How a few help all: cooperative crossing of lipid membranes by COSAN anions

David C. Malaspina , Huixia Lu, Francesc Teixidor , Clara Viñas and Jordi Faraudo

Institut de Ciencia de Materials de Barcelona, ICMAB-CSIC, Campus de la UAB, Bellaterra, Spain

jfaraudo@icmab.es

Cobaltabisdicarbollide (COSAN) nano-ions have an unexpectedly rich self-assembly behaviour, which can lead to vesicles and micelles without having a classical surfactant molecular architecture. The reason for that behaviour is that water stabilizes a particular rotameric form of these nano ions (the cisoid rotamer) that has a well-defined hydrophilic polar region and a hydrophobic apolar region, as shown by our electronic structure calculations (DFT) and molecular dynamics simulations (MD) [1].

This peculiar self-assembly behaviour has consequences on the ability of COSAN nanoions to cross biological membranes, a question of conceptual importance but also with practical consequences due to the potential applications of COSAN in boron neutron capture therapy (BNCT). Experimental results show that COSAN nanoíons are able to cross intact artificial phospholipid bilayers in spite of the high Born free energy estimated for these nano ions. Our molecular dynamics simulations [2] show that the permeation of COSAN anions across a lipid bilayer proceeds in a cooperative manner. Single nano-ions can enter the bilayer but permeation is hampered by a free energy barrier of about 8kBT. The interaction between these nano-ions inside a leaflet induces a flip-flop translocation mechanism with the formation of transient, elongated structure inside the membrane. This cooperative flip-flop allows an efficient distribution of COSAN anions in both leaflets of the bilayer. These results suggest the existence of a new mechanism for permeation of nano-ions across lipid membranes, relevant for those that have the appropriate self-assembly character.

Our simulations also show that the flip-flop mechanism depends strongly on the phospholipid composition. This simulation result provides an explanation for the different biodistribution of COSAN ions between different organs observed experimentally that indicate that COSAN anions are able to cross specific biological barriers.

Keywords:
nanoions,molecular dynamics, biomembranes

References:

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