New and Notable

How Thin Can Glass Be? New Ideas, New Approaches

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In this issue, Smith et al. (2003) describe monomolecular films of the phospholipid 1-palmitoyl-2-oleoyl phosphatidylcholine (POPC) that are metastable at very high surface pressures for protracted time periods. This observation may have important consequences for our understanding of the molecular basis for alveolar stability in lungs. Were the surface of alveoli to be coated with an extracellular fluid of ordinary composition, the surface forces would cause alveolar collapse. This does not occur because the very thin extracellular aqueous lining of the alveoli contains a unique material called pulmonary surfactant (PS). The surfactant material forms a monolayer and in some cases an associated multilayer at the air-water interface that lowers surface tension in the alveolar spaces to exceptionally low values (Schürch et al., 1976, 1978).

In mammals, PS is comprised of ~90% lipids by weight and 10% of four surfactant-associated proteins. Of the lipids, 85–90% are phospholipids, with dipalmitoyl phosphatidylcholine (DPPC) being, by far, the major component, constituting ~40% of total lipids. POPC is the second most common phospholipid species. It has long been understood that the monolayer at the air-water interface is comprised of lipids, but the question is, which one(s)?

Submitted August 7, 2003, and accepted for publication August 7, 2003.

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0006-3495/03/11/1/02 $2.00

When monolayers of the lipid constituents of PS are allowed to come to equilibrium with that constituent in a bulk phase, either a crystal at the surface, or the material dispersed in the subphase, the surface pressure achieved in the film is called the equilibrium surface pressure, or, sometimes, the equilibrium spreading pressure. When monomolecular films of PS or its constituents are compressed in surface balances at slow or "near equilibrium" up to moderate rates, they collapse into multilayers or vesicles at or very near the equilibrium surface pressure, in a range of 45–50 mN/m.

These pressures are lower than those that would be required to match the surface tension in the functional alveoli, especially at low lung volume (surface pressure is taken as force per unit of length exerted by the film or as the difference in surface tensions of a clean and a "covered" surface). During normal lung dynamics, the surface tensions vary over the range of <5–30 mN/m. Thus, for most of the lung's functional volume, surface pressures substantially above the equilibrium pressure would be needed.

During lung deflation, the rate of film compression can be anticipated to be moderately high. Rapid compression of some types of phospholipid films allows them to achieve the high surface pressures necessary in films in the lung. A fair body of work has shown that films highly enriched in DPPC can be compressed to high surface pressures near 70 mN/m, and that they can remain stable at the high pressure for fairly long periods. Many alveoli in the functioning lung can remain at low volume for extended periods. Should the surface pressure fall in films in these low-volume alveoli, they would become subject to high surface tension and would collapse. Monolayer films of intrinsically disordered phosphatidylcholines such as POPC at 37°C had been found to rapidly relapse to their equilibrium surface pressures even when they could be rapidly compressed to surface pressures somewhat above those values. The overall findings of these studies led to the view that only films composed of phosphatidylcholines that were at a temperature below the intrinsic temperature at which they were transformed into a fluid matrix could maintain the long-lived metastable state required for lung stability, that is, the lipid molecules must be capable of being highly ordered before the long-lived, high pressure metastable state could be entered. The characteristic temperature involved corresponds approximately to the gel-to-liquid crystalline transition temperature (it would be expected to be a few degrees higher because of the high pressures involved). The compression behavior of PS monolayers on Langmuir-Wilhelmy balances showed a plateau near the equilibrium spreading pressure, followed by a rise in surface pressure to very high values near 70 mN/m. This behavior had been interpreted as arising from "squeeze-out" of non-DPPC molecules to leave a film highly enriched in DPPC.

The work presented by Smith and colleagues provides the physical basis for another means to interpret the behavior of high pressure surfactant films. The properties of phospholipid films referred to above had been described using Langmuir-type balances. These all involve barriers around which or over which there may be material loss, including selective loss of more fluid components, especially at very high surface pressures. Smith et al. have employed a captive bubble surfactometer wherein there can be no loss of monolayer components except through overcompression into a collapsed state. Surface tension and, from it, surface pressure, are calculated from the bubble shape. They have found that, above a threshold compression rate, it is possible to compress films of pure POPC to surface pressures up to 70 mN/m. At the temperatures used in the study, 23–70°C, POPC is well above its characteristic ordered-to-fluid transition

temperature (it is $\sim -6^{\circ}$C in bilayers). These compressed POPC films were stable for extended periods at very high surface pressures. Stability was higher as the final surface pressure increased above the equilibrium value, a phenomenon seen in DPPC films before.

The possibility that POPC films were induced to undergo a fluid-to-solid first- or second-order phase transition as a result of being compressed rapidly was discounted by a series of experiments studying the stability of films over a range of temperatures. The POPC films did not undergo an observable thermal transition and are presumed to contain molecules with high intrinsic disorder over the temperature range studied. The explanation for how the films achieve the metastable high surface-pressure state is taken by Smith and colleagues to be that these films undergo a transformation similar to the formation of a glass-like state where the molecules are ''jammed'' in their metastable organization. The authors' explanation for the ''trapping'' or ''jamming'' is based on a model that assumes that the lipids are hard bodies like hockey pucks. But since the lipid chains are intrinsically disordered at the temperatures of the studies, there might be additional ''stability'' given to the glass-like state by entanglement of the disordered claims. This might add some ''flexibility'' to the metastable state, something that may be important to the lung in a moderately dynamic state. Such flexibility or malleability was suggested earlier (Peréz-Gil and Keough, 1998) when the possibility was described that the monolayer of PS at high surface pressure might form an ''alloy-like'' state having both strength and flexibility.

In the previous molecular interpretations of lung stability, it has been assumed that some form of enrichment of the surface film in DPPC over that in the whole PS was required. This work suggests an alternative possibility, that with sufficiently high rates of compression, such enrichment is not necessary. Now we need to ask ourselves about how well do we understand individual alveolar surface compression rates during exhalation. Also, one still needs to consider the observation that the lung deflation curve shows a temperature dependence similar to the order-disorder transition in DPPC (Clements, 1977).

So, given the right circumstances, perhaps glasses can be mighty thin—a molecule thick. They may be important in lung stability, but such structures may have potential impact and use in other conditions where ultrathin devices such as matrix embedded biosensors may be designed.

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