Title: Structure evaluation of protein-ligand binding from low resolution density map using deep learning

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Abstract:

The quality of protein structure data obtained from X-ray crystallography and cryo-EM is highly dependent on the resolution of the experimental data. We have developed a machine learning-based method to evaluate the quality of structural coordinates using electron density and coordinates obtained from X-ray crystallography as input data [1,2]. Our method (Quality Assessment based on Electron density map: QAEmap) uses a 3D-CNN, which is an extension of the Convolutional Neural Network (CNN) to three dimensions, to learn 3D structural information. One of the problems in learning the 3D structure of a protein is that the size of each protein differs, but we solved this problem by evaluating each atom. In other words, the learning and evaluation unit is a box centered on the target atom. Within this box, ligands or amino acids containing the target atom and their surrounding environment (polar interactions, hydrophobic interactions, non-covalent interactions with neighboring atoms, etc.) are included, and their information is learned and evaluated. The box correlation coefficient (bCC) is defined as the objective value. This is the correlation coefficient between the coordinates in the box centered on the atom of interest and the corresponding high-resolution electron density. If the bCC prediction can be done correctly, the correlation between protein coordinates and a putative high-resolution electron density map can be predicted even when only low-resolution data are available. We are currently developing a method to obtain correct docking poses even from low-resolution data using QAEmap. Since QAEmap gives a resolution-independent evaluation score, we hope to make structural modifications based on this score to enable coordinate determination independent of data resolution.

[1] 佐藤 美和, 宮口 郁子, 生物工学会誌, 2022, 100 巻, 11 号, pp. 603-606

[2] Miyaguchi, I. et al. Sci. Rep. 11, 1–13 (2021).