Phase transformations in lipids follow classical kinetics with small fractional dimensionalities

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The kinetics of the gel-to-crystal phase transformation have been studied dilatometrically for lipid dispersions of 1,2-palmitoyl-*sn*-glycerol-3-phosphatidylcholine (DPPC). A new crystallization procedure is introduced in which the sample is first briefly quenched to form a small population of nuclei followed by jumping to temperatures at which negligible nucleation takes place but at which growth of nuclei occurs. Kinetic data obtained this way fit the classical Kolmogorov-Avrami relation very well over all measured times, up to 95% crystallization, but the effective dimensionality of the growing domains is only $n=1.0-1.3$. For the same system, differential scanning calorimetry shows that the data for the crystal-to-gel phase transformation are well fit with $n\sim 1.1$ and the data for the gel-to-ripple phase transformation are well fit with $n\sim 0.8$. Among the different possible causes of the small value of n for the two transformations involving the gel and crystal phases, the most viable focuses upon circular domains growing within each bilayer and the finite-size effects present in particular geometry of lipid dispersions. The fact that the gel-to-ripple transformation has a pronounced one-dimensional character accounts for its n value being even smaller.

I. INTRODUCTION

Biological lipids in water form bilayers which are the basic structures of biomembranes.[1] In the most easily prepared and common model system the bilayers aggregate to form multilamellar dispersions which consist locally of stacks of bilayers separated by fairly uniform layers of water. These multilamellar vesicles are typical smectic-liquid-crystal systems. As the temperature is lowered, the chemically pure, prototypical lipid DPPC undergoes a main transition at 41.4 °C ($\Delta H/R_{\rm gas}=4000-5000$, $\Delta V/V=0.037$) (Ref. 2) from a fluid (F) phase in which the hydrocarbon chains are disordered to a ripple (R) phase in which the chains are more ordered but in which there is a periodic rippling of the bilayers.[3] Next, a "pretransition" occurs at 34 °C ($\Delta H/R_{\rm gas}\sim 500$, $\Delta V/V=0.003$) from the R phase to a gel (G) phase which has no ripples. Next, a subtransition occurs at 13.8 °C ($\Delta H/R_{\rm gas}=2000-2500$, $\Delta V/V=0.017$) (Ref. 4) from the G phase to a more crystalline (C) phase in which the hydrocarbon chains become positionally more ordered. All phases, F, R, G, and C, are smectic phases, but the water layer becomes smaller as the temperature is lowered through each transition.[5]

The original goal of this research was to find procedures for preparing the most perfect C phase, as will be discussed in Sec. IV. When our new procedure described in this paper was used, kinetic data for the GC-phase transformation form the G phase to the C phase could be fit very well over the entire range by the classical Kolmogorov-Avrami relation,[6-9] as is shown in Secs. IV–VI. This relation is briefly reviewed in Sec. III. However, the fit requires small fractional values of the parameter n, which in the theory is supposed to be the dimensionality of the growing domains. After presenting our results in Secs. IV–VI possible explanations for the small value of n are discussed in Sec. VII.

II. EXPERIMENTAL

Dilatometry was performed using a home-built instrument previously described.[10] The instrument was operated in a quench mode in which the temperature was lowered as rapidly as possible to a quenching temperature T_Q and then held constant while volumes were measured as a function of time. The thermal equilibration time for the apparatus, in contrast to the sample, was about one hour after the typical quench. Differential scanning calorimetry (DSC) was performed with a Microcal MC-1 calorimeter (Microcal Inc., Amherst, MA 01002) with heating rates R ranging from 1.3 to 88 deg/h. Fraction of conversion was obtained by integrating the excess specific heat, thereby giving an excess enthalpy, after subtracting a smooth base line fitted to the data well outside the transition region.

DPPC (1,2-palmitoyl-*sn*-glycerol-3-phosphatidylcholine) was obtained in lyophilized form from Avanti Polar Lipids (Birmingham, AL). Lipid purity was judged to be excellent from the small width of the main transition ($\sim 0.1°$). Dispersions were prepared by drying the lipid in a vacuum oven at 65 °C overnight, weighing, adding distilled and deionized water, and then repeatedly raising and lowering the temperature between 60 and 0.1 °C while vortexing vigorously. For dilatometry the samples consisted of about 1 g of lipid in about 10 g of water and the samples were degassed. For this sample mass the sensitivity of the dilatometer corresponds to 0.1% of the volume change of the CG phase transition. For calorimetry the samples averaged 30 mg of lipid in about 0.9 g of water. The sensitivity of the calorimeter is 5×10^{-5} cal/deg. This may be compared to maximum

excess specific heats for the CG and GR transitions in these samples of about 0.05 cal/deg.

