Lipid-Bilayer Assemblies on Polymer-Bearing Surfaces: The Nature of the Slip Plane in Asymmetric Boundary Lubrication

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ABSTRACT: Phospholipid—macromolecule complexes have been proposed to form highly efficient, lubricating boundary layers at artificial soft surfaces or at biological surfaces such as articular cartilage, where the friction reduction is attributed to the hydration lubrication mechanism acting at the exposed, hydrated head groups of the lipids. Here we measure, using a surface force balance, the normal and frictional interactions between model mica substrates across several different configurations of phosphatidylcholine (PC) lipid aggregates and adsorbed polymer (PEO) layers, to provide insight into the nature of such lubricating boundary layers in both symmetric and especially asymmetric configurations. Our results reveal that, irrespective of the configuration, the slip plane between the sliding surfaces reverts wherever possible to a bilayer—bilayer interface where hydration lubrication reduces the friction strongly. Where such an interface is not available, the sliding friction remains high. These findings may account for the low friction observed between both biological and synthetic hydrogel surfaces which may be asymmetrically coated with lipid-based boundary layers and fully support the hydration lubrication mechanism attributed to act at such boundary layers.

INTRODUCTION

Over the past decade, phosphatidylcholine (PC) lipids and their assemblies, such as bilayers and vesicles, have been identified as the active components of boundary layers that are exceptionally efficient in reducing friction between sliding surfaces in aqueous surrounding.1−5 This arises via the hydration lubrication mechanism:6,7 the hydration layers coating the phosphocholine groups exposed by such boundary layers are highly tenacious and so resist being squeezed out, yet at the same time they are rapidly relaxing and thus result in only a very weak frictional dissipation on sliding and shear past similar boundary layers. PCs are the most ubiquitous lipids in living systems, and PC-based boundary layers have been suggested as responsible for biolubrication of different tissues, particularly of articular cartilage in the major joints, where efficient lubrication is crucial for joint homeostasis.8−15

Early molecular-level studies of lubrication by lipid assemblies, generally in the form of lipid vesicles (liposomes), were usually performed on model smooth, rigid substrates, often by using a surface-forces balance, SFM (in which case the substrates were single crystal mica surfaces).16−17 Most biological surfaces, however (including cartilage), are rather soft and rough on a molecular scale. Likewise, materials of interest for biomedical devices and tissue engineering are often soft or gel-like18−20 and in this sense resemble biological tissues (indeed, articular cartilage itself may be considered a complex biological hydrogel). Thus, there is interest in elucidating at the molecular level the lubricating behavior of lipids and their assemblies on soft surfaces, both to better understand biological lubrication and from the point of view of biomedical materials where lubrication plays an important role, as in a range of applications.21−30

A number of nanotribological studies have examined the lubricating behavior of lipid assemblies on polymer-bearing surfaces, where the adsorbed, swollen polymer layer or gel layer is a good proxy for a soft surface.5,13,32 Gaisinskaya-Kipnis et al.31 studied the lubricating behavior of liposomes on a chitosan−alginate bilayer, while Seror et al.13 and Zhu et al.33 examined the interaction of surfaces bearing hyaluronan (hyaluronic acid, HA) complexed with liposomes. On the basis of these, Seror et al.13 proposed that the lubricating boundary layer on healthy articular cartilage comprises at its outer surface an HA/lipid complex. Such synergy between lipids and HA was recently demonstrated for lubrication at a tendon/sheath interface,34 while very recently, highly lubricious synthetic hydrogels have been created that mimic this idea of lipid-based boundary layers.35 The use of adsorbed polyelectrolytes (such as chitosan/alginate13 or HA33) as soft substrates for lipids was recently extended32 to the case of an adsorbed neutral polymer, poly(ethylene oxide) (PEO), which...
is ubiquitous in biomedical applications, such as in tissue engineering scaffolds,16–38 or as a stabilizer for drug-delivery vehicles.39–42

In most nanotribological studies of lipid-based lubrication to date the configurations used have been symmetric,1,3,17,32—that is, lipid assemblies or complexes, whether in the lamellar or vesicular phase, on one surface interacted with and slid past an identical lipid assembly on the other surface. In such a case the slip plane between the surfaces was always at the midplane between the lipid layers. Such symmetry, however, may not be representative of interactions between biological tissues, whose surfaces are not only soft and rough—and generally polymeric—but also structurally and chemically heterogeneous, so that opposing surfaces may each bear a different boundary layer. Thus, asymmetric boundary layers are likely to be the rule between interacting biological surfaces and thus differ from the symmetric vesicle-vesicle or bilayer-bilayer interactions examined to date. With this in mind, the present investigation extends our earlier SFB studies of lipids examined to date. With this in mind, the present

