Master Thesis subjects proposed by the *Engineering of Molecular NanoSystems* laboratory for 2022-2023 MSc in Chemistry and Materials engineering

1. Self-healing polymers using novel dynamic covalent bonds

Summary: Dynamic covalent chemical (DCC) bonds are functional groups that can hold parts of a molecule together via covalent bonds, but that can also break and reform or exchange. Polymer materials that contain such DCC bonds can have attractive properties, such as self-healing and recyclability. The physical, self-healing and recycling properties of polymer materials are an important topic of research in the FYSC lab at the VUB.
A novel type of dynamic covalent bond has been recently developed in the EMNS lab at the ULB. The aim of this project is to incorporate these novel DCC functional groups into polymer materials and study the resulting properties. You will introduce the appropriate functional groups to the pre-polymers by organic synthesis in the EMNS lab, polymerise the materials, and then characterise the resulting polymers in the FYSC lab.

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2. Diffusion and transport of organic anions.

Summary: Transport of ions across membranes is an important process in biology. Specialized proteins embedded within the cellular membranes take care of this. In our laboratory, we seek to mimic the action of these proteins with synthetic molecules that can transport ions across membranes.
Many important molecules in biology have anionic phosphate or carboxylate groups. The aim of this project is to study how different anionic molecules can cross the membrane. For this, you will prepare liposomes, spherical assemblies of lipids, as models for cell membranes. You will use fluorescence spectroscopy and other ion sensing methods to study if different carboxylates and phosphates can diffuse spontaneously across the membrane. Then, synthetic transporters will be added to the membranes, to study the rate at which these transport the different anions. You will analyse how the rate of diffusion and transport of the anions depends on their structure.

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3. 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.

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4. Development of magnetic nanoparticles for nucleic acid purification.

Summary: Extraction procedures based on the use of magnetic nanoparticles functionalized with organic complexing agents present many advantages arising from the inherent characteristics of these materials (large surface/volume ratio, easy collection using magnetic fields, fast operation) and are expected to bring major breakthroughs in analytical and separation sciences. This project lies in the framework of a collaboration with Quantoom Biosciences (UniverCells) whose objective is to develop a platform that encompasses DNA and RNA manufacturing and formulation, along with critical reagent supply, from sequence to large scale production. The student will investigate the purification process for RNA and DNA strands from synthetic mixtures using functionalized magnetic nanoparticles.

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5. Development of Magnetic nanoparticles for environmental applications.

Summary: Extraction procedures based on the use of magnetic nanoparticles functionalized with organic complexing agents present many advantages arising from the inherent characteristics of these materials (large surface/volume ratio, easy collection using magnetic fields, fast operation) and are expected to bring major breakthroughs in analytical and separation sciences for biomedical but also environmental applications. In the continuation of different projects held in the EMNS laboratory, this project will focus on water decontamination using magnetic/organic nanohybrids. The work will consist in the synthesis of the nanoparticles, the selection of suitable functionalization ligands (using NMR or other spectroscopic techniques) and the monitoring of the separation efficiency.

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6. Design of nucleic acids coated nanoparticles for RNA delivery in specific organs.

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 Research Laboratory of Human Reproduction (LRRH) and the *Laboratoire d'Histologie générale*, *Neuroanatomie et Neuropathologie* (*LHNN*) from the Erasme hospital to develop new RNA Delivery Systems based on gold nanoparticles. MiRNAs are small non-coding molecules, which offer new promising approaches in cancer therapy but also in fertility preservation. However, these miRNA have to be delivered to the right organ, which requires the development of new targeted 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 (brain or avory depending on the application).

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7. Design of plasmonic nanomaterials for the development of Lateral Flow ImmonuAssays.

Summary: Lateral Flow ImmunoAssays (LFIAs) widely used in human health for point of care testing, as these assays give a relatively quick response (typically 10-15 minutes), are of 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, Au/Ag alloyed or core-shell nanostructures would however represent more efficient options, as they should exhibit larger molar extinction coefficients than AuNPs (i.e., 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. New nanostructures will be synthesized and be integrated in such Lateral Flow Assays as colorimetric reporters.

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8. Development of Lateral Flow Assays for environmental applications.

Summary: Lateral Flow Assays (LFAs) are widely used in human health testing and environmental monitoring, as they give a relatively quick response (typically 10-15 minutes), are of low cost and can be performed by untrained personnel. 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. Gold nanoparticles (AuNPs) are typically used as optical transducers to visualize the test result but other plasmonic nanomaterials are being investigated. The most eminent example of a LFA is the pregnancy test. The objective here is to design systems to detect traces of phytosanitary products of concern on food and food crops. This will entail the identification and characterization of molecular receptors for the selective recognition of the target analyte/contaminant, the preparation of the functionalized colorimetric reporters (plasmonic nanomaterials) and the design of the test strip. The aim is to develop a straightforward system that can be used in citizen science experiments for the monitoring of consumer goods.

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9. 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.

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10. Development of chiral catalysts for the preparation of lactones of pharmaceutical interest.

Summary: Asymmetric reactions, which lead preferentially to the synthesis of one enantiomer over the other, are extremely challenging but essential for the pharmaceutical sector. Lactones (cyclic esters) are a regular motif of molecules with medicinal applications and the Hennecke group is developing chiral oragnocatalysts, derived from natural alkaloids, that show promising results for the preparation of chiral lactones. Mechanistic questions remain and the proposed project will focus on the study, by NMR and UV spectroscopies, of the binding mode and binding affinity of carboxylic acid-containing substrates to the alkaloid-based catalysts.

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