# Can Small Complex Chains Be Treated as Polymers?

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ABSTRACT: The interactions of supramolecular systems often depend on small and complex molecules. It is tempting though dangerous to apply polymer theory to these molecules that are normally considered to be too small to be polymers and too large to be rigid. Here, forces and adhesions between surfaces bearing several types of such molecules with both flexible and rigid parts are measured. The force/distance profiles follow closely the description given by polymer theory. It is shown for a wide variety of systems containing these molecules that if one obtains an effective radius of gyration $R_g$ of the molecules, polymer theory can be used to predict their adhesion energy. Conversely, if the adhesion energy for bilayers containing such small and complex molecules is measured, polymer theory allows to deduce the effective $R_g$ of the molecule.

## I. Introduction

Many colloidal systems or surfaces bear a wide variety of molecules that determine the interactions of those surfaces with their environment.[1−4] These molecules may have various sizes and flexibilities, and it is tempting to predict their behavior with polymer theory. The lower size threshold for a molecule made of the same monomers to be considered as a polymer is not clear and depends on bond flexibility. The situation is difficult enough for homopolymers, but for a complex (or heterogeneous) molecule made of different parts, predictions are even more complex. This paper addresses this question and aims to test the relevance of polymer theory for surfaces bearing linear heterogeneous molecules of intermediate size. Here, force/distance profiles and adhesion measurements are compared with expected behaviors obtained by applying polymer theory to heterogeneous molecules.

A good example of such systems is provided by bilayers of lipids with flexible segments in their headgroups. These segments (oligosaccharides, polysaccharides, peptides, etc.) govern the bilayer equilibrium distance and determine their adhesion energy. For neutral lipids these two parameters result from a competition between the van der Waals forces and the steep short-range repulsions which depend strongly on the headgroup size of the lipids.[4,5] By contrast, polymer chains produce a repulsion of the brush or mushroom type.[6−9] Many flexible segments present on membranes are larger than usual lipid headgroups but presumably too small to be considered as polymers. Functionalized lipids often provide such intermediate size headgroups,[4] but few studies address the question of the short-range part of the force/distance profile. Kuhl et al.[10] reported such interactions and showed the validity of polymer theory for surfaces bearing linear and homogeneous molecules of small size (2000 $M_w$ PEO chains). Here, we focus on molecules of similar sizes but with heterogeneous headgroups in which flexible parts are combined with more rigid ones.

## II. Material and Methods

Four glycolipids were synthesized with different headgroup flexibilities and sizes (500−1500 $M_w$) (Figure 1). These headgroups are composed of some of the following patterns: a short linear and flexible PEO chain (P), a lactose (L), and a more rigid and complex sugar (Lex).[11] The names of the glycolipids reflect their compositions: PLex, PL, PLLex, PLLexLex (Figure 1).

Two techniques, the surface force apparatus (SFA)[12] and vesicle micromanipulation,[13] were used to measure interactions between layers made of those glycolipids. SFA experiments allowed the measurement of force/distance profiles between two mica surfaces in a crossed cylindrical geometry (with a radius of curvature $R$ of about 2 cm), each bearing a glycolipid layer immersed in pure water.[12] In practice, the mica surfaces were coated with lipid bilayers by the Langmuir−Blodgett (LB) method. The monolayers in contact with mica were composed of a phospholipid (DOPC = 1,2-dioleoyl-*sn*-glycero-3-phosphocholine or DMPE = 1,2-dimyristoyl-$d_{54}$-*sn*-glycero-3-phosphoethanolamine) while the outer ones were composed either of pure glycolipids or of a mixture consisting of the phospholipid used for the inner layer and between 10% and 25% (mol/mol) of one of the glycolipids (Figure 2).

The second technique involved measurement of the adhesion energy between two osmotically controlled giant vesicles prepared from a mixture of one of the glycolipids and SOPC (1-stearoyl-2-oleoyl-*sn*-glycero-3-phosphocholine) in a 1:9 molecular ratio. The vesicles were manipulated in aqueous NaCl solution (200 mM) using the micropipet aspiration technique developed by Evans[13] and illustrated in Figure 3. The negative pressure ($\Delta P$) in the pipet controls the positive hydrostatic pressure in the vesicle and thus the mechanical tension $\tau_m$ in the vesicle membrane. One of the vesicles is held with low pressure and remains deformable while the other one is held under a high aspiration pressure to be almost rigid. The free energy of adhesion was measured using the contact angle $\theta_c$ and the tension $\tau_m$ of the flaccid vesicle membrane: $E_{adh} = \tau_m(1 - \cos\theta_c)$. The measurement of $\theta_c$ was numerically deduced from geometrical parameters as indicated by Evans.[13]

