Cyclic Compression and Decompression of a Lipid Bilayer

Ingrid Guha,[†,‡] Jakub Kedzierski,[†] and Behrouz Abedian*[,‡]

[†]MIT Lincoln Laboratory, Lexington, Massachusetts 02420, United States
[‡]Department of Mechanical Engineering, Tufts University, Medford, Massachusetts 02155, United States

ABSTRACT: In this study, we measure transient thicknesses of a lipid bilayer during electrostatic compression and decompression and deduce non-equilibrium molecular interactions of the surfactants' tails within the layer. The bilayer under investigation (sorbitan monooleate) is single-tailed and self-assembles between a water drop and hafnium oxide in dodecane. We detect minute changes in bilayer thickness (∼0.01 Å/s) resulting from step changes in electrostatic pressure. The dynamic response of the bilayer consists of an elastic response followed by an inelastic dissipative behavior. We observe a distinct asymmetry between the inelastic responses: compression triggers a linear reduction in thickness over time, whereas decompression induces a logarithmic increase in thickness.
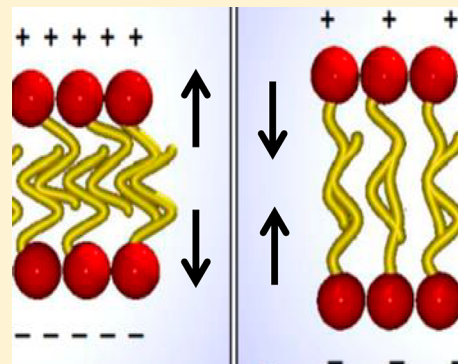
INTRODUCTION

Lipid bilayers are common in many systems ranging from human-devised water-in-oil emulsions[1,2] to nature-created biological systems.[3,4] Self-assembled bilayers are complex nanostructures,[5] and their physical properties can be affected by many factors.[6] Lipid tail interaction within the bilayer can affect a bilayer's physical and mechanical properties, such as its behavior during deformation, breakup, and cleavage. Measuring transient responses of these delicate nanoscale oil films under varying pressure can be used to develop a better understanding of the dynamics of systems containing lipid bilayers. In this study, we investigate the transient behavior of a self-assembled lipid bilayer during cyclic compression and decompression by subjecting it to step changes in the applied electrostatic pressure.

The steady-state thickness of a lipid bilayer varies with the applied electrostatic pressure, as verified in previous studies from capacitance measurements.[7−12] However, the transient properties of such systems remain largely unexplored. The few experiments that have measured transient thicknesses of lipid bilayers under non-equilibrium conditions are generally limited to small electrostatic pressures because of the fragile nature of lipid bilayers.[13]

In a previous study,[14] it was demonstrated that a lipid bilayer self-assembles between a water drop and a thin hafnium oxide film in the presence of dodecane and oleophilic surfactants. The motivation of this study was to demonstrate the use of a lipid bilayer as a hydrophobic dielectric in electrowetting systems in place of a fluoropolymer for the purposes of low-voltage electrowetting. In the setup, applying a voltage across the lipid bilayer—hafnium oxide dielectric stack exerts a controlled electrostatic pressure on the bilayer. The hafnium oxide film provides electrical stability so that the film may be subjected to a wide range of electrostatic pressures without rupturing. The

morphology of the interacting lipid tails for a compressed and uncompressed bilayer is depicted in Figure 1.
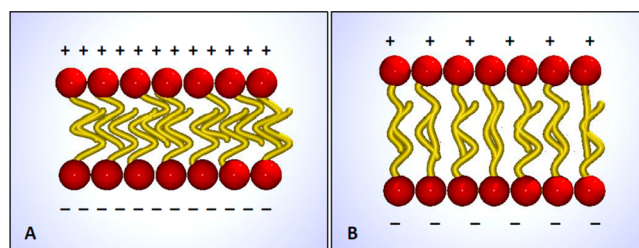

Figure 1. Schematic representation of a lipid bilayer under high and low electrostatic pressure. Red spheres depict the hydrophilic heads of the surfactant molecules that comprise the bilayer; yellow tails depict the hydrophobic lipid tails of the surfactant molecules. (A) When the voltage across the bilayer is increased, the hydrocarbon tails in the lipid bilayer fold under the high electrostatic pressure and the bilayer thins. (B) When the voltage across the bilayer is decreased, the bilayer decompresses under the lower electrostatic pressure and the bilayer thickness increases.

