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Transition from Complete to Partial Wetting within Membrane Compartments

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Liquid droplets at interfaces may exhibit zero or nonzero contact angles corresponding to complete and partial wetting, respectively. As one varies a certain control parameter such as temperature or liquid composition, the system may undergo a transition from complete to partial wetting. Such transitions have been found and intensively studied for fluid−fluid interfaces in binary mixtures[1] and for liquids at solid substrates.[2] Furthermore, liquid droplets at chemically patterned or topographically structured substrate surfaces can undergo morphological wetting transitions,[3] which reflect the freedom of contact angles for pinned contact lines.[4]

In this article, we provide the first experimental evidence that a transition between complete and partial wetting can also occur for an aqueous solution encapsulated within a lipid vesicle, i.e., for an aqueous solution in contact with a freely suspended lipid membrane.

Lipid vesicles have long been recognized as models for the cell membrane and have been widely applied to study properties of lipid membranes.[5] Recently, it has been found that giant unilamellar vesicles (several tens of microns in size and encapsulating volumes on the order of picoliters) loaded with aqueous solutions of water-soluble polymers may exhibit several spatial compartments formed by phase separation within the vesicle interior.[6,7] Thus, these artificial cell-like systems are a biomimetic setup for studying molecular crowding, fractionation, and protein sorting in cells.[6]

We encapsulate an aqueous solution composed of 4.05% poly(ethyleneglycol) (PEG) (molecular weight 8000 g/mol) and 2.22% dextran (molecular weight between 400 and 500 kDa) within giant vesicles, where 0.52% of the total dextran is labeled with fluorescein isothiocyanate and the composition of the aqueous solution is given in weight fractions. This solution is in the one-phase state at room temperature (see phase diagram in the Supporting Information). The vesicles are prepared in this solution using the method of electroformation (see Supporting Information). The membrane consists of 95.9% 1,2-dioleoyl-*sn*-glycero-3-phosphocholine (DOPC), 4.0% galbeta1-3galnacbeta1-4(neuacalpha2-3)galbeta1-4glcbeta1-1′-cer (G_{M1} Ganglioside) and 0.1% 1,2-dipalmitoyl-*sn*-glycero-3-phosphoethanolamine-*N*-(lissamine rhodamine B sulfonyl) (DPPE-Rhod) with the membrane composition given in mole fractions.

In order to obtain vesicles containing two phases, we raise the polymer concentration above the binodal (see Supporting Information) by deflation, i.e., by exposing the vesicles to a hypertonic medium. In order to balance the resulting osmotic pressure, water is forced out of the vesicle, the polymer concentration inside increases and phase separation occurs. To eliminate the fluorescence signal outside the vesicles and to make them sediment to the bottom of the chamber, they were first diluted in an isotonic solution containing 4.41% PEG and 1.45% dextran. The osmolarity of the medium was then increased stepwise (in 10−20% osmotic increments) by injecting a hypertonic solution containing 3.92% PEG, 2.14% dextran, and 3.27% sucrose into the working chamber. The system was left to equilibrate for at least 2 h after each consecutive injection.

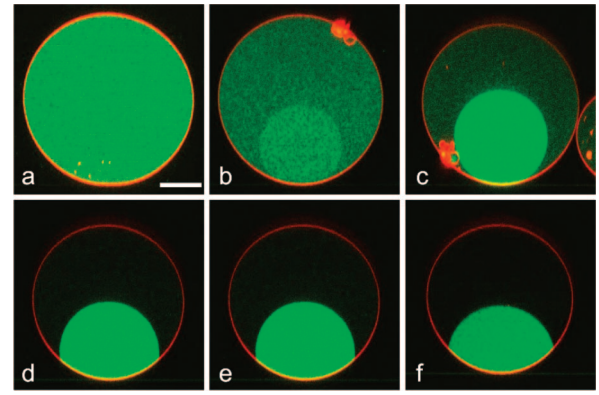

Figure 1. Confocal micrographs of a vesicle (vertical cross section), which contains a dextran-rich drop (green) undergoing wetting transition as the external osmolarity increases (see text for details). Note that these are images from confocal *z*-scans and the bottom of the vesicle is at the chamber bottom partially seen in f. Scale bar: 20 μm.

Figure 1 shows one example of such a vesicle (vertical cross section) with different polymer concentrations as observed by confocal microscopy. The membrane (red) is labeled with DPPE-Rhod, and the vesicle encapsulates fluorescent dextran (green). From Figure 1a to f, the osmolarity ratio, r, between the external medium and the initial internal polymer solution is 1.0, 1.1, 1.4, 1.6, 1.8, and 2.0, respectively. The first snapshot with $r = 1.0$ shows the vesicle before the phase separation occurs. As the osmolarity of the external medium increases, the polymer concentration is raised and phase separation occurs in the vesicle; see Figure 1b. The part with more intensive green fluorescence presents the dextran-rich phase, and the part with less fluorescence is the PEG-rich phase. The former is heavier than the latter. Thus the spherical dextran-rich droplet is always located at the bottom of the vesicle; see Figure 1c. When the external osmolarity is further increased, $r > 1.4$, the dextran-rich phase starts to wet the membrane (see Figure 1d) and the contact area between the dextran-rich phase and the membrane grows with increasing osmolarity ratio r (see Figure 1d−f). The morphology change of the dextran-rich droplet indicates a wetting transition from complete wetting of the PEG-rich phase or complete dewetting of the dextran-rich phase in Figure 1c to partial wetting in Figure 1d−f. Such wetting transitions were observed to occur for the majority of isolated vesicles in the sample.

