

TRACKING ATP-DEPENDENT PROTEIN DYNAMICS

Project title: Tracking ATP-Dependent Protein Dynamics
PRISMAS Research Area: Healthy people
Supervisor: Magnus Andersson
Hosting University: Umeå University
Partners:
Link to position: [Apply here](#)

1. Project summary:

Proteins rearrange their structures according to predefined patterns that are encoded into the amino acid sequence, and hence have developed throughout evolution. Determination of such structural dynamics and the corresponding time scales is critical to understand the biological function of proteins. In this project, we will develop a time-resolved X-ray solution scattering approach at the CoSAXS beamline to track ATP-dependent protein dynamics in real time. The structural interpretation will be obtained using supercomputer-based molecular dynamics simulations. We aim to determine kinetics and structural transition states of ATP-driven P-type ATPase membrane proteins. In particular, we will characterize regulation by membrane lipids and protein internal domains. The results will show structural rearrangements involved in regulation of ion transport, identify the time scales involved, and potentially provide better understanding of associated diseases.

2. Keywords

Structural biology, time-resolved X-ray solution scattering, membrane protein regulation, molecular dynamics simulations

3. Project outline

- **State of the art:**

Membrane protein regulation is a new frontier in structural biology and serves as a basis to understand associated diseases. In this project, we will develop a synchrotron-based methodology at MAX IV Laboratory to track regulatory processes involved in membrane protein transport in real time.

- **Project objectives:**

The project will focus on development of a time-resolved methodology at the CoSAXS beamline at MAX IV Laboratory. The developmental work includes both the experimental setup at the beamline as well as Python code for data analysis, visualization, and interpretation. The aim is to study regulation of membrane protein transporters in a lipid environment, which will be achieved by state-

of-the-art nanodisc technology (Fig. 1).

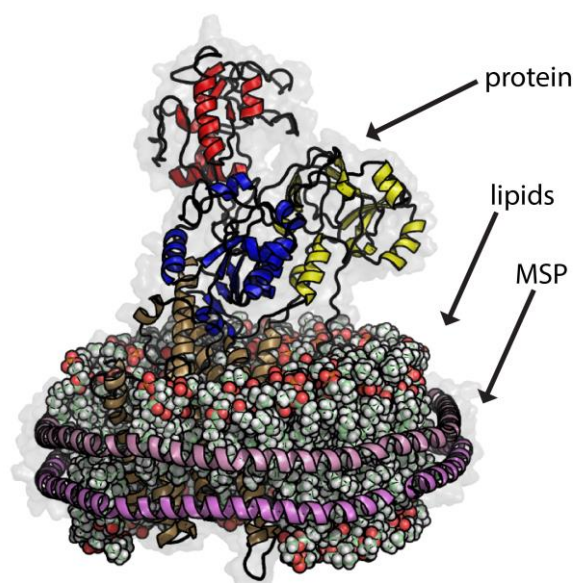


Figure 1

The PhD student will work in a research team with expertise in all aspects of the project – from the scattering technology and supercomputer-based simulations to membrane protein production and insertion into nanodiscs at controlled lipid composition. We have developed a time-resolved methodology for characterisation of ATP-dependent protein dynamics at the European Synchrotron Radiation Facility (ESRF) in Grenoble, France [1], which has enabled determination of intermediate-state structures and kinetics involved in muscle relaxation [2] (Fig. 2) and energy conversion [3]. The PhD student will also take part in experiments at the ESRF synchrotron.

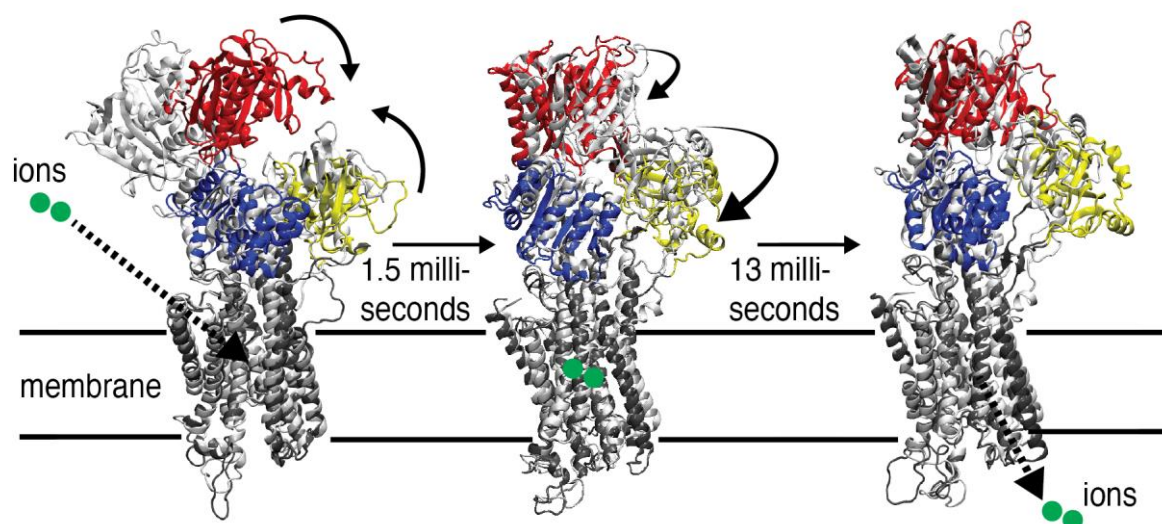


Figure 2

The PhD student will be trained in a highly interdisciplinary environment and obtain expertise in cutting-edge development of novel techniques in structural biology, which will provide excellent future opportunities in both academia and industry.

- **References:**

- [1] Orädd, F., Andersson, M. Tracking membrane protein dynamics in real time. *Journal of Membrane Biology*. 254:51-64, (2021).
- [2] Ravishankar, H., Pedersen, M.N., Eklund, M., Sitsel, A., Li, C., Duelli, A., Levantino, M., Wulff, M., Barth, A., Olesen, C., Nissen, P., Andersson, M. Tracking Ca^{2+} ATPase intermediates in real-time by X-ray solution scattering. *Science Advances*. 6(12):eaaz0981, (2020).
- [3] . Orädd, F., Ravishankar, H., Goodman, J., Rogne, P., Backman, L., Duelli, A., Pedersen, M.N., Levantino, M., Wolff, M., Wolf-Watz, M., Andersson, M. Tracking the ATP-binding response in adenylate kinase in real time. *Science Advances*. 7(47):eabi5514, (2021).

Link to PRISMAS overview: <https://www.maxiv.lu.se/prismas/>