In this study, we measure the thickness of a lipid bilayer over time in response to step changes in electrostatic pressure, created simply by increasing or decreasing the voltage applied across the membrane. This experimental setup can be used not only to anticipate the bilayer behavior in equilibrium but also to predict the dissipative responses of the bilayer under non-equilibrium conditions, when the polymer strands undergo bonding and debonding or folding and unfolding. The relaxation-time constants derived from the experiments in the

dissipative regimes can be related to the non-equilibrium molecular dynamics of the attached polymer strands.

A complex system, such as a lipid bilayer, often has many characteristic relaxation times that can range in magnitude from subnanoseconds to years.[15] Its transient behavior can be considered by introducing the Deborah number, defined as

$$De = \frac{\text{system relaxation time}}{\text{molecular interaction time}} \tag{1}$$

where the system relaxation time is the measurement time or the transient time and the molecular interaction time is related to the thermal vibration modes. For a polymer strand confined in a nanoscale bilayer, the molecular vibrations or collision times are dependent on molecular weight and temperature and are on the order of 10^{-11} s. Accordingly, given the measurement times in our experiments ($\sim$100 s), $De \gg 1$ for the cases we study. Thus, from a molecular dynamics perspective, the system is dissipative and irreversible, and is in a non-equilibrium state.

Hydrodynamic interactions of a polymer chain in the surrounding solvent will give rise to another characteristic time scale known as the Zimm relaxation time.[16] For a free ideal chain with length L, the Zimm relaxation time T_z has the form

$$T_z = C \frac{L^\nu \mu_0}{k_B T} \tag{2}$$

where μ_0 is the solvent viscosity coefficient, k_B the Boltzmann constant, T the temperature, ν an empirical exponent, and C a constant. Assuming that the polymer chain is in the form of a spherical coil, scaling laws can be used to find $\nu = 3$.[17] For a single free-folding DNA molecule on the order of micrometers, this exponent has been determined to be $\nu \sim 1.65$.[18] Setting $\nu = 3$ and taking μ_0 to be the viscosity of dodecane at room temperature, eq 2 predicts a time scale on the order of 10^{-8} s.

Resultant viscous flow of solvent into or out of the confined spaces of the planar bilayer introduces another time scale that, in addition to the viscosity, is related to the bilayer thickness and diameter as well as the sustained pressure difference. Using the parameters in our experimental setup and simplifications regarding the bilayer geometry, this time scale is on the order of seconds. The observed averaged thickness changes we report have much larger duration times, signifying that the viscous flow through the deforming bilayer cannot be responsible for the observed transient effect.

■ EXPERIMENTAL METHODS

In these experiments, a thin layer of hafnium oxide ($\sim$9 nm) was deposited onto the silicon electrode via thermal atomic layer deposition (ALD) using tetrakis ethylmethylamino hafnium (TEMAH) and water in an Oxford Instrument OpAL ALD system. Then 100 cycles of TEMAH dose (2 s), N_2 purge (7 s), H_2O dose (0.1 s), and N_2 purge (8 s) were performed at 300 °C. The TEMAH precursor was held at 80 °C and delivered using 300 sccm Ar carrier gas. Ellipsometry measurements indicated that the resulting hafnium oxide film was approximately 9 nm thick. With this technique, the expected surface roughness of the generated film is approximately 1.5–3 Å. The dielectric constant of the film was also measured to be 17.

Two cleaved pieces of wafer were positioned parallel to each other, with the hafnium oxide surfaces facing inward, spaced 600 μm apart. The parallel surfaces were submersed in dodecane with 10 mM sorbitan monooleate, and a small water drop ($\sim$1–2 mm diameter) was deposited between the two parallel surfaces (Figure 2). A nanoscale oil layer
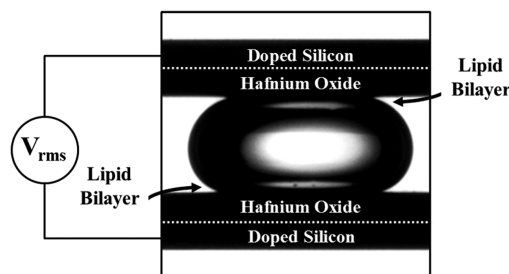

Figure 2. Experimental setup used to measure the thickness of the lipid bilayer. A water drop was placed between two parallel pieces of a doped silicon wafer coated with a thin film of hafnium oxide. The entire setup was submersed in dodecane. A voltage was applied between the two conductive silicon layers, and the thickness of the lipid bilayer was measured from the capacitance of the system, the capacitance of the hafnium oxide film, the relative permittivity of the oil, and the base width of the water drop.

autonomously formed between the surface of the water drop and the hafnium oxide under these conditions. We refer to this thin oil film as a lipid bilayer because it consists of two layers of adsorbed surfactant molecules (sorbitan monooleate) coating the oil–water and oil–hafnium oxide interfaces.

