Analyzing Model Bias in Cryo-EM Single-Particle Image Processing

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Abstract

Single particle cryogenic electron microscope (cryo-EM) has become a popular method to determine the structure of biological molecules to near-atomic resolution. When cryo-EM is applied to imaging biological molecules, the data is recorded in a micrograph containing many particle projections in unknown orientations. A big challenge of cryo-EM image analysis is that the signal to noise ratio is extremely low (SNR <0.1), because the molecules are photographed with low-exposure to minimize structural degradation caused by radiation. 2D clustering, a crucial step in cryo-EM analysis, is to group projections of similar particle orientations such that the resulting averages can greatly enhance the signal to noise ratio of those abundant views and allow them to be labeled. Meaningful clustering depends on good image alignment, for which all possible rotations and translations are exhaustively searched to find the most fitted solution. However, image alignment for highly noisy data can be strongly biased toward the reference model, which is referred as model bias phenomenon. In this talk, I will show how we investigate model bias from a mathematical and statistical perspective. We propose an index to quantify model bias and provide the consistency and asymptotic theorems. This is a joint work with Yi-Ching Yao, Wei-Hau Chang and I-Ping Tu.