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described in more detail elsewhere,44 while a schematic of configurations used have been symmetric,1,3,17,32,42 or as a stabilizer for drug-delivery

Preparation of Liposome-Coated and Bilayer-Coated Polymer-Bearing Surfaces. Polymer-bearing mica surfaces were prepared as follows. One mica surface mounted on a semicylindrical glass lens (ready for mounting into the SFB) was incubated for 14–16 h in 0.15 mg/mL PEO in 0.1 M KNO3 salt solution; then the excess polymer was first washed by rinsing in a large excess of 0.1 M KNO3 solution (~10 times) and then with water (~10 times). Next, the surface was incubated under a 0.5 mM DSPC-SUV dispersion for 12 h, following which the surfaces were rinsed multiple times by replacing the liposome solution by water. For the SFB bilayer experiments, surfaces were coated with PEO/DSPC as described above. After the adsorption of DSPC on PEO the excess DSPC liposomes were washed by rinsing in a large excess of water (~10 times). The DSPC liposomes on PEO were then immersed in water and heated in an oven under water for 2 h at 70 °C. This temperature is significantly higher than the main transition temperature of DSPC (54 °C), since supported bilayers are known to have a higher transition temperature than liposomes,43 and is sufficient to induce the fusion of liposomes on PEO and form a continuous bilayer as shown by microscopy.

Surface Force Balance (SFB). The SFB technique was used to measure normal Fz(D) and shear forces Fx(D) between polymer-modified mica surfaces in aqueous liquids. The detailed experimental procedure is described in more detail elsewhere,46,48 while a schematic with the main elements is shown in the inset of Figure 3B. Briefly, two freshly cleaned, atomically smooth mica sheets are back-silvered and glued onto optically polished silica lenses that are subsequently mounted in a crossed-cylindrical configuration into the SFB. White light multiple beam interferometry is employed to determine the absolute surface separation D and mean curvature radius R of the mica surfaces. The bottom surface is mounted on a pair of horizontal leaf springs which measure the normal surface forces (spring Kz, of constant 150 N/m), and the top surface is mounted onto a four-sector piezoelectric ceramic tube, which is suspended by a pair of vertical leaf springs (spring Kx, of constant 300 N/m). Lateral motion ∆x is applied to the top surface by applying equal but opposite voltages to the opposing outer sectors of the piezoelectric tube, with lateral velocity v in the range 10–600 nm/s. The normal and shear forces, Fz and Fx, respectively, are measured by detecting the deflection of the horizontal (Kz) and vertical (Kx) springs via the interference fringes and an air–gap capacitor, respectively. Prior to every experiment, the glassware was cleaned in piranha solution (70% H2SO4, 30% H2O2) and sonicated in pure water and ethanol for 10 min. Stainless steel tools were passivated in 30% aqueous solution of HNO3 at 80 °C for 30 min followed by sonication in pure water and ethanol for 10 min. All preparations were performed in a laminar hood to avoid particulate contamination. Metal tools were cleaned by using ethanol dispersed through a 0.45 μm pore-sized poly(ether sulfone) membrane filter from a pressure rinser.

The mean pressure, P, across the contact area A between the compressed surfaces can be directly evaluated from the dimensions of the flattened area, contact radius a, as P = Fz/A = Fx/2a. The flattening is mostly due to compression of the glue supporting the mica sheet, and a is measured from the flattening of the interference fringes. For smaller contact radii which cannot readily be measured from the fringe shape, Hertzian contact mechanics45 can be used for pressure evaluation, where a = (FR/K)1/3 and K is the effective elastic modulus (determined separately) of the glue/mica layers.

Atomic Force Microscopy (AFM). Surface topography was determined by using an atomic force microscope (MFP-3D SA, Oxford Instruments Asylum Research, Inc., Santa Barbara, CA). The surfaces were scanned in tapping mode under conductivity water by using a silicon nitride V-shaped cantilever having a nominal spring constant of 0.35 N/m with a pyramidal silicon tip with a nominal radius of 2 nm (SNL, Bruker).

