

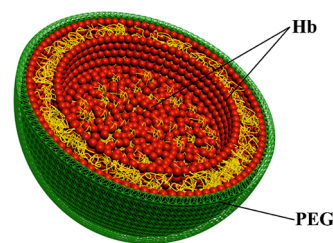
A Sanguine Solution for Artificial Blood

Doctors have long been able to combat the effects of blood loss and conditions that cause serious blood deficiencies using allogenic blood transfusions. However, donor blood is a vastly limited resource with a short shelf life, and blood banks around the world routinely experience acute shortages. To solve this problem, scientists have attempted to develop a variety of blood substitutes, including glutaraldehyde cross-linked polyhemoglobin and hemoglobin conjugated with various polymers, both of which avoid the toxicity caused by cell-free hemoglobin. However, these substitutes only mimic the oxygen-carrying capacity of red blood cells without replacing any of blood's other functions. Additionally, while free hemoglobin can be encapsulated in other ways, such as in biodegradable polymers or lipid vesicles, loading these vehicles with high con-

centrations while maintaining their presence in circulation remains a challenge.

To overcome these hurdles, Duan *et al.* (DOI: 10.1021/nn301735u) developed a new prototype for artificial blood that takes advantage of porous calcium carbonate nanoparticles as templates. The researchers developed hemoglobin spheres by co-precipitating CaCO₃ with hemoglobin, which enclosed hemoglobin inside the structures' pores. Loads were controllable by simply changing the initial hemoglobin concentration or adsorption time, with even more hemoglobin loading possible using covalent layer-by-layer assembly with glutaraldehyde as a cross-linker. The resulting structures were coated with biocompatible poly(ethylene glycol) to extend circulation time. Tests showed that these hemoglobin spheres retained oxygen-carrying

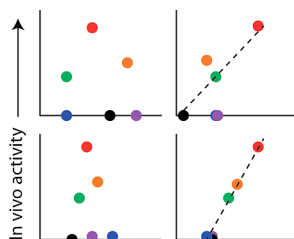
capacity similar to free hemoglobin and were able to withstand relatively high temperatures, unlike natural blood. The authors suggest that similar structures may hold promise as blood substitutes in the future.



Predicting siRNA beyond the Petri Dish

Developing effective pharmaceuticals remains an expensive, time-intensive, and resource-heavy process. Because animal testing is one of the largest investments in pharmaceutical development, researchers typically only proceed *in vivo* with biomaterials or compounds that show promise *in vitro*. In principle, this allows laboratories to test large numbers of compounds simultaneously at relatively low expense, reserving only the most promising for animal testing. However, *in vitro* testing can give misleading results, making a compound seem more or less promising than it actually is. This is especially true in the area of pharmaceuticals based on small interfering RNAs (siRNA), for which limited correlations between *in vitro* and *in vivo* performance exist.

To add to the current knowledge base, Whitehead *et al.* (DOI: 10.1021/nn301922x)



used existing data sets along with new experiments to develop correlations between *in vitro* and *in vivo* efficacy for lipid-like siRNA delivery vehicles known as lipidoids. Using hepatocellular targets as a model, the researchers varied several parameters, including the specific type of lipidoid, the type of cell used for *in vitro* experiments, the vehicles' siRNA

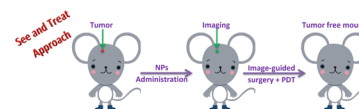
entrapment efficiency, zeta-potential, and nanoparticle size. Tests showed that maintaining consistency in formulating lipidoid delivery vehicles as either nanoparticles or complexes with siRNA led to greater correlation between *in vitro* and *in vivo* data. *In vitro* cell type also made a difference for *in vitro* correlation, with primary hepatocytes and HeLa cells yielding the most predictive data. While entrapment efficiency was predictive, zeta-potential and nanoparticle size were not. The authors suggest that these findings could offer guiding principles when designing siRNA delivery experiments.

