RESEARCH HIGHLIGHTS

Organic, carbon-based and soft materials MICROFABRICATION: POLYMER NANOPOTTERY

The controlled coiling of a tiny jet of polymer solution allows the construction of microstructures that resemble the familiar clay pottery of the macro world.

Published online 23 August 2010

Nano Lett. | The ability to make eversmaller patterns of silicon drove advances in computing technology. In much the same way, the ability to construct micrometer-scale objects in an accurate and repeatable manner is fundamental to the development of labon-a-chip technologies, which have a wide range of possible applications accompanied by considerable environmental, safety and economic benefits.

In a demonstration of their mastery of microfabrication, Ho-Young Kim and co-workers from Seoul National University in Korea and Harvard University in the USA¹ have now developed a technique they call 'nanopottery'. As with many microfabrication techniques, inspiration is taken from the macroscopic world—like the coiling of a rope as it is dropped onto a horizontal surface. In this scenario, the diameter of the coil is dependent on the flexibility of the rope and the rate at

Theory, modeling and simulation DRUG DELIVERY: SIMULATED SONOPORATION

New insights into the selforganization of a pore structure in the cell membrane could aid in cell-targeting drug delivery.

Published online 23 August 2010

Phys. Rev. Lett. | New approaches for the targeted delivery of drugs to diseased and injured tissue lie at the heart of biomedical materials research. Studies in this area generally focus on the design of delivery vehicles that can enter affected cells through existing biological pathways, but an alternative, noninvasive approach is to use pulses of electricity or ultrasound to induce the formation of pores in cell walls. Kenichiro Koshiyama and Takero Yano from Osaka University and Tetsuya Kodama from Tohoku University in Japan¹ have now modeled in detail the formation of ultrasound-driven pore formation (sonoporation) in a phospholipid bilayer—a component of the cell membrane.

The phospholipids in cell membranes often self-assemble into a bilayer with hydrophobic (water-repelling) lipid tails pointing inward. Sonoporation can induce the formation of pores in the space between the two lipid layers, but the process occurs on



A scanning electron microscopy image of an example of nanopottery produced through the controlled coiling of a polymer.

which it is dropped onto the surface. Kim and his team figured that the phenomenon is based on geometry and should therefore work on any scale—a theory they tested through polymer microfabrication using a process known as polymer electrospinning.

By exposing a droplet of polymer solution to a strong electric field, a fine 'jet' of the polymer can be drawn out and deposited on a suitable electrode substrate. On microscopic scales, however, a stable jet of polymer solution is difficult to produce because of the accumulation of surface charge. This kind of difficulty is not uncommon on small scales as electrostatic effects—often unimportant at macroscopic scales—become prominent.

After some experimentation, the researchers decided on the use of a sharp electrode instead of the conventional flat plate, providing better confinement of the electric field. Using this set-up, the researchers confirmed that the coiling effect could still be produced at microscopic scales, allowing them to construct a cylindrical polymer tube several micrometers in diameter (pictured). The team then developed a mathematical model of the jet and its coiling, showing that the coil radius can be changed by adjusting the concentration of polymer in solution and the strength of the applied electric field.

"In the future, we would like to use functional polymers to turn our nanopottery into useful microscale objects," explains Kim. "For example, if we could use a conducting polymer, then the coil shape would allow us to produce a microscale electromagnet."

Reference

 Kim, H.-Y., Lee, M., Park, K.J.,Kim, S. & Mahadeven, L. Nanopottery: coiling of electrospun polymer nanofibers. *Nano Lett.* 10, 2138 (2010).



A snapshot of simulations showing the formation of a stable pore structure in a phospholipid bilayer due to sonoporation.

the scale of nanoseconds, making it too fast to be analyzed experimentally. Koshiyama and his colleagues performed molecular dynamics simulations to probe the exact mechanism by which the pores form. They found that during sonoporation, the waves of ultrasound disturb the self-assembled phospholipids in a collective manner, providing sufficient energy for the surrounding water molecules to enter into the bilayer's hydrophobic core. In just several hundred picoseconds, these water molecules self-assemble into a cluster, pushing the phospholipids outwards and distorting the bilayer structure.

Depending on the size of the water cluster, it could be too small to be stable and would disappear after a few nanoseconds, or it could be too large to be contained in the bilayer, in which case the phospholipids re-organize around the cluster to open up water-filled pores in the cell membrane (see image).

The pores produced in their simulations are much smaller than those observed experimentally based on the transport of large molecules through lipid bilayers during sonoporation. The researchers therefore propose that their studies reveal the formation of pore nuclei that expand through the molecular stresses caused by prolonged ultrasonication. "The resulting larger-sized pores may enhance membrane permeabilization for large molecules such as drugs, although the detailed mechanisms underlying the diffusion of large molecules through ultrasound-generated pores still remain unknown," says Koshiyama.

Reference

 Koshiyama, K., Yano, T. & Kodama, T. Selforganization of a stable pore structure in a phospholipid bilayer. *Phys. Rev. Lett.* **105**, 018105 (2010).