Giant liposomes of controlled size and composition: Preparation, mechanisms, and applications as artificial cell models

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The potentiality to use giant liposomes, phospholipid bilayered vesicles with a size larger than 1 µm, as cell models has been well demonstrated. However, the current methodologies to obtain such artificial cells exhibit various problems. In particular, it is rather difficult to prepare liposomes with predefined size and desired inner contents. Here, we report novel methods to prepare liposomes of controlled size and well-defined inner composition. We discuss the underlying mechanisms leading to the generation of the liposomes and show a few examples where the prepared liposomes were used as artificial cell models.

First, we developed a methodology to control the liposome size by electroswelling a phospholipid film on a silicon substrate with a controlled chemical/physical micro-topography (phospholipid micro-patterns and silicon micro-structures).[1] By changing the surface properties (chemical composition and microstructures) of Si, it was possible to control both the molecular organization of the phospholipid film and the properties of the final vesicles. Combined with the micro-localization of the electric field, a good control on the size distribution was achieved (Figure 1). We also explored the process of the spontaneous generation of liposomes from an oil/water interface.[2] Finally, by using phospholipid-coated micro-droplets,[3] which were generated by emulsification or microfluidic techniques, as precursors of liposomes,[4] we prepared cell-sized liposomes encapsulating various biologically relevant complex medium.

Various experiments were performed on such well-defined artificial cells. We followed the *in situ* protein expression kinetics within individual liposomes (Figure 2). We also prepared a novel artificial system, in which the conformation of individual genomic DNA molecules encapsulated in a cell-mimicking structure was controlled by light, *i. e.*, by an external stimulus.[5]

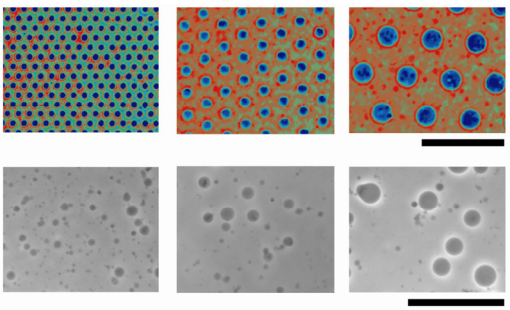

Fig. 1. Electroswelling a phospholipid film on a silicon substrate with an insulating silica layer (200 nm thick) containing micro-holes arranged in a hexagonal array. Top, reflection microscopy images (false colors) of the film organization for hole sizes of 7, 12, and 24 µm, respectively. Bottom, corresponding phase contrast images of the vesicles obtained after electroformation (2h, 2V, 10 Hz). Scale bars are 100 µm.

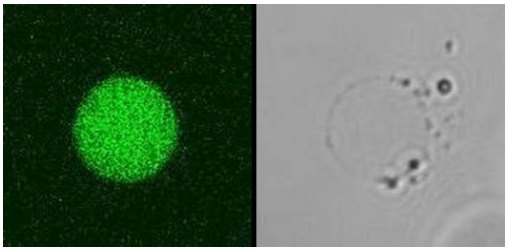

Fig. 2. Confocal fluorescence (left) and transmission (right) microscopy images of the GFP expression in a liposome obtained by the spontaneous transfer methodology[4]. Each image has a size 50µm × 50µm.

References

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