*Nature Reviews Molecular Cell Biology* | Published online 24 Jan 2018; doi:10.1038/nrm.2018.1

# Journal club

## CYTOSKELETON IN HIGH RESOLUTION

The pursuit of high-resolution structures of cytoskeletal filaments used to pose a great challenge to structural biologists. With a few exceptions, polymerization and crystallization are incompatible processes. The approach successfully taken for actin by Ken Holmes and coworkers in 1990 was to inhibit filament assembly to obtain the crystallographic atomic structure of the actin monomer and to then generate a model of the actin filament using this structure and high-resolution X-ray fibre diffraction data from aligned filaments. This was followed by the model of the acto-myosin complex by Rayment and Milligan in 1993, using what may have been the first instance of 'hybrid methods', whereby the high-resolution crystal structures of both myosin and actin were 'docked' into the low-resolution cryo-electron microscopy (cryo-EM) structure of actin filaments saturated with myosin molecules.

These structural breakthroughs in the actin field resounded with the microtubule community, who felt that structures of tubulin and microtubules should not lag behind. However, attempts to inhibit tubulin self-assembly in the 1980s and 1990s led nowhere. The efforts that ultimately resulted in the first structure of tubulin took advantage of the ease with which tubulin polymerizes into different types of assembly, rather than relying on assembly inhibition, and of the development of electron crystallography by Richard Henderson. Henderson's work culminated in the publication in 1990 of the first atomic model of a protein from electron microscopy data — the structure of bacteriorhodopsin. To create this landmark atomic model, Henderson *et al.* combined electron diffraction and images of many 2D crystals of bacteriorhodopsin, naturally occurring in purple bacteria, to generate a 3D map of the protein. This paper is filled with technical insights and it set the stage for resolving other protein structures, including tubulin (Nogales *et al.*, 1998). Of note, the electron crystallographic analysis of tubulin used aberrant polymers of anti-parallel protofilaments, assembled in the presence of zinc and stabilized by taxol.

Henderson, together with Joachim Frank and Jacques Dubochet, was a pioneer who laid the ground for the development of cryo-EM, for which last year all three were awarded a Nobel Prize in Chemistry. Today, actin and microtubules can be visualized at high resolution, both alone and interacting with the myriad binding partners that contribute to cytoskeletal function, thanks to the amazing recent developments in the cryo-EM field.

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The author declares no competing interests.

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