III. THEORY

The classical theory considers a model for phase transformations that initially consists of a fixed number N of randomly distributed nuclei each of which would proceed to grow to a volume $V_1(t)$ at time t if it did not meet another domain. The complication of domains meeting is accommodated in the following equation[8] by the factor $[1-X(t)]$:

$$dX/dt = N[1-X(t)]dV_1/dt \ , \tag{1}$$

where $X(t)$ is the fraction of sample transformed to the new phase. Equation (1) is easily solved to yield

$$X(t) = 1-\exp[-NV_1(t)] \ . \tag{2}$$

It is often supposed that a single domain will grow so that its radius increases linearly with time, corresponding to the equal probability of phase conversion any place on the domain surface. For reasonably smooth domains this leads to

$$V_1(t) = gr^n = gu^n t^n \ , \tag{3}$$

where u is the radial growth rate, g is a geometrical factor which would be $4\pi/3$ for spheres, and n is the effective dimensionality of the growing domain. The result of combining Eqs. (2) and (3),

$$\begin{aligned} X(t) &= 1-\exp(-Ngu^n t^n) \\ &= 1-\exp\{-[t/\tau(T)]^n\} \ , \end{aligned} \tag{4}$$

has been known for many years[6-8] and a different, completely rigorous, derivation was supplied by Evans.[9] [It might also be noted that, before learning of this classical theory, which is usually just called the Avrami theory, we had performed computer calculations (Fig. 2) that also are fit well by Eq. (4).] It has also been shown that if nucleation continues at a steady rate in the untransformed phase during the course of growth, then n should be replaced by $n+1$.[6,8,9]

One potential use of Eq. (4) was to determine whether the GC transformation takes place primarily within each bilayer, in which case one would expect the dimensionality n to be 2, or if the bilayers in these more ordered phases have strong enough three-dimensional couplings for the C-phase domains to grow to adjacent bilayers, in which case one would expect n to be 3.

IV. RESULTS FOR THE GC PHASE TRANSFORMATION

The time dependence of the volume change after rapid quenching was measured. Previous studies[4] have obtained the total volume change for samples quenched for as long as eight months and this was used to convert the data to the fraction remaining, $1-X(t)$, in the G phase. The results are shown in Fig. 1. For quenching temperature $T_Q = 0.5\,^\circ$C the GC transformation began immediately within our quenching time resolution, but for higher

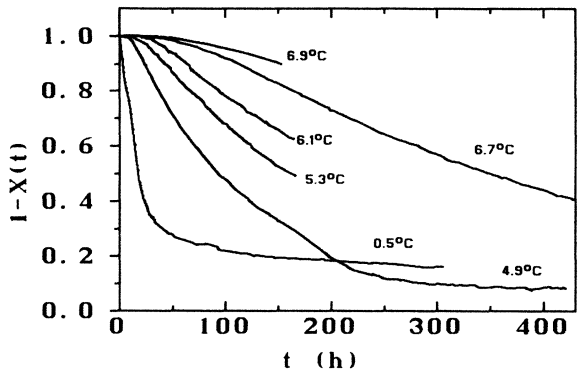

FIG. 1. Dilatometric measurements of the time dependence (in h) of the GC phase transformation for the quench temperatures T_Q indicated, where $1-X(t)$ is the fraction remaining in the G phase. Data for 0.5 and 4.9 °C are from Ref. 4.

$T_Q > 4\,^\circ$C, Fig. 1 shows an initial period during which there was very little GC transformation. This initial period is interpreted to be the time necessary for nuclei of the C phase to form. This was followed by a period of increased rate of GC transformation which is interpreted as the growth of the domains of the C phase.

After 300 h the extent of conversion for $T_Q = 0.5\,^\circ$C is less than for $T_Q = 4.9\,^\circ$C in Fig. 1. This has been interpreted[4] to be a consequence of the collisions between domains as they grow. The collision region would have a smaller density due to misorientation of the two colliding domains. For lower T_Q there are more nuclei so after all domains have grown and collided the average domain size is smaller and the total imperfect collision volume at the interface between domains is larger than when there are fewer nuclei for higher T_Q (See Fig. 2). Only after an extended period of time, longer than shown in Fig. 1,

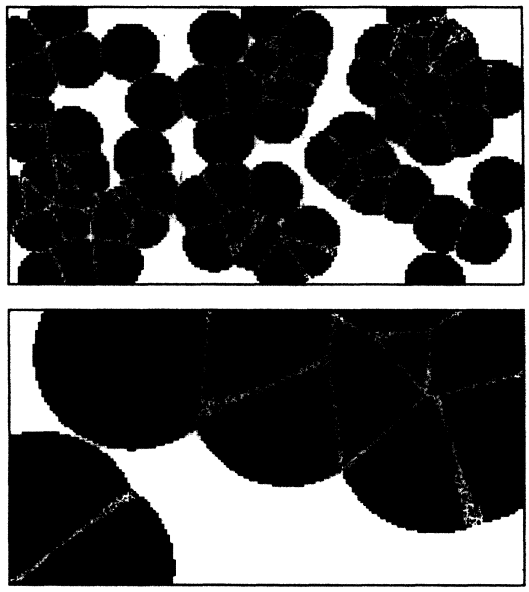

FIG. 2. Computer-generated domains with colliding region indicated. The fraction of conversion for both figures is 70%. (a) Lower T_Q; (b) higher T_Q.

