LSI SUPPORT FOR PhD-STUDENTS IN APPLIED AREAS

Combined neutron spectroscopy and simulation study of intrinsically disordered proteins

THE PURPOSE OF THE PHD PROJECT

Disordered proteins are highly flexible, making dynamics a key property to understand them. They are common and implicated in several diseases, such as Alzheimer's, why an understanding of disordered proteins may contribute to the resolution of medical issues. The project aims to investigate dynamical properties of the antibacterial, disordered, small protein Histatin 5, through a combined approach of computer simulations and quasi-elastic neutron scattering. Crowding effects are also of interest, why the dynamics at low and high protein concentration are considered.

USING A LARGE-SCALE INFRASTRUCTURE

The lack of a defined equilibrium structure in disordered proteins limits the number of feasible techniques that can be used. Neutron scattering uniquely accesses short-time diffusion, which is the relevant measure to compare with simulation (molecular dynamics) models. In addition to being able to investigate disordered proteins, it is also possible to achieve results at higher protein concentration, which many alternative techniques of probing disordered proteins are unable to do. Due to the pandemic, measurements were performed remote at the experimental station IN16B of Institute Laue-Langevin (ILL), France, which access relevant time scales on a global protein scale and an internal protein scale, respectively.

Figure 1: The IN16B experimental station at ILL.

The analysis was performed in close collaboration with Dr. Tilo Seydel, enabling competence development of the Ph.D. student in terms of data treatment, data analysis, and the theoretical background of neutron scattering.

RESULTS AND IMPACT

The neutron scattering data showed the dynamics to be sensitive to both salt content, temperature, and the protein concentration used. It was shown that approximations such as using effective shapes, rather than accounting for the ensemble feature of disordered proteins, is inadequate to predict dynamics. Compared with the few studies performed in this area, numbers have the same magnitude, though dynamics seem faster for this smaller protein. Considering crowding effects, there is a clear decrease in dynamics with increasing protein concentration. Comparison with simulations suggest qualitative agreement with experiments, capturing the strong decrease in dynamics with crowding, and yielding comparable numbers, though not having perfect agreement, which may depend on both assumptions and model adequacy.

Results have been presented at conferences “Neutrons for Life” (2021) and “Les Houches” (2021) and an article has been submitted for publication.

Familiarity with relevant software (MANTID, LAMP) and experience with in-house development of analysis frameworks has been attained.

Figure 2: Project discussion. Top left: Dr. Tilo Seydel, top right: Ph.D student Eric Fagerberg, bottom: Prof. Marie Skepö.

Contacts: Eric Fagerberg – PhD-student at Lund University, eric.fagerberg@teokem.lu.se
Marie Skepö – Supervisor at Lund University, marie.skepo@teokem.lu.se
Tilo Seydel – LSI Expert at Institut Laue-Langevin, seydel@ill.eu

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