Master thesis project

Modeling of membranes and proteins from neutron reflectometry data

Membrane proteins are complex biomacromolecules that perform essential regulatory functions in biological systems, as they facilitate transport over and interactions with lipid membranes such as our cell membranes. Thus, membrane proteins account for the majority of drug targets. Elucidating the structure and behavior of these proteins has been a central goal in structural biology for years.

Neutron reflectometry is a developing, structural, non-destructive technique that allows for probing the structure of biological systems at near-physiological conditions. Samples are prepared on silica substrates and irradiated by a collimated beam of neutrons, whereafter the reflectivity perpendicular to the surface is recorded. From this data, the structure of the sample is determined by refining intricate models.

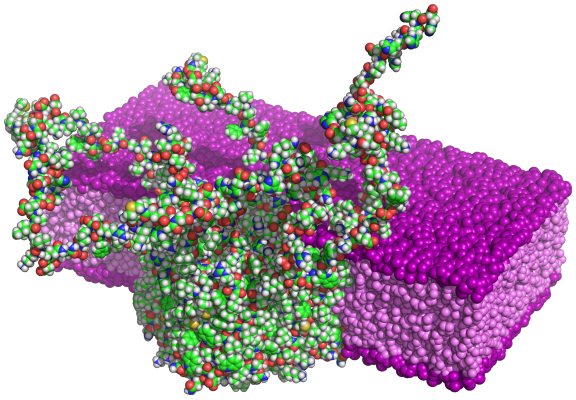

Figure 1: A membrane protein, Aquaporin, embedded in a model of a phospholipid membrane.

Information about the sample is acquired through elaborate modeling, where the constituents of the sample are usually modeled as simple "slabs" stacked in a layered structure. However, in order to refine models describing more delicate structures such as disordered proteins, novel, more direct modeling tools are needed. Scattering physics, and in particular soft matter materials science, routinely applies models of disordered domains of proteins, polymers, or other flexible molecules as simple random coils; however, the field of computational structural biology already utilizes numerous manners of predicting structures of proteins based on well established models for interactions.

This project proposes a novel model refinement approach, which aims to refine the structural conformations of disordered proteins embedded in a membrane by comparing recorded data to models of ensembles of structure determined by computational methods. From e.g. molecular dynamics trajectories or Monte Carlo generated ensembles, the proposed analysis pipeline would initiate by assembling a conformational ensemble for the disordered (parts of a) membrane protein in question.

The student will get hands-on experience with:

- Neutron reflectometry data and experiments
- Mathematics of scattering physics
- Development of data analysis algorithms
- Software development in Python
- Bioinformatics of protein modeling
- Statistics of model refinement

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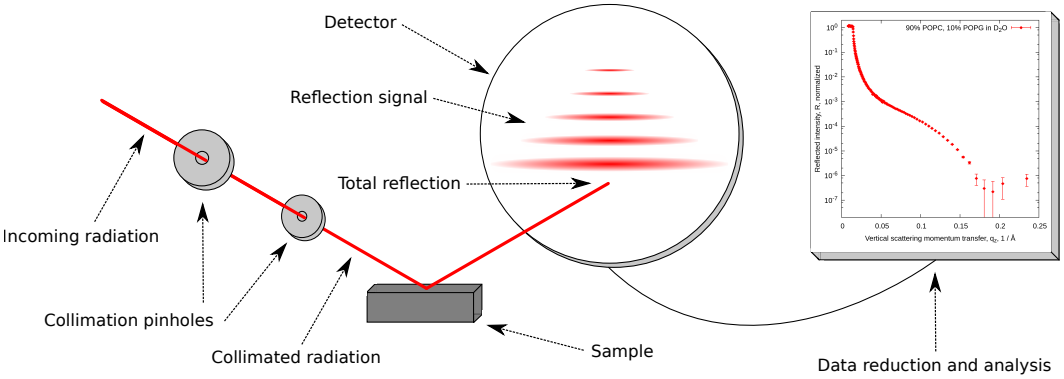

Figure 2: Schematic of a neutron reflectometry set up.