

NANOBIOTECHNOLOGY

Looking inside cell walls

Carbon nanotubes have been used to probe the properties of bilayer systems resembling living cell membranes. Such experiments could offer new insights into the working of cells.

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Carbon nanotubes are a natural choice for interfacing with the biological world because of their molecular scale, biocompatibility and stability in aqueous environments. Examples of applications that exploit these features include scanned-probe imaging of biomolecules¹ and biosensing². Nanotubes can also be used as electrical contacts to enzymes and other biomolecules³, and there are possible applications in drug delivery and cancer treatment⁴ as well. On page 185 of this issue Xinjian Zhou, Paul McEuen and co-workers⁵ at Cornell University in the US describe a new bio-application of these remarkable materials. They show that carbon nanotubes can be used to manipulate and sense proteins in experiments that might shed new light on important cellular processes.

The Cornell group place a nanotube on a silicon dioxide surface and then deposit a lipid bilayer on top of this to form a hybrid structure (Fig. 1). Lipid molecules consist of a hydrophilic tail and a hydrophobic headgroup. When placed in an aqueous environment, they tend to self-assemble into structures such as bilayer membranes in which the hydrophilic groups form the outer surfaces, protecting the hydrophobic core from the solution. Lipid bilayers play a major structural and organizational role in living cells, including bacterial, yeast, plant and animal systems: they form membranes that separate the inside of the cell from the outside environment, and internal structures from each other.

Cellular membranes also host the proteins that regulate molecular interactions between these regions, including the receptor proteins that play a central role in cell signalling. And because lipid bilayers are held together by hydrophilic and hydrophobic interactions, rather than covalent bonds, biomolecules embedded in these structures are free to diffuse laterally,

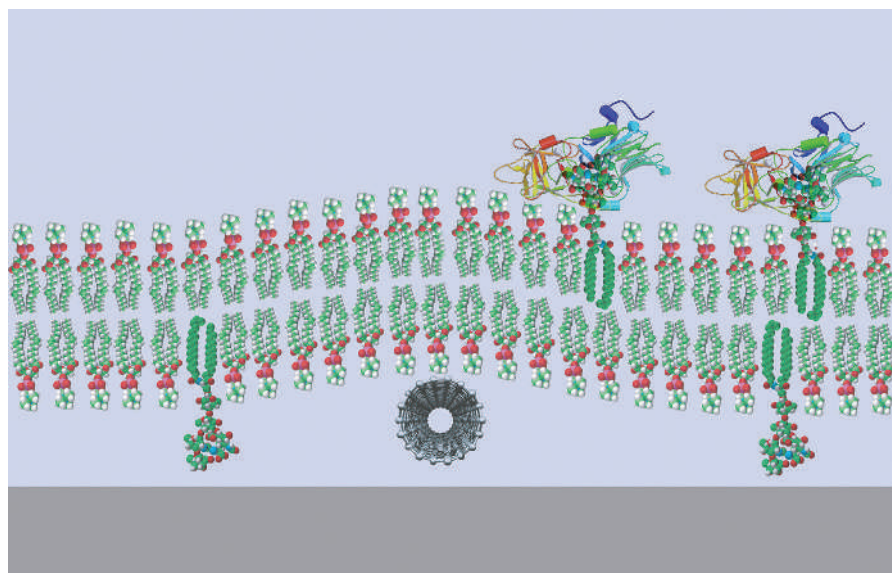


Figure 1 Hybrid nanostructures could be used to learn more about the behaviour of cell membranes. In this structure the carbon nanotube, which is sandwiched between a supported lipid bilayer (red and green) and an underlying substrate (grey), acts as a barrier to the diffusion of membrane-bound proteins (top) while, at the same time, allowing the lipids to diffuse across it. This mimics the behaviour of real cells, in which the cytoskeleton acts as a selective barrier to the diffusion of membrane proteins. The compact molecules below the bilayer are attachment points for the proteins.

although they cannot leave the plane of the membrane. However, it has become clear that other cellular structures, particularly the cytoskeleton, are able to restrict the mobility of membrane proteins without disrupting the membrane itself.

In some cases, the cytoskeleton acts as part of a barrier that completely blocks protein diffusion. This allows many cells — including neuronal, epithelial, and yeast cells — to divide their outer surfaces into different functional regions. In other cases, the cytoskeleton acts more like a series of ‘speed bumps’, reducing the diffusion rate of proteins⁶. Recent work⁷ suggests that this allows cells to rearrange receptor proteins into complex patterns that significantly modify cell–cell interactions.

Many aspects of the interactions between membrane proteins and the cytoskeleton are still not well understood,

so there is a significant need for artificial model systems that can be tightly controlled and defined with high precision. In particular, such a model system would need to allow the lipid membranes to diffuse freely without restricting the diffusion of the membrane proteins. Supported lipid bilayers, in which a lipid membrane is placed on a silicon dioxide surface, can act as proxies for biological lipid membranes, but by themselves they do not allow for the protein mobility to be modified. Photoresists and other materials have been used to pattern barriers into supported lipid bilayers⁸ but these barriers interrupt the membrane structure and impede the mobility of both proteins and lipids because they are much larger than the bending radius of the bilayer.

