【Grant-in-Aid for Scientific Research on Innovative Areas (Research in a proposed research area)】
Interdisciplinary Area

Title of Project : Novel measurement techniques for visualizing 'live' protein molecules at work

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【Purpose of the Research Project】

Genomic DNA encodes the amino acid sequences of proteins. In the evolution of life, random mutations and natural selection have made the proteins molecular machines that autonomously form stable tertiary structures, for their functions as catalysts, sensors, actuators, and scaffolds in organisms. The 3D structures determined by X-ray crystallography are inevitably static, but they provide convenient explanations of the protein functions, as if they were macro-scale machines.

However, most structural biological techniques cannot properly convey the dynamic aspects of protein structures. In this research program, we aim to develop innovative measurement techniques, to vividly describe protein structures at their sites of action (Fig. 1).

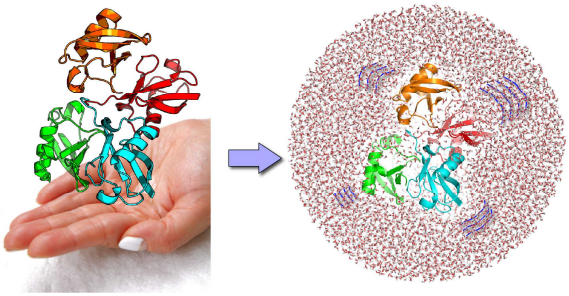

Figure 1: From a static view to a dynamic view.

【Content of the Research Project】

Nuclear magnetic resonance (NMR) and atomic force microscopy (AFM) are the methods of choice for characterizations of the time variations of protein structures. We must consider two fundamental problems, related to the "mean and distribution of motions" and the different structures between the "*in-vitro* and *in-situ* states" (See the Key Words section). We will solve the first problem by 1) "the integration of optical techniques into the high-speed AFM measurement" and 2) "the creation of crystal contact-free space in protein crystals" (Fig. 2). We will also address the second problem by 3) "the development of in-cell NMR measurement technology" and 4) "biologically-oriented application of optically detected magnetic resonance (ODMR), using nanodiamonds" (Fig. 2).

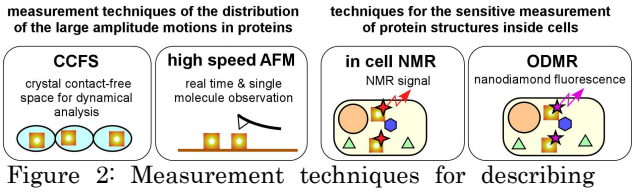

Figure 2: Measurement techniques for describing protein structures in action and on site.

Since new measurement techniques inevitably provide truly novel results, we will evaluate their precision by molecular dynamics simulations. We will also apply the new measurement techniques to specific biological targets to discover their potential applications and limitations, thus eventually accelerating the methodological development within a short time period.

【Expected Research Achievements and Scientific Significance】

The capabilities of Japanese life sciences research will be strengthened by developing innovative measurement techniques for protein dynamics. The applications of these novel techniques to a wide variety of biological problems will facilitate discoveries toward breakthroughs in life sciences.

【Key Words】

Problem of "mean and distribution of motions": Large motions give distorted mean structures. Therefore, the unbiased measurement of the distribution of motions is required.

Problem of "*in vitro* versus *in situ* states": A stable protein structure in a test tube and a biologically active structure in a cellular environment may differ, due to molecular crowding effects and interactions with other molecules.

【Term of Project】

FY2014-2018

【Budget Allocation】

1,171,000 Thousand Yen

【Homepage Address and Other Contact Information】

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