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

Science and Engineering (Interdisciplinary Science and Engineering)

Title of Project： Direct visualization of molecular recognition forces by high-resolution atomic force microscopy and spectroscopy

Hirofumi Yamada
(Kyoto University, Graduate School of Engineering, Professor)

Research Project Number：17H06122　Researcher Number：40283626
Research Area：　Nano/Micro science, Nanobioscience
Keyword：　Single-molecule force spectroscopy, Atomic force microscopy

【Purpose and Background of the Research】

Three-dimensional (3D) force mapping based on frequency modulation atomic force microscopy (FM-AFM) is a powerful technique, capable of directly visualizing hydration structures and charge distribution in solution. The method is also applied to mapping of recognition forces between biological molecules. However, the detection probability of binding forces is often low because the effective interaction time in the measurements is not sufficiently long, which means that essential improvements of the method are required.

In this project we further develop 3D force mapping method not only by the precise control of the AFM probe motion but also by the real-time analysis of the response signal, which allows us to visualize 3D molecular recognition forces and other several forces originating from hydration structures and/or charge density of the molecules.

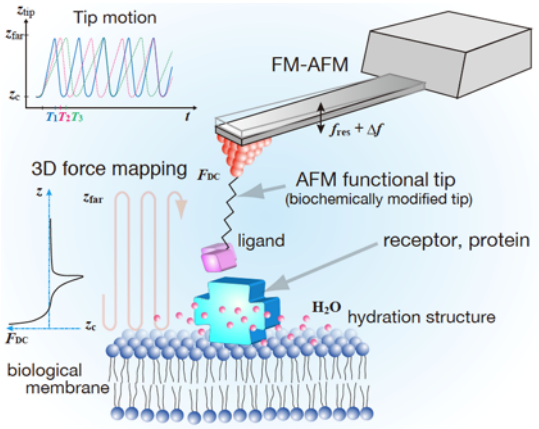

Fig. 1 3D molecular recognition force mapping

【Research Methods】

(1) Advanced 3D force mapping

Molecular binding forces are quantitatively detected in 3D force mapping by varying the interaction time of the probe tip in the vicinity of a target molecule. To minimize measurement disturbance possibly caused by the tip vibration in FM-AFM the natural oscillation driven by the thermal noise is utilized.

(2) Visualization of molecular recognition forces

Antibody-antigen binding: Oligomer formation of various IgG antibody molecules and the formation mechanism are investigated at the molecular level.

DNA-protein complex: DNA-protein complexes formed in the initial stage of eukaryotic DNA replication process are visualized and a series of the whole initial process is clarified.

(3) Visualization of hydration structures

Hydration shells/structures in the proximity of biological molecules having complex spatial structures are visualized by precise control of the probe tip. The relationship between hydration strictures and bio-functions in various protein molecules including ion channels is clarified

【Expected Research Achievements and Scientific Significance】

This project is expected to make a significant contribution directly to the molecularly-targeted therapy. In engineering applications it is directly connected to development of biomaterials such as biocompatible materials and biosensors. In addition it is expected to produce a huge spinoff effect in both industrial and social life aspects.

【Publications Relevant to the Project】

・S. Ido *et al*. “Immunoactive two-dimensional self-assembly of monoclonal antibodies in aqueous solution revealed by atomic force microscopy”, *Nature Materials*, **13**, 264-270 (2014).

・K. Umeda *et al*. “Molecular-scale quantitative charge density measurement of biological molecule by frequency modulation atomic force microscopy in aqueous solutions”, *Nanotechnology*, **26**, 285103 (2015).

【Term of Project】 FY2017-2021

【Budget Allocation】 141,900 Thousand Yen

【Homepage Address and Other Contact Information】

http://piezo.kuee.kyoto-u.ac.jp/
h-yamada@kuee.kyoto-u.ac.jp