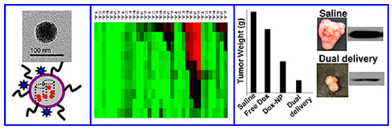
Resisting Resistance with a One-Two Punch

In an attempt to evade the resistance that can develop to chemotherapeutic agents, many cancers are treated with a combination of drugs. However, cancer cells often adapt and become resistant anyway, leading to treatment failure. Avoiding drug resistance has proven difficult because this problem can arise through multiple and dynamically acquired mechanisms, stemming from sources as varied as the expression of drug efflux pumps, antiapoptotic proteins, oncogenes, and cellular regulators of drug metabolism. To combat this problem, researchers have recently begun investigating the use of nanocarriers, which can sidestep resistance through endosomal chemotherapeutic delivery while also having the capability to deliver small interfering RNAs (siRNAs) to knock down drug-resistance genes.

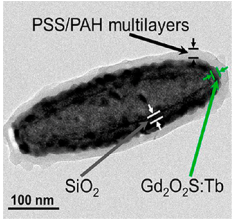
In a new study, Meng *et al.* (DOI: 10.1021/nn3044066) take advantage of both of these features by using nanoparticles to deliver a chemotherapeutic agent as well as siRNA to lower expression of a protein involved in drug resistance. Using a breast cancer cell line known to be resistant to the cancer therapeutic doxorubicin (Dox), the researchers performed high-throughput screening with various siRNAs to determine the best gene to knock down in order to overcome Dox resistance. Their search identified P-glycoprotein (Pgp), a drug efflux pump. Using this finding, the researchers developed mesoporous silica nanoparticle carriers to deliver Dox and the optimal siRNA against Pgp to tumors. *In vivo* tests showed that particles provided significantly higher tumor inhibition compared to particles carrying just Dox or the Pgp siRNA, or free Dox, although these effects were heterogeneous due to the tumor microenvironment. The authors suggest that this strategy could offer a novel way to treat drug-resistant cancers.



Watching Chemotherapy at Work

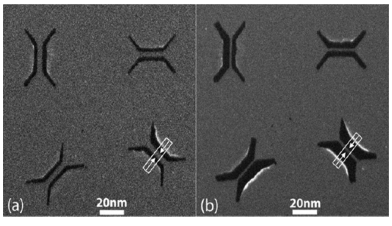
One of the holy grails of cancer therapy is the ability to target only cancer cells while reducing toxicity to normal, healthy cells. To accomplish this feat, scientists have explored coating nanoparticle drug-delivery vehicles with agents that release drugs only in the presence of specific stimuli. However, many physiologic factors can affect the nanoparticle distribution and drug-release rate. Measuring distribution and drug release *in vivo* after these nanoparticles are delivered systemically remains a challenge, making it more difficult to design the most effective chemotherapeutic nanocarriers rationally.

Toward this end, Chen *et al.* (DOI: 10.1021/nn304369m) have developed novel nanocapsules capable of acting as pH-responsive delivery vehicles for cancer drugs while also providing a radioluminescent signal that changes during drug release. Using ellipsoidal hollow silica nanorice as templates, the researchers crafted Gd_2O_2S-based nanoparticles doped with the rare earths Tb or Eu. Tests showed that these nanocapsules were stable under physiological temperatures and pH and had efficient energy conversion rates, making them suitable for radioluminescent applications. By coating them with layers of sodium poly(styrenesulfonate) (PSS) and poly(allylamine hydrochloride) PAH, the researchers made these nanoparticles suitable to release their cargo of the chemotherapeutic drug doxorubicin under the low-pH conditions present inside cancerous tumors. *In vitro* and *in vivo* experiments showed that it was possible to track drug release from these carriers using X-ray excited optical luminescence. The particles' composition also makes them suitable contrast agents for MRI. The authors suggest that radioluminescent particles could open the door to better drug nanovehicle design.



