Membrane Fusion in Intracellular Trafficking and Fertilisation:

Molecules, Forces, Energies and Networking

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Membrane fusion plays a key role in living matter. Naturally stable, membranes separate the inside from the outside of cells, and require specialised molecules, in order to fuse, whose mode of action is generally unknown. We will consider two examples of fusion: the one induced by SNARE proteins, and that involved in fertilisation. We will show how picoforces, nanodistances and energy measurements techniques can be used to produce information on how their molecular machineries work.

A large part of the intracellular trafficking is achieved by SNARE proteins that constitute the core of the membrane fusion machinery. The most well-known SNAREs are neuronal SNAREs that drive the release of neurotransmitters. Other proteins regulate the SNARE machinery, and among them, complexins allow fusion to be triggered upon the arrival of a signal. Using surface force measurements, we have obtained the description of the mechanism of action of SNARE proteins and of the one by which complexins do first facilitate the assembling of SNAREs, then clamp it, and then unclamp it.

As a second example, just before mammalian fertilisation, two cells only are located inside the zona pellucida: the oocyte and the spermatozoon. The latter moves, fluctuates and contacts the oocyte in a transient manner before it adheres and fuses with it. A force measuring technique sensitive to one molecular bond was used to investigate the separation between an oocyte and a spermatozoon. This approach, combined with gene knock-out, has allowed to show how the oocyte protein CD9-tetraspanin produces fusion-competent adhesion sites by spatially organising the receptors at the oocyte membrane, and it has also established that the sperm protein Izumo1 behaves as an adhesion protein.