Master Thesis subjects proposed by the *Engineering of Molecular NanoSystems* laboratory for 2021-2022
MSc in Biomedical Engineering

1. Preparation of Giant Unilamellar Vesicles using microfluidics and their application for transmembrane transport

**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, ~10 µm) 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 then characterise these GUVs and use them to study transmembrane transport by fluorescence microscopy.

**Contacts:** Hennie Valkenier (EMNS); hennie.valkenier@ulb.be
Benoit Scheid (TIPS); benoit.scheid@ulb.ac.be

2. Transmembrane transporters for anions.

**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. In this project you will start with the organic synthesis of a transporter, you will study 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.

**Contacts:** Hennie Valkenier (EMNS); hennie.valkenier@ulb.be
Alessio Cataldo (EMNS); Alessio.Cataldo@ulb.be

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

**Summary:** Chemotherapy drugs such as cyclophosphamide are highly gonadotoxic and 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.

**Contact:** Gilles Bruylants, gilles.bruylants@ulb.be

**Summary:** Lateral Flow ImmunoAssays (LFIs) widely used in human health for point of care testing, as these assays are relatively fast (typically 10-15 minutes), low cost and can be performed by untrained personnel. The most eminent example is the pregnancy test. The operating principle is straightforward and relies on the detection of a target analyte by a functionalized colored material and its binding on a test line. Typically, gold nanoparticles (AuNPs) are used as optical transducers to visualize the test result. This is mainly due to their high molar absorption coefficient in the visible region and their relatively high stability. Silver nanostructures would however represent a most promising option, as they exhibit a larger molar extinction coefficient than AuNPs (more than one order of magnitude for AgNPs compared to AuNPs of a similar size) resulting in a larger sensitivity. This is of great importance since this allows a decrease in the amount of material used (nanoparticles together with the expensive biomolecules, such as antibodies and viral recombinant proteins) and therefore considerably reduces the production cost of a test. The larger molar extinction coefficient could lead to the detection of smaller amounts of the target molecule, and hence allow detection at an earlier stage, which is a clear benefit for the patient treatment. These silver nanomaterials are however barely explored these days, due to their low stability. Thanks to a new functionalization strategy that was developed by the EMNS laboratory, these particles could advantageously be integrated in such Lateral Flow Assays. This work will be devoted to the integration of silver nanomaterials into a functional LFIA.

**Contact:** Gilles Bruylants, gilles.bruylants@ulb.be

7. Elaboration of micellar nanocatalysts 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.

**Contact:** Kristin Bartik; kristin.bartik@ulb.be