

Oligomerization of viral channel proteins along a bio-inspired pathway.

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Many viruses encode short membrane proteins which are render lipid membranes permeable to ions and even small molecules. The proteins need to form a quaternary structure in order to be functional. For some of these proteins detailed functional and even structural features are available. Whilst a detailed picture of the insertion of the membrane proteins into a bilayer via the translocon machinery is fairly established, formation of the quaternary structures is still in the dark. Nevertheless, in many cases these proteins are important drug targets in antiviral therapy.

When released from the translocon, the proteins are assumed to be in a monomeric stage. In case of polytopic membrane proteins the transmembrane helices have to fold into the tertiary structure during this stage. In the next stage, through lateral diffusion these proteins oligomerize forming functional pores. In a computational approach these stages are explored using a 2D docking approach and molecular dynamics (MD) simulations. The latter technique is used to assess ion selectivity of the proteins and to monitor assembly dynamics for predicting the oligomeric state. Results from proteins 8a of SARS-CoV and Vpu of HIV-1 are compared with experimental data.