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POLY(2-OXAZOLINE)S-BASED NANOVECTORS FOR PHOTODYNAMIC THERAPY

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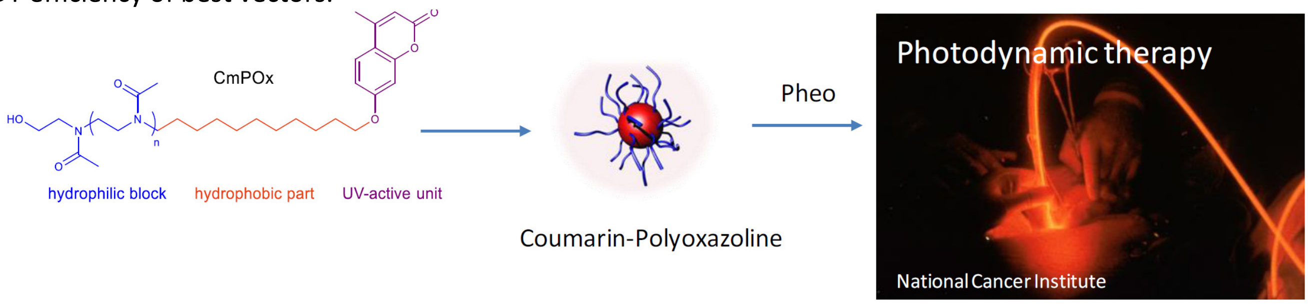
This research master's degree research project could be followed by a PhD	☐ YES	☒ **NO**

The future of medicine lies in nanomedicine: the use of nanometric vectors to deliver the desired molecules to the desired site. For diseases such as cancer, it is essential. Photodynamic therapy (PDT), a technique already clinically used, is based on the irradiation of a photosensitizer, which transfers its energy to oxygen, leading to reactive oxygen species that kill the local cells. PDT suffers today from an inadequate biodistribution of the photosensitizer, leading to a patient skin photosensitivity over several days. We have shown in previous studies that encapsulating the photosensitizer in a polymer vector strongly improves the PDT efficiency. However, our vectors are based on amphiphilic block copolymers, with a hydrophilic block constituted of poly(ethylene glycol) (PEG). In nanomedicine, 90 % of the vectors are also based on this polymer because it enables the vector to remain in the bloodstream for very long times, enabling its concentration in the desired area to be treated in ca. 2 days. If this looks like the magic component, in fact, it is not, because studies have been increasingly showing that upon several injections of PEG-based nanovectors, immune responses appear, and this leads to a rapid clearance of the vectors. We have begun to assess a new type of vectors, based on poly(2-oxazoline) for PDT. This internship is the follow up of this topic. The work of the trainee will consist in: - assessing the ability of forming polymeric nanovectors (micelles or polymer vesicles) with a range of poly(2-oxazolines), depending on their molecular weight and their composition. This will use different techniques for the characterization: static/dynamic light scattering, transmission electron microscopy (TEM), cryo-TEM, tensiometry - crosslinking the vectors by light, thanks to the presence of a photo-reactive group on the polymer chain. This provides more stability to the vectors. Crosslinking will be assessed by 1H NMR In collaboration with a biologist of our team, the trainee will attend the performing of biological tests to evaluate the PDT efficiency of best vectors.



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- Extended photo-induced endosome-like structures in Giant Vesicles promoted by block-copolymer nanocarriers
C. Montis et al. Nanoscale (2018) 10 15442 – 15446
- Polymeric micelles encapsulating photosensitizer: structure/ photodynamic therapy efficiency relation
L. Gibot et al. Biomacromolecules, 15(4) (2014)1443-1455

Keywords, areas of expertise	Polymers, nanomedicine, physical chemistry
Required skills for the internship	Rigorousness, scientific curiosity

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SYNTHÈSE ET CARACTÉRISATION DE NANOPLASTIQUES MODÈLES POUR ÉVALUATIONS ENVIRONNEMENTALES

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This research master's degree research project could be followed by a PhD	☐ YES ☒ **NO**

