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Kinetics for the Collapse of Trilayer Liquid-Crystalline Disks from a Monolayer at an Air–Water Interface

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Abstract

Unlike surfactants considered in previous studies, when phosphatidylcholine (PC) monolayers collapse at constant surface tension to form a 3D bulk phase, surface area decreases at rates that slow. The different kinetics could result from collapse by a distinct mechanism. Rather than the transfer of molecules all along the interface between the monolayer and bulk phase, PC films can collapse by the folding and subsequent sliding of a bilayer over the monolayer. By this mechanism, molecules can transfer to collapsed trilayers through a locus of constant size. In this article, we use the theory of nucleation and growth to show analytically that during collapse, the area can decrease at rates that decelerate when each individual structure grows through a region of fixed dimensions. We also show that binary films of 30% dihydrocholesterol (dchol) and dipalmitoyl phosphatidylcholine (DPPC), which have previously been shown to form a homogeneous monolayer from which trilayer disks grow through a point, collapse with rates of area decay that slow, in agreement with our analytical expressions.

1. Introduction

When monomolecular films at an air-water interface are held at constant surface tension (σ) below the equilibrium spreading tension (σ_e), area can change because of several processes. Films undergo a phase transformation to form a collapsed bulk phase that occupies less space at the interface than the monolayer. Under equilibrium conditions, collapse occurs at σ_e and limits access to lower σ . Monolayers, however, can reach σ below σ_e through nonequilibrium compressions. Area then changes both because of collapse and viscoelastic relaxations, which involve rearrangements of molecules within the monolayer. Constituents of the film might also evaporate or desorb, just as they would at $\sigma > \sigma_e$, and area would shrink accordingly. Collapse has traditionally been distinguished from these other processes by the manner in which area changes. Collapse has been considered to be the one process for which area decreases at rates that accelerate.^{1, 2}

Recent studies with insoluble films containing fluid phosphatidylcholines (PC) compressed to $\sigma < \sigma_e$ have demonstrated that area at constant σ decreases for prolonged periods at rates that slow,^{3–5} suggesting that in contrast to the traditional view collapse produces decelerating reductions in area. One possible explanation for the different kinetics is that for these films collapse proceeds by a nontraditional mechanism. In most films for which the kinetics of collapse have been studied previously, constituents transform at points along the interface between the monolayer and collapsed phase (Figure 1a); therefore, the rate of molecular transfer is proportional to the extent of the interface.^{6, 7} This process is similar to that of phase transitions in many bulk materials, for which transfer occurs all along the

interface between the two phases.⁸ Because in both cases the interface grows with time, the rate of transformation to the new phase increases. With PC films, for which collapse appears to produce a decrease in area that slows, the movement of constituents to the new phase may be restricted.

The bulk phase of hydrated PCs is a smectic liquid crystal, and monolayers of liquid-crystalline compounds can flow as a continuous lamella into collapsed bilayers through a narrow line or a point that may not enlarge as transformation proceeds (Figure 1b).^{9–18} Binary mixtures of dipalmitoyl phosphatidylcholine (DPPC) with dihydrocholesterol (dchol) form homogeneous films for which the liquid-crystalline collapse through a locus of constant size is particularly well documented. Microscopic images show that the collapse of 30% dchol/DPPC films initially forms bilayer disks on top of the monolayer. During compression and expansion, the collapsed structures grow and shrink by the transfer of molecules through a single point located at the edge of the disks.¹⁹ In this article, we first derive analytical expressions to determine if growth through the restricted locus should produce decelerating collapse. We then show that at constant $\sigma < \sigma_e$, the collapse of 30% dchol/DPPC films reduces the area at rates that slow and that fit the expressions obtained analytically.

