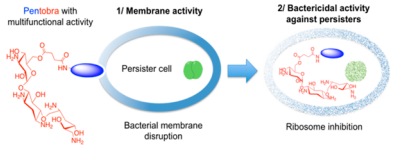
Fighting Back against Persisters

Antibiotic resistance continues to grow as a public health problem. Although this issue can largely be blamed on genetic variations that arise in bacterial populations through spontaneous mutation and horizontal gene transfer, part of the problem centers on subpopulations of bacteria known as persisters. These bacteria tolerate antibiotic treatment through a mechanism in which they reduce metabolic activity, allowing them to survive against drugs that typically target growth processes such as cell-wall, protein, and nucleic acid synthesis. These persistent bacteria then often revert to an actively growing state once treatment ceases, leading to recurrent and chronic infections.

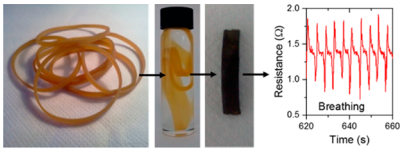
Seeking a novel way to target these persistent subpopulations, Schmidt *et al.* (DOI: 10.1021/nn502201a) engineered a persister-specific antibiotic that combines two synergistic antibiotic functions into a single molecule. The researchers started with tobramycin, an aminoglycoside antibiotic that targets bacterial ribosomes but is ineffective on its own against persisters, and antimicrobial peptides (AMPs), which kill by selectively disrupting the barrier function of bacterial membranes while alternatively or also translocating across membranes to bind intracellular targets. While AMPs' killing activity is lower than that of aminoglycosides, they depend less on bacterial cells' metabolic status. By incorporating 12 amino acids from AMPs into tobramycin, the researchers created a new composite antibiotic they named Pentobra. Tests showed that Pentobra induced nanoscopic Gaussian membrane curvature necessary for membrane permeabilization, allowing the drug to enter and to kill both Gram-negative and -positive bacteria selectively while sparing eukaryotic cells. The authors suggest that this strategy against persistent bacteria could offer a promising way to renovate traditional antibiotics.



Strike Up the Band: Graphene–Rubber Composites

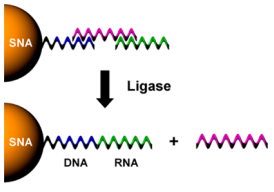
Strain sensors that are meant to be worn on the body must fulfill a variety of requirements that are not part of traditional strain sensing platforms. For example, they need to be light and flexible, sensitive enough to detect small-scale resistance changes that might arise from breathing, able to work at the high strains of joint flexion, and need to operate at high speeds and strain rates to accommodate fast, involuntary movements. Ideally, these sensors would also be producible in various geometries and inexpensive. Thus far, no reported material has simultaneously met all these requirements.

In a new study, Boland *et al.* (DOI: 10.1021/nn503454h) took a novel approach to developing flexible strain sensors by incorporating flakes of graphene into rubber bands. The researchers soaked store-bought rubber bands in toluene, causing the bands to swell, then transferred the bands to solutions of liquid-exfoliated graphene dispersed in solvent. Tests showed that rubber bands soaked in the graphene dispersions for times ranging from 15 min to 48 h had varying amounts of infused graphene, with concentrations increasing further in the bands after longer exposure times. These materials served as excellent strain sensors, with up to 10^4-fold increases in resistance when stretched and working at strains exceeding 800%. These sensors could also track dynamic strain at vibrational frequencies of at least 160 Hz. As proof of principle, the researchers were able to use the bands to monitor joint and muscle motion, breathing, and pulse. The authors suggest that these bands might be useful in continuous monitoring of bodily functions or woven into smart suits for babies, athletes, or rehabilitation patients.



