Manipulating Metastability in Lipid-based Multi-lamellar Particles

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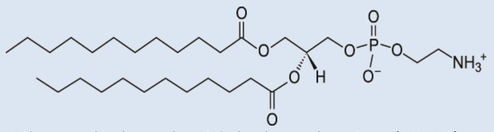
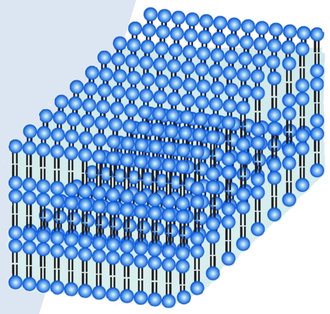
Phospholipids and their Self-Assembly

Phospholipids are a main component of cell membranes and can form various structures via the self-assembly process.

We study the phase-transition dynamics of DLPE bilayers in solution. DLPE is known to have a highly ordered crystalline structure at temperatures below 43°C [1,2].



Dilauroyl-phosphatidylethanolamine (DLPE)
12 carbon saturated chains, zwitterion

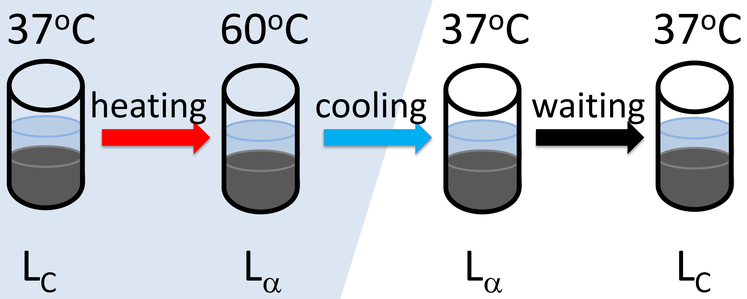


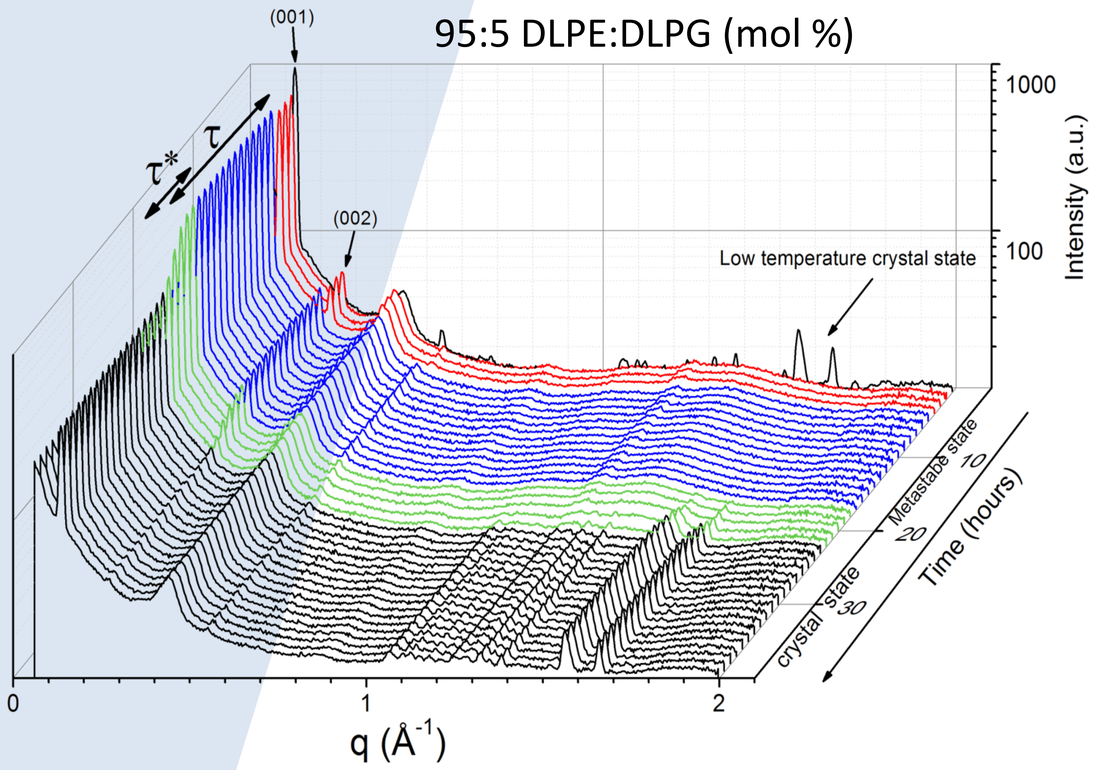
3D lamellar crystal

[1] Chang, H. & Epand, R. M (1983). *Biochimica et Biophysica Acta,* 728 (1983) 319-324
[2] Seddon, J. M., Harlos, K., & Marsh, D. (1983). *Journal of Biological Chemistry*, *258*(6), 3850–3854

