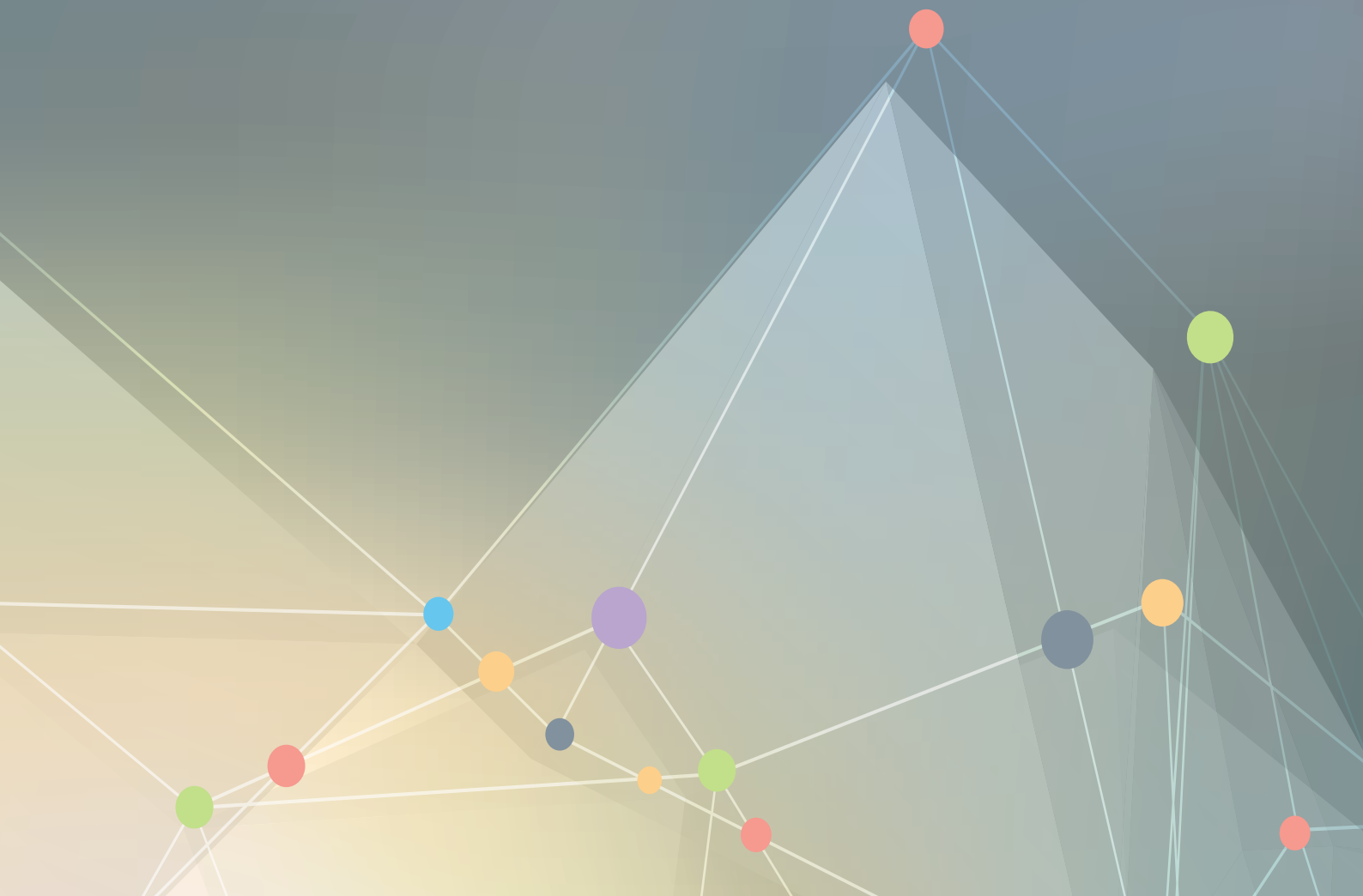
BOOK OF ABSTRACTS

Oral Presentations



C'Nano
THE NANOSCIENCE MEETING
2023

Poitiers
March, 15, 16 and 17

NanoBiosciences

(Last update: August 23th, 2022)

Description

The « Nanobiosciences » session is dedicated to the study of the organization of biological matter at the nanoscale and to the design of nanometric tools for sensing, imaging and therapy.

This year, we wish to make a special emphasis on the following topics:

- Biological structures at the nanoscale: coacervates, protein bodies, exosomes...
- Interfacing nanomaterials with living organisms: surface bio-engineering, targeting, intracellular trafficking, pharmacokinetics and biodistribution...
- Physical state of nanodrugs: nanoprecipitation, nanocristallisation...

All contributions related to the following topics (and more!) are also welcome:

- Lipid particles, self-assemblies, polymeric or inorganic particles, nanohybrids, lipoplexes, nanoemulsions
- Nanoprobes: magnetic, multiphotonic, plasmonic, photoacoustic
- Nanotherapeutics: radiopharmaceutics and radiosensitization, drug or gene-delivery, photodynamic and photothermal therapy, magnetic hyperthermia, protein therapy

Keywords

nanoprobes & nanocarriers (organic, inorganic, hybrids) for imaging & therapeutics, nanoprecipitation & other processes for biotechnologies, surface/particle (bio)functionalization, membrane interaction and intracellular trafficking

Scientific committee

Frédéric AFFOUARD (Univ. Lille – UMET, Lille)
Philippe BERTRAND (Univ. Poitiers – IC2MP, Poitiers)
Adeline BOIRE (INRAE – BIA, Nantes)
Fabienne GAUFFRE* (CNRS – ISCR, Rennes)
Nadine MILLOT* (Univ. Bourgogne – ICB, Dijon)
Stéphane MORNET (CNRS – ICMCB, Bordeaux)

** Session Coordinator*

Wednesday March 15th

3.30 pm – 6.00 pm

Room 11/12

Program of the session

Chairs: Adeline BOIRE & Nadine MILLOT

NANOBIOSCIENCES		
15:30	**Bio-inspired compartments based on liquid-liquid phase separation**	**Nicolas MARTIN** • *CNRS – CRPP, Bordeaux – France*
16:00	From the "Ouzo effect" to the chemoradiotherapy : elaboration of hybrid nanocapsules for encapsulation and therapy	**Déborah IGLICKI** • *Univ. Rennes - ISCR, France*
16:15	Lipid-based nanodrugs in complex biological media: structure, corona formation and disassembly mechanisms	**Frédéric GOBEAUX** • *CNRS - NIMBE, France*
16:30	Organization of collagen I fibers and tissue hardening: markers of fibrotic scarring after spinal cord injury in mice revealed by multiphoton-atomic force microscopy imaging	**Oscar SAAVEDRA-VILLANUEVA** • *Univ. Montpellier - L2C, France*
16:45	Coffee break	
17:15	Self-assembly of shape-complementary DNA origamis for lithographic applications	**Nicolas TRIOMPHE** • *CEA - CBS, France*
17:30	Tissue / Organ-Selective Non-Viral Intracellular Drug-Delivery	**Peter DALKO** • *CNRS - LCBPT, France*
17:45	Aryl diazonium salts encoded plasmonic nanoparticles for multiplex color Raman imaging	**Da LI** • *Univ. Paris Cité - LCBPT, France*

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Nicolas MARTIN

CNRS I Researcher

Paul Pascal Research Center

https://www.crpp.cnrs.fr/nicolas-martin/

Biography

Nicolas MARTIN is a CNRS researcher at Centre de Recherche Paul Pascal (CNRS, University of Bordeaux, France). After completing his PhD in 2014 at Ecole Normale Supérieure in Paris on polyelectrolyte-assisted protein folding, he spent 4 years as a post-doc in the group of Prof. Stephen Mann at the University of Bristol (UK) to work on synthetic cells. He joined CNRS in 2018 where his current research interests focus on the design and characterization of reactive and responsive coacervates based on polyelectrolytes, nucleic acids, peptides or amphiphiles to mimic the dynamic organization of membraneless organelles in cells and shed light on the emergence of self-assembled life-like compartments.

