The role of Cryo-electron microscopy in structural biology after the "resolution revolution"

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In 2017 R. Henderson, J.Frank and J Dubochet have been awarded the Nobel prize in Chemistry for having pioneered cyo electron microscopy (Cryo-EM) and Single Particle Analysis (SPA).

During the last few years Cryo-EM and SPA have grown from techniques able to produce low-resolution structures of protein complexes (aka blobology) to tools capable of achieving atomic and quasi-atomic resolution for complexes that nobody could solve with any other technique.

This incredible leap forward has made possible by introduction and adoption of new tools, in particular direct electron detectors (DED), ultra-stable cryo-microscope, such as Titan Krios, and the adoption of new SW for automatic data collection and processing.

Cryo-EM benefit of specific advantages, respect to other structural biology techniques such as NMR and X-ray diffraction:

- Crystallization or isotopic labelling is not needed.
- Amount of sample required is two orders of magnitude lower.
- Different functional conformation of a complex may be sorted out.

Cryo-EM has proved to be a very useful technique to be integrated with X-ray and NMR for structure-based drug design.

So it is no surprise that many structural biology groups all over the world are seeking access to this technology in order to find answers to their most relevant biological questions. Nevertheless most new comers to the field are struggling to overcome the adoption barrier that this technique may pose in term of: sample preparation and screening, automatic data acquisition and progressive users training.

In this presentation we will see how the fast pace of cryo-EM growth is going to change the structural biology landscape for the best.

In particular we will discuss the

- Glacios™ Cryo-TEM: A 200kV X-FEG autoloader-provided system capable of automatic screening of multiple grids and reduced footprint.
- The new Krios™ G3i: The latest Krios version with improved automation, increased cryo-performance and higher throughput.
- The new development of mED (Micro electron Diffraction): a technology that holds the promise to solve at high resolution, structures of nano-crystals . And at 0.1% of the cost of an XFEL.