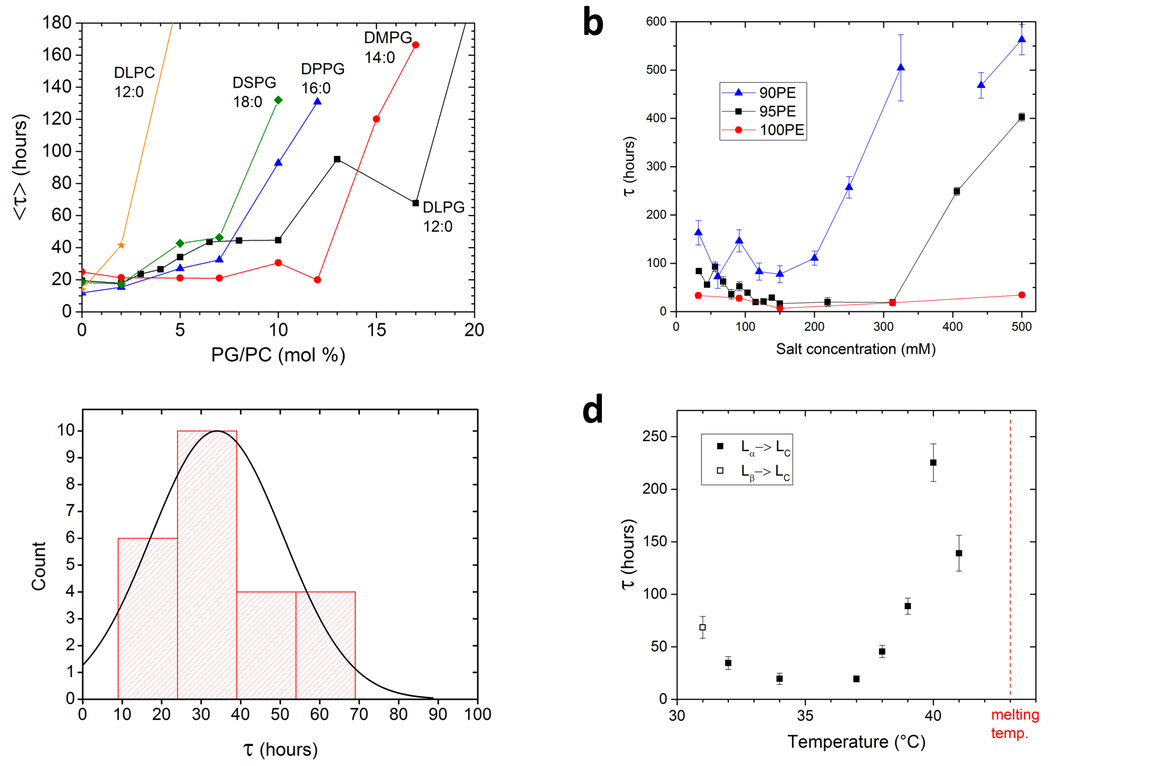
The Metastable Liquid-Crystal phase

Time resolved x-ray scattering experiments on DLPE:DLPG dispersions at full hydration. At 37°C, DLPE is in a crystalline phase. After heating to 60°C the hydrocarbon chains' correlations disappear (wide angle peaks) characteristic of MLVs in the liquid-crystal phase (L_α). Upon cooling to 37°C the L_α phase becomes metastable for tens of hours (denoted $\boldsymbol{\tau}$ – delay time) until a collective phase transition back to the crystalline state on a shorter time scale (denoted $\boldsymbol{\tau}^*$ – transition time).





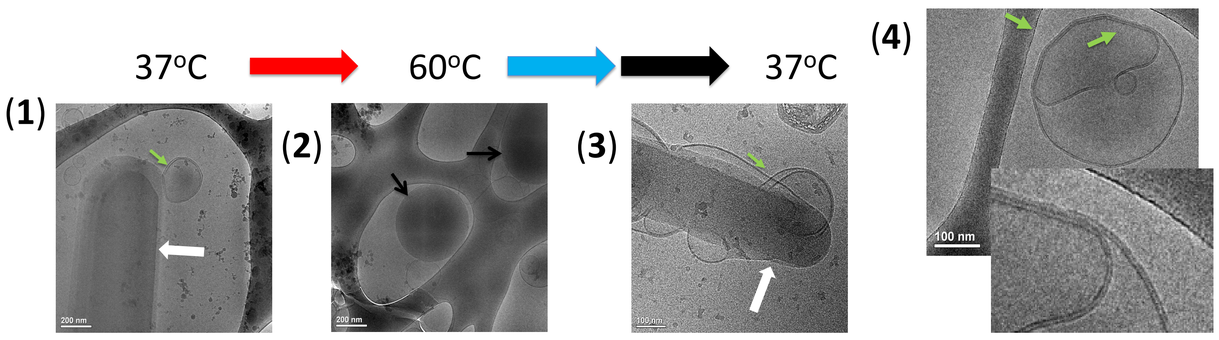
X-ray Scattering



a. The delay time (τ) strongly depends on the molar ratio of DLPE and a second lipid component, with varying hydrocarbon chain length or headgroup charge. **b**. Monovalent salt concentration in the solution has a non-monotonic effect on the delay time. Salt concentration effects seem to be connected to the charged headgroup (DLPG). **c**. Distribution of delay times for 24 samples at same conditions. **d**. Delay time increases when waiting temperature approaches the transition point.

Cryo-TEM

(**1**) A population of large crystals (>1μm) visible prior to heating. (**2**) At 60°C the crystals melt to form MLVs with water situated between the bilayers. Cooling back to 37°C, (**3**) reforming crystals and (**4**) sharp faceted liposomes.



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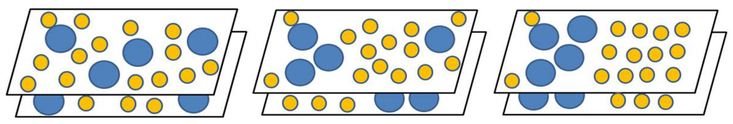
Competing forces for crystallization

DLPE crystallization ⟷ Lipid segregation
Membrane undulation
Membrane elasticity
Water & ion permeability
2D crystal's destabilization

60°C → 37°C → 37°C



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