In our setup, two identical lipid bilayers formed between the top and bottom surfaces of the water drop and the hafnium oxide films. The mirror symmetry in this setup allows the measurement of the bilayer properties to be more precise than in a setup containing only a single lipid bilayer where the water drop is charged relative to a ground electrode. This two-bilayer setup eliminates any uncertainties introduced into the experiment by the work function of an electrode contacting the water drop or the electrical charging and discharging of the water phase.

In addition to supporting the formation of a stable lipid bilayer on its surface, the hafnium oxide film also provides electrical stability during these experiments. The lipid bilayer is electrically fragile so that high electric fields cannot be applied solely across the bilayer without rupturing the membrane. However, the hafnium oxide provides an extra dielectric layer that prevents breakdown of the thin membrane and electrolysis.

This study focuses on the changes in thickness of this lipid bilayer over time in response to step increases and decreases in electrostatic pressure exerted on the film. When an electric potential is applied between the two silicon electrodes, the bilayer is subjected to an electrostatic pressure, which compresses the bilayer. However, the thickness of the bilayer is not the only voltage-dependent parameter; changing the voltage causes the contact angle with which the water drop wets the solid surface to increase or decrease because of the electrowetting effect.[19,20] Therefore, changes in electrostatic pressure caused an initial deformation of the shape of the water drop and a change in base area. This effect is limited to the first 1–2 s following a step change in voltage. No further change in shape occurred after the first 2 s, and the base area of the drop was assumed constant for the remainder of the experiment.

The thickness of the lipid bilayer was measured electrically; an Agilent LCR meter was used to measure the capacitance

across the hafnium oxide—lipid bilayer dielectric stack as well as the hafnium oxide film in air. The effective bilayer thickness was determined by modeling the hafnium oxide and lipid bilayer as two capacitors in series and calculating the resulting capacitance per area of the lipid bilayer (C_{oil}) using the following relation:

$$\frac{1}{C_{total}} = \frac{1}{C_{HfO_2}} + \frac{1}{C_{oil}} \tag{3}$$

where C_{total} is the capacitance per area of the lipid bilayer—hafnium oxide dielectric stack and C_{HfO_2} is the capacitance per area of the hafnium oxide film in air. The average thickness of the bilayer can be estimated using the dielectric constant of dodecane ($\varepsilon_{oil} = 2.1$) with the following relation:

$$C_{oil} = \frac{\varepsilon_0 \varepsilon_{oil}}{t_{oil}} \tag{4}$$

where ε_0 is the permittivity of vacuum, t_{oil} is the temporal and spatial average thickness of the lipid bilayer, and C_{oil} is the bilayer capacitance per unit area (Figure 3). This approach is
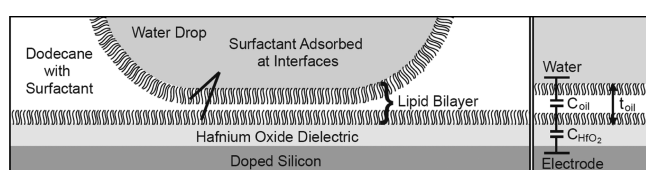

Figure 3. Electrical diagram of a single lipid bilayer within the experimental setup. The lipid bilayer functions as a capacitor in series with the thin hafnium oxide film.

used for each system to obtain the effective thickness of the lipid bilayer at a given voltage. For consistency, droplet diameter measurements were conducted before and after each measurement on the top and bottom electrodes.

Capacitance measurements of the hafnium oxide—lipid bilayer stack were recorded every few seconds for several minutes following a step change in applied voltage as the lipid bilayer transitioned from one equilibrium thickness to another. AC voltages (20 Hz, sinusoidal) were used for these experiments; the peak voltage alternated between 0.5 and 1.0 V. Because the mirror-image setup contains two identical

hafnium oxide—lipid bilayer stacks, the effective voltages applied across a single stack were half of these values (0.25 and 0.5 V).