does annealing of the microcrystallinity, i.e., increasing the density of the collision regions, take place. The results of fitting the data in Fig. 1 to Eq. (4) were rather poor, as would be expected if additional kinetic factors were present in the transformation that were not included in the theory. To fit the early times for the data taken at 4.9 and 6.7 °C required an n value ~ 2.7 and the later times required an n value smaller than 2. Some additional complications that may account for this will be discussed in Sec. VII. However, the microcrystallinity argument alone suggests that, to prepare the more perfect C phase, it is better to quench to the higher T_Q rather than to the lower T_Q, even though the initial rate of GC transformation is slower because to obtain simpler kinetics the slower process involving annealing of the collision regions should be minimized.

For quenching temperatures T_Q greater than 7 °C, no apparent GC transformation occurred for hundreds of hours after quenching, suggesting that the equilibrium phase transition temperature T_{CG} might be 7 °C. Once formed, however, the C phase does not transform back to the G phase until the temperature is raised above 13.8 °C. This latter temperature is actually the true equilibrium transition temperature T_{GC} as was originally shown by quenching samples at $T_Q < 7$ °C until the GC transformation was about half completed.[11] The temperature was then jumped to T_J between 7 and 13 °C and it was observed that the volume continued to decrease indicating that the C phase was the stable one and was growing at the expense of the metastable G phase. The reason for the lack of GC transformation in a freshly quenched sample with $7 < T_Q < 13$ °C is understood to be the very long time for nuclei of the C phase to form for such small amounts of undercooling.

The results in the preceding two paragraphs have led us to try a new way to prepare a more perfect C phase that would also provide kinetic data that are easier to analyze. This new way minimizes the colliding domain volume and it kinetically separates the nucleation step from the domain growth step. The sample is first quenched from the G phase to about 4–5 °C for several hours, during which time virtually no volume change takes place but during which the sample becomes seeded with nuclei. The temperature is then jumped to $T_J > 7$ °C at which temperature virtually no additional nucleation takes place and the volume decrease versus time is then measured. The data obtained this way should have a value of n representing the dimensionality of the domains in contrast to a value of $n+1$ if there were continuous nucleation as presumably occurs (but not necessarily with a constant rate) in the data in Fig. 1.

The data obtained using the new procedure are shown in Fig. 3. In preparation for taking the data shown in Fig. 3(a), the sample was cooled from the F phase to $T_Q = 4.5$ °C for 4 h and then jumped to $T_J = 8$ °C. After taking the data in Fig. 3(a) and in preparation for taking the data in Fig. 3(b) the sample was melted to the G phase, quenched to $T_Q = 4.1$ °C for 4 h, and then jumped to $T_J = 7$ °C. After taking the data in Fig. 3(b) the sample was requenched to 0.2 °C and an additional volume decrease was observed amounting to 5% of the decrease observed at 7 °C. In order to obtain the percentage GC transformation shown in Fig. 3(b), the total volume change was assumed to be the sum of the volume change at $T_J = 7$ °C and the additional 5% volume decrease at 0.2 °C. The total volume change obtained in this way was $\Delta V(\infty) = 0.0154$ ml/g which agrees within errors of the total volume change obtained from the samples incubated as long as eight months. In preparation for taking the data shown in Fig. 3(c) the sample was melted to the R

