-2019-23-million-people-falling-ill-from-unsafe-food-each-year-in-europe-is-just-the-tip-of-the-iceberg>

[2] Li 2019 et al., J Nanobiotechnol, 2019, 17, 59

Keywords: complex fluid analysis, bacteria concentration and detection, sensor, dairy production

P14/ Development of an instrumented physiological microdevice for the modelisation of human brain vasculature in tumoral context

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Glioblastoma is the most frequent and aggressive brain tumor. Conventional treatments are not sufficiently effective, and the development of new drugs can be hampered due to the blood-brain-barrier (BBB). Current studies aim at reproducing in vitro the cerebral vascular microenvironment, in a healthy or tumoral context, but often neglect the impacts of extra-cellular matrix (ECM) or flow conditions [1]. Nevertheless, the blood flow induces pressure and shear stress gradients, promoting angiogenesis, in healthy and tumoral environments [2]. With the objective of overcoming these gaps, this study focuses on the design, mold printing and casting of a microchip that can host a hydrogel mimicking the ECM, within which a cell coculture could organize as a vascular network. This network will be perfused to reproduce the blood flow.

The microchip design has been optimized to ease the demolding of the PDMS (polydimethylsiloxane) chip from the 3D printed PLA mold (polylactic acid), and facilitate plugging to a microfluidic system. The hydrogel was cast in the 1 mm x 1.4 mm central space of these chips, around a previously introduced 200 µm diameter needle. The hydrogel was composed of fibrin and type-I microfibrillar collagen. Gelation was too fast, and temperature were set at 4°C during manipulations to slow it down. Further works on the collagen microfibers is undergoing to increase hydrogel mechanical, such as a reticulation at 200°C for 24 h under vacuum (50 mbar). The needles were withdrawn after gelation, leaving a channel in which endothelial cells (HBEC-5i) will be seeded to mimic a venule. A syringe flow controller was used to perfuse the venule, modelling the blood flow and its effect on the BBB. In addition to the endothelial cells, three other human cell types were used. Pericytes (HP) have a major angiogenic role, while astrocytes (HA) reinforce the newly created vasculature. Glioblastoma tumoral cells (U87-MG) may enable the angiogenesis but also disturb the microenvironment. 2D tests were conducted to determine the adequate medium and cell proportions for the coculture.

All those steps get use closer to the development a 3D BBB capillary system, with human cells embedded in a collagen-based ECM cast into PDMS chips. The next steps will consist in system instrumentalization for the transport detection of drug candidates such as innovant nanocarriers. Applications for personalized medicine are to be expected with our system.

[1] Piantino, et al., *Frontiers in Toxicology*, 2021, doi: 10.3389/ftox.2021.656254

[2] Bouhira et al., *Biofabrication*, 2020, doi : 10.1088/1758-5090/ab5898

Keywords: Organ-on-Chip, blood-brain-barrier (BBB), glioblastoma, extracellular matrix, cell culture

P15/ Development of a complex vascular microarchitecture in a physiological microdevice to study the impact of a tumoral context on the brain angiogenesis and blood-brain barrier

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The blood-brain-barrier blocks the passage of many exogenous molecules into the brain, reducing treatment options for brain pathologies. In the case of multiform glioblastoma, the most frequent brain tumor, the evolution of the BBB remains uncertain. Developing a BBB-on-chip (BBBoC) model is particularly pertinent to compare its function in a healthy and tumoral context.

The BBB consists of a complex vascular network. The former BBBoC model was constructed with a single straight central channel seeded with endothelial cells and surrounded by a hydrogel matrix which may contains tumor and support cells. The complexification of the channel design brings the model closer to reality. Several biocompatible sacrificial materials were tested and compared: carbohydrate glass [1], gelatin [2], or a mixture of waxes [3]. They were assessed in terms of ease and rapidity of synthesis, molding and demolding (in a PDMS template obtained from 3D printing), shape conservation, and triggered dissolution, taking into account the constraints of cell preservation. Around those sacrificial materials, the hydrogel is cast. After gelation of the matrix, a buffered solution dissolves the material (different temperatures and protocols were tested), making way for a more complex network of about 100-200 μm diameter channels. The biocompatibility of the materials and the dissolution processes were assessed on glioblastoma cells (U87-MG) dispersed in the hydrogel (live-dead kit).

