CryoEM Structures of Macromolecules

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Single-particle cryo-electron microscopy (cryo-EM) is a mature methodology for routine structure determination of biomolecules with detailed features equivalent to those obtained by X-ray crystallography at comparable resolutions. More than 4,000 cryo-EM structures between 1-4 Å resolution have been deposited to the protein databank as in early 2021. It is feasible to utilize a standard 300 kV transmission electron microscope and direct electron detector to record images of vitrified apoferritin single particles for reconstructing its structure at 1.27 Å resolution. Quantitative validation analysis of the maps substantiates the resolvability of all atoms except hydrogen in the amino acids, water molecules, and metal ions. Such capability is not always achieved for any macromolecules because of their compositional and/or conformational heterogeneity. Nevertheless, an advanced data processing method can be used to sort out the structural variants of many biomolecules such as membrane ion channels and RNA from which novel chemical properties of the macromolecules can be derived at near-atomic resolution (2-3 Å). Furthermore, various computational and experimental methods have been used to validate these structures.