【Grant-in-Aid for Scientific Research (S)】

Broad Section B

Title of Project : Neutron Structural Biology for New Generation

Masaaki Sugiyama
(Kyoto University, Institute for Integrated Radiation and Nuclear Science, Professor)

Research Project Number : 18H05229 Researcher Number : 10253395
Keyword : protein dynamics, neutron scattering

【Purpose and Background of the Research】

In these days, not only structure but also dynamics has been highlighted to understand functions of biomacromolecules.

Figure 1 shows the relation between structure and dynamics, taking multi-domain protein (MurD) as an example. A hierarchic structure of the protein is shown in Fig.1(u): "amino acid reside" is a basic unit (10^{-11}-10^{-10} m), "domain" is a unit of 3D structure (10^{-10}-10^{-9} m), "whole structure" is constituted with the domains (10^{-9}-10^{-8} m), "complex / aggregates" is connected by other protein(s) and/or molecules(s) (>10^{-8} m). Next, based on MD simulation, the time range of dynamics of each structure is displayed on a spatio-temporal map (Fig.1(d)): Zones 1-4 correspond to the dynamics of amino acid reside (10^{-15}-10^{-12} s), domain (10^{-12}-10^{-9} s), whole structure (10^{-9}-10^{-6} s) and complex / aggregates (>10^{-6} s), respectively. Experimentally, there are several methods to observe the dynamics for Zones 1 and 4 but and there are not for Zones 2 and 3, namely an experimental "missing zone".

Neutron scatterings have possibilities to cover the missing zone in principle. However, the beam intensity was not enough to observe dynamics of protein in solution. Recently, the situation is going to change: J-PARC has supplied the brilliant beam and their spectrometers are having ability to observe the dynamics.

Purposes of this project are establishment of the methods to measure the protein dynamics in the missing zone and development of the analyzing method coupled with MD simulation by making full use of the latest neutron spectrometers.

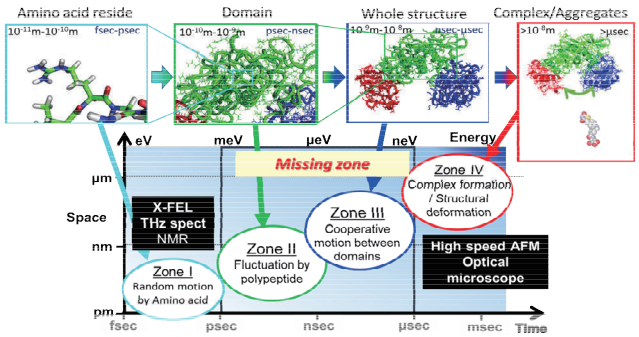

Figure 1. Relation between structure and dynamics in a multi-domain protein. (up) Hierarchic structure. (down) Dynamics of each structure on spatio-temporal map.

【Research Methods】

This project proceeds development and empirical studies. Three techniques, high level protein deuteration, measurement for protein dynamics with QENS, NSE and SANS, and data analysis coupled with MD simulation, will be developed. Then, by integrating the developed techniques, the protocol will be established to reveal protein dynamics in the missing zone. In the empirical study, the first targets are two proteins with high biological significances: MurD is a typical multi-domain protein and Hef is an intrinsically disordered protein. Then, the targets expand more.

【Expected Research Achievements and Scientific Significance】

This project will not only develop methods to cover the missing zone but also reveal dynamics of proteins with high biological significances. With these results, it is expected to reveal a transfer mechanism from random motion of amino-acid resides to cooperative motion between domains.

The developed methods will be open for all researches who are interesting of protein dynamics. Then, it is also expected that Japanese facilities such as J-PARC becomes center of neutrons biology. In addition, the most of project members are young and up-coming researches. Therefore, they will play a central role in this field in the next 10 years.

【Publications Relevant to the Project】

・P. Bernadó, M. Sugiyama, etal., BBA General Subjects, 1862 (2018) 253-274.
・R. Inoue, M. Sugiyama, etal., Sci. Rep., **6** (2016) 29208.

【Term of Project】 FY2018-2022

【Budget Allocation】 151,600 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.rri.kyoto-u.ac.jp/NSBNG