Bio-inspired compartments based on liquid-liquid phase separation

Living cells are self-organized soft matter systems whose hierarchical structure spans from the nanoscale up to the microscale. Compartmentalization at all these length-scales is crucial for the dynamic coordination of biochemical reactions in space and time. Beyond canonical membrane-bounded organelles, such as the nucleus or mitochondria, membrane-less condensates formed by liquid-liquid phase separation of proteins and polynucleotides are now widely recognized to be important intracellular organizers. Recent years have witnessed a growing interest in the bottom-up assembly of synthetic micro-compartments that mimic the structure and functions of these condensates and that can serve as modules to assemble synthetic cells. Our research focuses on the design of microdroplets produced by liquid-liquid phase separation in aqueous polymer solutions, such as coacervates, as bio-inspired functional compartments.[1] In this talk, I will in particular show that stimuli-responsive coacervate microdroplets provide a promising approach to assemble dynamic models of biomolecular condensates.[2,3] Although the systems we study are typically micrometre in size, I will also show that nanoscale processes do contribute to the observed phenomena, in particular at the interface of droplets.[4] Recent directions towards the construction of more advanced synthetic cells that integrate multiple functions in a droplet will also be discussed.[5]

Keywords:

Coacervates; bio-inspired self-assembly; stimuli-responsive systems; synthetic cells; membraneless organelles

References

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C'Nano THE NANOSCIENCE MEETING Poitiers March, 15, 16 and 17 2023

Keywords: Ouzo, nanoprecipitation, chemotherapy, radiotherapy, nanoparticle
Disciplinary fields involved: chemistry, biology

From the "Ouzo effect" to the chemoradiotherapy : elaboration of hybrid nanocapsules for encapsulation and therapy

Déborah Iglicki[1], Clément Goubault[2], Olivier Gazil[1, 3], Myrtil L. Kahn[4], Ulrich JARRY[5,6], Rémy Le Guével[7], Hélène Solhi[7], Soizic Chevance[1], Fabienne Gauffre[1].

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The "Ouzo effect" is a spontaneous emulsification generating metastable nanodroplets, without using surfactant or energy input.[1] This phenomenon occurs in ternary mixtures of a hydrophobic oil, a water-miscible solvent and water. Thus, the supersaturated oil aggregates into small droplets which are suspended in the continuous phase. This phenomenon has been used mainly for the formation of nanoparticles, nanocapsules, and drug encapsulation.[2] In our case, we used the "Ouzo effect" in the presence of nanoparticles to produce hybrid nanocapsules (~ 100 nm), called Hybridosomes®.[3] These are composed of an inorganic nanoparticle shell (Iron Oxide, Au, etc.) stabilized by a polymer (PEG-PAA, PVPA, etc.), that make them exceptionally robust. These nanocapsules have an internal volume enabling to load up to 170 $g.L^{-1}$ of hydrophobic molecule inside.[4] Thanks to a good knowledge of the phase diagrams, we have successfully developed a protocol to encapsulate different hydrophobic drugs (liquid or solid) in these hybrid capsules. In this work, we studied the encapsulation of drugs that have different characteristics (molecular, salt, crystalline...). The core/ shell complementary properties present a real potential for biomedical applications such as diagnostic (MRI, fluorescence imaging…) and therapy (radiotherapy, chemotherapy…). We therefore investigated the effectiveness of such nano-objects in the hepatocellular carcinoma with studying chemotherapeutic effects of a hydrophobic drug (sorafenib) combined with the radiotherapy enhancement (radiosensitizer gold nanoparticles[5]) *in vitro*.

References:

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Keywords: nanodrug ; structure ; biomolecular interactions
Disciplinary field involved: physical chemistry
Sustainable Development Goals: Good health & well-being (Goal 3)

Lipid-based nanodrugs in complex biological media: structure, corona formation and disassembly mechanisms

F. Gobeaux[1], S. Lepêtre[2], M. Varna[2], P. Couvreur[2], L. Massade[3], P. Guenoun[1], J.-Ph. Renault[1], S. Pin[1] et F. Testard[1]

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Despite undeniable promising results in *in vitro* and animal experiments, the behavior of nanodrugs in the human body is still poorly understood. Indeed, carrying pharmacodynamics studies in a living body is very complex. To tackle this issue, we have developed an *in vitro* methodology enabling to clarify the interactions between NPs and the components of the biological fluids.[1]

Of note, most studies on protein-NPs interactions deal with solid, mineral NPs and one of the most reported phenomena is the formation of a corona around the NPs. However, in the case of soft nano-assemblies (NAs), this is observation is not so obvious and disassembly phenomena could be more important. Our team has started to gather a large body of evidence of the complex interactions between soft NAs and blood components using squalene-based NAs as a model system.[1,2,4]

Through different examples, we'll show how combining cryo-transmission electron microscopy, x-ray and neutron scattering, and spectroscopic methods enabled us to determine the structure and colloidal stability of squalene-based NAs carrying nucleoside, peptide or siRNA.[1-4], to monitor their disassembly and to evidence different types of corona-like structure forming around the NAs.

Reference:
[1] Gobeaux et al. (2020) *Nanoscale* 12 2793-280910. [2] Caillaud et al. (2021) *International Journal of Pharmaceutics* 121117 [3] Dormont et al. (2019) *Journal of Controlled Release* 307 302-314. [4] Gobeaux et al. (2021) *in preparation*

Acknowledgment: This work was supported by public grants overseen by the French National Research Agency (ANR) as part of the "Investissements d'Avenir" program (Labex NanoSaclay, reference: ANR-10-LABX-0035).

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THE NANOSCIENCE MEETING
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Keywords: Multiphotonic, atomic force microscopy (AFM), nano-bio-mechanic, spinal cord injury (SCI)
Disciplinary fields involved: Physics, biology and medicine

Organization of collagen I fibers and tissue hardening: markers of fibrotic scarring after spinal cord injury in mice revealed by multiphoton-atomic force microscopy imaging

Oscar Saavedra-Villanueva[1], Clara Manesco[1], Marta Martin[1], Joshua de Lizaraga[1], Thierry Cloitre[1], Yannick Gerber[2], Florence E. Perrin[2], and Csilla Gergely[1]

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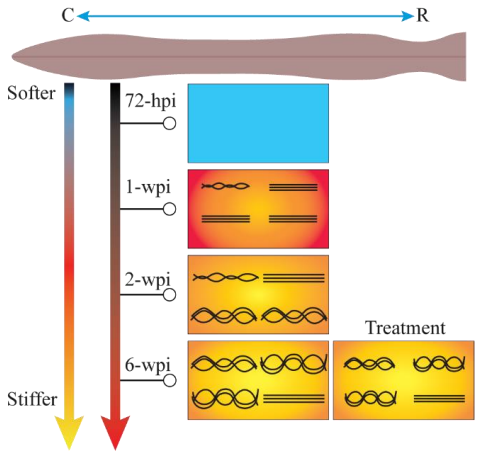
2. *MMDN, Université de Montpellier, EPHE, INSERM, Montpellier, France*

Spinal cord injury (SCI) is a dramatic disease leading to severe motor, sensitive and autonomic impairments. After the injury, the axonal regeneration is partly inhibited by the glial scar, acting as a physical and chemical barrier[1]. The scarring process involves microglia, astrocytes, and extracellular matrix components, such as collagen, composing the fibrotic part of the scar[2]. To investigate the role of collagen and microglia, we used a multimodal label-free imaging approach combining multiphoton and atomic force microscopies. The second harmonic generation signal exhibited by fibrillar collagen-I enables specifically monitoring it as a biomarker of the lesion. An increase in collagen density and the formation of more curved fibers over time after SCI are observed. Whereas 2-photon excitation microscopy (2PEF) showed the appearance and activation of microglia over millimeters in length near the injured area. Nano-mechanical investigations revealed a noticeable hardening of the injured area, correlated with collagen fibers' development. Additionally, we observed that inhibition of microglial proliferation by oral administration of GW2580 decreased the collagen density at the injured area. These observations indicate the concomitance of relevant structural and mechanical modifications during the fibrotic scar evolution.