## III. Polymer and Bilayer Interactions

When a surface is coated with polymers at elevated concentrations such that the molecules are close enough

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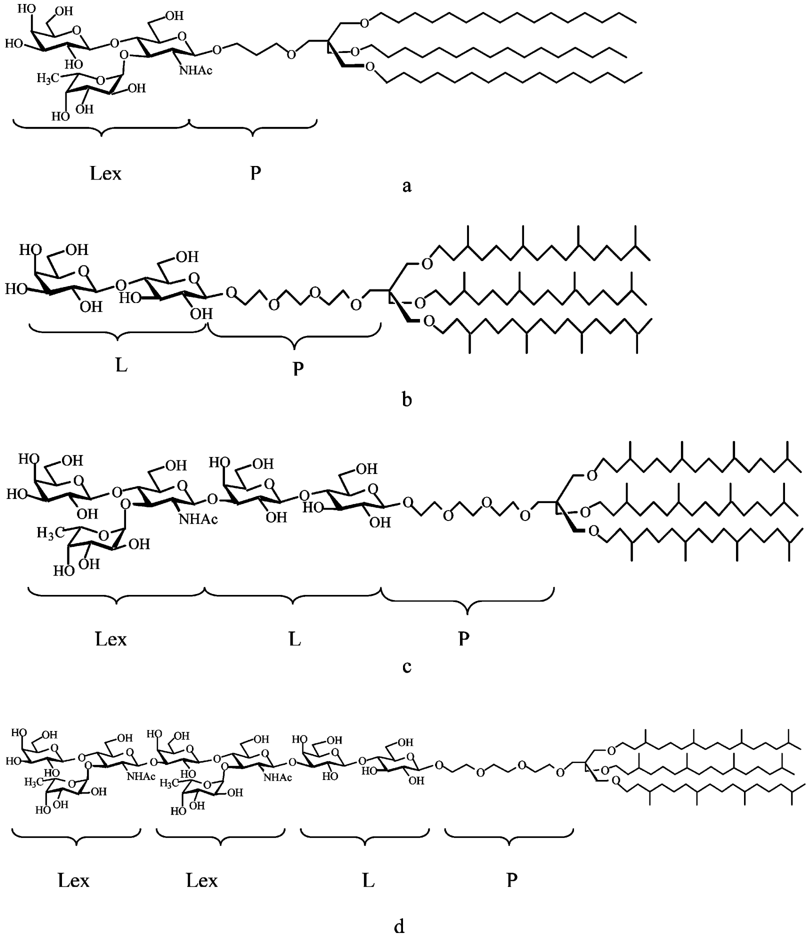

**Figure 1.** Glycolipids: (a) PLex is a Lex group connected to an aliphatic tail by a very short PEO chain, (b) PL is a lactose group connected to an aliphatic tail by a short PEO chain. (c) PLLex molecule is made of a PL molecule and one Lex group connected to the L group. (d) PLLexLex molecule is made of a PL molecule and two Lex group in series connected to L.

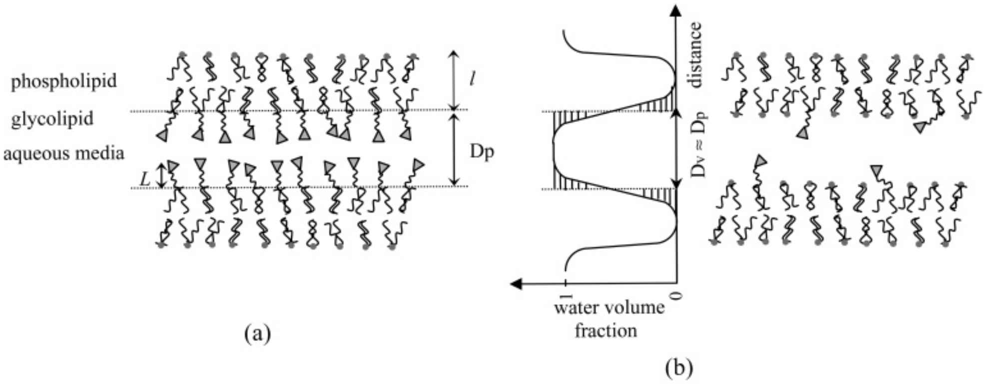

**Figure 2.** Representation of lipid bilayers in SFA experiments (a) for full coverage of glycolipids in the SFA experiments and (b) for partial coverage of glycolipids in SFA experiments or in vesicle experiments (in reality, in vesicles, the outer layer also contains some glycolipids). Lipid chains connected to circles symbolize phospholipids, whereas lipid chains connected to triangles (sugar headgroups) through small wiggles (PEO chains) symbolize glycolipids. The curve represents the water volume fraction (0 around the aliphatic chains and 1 in the gap between the layers). The distance $D_v$ is taken between the water density-weighted interface; the four striped zones have the same areas. $D_p$ is the distance between the surfaces as defined by the limit between the aliphatic tails and the headgroup of the glycolipids. When the density of glycolipids is small, which is always the case in vesicle experiments, the definitions of $D_p$ and $D_v$ give rise to similar distances $D$.

