Vesicle Origami

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The guided self-assembly of soft phospholipid vesicles, vesicle origami, remains a formidable challenge. In order to change the standard spherical form factor of a liposome, the forces at play during self-assembly must be understood and then influenced by introducing specific chemical modifications to the phospholipids. At the end of the process, liposomes with unprecedented properties are found such as, e.g., mechano-responsive vesicles that may find applications for targeting drugs to the occluded human artery segments after a heart attack or stroke [1].

Here, we correlate the biophysical findings of phospholipid monolayer studies (gracing-incidence X-ray diffraction, infrared reflection absorption spectroscopy, surface pressure/molecular area isotherms) with analogous bilayer measurements (small-angle X-ray scattering, differential scanning calorimetry, fluorescent dye release assays, microfluidics, cryogenic transition electron microscopy/tomography, animal toxicity assays). The results lead to insights into bilayer membrane interdigitation and its effect on vesicle membrane faceting and the induction of vesicle mechano-sensitivity [2]. The forces at play will then be fine-tuned by a next generation of synthetic phospholipids.

In particular, we introduce new 1,3- and 1,2-diamidophospholipids and their diester analogs as well as a phospholipid with a cyclic glycerol-backbone substitute. We show how membrane interdigitation leads to a stabilization of the critical temperatures found in bilayer systems over monolayer systems [3] and how the first order phase transitions can be removed by the addition of cholesterol.

In conclusion, we synthesize new types of phospholipids that yield fundamental insights into membrane self-assembly and lead to vesicle materials with unprecedented properties.

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