The bilayer thickness does not vary significantly with the frequency of the ac voltage waveform, except under very low frequencies when charge leaks through the bilayer and reduces the electrowetting effect. Although the thickness of the lipid bilayer is not significantly frequency-dependent, higher frequencies allowed for more stable capacitance readings at higher electric fields. An ac voltage waveform (100 Hz, sinusoidal) was used to measure the steady-state thicknesses at different voltages. The thickness measurements presented in this study were recorded at a sufficiently high frequency to produce stable, unfluctuating electrostatic compression across the bilayer for the range of electrostatic pressures presented.

■ RESULTS

The bilayer under investigation was formed from 10 mM sorbitan monooleate in dodecane and was confirmed to exhibit a pressure-dependent thickness under a steady-state condition (Figure 4). It self-assembles between a hafnium oxide film and a water droplet when the water is placed on the substrate in a surfactant-rich dodecane environment. The hafnium oxide film allows for high electric fields to be applied across the lipid bilayer without inducing electrical breakdown, enabling measurements of equilibrium bilayer thicknesses over a wide range of electrostatic pressures. Figure 4A shows equilibrium thicknesses of the bilayer resulting from different electric fields applied across the bilayer. As the applied electric field across the bilayer is increased, the bilayer thins out. Compression of the bilayer is fully reversible; the bilayer assumes a certain equilibrium thickness for a given voltage regardless of previously applied voltages short of electrical breakdown.

When the bilayer assumes its equilibrium average thickness for a given electrostatic pressure, the disjoining pressure arising from the repulsion between the adsorbed polymers within the bilayer is equal to and opposite the applied electrostatic pressure. The calculated average electrostatic pressure versus the bilayer thickness is provided in Figure 4B. Essentially, the electrostatic pressure squeezes the bilayer together, whereas a disjoining pressure pushes the two layers apart, as expected. If one attempts to estimate the observed disjoining pressure from
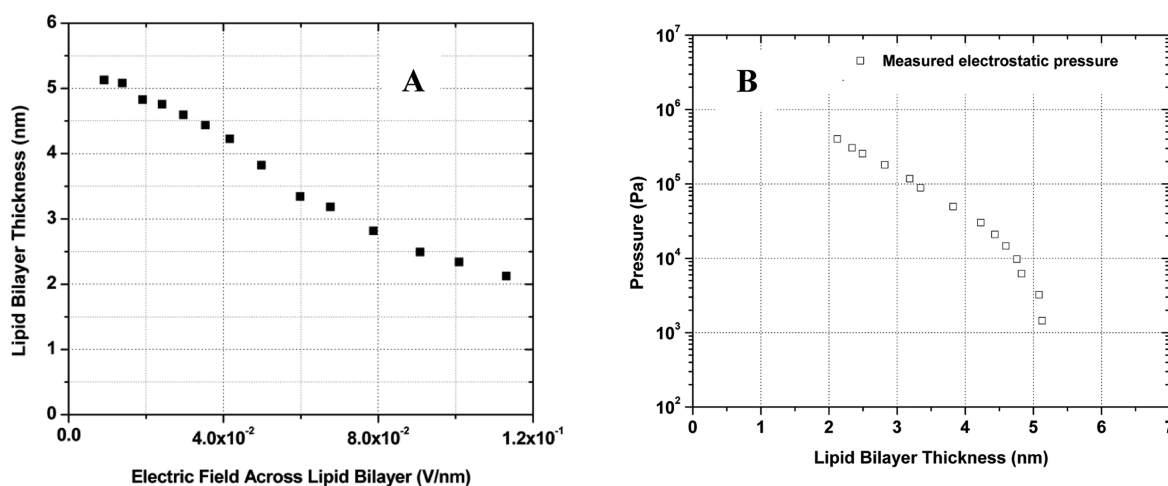

