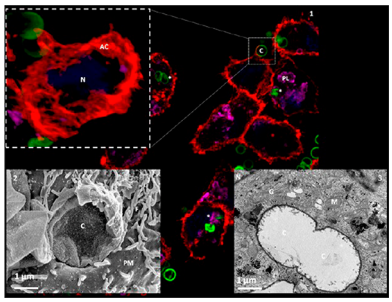
How Polyelectrolyte Multilayer Capsules Get Past the Velvet Rope

Polyelectrolyte multilayer (PEM) capsules are formed by sequentially laying down oppositely charged polyelectrolytes onto a spherical template and then chemically dissolving the template, leaving a hollow core. These empty casings are a promising delivery vehicle for biomedical applications, particularly due to their highly modifiable nature, making different functionalities easy to incorporate. Cargo molecules, including fluorophores, drugs, and proteins, can be placed inside. Other functional groups can be placed outside, imbuing these capsules with the ability to recognize cellular targets, to avoid immune system uptake, or to release their contents on command. However, despite these capsules' great potential, how they enter cells and their fate once inside is still largely unknown.

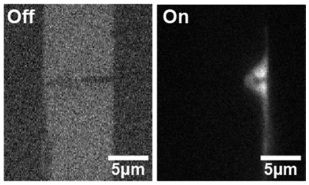
In a new study, Kastl *et al.* (DOI: 10.1021/nn306032k) sought to understand the internalization mechanism of PEM capsules in mammalian cells and their ultimate destination once internalized through a systematic study of various endocytic processes. Using a well-studied line of breast cancer cells as a model, the researchers carefully observed uptake of PEM capsules composed of polystyrene sulfonate/poly(allylamine hydrochloride) as a prototype of synthetic nondegradable capsules or poly-L-arginine/dextrane sulfate) as a prototype of biodegradable capsules. Rather than internalizing these capsules through invagination, the cells extended filopodia into a phagocytic cup to engulf them. Once inside, the capsules colocalized with lipid rafts, ultimately ending up in phagosomes. Through a thorough study of pharmacological and chemical inhibition of various endocytic pathways, the researchers found that electrostatic interactions influenced capsule internalization and ruled out clathrin- and caveolin-mediated endocytosis. The authors conclude that PEM capsule uptake combines lipid-raft-mediated macropinocytosis and phagocytosis, information that could help optimize their use.



Nanowires Mind the Chemical Store

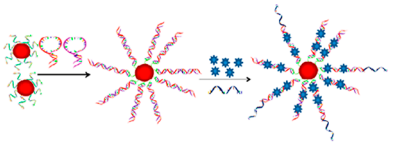
Scientists have long known that protein molecules' activity is inherently controlled by other molecules that serve as activation signals or energy sources. To develop new technologies that capitalize on protein functionalities, researchers must also develop effective ways to control the release of signaling chemicals. Researchers have looked to various solutions to manage the release of molecules such as ATP. However, each of these methods has critical drawbacks. For example, chemical concentrations can be readily controlled over the entire solution but cannot be controlled locally. Additionally, many of these methods require auxiliary equipment that hampers miniaturization into compact nanomechanical devices.

Seeking a new system to store and to release chemicals that can control protein activity, Lee *et al.* (DOI: 10.1021/nn402082v) developed "nano-storage" wires that discharge molecules under external electrical stimuli. The wires have three types of segments: a polypyrrole segment containing the chemical species of interest, a ferromagnetic nickel segment that allowed researchers to drive and deposit the nanostorage wires onto specific regions on an electrode surface, and a Au segment that provided good electrical contact with electrodes. Using ATP as their model chemical, the researchers show that when a negative bias was applied to the nanostorage wires, ATP was released, a process that could be repeated multiple times as voltage was turned off and on. The researchers were able to "write" nanostorage wires on solid substrates using a Ni needle as a pen, even showing their utility on flexible substrates. The authors suggest that this strategy could prove useful in a variety of applications, such as drug-delivery systems, biosensors, and biochips.