Graphene on the Cutting Edge

Graphene continues to attract attention for its unusual properties, including high mobility, strength, and thermal conductivity, making it a natural fit for a variety of interesting applications. Most of these applications rely on single-layer graphene being patterned into ribbons, gaps, or pores. Both theoretical and experimental studies have shown that the edges of these patterns can exert strong effects on graphene's electronic and magnetic properties, affecting its performance. Consequently, bringing these applications to fruition will rely on techniques to sculpt graphene edges controllably and reproducibly into desired patterns at the atomic scale. Thus far, it has not been possible to sculpt even a single ribbon or pore in multilayer or monolayer graphene without introducing defects nearby.



In their study, Xu *et al.* (DOI: 10.1021/nn3053582) introduce a new technique to pattern graphene reproducibly and cleanly, combining scanning transmission electron microscopy (STEM) and *in situ* heating to between 500 and 700 °C. By adjusting the dwell time—the time at which the electron beam is fixed at a given position—the researchers were able to alternate between destructive sculpting and imaging. Exposing the specimens to high temperatures during this procedure allowed the graphene lattice to self-repair, healing any introduced defects. Switching to imaging mode provided an opportunity to inspect the sculpted pattern and make adjustments. Using this technique, the researchers were able to create nanoribbons by moving the electron beam along two lines and nanopores by scanning the electron beam in a spiral. The authors suggest that this technique can eventually be computer automated to create more complex patterns.

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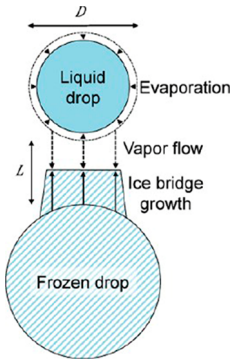
Giving Frost on Superhydrophobic Surfaces the Cold Shoulder

Superhydrophobic surfaces minimize contact and heat transfer between water and substrates, which may be useful for anti-icing applications. When superhydrophobic surfaces have robust nanoscale or hierarchical roughness, condensate collects in a suspended state and even has the potential to jump off the surface spontaneously using surface energy harvested from naturally occurring coalescence. Although recent research suggests that superhydrophobic surfaces cooled below zero have delayed condensation frosting compared to traditional filmwise and dropwise condensers, this result has been explained only in terms of the onset of freezing for individual drops. Researchers still know little about the interdrop freezing dynamics that lead drops of frozen condensate to contact and to freeze neighboring drops, advancing frost fronts.

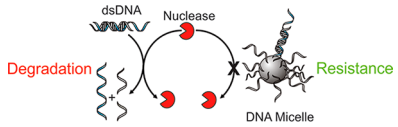
In a new study, Boreyko and Collier (DOI: 10.1021/nn3055048) further the knowledge of how frost fronts advance on hierarchical superhydrophobic surfaces. The researchers examined condensation frosting through microscopy on smooth and two-tier copper surfaces cooled and coated with a monolayer of 1-hexadecanethiol, creating hydrophobic and superhydrophobic surfaces. On the hydrophobic surface, condensate formed over time, gradually nucleating into larger drops and frosting uniformly into ice. However, on the superhydrophobic surface, formed condensate jumped from the surface, delaying the onset of frosting. However, frost eventually formed at the edges of the surface, with frozen droplets forming ice bridges to neighboring drops and freezing them, leading frost fronts to sweep gradually across the field. The authors suggest that superhydrophobic surfaces can delay frost growth but cannot prevent spreading frost fronts.



Indigestion: Protecting DNA from Nucleases

DNA has proven useful in numerous applications, in both clinical care and basic research. However, in the biological milieu, unmodified DNA is highly susceptible to degradation by enzymes, greatly limiting its practical use. To combat this problem, researchers have generated several DNA analogues capable of resisting enzymatic attack. However, these analogues can have unpredictable and undesirable biologic effects. As an alternative, recent studies have focused on two strategies to preserve DNA using nanotechnology-based approaches: either using gold nanoparticles to arrange oligonucleotides as a spherical brush or packing nucleic acids using DNA origami.

