

## What is the Surface Tension of a Lipid Bilayer Membrane?

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In a recent paper in this journal, Chiu et al. (1995) presented a molecular dynamics study of a planar lipid bilayer membrane in water with the explicit incorporation of a surface tension. Parallel to the membrane plane, a negative pressure of  $-100$  atmospheres was applied, derived from the measured surface tension of a monolayer at an air/water interface. The same approach was put forward by Feller et al. (1995).

The question as to what is the surface tension of a bilayer membrane goes far back in the literature. To my knowledge, it was first raised by de Gennes and Papoular in 1969 and taken up again in a paper by Brochard et al. (1976). The answer was that bilayer membranes of vesicles or cells (without concentration gradients across the membrane) have zero surface tension, because the free energy should be minimal with respect to the surface area of the membrane. This explained the great fluctuations in the shape of red cell membranes. Independently, the same argument was put forward by Tanford (1979), for membranes without high curvature, and by Israelachvili et al. (1977). The latter authors used this argument to develop a theory for the self-assembly of lipids in micelles or bilayers, either planar or vesicular, which proved to be very useful. Likewise, a theory for the exchange of lipid molecules between a bilayer and a monolayer at the air/water interface was worked out based on the assumption that the surface tension of a bilayer is zero, whereas that of a monolayer is finite (Jähnig, 1984). The predictions of this theory were in good agreement with experimental results on the equilibrium surface pressure of a monolayer in exchange with vesicle bilayers in the sub-phase (Schindler, 1980). Hence, although the surface tension of a bilayer membrane is not accessible directly, indirect measurements support the notion that it is zero.

White (1980) pointed out that the surface area is not necessarily the only variable that may change when a membrane tries to minimize its free energy. The volume of the membrane may also change, so that the free energy must not be minimal with respect to the area, i.e., the surface tension must not vanish. This implies a coupling between the area and the volume, which is weak, however, because a lipid molecule may expand laterally and shrink vertically while

keeping the volume constant. In essence, this happens at the lipid phase transition, the area changing by 20–30%, the volume only by 2–4%. Thus, for many purposes volume changes may be neglected, leaving the area as the relevant variable. Other variables that may permit the membrane to find an energy minimum at finite surface tension are the particle numbers of lipid molecules and associated water molecules. The first case pertains to black lipid membranes, which are in contact with a reservoir of lipid molecules at their boundary, the second to membranes that are not saturated with water. In these cases, a finite albeit small surface tension may exist.

The vanishing of the surface tension of a bilayer membrane may be understood by considering a membrane sheet in stacks of membranes at excess water or the membrane of a vesicle that is large enough that curvature effects can be neglected. If the surface tension for a given packing density were finite, because of attractive interactions between the hydrocarbon chains (arising mainly from their hydrophobic effect) the energy of the membrane could be lowered by reducing its area. Such a shrinkage is possible because the membrane is dispersed in water and free to compress or expand. Hence, the membrane will shrink, but not infinitely, because of repulsive interactions between the headgroups (steric repulsion between the hydrated headgroups and/or electrostatic repulsion between the charges on the headgroups). Actually, the membrane will adopt a state in which the attractive interactions between the hydrocarbon chains and the repulsive interactions between the headgroups balance each other. This is the case when the free energy is minimal with respect to the area of the membrane, i.e., when the derivative of the free energy with respect to the area vanishes, the surface tension is zero and the bilayer membrane has adopted a state with optimal packing of the lipid molecules.

The situation is different for a monolayer membrane spread at an air/water interface. Even if the packing of the lipid molecules is optimal so that the surface tension at the lipid/water interface vanishes, a finite surface tension arises from the lipid/air interface. Because the hydrocarbon chains are in contact with air, the surface tension is that of a hydrocarbon/air interface, which is  $\sim 30$  dyn/cm (Nagle, 1980; Jähnig, 1984). This value is in good agreement with the experimental result for the surface tension of a fluid monolayer at optimal packing of the lipids (Schindler, 1980).

The first molecular dynamics studies of bilayer membranes were performed by van der Ploeg and Berendsen (1983), who had already mentioned that the surface tension should be zero. Actually, in their studies they obtained a finite surface tension because they simulated a bilayer mem-

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brane in vacuum. In this case, the steric repulsions between the headgroups are too weak because of the lack of hydration and the attractive interactions between the hydrocarbon chains are too weak because of the lack of the hydrophobic effect. If the two effects do not balance each other, a finite surface tension may arise. In more recent studies of Egberts et al. (1994) and Tu et al. (1995), bilayer membranes in water were simulated at zero surface tension (by imposing an isotropic pressure of 1 atm). Good agreement with experimental data was obtained, which demonstrates that the inclusion of a finite surface tension as in the work of Chiu et al. (1995) and Feller et al. (1995) is not required. Direct comparison of membrane simulations with and without surface tension performed by Tieleman and Berendsen (1996) revealed no significant differences.

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