Cryo-EM: a crystallographer view

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Abstract

Cryo-electron microscopy (cryo-EM) has undergone an astonishing revolution in the last few years [1]. A limited, but significant, gain in resolution due to the implementation of new kind of sensors that detect electrons directly, without having to convert them to photons and, in turn, in photoelectrons, has allowed electron microscopy to overcome the barrier of the 4Å - 5Å resolution [2]. A resolution close or better than 3 Å allows, in fact, to trace the polypeptide chain, which means that detailed molecular models become available. The final result of this process is the production of electron density maps that looks similar or even better than an X-ray map at the same resolution. The reason is that the phase information is contained directly in the cryo-EM images.

Among the advantages of the technique, we have to mention the fact that: i) no crystals are needed; ii) a quite limited amount of sample is enough to carry out a complete analysis; iii) large and labile macromolecular complexes can be examined and, finally, iiii) the presence of two or three different conformations of the macromolecule can be distinguished. The major drawback is, at the moment, that only large molecules (i.e., about at least 150,000-200,000 Da) can be examined and the resolution is not yet comparable with that attainable by X-ray diffraction on single crystal.

A critical review of the comparison between classical protein crystallography and cryo-EM will be presented and discussed.

Biography

[1] Stuart, D., Subramaniam, S., and Abrescia, N.G. Nature Methods (2016) 8, 607-608
[2] Kuhlbrandt, W. The resolution revolution. Science (2014) 28, 1443-1444