SOCIÉTÉ CHIMIQUE DE GENÈVE

Vesicle Origami

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Most hydrated phospholipids self-assemble into spherical, soap-bubble like structures: vesicles. Here, we explore what happens if the vesicles are not spherical but facetted. In particular, we report on synthetic phospholipids and their vesicles that respond to mechanical stimulation. We explore the forces at play behind this phenomenon and its potential for targeted drug delivery.

The work is based on synthetic 1,3-diamidophospholipids. Due to the 1,3 substitution pattern the fatty acyl chains are more spread apart than those of standard 1,2-diesterphospholipids. This leads to interdigitation of the opposing Pad-PC-Pad bilayer leaflets and the formation of flat vesicle faces.[1] The vesicles release their cargo when they are exposed to elevated shear stresses; otherwise they remain tight. This opens up possibilities in purely physics based drug delivery where the high wall shear stresses, that are typically found in critically stenosed artery segments, trigger the release of a drug.[2]

1. Weinberger A., Tanasescu R., Stefaniu C., Fedotenko L.A., Favarger F., Ishikawa T., Brezesinski G., Marques C.M., Zumbuehl A. Bilayer properties of 1,3-diamidophospholipids. *Langmuir* **2015**, 31, 1879-1884.

2. Holme M.N., Fedotenko L. A., Abegg D., Althaus J., Babel L., Favarger F., Reiter R., Tanasescu R., Zaffalon P.-L., Ziegler A., Müller B., Saxer T., Zumbuehl A. Shear-stress sensitive lenticular vesicles for targeted drug delivery. *Nature Nanotechnol*. **2012**, 7, 536-543.

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