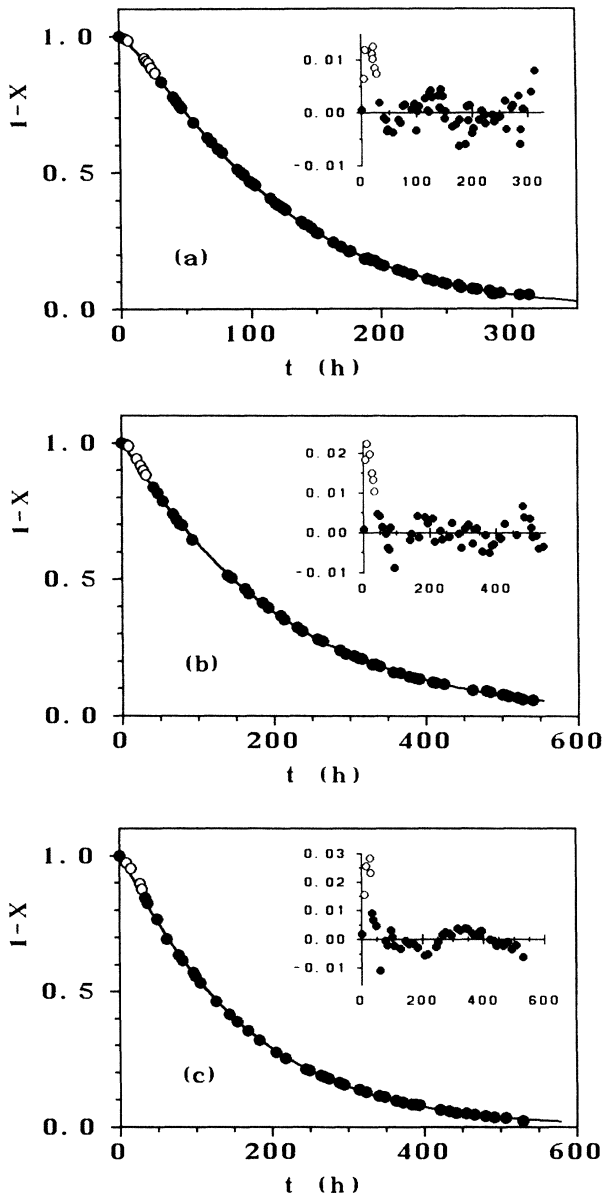

FIG. 3. The circles are data points for the fractional conversion from the G phase into the C phase vs time (h) using the new procedure. (a) $T_Q = 4.5$ °C for 4 h followed by $T_J = 8$ °C. (b) $T_Q = 4.1$ °C for 4 h followed by $T_J = 7$ °C. (c) $T_Q = 4.1$ °C for 7 h followed by $T_J = 10$ °C. The lines are the best fits to the data. The insets show the errors of the best fit to $1-X$ vs time. The distinction between open and solid circles is discussed in the text.

phase (37 °C), quenched to $T_Q = 4.1$ °C for 7 h, and jumped to $T_J = 10$ °C. After the data in Fig. 3(c) were taken, the sample was requenched to 1.2 °C and a small additional 2% volume decrease [and $\Delta V(\infty) = 0.0170$ ml/g] was observed which was used to obtain the fraction converted in Fig. 3(c).

The following formulas give the fits to the data represented by the solid lines in Figs. 3(a), 3(b), and 3(c), respectively:

$$\begin{aligned} &\text{(a) } 1 - X(t) = \exp(-0.0026 t^{1.23}) , \\ &\text{(b) } 1 - X(t) = \exp(-0.0035 t^{1.06}) , \\ &\text{(c) } 1 - X(t) = \exp(-0.0045 t^{1.06}) , \end{aligned} \tag{5}$$

where t is in hours. The early time data points indicated by the open circles in Fig. 3 were not used in the fits presented in Fig. 3. Whether or not these data points were used, their residual errors were positive for all three experiments. These positive, but small, deviations from Eq. (5) are consistent with a phenomenon observed before upon temperature jumping.[11] This phenomenon was interpreted as an initial, transient melting back of already formed C phase, perhaps due to the melting back of small domains and/or some dendritic protuberances with small radii of curvature becoming unstable at the higher temperature. The best fit obtained using these data points tends to increase n compared to the values given in Eq. (5), but by less than 0.1.

The best fits to the data with the constraint that $n = 2$ or 3 yielded mean-square fitting differences that were 300 and 1000 times greater, respectively, than those shown in Fig. 3. This demonstrates that the true value of n is considerably smaller than 2. The best fits to the data with the constraint that $n = 1$ yielded mean-square fitting differences that were, respectively, 37, 4.5, and 4.1 times as large as the best fit for unconstrained n for the data shown in Figs. 3(a)–3(c).

In Eq. (4) the coefficient of t^n has a factor of N, the number of domains formed at T_Q. For the three experiments shown in Fig. 3 this factor was not well controlled, so we do not think it is possible to obtain the growth rate u to high accuracy from the values of the coefficient of t^n given in Eq. (5). In a different experiment (data not shown) the sample was first quenched to 4.1 °C, then jumped first to $T_J = 7$ °C long enough to establish a rate of decrease in volume, followed by another jump to $T_J = 10$ °C. The fact that the rate of volume decrease changed very little after the second jump indicates that the growth rate u is fairly independent of T_J in the range 7–10 °C. From published results on other systems one expects a broad maximum in $u(T)$ at some temperature below the transition temperature[12,13] and our results are consistent with this occurring in the range 7–10 °C in our system.

V. RESULTS FOR THE CG PHASE TRANSFORMATION

We turn now to the CG-phase transformation which is considerably faster than the GC transformation, and our kinetic data are of a different sort. Differential scanning calorimeters employ a constant scanning rate $R_{\text{scan}} = dT/dt$. For heating scans this means that the apparent transition temperature of slow transitions will be elevated above the true equilibrium transition temperature. This is illustrated in Fig. 4 where the excess-specific-heat curve has been integrated once to give the excess enthalpy which is proportional to the fraction of sample that has been converted to the G phase. At the highest scanning rate shown in Fig. 4, the apparent transition temperature is over 10° higher than the equilibrium transition temperature.

