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Lipids Under Power Pressure

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Lipid phase transitions are very popular and interesting objects of biophysical investigation. They are, in general, easily visible by a whole host of physical techniques and, at least in chemically well defined model systems, readily open to thermodynamic analysis. X-ray diffraction on such systems is also relatively easy because of the low dimensionality of hydrated lipid specimens, the signal analysis is quite straightforward (at least in the case of multibilayer liposomes), and results in the essential parameters of bilayer and water layer thickness, from small-angle diffraction, and of hydrocarbon chain packing, from wide-angle data. As compared with single crystal structure analysis, the experimental and computational efforts are relatively small. With powerful synchrotron x-ray sources, the time resolution of modern experiments has been pushed down into the millisecond time domain, opening the field for direct approaches to the supramolecular dynamics through x-ray cinematographic observation.

The time-scale of milliseconds might look modest in the eyes of spectroscopists, at first sight, but it must not be overlooked that this is different from the usually quoted, fast time scales intrinsic to the techniques of molecular

(nuclear or electronic) spectroscopy. Although these techniques normally probe the molecular dynamics at or close to equilibrium by accumulating signals over a time period at least in the order of seconds, i.e., many times (by 5–12 orders of magnitude) larger than the motional correlation times in question, a time-resolved x-ray diffraction experiment is essentially a one-shot movie of a dynamic process.

By clever combination of time-resolved x-ray diffraction with physically well defined triggering mechanisms, lipid phase transitions can be studied in their mechanistic, structural, and thermodynamic aspects through one set of experiments. What more do we want? Indeed, there is more: by crossing the borders from equilibrium structure and thermodynamics to a non-equilibrium situation (as, e.g., in a large-amplitude jump), the linear response-regime can be left behind, and it becomes possible, and perhaps likely, that the mechanistic pathway changes and a bifurcation might occur. Knowledge in this field is still very limited for lipid systems.

Caffrey and his group have, in parallel with other groups (Gruner, 1987; Laggner and Kriechbaum, 1991), pioneered this field through systematic exploitation of the possibilities of synchrotron x-ray diffraction and rapid jump-relaxation techniques. In their most recent article (Cheng et al., 1994), they report on an improved p-jump experiment, providing an important additional source of information using simultaneous small- and wide-angle detection.

Pressure as a variable has the advantage over the more commonly used temperature perturbation, because it can be varied equally rapidly in both directions through the phase transition range, and it is homogeneous throughout the system (within the limits of sound velocity). A complication, of course, is the fact that both adiabatic p- or T-jumps are always accompanied by a corresponding change in the other variable. In T-jumps, this dissipates faster (through a pressure wave), whereas with p-jumps the temperature change fades out more slowly through

heat conduction. Combining information from both types of experiments and from static, near equilibrium studies is certainly wise.

Cheng et al. found a rather complex kinetic behavior for a seemingly simple transition, the $L_{\beta'}/L_{\alpha}$ process in a hydrated phosphatidylethanolamine lipid (DHPC). Most surprising is the fact that the melting transition (depressurization from β' to α , i.e., order-to-disorder) is a two-step process, invariate in its transit time with respect to the jump amplitude, whereas in the other direction (pressurization into the ordered β' -phase) the process is by one to two orders of magnitude faster and apparently one-step. The first, fast step in the order-disorder transition appears as a lateral dilation of the ordered hydrocarbon chain packing, without change in lattice type, and the second, rate-limiting step is the chain melting and the change in inter-bilayer hydration. On a similar lipid system (1-stearoyl-2-oleoyl-*sn*-3-phosphatidylethanolamine, SOPE), laser-induced T-jump experiments with a time resolution of 1 ms have indicated a one-step, martensitic transition process that occurs within the time of energy deposition (Kriechbaum et al., 1989). In the T-jump transition from the metastable ripple phase to the liquid crystalline phase of DPPC, a rapid, synchronous change of both the hydrocarbon chain packing and the interbilayer hydration was found (Rapp et al., 1883). There is no straightforward explanation for this discrepancy with the present results of Cheng et al. More, certainly, will be learned from a careful delineation of the temperature-pressure phase diagram of these systems.

Signs of transient structural intermediates upon jump-relaxation have been detected up to now in only a few lipid systems. Their nature and systematic significance for the underlying supramolecular rearrangements will have to be better defined. If these intermediates, however, prove to be bound to dynamic bifurcations (where is the threshold beyond which these occur?) between linear and nonlinear nonequilibrium situations under rapid jump conditions, a substantial expansion of

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our concepts of phase transitions in membrane lipids will be necessary. The intuitive coupling between energetic considerations and mechanisms, which is qualitatively insufficient, will have to be expanded by the time variable. In other words, new and increased emphasis will have to be put on power as a determining factor for transition mechanisms. And after all, power is the essence of signals.

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