DNA Packed into Sphere for Cancer Magic Bullet

DNA, with its nanoscale helix turn length and diameter, has proven useful for engineering nanosized structures. With its specific base-pair formation and programmable sequence, DNA can readily self-assemble into predetermined designs, with fabrication of complicated two- and three-dimensional nanostructures now possible through engineered hybridization processes. These nanostructures have been suggested for a variety of applications, such as molecular sensing, nanomachines, and drug delivery. Although spherical nucleic acids (SNAs), with oriented and densely functionalized DNA covalently attached to metallic nanoparticles, were pioneered nearly two decades ago and have been tested for cancer drug delivery, they have significant limitations. Those carrying paclitaxel have been challenging in terms of



covalently labeling the drug molecule and insufficient drug payload capacity.

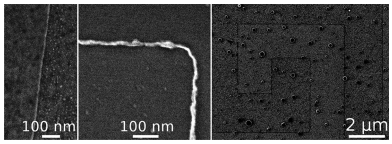
Seeking a new SNA system for cancer drug delivery, Zheng *et al.* (DOI: 10.1021/nn402344v) developed a nanoparticle-conjugated initiator that triggered DNA to hybridize on the nanoparticle surface into a long polymer, forming a shell. In a series of experiments, the researchers show that by controlling the concentration of the DNA initiator strand, they can control the size of the resulting SNA, which has further effects on cellular uptake, stability, biocompatibility, and surface functionalization. By inserting an apatamer that is specific to cancer cells with elevated expression of the protein nucleolin, the researchers were able to target their SNAs to specific cell types. By attaching fluorophores, the researchers could monitor internalization of these nanoparticles. Tests show a high drug loading capacity and enhanced killing of target cancer cells *in vitro*. The authors suggest that this new SNA platform could find potential applications in cancer therapies.

Published online August 27, 2013
10.1021/nn404111m

Water: The Secret Ingredient for Narrow Graphene Nanoribbons

Graphene has garnered increasing research interest due to its interesting and potentially useful electronic, optical, mechanical, and thermal properties. Its optical properties can be affected significantly by patterning this material into narrow graphene nanoribbons (GNRs). Bandgaps of GNRs have been shown to be tunable depending on width and edge configurations. Researchers have used a variety of methods to fabricate narrow GNRs, including various lithography methods, shadowing techniques, and processing of carbon nanotubes and graphite. However, few of these methods enable both scalable fabrication and the ability to position narrow GNRs on-chip—characteristics necessary for their industrial use in microelectronics.

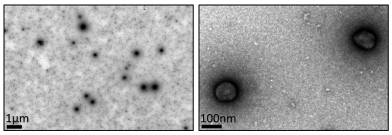
In a new study, Abramova *et al.* (DOI: 10.1021/nn403057t) develop a new method for preparing GNRs less than 10 nm wide through a top-down method they dub meniscus-mask lithography. The researchers first write a lithography pattern on graphene film so that the desired GNR position corresponds to the pattern edge. After the pattern is developed, they use reactive ion etching to etch the exposed graphene. After depositing a sacrificial metal layer, the pattern is then lifted off, and the structure is exposed again to reactive ion etching. Finally, the sacrificial metal layer is removed by wet etching. Through this process, the researchers found that narrow GNRs formed at the edge of the lithographic pattern. Further testing suggests that GNRs form through this method because an adsorbate, most likely atmospheric water, protects graphene in a wedge beside the sacrificial metal. The authors suggest that this facile method reliably produces GNRs with narrow widths without the need for high-resolution lithographic methods.



Minicircle DNA Gets around Viral Vectors

Transfecting cells with non-native genes has shown significant promise for medical therapy and basic research. Currently, most gene therapies use viral vectors to transfect cells. Although this approach provides highly efficient delivery, implementing this practice broadly for clinical applications faces safety concerns, such as the potential for these vectors to cause insertional mutagenesis. Consequently, researchers are increasingly focusing on developing nonviral vectors for gene delivery.