Today, plastic pollution has been recognized by the scientific community as a major environmental issue. Since the 1950s, the early beginning of plastic industrialisation, mankind has produced over 8 300 million metric tons of plastic1. In 2015, 75 % of this plastic ever produced has already been transformed into waste. About 5 000 million metric tons of plastic debris accumulate in landfills or were discarded in the natural environment (1).
Plastic is engineered to withstand. None of the commonly used plastics are biodegradable and plastic items once discarded in the environment, persist for years to decades (1). Plastic debris upon solar light and mechanical forces are oxidized and fragmented into smaller pieces (2).
Microplastic (1-5 mm) occurrence has been documented in a fair number of places on earth. However, there is a crucial knowledge gap towards the occurrence of microscopic plastic debris. Small microplastic (25 - 1000 µm) abundance in environmental samples is very scarcely documented. Nanoplastics are defined as particles within 1-999 nm (3). Nanoplastics have been detected for the first time recently in environmental samples in the North Atlantic sub-tropical gyre (4).
But the chemical structure of nanoplastic is not elucidated so far. For now environmental investigations like ecotoxicological studies have used polystyrene nanospheres but this very simple model does not reflect the complex structure of nanoplastic. In this investigation the master student will synthesize model nanoplastic from deep oxidized polymers using nano-milling techniques. The master student will thus characterize the nanoparticles by DLS, NTA, TEM, µ-FTIR, fluorescence and Py-GC-MS/MS. The reactivity of the nanoplastic synthesised towards heteroaggregation with natural organic matter will then be investigated. The interaction of the nanoplastics with porous media will also be investigated. Finally, the data obtained will help develop a method of extraction and quantification of nanoplastic from real samples (coral sediments).

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4. Ter Halle, A.; Jeanneau, L.; Martignac, M.; Jarde, E.; Pedrono, B.; Brach, L.; Gigault, J., 2017. Nanoplastic in the North Atlantic Subtropical Gyre. Environ. Sci. Technol. 51, 13689-13697.

Keywords, areas of expertise	nanoparticles, nanoplastic, plastic pollution, nano-milling, light diffusion scattering, electronic microscopy, fluorescence, hetero aggregation, diffusion, porous media
Required skills for the internship	analytical chemistry (DLS, NTA, TEM, µ-FTIR, fluorescence & Py-GC-MS/MS), colloids, rigor, autonomy, good communication skills

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HYBRID NANOPARTICLES FORMED BY ION-PAIRING – APPLICATIONS TO CATALYSIS

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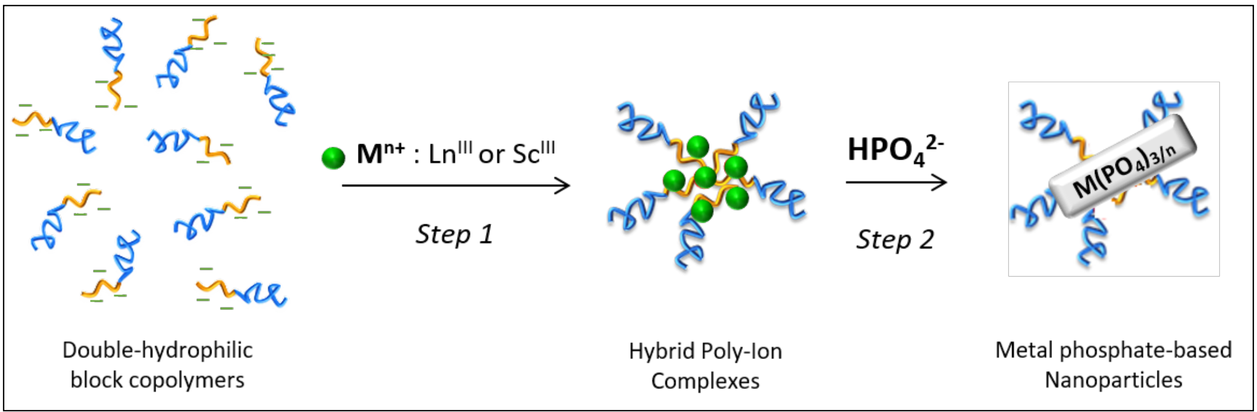
This research master's degree research project could be followed by a PhD	☐ YES	☐ NO