to overlap, the resulting layer is called a brush. In this case, the distance $s$ between the polymer chains is smaller than twice the brush thickness $L$. Alexander and de Gennes[14-16] have derived the expression for the repulsion of two such brushes as a function of the separation distance $D_p$ of the coated surfaces (Figure 2). For $D_p < 2L$, it is given by

$$E_{\text{brush}}(D_p) = \frac{4\beta k_B T}{s^3}\left[\frac{{D_p}^{7/4}}{7(2L)^{3/4}} + \frac{(2L)^{9/4}}{5{D_p}^{5/4}} - \frac{24}{35}L\right] \quad (1)$$

where $\beta$ is an unknown numerical factor,[17] independent of $s$ and $L$.

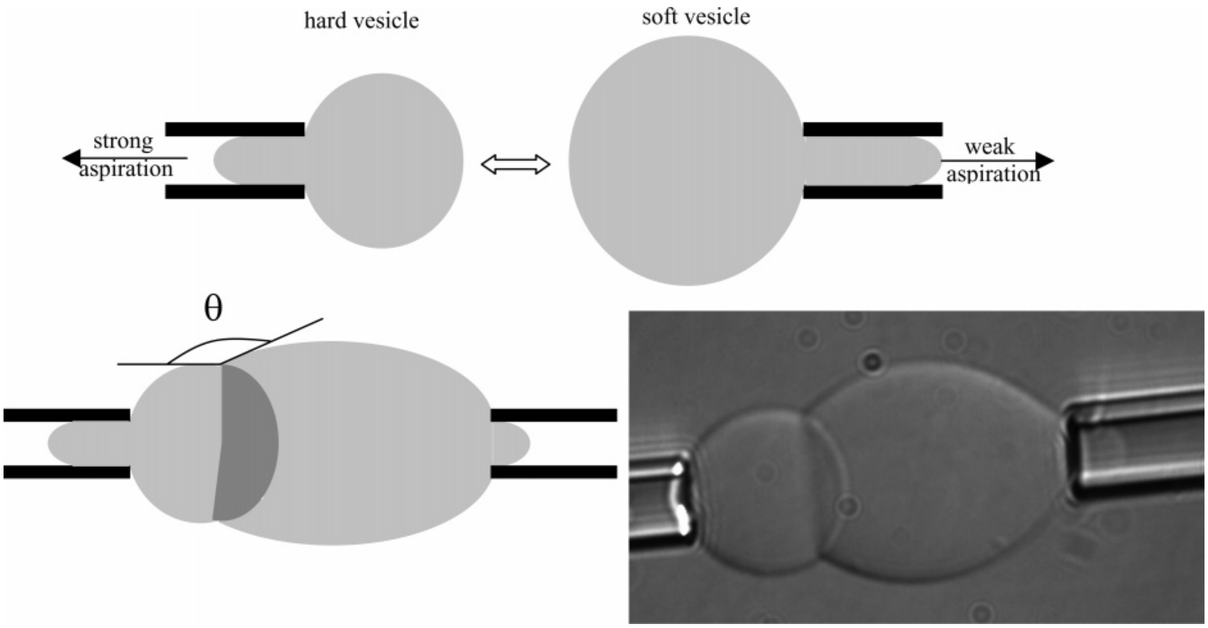

**Figure 3.** Principle underlying the measurement of adhesion energy by the micromanipulation of vesicles. The two osmotically controlled vesicles held in micropipets by aspiration are observed in interference contrast microscopy. The suction pressure applied to the micropipets allows the control of the tension of the vesicle bilayers. One of them (left) is pressurized into a tight-rigid sphere with large bilayer tension, whereas the adherent vesicle (right) is held with low pressure and remains deformable. The adhesion energy $W_{\mathrm{adh}}$ is obtained by determining the contact angle $\theta_{\mathrm{c}}$ of the two vesicles and the tension $\tau_{\mathrm{m}}$ of their membrane: $W_{\mathrm{adh}} = \tau_{\mathrm{m}}(1 - \cos\theta_{\mathrm{c}})$.