Cancer Theranostics That Hide, Seek, See, and Treat

Surgery, followed by chemotherapy, radiation, or both, is the typical sequence for treating cancerous tumors. However, surgical boundaries can be difficult to judge, and chemotherapy and radiation can fail due to variations in absorption, metabolism, and delivery to target tissues. Thus, doctors need more effective ways to delineate tumors during surgery and better adjuvant treatments that remove all remaining cancerous cells. Although the use of imaging agents has been explored since the middle of the last century, none offer sufficient specificity and sensitivity to cancerous tissues. Photodynamic therapies, in which photosensitizer molecules kill cells after stimulation with light, have been explored as a possibility to sterilize the tumor bed during surgery. However, these have lacked the penetration and tumor sensitivity necessary for successful treatment.

Seeking a new, multifaceted solution for each of these problems, Wang *et al.* (DOI: 10.1021/nn301633m) developed a new prototype treatment based on biocompatible and biodegradable polymeric nanoparticles. The researchers conjugated amine-functionalized polyacrylamide nanoparticles with the photosensitizer molecule 2-devinyl-2-(1-hexyloxyethyl)pyropheophorbide (HPPH). To this, they added the F3 peptide, a cancer-targeting moiety. They topped this ensemble with poly(ethylene glycol), which hides foreign material from the reticuloendothelial system and thus prolongs blood circulation. Tests showed that these combination particles biodegraded over time in porcine liver esterase and sodium hydroxide, which is a positive for limiting toxicity. Further investigations showed that the particles effectively targeted brain and breast cancer cells and made these cells visible with the

incorporated dye and had strong killing ability when stimulated with light but had low toxicity in darkness. The authors suggest that these multifunctional particles could be a boon for cancer theranostics.



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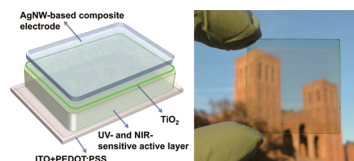
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A Clear Future for Polymer Solar Cells

■ Polymer solar cells (PSCs) have the potential to serve as the basis of visibly transparent photovoltaic devices that might be used in buildings or to charge portable electronics. To make these investigational devices a commercial reality, researchers have tried a variety of different tactics, including depositing transparent conductors, such as thin metal films, as top electrodes. However, these materials have typically led to either lower transparency or lower device efficiency. Although some solution-processable conductive materials have shown promise, these can damage the soft, polymeric, photoactive layers during deposition or have been incompatible from a chemical, physical, mechanical, or energetic angle.

In a new study, Chen *et al.* (DOI: 10.1021/nn3029327) evaluate a promising new way to surmount these difficulties using a different solution-processed electrode: a layer of highly transparent silver nanowire–metal oxide composite conducting film. The researchers created their PSC by sandwiching a photoactive polymer layer between a bottom electrode made of indium tin oxide and a top electrode of solution-processed silver nanowires that were spray-coated onto the photoactive layer with alcohol-based solvents. A thin layer of TiO₂ lay between this top electrode and the photoactive layer, enhancing the connection while protecting the fragile polymer. Tests showed that this device achieved a 4% power conversion

efficiency, collecting light in the near-infrared region, while maintaining a maximum transparency of 66% at 550 nm. The authors suggest that these solar cells could hold promise for a variety of applications where visible transparency is necessary.

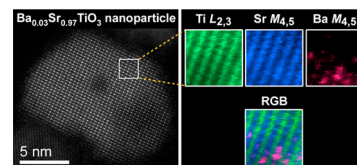


A Peek into Nanoparticle Dopant Clustering

■ Dopants can tailor the properties of nanoparticles, making them suitable for an enormous array of potential applications. How these atoms are distributed within nanoparticles can greatly affect the desired outcome and resulting performance of nanoparticle-based devices. Understanding their diffusion within materials could help researchers develop ways to optimize nanoparticles for various applications. However, directly characterizing the distribution of individual dopant atoms within nanocrystals remains a challenge. Some spectroscopic methods that are sensitive to dopants' physical properties have shown promise in investigating the local site symmetry and electronic structure of these impurities. Unfortunately, these methods often average across hundreds of thousands of nanostructures, giving little insight into distributions at the atomic scale. Other

methods are only good for certain nanoparticle–dopant combinations. No method thus far has offered single-atom chemical sensitivity.