With the development of nanosciences, nanocatalysis has clearly emerged as a domain at the interface between homogeneous and heterogeneous catalysis, which offer unique solutions to answer the demanding conditions for catalyst improvement.(1) This project aims at providing new sets of easy-to-prepare & easy-to-use hybrid original nanomaterials as recyclable green catalysts for organic synthesis in water. The preparation of the nanocatalysts relies on the co-assembly by electrostatic complexation of double-hydrophilic block copolymers and oppositely charged metal ions using only water as solvent.

Two families of nanocatalysts will be prepared (i) coacervated complex micelles or hybrid polyionic complexes (HPIC) (2) obtained by non-specific complexation of multivalent metal cations by double-hydrophilic block copolymers (PEO-b-poly(acrylate)) and (ii) metal-phosphate based nanoparticles obtained after addition of phosphate ions to HPICs (3) (Scheme 1).



Scheme 1. Synthesis via simple & fast mixing of (a) hybrid polyion complexes (HPICs) (step 1), and (b) metal-phosphate nanoparticles (step 2)

The metal ions (Mn+) themselves will drive the formation of the HPICs in addition to their functions as catalysts. The metal ions selected are LnIII and ScIII as water-tolerant LEWIS acids.

During this internship the objectives will be:
- to synthesize HPICs and phosphate-based nanoparticles
- to characterize the formed nanoobjects (size, composition) and to evaluate their stability
- to measure the catalytic activity of these water-tolerant LEWIS acid nanocatalysts on Mukayama-type reactions.4

References:
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(4) S. Kobayashi, M. Sugiura, H. Kitagawa, W. W. L. Lam, Chem. Rev. 2002, 102, 2227–2302.

Keywords, areas of expertise	nanocatalysts, polymers block-copolymer self-assembly, soft-matter
Required skills for the internship	Knowledge in polymer chemistry and characterization, basic knowledge in self-assembly

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NEW MULTIMODAL CONTRAST AGENT FOR X-RAYS TOMOGRAPHIC STUDIES OF BIOFILMS

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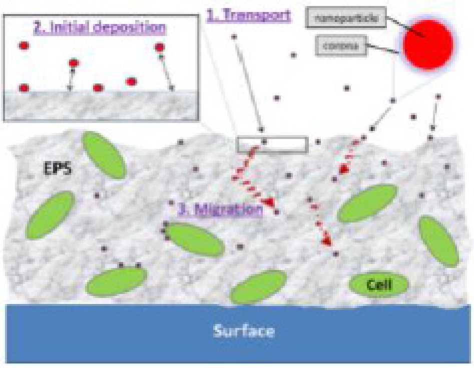
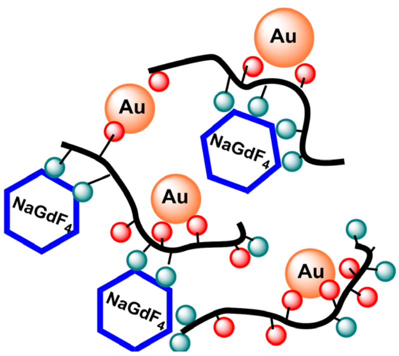
This research master's degree research project could be followed by a PhD ☐ YES ☒ **NO**	