2. Materials and Methods

DPPC (purity >99%) from Avanti Polar Lipids (Alabaster, AL) and 3 β -hydroxy-5 α -cholestane (dihydrocholesterol) (purity ~95%, Sigma Chemical Co., St. Louis, MO) were used without further characterization or purification. A mixture of chloroform and methanol (1:1 v/v) (Honeywell, Burdick & Jackson, Muskegon, MI) was used as a spreading solvent. Water was distilled and then filtered sequentially through mixed bed ion-exchange resins and organic free resins to deionize and remove organic impurities (Macropure, Ultrapure DI, and Organic Free Cartridges, Barnstead/Thermolyne, Dubuque, IA). *N*-2-hydroxyethylpiperazine-*N'*-2-ethane sulfonic acid (HEPES) (GibcoBRL brand, Life Technologies, Grand Island, NY), CaCl₂·2H₂O (J. T. Baker, Inc., Phillipsburg, NJ), and NaCl (Mallinckrodt Specialty Chemicals, Paris, KY) were purchased commercially and used without further analysis. Buffer used to suspend the bubble was filtered through 0.45 mm micropore filters (Millipore, Bedford, MA) to remove particulate contaminants.

These studies compressed films on a captive bubble apparatus described in previous publications.^{4,20,21} Our experiments used small volumes (~0.08 μ L) of 30% dchol/DPPC (mol/mol) solutions in chloroform/methanol (1:1 v/v) spread on air bubbles (100–120 μ L) floating in 150mMNaCl + 1.5mMCaCl₂ + 10mMHEPES, pH7.0 (HSC), below a dome of agarose gel. The spreading solvent was removed by exhaustive exchange of the subphase while the film was held at a constant surface tension of approximately 32 mN/m.²⁰ The films were then compressed and expanded by varying the hydrostatic pressure applied to the subphase using a stepper-motor-driven syringe pump (MBP 2000, Advanced Liquid Handling, Milwaukee, WI) to infuse and withdraw buffer from the chamber.⁴ Measurements of the bubble's height and diameter by a CCD camera allow calculations of surface tension and surface area.^{22,23} Buffer temperature was monitored with a thermistor probe (YSI, Yellow Springs, OH) and manipulated by a temperature controller (Cole-Palmer, Vernon Hills, IL) and heating pads (Minco, Minneapolis, MN) applied along the sides of the bubble chamber.

3. Theory

In this section, we first obtain a general mathematical expression for the variation of area during collapse at constant σ below σ_e . The model neglects effects of dissolution,

evaporation, adsorption, and viscoelastic relaxation of the film and assumes that area decreases only because of a single collapse mechanism that proceeds by nucleation and growth. We then consider the variation in kinetics that would occur for the same mechanism of growth but with two limiting forms of nucleation. Finally, we obtain a specific expression for the rates at which individual collapsed structures grow when the transfer of molecules occurs through a locus of constant dimensions.

3.1. Kinetics of Collapse Resulting from Nucleation and Growth

Derivations of the expressions for collapse presented here are based on theories developed for bulk materials (e.g., ref 8), adapted for the collapse of a 2D monolayer. The resulting equations are similar to those reported previously for specific forms of collapse^{6, 7, 24} but are derived in a manner that easily allows the consideration of general cases.

During the collapse of an insoluble monolayer at an air-water interface, the total interfacial area (A) consists of regions occupied by the monolayer (A_m) and collapsed structures (A_c) such that

$$A = A_m + A_c \quad (1)$$

The interfacial area is A_0 before collapse begins and A_∞ after collapse of the entire monolayer.

An expression for A as a function of time requires the relationship between A_m and A_c and their evolution as collapse progresses. Transfer of molecules between the two phases produces a decrease in A_m and an increase in the volume of the collapsed phase (V_c), related by

$$\rho dV_c = -\Gamma dA_m \quad (2)$$

where ρ is the molecular density of surfactant in the collapsed phase and Γ is the molecular surface concentration within the monolayer. Assuming that during the transformation ρ and Γ are constant, integration of eq 2 provides a relationship between the extent of monolayer and the collapsed phase,

$$V_c = sA_c = -\frac{\Gamma}{\rho}(A_m - A_0) \quad (3)$$

where s is a shape function that relates the volume and area occupied by collapsed structures and could be a function of time.