The next step will be to check the viability of endothelial cells seeded in the channels, and of the support cells (astrocytes and pericytes) seeded within the hydrogel. The perfusion of this vascular network, with a biological fluid, will reproduce the blood flow to study the angiogenesis phenomenon and the obtention of the blood-brain barrier functions with or without cancer cells in the matrix.

[1] Miller et al, Nature Materials, 2012, 11, 778

[2] Golden et Tien, Lab on a Chip, 2007, 7, 720

[3] Wan et al., Micromachines, 2020, 11, 907

Keywords: microfluidic, brain cancer, sacrificial biomaterials, vascularization, tumor-on-chip

P16/ Inhibition of *Pseudomonas aeruginosa* by combining honey and *Staphylococcus epidermidis* in agarose hydrogels

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Skin wounds are a gateway for bacteria to infect patients. However, preventing infection with antibiotics or other bactericidal agents contributes to the emergence and spreading of resistance to these essential therapeutic agents. Therefore, novel ways for anti-pathogen therapy are needed, dedicated to the prevention in particular. Playing with skin microbiota is one of these new ways. More specifically, *Staphylococcus epidermidis* (*S. epidermidis*), a skin commensal bacterium, can have a “probiotic” function by preventing colonization of the host by severe pathogens [1].

We studied the antibacterial effect of *S. epidermidis* encapsulated in agarose hydrogel (AH) supplemented with honey against pathogens. We found that the supplementation with honey enhanced the potential of *S. epidermidis* to inhibit the growth of *Pseudomonas aeruginosa* (*P. aeruginosa*), a bacterial species particularly harmful due to its facility to become resistant. The inhibition was concentration-dependent and complete from 2.4×10^2 CFU of *S. epidermidis* per mL of hydrogel. Supplementary results on other pathogens (*Staphylococcus aureus*, *Acinetobacter baumannii*) suggest that the intensity of the inhibition significantly varies with the species. A direct effect of the viscoelastic or hydration properties of the *S. epidermidis* + honey AHs on the pathogen growth could be excluded, whereas the ATR-FTIR fingerprints of extracts from the *S. epidermidis* + honey AHs suggest slight changes in the metabolism of *S. epidermidis* in these hydrogels. The morphology of *S. epidermidis* cells encapsulated in *S. epidermidis* + honey AHs is also modified in these conditions. The identification and quantification of proteins contained in the extracts is on-going, which should contribute to explain these promising results.

[1] T. Nakatsuji et al., Sci Adv, 2018, 4(2), doi: 10.1126/SCIADV.AAO4502

P17/ Cell & tissue engineering at FEMTO-ST/MN2S/BIND

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The BIND (BioInterfaces aNd Devices) team [1] is interested in the design of high-performance microdevices (lab-on-chip / organ-on-chip for instance) for the detection and quantification of biological elements in flow and complex fluids. They combine actuators, biosensors and bioengineering for active control and multi-scale characterization of biofluids. Our researches cover areas from the fundamental research to the patient in collaboration with health actors, with applications in innovative therapy, personalized medicine, contamination detection, drug qualification, and protein structure & function characterizations. Our research is focused on five axes: microsystems for life sciences, label-free detection, physical chemistry of surface/interface, characterization of fluids, and physiological microchips.

The team relies on multidisciplinary skills in biochemistry, biology (including eukaryote and prokaryote cell & tissue engineering & characterizations), engineering sciences, surface chemistry and on a strong technological expertise embodied by the national micro/nanofabrication platform Mimento [2], part of the Renatech french network [3].

In bioengineering, elements at the micro-nano or macro-scale (proteins, vesicles, bacteria, cells or tissues) are first cultivated and/or isolated and then characterized through diverse multi-scale techniques up and/or down microdevices. Using conventional viability and toxicity assays on unconventional functionalized materials, the biocompatibility and anti-microbial activities of functionalized surfaces can also be measured. As such, a project just finished demonstrating a kinetic approach to synergize bactericidal efficacy and biocompatibility of silver-based sol-gel coatings for biomedical applications.

