The characterization of structure and associated conformational changes of biological macromolecular complexes is important to understand how macromolecular assemblies fulfill their complex roles in the living cell, and it plays an important role in the development of new drugs to treat human diseases. Several techniques may be used to determine the 3D macromolecular structure. X-ray crystallography technique may yield atomic resolution of the structure but requires crystallization of the biological material. However, crystallization of complexes with conformational flexibility is difficult, which is often the case with large macromolecular complexes. Nuclear magnetic resonance (NMR) may provide unique information about dynamics and interactions but atomic structure determination is restricted to small complexes. Cryoelectron transmission microscopy (cryo-EM) allows studying frozen-hydrated samples within a thin layer of noncrystalline form of solid water, called amorphous ice, at cryogenic temperatures (generally liquid nitrogen temperatures). Thus, cryo-EM allows the observation of biological specimens in close-to-physiological conditions as well as studying flexible complexes. Single Particle Analysis and Single Particle Tomography are two cryo-EM approaches that are extensively used for obtaining 3D structural information of biological macromolecular complexes.

The 3D cryo-EM field has been experiencing a very fast evolution in recent years. New technological developments (e.g., direct detector devices (DDD), phase plates, and supercomputing platforms) and new image processing methods have opened the way to obtain quasi-atomic resolution for a large range of macromolecular complexes, including relatively small ones (less than 300 kDa). Moreover, the new technological developments have increased the richness of the data, requiring novel image processing methods to extract all the available structural information. Also, these recent developments now allow extracting the information about the dynamics of complexes by exploring the conformational heterogeneity of the sample. Finally, old questions such as how to validate the reconstructed EM density map or how to measure its resolution are just as topical as ever.

This special issue aims at providing a platform for discussion of the cutting-edge cryo-EM image analysis and 3D reconstruction methods and their structural biology and biomedical applications.

Potential topics include, but are not limited to:

- Advances in DDD movie processing and phase plate image processing
- Automated data collection, selection, and processing
- Quality, ranking, and validation of cryo-EM maps
- 3DEM map interpretation, including map fitting with available atomic resolution structures
- Computational analysis of sample heterogeneity/flexibility
- Applications of the state-of-the-art cryo-EM image analysis and 3D reconstruction methods in structural biology and biomedical research

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