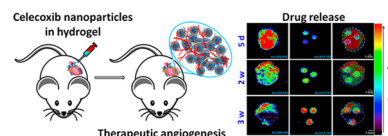


Building Blood Vessels with Celecoxib

Angiogenesis plays critical roles in preventing ischemic necrosis and recovery of tissue damaged by hypoxia, such as after myocardial infarction or ischemic stroke. Traditionally, angiogenic growth factors, chemokines, or gene therapy (to stimulate production of vascular endothelial growth factor) have been the primary means of spurring therapeutic angiogenesis. However, these macromolecules are expensive, may be toxic, and are subject to fast enzymatic and chemical degradation, with their hydrophilicity also contributing to rapid clearance from tissues. Although evoking angiogenesis with small-molecule drugs carried by nanoparticles could be a promising alternative, finding the right drug that does not confer appreciable toxicity and is not hydrophilic remains a challenge.

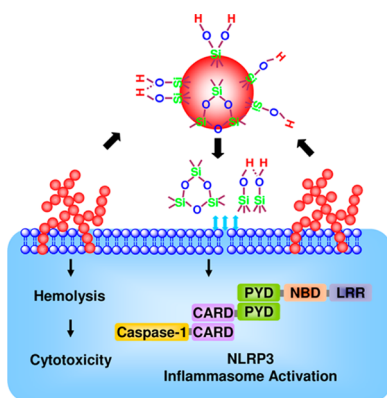
In a new study, Margulis *et al.* (DOI: 10.1021/acsnano.5b04137) evaluated whether nanoparticles of celecoxib, a small lipophilic nonsteroidal anti-inflammatory drug traditionally used as a painkiller, could induce angiogenesis. Although most studies have shown that celecoxib downregulates angiogenesis through various pathways, recent reports suggest that it could promote vascularization in tumors. To investigate, the researchers prepared celecoxib nanoparticles using supercritical CO₂ extraction from a volatile oil-in-water microemulsion. After incorporating the resulting nanoparticles in a biocompatible hydrogel, the researchers injected it subcutaneously into mice. Within days, these patches showed a 4-fold increase in blood vessel count compared to those injected with just the vehicle. This boost in vascularization was comparable

to that of nanoparticles of deferoxamine, a well-established vascularization promoter. Further experiments showed that celecoxib nanoparticles promoted significant vascularization of ischemic myocardium, preventing the progression of heart failure. The authors suggest that celecoxib nanoparticles could hold promise in treating diabetes, stroke, traumatic injuries, and other ischemic conditions.



Making Fumed Silica Less Toxic

The production of fumed silica nanoparticles, a product used in food, pharmaceuticals, electronics, rubber, plastics, paints, desiccants, and cosmetics, is growing each year and is expected to reach a production volume of 1.7 million metric tons by 2018. This material is generally recognized as safe for food additives and food packaging by the Food and Drug Administration, and no environmental or health risks have been reported. However, some experiments suggest that fumed silica could generate cytotoxicity and pro-inflammatory effects *in vitro* and *in vivo* and additionally cause DNA damage, glutathione depletion, and red blood cell lysis, among other hazardous effects. A recent report suggests that these effects could be attributed to specific surface properties as a result of the reconstruction of strained three-membered rings and surface display of silanol groups.



To determine if these effects might be avoidable, Sun *et al.* (DOI: 10.1021/acsnano.5b03443) investigated whether adjusting the silanol display through calcination or doping could change fumed silica's hazard

potential. Experiments showed that calcination indeed tempered cytokine production in macrophages and acute inflammation in the lung, but this modification was easily reversed when calcined particles were rehydrated. To induce a more permanent change, the researchers doped fumed silica nanoparticles with Ti and Al using flame spray pyrolysis. Further study showed that these modifications reduced surface silanol density and expression of three-membered siloxane rings, in turn reducing hydroxyl radical generation, membrane perturbation, potassium efflux, NLRP3 inflammasome activation, and cytotoxicity in THP-1 cells. The authors suggest that these modifications provide a stable means for reducing fumed silica's hazard potential.

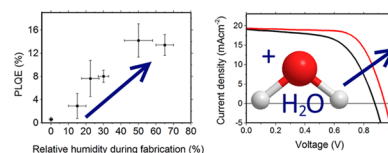
Best Bet Is Wet for Hybrid Lead Halide Perovskite Films

Hybrid organic-inorganic perovskite solar cells have recently experienced a meteoric rise in efficiency, from 3.8% to over 20% certified efficiency in less than 5 years. Most work to improve the performance of these devices further has focused on optimizing the absorber material and charge collection layers, ignoring the impact of environmental factors on device fabrication. However, some evidence suggests that local humidity could dramatically affect the ability to form high-quality absorber films, even though this variable is mostly uncontrolled between research laboratories working on these devices. Thus far, there is only fragmented understanding of the impact of moisture on perovskite film performance.

In a new study, Eperon *et al.* (DOI: 10.1021/acsnano.5b03626) sought to fill this gap through a comprehensive comparison of

methylammonium lead halide perovskite films prepared under wet and dry conditions. Their experiments show that films formed in high humidity conditions have less continuous morphology yet form faster with significantly improved photoluminescence, a sign of higher film quality. Testing these films in photovoltaic devices, the researchers found that those exposed to moisture either in the precursor solution or in the atmosphere during formation had significantly higher open-circuit voltages, leading to better overall device performance. Photovoltaic performance and photoluminescence could also be improved by post-treating films prepared under dry conditions with moisture. Further investigation suggests that the benefits of moisture derive from a reduction in the films' trap densities caused by water repairing imperfections in the perovskite

lattice. These results suggest that moisture plays a critical role in creating the most efficient perovskite solar cells and should be controlled for in future studies.