Collapse here was assumed to start with the formation of nuclei, an energy-activated process that results from statistical fluctuations in the monolayer^{6,7,25-27} and that could occur at defects, where the activation energy is lower. When nucleation is homogeneous, such that the probability of forming a nucleus is the same for all elements of the monolayer, or defects that lead to nucleation are randomly distributed over the interface, the number of nuclei formed at each instant is proportional to A_m and is expressed as IA_m , where I is the nucleation rate per unit area. Individual collapsed structures nucleate at different times (\hat{t}) and then grow. At a later time (t), the structures occupy a volume (v_τ) that is a function of ($t - \tau$). The number of nuclei created between times τ and $\tau + d\tau$ is then $IA_m d\tau$, and the increase in V_c that results from those nuclei at time t is

$$dV_c = IA_m v_\tau d\tau \quad (4)$$

After integration, a combination of eqs 2 and 4 yields the area occupied by the monolayer at time t ,

$$\frac{A_m}{A_0} = \exp \left[-\frac{\rho}{\Gamma} \int_0^t I v_\tau d\tau \right] \quad (5)$$

Combination of eqs 1, 3, and 5 yields

$$\frac{A}{A_0} = \left(1 - \frac{\Gamma}{\rho s} \right) \exp \left[-\frac{\rho}{\Gamma} \int_0^t I v_\tau d\tau \right] + \frac{\Gamma}{\rho s} \quad (6)$$

The shape function s assumes a simple form for the system considered here. The disks created by the collapse of 30% dchol-DPPC are uniform in thickness.¹⁹ Therefore, s can be taken as constant or approximately constant during the transformation. Equation 6 then becomes

$$\frac{A}{A_0} = \left(1 - \frac{A_\infty}{A_0} \right) \exp \left[-\frac{\rho}{\Gamma} \int_0^t I v_\tau d\tau \right] + \frac{A_\infty}{A_0} \quad (7)$$

which can also be expressed in terms of a normalized area (A^*),

$$A^* = \frac{A - A_\infty}{A_0 - A_\infty} = \exp \left[-\frac{\rho}{\Gamma} \int_0^t I v_\tau d\tau \right] \quad (8)$$

As collapse progresses, the proportion of area occupied by the collapsed phase grows, and individual structures impinge upon each other. As A_c increases, A_m diminishes, slowing the final speed of collapse. In the derivation of the collapse equation, A_m limits nucleation and growth through eqs 4 and 2, respectively. Combination of those equations therefore considers the slowing rates of collapse that occur at the end of any transformation.^{6, 8, 28}

The kinetics of phase transitions in 3D materials are commonly expressed in terms of the equation

$$1 - \zeta = \exp(-k_n t^n) \quad (9)$$

where ζ is the fraction of material transformed to the new phase, k_n is a constant, and n is a real number. Different mechanisms for the transformation are reflected in variations of n . The comparable expression for collapse would be

$$A^* = \exp(-k_n t^n) \quad (10)$$

The integral in the exponential term of eq 8 does not necessarily reduce to the single term $k_n t^n$. After expanding the integral in a series of the form $\sum_{p=1} k_p t^{(pn)}$, where p is an integer, if only the leading term is considered, then eq 8 can be approximated by eq 10 at small times. In the analysis of experimental data, values of n can then be used to identify different mechanisms of collapse. When $n > 1$, rates of area decay accelerate, but when $n = 1$, area decreases during the entire transformation with rates that slow.

3.2. Rates of Nucleation

The temporal dependence of I , the rate of nucleation, affects the kinetics of collapse. Here we consider the two limiting cases of progressive and instantaneous nucleation.^{6, 8} Progressive nucleation occurs when nuclei form during the entire process. Each point of the monolayer has the same probability of developing a nucleus, and that probability does not

change with time, resulting in a constant I . The number of nuclei formed at each instant is then proportional to A_m . Instantaneous nucleation, in contrast, occurs when nuclei form only at the beginning of the transformation, such that $\tau = 0$ for each nucleus, and no nucleation occurs at subsequent times. For that case, $I = I_0\delta(0)$, where δ is the Dirac delta. Even for the same mechanism of growth, these two limiting cases of nucleation result in different kinetics of collapse.

