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Individual-Particle Electron Tomography (IPET): An approach to study flexible protein structure and dynamics

Proteins have the unique ability to function specifically and efficiently, which is attained through its three-dimensional (3D) structures and flexibility, as well as necessary conformational changes. However, structural study on proteins that have large-scale flexibility, dynamics, and heterogeneity is challenging by current techniques, including X-ray crystallography, nuclear magnetic resonance (NMR) spectrum, small angle scattering (SAXS) and electron microscopy (EM) single-particle reconstruction. A fundamental approach to study the structure of flexible proteins should be based on the signal from each individual protein molecule itself instead of averaging from different protein molecules. EM provide a novel tool to image each individual molecule at atomic resolution level; while electron tomography (ET) provide an approach to image a targeted molecule from a series of tilt angles. Although the signal obtained from an individual molecule has been believed for decades to be too weak to achieve any 3D structure with a meaningful resolution, we recently re-investigated this possibility carefully and proposed an individual-particle electron tomography (IPET) approach with a "focused electron tomography reconstruction" (FETR) algorithm to improve the 3D structure resolution *via* decreasing the reconstructing image size with an iterative refinement process. IPET does not require a pre-given initial model, class averaging of multiple molecules or an extended ordered lattice, but can provide near one nanometer resolution 3D structure from an individual protein molecule. Through the structure determination of each individual molecule, the comparison of these molecular structures provides a new opportunity to reveal the dynamic character, equilibrium fluctuation, mechanism, aggregation and even structural changes in proteins during a chemical reaction or biological event.

Biography

Gang Ren is a Staff Scientist and Lab Director at Molecular Foundry, LBNL. He has received his BS and MS in Theoretical Physics at Lanzhou University and PhD in Material Physics at University of Science and Tech Beijing. He has received his Post-doctorate training at Scripps Research Institute. He has started his research lab at UCSF in 2006 and then transfer to LBL in 2010. His research group is supported by DOE, NIH and Industry funds. He has published more than 70 papers in reputed journals and has been serving as an Editorial Board Member of numerous journals.

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