Cryo-EM Macromolecular Structure Determination at Atomic Resolution

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Cryo-EM has the resolving power to visualize atomic detail of biomolecules. We utilize standard 300 kV transmission electron microscopes (Titan Krios) to image protein complexes in our Stanford-SLAC Cryo-EM Center. We have found to be readily feasible to record sufficient images of vitrified apoferritin in less than ¾ a day for reconstructing its structure at ~1.27-1.34 Å resolution with either a K3 camera and an energy filter or a falcon detector without an energy filter [1]. A quantitative analysis of the maps substantiates the resolvability of all atoms except hydrogen in all the amino acids, water molecules and metal ions. Such capability is not always achieved for all macromolecules because of their compositional and/or conformational heterogeneity. Nevertheless, advanced data processing method can be used to sort out the structure variants from which novel chemical properties of the macromolecules can be derived. Biological examples will be presented how the current technology is applied.

Reference

[1] K. Zhang, G.D. Pintilie, S. Li, M.F. Schmid and W. Chiu, "Resolving individual atoms of protein complex by cryo-electron microscopy," *Cell Res* **30,** 1136-1139 (2020).