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Membrane Fusion Proteins as Nanomachines

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Membrane fusion is key to fertilization, virus infection, and neurotransmission. Specific proteins work like nanomachines to stitch together fluid, yet highly ordered lipid bilayers. The energy gained from large exothermic conformational changes of these proteins is utilized to fuse lipid bilayers that do not fuse spontaneously. Structural studies using x-ray crystallography and NMR spectroscopy have yielded detailed information about architecture and inner workings of these molecular machines. The question now is: how is mechanical energy gained from such protein transformations harnessed to transform membrane topology? To answer this question, we have determined that a boomerang-shaped structure of the influenza fusion peptide is critical to generate a high-energy binding intermediate in the target membrane and to return the "boomerang" to its place of release near the viral membrane for completion of the fusion cycle. In presynaptic exocytosis, receptor and acceptor SNAREs are zippered to form a helical bundle that is arrested shortly before the membrane. Ca binding to interlocked synaptotagmin releases the fusion block. Structural NMR and single molecule fluorescence data are combined to arrive at and further refine this picture.