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Diffusion driving the formation of functional nanoscale machines in cell membranes

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A great fraction of functions in cells is taken care of by membrane proteins. Their biological relevance is thereby quite exceptional, yet they do not work alone. Instead, to become functional, membrane proteins require an appropriate pool of lipids around them, and the lipids have an important function as they modulate or even govern the activation of the proteins in question through specific or membrane-mediated interactions. The key process driving the formation of functional nanoscale protein-lipid units (lipid rafts) is diffusion.

While lateral diffusion of lipids in protein-free membranes is quite well understood [1], the situation is more complicated in cases where lipids diffuse under the influence of proteins [2]. More complications arise when crowding with proteins comes into play [3]. Understanding the dynamics under crowding is highly relevant since native cell membranes are usually very crowded, typical protein:lipid molar ratios being around 1:50–1:100 [4]. What is more, membrane-spanning proteins are influenced by the transmembrane distribution of lipids around them, thus diffusion of lipids across membranes (flip-flop/translocation) is also a matter to worry about in order to understand the conditions where membrane proteins are able to fulfill their cellular commitments.

Here we discuss perspectives based on most recent atomistic and coarse-grained molecular simulations on the dynamics of lipids with proteins. We discuss, e.g., how they form functional nanoscale units, how lipids migrate into the specific lipid binding sites in membrane proteins, how lipids and proteins move in unison as collective units with long lifetimes, and how proteins control the translocation of lipids across lipid membranes.

References

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