Supplementary Material (ESI) for Soft Matter

Supplemental Information

for

Liposil-Supported Lipid Bilayers as a Hybrid Platform for Drug Delivery

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S(i): Thermally induced lipid mixing

To further confirm the presence of the outer phospholipid bilayer on the $B_{in}/S/B_o$ constructs, additional DSC experiments were conducted. $B_{in}/S/B_o$ constructs, in which the external bilayer was composed of DMPC, were scanned from 5 to 65 ^oC at 10 ^oC/min on the Mettler-Toledo 822e. Initial scans showed thermal events at 24, 43, and 55 ^oC. The 24-^oC peak and the 55-^oC peak correspond to the main gel to liquid crystalline phase transitions for DMPC bilayers and DODAB encased in a silica shell, respectively, indicating that both bilayers are indeed present. The peak at 43 ^oC could be attributed to either a mixed phase including both lipids (such as might occur within defects in the silica layer), or to free DODAB vesicles that were not completely confined by the silica layer (see main text, Fig. 2C). Upon repeated scanning of the samples, the peaks at 24 and 55 ^oC are progressively diminished, while the peak at 43 ^oC increases in enthalpy. This finding suggests that the 43-^oC peak indeed represents a mixed phase including both DMPC and DODAB, and further that each time the sample is raised to 65 ^oC the mixing proceeds. It is possible that this thermally induced fusion of the two bilayers could be exploited as the stimulus for furthering the release of encapsulated drug.

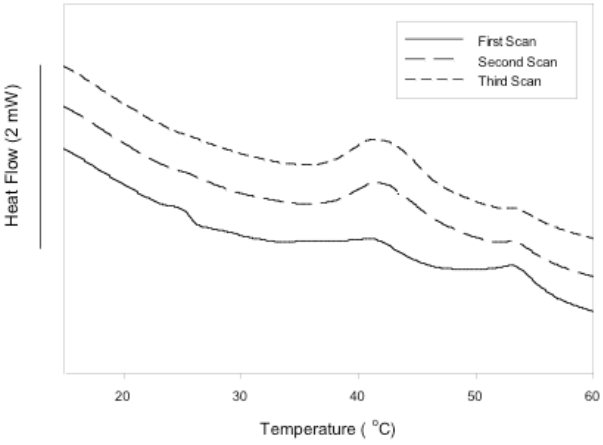

Fig. S-1. Thermal scans of DODAB/Si/DMPC constructs
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The notion that the 43-^{o}C peak does represent a mixed phase is substantiated by additional experiments conducted on $B_{in}/S/B_o$ constructs, in which the external bilayer was composed of DOPC. In this case, no peak at 43 ^{o}C was seen (data not shown). Since the same protocol was used for the deposition of the silica shell in both cases, it follows that the discrepancy between the two types of constructs is related to the external phospholipid bilayer, rather than the silica coating.

In the absence of silica, mixing does occur between DODAB and DMPC, but it appears to be less marked, as the DMPC peak is not eliminated even after three scans, and the intermediate peak is less pronounced (Fig. S-2). In this case, the peak for DODAB falls at 45 ^{o}C on the first scan, as it is not bound by the silica shell (main text, Fig. 2). On the second and third scans, the DODAB peak is shifted progressively to lower temperature, indicating the progressive mixing with the lower-melting DMPC.

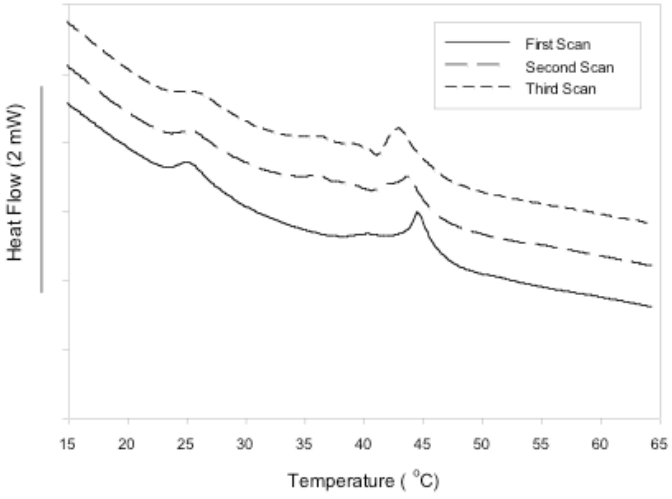

Fig. S-2. Thermal scans of a mixed sample of DODAB vesicles and DMPC vesicles. The 40-μL DSC crucibles contained 15 μL each of DODAB vesicles and DMPC vesicles (each at 10 mg/mL).