The data in Fig. 4 can also be fit to a suitably extended Kolmogorov-Avrami–type equation.[14] Beginning with Eq. (2), one must recognize that the rate of increase $u = dr/dt$ in mean domain radius r will depend upon how much the sample is superheated. Assuming that all N nuclei of G phase are formed shortly after the true equilibrium transition temperature T_m is reached, this leads to

$$r(T) = \int_{T_m}^{T} u(T')dT'/R_{\text{scan}} = I(T)/R_{\text{scan}} , \tag{6}$$

where the last equality defines the integral $I(T)$. Together with Eq. (2) this yields

$$X(T) = 1 - \exp\{-Ng[I(T)/R_{\text{scan}}]^n\} . \tag{7}$$

The effective dimensionality n should then appear as the slope in a plot of $\ln\{\ln[1 - X(T)]\}$ versus $\ln(1/R_{\text{scan}})$ for any fixed temperature. Figure 5 shows such a plot for three temperatures for which the slope of n is about 1.1. Furthermore, if Eq. (6) is valid, then plots of R $\ln[1 - X(T)]^{1/n}$ as a function of temperature for different scan rates should be superposable. Figure 6 shows that this is indeed the case in the temperature range consisting of more than 5° of superheating. One possible reason that the curves are not superposed for lower temperatures is due to the breakdown of the assumption that all nuclei form shortly after the true transition temperature is reached. Another possible reason is that even our best-formed C phase was not perfect and there may be premelting below T_m.

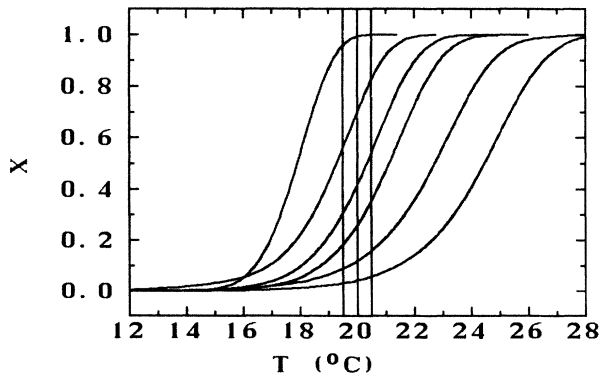

FIG. 4. Fraction of CG transformation as determined by integrating DSC traces for the subgel transition at scan rates of 1.3, 4, 7.5, 13, 34, and 88 °C/h,reading from left to right on the figure. The three vertical lines correspond to the three temperatures used in Fig. 5. Samples were incubated under the same conditions as the sample in Fig. 3(c).

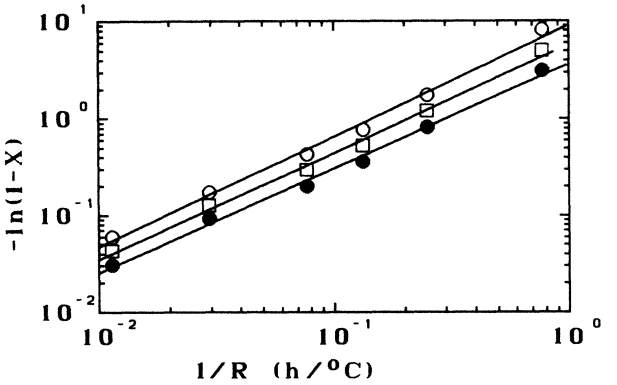

FIG. 5. Determination of n according to Eq. (7) at the three temperatures indicated in Fig. 4. Solid circle: $T=19.5\,^{\circ}\mathrm{C}$ and $n=1.08$. Open circle: $T=20.0\,^{\circ}\mathrm{C}$ and $n=1.10$. Open square: $T=20.5\,^{\circ}\mathrm{C}$ and $n=1.14$.

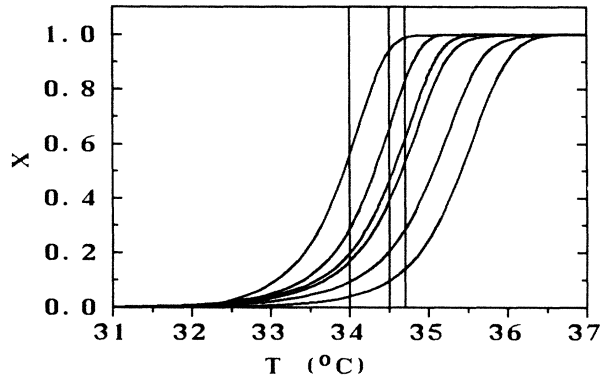

FIG. 7. Fraction of GR transformation as determined by integrating DSC traces for the pretransition vs temperature $T\,(^{\circ}\mathrm{C})$ at scan rates of 1.3, 4, 7.5, 13, 34, and 88 °C/h, reading from left to right on the figure. The three vertical lines correspond to the three temperatures used in Fig. 8.

