Drug delivery through cell membranes: What can we learn from Molecular Dynamics simulations

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Membranes constitute an important component of cells. Not only they give support for trans-membrane proteins to anchor in, but act also as natural barriers against free translocation of molecules and nutrients as they prevents them from going in or out of the cell. Such is the case for many ions, charged compounds and large polar molecules, e.g., drugs that in order to be effective need to cross these barriers. Different strategies have been developed during the past decades to transfer molecules of variable sizes and chemical properties across membranes of a cell. These include the use of nanomaterials such as carbon nanotubes and fullerenes as carriers, or enhancement of membranes permeability by electroporation. Regardless of the method used to vectorize small fragments or molecules inside cell compartments, understanding their interaction with biological membranes and their behavior while they penetrate their hydrophobic core is of crucial importance. The direct observation of such events is not possible with conventional techniques. Furthermore, due to the complexity and heterogeneity of cell membranes, it is difficult to describe and characterize their behavior in terms of atomically resolved processes.

Atomistic simulations in general and Molecular Dynamics (MD) simulations in particular, have proven to be effective for providing insights into both the structure and the dynamics of model lipid membranes in general. Here we provide a review of the progress made so far in modeling transport phenomena across such membranes. We show how such "computer experiments" provide significant insights into the transport of a wide variety of components. We discuss in particular, based on our recent investigations how transport of species ranging from small amino acids to large molecules occurs by direct translocation, and how it might be enhanced by anchoring them to nanomaterials or by subjecting the systems to high electric fields.