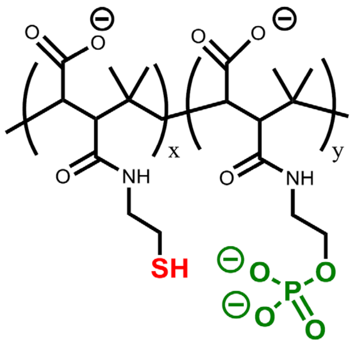
Biofilms are bacterial colonies that grows onto surfaces typically at the interface between a solid and a liquid, and are made of cells enclosed in a so-called “extracellular matrix” of polymeric nature. Therefore, a biofilm is fundamentally a heterogeneous and porous structure. The understanding of the internal structure of a biofilm and the way it organizes itself in complex media is a hot research topic, requiring specific imaging techniques.
In order to study biofilms growing onto rough surface even in opaque medium, the team of Y. Davit (IMFT) has developed an approach based on computer assisted X-rays tomography (X-CT), using BaSO4 as contrast agent.(1)
The objective of this training is to substitute BaSO4 microcrystals by aggregates of inorganic nanoparticles containing elements of high Z values thus showing very good contrast agent properties (2). We have selected gold nanoparticles (Au NPs), and lanthanide fluorides such as NaGdF4. Such an aggregate could then be used as a multimodal probe for multiple threshold X-ray imaging (3). However the interaction of nanoparticles (of any kind) with a biofilm is the result of several constraints: the nanoparticles’ size, their charge, and their surface ligands [fig. A].(4)
To ensure a strong and specific grafting between the polymer and inorganic NPs, we will design a polymer carrying aurophilic



A: interaction nanoparticle and biofilm



B: proposed nanohybrid architecture



C : target polymer

thiol SH groups and phosphate groups as early-d metal binging moieties. We will explore the use of the reactive and commercially available poly-alt-isobutylene-maleic anhydride as polymer backbone, in a strategy similar to published work [fig., left](5). Our targets are aggregates nanohybrids constituted of gold and NaGdF4 nanoparticles with an average diameter of 20nm. As NaGdF4-NPs are already available in the lab, we consider two main tasks: first the preparation of two of the nanohybrids components (AuNPs and Thiol containing polymer), followed by their assembly to yield {NPsAu:NaGdF4}@polymer. For each steps, suitable analytical techniques will be employed: NMR, Uv-vis, TEM, DLS… The X-CT performances of such nanoprobes will be tested in a model biofilm

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5. W. Wang, X. Ji, L. Du and H. Mattoussi, The Journal of Physical Chemistry C, 2017, 121, 22901-22913.

Keywords, areas of expertise	nanoscience, soft matter, polymers, imaging
Required skills for the internship	synthetic chemistry skills, broad scientific curiosity, motivation and enthusiasm for the project

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"ALGABOT": NIR-PHOTOCONTROL OF THE PHOTOTACTICITY OF UNICELLULAR ALGAE

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This research master's degree research project could be followed by a PhD	☐ YES	☒ **NO**

"Micro-robotics" relies on the general idea of using living cells as the active "engine" to propel a larger structure, the "robot", under the control of an external physical stimulus. Such a device is foreseen inter alia as a smart approach of drug delivery.[1] The external stimulus gradients act as a guideline and as a power controller. Advanced reported examples concern magnetic control ("magnetotaxis") achieved by hybridization of mobile single cell (sperm cell, Bacteria, Algae…) with magnetic field-sensitive iron-oxide nanoparticles (IONPs).[2] Less frequent is the control with light ("phototaxis"). For this purpose, one would classically chose photosynthetic mobile Prokaryotes (Bacteria) or Eukaryotes (Euglenophytes, Chlorophytes...). Indeed, light not only fuels the photosynthetic machinery but is also used to guide the cell's displacements thanks to non-photosynthetic receptors (i.e. channelrhodopsins, flavoproteins).[3] Yet, the penetration of the excitation light in the culture medium remains a problem.
Able to reemit visible photons upon excitation with highly penetrating near infra-red (NIR) light,[4] up-converting nanoparticles (UCNPs) are attractive local sources of visible light, bypassing the medium's limitations due to light absorption. The aim of the present internship is to assemble a photocontrolable biohybrid microswimmer using electrostatic interactions.