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[2] Z. Li et al., "Fibrotic Scar After Spinal Cord Injury: Crosstalk With Other Cells, Cellular Origin, Function, and Mechanism," Frontiers in Cellular Neuroscience, vol. 15. Frontiers Media S.A., Aug. 26, 2021. doi: 10.3389/fncel.2021.720938.

Acknowledgment:

This work was publicly funded through ANR (the French National Research Agency) under the "Investissements d'avenir" program with the reference ANR-16-IDEX-0006.

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Poitiers
March, 15, 16 and 17

Keywords: DNA origami, self-assembly, shape-complementarity
Disciplinary fields involved : Biology, Chemistry, Physics
Sustainable Development Goals* eventually involved in your research: Sustainable consumption and production (Goal 12) and Climate Action (Goal 13)

Self-assembly of shape-complementary DNA origamis for lithographic applications

Nicolas Triomphe[1,2], Ludwig Rotsen[1,2], Guido Rademaker[2], Raluca Tiron[2], Gaëtan Bellot[1]

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2. *Univ. Grenoble Alpes, CEA, Leti, F-38000, Grenoble, France*

In nanotechnology in general and in semiconductor industry in particular, there is an ever-increasing need for smaller and more complex features at an ever-lower cost. To address the challenge of patterning at sub-10 nm scale, novel patterning strategies must be envisioned. I will present the method of DNA (desoxyribonucleic acid) origami nanostructures self-assembly as a new approach. DNA origamis are built by programming the assembly of DNA molecules through base pairing. By virtue of its inherent small helix diameter (2 nm), DNA can be programmed to self-organize into various 2D and 3D morphologies at nano-scale resolution [1, 2]. Therefore, DNA is a promising mask material for bottom-up lithography techniques.

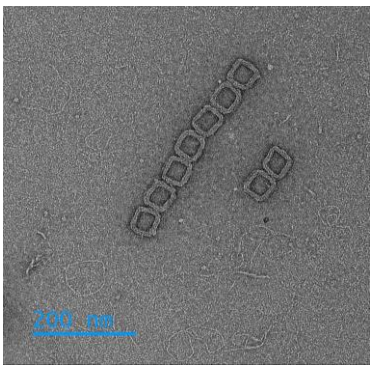

Figure 1: TEM image of DNA origamis self-assembling into a line.

Although DNA origamis are limited in size (from tenths to a hundred nanometers), 2D and 3D patterning and high molecular weight objects are obtained through binding of numerous origamis [3, 4]. Shape-complementarity is a powerful way to do so, allowing to create reversible DNA nanostructures [5]. By using this feature, we develop new origamis for 1D (see Figure 1: TEM image of DNA origamis self-assembling into a line.Figure 1) and 2D patterns. The focus will be brought on the 1D objects as well as the parameters and phenomena driving their self-assembly, which bring key information about to optimize shape-complementary binding.

References:

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Keywords : Drug-delivery; redox probe; imaging; pancreas.
Disciplinary fields involved: Chemistry / chemical biology
Sustainable Development Goals* eventually involved in your research: Good Health and Well-Being; Ensuring healthy lives and promoting the well-being for all at all ages is essential to sustainable development.

Tissue / Organ-Selective Non-Viral Intracellular Drug-Delivery

Amit Kumar[a], Zoeisha S. Chinoy[b], Anna Barosi[a], Petra Dunkel[a], Gauvin Hemery[b], Gregory Ramniceanu[c], Elisabeth Garanger[b], Sébastien Lecommandoux[b], Daniel Scherman[c], Lucie Sancey[d], Véronique Josserand[d], Julien Vollaire[d], Hamid Dhimane[a], Olivier Sandre[b]*, Bich-Thuy Doan[c]*, and Peter I. Dalko[a]*

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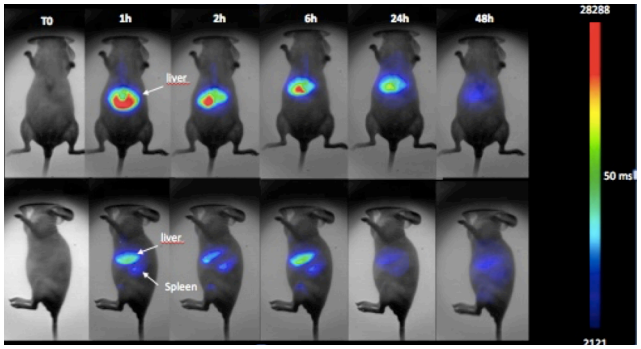
A conceptually novel redox-sensitized polymersome family was developed[1,2] that may be regarded in many aspects as "synthetic virus" analogs: they have the classical size of many viruses and have transfection ability (without the replication ability, of course). Structurally they are close to liposomes, while they are considerably more stable and robust: their membrane thickness (14 nm thick diblock copolymer bilayers in our case) imparts them with several advantages such as colloidal stability, fluidity, and tunable permeability. The challenging task of encapsulation of a variety of drugs and in particular of large protein and plasmid sequences were solved and the transfection ability of the surface-modified nano-cargo was demonstrated in eukaryotic cells. The incorporation of tracers such as superparamagnetic iron oxide nanoparticles (SPIONs) for MRI imaging and fluorescent gold nanocrystal for optical (SWIR) imaging were solved and were used to follow the biodistribution of the nanomaterials in vivo (mice). It was observed, that intraperitoneal administration resulted in selective accumulation of the Ps in the pancreas and in the surrounding adipose tissues in mice.



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Keywords: aryl diazonium salts, plasmonic nanoparticles, SERS, bioimaging, anti-counterfeiting

Disciplinary fields involved: Chemistry, Biology

Sustainable Development Goals* eventually involved in your research: Industries, innovation and infrastructure (Goal 9)

Aryl diazonium salts encoded plasmonic nanoparticles for multiplex color Raman imaging

Da Li[1], Philippe Nizard[1], Delphine Onidas[1], Vincent Nöel[2], Florence Gazeau[3], Giorgio Mattana[2], Yun Luo[1] and Claire Mangeney[1]

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Sensing and imaging technologies based on the use of nanoscale tools have received growing interest these last decades. Among the portfolio of reported bioimaging nanotools, labels based on optically encoded metallic nanoparticles (NPs) are particularly attractive as they are efficient Raman signal-enhancing materials, giving rise to intense surface-enhanced Raman spectroscopy (SERS) signals. As an alternative to fluorescent probes, the popularity of SERS tags has increased in recent decades.[1] Indeed, unlike the broad spectral feature of fluorescence probes, SERS tags provide multiple sets of narrow peaks, resulting in low spectral overlap and high multiplexing ability. In this talk, we will describe the potential of aryl diazonium salt-encoded silver NPs as contrast agents for Raman imaging. Compared to thiol self-assembled monolayers which are commonly employed for the preparation of SERS tags, aryl diazonium salts present several advantages, such as: (i) the formation of strong interfacial bonds with the supporting NPs, (ii) the presence of intense SERS fingerprints, (iii) the possibility to create multilayers with various functions. The formation of multilayers has been exploited here to introduce straightforwardly several SERS labels along the grafted polyaryl chains and post-functionalization moieties at their end. This new generation of SERS encoded NPs are efficient labels for Raman bioimaging inside cells or anticounterfeiting applications to secure hand-writing and inkjet-printed marks. Therefore, the aryl diazonium salt-based approach will not only pave a new way for the functionalization of metallic NPs by multilayers but also provide a general strategy to design SERS-encoded NPs[2-4].