In a step toward that goal, Keeney *et al.* (DOI: 10.1021/nn402657d) combined polymeric vectors with minicircle (MC) DNA, supercoiled DNA molecules trimmed of bacterial plasmid backbones. Recent studies have

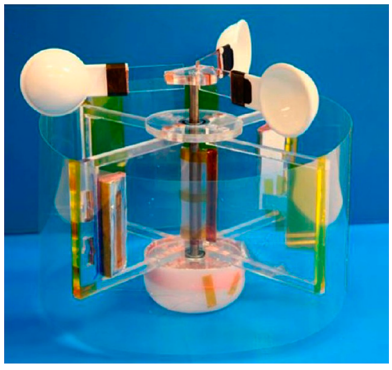


shown that MC DNA can increase transgene expression more than 100-fold over plasma DNA, although MC DNA alone suffers from low transfection efficiency. To boost this efficiency, the researchers combined MC DNA with poly(β-amino ester)s (PBAEs), which are biodegradable polymers with broadly tunable structural diversity. The researchers synthesized 18 PBAEs with different chemical structures, then complexed the cationic polymer with MC DNA to form nanoparticles. Testing these nanoparticles *in vitro* using green fluorescent protein as the transgene, the researchers found that transfection efficiency differs significantly depending on the PBAEs' chemistry. A few of the PBAE polymers allowed MC DNA delivery at levels comparable to or even surpassing Lipofectamine 2000, a popular reagent for enhancing transfection. When studied *in vivo* in a mouse model, a lead PBAE/MC DNA nanoparticle formulation enhanced protein expression two-fold compared to MC DNA alone. The authors suggest that these results show the promise of PBAE-based nanoparticles as a valuable tool for gene therapy.

Renewable Energy, Blowing in the Ambient Wind

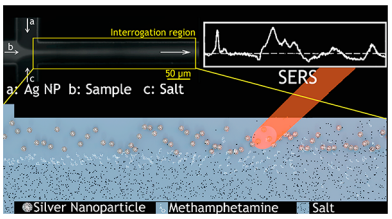
Finding sustainable and self-sufficient sources of energy continues to be a prominent research focus. Nanogenerators that convert small-scale mechanical energy into electricity are one solution to this problem. Although wind energy is considered to be one of the most important renewable and "green" energy sources, the conventional approach toward generating electricity from wind requires large wind turbines, high installation costs, and high wind speeds to turn the blades, preventing harvesting wind energy from the slower wind speeds around houses and in cities.

Seeking a new way to harvest energy from even weak winds, Xie *et al.* (DOI: 10.1021/nn402477h) developed a new type of nanogenerator that relies on the triboelectric effect to generate charge. This novel device has conventional wind cups at the top of a rotating shaft. A flexible and soft rotor blade made out of a polyester film is connected to the shaft and rotates with it. Attached to the end of this blade is a polytetrafluoroethylene film, which serves as a triboelectric layer. To increase surface roughness, and therefore maximize triboelectric charge density, the researchers etched this film to form nanowires-like structures on the surface. As wind energy turns the shaft, this film sweeps across two aluminum-covered plates that serve as stators, generating triboelectric charges. Under a mild wind speed of about 15 m/s, this nanogenerator delivered an open-circuit voltage of 250 V and a short-circuit current of 0.25 mA, which was capable of driving more than 100 LEDs. The authors suggest that this device could also be powered by ocean currents, providing another outlet for energy harvesting.



Shining a New Searchlight on Drugs of Abuse

Developing a quick and cost-effective method to identify drugs of abuse in biological fluids, especially saliva, would be tremendously useful for healthcare, forensic, and home testing applications. Currently, drug testing is usually carried out in laboratories through enzyme-linked immunosorbent assay, gas chromatography with mass spectrometry, or high-performance liquid chromatography. These methods typically require expensive reagents, trained personnel, and several hours to complete. Although home testing kits usually rely on a colorimetric assay, these tests can screen for only a limited number of substances, require large sample volumes, and the subjective nature of their readout can be misinterpreted.