Figure 4. Quantifying the pressure-dependent nature of the lipid bilayer thickness. (A) Equilibrium bilayer thickness as a function of electric field applied across the bilayer. As the electric field increases, the bilayer thins. (B) Electrostatic pressure at equilibrium for a range of bilayer thicknesses.
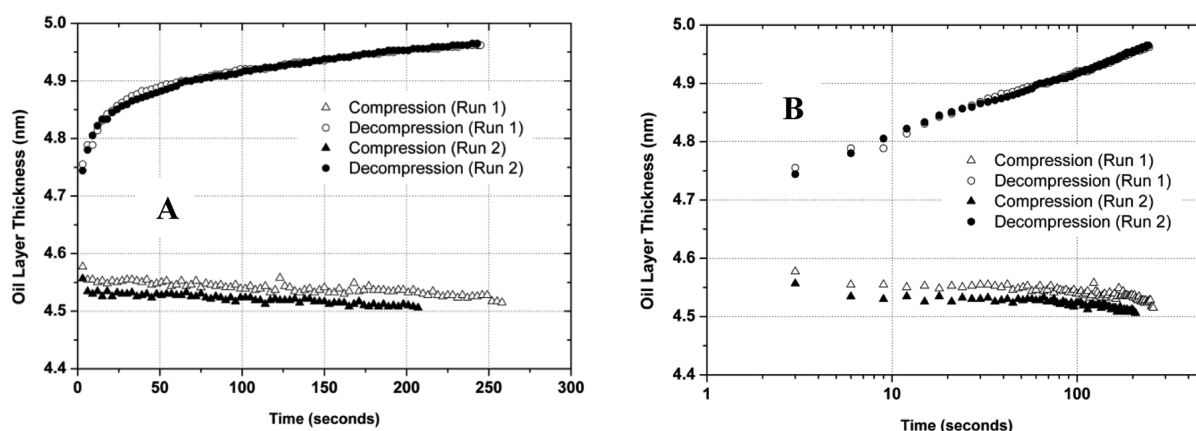
Figure 5. Transient thicknesses of the lipid bilayer during compression and decompression. (A) Linear plot of bilayer thicknesses versus time. During compression, the bilayer reaches its near-equilibrium thickness within the first few seconds and then gradually linearly decreases in thickness afterward. During decompression, the bilayer thickness increases logarithmically with time, slowly reaching its equilibrium height at the lower electrostatic pressure. (B) Logarithmic plot of the data presented in part (A). The decompression runs show a clear logarithmic trend.

deGenne's densely packed polymer brush repulsion,[21] an unrealistically low packing density of the surfactants in the bilayer is obtained. Using a sawtooth actuation system for this setup,[22] the packing density of surfactants is estimated to be ~6.75×10^{18} molecules/m^2. Accordingly, with a surfactant base area in the range of 30–50 Å^2, the two opposing interfaces of the bilayer are nearly packed.

Figure 5 shows samples of transient thicknesses of the bilayer during cyclic compression and decompression, induced by step changes in electrostatic pressure. The transient thicknesses reveal a distinct asymmetry in the compression and decompression responses. During compression, the bilayer reaches its near-equilibrium thickness within a matter of seconds and then slowly decreases in thickness linearly afterward. During decompression, when the voltage across the membrane is decreased, the bilayer thickness increases logarithmically with respect to time. The similarity between the two runs (performed back-to-back) illustrates the full reversibility of the bilayer compression and decompression and repeatability of the experiment.

◼ DISCUSSION

The different trends suggest an asymmetry in the mechanism of molecular interactions between the adsorbed molecules comprising the lipid bilayer during compression and decompression. We hypothesize that the interactions between the lipid tails affect the rate at which the two layers pull apart. Hydrodynamic effects cannot account for the asymmetric trends during compression and decompression, even when considering the viscoelectric effect, which describes modest changes in fluid viscosity when the direction of flow is perpendicular to the direction of the applied electric field.[23] Thus the dynamic changes in lipid bilayer thickness in response to pressure changes appear to depend upon the interactions of molecules within the polymer brush rather than the hydrodynamic effects of squeezing a thin liquid film.

A closer examination of the data presented suggests that the observed asymmetric behavior exists for both short and long responses of the bilayer for step changes in electrostatic pressure. In the experiments, the equilibrium thicknesses of the bilayer for the two final states are 4.5 and 5 nm. Accordingly, the total thickness change in both directions is ~5 Å. During the compression process, the bilayer collapses by approximately

4 Å within the first second before exhibiting a linear decline in thickness with time. In the opposite direction, the bilayer has an initial response thickness change of roughly 2 Å and then proceeds to a logarithmic increase in thickness with time. The dissimilarity of the initial responses in the two directions confirms that (1) hydrodynamics cannot be responsible for the initial responses of the bilayer, otherwise one would expect an analogous behavior given that the oil flow in this nanometer-size gap is Stokesian, and (2) if the hydrodynamic resistance in these conditions is discounted, the responses should be associated with the initial folding and unfolding or bonding and debonding of the attached polymer tails in the bilayer. Therefore, in the case of a step change in force, the polymer tails are more inclined to fold than to unfold.