**RESULTS AND DISCUSSION**

Dynamic Light Scattering and AFM Imaging. Figure 1 shows the size distribution of the PEO and DSPC-SUVs as
determined by DLS. The peak dimension of the SUVs in water was 90 ± 10 nm, while the hydrodynamic diameter of the PEO molecules in 0.1 M KNO₃ was 23 nm. It is of interest that DLS from a mixture of the liposomes and the PEO in water revealed a single peak similar in size to that of the liposomes alone; this suggests that the PEO adsorbs quite strongly onto the lipid vesicles, forming a thin adsorbed layer. This is in line with the results of our earlier study on similar DSPC-SUV/PEO mixtures in 0.1 M KNO₃. A detailed consideration of the adsorbance onto the vesicles of the available PEO in the liposome/polymer mixture indicates a thin (<5 nm) adsorbed PEO layer on the vesicle surfaces, consistent with the DLS peak diameter (Figure 1) which shows little change as a result of the PEO adsorbance.

AFM tapping mode images of the DSPC-SUVs adsorbed on PEO-coated mica at room temperature, both following overnight adsorption of the liposomes and following heating to 70 °C, are shown in Figure 2. Figure 2A shows the AFM image of the liposomes on PEO. The measured height of 10 ± 1 nm and lateral dimension of ~100 nm correspond to adsorbed, flattened vesicles, though the height is significantly lower than the DLS-measured dimension. This is believed to be partly due to a somewhat flattened configuration arising from the adsorption and probably more as an artifact from the tapping mode imaging, where the soft nature of the vesicles on the adsorbed PEO layer likely results in compression of the liposomes during the imaging. This is in line with similar indications of an earlier AFM tapping mode study of lipid vesicles adsorbed on a mica surface. We attribute the DSPC-SUV adsorption on the weakly polar PEO monomers to the large dipole of the zwitterionic phosphocholine groups at the outer PC liposomes surface. The partial coverage of the vesicles on the surface (Figure 2A) may be due to removal of some of them by the AFM tip during the tapping mode scanning, since cryo-SEM images of similar vesicles on PEO indicate a much denser coverage. Following heating at 70 °C for 2 h, the AFM micrograph (Figure 2B) shows clearly that the DSPC liposomes adsorbed on the PEO-coated mica transformed into a continuous bilayer phase, in line with earlier studies of adsorbed DSPC-SUVs following heating. It is of interest that the small defects shown in Figure 2B have a depth...
corresponding to one leaflet height (ca. 2 nm); this may arise from the removal of trace amounts of the top leaflet on passage through the air–water interface necessary for the AFM measurements (such passage is not needed for the SFB measurements).

**Surface Interactions between Lipid- and Polymer-Bearing Substrates.** Normal and shear force profiles from the surface force balance (SFB) experiments are generally based on between two and three independent experiments (different pairs of mica sheets) for each configuration and different contact points between each pair of mica sheets.

**Forces between Bare and Polymer-Bearing Surfaces across a Liposome Layer.** Following the approach to contact between bare mica surfaces across water, to establish the absence of contamination and determine the absolute zero of surface separation (these control profiles are shown as cross data symbols in Figures 3 and 5), the PEO layer was adsorbed on one surface, followed by incubation in DSPC-SUVs dispersion for 12 h as described earlier (see the Experimental Section). Figures 3A,C summarize the normal force profile \( F_n(D)/R \) vs surface separation \( D \) between a DSPC-SUV/PEO-coated mica surfaces against a rigid (bare) mica surface and against a soft, polymer-coated mica surface, respectively, as indicated in the cartoons. The applied loads \( F_n(D) \) are normalized by the mean radius of curvature \( R \) of the interacting surfaces as \( F_n(D)/R \), which in the Derjaguin approximation,\(^{35,69} \) valid here, gives the interaction energy/unit area for flat parallel surfaces obeying the same force–distance law and is used to normalize the data with respect to different surface curvatures. Long-range repulsion was measured, likely of steric origin due to the vesicle layers adsorbed on the PEO-coated mica, commencing at \( D \approx 130 \pm 30 \) nm in both cases (Figures 3A,C). With progressive compression, a sharp increase in repulsion was measured, with an effective hard wall (i.e., limiting thickness at high compressions) of 15 ± 1 nm in the case of DSPC-SUV/PEO-coated mica surfaces against bare mica and 19 ± 2 nm for DSPC-SUVs/PEO-coated mica surfaces against a PEO layer. Shear forces \( F_s \) were measured simultaneously with the normal load \( F_n \) in the different configurations by recording directly the \( F_s \) vs time traces as provided by the SFB from the bending of the shear springs \( K_s \) under the lateral motion \( \Delta x_s \) (inset to Figure 3B). Typical traces are shown in Figure 4. The respective \( F_s \) vs \( F_n \) values between DSPC-SUVs/PEO-coated mica surfaces and bare mica or PEO-coated mica under pure water are summarized in Figures 3B and 3D, respectively. The measured friction coefficients \( \mu = F_s/F_n \) were low for both configurations, ranging from \( \mu \approx 5 \times 10^{-5} \) to \( \mu \approx 8 \times 10^{-4} \) at maximal contact stresses of 70–75 atm, comparable with the highest physiological pressures\(^{47,48} \); the variance in \( \mu \) may arise from differing local surface structure of the vesicle/PEO complex at different contact points between the surfaces.

