Combining experiments and computations to gain structural and functional information: some examples from Red Blood Cell membrane proteins

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Membrane proteins are among the main components of cell membranes. They are involved in major cellular processes, like transport, signal transduction and they participate in cell-cell recognition. Membrane proteins are embedded in a complex lipid environment, which poses problems in their extraction and in the resolution of their 3D structure. As a result, the number of 3D structures remains extremely small despite recent improvements in expression and purification strategies. Alternative approaches are thus required to increase and to improve structural information and to better understand functional properties. Molecular modeling and bioinformatics methods when coupled to experimental data are valuable tools that help gaining structural information.

As an example, I will describe the results of a close and fruitful dialogue between *in silico* methods and experiments that helped in elucidating the transport site of Band III protein, a major anion exchanger (AE1) in the red blood cell (RBC). I will also describe the case of the TSPO protein, a membrane cholesterol transporter in the RBC, focusing on the difficulties in the interpretation of low-resolution electron microscopy data. I will illustrate how molecular dynamics simulations help to interpret conductance measurements for two transporters, the urea transporter and the aquaporin. Finally, I will show how thermodynamics properties can be efficiently calculated from simulations and compared to experiments.