In the long responses, the logarithmic increase during the decompression step indicates that an individual lipid tail in the bilayer should pass through an energy potential well to reach its final equilibrium configuration. During compression, on the other hand, the linear thickness decrease with time can be associated with the Brownian motion of the attached entangled tails. The data in Figure 5 can be used to corroborate these two assertions. One is reminded that the calculated thickness measurements are average values over the bilayer area. Therefore, at each time, the change in bilayer thickness should be proportional to the number of the polymer tails that shift from one equilibrium state to another. The transient bilayer thickness $h(t)$ may then be written in the form

$$h(t) - h_i = \pm \frac{\Gamma(t)}{\Gamma_o} \Delta l \tag{5}$$

where h_i is the bilayer thickness immediately after its short response, $\Gamma(t)$ the population density of configured polymer tails, Γ_o the total population density of the polymer tails, and Δl the effective distance over which the tails make random adjustments. The ± sign corresponds to the decompression and compression steps in the cycle. The transient thickness change during decompression may now be written as

$$\frac{t}{\tau} = \exp\left(\alpha \frac{\Gamma(t)}{\Gamma_o} \frac{\Delta l}{\lambda} \right) \tag{6}$$

where τ and λ are characteristic time and length scales, respectively, and α is a proportionality constant that should be

of order unity for Arrhenius-type reactions. Taking λ as the length scale that is related to the Brownian fluctuations of the confined tails, it can be estimated as the ratio of molecular kinetic energy over the force field difference $\Delta\Pi_e$ that is imposed for such a jump in the form $\lambda = k_BT/\Delta\Pi_e$. If the coefficient α is assumed to be unity and the net force field difference is calculated from the electrostatic pressure change, the average length of the molecular jump Δl during a decompression experiment can be deduced from the data in Figure 5B. With some algebra, one can show that $\Delta l \cong 2.6$ Å, very close to the total thickness change of the bilayer during a decompression step.

The empirical correlation for the thickness change during a compression step can be written as

$$h_i - h(t) = \frac{t}{\tau'} \tag{7}$$

with the characteristic time τ' related to the molecular vibrations of the tails in a viscous fluid. One can show the Zimm relaxation time calculated using the inferred polymer tail length and setting $\nu = 3$ will result in time scales much larger than the one deduced from the data. Such a calculation is for a free polymer chain, and the fact that the two time scales do not match is not entirely surprising. Alternatively, if one considers an attached polymer tail with length L whose open end travels in a viscous fluid for a total length $\Delta l'$, one can derive a time constant that is on the order of $L^2 \mu_o \Delta l'/k_BT$. If one uses the estimated value for L (~ 2.6 nm) and τ' from the reported data above, $\Delta l'$ can also be estimated for this case to be 0.05 Å. This calculated value is remarkably close to the observed thickness change during this transition.

The same authors of this paper have also recently conducted electrical interactions of the surfactant tails[24] using the same experimental setup that also supports the conclusions that these bilayers are indeed of uniform thickness and the tail–tail interactions are dominated by their Brownian motion.

The interpretation of the experimental data and its related analysis given above hinges to some extent on uniformity of the lipid bilayer thickness between the water drop and the insulated electrodes. Besides the edge effects that are neglected in our approach, several factors can disrupt the uniform thickness of the bilayers such as formation of micelles on the electrodes, instantaneous evolution of microsized oil drops under the water drop, and occasional nonuniformity of the HfO_2 layer. In all such cases during application of a voltage on the electrodes, the nonuniform thickness of the drop gives rise to an asymmetric electrostatic force on the water drop, making it become nonstationary. Accordingly, a steady state of the drop with the application of the voltage can occur only with a perfectly symmetric water drop sandwiched between an autonomously formed two-lipid bilayer.