VI. RESULT FOR THE GR PHASE TRANSFORMATION

The GR transformation from the G to the R phase has also been studied using DSC in exactly the same way as the CG transformation was studied in the previous section. The result for fraction of conversion as a function of temperature for different scanning rates is shown in Fig. 7. The plot of $\ln\{\ln[1-X(T)]\}$ versus $\ln(1/R_{\mathrm{scan}})$ is shown in Fig. 8 for three different temperatures with slopes $n=0.70$, 0.78, and 0.78, respectively.

VII. DISCUSSION

The first conclusion of this research is that the GC-, CG-, and GR-phase transformations follow classical Kolmogorov-Avrami growth kinetics, i.e., Eq. (4), very closely, with only two adjustable fitting parameters. This theory has previously been used extensively to fit crystallization kinetics for a variety of materials,[6,14–29] but it has not previously been employed to study lipid phase transformations nor, to our knowledge, has it been employed to study melting phase transformations for any system. For many systems, especially polymers, Eq. (4) only provides a good fit for early times when less than about 50% of the sample is crystallized because of the onset of various kinds of secondary effects that are not included in the classical theory.[16,17,25–29] Similarly, the kinetic data in Fig. 1 for quenches below 7 °C for long periods of time were not well fit by Eq. (4). However, adoption of our new experimental procedure for GC crystallization appears to minimize any secondary effects as evidenced by the fact that Eq. (4) fits the data in Fig. 3 extremely well from the shortest times to the longest times measured at which the phase transformation was about 95% complete. The key aspect of our experimental procedure is first to quench the sample to form nuclei followed by a jump to a temperature at which further nucleation is very slow compared to the duration of the experiment. This procedure effectively separates the primary nucleation process from the growth process and avoids any concerns over time (or degree of conversion) dependent rates of nucleation during the growth process.

The secondary conclusion of this research is that the effective dimensionality for the growth of domains is only

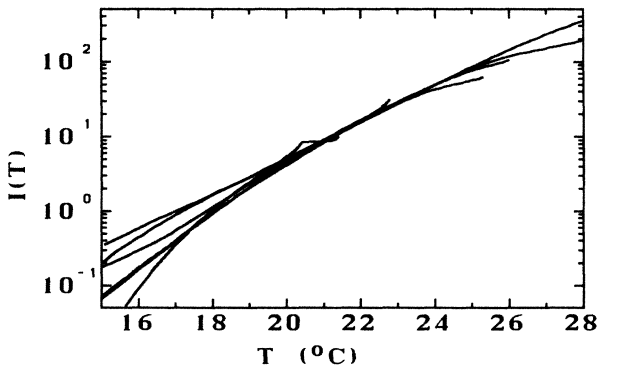

FIG. 6. Determination of $I(T)$ defined in Eq. (7) calculated from data of Fig. 4 using $n=1.1$ for various scanning rates.

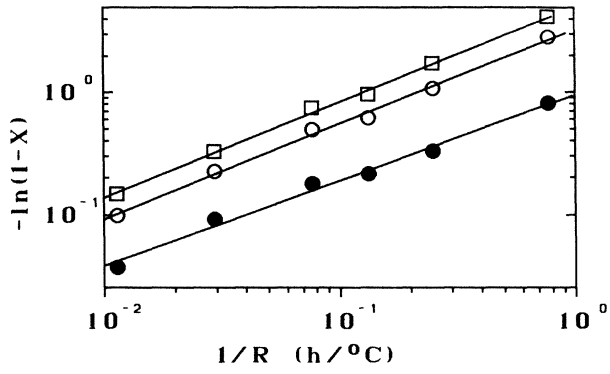

FIG. 8. Determination of n according to Eq. (7) at the three temperatures indicated in Fig. 7. Solid circles: $T=34.0\,^{\circ}\mathrm{C}$ and $n=0.70$. Open circles: $T=34.5\,^{\circ}\mathrm{C}$ and $n=0.78$. Open squares: $T=34.7\,^{\circ}\mathrm{C}$ and $n=0.78$.

$n = 1.0-1.3$ for the GC- and CG-phase transformations and only $n \sim 0.8$ for the GR-phase transformation. Although these effective dimensionalities n are far smaller than what one would naively expect from the theory, the goodness of the fit suggests that the theory is still relevant, and that some explanation for the small measured values of n should first be sought within the context of the general Kolmogorov-Avrami theory. Several other systems appear to have the expected integer values of n,[15,17-20] but in many other systems the value of n is smaller and not necessarily integral.[14,16,21-28] A number of explanations have been offered, many of which are specific to the particular system studied and some of these will be included in the ensuing discussion.