**Forces between Rigid and Soft Surfaces across Lipid Bilayers.** Forces were measured also between DSPC bilayers adsorbed to the PEO-coated mica substrates, formed by heating the DSPC-SUVs as described earlier, and are shown in Figure 5. Figures 5A, 5C, and 5E show the normal force profiles for the configurations when a bilayer on PEO-coated mica, lower surface, interacts with bare mica, a PEO-coated mica, or a similar lipid bilayer on PEO-coated mica, respectively, as shown in the respective inset cartoons. The long-ranged repulsions in the three configurations (Figures 5A, 5C, and 5E) commenced at surface separations \( D \) in the range ca. 60, 48, and 90 nm, respectively, significantly smaller than the \( D \approx 130 \pm 30 \) nm range of repulsion onset with adsorbed liposomes (Figures 3A,C). On progressive compression, a sharp increase in repulsion was observed in all three cases, with effective “hard wall” separations (i.e., limiting thickness at high compressions) of 10 ± 1, 15 ± 1, and 19 ± 1 nm for the configurations shown in Figures 5A, 5C, and 5E, respectively.

Shear force \( F_s \) vs normal force \( F_n \) profiles for the three configurations of Figures 5A, 5C, and 5E, measured from shear force traces as in Figure 4, are shown in Figures 5B, 5D, and 5F respectively, where \( \mu \) values shown correspond to \( F_s/F_n \) at the adjacent extremal data points. The configurations where a single bilayer is compressed against either a bare or a PEO-coated mica substrate (Figures 5B,D), the shear forces, while somewhat scattered, were characterized by much higher friction than was the case for the sheared liposome layers (Figures 3B,D). Thus, for the PEO/DSPC bilayer sliding either against bare mica (Figure 5B) or against PEO-coated mica (Figure 5D), the friction coefficient was in the range \( \mu \approx 0.06–0.4 \) (compared with \( \mu \approx 5 \times 10^{-5} \) for the sheared DSPC vesicles). Further increase in normal load for these configurations resulted in rigid coupling between the surfaces, implying the friction was higher than the highest shear forces that could be applied in the SFB, so that no sliding between the surfaces occurred. In contrast, for the symmetric case of two PEO-coated mica surfaces each bearing a DSPC bilayer sliding past each other (configuration inset to Figure 5E), the friction was very much lower, as shown in Figure 5F,
with \( \mu \approx 2 \times 10^{-3} - 8 \times 10^{-3} \) at a maximal pressure of 50 atm. The significance of these results is considered in the following section.

The present study extends our earlier investigation of the lubrication properties between layers of gel-phase liposomes on surface-adsorbed neutral polymers, interacting in symmetric configurations,\(^{32}\) to asymmetric configurations as well as to the case of these lipids, in an extended lamellar phase (bilayers) interacting in both symmetric and asymmetric configurations.\(^{3,4}\) Our main findings with these different configurations provide important insight into the nature of the slip plane between such lipid assemblies and thereby support for a recent model of boundary lubricating layers on healthy articular cartilage.\(^{12,13}\)

We first consider briefly the normal interactions between the PEO/lipid bearing surfaces in the five different configurations shown in Figures 3 and 5, for which we label I–V, corresponding to the schematic configurations inset in Figures 3A, 3C, 5A, 5C, and 5E, respectively. We may attempt to attribute the onset of interactions in these different configurations as follows. We recall that the onset of normal interactions between mica surfaces bearing adsorbed layers of PEO (of molecular weight 110K) is ca. 70 nm,\(^{32,44}\) so that the thickness of each uncompressed layer is \( L_{\text{PEO}} \approx 35 \text{ nm} \). The DSPC-SUVs have a peak diameter \( L_{\text{liposome}} \approx 90 \text{ nm} \) (from the DLS data of Figure 1). Thus, a liposome layer having this full thickness (\(~90 \text{ nm}\)) adsorbed on the PEO would have a mean thickness \( L_{\text{PEO}} + L_{\text{liposome}} \approx 125 \text{ nm} \). Likewise, when the PEO/liposome layer interacts with an additional adsorbed PEO layer (Figure 3C), the onset of repulsion would be at surface separation \( 2 L_{\text{PEO}} + L_{\text{liposome}} \approx 160 \text{ nm} \). These values are consistent with the onset of repulsion observed in Figure 3A (configuration I) and Figure 3C (configuration II). In practice, however, and as indicated in Figure 2, the thickness of the PEO-attached vesicle layer is likely significantly less than \( L_{\text{liposome}} \). We believe rather that an overlayer of loosely adsorbed liposomes contributes to the larger onset distances, as has been observed in several earlier studies,\(^{3,4}\) and that the effective combined thickness of the PEO-attached layer together with this loosely attached overlayer is ca. \( L_{\text{liposome}} \). We believe that an overlayer of loosely adsorbed liposomes contributes to the larger onset distances, as has been observed in several earlier studies,\(^{3,4}\) and that the effective combined thickness of the PEO-attached layer together with this loosely attached overlayer is ca. \( L_{\text{liposome}} \).