We have also argued that the lipid bilayer in this study is in a quasi-equilibrium state with a temporal average estimated thickness. As discussed previously,[14] this system will reach a stable condition only if the driving voltage frequency is larger than 20 Hz. However, because of applied ac voltage across the bilayers, one concern would be how the voltage fluctuations would give rise to bilayer thickness fluctuations. If prominent, the thickness oscillations can induce a rippling effect of the droplet. There was no observable vibration of the drop when the measurements were conducted. To estimate such thickness fluctuations, we can use a first-order approximation of how the bilayer thickness $h(t)$ is also dependent on the applied voltage

frequency ω. To this end, we expand $h = h(t \pm \Delta t)$, where $\Delta t = 1/\omega$ is the time period of oscillations, in terms of Δt in the form

$$h(t \pm \Delta t) = h(t) \pm \left.\frac{dh}{dt}\right|_{t;\Delta t=0} \Delta t + HOT$$

The maximum thickness changes due to ac voltage could be estimated from the second term on the right-hand side of this expansion, $\Delta h \cong (dh/dt)|_{\omega\to\infty} (1/\omega)$. For $dh/dt = 0.01$ nm/s (from Figure 5) and $20 < \omega < 1000$, one can conclude that shifting thickness should be on the order of ≤ 0.005 nm. At the same time, the initial response of the bilayer in our setup in terms of the rate of change of thickness is on the order of 0.1 nm/s. With this rate, the thickness fluctuations are estimated to have a maximum of 0.05 nm. The calculated thickness fluctuations turn out to be two orders of magnitude smaller than the measured thicknesses and give credence to our experimental observations that the driving frequencies have a secondary effect on the tested bilayer thickness changes.

While the analysis in this section has provided additional support for the experimental data, one is cautioned in generalizing the findings of this work for all bilayers. Up to the present, despite many attempts, we have not been able to conduct experiments with other oil surfactants that could exhibit such distinct and well-defined asymmetric behavior. It would also be of interest to see if other techniques such as dual polarization interferometry and quartz crystal microbalance with dissipation monitoring can be used in similar setups to measure time evolution of the transient behavior of bilayers.

■ CONCLUSIONS

Surfactant tails have a variety of physicochemical properties that influence natural and synthetic processes. In this study, transient interactions of opposing surfactant tails in a lipid bilayer were deduced from thickness evolution of the bilayer subjected to an electrostatic pressure step function. The symmetric arrangement of the electrodes mitigated the effects of the electrical working potential that can often distort such measurements. In this setup, the cyclic tests comprised of changes of applied voltage from 0.5 to 1.0 V and vice versa. A step voltage increase resulted in a sudden thickness change on the order of 4.5 Å after which it was observed that the bilayer thickness decreases gradually and linearly with time to an eventual thickness change of 5 Å. This total change of thickness of 0.5 Å could be related to dissipative fluctuations of the surfactant tail in the base viscous fluid. This behavior might well characterize the folding or tangling mechanism of interacting tails. Tangled or folded tails, on the other hand, showed a remarkably different response. During the decompression step, the initial expansion turned out to be more restrained followed by a logarithmic increase in thickness that we could successfully relate to an unfolding/untangling jump due to thermal vibrations of the tails.

■ AUTHOR INFORMATION

Corresponding Author
*E-mail: Behrouz.Abedian@tufts.edu. Tel: 617-627-3012.
Notes
The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

conclusions, and recommendations are those of the authors and are not necessarily endorsed by the United States Government.

■ REFERENCES

(1) Horikoshi, S.; Akao, Y.; Ogura, T.; Sakai, H.; Abe, M.; Serpone, N. On the Stability of Surfactant-Free Water-in-Oil Emulsions and Synthesis of Hollow SiO_2 Nanospheres. *Colloids Surf., A* **2010**, *372* (1−3), 55−60.

(2) Wang, J.; Yang, F.; Tan, J.; Liu, G.; Xu, J.; Sun, D. Pickering Emulsions Stabilized by a Lipophilic Surfactant and Hydrophilic Platelike Particles. *Langmuir* **2010**, *26* (8), 5397−5404.

(3) Hurtley, S. M. Crossing the Bilayer. *Science* **2005**, *2*, 1451.

(4) Nohturfft, A.; Losick, R. Fats, Flies, and Palmitate. *Science* **2002**, *296*, 857−858.

(5) Nagle, J. F.; Tristram-Nagle, S. Structure of Lipid Bilayers. *Biochim. Biophys. Acta* **2000**, *1469*, 159−195.