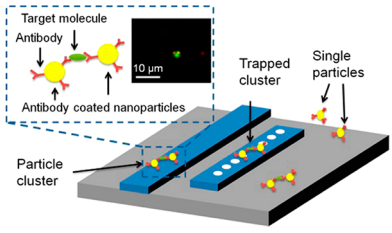
Investigating a third alternative, Rush *et al.* (DOI: 10.1021/nn305030g) fortified single-stranded oligonucleotides against enzymatic attack by packing them densely in organic polymeric micellar nanoparticles. The researchers conjugated about 200 strands apiece to a hydrophobic organic polymer core, creating a dense corona. Using this method, they formed two different types of particles carrying DNA with different sequences. When they exposed these particles to a selective endonuclease, a variety of assays showed that the DNA packed into these nanoparticles was well-protected. The findings were similar for a nonspecific exonuclease. Although tests showed that the exonuclease succeeded in removing a few of the outer bases, the vast majority of the sequences were preserved. In a final test, the researchers exposed the particles to snake venom phosphodiesterase, an aggressive exonuclease. Findings showed that DNA packed on the nanoparticles exhibited exceptional resistance to degradation. The authors suggest that this method could be used to protect DNA for both *in vivo* and *in vitro* applications.



Catching Proteins and Particles in a Microcavity Trap

Developing improved methods for sensing particles and biological molecules is essential for moving forward in fields including medical diagnostics, environmental monitoring, and basic research. Researchers have made progress to this end, crafting impressive electronic and photonic devices that sense a variety of molecules. However, these tools typically perform this function by binding molecules to a functionalized surface, rendering them suitable only for single use, restricting them to predetermined particles and molecules, and making them susceptible to a diffusion bottleneck.

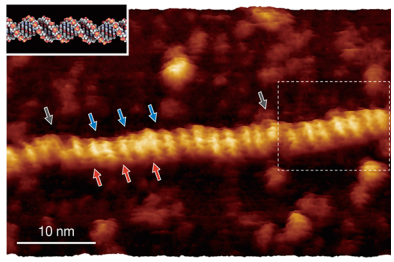
Seeking a way to avoid these drawbacks, Lin and Crozier (DOI: 10.1021/nn305826j) developed a method that uses optical forces to trap and to detect particles within waveguide-coupled silicon microcavities. As a proof of principle, the researchers used this method to trap polystyrene particles. They employed a single laser operating at a wavelength of 1500 nm to trap particles within microdonuts and a second laser, operating at the same wavelength, to perform the sensing function. Tests show a linear increase of the microdonut resonance wavelength with the number of trapped particles within. To improve the sensitivity of this setup, the researchers next investigated using nanobeam photonic crystal cavities instead of microdonuts. Indeed, these microcavities provided even larger resonance shifts. Finally, the researchers tested this method's ability to sense protein molecules, coating the polystyrene particles with green fluorescent protein. Experiments show that optical trapping provides an accurate way to detect the concentrations of these target molecules. The authors suggest that this technique could find sensing applications in a wide range of fields.



Seeing DNA in a New Light

More than half a century ago, using X-ray diffraction, DNA was found to form a double helix. Since then, there has been a drive to visualize the submolecular features of this hallmark structure directly. Atomic force microscopy (AFM) has come close, showing the biologically active structure of this genetic molecule in water. Two problems with this approach are that AFM not only structurally deforms DNA due to the strong interactions with the AFM probe tip, but the large AFM probe typically prevents imaging submolecular features as small as the simple helical periodicity.

