Faceted Vesicles from Interdigitating 1,3-Diamidophospholipids

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Abstract
The guided self-assembly of nonspherical phospholipid vesicles or liposomes may lead to interesting applications such as mechano-responsive drug delivery systems [1]. However, in order to form true facetted vesicles, first the underlying physical forces at play have to be understood.

We approach the problem by organic synthesis of unprecedented phospholipid structures. The highly pure compounds are then submitted to biophysical testing of both their monolayer and bilayer characteristics (surface pressure/molecular area isotherms, gracing incidence angle X-ray diffraction, infrared reflection absorption spectrometry, Brewster-angle microscopy, small-angle X-ray scattering, cryogenic transition electron microscopy, fluorescence release, microfluidics, etc.)

The results from the 1,3-diamidophospholipid Pad-PC-Pad (**1**) show a fully interdigitated, flat bilayer membrane at temperatures below the main phase transition of 37 °C. Above the phase transition a cooperative first order transition into a non-interdigitated bilayer Lα phase is observed. This fluid membrane can be extruded into large unilamellar vesicles of 100 nm. Upon cooling to room temperature, various faceted vesicle types form such as lenticular vesicles, or d-form vesicles [2]. The formed membrane defects are attenuated when the system is agitated on a vortex shaker [1]. If no external force is applied, the vesicles retain their cargo. This is unlike natural phospholipid vesicles that either release or do not release their cargo under either conditions.

The insights gained from this first generation artificial phospholipid system have flown into several new structures that will be discussed, such as 1,2-diamidophospholipids or 1,3-diureaphospholipids.

Overall, the biophysical forces at play will be discussed as well as potential applications for physics-based targeted drug delivery of a vasodilator to the site of an occluded blood artery after a heart attack.

References

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[2] R. Tanasescu, M. A. Lanz, D. Mueller, S. Tassler, T. Ishikawa, R. Reiter, G. Brezesinski, A. Zumbuehl, Langmuir, *in press*.

Figures

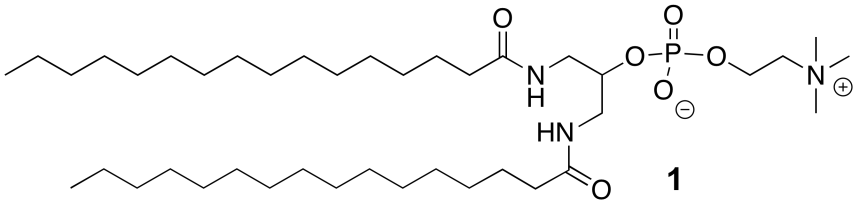

Figure 1. Structure of the 1,3-Diamidophospholipid Pad-PC-Pad (**1**).