(6) Mashangi, A.; Partovi-Azar, P.; Jadidi, T.; Nafari, N.; Maass, P.; Tabar, M.; Bonn, M.; Bakker, H. J. Hydration Strongly Affects the Molecular and Electronic Structure of Membrane Phospholipids. *J. Chem. Phys.* **2012**, *136*, 114705−114709.

(7) Bamberg, E.; Benz, R. Voltage-Induced Thickness Changes of Lipid Bilayer Membranes and the Effect of an Electric Field on Gramicidin A Channel Formation. *Biochim. Biophys. Acta* **1976**, *426*, 570−580.

(8) Srikoundinya, P.; Steckl, A. Voltage Control of Droplet Interface Bilayer Lipid Membrane Dimensions. *Langmuir* **2011**, *27* (2), 618−626.

(9) Toyama, S.; Nakamura, A.; Toda, F. Measurement of Voltage Dependence of Capacitance of Planar Bilayer Lipid Membrane With a Patch Clamp Amplifier. *Biophys. J.* **1991**, *59*, 939−944.

(10) White, S. H. Thickness Changes in Lipid Bilayer Membranes. *Biochim. Biophys. Acta* **1970**, *196*, 354−357.

(11) White, S. H. A Study of Lipid Bilayer Membrane Stability Using Precise Measurements of Specific Capacitance. *Biophys. J.* **1970**, *10* (12), 1127−1148.

(12) Gross, L. C. M.; Heron, A. J.; Baca, S. C.; Wallace, M. I. Determining Membrane Capacitance by Dynamic Control of Droplet Interface Bilayer Area. *Langmuir* **2011**, *27*, 14335−14342.

(13) Benz, R.; Janko, K. Voltage-Induced Capacitance Relaxation of Lipid Bilayer Membranes Effects of Membrane Composition. *Biochim. Biophys. Acta* **1976**, *455*, 721−738.

(14) Guha, I. F.; Kedzierski, J.; Abedian, B. Low-Voltage Electrowetting on a Lipid Bilayer Formed on Hafnium Oxide. *Appl. Phys. Lett.* **2011**, *99*, 024105-1−024105-3.

(15) Israelachvili, J. N. *Intermolecular and Surface Forces*, 3rd ed.; Elsevier: Waltham, MA, 2011.

(16) Zimm, B. H. Dynamics of Polymer Molecules in Dilute Solution: Viscoelasticity, Flow Birefringence and Dielectric Loss. *J. Chem. Phys.* **1956**, *24* (2), 269−278.

(17) De Gennes, P. G. Dynamics of Entangled Polymer Solutions. I. The Rouse Model. *Macromolecules* **1976**, *9* (4), 587−593.

(18) Perkins, T. T.; Quake, S. R.; Smith, D. E.; Chu, S. Relaxation of a Single DNA Molecule Observed by Optical Microscopy. *Science* **1994**, *264*, 822−826.

(19) Seyrat, E.; Hayes, R. A. Amorphous Fluoropolymers as Insulators for Reversible Low-Voltage Electrowetting. *J. Appl. Phys.* **2001**, *90* (3), 1383−1386.

(20) Mugele, F.; Baret, J.-C. Electrowetting: From Basics to Applications. *J. Phys.: Condens. Matter* **2005**, *17*, R705−R774.

(21) de Gennes, P. G. Polymers at an Interface: A Simplified View. *Adv. Colloid Interface Sci.* **1987**, *27*, 189−209.

(22) Kedzierski, J.; Barta, R.; Berry, S.; Guha, I.; Abedian, B. Validation of the Trapped Charge Model of Electrowetting Contact Angle Saturation on Lipid Bilayers. *J. Appl. Phys.* **2013**, *114*, 024901-1−024901-7.

(23) Andrade, E. N.; da, C.; Hart, J. The Effect of an Electric Field on the Viscosity of Liquids. III. *Proc. R. Soc. London, Ser. A* **1954**, *225*, 463−472.

(24) Guha, I. F.; Kedzierski, J.; Abedian, B. Electrical Conductance Across Self-Assembled Lipid Bilayers. *J. Appl. Phys.* **2013**, *113*, 54301-1−54301-5.

8474

dx.doi.org/10.1021/jp309796r | *J. Phys. Chem. B* 2013, 117, 8469−8474