References:

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Thursday March 16th

10.30 am – 12.30 am

Room 11/12

Program of the session

Chairs: Frédéric AFFOUARD & Fabienne GAUFFRE

NANOBIOSCIENCES		
10:30	**Nanodroplets to study crystallization and jellification phenomena using dropletbased microfluidics**	**Nadine CANDONI** • *AMU – CINaM, Marseille – France*
11:00	Design and performances of a 3D designed microfluidic cell for LSPR biosensing: A proof of concept study toward rapid bio-detection of pathogen targets	**Walid AIT MAMMAR** • *Sorbonne Univ. - LRS, France*
11:15	Nanoscale dynamic localization of single nanoparticles over an extended thickness at depth in complex (bio)environments	**Quentin GRESIL**• *CNRS - LP2N, France*
11:30	QD vs. organic dye in FRET biosensors: which one would you chose?	**Chloé GRAZON** • *CNRS - ISM, France*
11:45	Synthesis of hybrid nanoparticles to target extracellular vesicles	**Mélanie ROMAIN** • *Univ.Bourgogne - ICB, France*
12:00	Quantum dots micropatterning: towards biofunctionalization and nano-imaging	**Cyrille VEZY** • *UTT - L2n, France*
12:15	Use of core-satellite polymer-metal nanocomposites to remodel the tumor microenvironment of pancreatic cancer via combined therapies	**Jordan ROBERT** • *Univ. Montréal - GRSTB, Montréal*

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Nadine CANDONI

University of Aix-Marseille I Professor

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Biography

Nadine CANDONI is Head of the Biomedical Engineering Department of Polytech Marseille. She graduated in Physics and Chemistry at ENSCPB (1992) and obtained a PhD in Condensed Matter, Chemistry and Organization at Paris VI (1998). Nadine Candoni is professor at the Centre Interdisciplinaire de Nanoscience de Marseille (CINaM-UMR7325), which she joined in 1999. She first studied physico-chemical properties of individual molecules with Atomic Force Microscopy and Mechanically Controlled Breaking Junction. Nadine CANDONI is currently leading studies on nano-droplets (nL) for chemical reactions of solutes, using droplet-based microfluidics. She investigates from the generation of these nanoscale droplets to physicochemical properties of solute aggregation. Applications of her work concern crystallization of proteins and active pharmaceutical ingredients and jellification of biomimetic microparticles for Biomedical interests. She is the author of more than 70 publications and book chapters.

Nanodroplets to study crystallization and jellification phenomena using droplet-based microfluidics

We study crystallization of pharmaceutical molecules (proteins and active pharmaceutical ingredients) and jellification of biomimetic microparticles in nano-droplets (volume of nL), using droplet-based microfluidics:

- In crystallization in solution, the nucleation step determines the physical properties of crystals. However, the stochastic nature of the nucleation step requires a large number of experiments to obtain reliable data through statistical analysis. Using droplet-based microfluidics, experiments are carried out in hundreds of nano-droplets used as nano-crystallizers, while saving time and material. The size and frequency of the droplets are controlled without using surfactants [1]. We developed a versatile and easy-to-use microfluidic platform for non-specialists in microfluidics to: directly solubilize the powder of molecule of interest for solubility determination[2]; study nucleation kinetics[3] and polymorphism [4], generate a chemical library for crystallization condition screening[5], measure the concentration of the droplets by UV spectroscopy [6], validate polymorphism by Raman spectroscopy [2] and determine structure by X-ray diffraction [7].
- The Biomedical application aims to generate red blood cell mimes to validate an ultrasound tool for the diagnosis of red blood cell hyper-aggregation involved in thrombosis and diabetes. Therefore, calibrated microparticles are produced from nano-droplets of sodium alginate solution, by a contraction method [8]. They are jelled with calcium chloride giving deformable porous microparticles that are characterized in terms of mechanical properties, by Atomic Force Microscopy (AFM) and by manipulation with micro-clamps, and in term of structure by Scanning Electron Microscopy (SEM). [9]

Keywords:

Droplet-based microfluidcs; Crystallization; Polymorphism; Jellification; Biomimetic microparticles

References

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C'Nano
THE NANOSCIENCE MEETING
Poitiers
March, 15, 16 and 17
2023

Keywords: Gold nanoparticles, Immunosensor, Microfluidic chip, optical transduction
Disciplinary fields involved: Chemistry, Physics, Biology
Sustainable Development Goals* eventually involved in your research: Good Health and Well-Being (Goal 3)

Design and performances of a 3D designed microfluidic cell for LSPR biosensing: A proof of concept study toward rapid bio-detection of pathogen targets

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Food safety is a major public health concern, with foodborne diseases affecting 10% of the worldwide population according to the WHO. These foodborne diseases are often hard to tackle due to insufficient tracking of contaminated food. Therefore, on-site rapid testing constitutes an effective way for preventing foodborne contaminations. [1,2]

In this project, we developed a LSPR-based, solid-phase sandwich-type immunosensor capable of performing qualitative and quantitative measurements of a given target. Glass slides and AuNP were first functionalized with antibodies. Capture of target by antibody immobilized on glass slides was in turn revealed by adding AuNP bioconjugated to the same antibody (Fig.1 (a)) [3]. This produced a red color on the glass slide owing to the LSPR band of the AuNP whose intensity is related to the concentration of target and that is observable by the naked eye after 30 min incubation (Fig.1 (d)). Target detection was validated by scanning electronic microscopy analysis of the sensor surface (Fig1. (b)).

A proof-of-concept of our designed chip has been achieved with rabbit antibody (r-IgG) as a model target for which a limit of detection around 14 ng/mL was reached. The on-site detection aspect of the project is addressed using a lightweight portable spectrometer provided by our industrial collaborator "Goyalab" connectable to a computer or a smartphone. This last allowed to establish a dose-response curve for our model target (Fig.1 (e,f)) that was validated by absorption measurements carried out using a benchtop uv-vis spectrometer. In addition, we developed a 3D designed microfluidic chip for LSPR biosensing (Fig.1 (c)). Our next goal is to employ this setup to detect some allergens and toxins. This system would open avenues in the development of a portable and user-friendly immunosensor where the user may detect on-site a low concentration of pathogen from only a few drops of sample. [4]