Having a Ball with siRNA

Small interfering RNA (siRNA) continues to be a useful tool in biomedical research, with utility for knocking down targeted proteins by degrading mRNAs in a sequence-specific manner. Because siRNAs suffer from inherent chemical instability in cells that hampers their chances of successful delivery, researchers have developed a variety of methods to improve their resilience, including several that involve conjugating siRNA to the surfaces of nanoscale materials. These constructs are usually synthesized by functionalizing an oligonucleotide with an unnatural binding group, such as an alkylthiol or alkylamine, which can then be absorbed onto a particle of interest. Although this technique has been successful, it also requires a specialty oligonucleotide to be synthesized for every different nanoconstruct. Developing a universal construct that could be used with any siRNA or nanoparticle could offer a more facile approach.



Toward that end, Rouge *et al.* (DOI: 10.1021/nn503601s) made siRNA–nanoparticle constructs using a universal DNA-based spherical nucleic acid (SNA) nanoparticle conjugate and a T4 DNA ligase-catalyzed reaction. After functionalizing Au nanoparticles with DNA anchor strands, the researchers hybridized these to customized DNA bridges that extended sticky ends outside the sphere. They then hybridized these sticky ends to siRNAs. Results showed that these constructs were readily taken up into cells in culture and were able to reduce expression of green fluorescent protein by more than half. Constructs that carried two different types of siRNA also demonstrated successful knockdown. The authors suggest that this approach opens up a rapid route for preparing RNA–nanoparticle constructs that are able to target multiple messenger RNAs at the same time.

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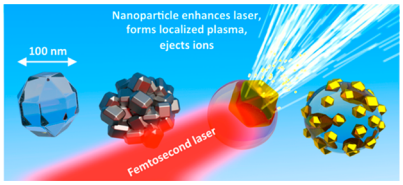
Liquid Manipulation, by a Hair

Manipulating liquid droplets controllably is key to many fields, including printing, patterning, bioassays, nanomaterials fabrication, and chemical reactions. In typical liquid manipulation systems, fluid is transferred by components including channels, nozzles, or tubes. However, these closed systems pose several challenges, including high flow resistances and high risks of clogging. Open systems could offer advantages due to their lower hydrodynamic resistances and ease in fabrication and processing. Many researchers have developed artificial fibrous systems to move liquid droplets that mimic systems in nature, such as those that collect water from humid air much like spider silks and cactus spines. However, most of this work has focused on the self-propelling behavior of liquid droplets on conical fibers driven by the surface physicochemical gradient, while little research has mentioned using these agents for efficient liquid transfer.

In a new study, Wang *et al.* (DOI: 10.1021/nn503463y) developed a novel approach to liquid transfer by using surface-structured conical copper wires (SCCWs) to mimic the hairs on Chinese brushes that deliver ink. Using cylindrical copper wires with diameters of 250 μm as the starting material, the researchers used a dynamic electrochemical approach to fabricate conical wires with *ca.* 100 nm tips and tunably rough surfaces at many scales. By optimizing the apex angle and the tilt angle of individual SCCWs, these artificial hairs demonstrated the ability to hold over 400 times greater than their own volume at their tips. The authors suggest that these bio-inspired materials could offer a new way to manipulate liquid controllably and with high efficiency.

Explosion of Data on Localized Light Absorption

Nanoscale structures can locally enhance a laser field, leading to interesting technologies such as Au nanoparticles that can selectively destroy tumor tissues when irradiated while sparing nearby healthy tissues and nanostructures that can accelerate electrons when irradiated, potentially leading to miniature particle accelerators. However, refining and realizing these concepts requires better understanding of how nanostructures respond to laser fields near the damage threshold. Studying nanomaterials at strong laser fields poses many challenges, including the fact that these intense lasers damage nanoparticles and the effects of the lasers can differ dramatically with subtle variations between nanomaterial samples and even with particle orientation.