As the separation distance $D_{\mathrm{p}}$ approaches zero, eq 1 can be approximated[10] by

$$E_{\mathrm{brush}}(D_{\mathrm{p}}) \propto \mathrm{e}^{-\pi D_{\mathrm{p}}/L} \tag{2}$$

In contrast, low polymer surface concentrations with no chain overlap ($s > 2L$) correspond to the mushroom regime which produces an exponential repulsion profile as the surfaces get close to the contact:[10,18]

$$E_{\mathrm{mushroom}}(D_{\mathrm{p}}) = 36\Gamma k_{\mathrm{B}}T\mathrm{e}^{-D_{\mathrm{p}}/R_{\mathrm{g}}} \tag{3}$$

where $\Gamma$ is the density of anchored polymers ($\Gamma = 1/s^2$) and $R_{\mathrm{g}}$ is the radius of gyration of the polymer.

One may note that at the limit between brush and mushroom regimes ($s \approx 2L$) steric repulsion due to the polymer effect can be described by either eq 2 or eq 3, which supposes that for intermediate polymer surface concentration $L/\pi$ has to tend to $R_{\mathrm{g}}$.

Lipid bilayers involving glycolipids such as those mentioned above differ from pure phospholipid bilayers by the presence of protruding large headgroups. A schematic of such lipid bilayers (either in SFA or in vesicles experiments) is given in Figure 2: a layer of thickness $l$ comprising the phospholipids and/or the aliphatic tails of the glycolipids, from which protrude large linear and heterogeneous groups (the glycolipid headgroups: PEO plus polysaccharides). These prominent chains give rise to steric interactions that we may consider similar to those produced by polymers.

The equilibrium distance between two of these lipid bilayers is obtained by minimizing (relative to their separation distance) the free energy of interaction between them. This energy is comprised of many contribution elements: van der Waals attraction, steric repulsion due the protruding headgroups, undulation (or Helfrich) repulsion[19] which comes from spontaneous membrane undulations under thermal fluctuations and interactions due to hydration,[20] and protrusion effects.[21] One may note that these latter two interactions are not relevant here since the repulsions they generate have shorter range than the distances involved in the present SFA or vesicles experiments. At distances longer than the equilibrium distance, van der Waals attraction dominates the interaction profile, while at shorter distances, steric repulsion due to glycolipid headgroup and Helfrich undulations is predominant.

In SFA experiments, the bilayers are fixed on mica surfaces, and the distance between the surfaces can be modified through the mechanical force which is applied to the surfaces. Therefore, at separation distances smaller than the equilibrium distance, the interaction between the bilayers is repulsive due exclusively to the steric repulsions of the glycolipid headgroups. Indeed, the bilayers are not free to fluctuate and do not generate Helfrich repulsion. The particular characteristics of this technique permit the testing of the polymer aspect of the steric interaction.

By contrast, in the vesicle adhesion energy experiments, lipid bilayers are free to fluctuate, and the distance separating two vesicles is thus the equilibrium distance that results from the minimization of the free energy.

In the case of two interacting bilayers as shown in Figure 2b, the van der Waals attraction contributes to the interaction energy with a power law distance dependence given by[22]

$$E_{\mathrm{vdW}}(D_{\mathrm{v}}) = \frac{H}{12\pi}\left[\frac{1}{{D_{\mathrm{v}}}^2} - \frac{2}{(D_{\mathrm{v}} + l)^2} + \frac{1}{(D_{\mathrm{v}} + 2l)^2}\right] \tag{4}$$

where $H$ is the Hamaker constant and $l$ the bilayer thickness.

The Helfrich entropic repulsion also follows a power law distance dependence.[19] The expression derived in ref 23 is suitable for lipid bilayers and will be used here:

$$E_{\mathrm{Helfrich}}(D_{\mathrm{v}}) = \frac{(k_{\mathrm{B}}T)^2}{1.6\pi^2 k_{\mathrm{c}}}\frac{1}{{D_{\mathrm{v}}}^2} \qquad (5)$$

where $k_c$ is the bilayer rigidity modulus of curvature.

These two contributions depend on the separation distance $D_v$ between the vesicles defined as the distance between the density-weighted interfaces (Figure 2b) because of the soft nature of bilayers.