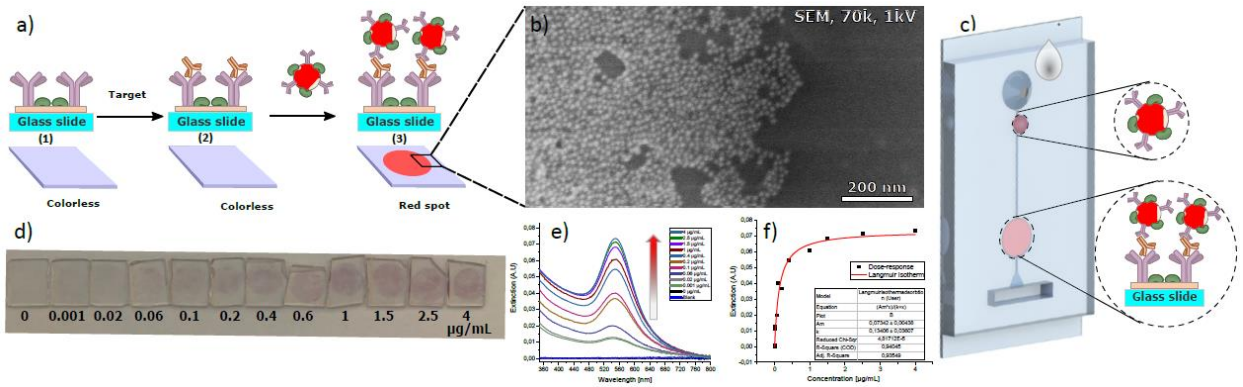

Figure 1 a) Schematic presentation of the sandwich type immunosensor. (1) Immobilisation of antibody (purple) on the glass surface and blocking step with BSA (green), (2) Incubation of target (orange), (3) Revelation with antibody-conjugated AuNPs (red spheres), b) SEM image of the border of the red spot, c) 3D design of the microfluidic device, d) Photos of glass sides exposed to increasing concentrations of r-IgG, showing increasing intensity of the red spot, e) extinction spectra of glass sides showing increasing intensity of the LSPR band, f) dose-response curve fitted by Langmuir isotherm.

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C'Nano
THE NANOSCIENCE MEETING
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2023

Keywords: Single-particle-tracking, 3d microscopy, diffusion, brain extracellular space
Disciplinary field involved: Physics

Nanoscale dynamic localization of single nanoparticles over an extended thickness at depth in complex (bio)environments

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The nanoscale architecture of living organs is often heterogeneous and tortuous. In the brain extracellular space (ECS), for instance, this complex maze is delimited by cellular walls where ions and signaling molecules diffuse, and its architecture is acknowledged to be important for proper function [1]. However, its precise structure is still mostly unknown. To address this challenge, recent advances in single-particle tracking based on SWIR emitting single-walled carbon nanotubes (SWCNTs) opened the avenue for exploring the ECS at the nanoscale at depth in living tissue [1]. However, in current approaches, the point spread function (PSF) limits the tracking of fluorescent nanoparticles to a narrow depth (typ. <1µm) around the two-dimensional imaging plane, restricting access to the axial information of the structure under study. PSF engineering can overcome this limitation by changing the shape of the PSF through phase modulation of the fluorescence signal [2], but it still needs to be adapted to the SWIR domain and in the context of dynamic imaging at depth. First, we will present single-particle-tracking using a novel design of annular binary phase mask [3] that extends the PSF in the axial direction over several microns. The modified PSF allows two-dimensional imaging of diffusing nanoparticles at depth and in a volume without adapting the tracking algorithm. Second, we will show how three-dimensional tracking of SWCNTs can be achieved over extended depths using a customized double-helix phase mask [4] operating in the SWIR. Applications to the study of the brain ECS structure will then be presented.

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Keywords: biosensor, FRET, fluorescence
Disciplinary field involved: chemistry, photonics
Sustainable Development Goals* eventually involved in your research: none

QD vs. organic dye in FRET biosensors: which one would you chose?

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Förster resonance energy transfer (FRET) is a widely used and an ideal transduction modality for fluorescent based biosensors as it offers high signal to noise with a visibly detectable signal. While intense efforts are ongoing to improve the limit of detection and dynamic range of biosensors based on biomolecule optimization, the selection of and relative location of the dye remain understudied. Herein, we describe a study comparing the nature of the dye, i.e., organic fluorophore (Cy5 or Texas Red) vs inorganic nanoparticle (QD) and the position of the FRET donor or acceptor on the bioreceptor. Using a recently discovered transcription factor (TF) – DNA biosensor for progesterone, we examine four different biosensor configurations and report the quantum yield, lifetime, FRET efficiency, IC50, and limit of detection. We identify key molecular parameters driving sensor performance in each biosensor configuration. Finally, we provide set of design parameters to enable one to select the fluorophore system for their future FRET assays and new diagnostic devices.

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Keywords: Nanoparticles, Extracellular vesicles, Microfluidics, Diagnosis
Disciplinary fields involved: Chemistry, Physics, Biology
Sustainable Dev. Goals* eventually involved in your research: Good Health and well-being (Goal 3)

Synthesis of hybrid nanoparticles to target extracellular vesicles

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Extracellular vesicles (EVs) present a growing field of interest due to their ability for biological content transport during intercellular communication and their noteworthy release in biofluids, making them promising biomakers for theranostic applications. However, it is very difficult to specifically target, isolate or characterize them because their circulation happens in complex samples (blood…) containing all subclass of EVs released continuously from different tissue/fluid cells. There, sub-populations of interests are minor and difficult to reach. This project aims to separate EVs sub-populations thanks to an acoustofluidic device combining microfluidic and electroacoustic modules to efficiently align and sort submicron biological particles based on physico-chemical properties [1]. In order to refine the sorting, targeted EVs will be spiked by hybrid nanoparticles (NPs), thus also facilitating EVs characterization.
Gold NPs are used for this purpose, and functionalized depending on the biomarkers of interests. A first linker grafting step is carried out, leading to stable suspensions. Studies with UV-Visible spectroscopy and SPR assays enable to define the optimum grafting conditions for this step [2]. The next step of covalent conjugation of recognition biomolecules is carried out with different proteins: cytochrome C chosen to define grafting conditions on the NPs, and then various antibodies chosen to selectively target some EVs. Various characterizations highlight the grafting of additional layers and maintained stability at each step of the synthesis. Then preliminary tests were carried out to study selective attachment in a complex media of the hybrid NPs to polymer microparticles, used as model EVs and functionalized with albumin. They show encouraging results which require further investigations.

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C'Nano
THE NANOSCIENCE MEETING
Poitiers
March, 15, 16 and 17
2023

Keywords: FRET, Quantum dots, nanoimaging, Cell adhesion, Biology
Disciplinary fields involved : Physics, surface materials, biophysics

Quantum dots micropatterning: towards biofunctionalization and nano-imaging

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   University of Technology of Troyes, Troyes France
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   Ecole Supérieure de Physique et de Chimie Industrielles, Paris, France

During adhesion and migration, single cells interact with their environment through various physicochemical force and sensing. Such highly specific interactions between the cell and the extra-cellular matrix are mainly controlled by integrins, in cooperation with many other proteins. But geometrical and mechanical constraints provided by *in situ* micro-environment must be mimicked in single-cell adhesion studies if one does not want to produce artifactual results [1]. Then, we propose a FRET-based imaging technique that will integrate in its core this micro structuration necessity: Non-radiative Excitation Fluorescence (NEF) nanoscopy. Using a monolayer of quantum dots as donors, NEF imaging allow selective observations of membrane components and quantitative measurement of cell-substrate distances, reaching a nanometric axial resolution without high laser irradiance nor long time acquisitions (Figure A). In order to combine NEFM and the micro structuration necessity, we have developed an innovative method to create micropatterns of highly concentrated quantum dots monolayer at large scale (Figure B) to organize them spatially by using photolithography and silanization processes. The obtained micropatterns will be used as a scaffold for surface structuration of the adhesion protein (fibronectin, laminin, RGD peptides, etc.) specifically recognized by integrins. We will show that FRET can be obtained, that it is possible to specifically bind any kind of his-tag proteins on the micropatterns and therefore that our approach is relevant for biofunctionalization and nano-imaging issues.