Similarly, the onset of monotonically increasing repulsive interactions with a single bilayer (thickness \( L_{\text{bilayer}} \approx 5 \text{ nm} \)) and either one or two adsorbed PEO layers is expected around \( L_{\text{PEO}} + L_{\text{bilayer}} \approx 40 \text{ nm} \) or \( 2 L_{\text{PEO}} + L_{\text{bilayer}} \approx 75 \text{ nm} \), consistent with the profiles in Figure 5A (configuration III) and Figure 5C (configuration IV), respectively. The repulsion onset in Figure 5E (configuration V) is likewise consistent with the expected \( 2(L_{\text{PEO}} + L_{\text{bilayer}}) \approx 80 \text{ nm} \). While there is some uncertainty in the point where the scatter in the data begins to

**Figure 4.** Typical shear traces of the frictional force \( F_s(t) \) between two mica surfaces bearing liposomes and PEO in different configurations. (A) DSPC-SUVs adsorbed on PEO-coated mica against PEO-coated mica (corresponding to Figures 3C and 3D). (B) PEO/DSPC bilayer against PEO/DSPC bilayer (corresponding to Figures 5E and 5F). (C) PEO/DSPC bilayer against PEO (corresponding to Figures 5C and 5D). In all cases the top trace shows the back-and-forth lateral motion applied to the top mica surface, while the lower traces are the corresponding shear forces transmitted to the lower surface. The load \( F_n \) and measured shear forces \( F_s \), as well as the mean contact pressures and \( D \) values, are given for each trace.
increase monotonically (i.e., the separation at onset-of-repulsion), the high-compression (or “hard wall”) limits for the various configurations are much better defined. For the adsorbed PEO, the DSPC-SUVs, and the DSPC bilayers, these are respectively $L_{PEO\text{(HW)}} = 4.5 \pm 1$ nm and $L_{liposome\text{(HW)}} = 2L_{bayer} = 10 \pm 1$ nm (since the limiting thickness of a compressed liposome is that of two bilayers). Thus, the “hard-wall” separations for the configurations I–V of Figures 3A,C and Figure 5A,C,E, by inspection of the respective schematic cartoons, are expected to be respectively $L_{PEO\text{(HW)}} + L_{liposome\text{(HW)}} = 14.5$ nm; $2L_{PEO\text{(HW)}} + L_{liposome\text{(HW)}} = 19$ nm; $L_{PEO\text{(HW)}} + L_{bayer} = 9.5$ nm; $2L_{PEO\text{(HW)}} + L_{bayer} = 14$ nm; and $2(L_{PEO\text{(HW)}} + L_{liposome}) = 19$ nm. These values are indeed very close to the measured values, as reported in the Results section and summarized in Table 1, and thus fully consistent with the different configurations shown.

The reduction in friction afforded by the different configurations is summarized in Table 1.

The values of $\mu_i$ in Table 1 may be readily understood in terms of the hydration lubrication paradigm. Low values of the friction in our configurations are expected whenever highly hydrated, phosphocholine-exposing lipid layers slide past each other via the hydration lubrication mechanism (where fluid but tenaciously attached hydration layers mediate the sliding); that is, when the slip plane is between the sliding surfaces is between bilayers. At other interfaces, friction is expected to be higher. An example is illustrated in Figure 6, which shows the configuration of Figure 3A (configuration I).

| configuration | system | friction coefficient ($\mu_i$) | $P_{max}$ (atm) | "hard wall" separation (nm) |
|---------------|--------|-------------------------------|-----------------|-----------------------------|
| I             | PE0/DSPC vesicles vs bare mica | 0.00005–0.00006 | ~70 | 15 ± 1 |
| II            | PE0/DSPC vesicles vs PEO | 0.0016–0.00084 | ~75 | 19 ± 2 |
| III           | PE0/DSPC bilayer vs bare mica | 0.06–0.4 | ~17 | 10 ± 1 |
| IV            | PE0/DSPC bilayer vs PEO | 0.06–0.34 | ~15 | 15 ± 1 |
| V             | PE0/DSPC bilayer vs PEO/DSPC bilayer | 0.003–0.008 | ~50 | 19 ± 1 |

