

### GM02

#### *Experiments in electron microscopy: from metals to nerves*

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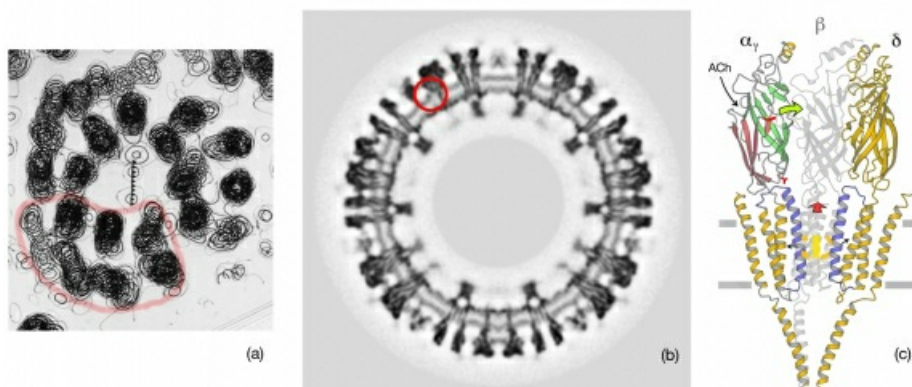
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Electron microscopy has become a major tool for biological structure research. My talk will recount experiments from my own research contributing to advances in this field, following on from electron crystallographic studies of metals. These experiments involve EM developments, such as low-dose imaging and millisecond time-resolved microscopy, and structural studies of proteins in membranes, including bacteriorhodopsin (with Richard Henderson, (a) in figure), gap junctions, membrane-associated ribosomes and nuclear pores [1-2]. Most recent work has centred around the structure and mechanism of the acetylcholine receptor ion channel, imaged and analysed in its unperturbed native membrane ([3]; (b) in figure). The talk will highlight studies on helical membrane tubes, beginning with the structure of the receptor at near-atomic resolution, obtained by cryo-EM in 2005. I will give a mechanical description of how the receptor works in mediating fast synaptic transmission ((c) in figure), based on spray-freeze-trapping experiments to capture the protein in the transient open-channel form. A model will be presented for the role played by lipids in enabling this transient conformational change, based on their segregated distribution next to the channels in the outer leaflet of the bilayer, where the structural changes are greatest. These experiments, recapitulating almost perfectly the conditions that exist at the synapse in living tissue, underscore the unique potential of cryo-EM for probing a biological mechanism in a physiological setting.

[1] Unwin, P.N.T. & Henderson, R. (1975). *J. Mol. Biol.* 94, 425-440.

[2] Berriman, J. & Unwin, N. (1994). *J. Ultramicrosc.* 56, 241-252.

[3] Unwin, N. (2013). *Quart. Rev. Biophys.* 46, 283-322.



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