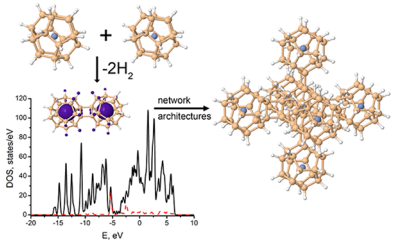
In a new study, Ido *et al.* (DOI: 10.1021/nn400071n) reveal the quintessential genetic molecule's submolecular features using AFM with frequency modulation detection (FM-AFM). This method enhances force sensitivity compared to other AFM methods. The researchers used FM-AFM on the bacterial plasmid pUC18, a closed circular DNA composed of 2686 base pairs. Their high-resolution images clearly showed deep grooves of two different widths between the sugar–phosphate backbones of DNA, which they attributed to the B-DNA's major and minor grooves. Comparing these experimental images with simulated DNA images based on atomic coordinate data from the Protein Data Bank, the researchers located the molecule's individual phosphate groups. They extrapolated these findings to DNA tiles, identifying the major and minor grooves in these nanostructures and two different unit connections between individual tiles, corresponding to two different major and minor groove arrangements between DNA's sticky ends. The authors suggest that this technique will be useful in investigating other nanostructures based on DNA.



Doped Hydrogenated Si Clusters: Attractive Building Blocks

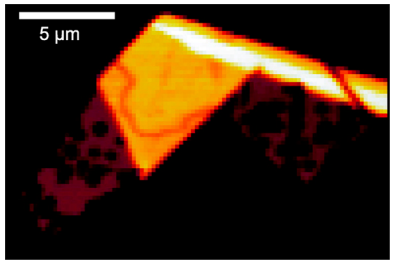
Multidoped endohedral clusters have cage-like geometries and easy-to-tune electronic properties that make these molecules promising building blocks for nanoscale structures. Hydrogenated transition-metal-doped Si clusters are especially interesting because the minimized interactions between the cage structure and their dopants preserve the encapsulated dopants' high magnetic moments. Such properties make these molecules promising components for applications that rely on magnetism, such as data storage or spin-based electronic devices. However, although these molecules are promising individually, assembling them into larger units remains a pivotal problem.

Attacking this problem using quantitative first-principles calculations, Palagin and Reuter (DOI: 10.1021/nn3058888) suggest that the degree of hydrogenation could hold the solution to this problem. The researchers performed density functional theory (DFT)-based global geometry optimizations for prototypical $CrSi_{20}H_{20}$ cages with different numbers of H vacancies built into the structures. Taking up to 8 H atoms continued to produce cages with distortions but maintained their structural integrity. When H atoms were removed by twos, the vacancies were paired, with sets of vacancies located at opposite ends of the cage. Further investigation showed that these paired vacancies can act as docking sites to join molecules through Si–Si double bridge bonds, effectively fusing clusters together. Depending on the number and location of H vacancies, the researchers show that the cages can be polymerized into one-dimensional chains, two-dimensional sheets, or more complicated three-dimensional structures. They suggest that dehydrogenation could be key to using these unique molecules to construct highly magnetic materials.



Hydrogen-Plasma Reactions with Graphene: The Hole Story

Graphene's unusual electronic, mechanical, and optical properties have made it a highly desirable material to exploit for a variety of technological applications. To tailor its properties based on particular needs, researchers have looked for ways to chemically modify and to functionalize graphene. One way is treatment with plasma at elevated temperatures. At the present, however, how hydrogen plasma reacts with mono- and multilayer graphene has not been well elucidated.



To understand the interactions between hydrogen plasma and graphene, Diankov *et al.* (DOI: 10.1021/nn304903m) explore this phenomenon using microscopy and Raman spectroscopy. The researchers exposed monolayer and multilayer graphene sheets on SiO_2 substrates to remote hydrogen plasma in a tube furnace. Atomic force microscopy images, supported by Raman spectra, show that monolayer graphene developed numerous circular isotropic etch pits and etching from the sheet edges. However, multilayer graphene was etched very little, with the numbers of pits about 2 orders of magnitude lower than for monolayer graphene. Additionally, the multilayer graphene pits were anisotropic and hexagonal in shape, arising from pre-existing defects. For both types of samples, the etch rate was highly dependent on temperature, being very slow at room temperature, peaking at 400 °C, and being completely suppressed at 700 °C. When graphene samples were placed on the much smoother substrate mica, the results were the same, suggesting that substrate roughness was not a factor. The authors suggest that substrate polarity or charged impurities within the substrate could be responsible for monolayer graphene's high reactivity.