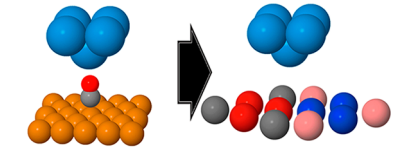


In a new study, Andreou *et al.* (DOI: 10.1021/nn402563f) find a potential solution to these problems by combining surface-enhanced Raman spectroscopy (SERS) with microfluidics. The researchers developed a three-pronged microfluidics platform in which a saliva sample is introduced in a centrally located stream. Ag nanoparticles are flowed in one side stream. Lithium salt, which acts as an aggregator to the Ag nanoparticles so they can be used for SERS, is flowed in another side stream. In this scenario, the analyte first has a chance to bind to the nanoparticles before the salt aggregates them; these aggregates are then probed with spectroscopy further down the channel. Using methamphetamine as their model drug of abuse, the researchers show that this method effectively identified at concentrations as low as 10 nM. The authors suggest that this cartridge-based method could also be used in other applications, such as groundwater analysis or toxin detection.

A Handy Tip for Better Atomic Identification

Noncontact atomic force microscopy has become a useful tool for surface chemistry analysis. This technique can not only discriminate between different atomic species, but also distinguish between the same atomic species in different local environments. Because this technique relies on measuring forces between the tip of the microscope's cantilever and the sample, the ability to distinguish between different types of adatoms depends strongly on the tip state, with a poorly defined tip preventing reliable atom identification.

Seeking a way to characterize the tip reliably and to engineer a specific tip apex, Welker *et al.* (DOI: 10.1021/nn403106v) developed a method they call CO front atom identification (COFI). Their method involves scanning a clean tip over a CO molecule adsorbed on a Cu(111) sample, showing the front atom's angular bonding symmetry. By softly poking the tip into the sample, the tip apex's configuration was changed without contaminating it with Cu atoms. The angular bonding symmetry of the tip was then characterized again over the CO. This procedure can be repeated until the preferred bonding symmetry is obtained. To test the utility of this method, the researchers took spectroscopic measurements of a Si(111)-7 × 7 sample, which contains four inequivalent adatom types, using COFI to ensure tip integrity after measurements. Their results, using four different tip states, distinguished between all four different adatoms. The authors suggest that their COFI method provides a well-defined tip for atomic force measurements, which could help improve metrology on the nanoscale.



Taking a Closer Look at Single-Molecule Magnets

Single-molecule magnets (SMMs) could be used for a variety of potential applications, such as information storage, molecular spintronics, or quantum computation. Such applications will depend on SMMs being adsorbed onto solid substrates, with their electronic structures and magnetic properties well characterized and individual SMMs accessible. To characterize SMMs, previous studies have placed these materials onto substrates that exert a variety of different effects. For example, the interaction between noble metal substrates, such as Au, and SMMs can be strong, changing the electronic structure and magnetic properties of the SMM. With inert insulating substrates, such as SiO_2, the interactions can be so weak that the deposited SMMs move around and aggregate.

To gain a better understanding of these materials, Sun *et al.* (DOI: 10.1021/nn401827h) used the semimetallic substrate Bi(111), which has intermediate effects, to characterize a model SMM, manganese-12-acetate (Mn_{12}). The researchers gently deposited individual Mn_{12} on the surface using a scanning tunneling microscope (STM) tip. Resulting STM images showed two different orientations for the deposited molecules, side-lying and flat-lying. Energy-resolved spectroscopic mapping allowed the researchers to view several molecular orbitals around individual Mn_{12} molecules. For the flat-lying molecules, the energy gap between the highest occupied molecular orbital and the lowest unoccupied molecular orbital is only 40% of the gap for a free Mn_{12} molecule due to interactions with the Bi(111) surface. However, images show that the local lattices of Bi(111) are intact, suggesting that these interactions are not strong. The authors suggest that these results provide a first look at the local structure and electronic properties of individual Mn_{12} molecules on a semimetal substrate.