Single-particle cryo-EM: Visualization of biological molecules in their native states

The aim of Structural Biology is to explain life processes in terms of macromolecular interactions in the cell. These interactions typically involve more than two partners, and can run up to dozens. A full description will need to characterize all structures on the atomic level, and the way these structures change in the process. Because of the crowded environment of the cell, such high-resolution characterization is presently only possible when the group of interacting molecules (often organized into processive "molecular machines") is isolated and studied in vitro. While X-ray crystallography has provided structures of a large number of molecular structures, the need for crystals diffracting to high resolution has severely limited the number of biological molecules and the range of conformers that can be studied with this technique. Single-particle cryo-electron microscopy is about to fill this gap, allowing functional processes to be studied in great detail without imposing restraints on the structures. There are many examples now for this expansion of Structural Biology toward a full characterization of a functional process. Future developments of single-particle cryo-EM include the study of short-lived intermediates in a nonequilibrium system by time-resolved techniques, and the characterization of continuous structural changes using data mining from large ensembles of molecule images.

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