

Protein and water dynamics at the atomic level

This project aims at pushing the boundaries for applications of neutrons in structural biology and paving the way for the use of neutron diffraction to extract information on protein and water dynamics at the atomic level.

The last 20 years of development of the experimental methods for protein structure determination by X-ray diffraction has led to an exponential growth of known protein structures. In contrast, the number of structures determined solely by neutron diffraction is still relatively limited (<50 in the PDB) and mostly based on data measured at medium to low resolution. The majority of these studies have been conducted with the purpose of locating functionally important hydrogen atoms.

The function of a protein is intimately linked to its dynamics, e.g. the action of the protein is accompanied by structural changes. The atomic displacement parameters (ADPs or temperature factors) contain information on structural flexibility and on structural dynamics in general. However, the ADPs from conventional refinements based on X-ray data also include contributions from disorder, and also suffer deficiencies in the model with respect to the electron distribution, making their relevance to dynamics difficult to interpret. In contrast, high resolution neutron diffraction data provide unbiased anisotropic ADPs that only reflect protein dynamics. This unique access to the determination of unbiased anisotropic ADPs, enables a comparison between neutron and X-ray derived displacement parameters as well as their link to the dynamic nature of the protein.

Perdeuteration is crucial in reducing the background arising from incoherent scattering of hydrogen. However, it is also known that this isotopic substitution affects the overall properties of a given protein. The investigation of the effect of deuteration on local dynamics will constitute an important part of this project.

The student will work in close collaboration with both ILL and UCPH supervisors. The research work includes the following:

- Expression, purification and crystallization of perdeuterated protein
- Collection of high resolution single crystal neutron and X-ray diffraction data
- Optimization of processing high resolution neutron diffraction data from protein crystals
- Structure refinement based on the neutron and X-ray diffraction data.
- Analysis of the effects of deuteration
- Extensive analysis of protein and water dynamics and relation between obtained X-ray and neutron derived results