It is currently fashionable, whenever confronted with a low fractional dimensionality, to suggest that the domains might be growing in a fractal mode. In some previous work we invoked the possibility of dendritic protuberances to explain some complicated kinetic phenomena[11] and this could also account for the systematic deviations of the early time points in Fig. 3 from the classical theory as mentioned in Sec. IV. It might also be noted that fractal dendritic growth can be induced with very rapid supercooling of lipid monolayers through the FR transition,[30] although these incipient fractal domains anneal to circular domains within minutes. We find it difficult to understand how domain growth for our much slower phase transformations would become dendritic or anything but globular in either two dimensions (growth within individual bilayers) or in three dimensions. Until some direct evidence is obtained for this possibility, we will not discard it, but we think other possibilities should be discussed.

A very simple possible explanation for the small effective dimensionality n is that each individual domain does not grow with constant radial growth rate u, but with a growth rate which slows down for larger domains, in such a way as to satisfy Eq. (3). For $n = 1.2$ for the GC transformation this would require $r(t) \sim t^{0.6}$ which is equivalent to $u(r) \sim r^{-2.3}$, assuming two-dimensional domain growth. If three-dimensional domain growth is assumed, then $r(t) \sim t^{0.4}$ and $u(r) \sim r^{-3/2}$. One possible mechanism that would alter the linear time dependence of $r(t)$ is if the transformation is diffusion controlled, in which case $r(t)$ would scale as $t^{1/2}$ for lipid phase transformations for which the order parameter should be nonconserved.[31] However, it is unclear to us that there is any plausible diffusion that could control the kinetics of domain growth. Certainly, there is no need for lipid diffusion in these phase transformations. There is a requirement for water diffusion between the excess water phase and the interbilayer water region; this will be discussed and rejected later. A simple calculation based on the paper of Chan[32] indicates that thermal diffusion can not be the rate limiting step. Therefore, we are inclined to suppose that the phase transformations in these lipid systems are interface controlled, and the radial growth rate of individual domains would be expected to be constant in time,[32,33] as has been verified experimentally in a variety of polymeric and liquid crystalline systems.[12,34,35]

Another tentative explanation for the small value of n assumes first that domain growth is basically two dimensional and confined to individual bilayers. The novel element involves the underlying geometry of these bilayers in multilamellar dispersions. Instead of each bilayer being an infinite sheet, many are topologically spherical and the stacks of bilayers are like the layers of an onion. A single domain growing in a small spherical bilayer would slow down compared to Eq. (3) and eventually stop growing even before the sample were fully transformed. Other bilayers may have even more complex geometries with narrow necks separating one region of a single bilayer from another. Again, when the domain grows through the necks, growth is slower compared to Eq. (3). The slowing down due to both of these suggested possibilities would be qualitatively similar to having a lowered dimensionality compared to $d = 2$ in Eq. (4). Making this suggestion into a more quantitative theory appears difficult, although calculations have indicated that finite-size effects can effectively reduce n from its normal value, and the amount of the reduction ranges from 0 to 1.[36] At this time the strongest evidence in favor of this suggestion is the fact that the same value of the fractional dimensionality is found for the cooling or GC-phase transformation as for the heating or CG-phase transformation, which is consistent with the idea that n is determined by some underlying geometrical constraint that exists in both the G and the C phases.

A final tentative explanation for small values of n in Eq. (4) is connected with the necessity for water to leave the space between bilayers when transforming into the C phase. Given the geometry of multilamellar dispersions described in the preceding paragraph, much of this water must pass through one or more bilayers before reaching the excess water phase. Although it has not been measured in the C phase, it is reasonable to suppose that the permeability to water of the C-phase bilayer is considerably lower than for the G-phase lipid. Therefore, as a greater fraction of each bilayer is converted to the C phase, pushing out additional water becomes more difficult which would slow down the rate of GC-phase transformation. The fatal flaw with this explanation is that it suggests that the CG-phase transformation should proceed more rapidly, consistent with a larger value of n, and this is not observed.

The failure of the classical theory to fit the data in Fig. 1 which was taken for lower quench temperatures may come from the proposed collision of domains, but this would presumably not be so effective for short and intermediate times, so we wish to present another possible explanation. For $T_Q < 7\,^{\circ}\mathrm{C}$, domains will presumably form continuously, so the effective dimensionality should be increased to $n+1$ as mentioned in Sec. III. However, as C-phase formation proceeds, kinetic limitations on pushing out the water mentioned in the preceding paragraph would slow down the rate of nucleation of new C-phase domains. This would reduce the effective value of n at later times, consistent with the results mentioned in Sec. IV.

