Endocytosis across scales: from molecular structures to a functional process

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Clathrin-mediated endocytosis (CME) is the main mechanism by which eukaryotic cells internalize and recycle most membrane proteins. Mutations affecting endocytosis have been directly linked to cancer as well as to Alzheimer[1] and Stiff-man[2] diseases. The CME is driven by different Adaptor and Modulator Proteins, which solely interact with the inner leaflet of the cell membrane.

By exploiting techniques such as ellipsometry, pressure–area isotherms and Neutron Reflectometry (NR), the aim of this work has been to investigate the binding and resultant structures formed by the adaptor protein CALM and by the modulator FCHo2 on association with lipid monolayers enriched in either phosphatidyl-inositol-4,5-diphosphate (PIP2), or 1-palmitoyl-2-oleoyl-sn-glycero-3-phospho-L-serine (POPS). In particular, Neutron Reflectometry allowed us to determine the position and orientation of both CALM and truncated versions of FCHo2 with respect to the membrane. The resultant position of the CALM atomic structure[3] on the membrane made biological sense (Figure 1). Regarding FCHo2, a 4-layer-model, which fit well to the NR data, allowed the general orientation of the protein as well as the relative positions of the protein's individual domains to be determined.

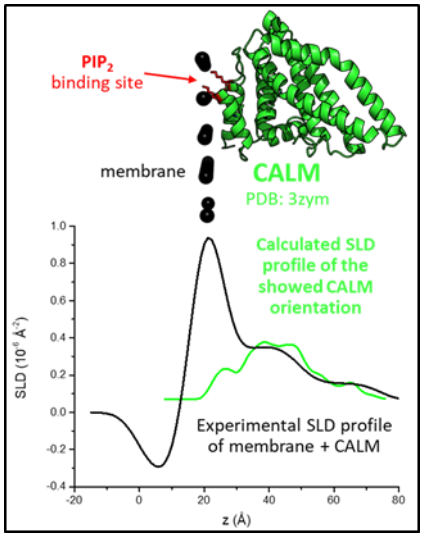

Figure 1. Best orientation of CALM obtained from Neutron Reflectometry. The experimental SLD profile obtained from the fitting and the calculated SLD profile of CALM are shown.

References

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