Carbon nanotubes, because of their nanometre scale, do not suffer from this

problem, which makes them very attractive for experiments like this. Indeed, Zhou and colleagues report that individual lipids, labelled with fluorescent markers, can diffuse over the nanotubes, indicating that continuous lipid bilayers can form over these structures (Fig. 1). Moreover, when they attach a tetanus toxin protein to the lipid membrane, the diffusion rate is less and falls dramatically as the width of the nanotube is increased from 1 to 3 nm. It is this ability to mimic what happens to proteins in real cells that makes the approach so potentially useful. Further development of techniques for patterning nanotube networks, including the ability to create arrays of regularly spaced carbon nanotubes, will have immediate impact on understanding how the complex mobility of membrane proteins influences their signalling function.

The close proximity of the lipid bilayer to the nanotube also offers the possibility of sensing chemical changes by monitoring the electrical properties of the nanotubes. This could, for instance, allow protein diffusion to be tracked without the use of fluorescent tags. Label-free detection systems that do not involve the use of fluorescent or radioactive tags have many advantages in biomedical applications: in particular, they do not alter the physical properties of the systems being studied, and they are also simpler and less expensive than existing methods. Zhou and colleagues explore this possibility by demonstrating, as a proof-of-principle experiment, that the conductance of a nanotube is sensitive to both the formation of a lipid bilayer on top of it, and also to the binding of proteins to ligands embedded in the bilayer.

Further work will likely lead to improvements in sensitivity that allow single-molecule detection. Thus we can look forward to having artificial structures that not only mimic the complex behaviour of cell membranes and membrane proteins, but also have the ability to track molecular diffusion in real time.

References

1. Wong, S. S., Joselevich, E., Woolley, A. T., Cheung, C. L. & Lieber, C. M. *Nature* **394**, 52–55 (1998).
2. Balasubramanian, K. & Burghard, M. *Anal. Bioanal. Chem.* **385**, 452–468 (2006).
3. Besteman, K., Lee, J. O., Wiertz, F. G. M., Heering, H. A. & Dekker, C. *Nano Lett.* **3**, 727–730 (2003).
4. Kam, N. W. S., O'Connell, M., Wisdom, J. A. & Dai, H. J. *Proc. Natl Acad. Sci. USA* **102**, 11600–11605 (2005).
5. Zhou, X., Moran-Mirabel, J. M., Craighead, H. G. & McEuen, P. L. *Nature Nanotech.* **2**, 185–190 (2007).
6. Jacobson, K. A. et al. *Biochim. Biophys. Acta* **1330**, 138–44 (1997).
7. Mossman, K. D., Campi, G., Groves, J. T. & Dustin, M. L. *Science* **310**, 1191–1193 (2005).
8. Groves, J. T. & Boxer, S. G. *Acc. Chem. Res.* **35**, 149–157 (2002).

OPTICAL MATERIALS

Nanowire lasers go organic

With templates, it is possible to make large arrays of polymer nanostructures with adjustable shapes and sizes. Researchers are now adopting these techniques to make compact, subwavelength, polymer nanowire lasers.

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Over the past two decades, organic materials have shown great potential for use in high-performance optoelectronic devices, with rapid progress in the development of light-emitting and photovoltaic devices, as well as lasers and optical amplifiers. The first demonstrations of organic optoelectronic devices were made possible by the successful application of well-known vacuum thin-film deposition techniques to organic materials^{1,2}. Whereas early experiments focused on light-emitting and photovoltaic devices, the observation of lasing from an organic thin film soon followed^{3–5}.

The features that make organic-based lasers so attractive are a high degree of spectral tunability, large stimulated emission cross-sections, and the potential for simple high-throughput fabrication. The ease of fabrication has made it possible to produce organic

lasers using a wide variety of optical microcavities. Inspired by existing inorganic semiconductor lasers, organic materials have been used in conjunction with optical gratings, distributed Bragg reflectors and photonic crystals.

On page 180 of this issue, Deirdre O'Carroll, Ingo Lieberwirth and Gareth Redmond at the Tyndall National Institute in Cork, Ireland and the Max Planck Institute for Polymer Research in Mainz, Germany have extended this flexibility of structuring organic materials to fabricate subwavelength optical nanowire lasers⁶. They used a widely applicable templating method to grow arrays of vertically aligned cylindrical polymer wires (Fig. 1a) with optically flat end facets, such that each wire functions as a miniature optical cavity. Photons incident from an external pump laser are absorbed by the nanowire, leading to fluorescence from the polymer, followed by spectral line narrowing and lasing at higher pump intensities (Fig. 1b). The observed lasing wavelength is determined by the nanowire length: the condition for a resonant optical standing wave in the

cylindrical nanowire is that the wire length is a half-integer multiple of the emitted wavelength. The clear observation of these cavity resonances (Fabry-Pérot resonances) and lasing is an encouraging step for the further development of polymer nanowire optoelectronics. Moreover, this work may contribute to the realization of subwavelength integrated organic photonic devices.

Historically, organics have played an important role in the development of tunable lasers, some of the earliest examples of which were based on solutions of fluorescent dyes. Research into organic solid-state lasers has been motivated by the idea of combining the lasing medium and cavity in a single microscale device that could be easily integrated into numerous applications. In the early 1970s, lasing from a single crystal of fluorene doped with anthracene was demonstrated, where the stimulated emission originates from anthracene impurities, and the reflective crystal facets form the microcavity⁷.

Undoped single crystals offer an even simpler platform for organic lasers, eliminating the need to introduce foreign