## IV. Results and Discussion

**Polymer-like Interactions from SFA Force/Distance Profiles.** The four force/distance profiles probed with the SFA technique were respectively those of monolayers of purePLex (Figure 4a), pure PLLex (Figure 4b), a 1:3 PLex/DMPE mixture (Figure 5a), and a 1:9 mixture of PLLex/DOPC (Figure 5b). Figures 4 and 5 display the short-range portion of the profiles due, as explained above, to the glycolipid headgroups. This steric interaction can be compared directly with the one given by the polymer theory. Because of the high glycolipid density, the brush character of surfaces fully covered with glycolipids (PLex or PLLex) (eq 1) can first be tested by fitting their force/distance profiles (Figure 4) using eq 1. For our systems, $s$, $L$, and $D_p$ in eq 1 can respectively be seen as the distance between two glycolipids, the thickness of the layer made of the glycolipid headgroups, and the distance between the surfaces defined by the limit between the aliphatic tails and the headgroup of the glycolipids (see Figure 2a). $s$ is not an adjustable parameter since it has been obtained independently by compression isotherm measurements before Langmuir–Blodgett deposition. In this study $s$ is equal to 0.95 ± 0.05 nm for both PL and PLLex. The fit parameters $\beta$ and $L$ are given in Table 1. Figure 4 shows that fits are very good and accurate. Indeed, their ranges of adjustment are extremely narrow. The short and long dashed line in Figure 4b show how the best fit is changed when $L$ is shifted by +0.05 nm and −0.2 nm from its optimal value. Similarly, a small variation of $\beta$ would lead to a significant vertical translation of the curves.

The small thickness $L = s$ obtained for PLex layer indicates that despite the high coating density of PLex molecules, conditions approach the limit ($L = s/2$) between the brush and the mushroom regime. According to eqs 2 and 3, in that limit, $L/\pi$ should tend to $R_g$. By reducing the PLex density by a factor of 4 (1:3 PLex/DMPE mixture), the mushroom regime should therefore be fully reached. Indeed, the force/distance profile (Figure 5a) has successfully been fitted with the exponential law given by eq 3. Like $s$, $\Gamma = 1/s^2$ is not an adjustable parameter since it has been obtained independently by compression isotherm measurements. For the 1:3 PLex/DMPE mixture $\Gamma = 0.35$ nm$^{-2}$. From the fit (Figure 5a), an effective $R_g$ value of 0.32 nm (see Table 1) could be obtained. As expected, this value is close to that obtained for $L/\pi$ (0.33 nm).

For a layer of pure PLLex, the thickness value ($L$ = 2 nm = $2s$, see Table 1) shows that the system is far from the mushroom regime. Nevertheless, if the PLLex molecule is diluted by a factor 10 in DOPC (1:9 of PLLex/DOPC mixture), the mushroom regime should be reached ($\Gamma = 0.1$ nm$^{-2}$). Indeed, the corresponding force/distance profile (Figure 5) fits well with the exponential law of eq 3. The strong difference between the $R_g$ value (0.52 nm, Table 1) and the $L/\pi$ value (0.64 nm) obtained with a brush regime (eq 2) shows that in this case the layer is far from the limit between brush and mushroom regimes.

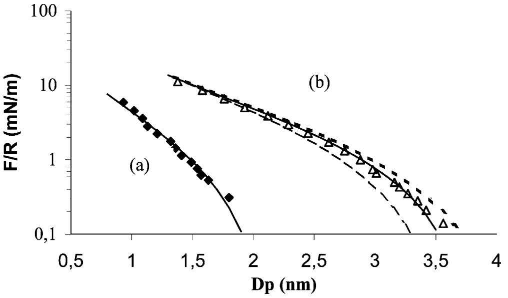

**Figure 4.** Force/distance profile for surfaces covered by a (a) PLex and (b) PLLex. The solid lines are best fits for $\beta$, $L$ with the brush regime obtained from eq 1. The short and long dashed lines have been plotted to show the accuracy of the fit: they are the best fits for $\beta$ with the brush regime obtained from eq 1 when shifting $L$ by +0.05 nm and −0.2 nm from the value given in Table 1. A variation of $\beta$ leads to a vertical translation of the curves. $D_p$ is defined in Figure 2a.

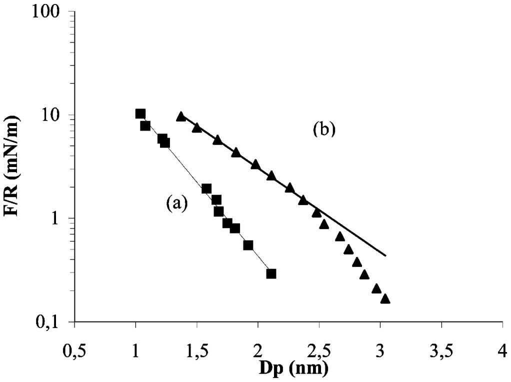

**Figure 5.** Force/distance profiles between surfaces covered by a monolayer of (a) a 1:3 mixture of PLex/DMPE and (b) a 1:9 mixture of PLLex/DOPC. The solid lines are fits of the mushroom regime at short distances obtained from eq 3. When the repulsion decreases at longer distances, the data points cannot be fitted anymore because the exponential approximation stops being valid. $D_p$ is defined in Figure 2a.