In a new study, Rossell *et al.* (DOI: 10.1021/nn3021212) suggest a new combined method that brings together scanning transmission electron microscopy (STEM) with electron energy loss spectroscopy (EELS) to peer at individual dopant atoms in nanocrystals. Testing their method on barium atoms in SrTiO₃ nanocrystals, an approach used to suppress the native nanocrystals' intrinsic quantum fluctuations and induce ferroelectric transitions, the researchers started with STEM. Results revealed atomic columns, with Ba ions showing up as occasional higher-intensity columns due to their higher atomic number. However, this method required a relatively thin sample. Combining STEM with EELS provided identification of Ba in thicker

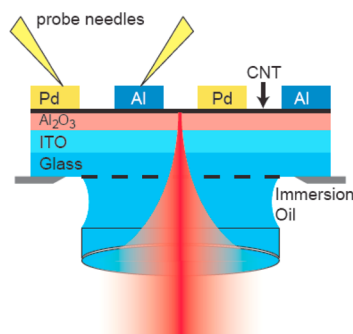


samples, revealing clustering that explains previous findings of polar nanoregions in this doped material. The authors suggest that STEM-EELS could offer a useful way to map dopants and to improve their use in various nanomaterials.

Mapping Nanotube-Based Voltaics

■ Semiconducting single-walled carbon nanotubes (S-SWCNTs) have exceptional electronic and optoelectronic properties that make these materials a promising choice for a variety of applications. The performance of S-SWCNT arrays depends largely on the physics of S-SWCNT–metal contacts; their electrostatic potential configuration determines the charge carrier transmission efficiency as well as photovoltaic response. However, previous optical studies relying on opaque S-SWCNT arrays have only been able to investigate the device channel.

To provide new insight, Engel *et al.* (DOI: 10.1021/nn302416e) embarked on an investigation of S-SWCNT arrays using optically transparent devices constructed of solution-processed S-SWCNTs on glass substrates coated with indium tin oxide. Using Al and Pd as contact metals, and thus inducing a built-in electric field across the array, the

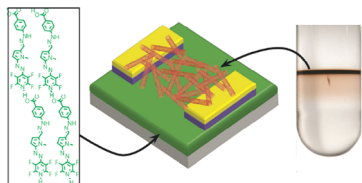


researchers took photocurrent images with a spatial resolution of 250 nm from the underside of the devices. Their results provide experimental evidence that photocurrent generation in devices with different metal contacts is maximized near the channel

center and not at the device contacts. The two different contacts result in different photocurrent signals and built-in electric fields. Their results suggest that it is possible to maximize positive photocurrent by shortening the channel length between adjacent contacts below the average S-SWCNT length. Using devices equipped with local metal gates, the researchers also show that it is possible to control the spatial dependence of photocurrent generation using external electrostatic fields. The authors suggest that these results could help optimize optoelectronic devices based on S-SWCNT arrays.

Testing Limits with Hybrid Molecular Dielectrics

Thin films made from a heterogeneous mixture of semiconducting and metallic carbon nanotubes (CNTs) have shown promise in a number of different applications, including large-area printed electronics, high-frequency devices, and light-emitting diodes. However, the metallic content harms the performance of thin-film transistors made from these materials. In addition, particular aspects of their gate dielectrics, such as capacitive coupling to the channel, interfacial scattering, and



trapped charges, can further limit device performance. Research devoted to improving operation of CNT thin-film transistors has tended to focus on individual features of the nanotubes or the gate dielectrics that independently affect performance without simultaneously working on both features.