There are four possible slip planes, as indicated in Figure 6, where interfacial slip may occur. At interface 1, between a PC bilayer and the mica surface, the interaction is between the zwitterionic phosphocholine groups and the negatively charged mica surface, which we know is attractive as PC vesicles adsorb readily to bare mica in aqueous media. This is confirmed by direct measurements showing that sliding of two mica surfaces across a single lipid bilayer (where no headgroup/headgroup interface exists) results in high friction, consistent with this attraction. Likewise, interface 3 (PE0/bilayer) is attractive, as PEO adsorbs to PC liposomes (from Figure 1 and liposome/PEO adsorption seen directly in Figure 2A), as is interface 4 (PE0/mica), since PEO adsorbs onto the mica. Shear of these interfaces is associated with hysteretic breaking and re-forming of adhesive bonds and thus with high frictional energy dissipation and a high friction coefficient. We conclude that slip for this configuration occurs at interface 2, where the hydrated phosphocholine headgroup layers of the PC bilayers repel and slide past each other via the hydration lubrication mechanism. This is indeed consistent with the low values of $\mu_i$ seen for configuration I (Figure 3B, as well as Figures 3D and 4A), which are similar to values seen in earlier studies where lipidome-bearing mica surfaces slide past each other. Likewise, we may identify the different interfaces in each of the other configurations II–V. In configuration II (Figure 3C),
the slip plane can again be at a bilayer—bilayer interface within the compressed lipidosome layer (as interface 2 in Figure 6), so that the sliding friction takes place via hydration lubrication and \( \mu \) is low. As seen in Table 1, the range of \( \mu \) for configuration II \((\mu_{II} \approx 6 \times 10^{-3} - 2 \times 10^{-5})\) is somewhat higher than for configuration I \((\mu_{I} \approx 7 \times 10^{-5} - 5 \times 10^{-7})\); this may be due to the effect of an additional soft adsorbed PEO layer separating the surfaces in the former case. Thus, although the slip plane is at the bilayer—bilayer interface 2 (Figure 6), viscoelastic distortion of the PEO layers as the surfaces slide past each other may result in additional energy dissipation; distortion during sliding of the two PEO layers in configuration II may therefore lead to greater frictional losses in this way than for the single PEO layer in configuration I, leading to a higher \( \mu \). In both cases I and II, however, the presence of the PC vesicles implies the availability of a bilayer—bilayer interface that may act as a low-friction slip plane.

In contrast, the presence of a single bilayer between the surfaces, as in configurations III and IV (Figures 5A,C), results in very different shear behavior, with much higher friction coefficients (Figures 5B,D and Table 1). The reason for this is clear: there is no longer an available bilayer—bilayer interface which can act as a slip plane. In these configurations, the interface which might act as potential slip planes are all between attracting species: mica/PEO, PEO/bilayer, and bilayer/mica (for configuration III) or bilayer/PEO (configuration IV). Thus, from Table 1, the measured friction coefficients \( \mu_{III} \) and \( \mu_{IV} \) for configurations III and IV are in the range \( 0.06 - 0.3 \) \( \mu \), far higher than \( \mu_{II} \) or \( \mu_{I} \), reflecting the higher energy dissipation associated with sliding of attracting surfaces (where the scatter in the data may be attributed to surface heterogeneity). Addition of a second bilayer, to form a symmetric mica/PEO/bilayer configuration as in Figure 5E, recovers to a large extent the hydration lubrication mechanism, where the slip lane has reverted to the bilayer—bilayer interface, with an associated much-lower friction coefficient \( \mu_{IE} \approx (2-8) \times 10^{-3} \). We note that \( \mu_{IE} \) is higher than \( \mu_{II} \) or \( \mu_{I} \), which are also associated with bilayer—bilayer slip (interface 2 in Figure 6). We attribute this to the more defect-free nature of the close-packed vesicle bilayers across the slip plane (as seen in cryo-SEM images \( ^{34,35} \)), relative to the defect-rich bilayers (Figure 2B) formed by heating and rupture of the liposomes. As a general comment, if there is a large difference—say an order of magnitude or more—between the friction across two possible slip planes, we expect the slip will likely occur almost exclusively at the plane with the lower friction. Where the friction coefficients are not too different, however—say within a factor of 2 or so—some combination of slip may occur at the two interfaces, and this may apply to the high-friction slip planes in configurations III and IV.

