Minimum free energy transformation paths in membrane fusion

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Abstract

Collective phenomena in membranes are those which involve the cooperative reorganization of many lipid molecules. Among others, membrane fusion and fission reactions are two fundamental processes in biological cells, involved in intracellular trafficking and viral infection. Membrane fusion is a process of merging two separate membrane compartments during exocytosis. It is tightly regulated by proteins, such as SNARE proteins, which involved in neuronal exocytosis. In order for fusion to start, a synaptic vesicle containing neurotransmitters must be in close opposition with a target neuronal membrane. SNARE proteins of the vesicle and target membrane self-organize into a trans-SNARE complex and bring the vesicle and the membrane in close opposition. However the role of the transmembrane domains of the SNARE proteins is less well understood. It has been demonstrated that such domains are not just protein anchors for the self-organizing parts, but play an active role in facilitating formation of fusion intermediate states. Here we will demonstrate how transmembrane domains of SNARE proteins can low the free energy of the first fusion intermediate state, so-called stalk state.

As a method we used coarse-grained[1] molecular dynamics simulations in conjunction with the so-called string method[2]. The string method is the free energy calculation method which provides the minimum free energy path of a transformation. Using lipid density as a collective order parameter[3] to describe membrane states along a transformation path we obtained minimum free energy paths for the first fusion intermediate state (stalk) and investigated how different parameters such as lipid spontaneous curvature, membrane dehydration and tension, presence of fusion peptides can low the free energy barrier and increase stability of the stalk state.

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[1] S. Marrink, H. Risselada, S. Yefimov, D Tieleman, and A. de Vries, J. Phys. Chem. B **111** 7812 (2007).

[2] W. E, W. Ren, and E. Vanden-Eijnden, J. Chem. Phys. **126** 164103 (2007).

[3] Y. Smirnova and M. Müller, J. Chem. Phys. **143** 243155 (2015).