S(ii): Size distribution of $B_{in}/S/B_o$ constructs

Particle size was monitored during and after the synthesis of $B_{in}/S/B_o$ constructs by dynamic light scattering (DLS). Although the template DODAB vesicles were very monodisperse, showing a narrow distribution around the mean of 180 nm, the final constructs were much more broadly distributed. DLS measurements of the finished three-layer construct (DODAB/Si/POPC) show an increase in the mean diameter to 250 nm as well as a noticeable increase in the polydispersity of the sample (Fig. S-3). This net increase in diameter cannot be fully accounted for by simple uniform enlargement in particulate dimensions across the sampled populations due to the accretion of the silica layer and the outer bilayer of the liposil construct, which contribute only an additional 5-10 nm and 3-6 nm, respectively.

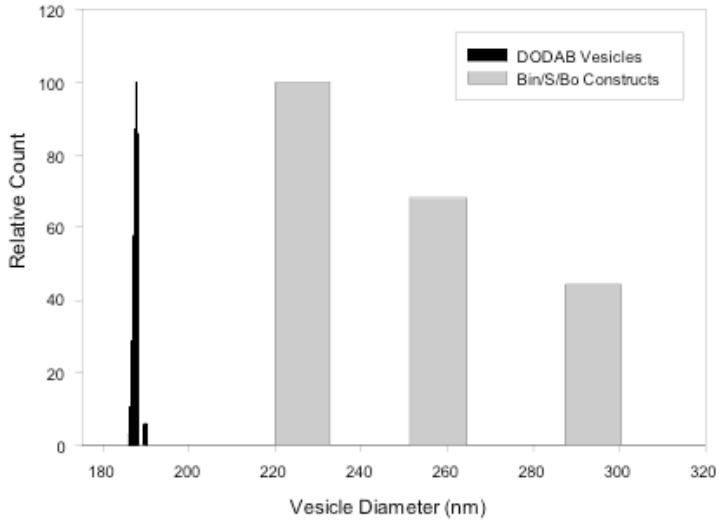

Fig. S-3. Dynamic light scattering measurements showing the range of diameters for DODAB liposome templates and completed $B_{in}/S/B_o$ liposil constructs.

These results are at variance with those reported previously by Hubert and co-workers under comparable synthesis conditions[1]. At present, we do not fully understand the origin of this discrepancy, but speculate it originates from a combination of three primary factors: (1) plausible vesicular deformations and aggregation during the course of sol-gel reaction, which is common to many colloid-vesicular complexes[2]; (2) heterogeneous deposition of silica onto different particles within the population – evident in some TEM images; and (3) formation of small aggregates of linked silica coated particles–also seen in some TEM images and reported earlier by others[3,4]. We emphasize that regardless of the origin of the particle enlargement, it appears to have no significant bearing on the integrity and function of the sealed DODAB vesicle or the outer bilayer coating. This suggests that aggregated particles probably behave similar to their solitary counterparts in terms of cargo containment and controlled release as well as lipid-based passivation or targeting.

S(iii) Coating liposils with external bilayer containing Texas Red causes color change

As mentioned in the main text, both fluorescence spectroscopy and casual observation indicate that the Texas Red doped phospholipids associate with the silica-coated particles (Fig. S-4).

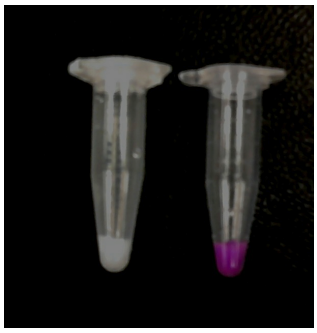

Fig. S-4. Washed pellets composed of silica-coated DODAB (left), or the Bin/S/Bo constructs containing 1 mol% Texas Red in the outer DMPC bilayer (right).

References

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