

Realization of new image-based structure analysis method for 3-D structural analysis of biology

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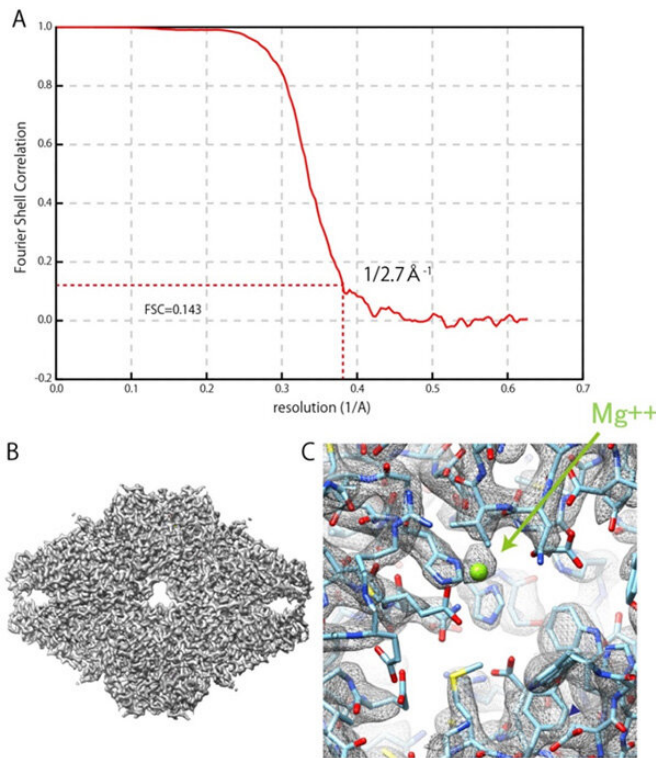


Figure A is Fourier Shell Correlation. This figure shows resolution is 0.27nm at FSC=0.143. Figure B is a map of 3D reconstruction. Figure C shows a Mg²⁺ ion at the enzyme active site. Credit: JEOL

In basic biology, medical sciences and pharmaceutical sciences, structural analyses of membrane proteins are important, and single-particle analysis by cryoEM is now very powerful method. Japanese researchers have developed the image-based structure analysis (IBSA) method, an improved method of single-particle analysis that enables structural analysis in a lipid membrane. This development has made it possible to analyze the structures of membrane proteins in vivo.

Single-particle analysis, a cryo-electron microscopy method, does not require crystallization of the sample as in X-ray crystal structure analysis, and there is no [upper limit](#) on the molecular weight of the sample as in nuclear magnetic resonance spectroscopy. Since atomic resolution can be achieved with very few aqueous samples, single-particle analysis has established a position as one of the basic technologies for structural analysis.

However, this method requires a large number of images of randomly placed target [protein](#) particles. Purification of proteins is necessary in single-particle analysis and in the case of membrane proteins, detergent solubilization is required for this purification. This changes the [molecular structure](#). Therefore, it is difficult to analyze the structure of membrane proteins in a real environment.

Research on the correlation between structure and function of membrane proteins requires a method that can elucidate their three-dimensional structure at the molecular level in the cell membrane. A method for resolving this problem could be the IBSA method invented by Professor Fujiyoshi of Tokyo Medical and Dental University. It captures tilted and non-tilted images of the sample, improving the reliability of 3-D reconstruction while taking advantage of single-particle analysis. It is a method of analyzing the structure of proteins in real biological membranes.

For this project, JEOL produced a [cryo-electron microscope](#) with a cryo-stage equipped with a sample autoloader and an automated liquid nitrogen supply system. For the IBSA method, the algorithm was constructed and verified, and sample preparation conditions were verified. Structural analysis using a cryo-electron microscope with the IBSA method obtained a resolution of 0.27 nm for β -galactosidase (which is an enzyme), by FSC

(Fourier Shell Correlation) evaluation (FSC = 0.143).

Structural analysis with a cryo-electron microscope does not require the sample to be crystalline, unlike X-ray crystal structure [analysis](#). Therefore, it enables [structural analysis](#) of proteins that cannot produce crystals. By using a cryo-electron microscope with the IBSA method, the structure of membrane proteins in a biological membrane can be analyzed, which could elucidate physiological functions of membrane proteins and drug discovery research.

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