**Table 1. Values (in nm) of the Radius of Gyration $R_g$ and of the Parameters $\beta$ and $L$ As Defined in the Text[a]**

| | $\beta$ | $L$ | $R_g$ |
|---|---|---|---|
| PLex 100% | | | |
| Figure 6a **—** | **0.1** | **1.0** | |
| Figure 6a - - - | 1.2 | 0.8 | |
| Figure 6a — | | | 0.21 |
| PLLex 100% | | | |
| Figure 6a **—** | **0.1** | **2.0** | |
| Figure 6a - - - | 2.96 | 1.2 | |
| Figure 6a — | | | 0.37 |
| PLex/DMPE 1:3 | | | |
| Figure 7a **—** | | | **0.32** |
| Figure 7a - - - | 0.1 | 1.9 | |
| Figure 7a — | 1.2 | 1.2 | |
| PLLex/DOPC 1:9 | | | |
| Figure 7a **—** | | | **0.52** |
| Figure 7a - - - | 0.1 | 4.7 | |
| Figure 7a — | 2.96 | 1.7 | |

[a] $\beta$, $L$: obtained by fitting force/distance profiles with eq 1 (brush regime). $R_g$: obtained by fitting force/distance profiles with eq 3 (mushroom regime).

In the Appendix, we demonstrate that fitting force/distance profiles of high glycolipid surface densities (pure PLex and pure PLLex layers) with the mushroom regime is not appropriate. Conversely, eq 1 relative to

**Table 2. Vesicles' Free Adhesion Energy, Measured and Calculated, and Interaction Parameters for the Calculation of the Adhesion Energy; Equilibrium Distance $D_{eq}$ and Calculated Adhesion Energy Are Obtained by Minimizing the Sum of the Different Energetic Contributions ($E_{vdW}$, $E_{mushroom}$, $E_{Helfrich}$)**

| | $E_{adh}$ ($\mu$J/m$^2$) measured | $E_{adh}$ ($\mu$J/m$^2$) calculated | $R_g$ (nm) | $D_{eq}$ (nm) | $E_{vdW}$ ($\mu$J/m$^2$) | $E_{mushroom}$ ($\mu$J/m$^2$) | $E_{Helfrich}$ ($\mu$J/m$^2$) |
|---|---|---|---|---|---|---|---|
| PL−PL | 9.5 ± 0.5 | 9.8 | 0.41[a] | 3.3 | 15.7 | 4.8 | 1.1 |
| PLLex−PL | 5.4 ± 1 | 5.9 | 0.47[b] | 4.1 | 9.1 | 2.4 | 0.7 |
| PLLex−PLLex | 4.5 ± 2 | 4.0 | 0.52[c] | 4.7 | 6.4 | 1.8 | 0.6 |
| PLLexLex−PLLex Lex | 4.5 ± 2 | 3.0 | 0.52 ± 0.07[d] | 5.2 | 4.9 | 1.4 | 0.5 |

[a] Estimated from the molecular structure (see text). [b] Averaged from the $R_g$ values of PLLex and PL. [c] Deduced from the fits of the force/distance profiles measured by SFA. [d] Calculated from the adhesion energy data (see text).

the brush regime is not suitable for coherently fitting the repulsion produced by the 1:3 of PLex/DMPE mixture and the 1:9 of PLLex/DOPC mixture.

The SFA experiments have shown that the steric repulsion due to large linear and heterogeneous groups (the glycolipid headgroups) are close to those produced by polymers in a brush or mushroom regime. By fitting force/distance profiles, an effective value of the gyration radius of PLex and PLLex headgroups is obtained. It is therefore tempting to use these effective radii of gyration to test whether we can predict the adhesion energy of two vesicles bearing such molecules.

**Vesicles Adhesion Energy.** Giant vesicles composed of a mixture (approximately 1:9) of PL, PLLex, or PLLexLex and SOPC have been used to measure the adhesion energy of the four following pairs: PLLex−PLLex, PL−PL, PLLex−PL, and PLLexLex−PLLexLex. The experimental results (Table 2) show that, as expected, the adhesion energies vary monotonically with the size of the headgroups. The larger the headgroups, the larger the steric repulsion and therefore the smaller the adhesion energies.