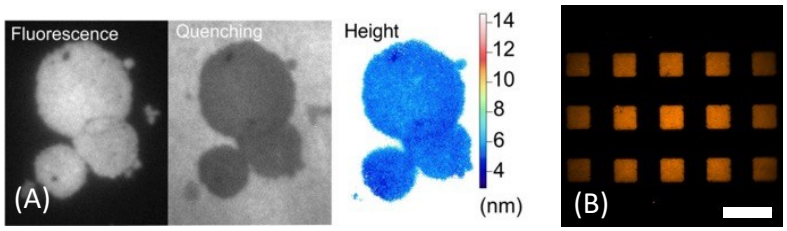

Figure: (A) Example of NEF imaging on giant vesicle: (Fluorescence) FRET signal of acceptor; (Quenching) Quantum dots monolayer as donor; (Height) Calculated distribution of proximity with substrate [2].
(B) Example of quantum dots micropatterns, colorized TIRF images. Scale bar: 50 µm)

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Acknowledgment:

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Thursday March 16th

3.30 pm – 6.00 pm

Room 11/12

Program of the session

Chairs: Philippe BERTRAND & Stéphane MORNET

NANOBIOSCIENCES		
15:30	**Translation to the clinic of an ultrasmall nanoparticle for treatment of cancer in combination with radiotherapy**	**François LUX** • Univ. Claude Bernard – ILM, Lyon – France
16:00	Biocompatible oily ferrofluid for better thermal tumor ablation efficiency	**Clément VECCO GARDA** • *CNRS - ICMCB, France*
16:15	Design of Iron Oxide Nanoparticles for imaging and active targeting: theranostic in one formulation	**Maria DE LOS ANGELES RAMIREZ** • *Univ. Strasbourg - IPCMS, France*
16:30	Impact of shape and defects of Iron Oxide Nanoparticles on photothermia and magnetic hyperthermia therapies	**Sylvie BEGIN COLIN** • *Univ. Strasbourg - IPCMS, France*
16:45	Synthesis, Characterization and Cellular Internalization of Anisotropic Magnetic Nanoparticles	**Jean-Michel SIAUGUE** • *Sorbonne Univ. - PHENIX, France*
17:00	Coffee & tea break	
17:30	Targeted thermal or mechanical Nanotherapy of pancreatic adenocarcinoma: efficacy and mechanisms	**Loubna LAIB** • *INSA Toulouse - LPCNO, France*
17:45	Bioimaging with persistent luminescence nanoparticles	**Cyrille RICHARD** • *CNRS. - UTCBS, France*
18:00	Luminescence nanothermometry for the control and understanding of heat-induced process and the fate of nanothermometers in vitro and in vivo	**Mahshid HASHEMKHANI** • *Univ. Paris Cité - MSC, France*
18:15	Synthesis & Functionalization of Hybrid Plasmon-semiconductor Nanoparticles for Cancer Photodynamic Therapy	**Thomas PONS** • *INSERM - LPEM, France*

François LUX

University of Lyon 1 I Assistant professor

Institute of Light and Matter

https://ilm.univ-lyon1.fr/index.php?option=com_directory&task=profile&id=73

Biography

Dr François LUX is a chemist, born in Le Mans in 1980. He was graduated by Ecole Normale Supérieure de Lyon and was laureate of Agregation of chemistry in 2003. In 2007, he received his PhD degree for his work on the synthesis and functionalization of lanthanides complexes. In 2009, he was recruited as assistant professor in the FENNEC team of Pr Olivier Tillement in Institute of Light and Mater of university Lyon 1. He was one of the co-inventor of the AGuIX nanoparticles currently in phase 2 clinical trial for the treatment of cancer in combination with radiation therapy and of MexCD1 polymer in phase 1 clinical trial for the treamtment of Wilson disease. He is co-founder of NH TherAguiX and MexBrain companies that are developping these two products. He has co-authored 116 scientific papers and 29 patents mostly on nanohybrids and their biomedical applications. He displays h-index of 35.

Translation to the clinic of an ultrasmall nanoparticle for treatment of cancer in combination with radiotherapy

During the last decades, ultrasmall inorganic nanoparticles have attracted growing interest due to their favorable properties for biomedical applications including tumor penetration by enhanced permeability and retention effect and easy elimination by the kidneys [1]. AGuIX nanoparticles are such king of ultrasmall nanoparticles designed for enhancement of radiotherapy. They are composed of a polysiloxane matrix on which gadolinium chelates are covalently grafted and display hydrodynamic diameter close to 5 nm [2]. Due to the presence of gadolinium atoms, AGuIX can be followed by MRI after intravenous administration and can act as radiosensitizers during treatment by radiotherapy. Their efficacy has been tested in more than twelve animal models of cancer before final translation in the clinic [3]. The synthesis of the nanoparticles has been optimized and scaled up and regulatory toxicity tests on two animal species have demonstrated very good tolerance profile. Consequently, the particles have been translated to the clinic first for treating brain metastases by whole brain radiation therapy (Phase I clinical trial NanoRad). During this clinical trial, no evidence of toxicity was shown and a clear targeting of the metastases has been demonstrated [4]. First encouraging insights have been shown also for the radioensitizing potential of these nanoparticles [5]. Following the success of this first clinical trial, phase 2 clinical trials have begun on the same indication and on others in France and in the US.

Keywords:

Ultrasmall nanoparticles; Clinic; Cancer; Radiosensitization; Gadolinium

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C'Nano THE NANOSCIENCE MEETING 2023
Poitiers March, 15, 16 and 17

Keywords : Magnetic hyperthermia, Magnetic nanoparticles, Thermoablation, Optical imaging
Disciplinary fields involved: Chemistry, Biology, Physico-chemistry
Sustainable Development Goals: Ensure healthy lives and promote well-being for all at all ages (Goal 3)

Biocompatible oily ferrofluid for better thermal tumor ablation efficiency

Clément Vecco-Garda[1], Pauline Jeanjean[2], Coralie Genevois[2,3,4], Franck Couillaud[2,3], Olivier Sandre[5], Stéphane Mornet[1,4]

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Aqueous ferrofluids used in magnetic hyperthermia (MHT) treatment, require huge amounts of magnetic nanoparticles (MNPs) to achieve complete tumor ablation. Different approaches have been developed to improve the heating power of MNPs such as changing their composition [1]. However, these parameters must respect biocompatibility criteria [2]. Another way consists of replacing the aqueous dispersion medium of the MNPs by a medium with better thermal inertia to better manage heat transfers such as biocompatible oily media.

The colloidal stabilization of MNPs in Miglyol® type oils were performed by chemisorption of phospholipids on their surface. We studied the impact of the surface grafting density of phospholipid and the influence of their chemical nature on the final redispersion behaviors in the oils. The heating properties of these oils were evaluated under magnetic induction. For *in vivo* studies indocyanine green, a near IR dye, was incorporated in the oily medium to localize the ferrofluid by fluorescent imaging. The fluorescent magnetic oil was injected directly into the subcutaneous tumor and MHT generated using an *in vivo* setup was monitored by optical imaging. The conditions of surface grafting density of phospholipid to reach the stabilization of MNPs in Miglyol® were determined in different types of oils for a narrow range of phospholipid grafting [3]. The heating properties of these magnetic oils proved that the dispersion of MNPs in a lipid phase permits to increase almost 10 times the thermal power compared with the aqueous ferrofluids. In same alternative magnetic field conditions, specific adsorption rate (SAR) of MNPs dispersed in water was 295 $W.g^{-1}$ while dispersed in oil the SAR was 2605 $W.g^{-1}$. RM1-Fluc tumors injected with magnetic oil were submitted to magnetic induction and the viability was followed by bioluminescence imaging (BLI). The results showed that after injection of a microvolume of oil, it was possible to observe a decrease of BLI signal attesting of a partial thermoablation of the tumor after a single treatment located near the injection site.