[1] <https://teams.femto-st.fr/BIND/>

[2] <https://www.femto-st.fr/fr/Plateformes-technologiques/Mimento-presentation>

[3] <https://www.renatech.org/>

Keywords: cell and tissue engineering, biocompatibility, characterizations

P18/ Lab-on-chips & organ-on-chips at FEMTO-ST/MN2S/BIND

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The BIND team (BioInterfaces aNd Devices) [1] is going from fundamental research to the patient through a better understanding of biological phenomena in close collaboration with health actors and using our expertise in bio-interfaces and innovative microsystems for biological fluids analysis and organ-on-chip development. The group relies on multidisciplinary skills in biochemistry, biology, engineering sciences and on a strong technological expertise embodied by the use of Mimento [2], a national micro-nanofabrication platform part of the Renatech french network [3].

We currently focus our research efforts in five main axes: (1) Microsystems for life sciences: clean-room based fabrication and integration of complex analytical systems. (2) Label-free detection: multi-parameter detection with optimized bio interface using acoustic or optical transductions.

Physical chemistry of surface/interface: understanding and control of surface properties for biological interaction. (3) Characterization of fluids: characterization of biofluids for diagnosis, biological purpose or agrofood process monitoring. (4) Bio-on-a-chip: development of organ/tumor/tissue on chip for in vitro study of biological response.

After designing the chips, during or after their microfabrication, the surfaces are prepared by structuration or functionalization. Several goals are pursued, either to enhance the biocompatibility, biosafety of the materials, or for lab-on-chip to specifically recognize biomarkers or other biological compounds. Depending on the purpose of the microdevice, different materials are used: polymers, thermoplastics, resins, silicon, glass and piezoelectric materials. Piezoelectric materials are employed in particular when we want to integrate functions such as sorting, isolation of biological elements and detection of specific elements with good sensitivity in a complex fluid. By integrating sensors into the microdevice, and therefore into microfluidic channels or bioreactors, we can reproduce and monitor physiological mechanisms. This provides a better understanding of biological mechanisms with significant control over parameters such as shear, velocity and pressure of the biofluids within the channels.

The microfluidic circuits, bioreactors and sensors are designed and optimized using COMSOL Multiphysics® software. The instrumentation of organ-on-chip is another objective of the team. With the adjunction of mammal or bacterial 2D or 3D cell culture in hydrogels, we develop physiological microsystems. Biological fluids can mimic the blood or lymph flow, to reproduce in our microchips healthy and pathological vascularized human tissues, and validate in vitro the efficiency and safety of innovations for health: antibacterial surfaces or biological drugs for instance.

[1] <https://teams.femto-st.fr/BIND/>

[2] <https://www.femto-st.fr/fr/Plateformes-technologiques/Mimento-presentation>

[3] <https://www.renatech.org/>

Keywords: microfabrication, biochemistry, microfluidic device, physiological microsystems

P19/ Electropolymerization of pyrrole-based metal N-Heterocyclic carbenes for antibacterial applications

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N-heterocyclic carbenes (NHCs) are strong σ -donor ligands capable of coordinating a large proportion of transition metals. Metal-NHC complexes have been firstly used for catalytic applications and are now seen as good and flexible moieties for the development of biologically active molecules [1]. Researchers have synthesized metal-NHC derivatives for antimicrobial and anticancer applications that have shown encouraging results, both *in vitro* and *in vivo* [2]. However, only simple complexes were tested and the possibility to use polymeric metal-NHC as bioactive materials is yet to be investigated. In this work, a new strategy has been explored to develop antibacterial surfaces from electroactive metal-NHC monomers. To achieve this purpose, a series of pyrrole-functionalized NHC complexes containing various transition metals (Cu, Ru, Rh, Ag, Au) were synthesized using mechanochemistry or classical solvent synthesis. The electropolymerization was carried out on gold surfaces using cyclic voltammetry to produce polypyrrole films. The obtained polymeric materials were fully characterized by Fourier Transform InfraRed spectroscopy (FT-IR), X-ray photoelectron spectroscopy (XPS), scanning electron microscopy (SEM), profilometry and water contact angle (WCA) analyses. The antibacterial activity of these novel materials has been measured against four different bacterial strains by the halo inhibition method. The metal-containing polypyrrole surfaces have shown good antibacterial activity that depends on the nature of the metal and the bacterial strain.

