Why do proteins remain well dispersed in membranes?

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Cell membranes contain many inclusions (such as protein membranes) which deform the underlying lipid bilayer, by thinning or thickening it to match the thickness of the transmembrane domain of the protein. This deformation engenders between the included objects an interaction, which simple elastic theories predict to be attractive. Combined with the high concentration of inclusions, such an attraction should lead to their aggregation. However, a large majority of membrane proteins remain well dispersed.

To solve this long-standing puzzle, we use a complete elastic theory for the deformation [1] in order to determine the interaction potential between gramicidin channels in membranes by fitting small-angle X-ray

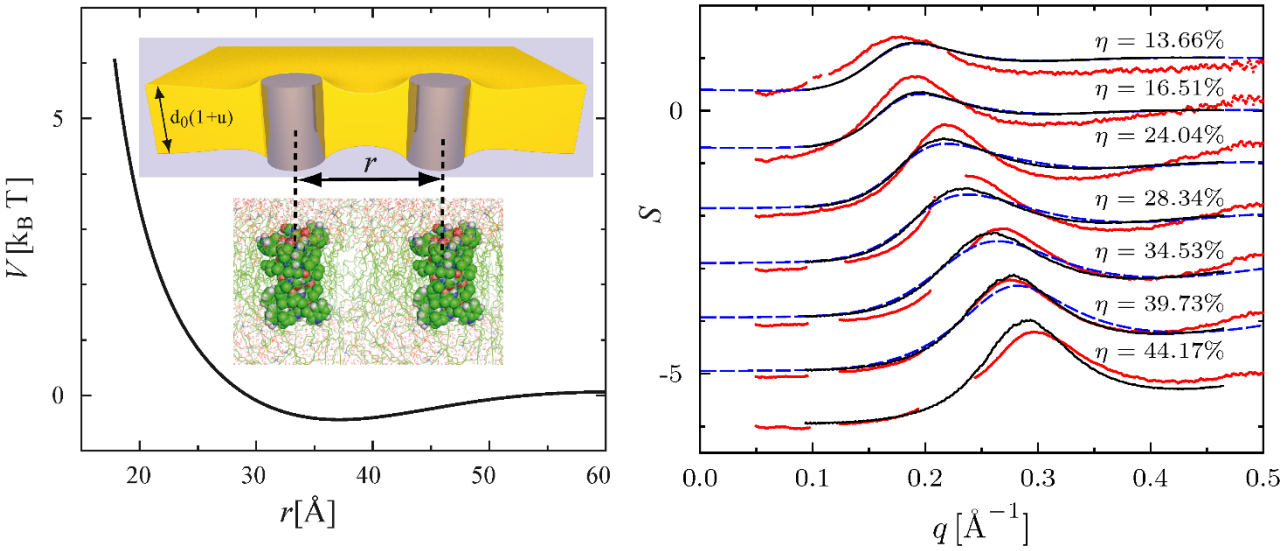

Figure 1 Left: Interaction potential $V(r)$ between two gramicidin channels in a DLPC membrane. The curve corresponds to our best fit of the experimental data. Inset: elastic model of the membrane, with the channels described as rigid cylinders; a more realistic representation is given below. Right: Structure factors $S(q)$ for the same system at different surface fractions η of inclusions (red solid lines) and best fits using the interaction potential on the left. The fits are obtained via Monte Carlo simulations (solid black lines) or using the HNC approximation (dashed blue lines).

scattering data recorded at varying channel concentration [2]. We show [3] that the essential ingredient is the preferred slope at contact, which induces a short-range repulsion. In phospholipid (DLPC) bilayers, the membrane thickness decreases with an angle of about 30° away from contact.

We confirm our results by predicting (with no adjustable parameters) numerical simulations for the interaction of gramicidin channels in other types of membranes as well as experimental conductivity data for the lifetime of the channels in DOPC, bringing together three completely different experimental techniques within one theoretical framework.

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