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March, 15, 16 and 17
2023

Design of Iron Oxide Nanoparticles for imaging and ative targeting: theranostic in one formulation

Maria de los Angeles Ramirez[1], Barbara Freis[1], Christine Affolter-Zbaraszczuk[2], Florent Meyer[2], Thomas Gevart3, Céline Henoumont3, Sophie Laurent3, Sylvie Bégin Colin[1]

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2 Inserm U1121, Centre de recherche en biomédecine de Strasbourg, Strasbourg, France

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Among females, breast cancer is the most diagnosed cancer and the leading cause of cancer death[1]. There is a strong need of new treatments without side effects[2]. In nanomedicine, the goal is to develop multimodal nanoparticles (NPs) to speed up targeted diagnosis, to increase its sensitivity, reliability and specificity for a better management of the disease. The selective accumulation of NPs in desired organs to enable precise diagnosis and targeted therapy remains an important issue.

Most of developed NPs accumulate, after intravenous injection, in eliminatory organs anddeveloped NPs accumulate, after intravenous injection, in eliminatory organs and developed NPs accumulate, after intravenous injection, in eliminatory organs and only low amounts are seen accumulating in tumors. For a precise treatment, active targeting with affinity ligands to achieve tumor specificity is crucial. Among NPs developed for nanomedicine, superparamagnetic iron oxide nanoparticles (IONPs) are promising as they may be designed to display multimodal therapy. Indeed, besides being excellent T2 contrast agents for MRI, IONPs are promising as therapeutic agents by hyperthermia when suitably designed.

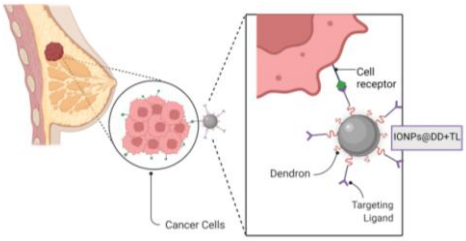

Figure 1 DIONPs functionalized with Targeting Ligand (TL) to recognize overexpressed receptors on breast cancer cells

In that context, we developed IONPs coated with a dendron molecule (DIONPs), which have been demonstrated in several *in vitro* and *in vivo* studies to display antifouling properties. We have studied the targeting of breast cancer cells by coupling selected targeting ligands (TL) on the nanoparticles' surface. We have chosen peptides with high affinity for specific membrane receptors overexpressed in these cancer cell lines: MDA-MB-231 (triple negative) and MCF-7 (ER+).

We succeeded in establishing a reproducible method for the coupling of the TL and for the quantification of their amount at the surface of our nanoparticles, which is a challenge today to better master the selective accumulation of DIONPs in cancer cells. Following the same strategy, we also performed the coupling of chelating agents, with this approach the nanoparticles can be followed in vivo by chelating agents, with this approach the nanoparticles can be followed *in vivo* by molecular imaging like PET-CT or SPECT. The internalization in breast cancer cells when the TL was present was higher compared with same DIONPs without TL, showing the efficiency of active targeting. We have also compared the internalisation of IONPs with different shapes showing an impact of the shape and aggregation state on the internalisation yield. Then, cells internalizing DIONPS have been submitted to magnetic hyperthermia and photothermia treatments. No size andshape effects were evidenced with photothermia when the opposite was observed shape effects were evidenced with photothermia when the opposite was observed found the most efficient.

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Keywords: iron oxide nanoparticles, dendron molecules, magnetic hyperthermia, photothermia, defects effect
Disciplinary fields involved: Materials Chemistry

Impact of shape and defects of Iron Oxide Nanoparticles on photothermia and magnetic hyperthermia therapies

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   Laboratory Name, Department Name, Line research organization or University 1, Line research organization or

In nanomedicine, the goal is to develop multimodal nanoparticles (NPs) to speed up targeted diagnosis, to increase its sensitivity, reliability and specificity for a better management of the disease. Besides being excellent T2 contrast agents for MRI, iron oxide NPs are promising as therapeutic agents by magnetic hyperthermia when correctly designed (high magneto-crystalline anisotropy) and they also have an interest for photothermal treatment[1]. Recently, it has been reported that the defects in nanoparticles may have a strong influence on therapeutic efficiency of both treatments [2][3]. So, defect evaluation on different sized and shaped NPs is a crucial point to find the best NPs design for ensuring multimodal therapies.
We have thus optimized the reproducible synthesis of iron oxides NPs with different sizes (10 and 20 nm) and shapes (nanocubes and nanoplates) by the thermal decomposition approach by tuning synthesis parameters such as the reaction temperature, the heating rate and the nature of surfactant. The synthesis conditions to obtain high yield in nanoplates have been optimized using artificial intelligence algorithms. Then, defects such as dislocation or antiphase boundaries were evaluated by XRD and FFT studies on HRTEM images and by calculating band gaps and Urbach energies. NPs behaviors towards the different kinds of therapies were investigated both in suspension in water and viscous media and in cancerous cells allowing to establish the key role of defects and NPs design for ensuring a multimodal therapy.

Acknowledgment
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a I·∃yŜűƛÔ yl·y2LJI·₪ûƛÔfŜă ó a b tăú ØƛűK Ŝf2y∃I·úŜŘ ăKI·LJŜ ădzÕK I·ă yl·y2₪2Řă I·₪Ŝ 2Ŧ ∃₪ŜI·ú ƛyűŜ₪Ŝăű ŦŻ₪ ōƛ2πI·LJLJfƛÔI·ûƛ2yã I·ă ûKŜè y2úI·ōfè ŜÈKƛōƛű Kƛ∃KŜ₪ KŜI·ûƛy∃ ŜŦŦΛÔƛŜyÕƛŜă I·yŘ I· LJ₪2f2y∃ŜŘ ₪ŜűŜyűƛ2y ƛy ůdzY2dz₪ ăƛűŜă ûKI·y ûKŜƛ₪ ăLJKŜ₪ΛÔI·f Õ2dzyűŜ₪LJI·₪ûă ᴹΦ ¢KŜ Y I·ƛy ƛăădzŜ Řdzₙƛy∃ ÔŜffă ƛyűŜ₪yl·fΛÎI·ûƛ2y ƛă ú2 I·Ø2ƛŘ ŜyŘ2ă2Y I·f Ŝyű₪I·LJY Ŝyű 2Ŧ yl·y2LJI·₪ûƛÔfŜăΣ ØKΛÔK LJ₪ŜØŜyű ûKŜY Ŧ₪2Y ƛyűŜ₪I·ÔûƛyΣ ØƛűK ƛyű₪I·ÔŜffdzfI·₪ Õ2Y LJ2yŜyűă I·yŘ ŘŜŐ₪ŜI·ăŜ ûKŜƛ₪ KŜI·ûƛy∃ ŜŦΛÔƛŜyÕè Φ aŜY ō₪I·yŜ ú₪I·yãf2ÕI·ûƛ2y LJKŜy2YŜyl· KI·ØŜ I·f₪ŜI·Řè ōŜŜy 2ōăŜ₪ØŜŘ ØƛűK ă2Y Ŝ I·yƛă2ú₪2LJΛÔ yl·y2LJI·₪ûƛÔfŜăΦ {dzÕK LJ₪2ÕŜää I·ff2Øă ûKŜ ƛyűŜ₪yl·fΛÎI·ûƛ2y 2Ŧ ûKŜăŜ 2ō?ŜÕűă ŘƛŜ₪ŜÕűfè ƛy ûKŜ Õè ü2LJfI·ăY Σ ØƛűK2dzú ōŜƛy∃ ú₪I·LJLJŜŘ ƛy Ŝy Ř2ă2Y Ŝă ᴴΦ

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<u>**wŜŦŜ₪Ŝy ÕŜăY**</u>

ώмв I·ú {₪ƛ]I·yűK I Φ Ŝű I·fΦΣ *J. Phys. Chem. C* **нлмс**Σ *120*Σ мллуспмллфо Т ō ú {Kdz]fI· {Φ Ŝű I·fΦΣ *Adv. Healthcare Mater.* **нлмр**Σ *4*Σ утпπуунΦ ώнв I·ú Y2ăűI·₪Ŝf2ă YΦ Ŝű I·fΦΣ *Nature Nanotech.* **нллт**Σ *2*Σ млуппмо Т ōú aƛff2ű bΦ Ŝű I·fΦΣ *Dalton Trans.* **нлмр**Σ *44*Σ тофптпсΦ ώов {λI·dz∃dzŜ ₩πaΦ Ŝű I·fΦΣ *Angew. Chem. Int. Ed.* **нлмл**Σ *49*Σ ууфтπуфлмΦ

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Targeted thermal or mechanical Nanotherapy of pancreatic adenocarcinoma efficacy and mechanisms.