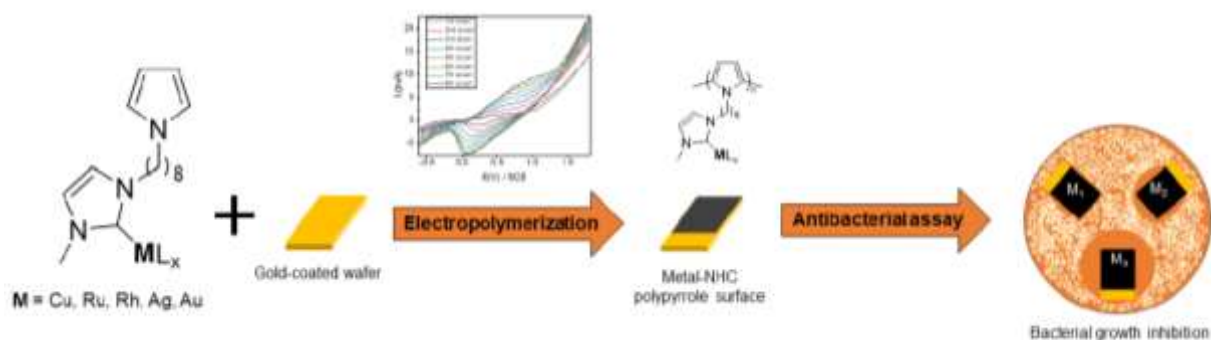


Figure 1. Preparation of polypyrrole metal-NHC surfaces and measure of their antibacterial properties.

[1] Jalal, M. et al., Mater. Today Proc., 2020, 31, S122

[2] Nayak, S. and Gaonkar, S. L., ChemMedChem, 2021, 16(9), 1360

Keywords: N-heterocyclic carbenes, electropolymerization, polypyrrole, antibacterial materials

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VI. Practical information and access

Conference place

Faculté des Sciences et Techniques (FST)

Université de Haute-Alsace (UHA)

18 rue des Frères Lumière

68093 MULHOUSE

To enter the building: +33 (0)3 89 60 88 04



Illberg Campus map



How to get there?

By tram

Tram 2 – Illberg station (from *Gare Central* station: **Tram 1**, **Tram 3** or **TramTrain** until *Porte Jeune* station; then, **Tram 2** until Illberg station).

<https://www.solea.info/se-deplacer/horaires-des-lignes/votre-itineraire>

By car

Mulhouse is at the junction of the A36 (5h from Paris) and A35 highways. From the highway, take *Les Coteaux* exit to the RD 68 (expressway).

Parking available near the Faculté des Sciences et Techniques (see Illberg Campus map).

By train

Regular connections Paris-Mulhouse (3h30) and Strasbourg-Mulhouse (1h), then tram from *Centrale Station* (20 min) (see above for access with tram).

www.sncf-connect.com

By plane

Airport *Euroairport Basel-Mulhouse* (30 km from Mulhouse); then shuttle to *Saint-Louis train station*; then train to Mulhouse central station; then tram from *Centrale Station* (20 min) (see above for access with tram).

www.euroairport.com

Public transport in Mulhouse

Tram

Tram 1: from *Gare Centrale* station to *Châtaignier* station.

Tram 2: from *Nouveau Bassin* station to *Nations* station.

Tram 3 and **TrainTrain:** from *Gare Centrale* station to *Lutterbach gare* station (further to *Thann* station for *TramTrain*).

<https://www.solea.info/se-deplacer/horaires-des-lignes/votre-itineraire>



Last **Tram 2** at *Palais des Sports* station at **23:40** (direction *Nouveau Bassin* station)
Last **Tram 3** at *Zu-Rhein* station at **23:08** (direction *Gare Centrale* station)

See simplified plan of public transport in next page