As mentioned above, the adhesion energy of two bilayers results from the balance between the van der Waals attraction and the repulsion that includes entropic (Helfrich undulations) and steric contributions (polymer effect). Note that when the density of glycolipids is small, which is always the case in vesicle experiments, $D_p$ and $D_v$ resolve to a common distance $D$. Assuming the additivity of these three contributions (the approximation of additivity introduces an error smaller than the experimental one),[24] the adhesion energy is calculated by minimizing the sum of these contributions (eqs 1−5). This requires the knowledge of several parameters: $H$ and $l$ (eq 4), $k_c$ (eq 5), and $R_g$ and Γ (eq 3) since the polymer effect of the glycolipid heads is of the mushroom type as suggested by SFA results for a small concentration of glycolipids. In the case of vesicles made with PLLex and SOPC, all these parameters are known. $R_g$, obtained by SFA experiments, is equal to 0.52 nm, and Γ, given by monolayer compression isotherms, is about 0.1 nm$^{-2}$. For SOPC, the Hamaker constant $H$ is equal to $7 \times 10^{-21}$ J,[25] but for pure glycolipid vesicles like those formed of digalactosyldiglyceride (DGDG), $H$ is higher ($H = 25 \times 10^{-21}$ J).[25] $H$ was therefore chosen equal to $9.5 \times 10^{-21}$ J for the vesicles with 87% of SOPC and 13% of glycolipid in surface. The thickness used in the fits is that of SOPC: $l = 4.06$ nm (as measured in ref 5). $k_c$ is equal to $9 \times 10^{-20}$ J, as in ref 24. The adhesion energy for PLLex vesicles, calculated with these parameters, is equal to 4.0 $\mu$J/m$^2$, and the details of energetic contributions as well as the related equilibrium distances can be found in Table 2. This result is in excellent agreement with the value experimentally measured (4.5 ± 2 $\mu$J/m$^2$).

For both the PL−PL pair and the antisymmetric PLLex−PL pair, all the parameters required to calculate the adhesion energy are the same as for the PLLex−PLLex system, except the $R_g$ value which is unknown for the PL molecule. Nevertheless, the PL headgroup is a linear and flexible chain with 16 beads, of which 14 have C−C or C−O bonds (≈0.15 nm) and two are sugar cycles (≈0.4 nm). These can be seen as ideally flexible chains for which $R_g$ is given by $R_g = aN^{3/5}/6^{1/2}$ ($a$ being the weighted average bead size and $N$ the number of beads).[10,26] $a$ is roughly equal to 0.18 nm; therefore, $R_g \approx 0.41$ nm. For the asymmetric PLLex−PL system, $R_g$ can be taken equal to 0.47 nm, which is the averaged of the $R_g$ of the PL−PL system (0.41 nm) and of the PLLex−PLLex one (0.52 nm obtained from the force/distance fits). As can be seen in Table 2, the calculated adhesion energies are consistent with the ones obtained experimentally. Moreover, the adhesion energy is very sensitive to a small variation of $R_g$ as illustrated below in the discussion of the PLLexLex case.

The good agreement between the calculated adhesion energies and the experimental values confirms the above-mentioned SFA results, stressing that the interaction of lipids with large headgroups can be described in the same way as for polymers.

We have just seen that the use of independently obtained effective $R_g$ values allows for the accurate prediction of the adhesion energy. It is interesting to test whether the reverse is true. Is it possible in the last system (the PLLexLex−PLLexLex pair) to deduce a consistent $R_g$ value of the complex PLLexLex chain from the measured adhesion energy and its calculation? Given the error bar, the adhesion energy of the PLLexLex−PLLexLex system lies (see Table 2) between 2.5 and 6.5 $\mu$J/m$^2$. Therefore, $R_g$ should be equal to 0.52 ± 0.07 nm. This is compatible with the fact that it should be slightly larger than the one of PLLex. Therefore, even for a very complex molecule that produces small adhesion energy, the accuracy of the $R_g$ value is still high.

## V. Conclusion

In this work, we have used two very different techniques: the surface force apparatus which gives force/distance profiles and a micromanipulation system for measuring the adhesion energy of vesicles. With each technique, we have studied four different configurations involving either different molecules or different densities. Moreover, the molecules differed by the length of the flexible chain and its composition and also by the introduction of one or two rigid groups.