## CONCLUSIONS

In summary, our findings show that surfaces interacting via boundary layers comprising PC lipid aggregates, which may be adsorbed onto or complexed with other molecules, will experience low friction, enabled by hydration lubrication, in both symmetric and asymmetric configurations, whenever sliding may occur across a slip plane between their highly hydrated phosphocholine groups. This finding is of interest for both biological tissues and for synthetic materials. In particular, it supports the recent proposal\(^ {12,13,33} \) that the low friction of the articular cartilage coating the major mammalian joints, which is essential for their homeostasis, is due to a boundary layer exposing PC lipids complexed with hyaluronan and other macromolecules.\(^ {1,2,5,34} \) Such lipid—HA complexes may expose both liposomes\(^ {35} \) and multilayer lipid structures,\(^ {56} \) and two such layers facing each other will in general be structurally asymmetric and may also experience attractive interactions due to HA bridging.\(^ {56} \) Our results reveal that as long as a slip plane may be located between hydrated phosphocholine groups in bilayer structures, including, as we show, the internal surfaces of compressed lipid vesicles, the friction will remain low via the hydration lubrication mechanism. For the case of synthetic materials, a very recent study\(^ {35} \) has shown that the presence of PC lipid bilayers or multilayers at the surface of hydrogels can provide excellent lubrication with different surfaces, despite the asymmetric lipid structure on hydrogel and its counter surface, indicating a slip plane between lipid bilayers in line with our present findings.

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### Notes

The authors declare no competing financial interest.

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### REFERENCES

1. Raj, A.; Wang, M.; Zander, T.; Wieland, D. C. F.; Liu, X.; An, J.; Garamus, V. M.; Willumeit-Römer, R.; Fielden, M.; Claesson, P. M.; Dédinaitė, A. Lubrication synergy: Mixture of hyaluronan and dipalmitoylphosphatidylcholine (DPPC) vesicles. J. Colloid Interface Sci. 2017, 488, 225–233.
2. Wang, M.; Liu, C.; Thormann, E.; Dédinaitė, A. Hyaluronan and Phospholipid Association in Biolubrication. Biomacromolecules 2013, 14 (12), 4198–4206.
3. Goldberg, R.; Schroeder, A.; Silbert, G.; Turjeman, K.; Barenholz, Y.; Klein, J. Boundary Lubricants with Exceptionally Low Friction Coefficients Based on 2D Close-Packed Phosphatidylcholine Liposomes. Adv. Mater. 2011, 23, 3517–3521.
4. Sorkin, R.; Kampf, N.; Dror, Y.; Shimon, E.; Klein, J. Origins of extreme boundary lubrication by phosphatidylcholine liposomes. Biomacromolecules 2013, 34, 5465–5475.

https://dx.doi.org/10.1021/acs.langmuir.0c02956
Langmuir 2020, 36, 15583–15591
(5) Trunfio-Sarfghiu, A.-M.; Berthier, Y.; Meurisse, M.-H.; Rieu, J.-P. Role of Nanomechanical Properties in the Tribological Performance of Phospholipid Biomimetic Surfaces. Langmuir 2008, 24, 8765–8771.

(6) Klein, J. Hydration lubrication. Friction 2013, 1, 1–23.

(7) Briscoe, W. H.; Titimuss, S.; Tiberg, F.; Thomas, R. K.; McGillivray, D. J.; Klein, J. Boundary lubrication under water. Nature 2000, 444, 191–194.

(8) Hills, B. A. Boundary lubrication in vivo. Proc. Inst. Mech. Eng., Part H 2000, 214 (H1), 83–94.

(9) Hills, B. A. Surface active phospholipid: a Pandora’s box of clinical applications. II: Barrier and lubricating properties. Int. Med. J. 2002, 32, 242–251.

(10) Hills, B. A.; Jay, G. D. Identity of the joint lubricant. J. Rheumatology 2002, 29, 200–201.

(11) Hills, B. A.; Butler, B. D. Surfactants identified in synovial fluid and their ability to act as boundary lubricants. Ann. Rheum. Dis. 1984, 43, 641–648.

(12) Jahn, S.; Seror, J.; Klein, J. Lubrication of articular cartilage. Annu. Rev. Biomed. Eng. 2016, 18, 235–258.

(13) Seror, J.; Zhu, L.; Goldberg, R.; Day, A. J.; Klein, J. Supramolecular synergy in the boundary lubrication of synovial joints. Nat. Commun. 2015, 6, 6497.