A close look at the collapse equation (eq 8) shows that, regardless of the manner in which nuclei grow, slowing rates of area decay, with $n > 1$ in eq 10, cannot be obtained in the initial stages of collapse with progressive nucleation. This point is evident if we express the volume of individual structures as a series expansion

$$v_\tau = \sum_{p=1} \beta_p (t - \tau)^{pm} \quad (11)$$

where β_p are constant coefficients and m is a positive real number. For the case of progressive nucleation, where I is constant, the integral in the exponential term of eq 8 gives

$$\int_0^t I v_\tau d\tau = I \left[\sum_{p=1} \frac{\beta_p}{pm+1} (t)^{pm+1} \right] \quad (12)$$

At small times, where higher-order terms can be ignored, $n = m + 1 > 1$, resulting in accelerating rates of collapse. In contrast, if nucleation is instantaneous, then $I = I_0 \delta(0)$, and

$$\int_0^t I_0 \delta(0) v_\tau d\tau = I_0 \sum_{p=1} \beta_p t^{pm} \quad (13)$$

Equations 12 and 13 show that, as with the transformation of bulk materials, instantaneous and progressive nucleation produce values of n that differ by 1.^{6, 8, 29} Equation 13 also shows that for instantaneous nucleation $n = m$ could be less than or equal to 1, and the decrease in area could slow.

3.3. Rates of Growth for the Transfer of Molecules through a Single Point

The rate at which individual collapsed structures grow is limited by how fast molecules can transfer from the monolayer. By analogy to the transformation of bulk phases, the driving force for collapse is the difference in the molecular free energies between the two phases, which in this case is equal to the difference in the chemical potentials, $\Delta\mu$, between the monolayer and collapsed phase. During a phase transition and in the absence of any other irreversible process, molecules move to the phase with lower free energy.³⁰ A usual assumption is that ϕ , the flux of molecules that transfer to the new phase with flux defined as the rate of molecular transfer per interfacial unit, is a linear function of the driving force.^{31,32} For bulk materials at constant temperature, this assumption results in a constant rate of radial growth for spherical particles, and has been successfully employed to predict the kinetics of many phase transitions.³³ For collapse at constant σ , a reasonable assumption for any mechanism is that when no other effect opposes the growth of the collapsed phase, ϕ from the monolayer to each collapsed structure is constant.

Rates of molecular transfer to each individual collapsed structure, \dot{n}_i , depend on the extent of the interface at which transfer occurs. Previous models^{6,7} have considered transfer that occurs all along an interface of length l , and the flux, $\phi = \dot{n}_i/l$, was assumed to be constant.

The growth of structures then produces an increase in \dot{n} , which leads to accelerating decreases in area.

When collapsed disks grow through a region of the interface that has dimensions that remain unchanged (Figure 1b), both ϕ and \dot{n} would be constant. The disks will grow to accommodate the molecules that enter, and assuming that the liquid-crystalline phase is incompressible,

$$\dot{n} = \rho \dot{v}_\tau \quad (14)$$

Integration of eq 14 yields

$$v_\tau = \frac{\dot{n}}{\rho}(t - \tau) \quad (15)$$

For instantaneous nucleation, the decrease in interfacial area from collapse, obtained by combining eqs 8 and 15, is

$$A^* = \exp\left[-\frac{I_0 \dot{n}}{\Gamma} t\right] \quad (16)$$

Unlike previous models of collapse^{6,7} at constant σ below σ_c , eq 16 predicts an exponential decay of A^* with time and therefore a decrease in area that slows during the entire transformation. Progressive nucleation could also produce an exponential decay in A^* if collapsed structures that enlarge according to eq 15 at some point stop growing. Microscopic studies indicate that the growth of disks formed above dchol-DPPC monolayers can terminate.¹⁹ A simple model for this situation considers structures that grow only for a period t_1 after nucleation. The initial stages of collapse at $t < t_1$ would then correspond to an accelerated decrease in area of