The SFA experiments allowed to directly observe the influence of the steric repulsion produced by the glycolipid headgroups on the force/distance profiles, show-

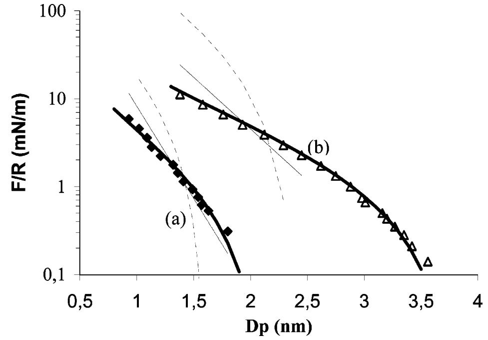

**Figure 6.** Force/distance profile for surfaces covered by a (a) PLex and (b) PLLex. The solid bold lines are best fits for $\beta$, $L$ with the brush regime obtained from eq 1 (the same as in Figure 4). The solid thin lines are the best fits obtained with the mushroom regime (eq 3). The short dashed lines are the best fits obtained by fixing $\beta = 1.2$ for PLex and $\beta = 2.96$ for PLLex (see Figure 7).

ing their polymer-like nature. For the PLex and PLLex chains, a value of their effective $R_g$ could be deduced from experiments. For the PL chain (linear and without rigid moiety), a value of $R_g$ could be obtained from a crude structural argument. With these effective $R_g$ values the calculation for three systems of the adhesion energy of two bilayers bearing these molecules has been done. The excellent agreement with the micropipet experimental value could show that the use of independently obtained $R_g$ values allows accurate prediction of the vesicles' adhesion energies. For the more complex PLLexLex chain, a reliable $R_g$ could be deduced from the measured adhesion energy and the calculation using polymer scaling theory.

Finally, this extended study shows that the behavior of small linear heterogeneous molecules is consistent with polymer scaling theory. This conclusion supported by the present study is likely to have some limitations, such as, if the rigid part were much larger than the flexible part of the molecules. However, this point will remain unclear until measurements are done with such molecules. Nevertheless, the main conclusion applies to a majority of the functionalized lipids used in soft matter physicochemistry.

## Appendix

Figure 4 shows that the relationship describing the interaction between two polymer brushes (eq 1) provides a good description of the interaction between surfaces with high glycolipid densities.

Figure 5 illustrates that a mushroom interaction (eq 3) can nicely account for the interaction between surfaces with low density of glycolipids close to the contact.

In eq 3, only $R_g$ is a fit parameter since $\Gamma$ is independently obtained by compression isotherm measurements. The force at $D = 0$ is therefore fixed. In pure Plex and PLLex layers $\Gamma$ is equal to 1.1 and 0.35 nm$^{-2}$ (0.1 nm$^{-2}$) in the 3:1 PLex/DMPE mixture (9:1 PLLex/DOPC mixture). Figure 6 clearly shows that attempts to fit the force/distance profiles of the dense layers (pure PLex (curve a) and pure PLLex (curve b)) with the mushroom relation (eq 3) do not give satisfactory results.

In eq 1, not only $L$ but also $\beta$ are parameters. However, $\beta$ depends neither on $L$ nor on $s$. To determine whether the brush interaction (eq 1) could also describe the force/distance profile obtained with low density of glycolipids, $\beta$ should be fixed to the value obtained for high coverage of glycolipids ($\beta \approx 0.1$ for both PLex and PLLex layers). Figure 7 shows that the best fits obtained are still very far from experimental curves. Better fits (see Figure 7) could be obtained by also fitting $\beta$ (see Table 1). However, with such $\beta$ values the fits for the denser surfaces are irrelevant (see Figure 6 and Table 1).

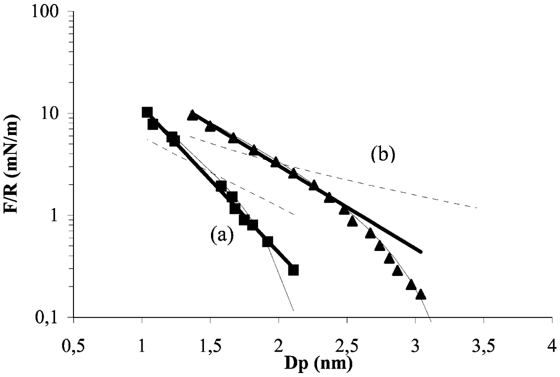

**Figure 7.** Force/distance profiles between surfaces covered by a monolayer of (a) a 1:3 mixture of PLex/DMPE and (b) a 1:9 mixture of PLLex/DOPC. The solid bold lines are the best fits with the mushroom regime at short distances obtained from eq 3 (the same as in Figure 5). The short dashed lines are the best fits obtained with the brush regime (eq 1) with $\beta = 0.1$ (value which provides the best "brush" fits for the pure PLex and pure PLLex force/distance profiles (see Figure 4 or Figure 6). The solid thin lines are the best fits obtained with the brush regime by allowing $\beta$ to be different from 0.1.

The main conclusion of this Appendix is that the steric repulsion due to the glycolipid headgroups can be well described by the polymer theory. As in the case of real polymers, the expressions depend on the surface densities of the glycolipids.

## References and Notes

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