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Harnessing the power of electrons to unravel atomic level structures of macromolecules

The field of structural biology provides us with detailed 3D atomic structures of macromolecules such as proteins. By understanding the 3D structure of an object, we can understand the functional properties more intimately and thus help to fix any malfunctions or prevent severe problems from occurring (i.e., producing more effective drugs against pathogens, design of vaccines etc.,). The current landscape of macromolecular structural biology has rapidly changed in the past decade due to rapid advancements in cryogenic electron microscopy (cryoEM)[1]. In particular, the technique of single particle analysis has transformed the way we analyze structures at the molecular level. By removing the need to crystallize your target protein(s) allows imaging in a more native state, whilst vastly saving on sample amount > 100-fold. These factors combined with the improvements in hardware (cryoEM grids, microscopes, detectors) and sophisticated 3D reconstruction software[2,3] can allow for high resolution reconstructions of protein molecules. A key advantage of this technique is that heterogenous samples (i.e., protein that adopts several conformational states) can be effectively separated by the software, allowing the concept of 'multiple structures from one cryoEM grid' to come to fruition[4]. I will present some recent studies that highlight the unique power of cryoEM and some of the future perspectives within the field to further advance the structural biology field.

（1） K. Vinothkumar & R. Henderson, Quarterly Review of Biophysics, 2016
（2） Zivanov *et al*, IUCrJ, 2020
（3） A. Punjani & D. Fleet, Journal of Structural Biology, 2021
（4） S. Scheres, Methods in Enzymology, 2016