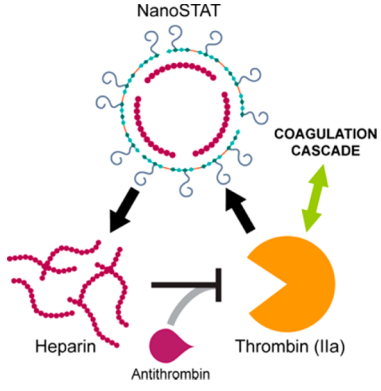


In a new study, Hickstein *et al.* (DOI: 10.1021/nn503199v) overcome these hurdles through a new method that images localized nanoscale plasma created when an isolated nanoparticle is irradiated with a short but strong laser pulse that is slightly below the plasma formation threshold of the bulk material. Here, the nanoparticle itself enhances the laser field in localized regions, ejecting ions in a direction that can be used to determine the location of the plasma. Using this technique, which they call plasma explosion imaging, the researchers observe dramatic differences in how four different nanoparticles of four different compositions and shapes respond to strong laser fields. Their results show subwavelength focusing in NaCl crystals, symmetric absorption in TiO_2 aggregates, surface enhancement in dielectric particles containing a single Au nanoparticle, and interparticle hotspots in dielectric particles containing several smaller Au nanoparticles. The authors suggest that, in the future, this method might be extended to more complex nanostructures and stronger laser intensities.

Tighter Control of Anticoagulation

Many biological processes use feedback loops to maintain homeostasis. One such process is blood coagulation, which uses a protease-driven positive-feedback cascade to stop blood loss from injured vessels by forming clots. Dysregulation of this process, either through disease or medication, can lead to life-threatening hemorrhaging or thrombosis that causes pulmonary embolism, stroke, or organ infarction. Patients at risk of thrombocytic conditions often receive anticoagulant medications, the levels of which must be tightly controlled to prevent both clots and bleeds. Because this therapeutic window is exceedingly narrow, the need for new formulations of anticoagulants that effectively prevent thrombosis while protecting against over- or under-treatment remains high.

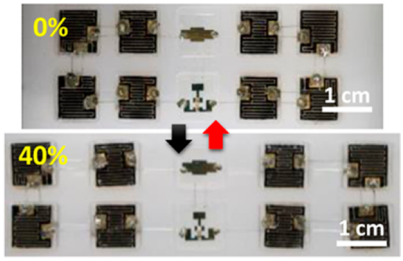
In a new study, Lin *et al.* (DOI: 10.1021/nn501129q) increased the safety profile of unfractionated heparin, the prototypical clinical anticoagulant, by reformulating it into a self-assembled nanocomplex that only releases heparin in the presence of thrombin, a key protease of the coagulation cascade. This so-named nanoscale self-titrating activatable therapeutic, or nanoSTAT, relies on leveraging the charge interaction of PEGylated cationic peptides composed of thrombin-cleavable substrates with naturally ionic heparin. Numerous assays, including in plasma and *in vivo*, show that nanoSTAT keeps heparin enclosed until it encounters thrombin, at which time it releases its payload. Additional tests in mouse models indicate that this reformulated anticoagulant does not increase bleeding risk, unlike free heparin, while also significantly decreases clotting risk in animals predisposed to pulmonary thromboembolism. The authors suggest that nanoSTAT could offer a viable option for safer anticoagulant therapy.



Microsupercapacitor Arrays Take the Strain

Stretchable electronics are a growing area of research, with a bevy of applications in medical, environmental, and electronics industries. With this surge in interest for stretchable electronics comes a need for equally stretchable energy storage devices that can operate without an external wire connection to a power source. Although supercapacitors could offer a promising power source, few have been designed on stretchable substrates.

