Master Project Topics:

**Research at the Biochemistry and Structural Biology lab**
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Our lab focuses on deciphering the structure, dynamics, and mechanisms of membrane proteins. We focus on understanding the molecular basis of membrane transporters in normal physiology and in pathogenesis. We aim to decipher mechanisms involved in key processes such as adaptation to environmental stress, drug resistance or mutation-induced protein misfolding. We employ a heuristic approach which combines functional characterization with in-depth structural and biophysical characterization with a focus on protein dynamics.

Our experimental toolkit comprises cutting-edge techniques to characterize dynamics and structures of challenging proteins :

* Hydrogen-Deuterium Exchange Mass Spectrometry (HDX-MS) for insights into protein structure and interactions.
* Native Mass Spectrometry to investigate protein-lipid complexes in their native state.
* Single-Molecule FRET (smFRET) for studying conformational dynamics.
* X-ray crystallography and cryogenic electron microscopy for high-resolution structures
* AI-base structural predictions

Why Join Us?

Our research unit is located in building BC of La Plaine Campus. We offer a stimulating research environment, comprising a diverse team of PhD students, postdoctoral fellows, and researchers. In our lab, you will:

* Gain experience in advanced biophysical techniques
* Work on impactful projects with potential applications in drug resistance and therapeutics.

Who We Are Looking For

We are seeking master’s students who are:

* Interested in protein biochemistry and the biophysical study of membrane proteins.
* Motivated to explore challenging research questions in the field of membrane transport and associated pathologies, and drug resistance.
* Keen to develop new technical skills and contribute to ongoing projects in a collaborative atmosphere.

What You’ll Do - Master thesis projects

1. **How the lipid environment influences multidrug efflux pumps**

Multidrug transporters play an essential role in the emergence of multidrug-resistant bacterial strains. Developing suitable strategies requires a fundamental understanding, at the molecular level, of how they operate. Our laboratory has demonstrated that the membrane in which these transporters are embedded plays a crucial role in the recognition of different antibiotics and in the efficacy of transport. The molecular basis of these protein-lipid interactions are currently poorly understood. This project utilizes tools that allow for the direct study of proteins in their native membrane, in order to observe their dynamics and function in response to a physiologically relevant environment.

**Duration:** 6-9 months
**Techniques**: bacterial transformation, growth, protein expression, protein purification and characterization, SDS-PAGE and Western blot, chromatography, HDX-MS, native MS, transport assay, fluorescence spectroscopy.

1. **Decipher the molecular mechanism of phytohormones transporters**

Like hormones in animals, phytohormones act in cells and tissues distant from their site of origin, involving three essential steps for function: synthesis, transport, and reception. Phytohormones must rely on specialized transporters to cross cell membranes for both export from the producing cell and import into the target cell where reception takes place. Intrinsically disordered regions (IDRs) of phytohormone transporters play a significant role in regulation through interactions with inhibitors and activators. However, the exact mechanisms by which IDRs achieve this remain poorly understood. We will use approaches spanning from biochemistry and biophysics to plant phenotypes to determine how phytohormone transporters modulate their activity and structure in response to different stimuli targeting their IDRs.

**Duration**: 6-9 months
**Techniques**: protein expression, protein purification and characterization, SDS-PAGE and Western blot, chromatography, HDX-MS, transport assay, fluorescence spectroscopy, transformation and in vivo phenotyping of Arabidopsis thaliana

1. **Development of novel approaches for studying membrane protein dynamics.**

Membrane proteins interact with their surrounding environment to modulate their conformation and activity. How this happens at a molecular level is unknown because the tools to observe these interactions are lacking. In this project, you will evaluate and compare different methods of isolation of membrane transporters in native environments, using either polymer-based or protein-based approaches. How the native membrane affects the activity will be evaluated using different biochemical assays. The conformational changes will be monitored using high-end biophysical approaches, such as DEER spectroscopy and HDX-MS.

**Duration:** 6-9 months
**Techniques**: bacterial transformation, growth, protein expression, protein purification and characterization, SDS-PAGE and Western Blot, negative stain EM, chromatography, HDX-MS, DEER spectroscopy, transport assays.

### **Understanding the Molecular Basis of Cystic Fibrosis**

Cystic fibrosis (CF) is a life-threatening genetic disorder caused by mutations in the CFTR (Cystic Fibrosis Transmembrane Conductance Regulator) gene, leading to defective chloride ion transport and the buildup of thick mucus in the lungs and other organs. This disrupts normal cellular function and causes severe respiratory and digestive complications.

Our goal is to investigate, at the molecular level, how mutations in the CFTR channel result in protein misfolding of this essential chloride channel, ultimately leading to cystic fibrosis. We focus on understanding how protein dynamics enable proper function while also contributing to mutation-induced dysfunction.

In addition to this fundamental research, we aim to develop nanobody-based therapeutic strategies to combat various forms of cystic fibrosis. To achieve a comprehensive understanding of the process, we employ a wide range of methodologies, including X-ray crystallography and cell culture.

**Duration:** 6–9 months
**Techniques:** Recombinant protein expression, protein purification and characterization, SDS-PAGE, Western Blot, X-ray crystallography, cryo-EM, HDX-MS, mammalian cell culture, fluorescence spectroscopy.

### **Novel Regulatory Mechanisms in Mycobacterium tuberculosis**

Tuberculosis (TB), caused by Mycobacterium tuberculosis, remains one of the most persistent and deadly infectious diseases worldwide. The bacterium’s ability to survive and adapt to hostile environments within the host makes it particularly difficult to eradicate, contributing to its continued global health burden.

Our group has identified a novel bacterial system in mycobacteria that links membrane transport to gene transcription. This previously unknown membrane transporter plays a critical role in the adaptation of pathogens like Mycobacterium tuberculosis to stress conditions.

We aim to investigate the structure and function of these proteins and their role in virulence. Using a comprehensive experimental approach, we will explore how membrane transport directly regulates gene transcription. Additionally, we will study the evolutionary origins of this novel system.

**Duration:** 6–9 months
**Techniques:** Recombinant protein expression, protein purification and characterization, SDS-PAGE, Western Blot, X-ray crystallography, cryo-EM, HDX-MS, mammalian cell culture, fluorescence spectroscopy.