The Institute of Biochemistry and Biophysics of Polish Academy of Sciences is offering one PhD position in the project PreludiumBIS NCN: High Resolution analysis of hydrogen-deuterium exchange experiments monitored by mass spectrometry

Descrpition:

The aim of that project is to develop a novel algorithm for high-resolution analysis of the Hydrogen Deuterium eXchange Mass Spectrometry (HDX-MS) data to provide a better understanding of protein structures. Algorithm is going to be tested on existing datasets and from proteins measured during that project. Proteins are involved in virtually every biological process in any living cell. From a chemical point of view, proteins are by far the most structurally complex and functionally sophisticated molecules known. The function of a protein is determined by its structure. Protein structure is dynamic as it is constantly undergoing conformational motions (changing from one conformation to another). Conformational changes are a result of the interactions with other proteins, ligands, and the environment. “Traditional” methods of structural research such as crystallography (X-Ray) and nuclear magnetic resonance (NMR) provide high quality, atomic-resolution data. However, they are time-consuming, demanding significant quantities of material, are limited in protein size, as well as the possibility of crystallization in the case of X-Ray. Limitations resulting only from the size of a protein or its ability to crystallize were largely overcome thanks to electron microscopy (CryoEM). The dynamics of the structure can be studied NMR, which is limited by the size of protein and laboriousness of procedures. Finally, classical methods are not suitable for testing about 30% of the proteome. These are largely Intrinsically Disordered Proteins (IDP), or proteins consisting long (>40 residues) intrinsically disordered regions (IDRs). As a result, such proteins do not have a single, stable 3D structure. It is estimated that IDR represents 52-67% and IDP ~30% of the eukaryotic protein. IDPs are over-represented in such key biological processes as transcription, chromatin remodeling, cell signaling, cell signaling, etc. For this reason, they can be a valuable therapeutic target. Hydrogen-deuterium (H/D) exchange monitored by mass spectrometry (HDX-MS) provides complementary data to structural studies on complex systems by providing insight into the protein dynamics axis, which is in many cases of primary functional importance. HDX-MS and NMR are only one technique providing information about structure dynamics, contrary to the NMR, it is not affected by its limitations. The current most important limitation of the HDX-MS method is the resolution limited to the length of the measured peptides. It is also the biggest difference compared to NMR, which provides information with atomic accuracy. However, all the advantages of HDX-MS, including the ability to study proteins not available for NMR and X-Ray, the relative simplicity and ease of the method, make improving HDX-MS resolution would be extremely useful for molecular biology. However, we believe that from this type of data we can obtain high-resolution information in nearly single amid resolution. Single-residue deuterium uptake can be compared with the information obtained by NMR because it is not limited by the length of the peptides. However, unlike NMR or X-Ray, it allows the study of much larger systems, such as unstructured proteins. Also, this approach allows re-examining data from previous experiments and extracting additional information without repeating the measurement. This enables getting more insight from data assumpted as exploited.

Project Leader: prof. Michał Dadlez

Duration: 48 months

Job Status: PhD scholarship in Doctoral School

Offer Starting Date: 01.10.2020

Salary: 5000 PLN/month, 6000 PLN/month after midterm evaluation, brut

Requirements:

- MSc or equivalent in computational biology, physics, biophysics
- Strong biological background and interest in proteomics
- Fluency in English
- high programming skills, with particular emphasis at R language and the Shiny framework
- Motivation and the ability to solve research problems on their own
- Ability to work in a team and good interpersonal skills
- At least one scientific publication published in a journal indexed by JCR

Required documents:

1. Curriculum Vitae; including publication list
2. Diploma
3. Relevant documents

Please submit the following documents to: sn@ibb.waw.pl

Application deadline: 20.09.2020 (23:59:59 GMT+2)