$$A^* = \exp\left[\frac{I \dot{n}}{2\Gamma} t^2\right] \quad (17)$$

Although some structures stop growing at $t > t_1$, new ones appear. The argument of the exponential function in eq 8, with v_τ given by eq 15 and I , \dot{n} , and Γ being constant, then becomes

$$-\frac{I \dot{n}}{\Gamma} \left[\int_0^t (t - \tau) d\tau - \int_{t_1}^t (t - t^*) dt^* \right] = -\frac{I \dot{n}}{\Gamma} \left[t_1 t - \frac{t_1^2}{2} \right] \quad (18)$$

Therefore,

$$A^* = \alpha \exp\left[-\frac{I \dot{n} t_1}{\Gamma} t\right] \quad \text{for } t > t_1 \quad (19)$$

where α is a constant that results from the second term of eq 18. Progressive nucleation followed by growth that stops, as well as instantaneous nucleation, could produce slowing decreases in area.

4. Experimental Results

A comparison of the decay in area predicted by eq 16 with experimental results requires measurements of collapse at constant $\sigma < \sigma_c$. Because films of 30% dchol-DPPC form trilayer disks that grow through a point,¹⁹ we use those films for our measurements. Prior to

other measurements, we determined σ_e . After compression to a σ at which a fast decrease in area indicated the onset of collapse, the interfacial film was allowed to relax at constant area to equilibrium. At 26 °C, σ_e for the DPPC–dchol mixture was 21.5 ± 0.1 mN/m.

For the experiments reported here, the DPPC-dchol monolayers at 26 °C were compressed from just above σ_e to 18.1 mN/m. Surface tension was then held constant while surface area fell. Initial rates of area decrease, measured as $1/A \, dA/dt$ between 0 and 5 min, were $-0.011 \pm 0.008 \, \text{min}^{-1}$. Plots of interfacial area versus time at 18.1 ± 0.2 mN/m (Figure 2), recorded in some cases for over 12 h and through more than a 50% reduction in area, had positive curvature at all times. Just after σ reached a constant value, the area decreased at a rate that was rapid but then slowed gradually. Comparing these results with analytical expressions requires the calculation of the normalized area, A^* , for which we assumed that the monolayer transformed completely to a trilayer and that A_∞ equaled $1/3 A_0$. Plots of $\ln(A^*)$ as a function of time showed that after an initial period, area decreased exponentially (Figure 2). The slope of the linear portion of the $\ln(A^*)$ versus t curves was $(-4 \pm 2) \times 10^{-4} \, \text{min}^{-1}$ (mean \pm standard deviation for seven experiments), and r^2 for each linear fit was greater than 0.98. Although the rates at which area decreased varied among individual measurements, experiments consistently demonstrated that area decreased with slowing rates for prolonged periods and that after an initial faster decrease the decay became exponential.

5. Discussion

Unlike most monolayers studied previously,^{2,6,7,34} at constant $\sigma < \sigma_e$, the area of at least some fluid PC monolayers decreases at slowing rates. This behavior raises the possibility that PC films collapse through a distinct mechanism. We show here that, in contrast to collapse that occurs along an expanding interface, the formation of a liquid-crystalline phase by the transfer of molecules through a region of invariable dimensions can result in a decrease of area at rates that slow. Our theoretical analysis agrees with kinetic measurements on DPPC–dchol films that collapse through a point.

Restricted collapse is not the only process that at constant σ could contribute to an interfacial area that decreases at decelerating rates. Following any dynamic compression, including those at surface tensions above σ_e where collapse does not occur, viscoelastic relaxation produces a decaying change in area.³⁵ That process, however, usually lasts less than tens of minutes^{2, 4} and produces changes in area that are quite limited. Experimental results for DPPC–dchol monolayers at constant σ show an initial rapid decrease in area, followed by a slower decrease at rates that diminish for more than 12 h (Figure 2). We attribute the initial rapid change in area to viscoelastic relaxation and the subsequent slower changes to collapse.