For the GR transition, or the pretransition as it is usually called in the lipid literature, we obtain even smaller effective dimensionalities with n about 0.7–0.8. We have

also reanalyzed the DSC data of Cho, Choy, and Young,[37] which they analyzed assuming simple exponential relaxation. We have replotted their GR conversion data at three different incubation temperatures and we find very good straight lines with values of n between 0.8 and 0.9. Figure 9 shows the result for only one incubation temperature. Also shown in Fig. 9 is the fitted line when conventional first-order kinetics were assumed. For n values so close to one the simple exponential relaxation fits the data reasonably well; however, n is not always so close to one. In an ESR study by Tsuchida *et al.*,[38] the GR transition conversion ratio data could not be fitted to a single exponential but required at least two exponentials. We have replotted the data (not shown) using Eq. (4) and we find that the fit is quite satisfactory (with only two parameters rather than three required for a double exponential fit) with n values between 0.5 and 0.8 depending upon temperature.

The fact that the value of n is less than or equal to one for the GR transition can be understood as follows. In a recent electron microscopy study[39] it was shown that the formation of the ripple phase starts by having narrow bands of ripples which then grow in the direction perpendicular to the length of the band and the density of rippling is not changed in the process. This shows that the growth of the ripple phase has basic one-dimensional character. The fact that our measured value of n is slightly smaller than unity may perhaps be related to geometric restrictions of different banded domains having different orientation which introduces an additional complication not included in the theory.

The reverse transformation (RG), on the other hand, does not seem to follow the Avrami formalism as can be seen in Fig. 9 which shows that data of Cho *et al.*[37] for the RG transformation do not fall on a straight line. The failure of the theory for the RG transition is not surprising because the same electron microscopy study[39] shows that loss of the ripple phase occurs by increasing the spacing between each ripple rather than by formation of domains. Therefore, the Kolmogorov-Avrami theory would not be expected to apply for the RG-phase transformation, in contrast to its apparent success for the CG-, GC-, and GR-phase transformations in DPPC bilayers.

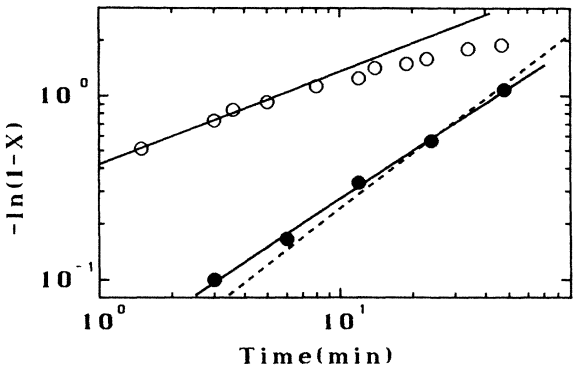

FIG. 9. Fractional conversion data by DSC from Cho *et al.* (Ref. 37). The solid circles are for the GR conversion at 33.3 °C. The solid line through them is the best straight-line fit to the data with a slope $n=0.86$. The dashed line is the best fit if $n=1$ is assumed, or assuming simple exponential. The open circles are for the RG conversion with the solid line the best fit to the first four data points, and the slope $n=0.51$.

Although the main transition is too fast for our instrumentation, we would also expect the Kolmogorov-Avrami theory to be the appropriate one for analysis of kinetic data. In contrast to the RG transition for which the ideal value of n would seem to be 1, it would appear more likely that the ideal value of n would be 2 for the main transition, but possibly with some reductions from 2 due to the geometry of multilamellar vesicles. It would also be of interest to determine n for unilamellar vesicles of various sizes to test whether the geometry does play a role in determining n. On the other hand, due to the much smaller time scale of the main transition, heat diffusion could become the rate limiting step. If so, it would not be surprising if n were close to or even smaller than 1 since the radius of domains would grow as $t^{1/2}$ when the growth is diffusion controlled.[31]

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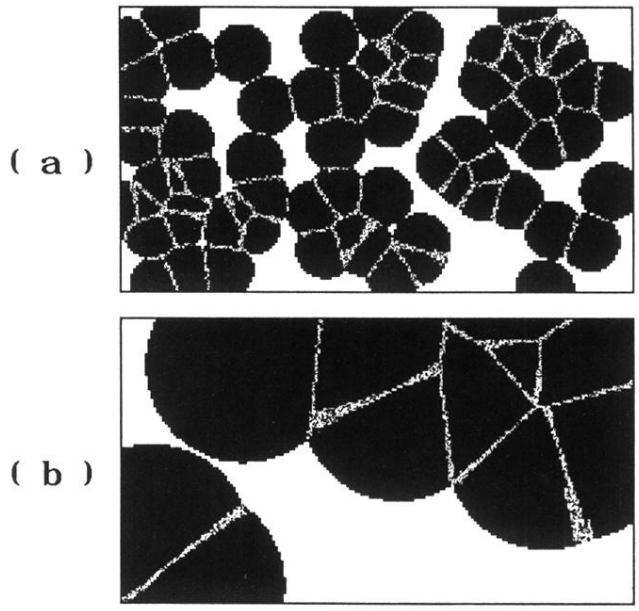

FIG. 2. Computer-generated domains with colliding region indicated. The fraction of conversion for both figures is 70%. (a) Lower T_Q; (b) higher T_Q.