Seeking to address this opportunity, Hong *et al.* (DOI: 10.1021/nn503799j) developed microsupercapacitor arrays on a deformable substrate that consists of relatively rigid islands for active devices embedded in a soft and stretchable thin film. The islands are made of a stiff polymer (polydimethylsiloxane, PDMS)

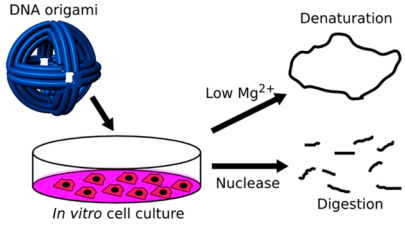


with a high Young's modulus, while the thin film is made of a mixture of Ecoflex and PDMS with a significantly lower Young's modulus. On the stiff islands, the researchers placed microsupercapacitors composed with layer-by-layer assembly of multiwall carbon nanotubes with metal oxide and polymer electrodes. They connected these with the liquid metal Galinstan. Tests showed that this device exhibited high electrochemical performance under a variety of mechanical deformations, such as bending, twisting, and uniaxial strain of up to 40%. This level of strain had little effect on the PDMS islands, while the thin film withstood extraordinary stretching. When integrated into a circuit, the microsupercapacitors increased the output voltage beyond the electrolyte used, effectively lighting LEDs of various voltages. The authors suggest these results show the viability of this design for energy storage for flexible, stretchable electronics.

Turning DNA Nanostructures into Survivors

DNA has offered a revolutionary material for creating nanostructures, with the ability to form virtually any geometry and display sophisticated capabilities. These features have made DNA nanostructures an attractive platform for various biomedical applications. To test the viability of DNA nanostructures for these uses, *in vitro* tissue culture model systems are an obvious choice. However, tissue cultures use conditions that could affect the integrity of these materials. These include fetal bovine serum (FBS), which contains nucleases capable of digesting DNA nanostructures, and divalent cation concentrations significantly below conditions used to fold these nanostructures, which could lead to denaturation.

To determine if these conditions significantly affect the form and function of DNA nanostructures, Hahn *et al.* (DOI: 10.1021/nn503513p) systematically tested both conditions that could alter the viability of these materials in tissue culture as well as fixes that could preserve their integrity. Using four different DNA nanostructures, including nano-octohedrons, nanotubes, nanorods, and a nanorobot, the researchers found that all four designs were significantly digested after 24 h when medium was supplemented with greater than 5% FBS. Similarly, all but the nanotube was significantly denatured after 24 h when cations were depleted in normal tissue culture medium. Inactivating the FBS with heat was incompatible with normal tissue growth, but supplementing with actin protein reduced FBS nuclease activity. Similarly, supplementing tissue cultures with Mg^{2+} reduced denaturation, while leaving cell growth unaffected. The authors suggest that researchers using tissue culture systems to test DNA nanomaterials' viability must consider these factors in their studies.



Polymers on the Move

As polymer chains move from dilute to overlap concentrations, critical fluctuations emerge over extended distances. Near the overlap concentration, polymer solutions likely become mosaics, with some spatial regions that are locally dilute having free translational motion of chains and other regions with higher concentrations having slower, more restricted mobility. As the polymer concentration increases, chain entanglements would probably further limit correlated motion to smaller and smaller pockets, according to scaling laws that describe cooperative diffusion. Decades ago, experimental dynamics between correlated regions in polymer solutions were obtained using dynamic light scattering. However, because the intrinsic scale of segmental motion in synthetic polymers is below the diffraction limit of this technique, researchers still know little about the true dynamics of polymer mobility fluctuations near overlap concentrations.

To address this regime, King *et al.* (DOI: 10.1021/nn502856t) used a combination of stimulated emission depletion microscopy (STED) and fluorescence correlation microscopy (FCS). The researchers dissolved end-labeled polystyrene, which served as a tracer, in toluene, then mixed these with matrix polystyrene at concentrations that varied from dilute to more than 10 times the overlap concentration. Results showed that for dilute solutions, the intensity−intensity correlation function follows a single diffusion process. However, at the overlap concentration, the technique showed an additional relaxation process. The researchers identified the slower mode as self-diffusion and the faster mode as correlated segment fluctuations that reflect the cooperative diffusion coefficient. The authors suggest that STED-FCS provides a way to visualize heterogeneous dynamics in polymer systems.