Transformation by any mechanism also slows during its later stages. The shrinking monolayer provides fewer sites for nucleation. The enlarging nuclei encounter each other, and the resulting impingement slows growth. Consequently, even transformations that initially accelerate eventually slow. Our analysis shows that for collapse through a region of constant dimensions, area can decrease with slowing rates during the entire transformation. Following instantaneous nucleation, when only growth affects the rate of transformation, the area of individual isolated nuclei would increase as a linear function of time. Impingement of the randomly spaced nuclei, however, slows the transformation, which proceeds linearly only for the earliest portions of the exponential decay (eq 16).

Area cannot decrease at rates that slow throughout the transformation by traditional mechanisms. If molecules transfer from the monolayer to the collapsed phase at any point

along the interface (Figure 1a), then the radius of collapsed trilayer disks at constant σ would grow at a constant rate.⁶ The kinetics of transformation that result from this growth, expressed as an exponential function in the form of eq 10, gives $n = 2$; therefore, area would decay at rates that accelerate. The analysis presented here, in contrast, shows that when transfer to each disk occurs through a restricted locus with constant dimensions, A^* can decay exponentially ($n = 1$), in agreement with experimental results for DPPC-dchol (Figure 2).

The model of growth through a fixed region, eq 15, predicts exponential decay, eq 16, only under specific circumstances, such as with instantaneous nucleation. Because defects usually reduce the activation energy necessary to form a nucleus, instantaneous nucleation generally occurs at these points. Previous studies demonstrate that the formation of an initial fold requires a large activation energy and that therefore nucleation is more likely to occur at defects.^{10,36} For collapse of DPPC-dchol, instantaneous nucleation is then a reasonable possibility.

Nucleation that is progressive could also produce slowing rates of collapse if the collapsed disks stop growing. When collapse occurs through a restricted point (Figure 1b), the viscous dissipation caused by both the sliding of the bilayer on top of the monolayer and the rearrangement of molecules within the disk would become more important as disks enlarge and slow the growth of individual collapsed trilayers. At some point, roughness on a molecular scale could bring further growth to a halt. Although the dissipation would probably produce rates of growth that decrease gradually, rather than the abrupt change considered here, the simple analysis that leads to eq 19 effectively shows how the cessation of growth could affect the kinetics of collapse. Our model predicts that initially, when all the disks are growing according to eq 15, the decrease in area would accelerate. The kinetics would change to a decelerating process only after the interval t_1 , required for the disks to reach the point at which growth stops. Experimentally, if the time for viscoelastic relaxation is greater than t_1 , then the initial accelerating stage would not be observed. The change in area after t_1 , however, would still accelerate if growth occurs through a traditional mechanism. Although the pattern of nucleation in the DPPC-dchol monolayers, or in other films that undergo liquid-crystalline collapse, has not yet been determined, instantaneous nucleation or progressive nucleation with structures that stop growing both seem plausible.^{12, 13, 19} The model of liquid-crystalline collapse presented here, in which the transfer of molecules occurs through restricted loci, therefore provides a reasonable explanation for the observed slowing kinetics of collapse.

6. Concluding Remarks

Experimental measurements show that the collapse of homogeneous DPPC-dchol monolayers at constant σ reduces the interfacial area at rates that slow. Analytical expressions developed here demonstrate that transfer between the monolayer and a liquid-crystalline collapsed phase that occurs through a locus of constant dimensions (Figure 1b) can explain the observed decelerating changes in area.