In contrast to the dextran-rich droplet, the vesicle seems to remain spherical throughout the whole experiment. The volume of the vesicle decreases with increasing osmolarity. The excess area gained in this way forms a cluster of interconnected small vesicles and lipid aggregates. This cluster diffuses with the membrane and was not always located in the focal plane as in Figure 1b, c (more details on this lipid cluster can be found in the Supporting Information).

By fitting the vesicle and the drop contours in the acquired images with spherical caps, we obtain the vesicle volume and the contact

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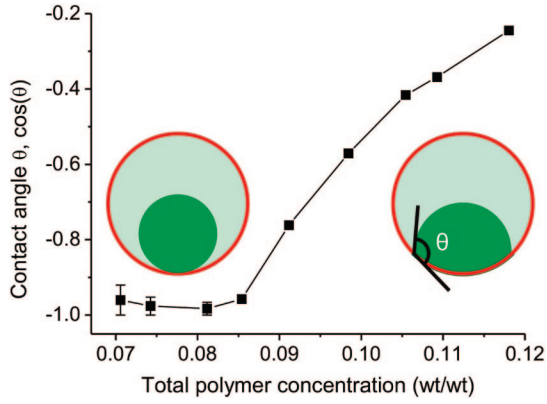

Figure 2. Cosine of the contact angles versus total polymer concentration in the vesicle. The weight ratio between dextran and PEG is 0.55. The insets schematically illustrate the dewetted and wetted states.

angle, θ, between the dextran-rich phase and the membrane (see inset in Figure 2) under different osmolarity conditions. Because the membrane is permeable only to water but not to the polymers, the number of polymer molecules inside the vesicle is fixed and the decrease of vesicle volume is due to the loss of water. Thus we can calculate the total polymer concentration in the vesicle for each osmolarity ratio r. The initial polymer concentration corresponding to $r = 1.0$, as in Figure 1a, was considered to be the same as that in the polymer solution, in which the vesicles were prepared.

The cosine of the contact angle θ defines the wettability via

$$\cos(\theta) \equiv (\Sigma_{pm} - \Sigma_{dm})/\Sigma_{pd} \quad (1)$$

where Σ_{pm}, Σ_{dm}, and Σ_{pd} are the interfacial tensions at the interfaces between the PEG-rich phase and the membrane (*pm*), the dextran-rich phase and the membrane (*dm*), and the PEG-rich phase and the dextran-rich phase (*pd*). Here, the normal components of Σ_{pm} and Σ_{dm} have been neglected because the vesicle is approximately spherical. In addition, we have assumed that no long-range interactions are present, which allows us to ignore the effect of the external medium. The wettability as a function of the total polymer concentration inside the vesicle is given in Figure 2 (such wetting transitions were monitored for 10 other vesicles). A sharp change in the contact angle is observed for polymer concentration $\cong$ 8.5 wt %, indicating a wetting transition. For contact angles larger than 170°, the error in the measured value for θ increases, as illustrated by the error bars in Figure 2. This reflects the resolution limits of optical microscopy and slight deformations of the dextran-rich droplet (sessile shape) by gravity. Thus, directly from the contact angle behavior, one cannot conclude whether this wetting transition is of first or second order. We are not aware of experimental techniques, by which one could measure the contact angle in the present system with a higher precision. Vesicle simulations based on dissipative particle dynamics[8] may offer a possible way to reveal the order of this wetting transition. Work in this direction is in progress.

We consider a possible mechanism involved in the observed wetting transition. When the polymer solution is close to the mixing point, namely at a polymer concentration close to and above the binodal, Σ_{pd} is extremely low. It is smaller than $|\Sigma_{pm} - \Sigma_{dm}|$, which is why the dextran phase minimizes its contact with the membrane. The membrane is fully wetted by the PEG-rich phase. Both Σ_{pd} and $|\Sigma_{pm} - \Sigma_{dm}|$ increase with increasing polymer concentration, but Σ_{pd} increases faster than $|\Sigma_{pm} - \Sigma_{dm}|$. When $\Sigma_{pd} = |\Sigma_{pm} - \Sigma_{dm}|$, the wetting transition occurs, and the dextran-rich phase starts to wet the membrane. After this transition point, the wettability of the dextran-rich phase increases with the polymer concentration as shown in Figure 2.

In contrast to conventional surfaces (solid or bulk liquid), there is a constant water exchange through the lipid bilayer. In addition, this bilayer is rather flexible and, thus, can easily adapt its shape. In the experiments described here, this flexibility allows the membrane to deposit the excess area arising from the deflation of the vesicle in a small lipid aggregate and to keep the overall vesicle shape close to a sphere. We can then use the simplified description as given by eq 1 without addressing the delicate question of membrane tension, which can have several contributions arising from mechanical forces and constraints as well as from the different composition of the external and internal solution. The interfacial tensions in eq 1 will depend on the molecular structure of the lipid bilayer and on the interactions between the lipid head groups and the two polymer phases. Thus, these tensions can be varied by changing the membrane composition. Of particular interest would be to study wetting phenomena in vesicles containing domains of various compositions. The interfacial tensions in eq 1 will also be affected by the mechanical tension within the membrane, which can be manipulated by exerting an external pressure on the vesicle through a micropipette.

In our future work we want to consider additional factors, which might influence the wetting transition, such as the vesicle excess area, membrane tension, and curvature. Having reported a wetting transition on membranes for the first time opens the possibility to explore a number of biologically relevant systems. Wetting transitions in membrane-confined biological systems (vesicles or cells) could be used to locally regulate cellular processes such as protein synthesis, to restrict chemical reactions to particular segments of the membrane surface, or to stop such reactions by dewetting.

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Supporting Information Available: Materials, phase diagram of the polymer aqueous solution, vesicle preparation and characterization. This material is available free of charge via the Internet at http://pubs.acs.org.

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