

**Master Thesis subjects proposed by the
Engineering of Molecular NanoSystems laboratory in 2019-2020.
MSc in Biomedical Engineering**

1. Elaboration of micellar nanodevices for biomass conversion in water.

Summary: There is currently great interest in development of environmental-friendly synthetic processes and, in this context, the replacement of commonly-used volatile organic solvents by water is of prime interest. Water is a solvent with little environmental impact but its use has been limited because organic substrates are often poorly soluble in water. Micellar systems represent one of the simplest methods to achieve organic transformation in an aqueous environment. In collaboration with the University of Padova, we are investigating the potential of vanadium-based catalysts in aqueous micellar media for the hydrolysis of lignin. The work will consist in monitoring the conversion using model substrates in order to identify the key parameters to control for optimum conversion. This will entail work in the wet-lab and the set-up of HPLC and NMR protocols to characterize the systems and reactions.

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2. Transmembrane transporters for phosphates.

Summary: The cell membrane is an apolar barrier for the free diffusion of ions. In-vivo, specialized proteins embedded within the cellular membranes take care of the transport of ions. In our laboratory, we seek to mimic the action of these proteins with synthetic organic molecules that can transport ions across membranes. The aim of this project is to develop and test potential anion transporters. We are particularly interested in molecules that can carry chloride and phosphate anions across lipid bilayers. After the organic synthesis of a transporter, you will evaluate if the compound is able to bind anions and if it can function as a transporter. For this, you will prepare liposomes, spherical assemblies of lipids, as models for cell membranes. The transmembrane transport of the anions will be studied with fluorescence spectroscopy by monitoring the emission of dyes which are encapsulated in the liposome. The mechanism of transport will be investigated by varying salt solutions and lipid composition.

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3. Preparation of Giant Unilamellar Vesicles using microfluidics

Summary: In the EMNS laboratory, vesicles prepared from natural lipids (liposomes) are used as models for cell membranes to study processes like transmembrane transport and cell targeting. With standard procedures, vesicles with diameters of up to 200 nm are easily made, but the preparation of giant unilamellar vesicles (GUVs, $\sim 10 \mu\text{m}$) is still a challenge. The TIPS laboratory is specialized in microfluidics, which can be used to prepare droplets and vesicles. The aim of this collaborative project is to develop a method to prepare GUVs as membrane model system by microfluidics. You will use a home-made 3D-printed micro-emulsion generator to produce double emulsions and screen the conditions (fluid viscosities, lipid solutions and concentration, flow rates, geometry) to identify the optimal regime for generating stable GUVs, with minimal organic solvent present. You will characterise these GUVs (DSC, ^1H NMR spectroscopy) and compare transmembrane transport into these GUVs with those prepared by classical methods.

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4. Nucleic acids driven assembly of nanoparticles at the surface of biological membranes.

Summary: Gold nanoparticles (GNPs) are of particular interest for biomedical diagnostic and therapeutic applications because of their remarkable optical properties, ease of surface functionalization and presumed biocompatibility. In particular, the photothermal properties of GNPs and ease of detection using photoacoustic imaging make them an ideal theranostic tool. For in vivo applications however, the plasmon band (LSPR) of GNPs, which falls in the visible range, is not ideal and the near-IR would be more suitable. This shift can be obtained by the controlled assembly of the GNPs. This project will aim at controlling the assembly of GNPs at the surface of a target membrane using a bioinspired strategy based on the use of nucleic acids. Nanoparticles will be synthesized and functionalized with different DNA oligonucleotides encoding for the targeting of membranes functionalized with a complementary strand but also for their assembly at the surface.

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5. Design of nucleic acids coated nanoparticles for miRNA delivery in ovarian cells.

Summary: Chemotherapy drugs such as cyclophosphamide are highly gonadotoxic and can lead to ovarian reserve depletion, causing infertility and thus strongly affecting the quality of life in young patients. The EMNS laboratory works in collaboration with the Laboratory of Human Reproduction from the Erasme hospital that has recently identified microRNAs as therapeutic options to preserve fertility during chemotherapy exposure. MiRNAs are small non-coding molecules, which offer new promising approaches in cancer therapy but also in fertility preservation, as they play a key role in ovarian function. However, these miRNA have to be delivered to the ovarian cells, which requires the development of new delivery systems. Gold nanoparticles (GNPs) are promising vectors, which have already been successfully used for nucleic acid delivery. In this study, we propose a new approach of GNPs surface functionalization based on calix[4]arenes which can be used to control the anchoring of synthetic miRNA nucleotides and/or of other ligands (peptides) for organ specific targeting. The goal of this project is to create novel ovarian protective drugs by combining the favorable characteristics of miRNAs and the cutting-edge technology of GNPs.

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