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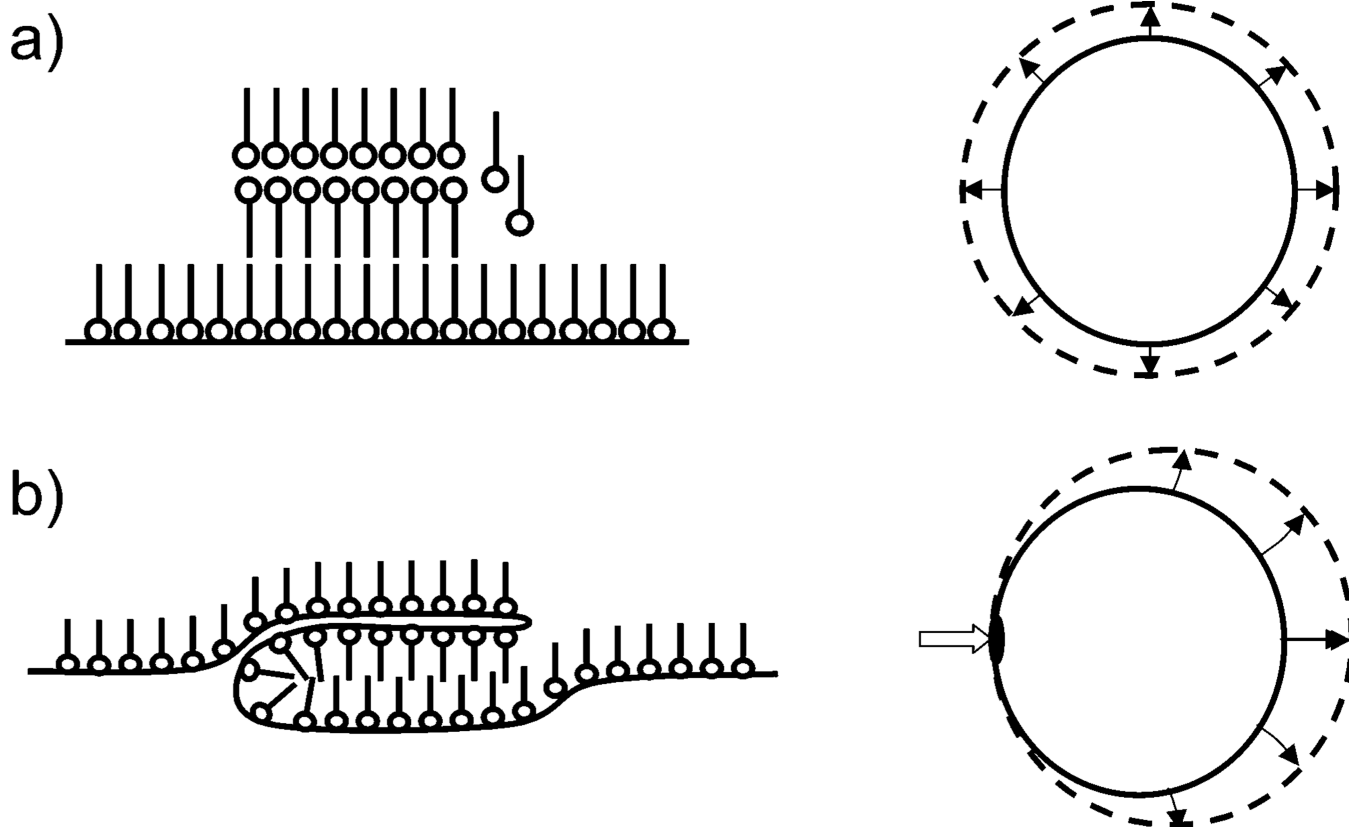


Figure 1. Mechanisms for the formation of trilayer collapsed structures. For the two mechanisms shown, the picture to the left represents a side view, and the right diagram gives the top view. Solid arrows indicate the direction of growth, and the thick white arrow in part b indicates the transfer of molecules. (a) Surfactant molecules detach from the monolayer and attach to the collapsed structure along its perimeter. (b) Collapse proceeds by the flow of continuous lamellae into the collapsed phase.