In an effort to enhance the performance of CNT thin-film transistors, Sangwan *et al.* (DOI: 10.1021/nn302768h) changed both parameters at once. The researchers developed a new gate dielectric based on vapor-deposited self-assembled nanodielectrics (V-SAND). On heavily doped Si/SiO₂ substrates covered by a native oxide layer, they placed Al₂O₃ by several cycles of atomic layer deposition. They then evaporated a V-SAND organic layer, topped by another several deposition cycles of Al₂O₃. The researchers attached gold elec-

trodes to this gate dielectric, which they dubbed VA-SAND, then laid a CNT thin film on top whose nanotube content was composed of 99% semiconducting nanotubes, purified by a density gradient ultracentrifugation method. Tests showed that, under ambient conditions, the devices displayed low operating voltages, low subthreshold swings, high normalized on-state conductance, high transconductance, and high intrinsic field-effect mobilities with high on/off ratios. The authors suggest that these parameters, which approach the fundamental performance limits for CNT thin-film transistors, could be attractive for numerous applications.

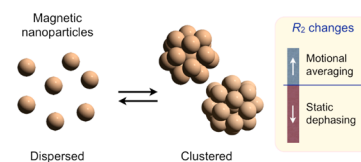
Analyzing the Attraction of Magnetic Nanoparticles

Nanoparticles have drawn increasing attention for use in a variety of biosensing applications, including drug discovery and clinical diagnostics. In particular, magnetic nanoparticles (MNPs) can generate exceptionally distinct and strong signals in typically low magnetic biological media. Several recently developed assays rely on the phenomenon of magnetic relaxation switching, in which clustered MNPs change the transverse relaxation (R_2) of water protons, detectable by nuclear magnetic resonance imaging. Although these assays have been successfully used to detect several targets, scientists have not yet elucidated their working mechanism or how varying different assay factors might affect results.

To fill in these gaps, Min *et al.* (DOI: 10.1021/nn301615b) embarked on the comprehensive

characterization of a magnetic relaxation switching assay. As a model, they used avidin–biotin interactions with biotinylated MNPs. The researchers prepared a panel of MNPs with four different compositions, including cross-linked iron oxide, ferrite, Mn-doped ferrite, and elemental iron, ranging in size from 8 to 22 nm. Tests showed that MNP size governed the R_2 mode, with smaller MNPs remaining in a motional averaging mode and larger MNPs assuming a static dephasing mode. Regardless of size, nanoclusters formed by the MNPs had a fractal structure, with a fractal dimension of about 2.4. Their findings suggest that magnetic relaxation switching assays' detection sensitivity might be enhanced by using MNPs with higher transverse mode relaxation,

optimizing the ratio between MNPs and molecular targets, and maximizing the binding sites per MNP, which leads to denser and larger nanoclusters. The authors suggest that these improvements could help MNPs become a more powerful tool for molecular detection.



Ambipolar Field-Effect Transistor: Conducting New Ideas

Ambipolar field-effect transistors (FETs) have the unique capability of being able to switch between n- and p-type transport behavior based on the applied gate voltage. Over the years, these dual-nature FETs have been developed from an increasingly large array of materials, including single-molecule FETs. These molecular devices offer opportunities not just for practical applications but also for fundamental studies on transport switching in the same molecule and on understanding how the highest occupied and lowest unoccupied molecular orbitals (HOMO and LUMO, respectively) factor into this unusual conduction behavior.

In a new study, Díez-Pérez *et al.* (DOI: 10.1021/nn302090t) examine a newly discovered single-molecule ambipolar FET that switches between n- and p-type conduction

at room temperature. The molecule at the heart of this FET is a pyrrolidine-substituted perylenetetracarboxylic diimide (PTCDI) block. The researchers bridged this molecule between Au source and drain electrodes to form a molecular junction immersed in an electrolyte, with charge transport being controlled by an electrochemical gate immersed in the same solution. Optical absorption spectroscopy and electrochemical measurements suggest that the substitution results in a smaller HOMO–LUMO gap and a shift of the HOMO closer to the electrodes' Fermi energy levels compared to the unsubstituted molecule. Although both molecules showed n-type behavior at negative voltages, the substituted molecule switched to p-type behavior at positive voltages, which the researchers attribute to an adiabatic two-step tunneling

process. The authors suggest that this single-molecule FET could be useful for future organic electrical devices in which conductance could be tuned through a small applied gate voltage.