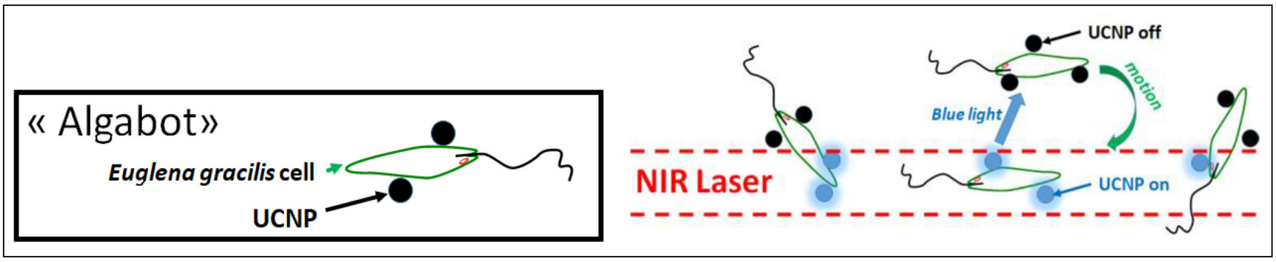

Figure: Left: scheme of the biohybrid "Algabot" Right principle of the gathering of "algabots" upon NIR light exposure

Our approach is to adapt strategies known on IONPs to UCNPs in particular the simple cell–nanoparticle interaction via electrostatic interaction. The surface of 20nm-UCNPs, already available in the lab, will be modified to make them cationic, enabling them to bind to the anionic surface of flagellated Euglena gracilis. Self-assembly is expected to take place upon exposure of living cells to such particles. Phototaxis alteration will then be measured by inducing cell gathering under NIR-laser exposure. Simple synthetic chemistry will be needed, and standard colloid characterization techniques will be used (Electronic microscopies, DLS), with also UCNP luminescence recordings. Algae recording will be done in partnership with specialized laboratories. Curiosity, creativity and adaptability are highly sought qualities.

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Keywords, areas of expertise	nanoscience, soft matter, imaging
Required skills for the internship	synthetic chemistry skills, broad scientific curiosity, motivation and enthusiasm for the project

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THE EFFECT OF CHAOTIC EXCITATION ON LUMINESCENT NANOPARTICLES

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This research master's degree research project could be followed by a PhD	☒ **YES** ☐ NO

In this project, we will screen rationally generated chaotic excitation patterns leading to optimized upconversion emission in nanomaterials.
Upconverting nanoparticles are fascinating objects that possess unique luminescence properties: they are able to convert near infrared incident light (e.g. 980 nm) into higher energy photons, ranging from UV to NIR (800 nm). They are currently receiving a lot of attention, with a wide array of potential applications, ranging from biomedical (imaging, theranostics) to the improvement of solar cells (recovery of sub bandgap photons), and even in display technology (JACS, 2018 140 35 10923-10931). The particles that we synthesize routinely in the laboratory are composed of a NaYF4 matrix doped with sensitizing and emitting lanthanide ions (Yb and Tm).
Until now, upconverting nanoparticles have been excited either by continuous wave lasers, or by pulsed lasers but with rather simple excitation patterns. Recently it has been shown that the width of the excitation pulses had an influence on the emission characteristics (JACS 2018 140 17 5714-5718).
In this project, we wish to explore the influence of chaotic excitation on lanthanide-based upconversion. The expected outcomes could be an enhancement of the upconversion phenomenon, or an alteration of the intensities of the various emission bands.
To achieve chaotic excitation, a simple electronics system will be assembled consisting of a digital-to-analog converter, controlled on the computer side by a basic MATLAB routine. This will produce signals with chaotically interspersed duty cycles, and they will be used as triggers for the pulsed laser to excite the nanoparticles. The effect of this complex, highly tunable excitation on the upconversion phenomenon will be analysed using a modified fluorimeter already available in the group.

The tasks to be undertaken by the student are:
-Synthesis and characterization of upconverting nanoparticles following routine procedures.
-Implementation of the DAC and MATLAB routine (obtained from Prof Parmananda's group at IIT Bombay). Interfacing with the laser.
-Evaluation of the effect of chaotic excitation on upconversion.

The relative importance of each task can be modulated depending on the student's background and skills.

Keywords, areas of expertise	Physical chemistry, Materials Science, Luminescence, Upconversion.
Required skills for the internship	Bachelor's degree in Applied Chemistry or Physics.