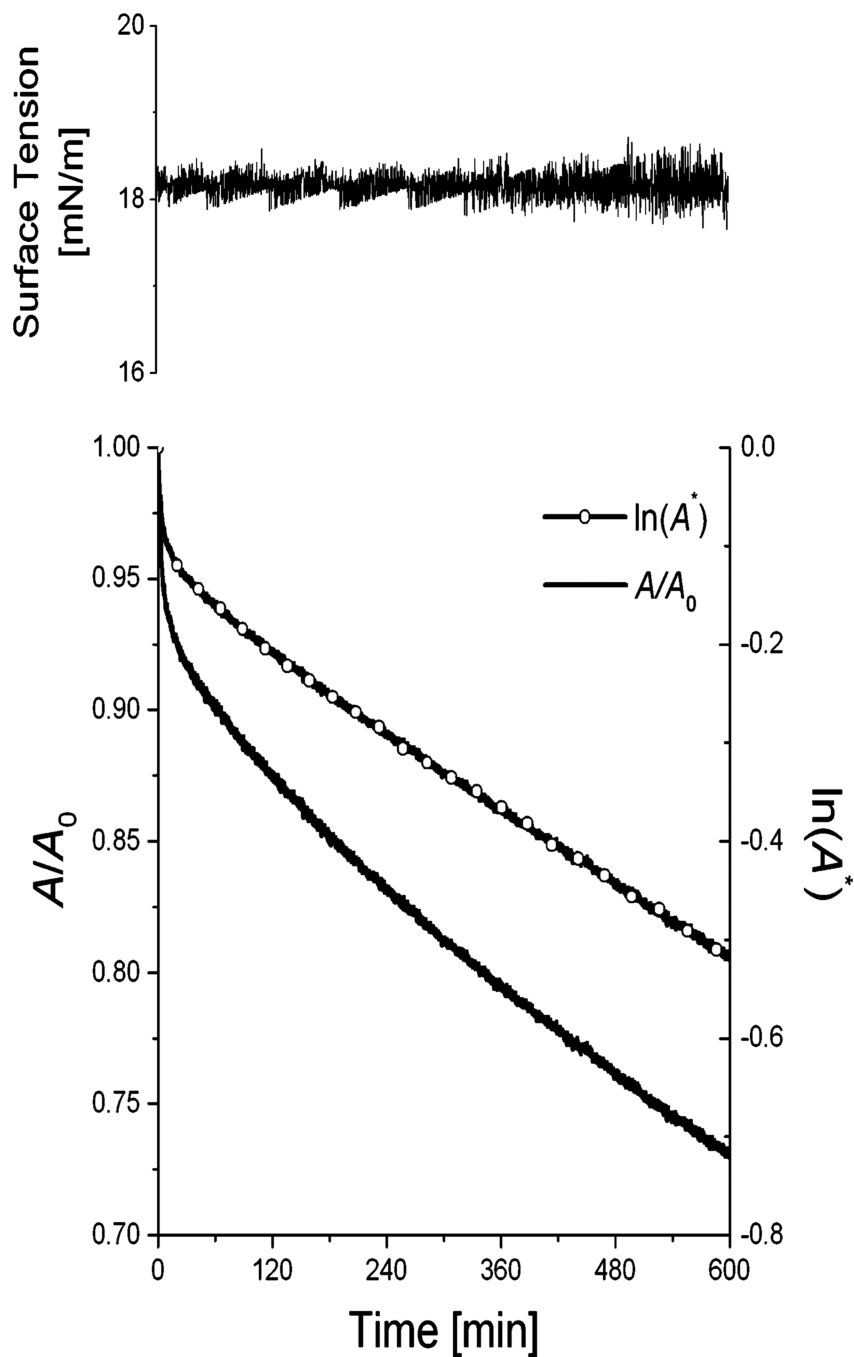


Figure 2. Decay in area observed during the collapse of DPPC–dchol monolayers. The measurements were performed at a constant σ of 18.1 ± 0.2 mN/m. Interfacial area decreases at rates that slow during the entire measurement, and after a faster initial decay, the normalized area, A^* , becomes exponential. Curves are representative of seven experiments.