(14) Duan, Y.; Liu, Y.; Zhang, C.; Chen, Z.; Wen, S. Insight into the Tribological Behavior of Liposomes in Artificial Joints. Langmuir 2016, 32, 10957–10966.

(15) Schmidt, T. A.; Gastelum, N. S.; Nguyen, Q. T.; Schumacher, B. L.; Sah, R. L. Boundary lubrication of articular cartilage - Role of synovial fluid constituents. Arthritis Rheum. 2007, 56 (3), 882–891.

(16) Sorkin, R.; Dror, Y.; Kampf, N.; Klein, J. Mechanical stability and lubrication by phosphatidylcholine boundary layers in the vesicular and in the extended lamellar phases. Langmuir 2014, 30, 5005–5014.

(17) Yu, J.; Banquy, X.; Greene, G. W.; Lowrey, D. D.; Israelachvili, J. N. The Boundary Lubrication of Chemically Grafted and Cross-Linked Hyaluronic Acid in Phosphate Buffered Saline and Lipid Solutions Measured by the Surface Forces Apparatus. Langmuir 2012, 28, 2244–2250.

(18) Green, J. J.; Elisseef, J. H. Mimicking biological functionality with polymers for biomedical applications. Nature 2016, 540, 386.

(19) Peppas, N. A.; Hilt, J. Z.; Khademhosseini, A.; Langer, R. Hydrolgys in Biology and Medicine: From Molecular Principles to Biomaterials. Adv. Mater. 2006, 18, 1345–1360.

(20) Hoffmann, A. S. Hydrogels for biomedical applications. Adv. Drug Delivery Rev. 2002, 54 (1), 3–12.

(21) Bernard, M.; Jubeli, E.; Pungente, M. D.; Yagoubi, N. Biocompatibility of polymer-based biomaterials and medical devices – regulations, in vitro screening and risk-management. Biomater. Sci. 2018, 6, 2025–2053.

(22) Cao, D.; Zhang, Y.; Cui, Z.; Du, Y.; Shi, Z. New strategy for design and fabrication of polymer hydrogel with tunable porosity as artificial corneal skirt. Mater. Sci. Eng. C 2017, 70, 665–672.

(23) Goda, T.; Ishihara, K. Soft contact lens biomaterials from bioinspired phospholipid polymers. Expert Rev. Med. Devices 2006, 3, 167–174.

(24) Kim, B. S.; Hrkach, J. S.; Langer, R. Biodegradable photo-crosslinked poly(ether-ester) network for lubricious coatings. Biomaterals 2000, 21, 259–265.

(25) MacNeil, S. Biomaterials for tissue engineering of skin. Mater. Today 2008, 11 (5), 26–35.

(26) Le Meins, J-F.; Schatz, C.; Lecommandoux, S.; Sandre, O. Hybrid polymer/lipid vesicles: state of the art and future perspectives. Mater. Today 2013, 16 (10), 397–402.

(27) Suh, J. K. F.; Matthew, H. W. T. Application of chitosan-based polysaccharide biomaterials in cartilage tissue engineering: a review. Biomaterials 2000, 21 (24), 2589–2598.
rated Phosphatidylcholine Mixtures. *Langmuir* 2019, 35 (48), 15459–15468.

(50) Chai, L.; Klein, J. Role of ion ligands in the attachment of poly(ethylene oxide) to a charged surface. *J. Am. Chem. Soc.* 2005, 127, 1104–1105.

(51) Tabor, D Friction as a dissipative process. In *Fundamentals of Friction: Macroscopic and Microscopic Processes*; Pollock, H., Singer, I. L., Eds.; Kluwer: Dordrecht, 1992; pp 3–20.

(52) Hu, Y.-x.; Ma, T.-b.; Wang, H. Energy dissipation in atomic-scale friction. *Friction* 2013, 1 (1), 24–40.

(53) Murakami, T.; Yarimitsu, S.; Nakashima, K.; Sawae, Y.; Sakai, N. Influence of synovia constituents on tribological behaviors of articular cartilage. *Friction* 2013, 1 (2), 150–162.

(54) Schmidt, T. A.; Sah, R. L. Effect of synovial fluid on boundary lubrication of articular cartilage. *Osteoarthritis and Cartilage* 2007, 15 (1), 35–47.

(55) Pasquali-Ronchetti, I.; Quaglino, D.; Mori, G.; Baccelli, B.; Ghosh, P. Hyaluronan—Phospholipid Interactions. *J. Struct. Biol.* 1997, 120, 1–10.

(56) Lin, W.; Liu, Z.; Kampf, N.; Klein, J. The Role of Hyaluronic Acid in Cartilage Boundary Lubrication. *Cells* 2020, 9 (7), 1606.