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Magnetic nanoparticles (MNPs) are already widely studied in nanomedicine, particularly as MRI contrast agents or therapeutic agents by magnetic hyperthermia. The first clinical trial using nanotherapy was conduct in 2011 to treat high-grade brain tumors. Currently, the efficacy of nanotherapy combined with radiotherapy is investigated as a new treatment against prostate cancer. However, the benefit on life expectancy remains negligible and neither radiotherapy nor magnetic hyperthermia can distinguish between normal and cancerous tissues, responsible of adverse effects. Our strategy is based on the vectorization of iron oxide magnetic nanoparticles called NanoFlowers (NFs) capable of recognizing targeted cells and therefore specifically treating cancerous tissue throught the application of an external magnetic field, minimizing damage to healthy tissue. Under a high frequency magnetic field (AMF) exposure, the heat of NFs will specifically eradicate these cells, without macroscopic temperature elevation. Therefore, the rotation of the NFs under a low frequency rotating magnetic field (RMF) application generates mechanical forces leading to cell destruction. As a proof of concept, we have chosen a model of pancreatic adenocarcinoma (PDAC), a cancer with a very poor prognosis. The therapeutic failure is especially due to the development of multidrug resistance resulting from many mechanisms such as the lysosomal sequestration of chemotherapies. Moreover, tumor microenvironment plays a critical role in the development of PDAC resistance. By secreting extracellular matrix proteins, Cancer-Associated Fibroblasts (CAFs) create notably a physical barrier that limits the penetration and the efficacy of treatments (chemotherapy and radiotherapy). PDAC cancer cells and CAFs can overexpress the type 2 cholecystokinin (CCK2) receptor that is internalized after its activation. The graft of a specific agonist of the CCK2 receptor, the Gastrin, at the Nanoflower surface (NF@Gastrin) allows their accumulation into the lysosomes of pancreatic cancer cells and CAFs overexpressing the CCK2 receptor. The RMF (1Hz, 40 mT) or AMF (275 kHz, 30 mT) application kills up to 45% of cancer cells and CAFs that have internalized NF@Gastrin, slows down their proliferation without affecting cells lacking the nanoparticles. These two strategies also inhibit cell migration and stimulate the expression of Damage-Associated Molecular Pattern (DAMP) proteins such as Calreticulin and HSP70, well known to induce an immunogenic anti-tumoral response. Current studies are performed to determine the impact of these two strategies, consisting in thermal or mechanical energy delivery through magnetic nanoparticles excited by an external magnetic field, on spheroids & preclinical *in vivo* models.

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Bioimaging with persistent luminescence nanoparticles

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Persistent luminescence is the property of some materials that can store excitation energy and then slowly release photons for minutes to a few hours after the excitation source is turned off. These phosphors have long been of great research interest and are nowadays commercialized as night or dark environment vision materials for a wide range of applications such as security signs or emergency route signage.

A couple of years ago, our lab has shown that this property can also exist in nanoparticles.[1] We will present some nanophosphors we have developed,[2] and we will show how their composition and their surface modification can affect their use.[3]

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Disciplinary fields involved: Chemistry, Physics, Biology
Sustainable Development Goals* eventually involved in your research: 9.5, 4, 4.4, 3.5, 3.8, 17.6, and 1.4

Luminescence nanothermometry for the control and understanding of heat-induced process and the fate of nanothermometers *in vitro* and *in vivo*

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For centuries mankind has been aware of the intrinsic relationship between temperature and health, such as fever (increased body temperature in the face of infectious or inflammatory processes). The temperature of a given organ is a consequence of the delicate balance between several factors including external temperature, metabolic activity, and blood perfusion[1,2]. To be effective, thermal monitoring should be achieved remotely, without perturbing the temperature of the tissue while measuring, also avoiding physical alterations of the organ under investigation.

Most conventional thermal-sensing technologies are invasive- as they require the insertion of microscopic thermal sensors like thermocouples- while noninvasive thermal imaging by infrared cameras only allows measurement of surface temperature. Luminescence thermometry represents an alternative technique that overcomes these limitations measuring the change in the temperature by change in the luminescence of NPs heated by a laser [3]. We designed and synthetized nontoxic Ag2S quantum dots with different coating using microwave (Figure 1). The temperature-dependent luminescence of NPs was measured in the solution (data not shown) and then the fate of NPs in fibroblast showed the luminescence-dependent according to the coating of the NPs. The decrease in the luminescence of AS-DTDTPA could be due to the presence of thiol groups that act as reactive oxygen species (ROS) scavenger. The presence of only AS-PEG and AS-Ag NPs increased ROS in fibroblast proving the ability of those NPs as ROS-promoter. Moreover, the generation of ROS in NPs with ROS-scavenger (NAC) and ROS-promoter (LPS) decreased and enhanced significantly the ROS, respectively. The luminescence AS NPs gives us the opportunity to track the NPs in the body and measure the exact temperature of tissue.

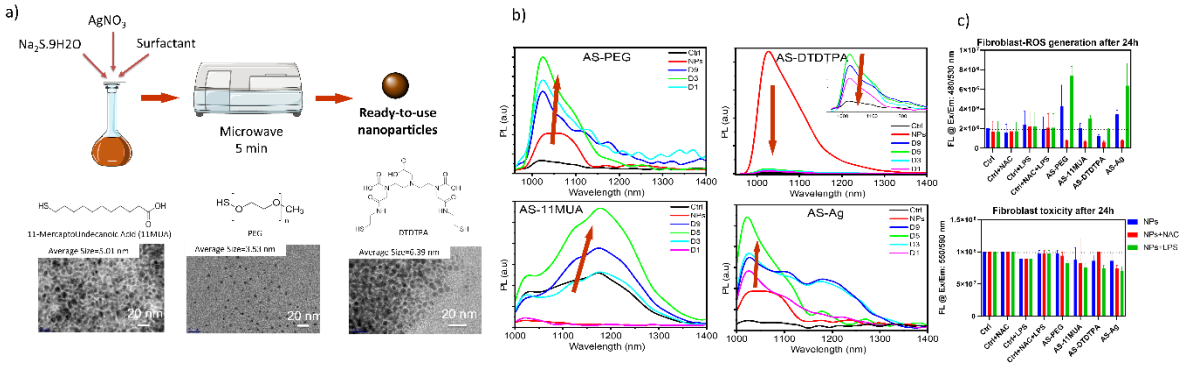

Figure 1: (a) the synthesis of AS NPs with different coating. (b) The photoluminescence of different AS NPs in fibroblasts from day 1 to 9. (c) ROS generation by DCFH-DA.

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