Membrane Fusion: Molecular insights from all-atom and coarse-grained simulations

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How do membrane bilayers fuse? The question and its answer are fundamental to improving drug delivery and to understanding biological activity. With the continuing power of computers it has become possible to ask questions of much larger assemblies of molecules and thus to begin suggesting the molecular behavior that underlies such things as membrane fusion.

We have been performing coarse-grained simulations of membrane fusion (Phys Rev Lett 91:188102) and have suggested that an important stage in fusion is created by splay of the alkane chains in the two lipid bilayers. As the lipids splay, it becomes possible for two alkane chains to meet within the interfacial zone between bilayers and for the process of fusion to proceed to a stalk intermediate and then to complete fusion.

More recent work has been performing all-atom simulations of two bilayers and exploring the potential of mean force as these bilayers approach one another. Results have shown tilting of headgroups and repositioning of membrane lipids as the two bilayers approach one another. This suggests that a repositioning of membrane lipids and water/salt is critical for fusion to initiate.

From these findings it is possible to begin understanding the role of salt and protein in mediating fusion as well as thinking about how modifications to the lipids and the geometry can influence the fusion event.

The research to be presented includes work from both Sandia National Labs and Johns Hopkins and includes contributions to the research from: Mark Stevens, Paul Crozier, Anastasia Gentilcore, Jonathan Sachs, and Jan Hoh.