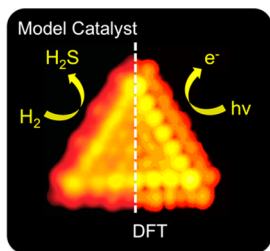


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Living on the Edge of MoS₂ Catalysts

MoS₂ has served for decades as a remarkably versatile catalyst, used for hydrotreating in oil refineries to remove sulfur and nitrogen heteroatoms and to control hydrogenation, as well as for the hydrogen evolution reaction in photoelectrochemical cells for water splitting. The active sites for catalysis are the undercoordinated edge sites of the layers in MoS₂. These sites have the adaptable ability to dissociate H₂ for hydrogenation reactions, associate H for hydrogen evolution, and bind heteroatoms in hydrocarbons during the hydrogenolysis of S and N. Researchers have used a variety of techniques to investigate how MoS₂ manages these feats, reaping data from scanning tunneling microscopy (STM), Fourier transform infrared spectroscopy, temperature-programmed reduction studies, high-resolution transmission electron microscopy, and



ambient pressure X-ray photoelectron spectroscopy (AP-XPS). However, a spectroscopic signature of the active MoS₂ edges under working conditions was still missing.

To remedy that absence, Bruix *et al.* (DOI: 10.1021/acsnano.5b03199) combined AP-XPS, STM, and density functional theory (DFT) calculations to determine the resulting edge structures that arise when activating single-layer MoS₂ nanoparticles with

hydrogen gas at conditions that resemble hydrotreating catalysis or hydrogen evolution. Results showed a consistent core level shift for the edge Mo atoms, which move counterintuitively toward higher binding energies when the active edges are reduced. This shift appears to result from variations in the metallic character of the Mo edge, which is lost when sulfur dimers are replaced by more reducing sulfur ion species. The authors suggest that these changes should also be observable by near-edge X-ray absorption or resonant inelastic X-ray scattering experiments, which could shed further light on the mechanism(s) of this catalyst.

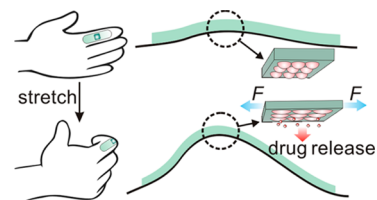
Drugs from Wearable Elastomer Films: Not a Stretch

Researchers have developed various stimuli-triggered drug delivery systems that rely on a host of internal physiological signals, such as pH, enzymatic activity, and glucose levels, or external signals such as light, temperature, and ultrasound. However, these systems come with challenges that significantly limit their use. For example, internal triggers can hamper precise dosing in the complex physiological environment, and external triggers require additional instrumentation to implement. For targeted spatiotemporal drug release, mechanical strain-based stimulus could hold advantages over other systems. This drug delivery method could link release to strain variations in muscles, organs, tendons, and bone joints, compression in cartilage and bones, or shear force in blood vessels. However, to date, strain-triggered

drug release systems have not been well explored.

In a new study, Di *et al.* (DOI: 10.1021/acsnano.5b03975) report the details of a wearable, tensile strain-triggered drug delivery device consisting of a stretchable elastomer and cross-linked microgel depots containing drug-loaded nanoparticles. The encapsulated drug is passively released into the matrix of the microdepots, remaining there until a tensile strain is applied. Then, an enlarged surface area and Poisson's ratio-induced compression on the microdepots promote release. The researchers tested their system using the cancer drug doxorubicin hydrochloride, the broad-spectrum antibiotic ciprofloxacin, and insulin, incorporating microneedles into the elastomer for this last delivery system to promote release further.

Tests showed that each system effectively released its drug payload gradually with either regular joint motions or active stretching. The authors suggest that this mechanical strain-based drug delivery system could eventually be useful for sustained or pulsed release for a variety of uses externally or internally.



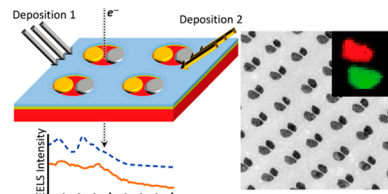
Making the Perfect Pairs

Plasmonic noble metal nanostructures have been investigated for a variety of applications ranging from molecular sensing to light manipulation. Because their optical properties strongly relate to their morphology, there is a great need to develop fabrication methods to control the geometry of these structures precisely while also producing high yields. Among the structures most in demand are dimers, which have shown the ability to confine and to localize the electromagnetic field at nanoscale ranges and provide near-field enhancements by several orders of magnitude, forming plasmonic hot-spots useful for a range of fundamental studies and practical applications.

In a new study, Zhang *et al.* (DOI: 10.1021/acsnano.5b03090) describe a method that

combines nanoimprinting lithography and shadow evaporation to produce wafer-scale, high-density Au–Au, Ag–Ag, or mixed dimers of Au–Ag, all with sub-10-nm gap configurations. The authors patterned dimers on Si or Si₃N₄ substrates, then coated the substrates with a layer of poly(methyl glutarimide) (PMGI) followed by a layer of poly(methyl methacrylate) (PMMA). They then nanoimprinted the PMMA layer to create a hole pattern with pillars generated using nanosphere lithography. Finally, the substrate was reactive-ion-etched to remove the PMGI layer through the holes, followed by shadow evaporation of the noble metals. The residual metallic sheet over the PMMA layer was then removed by lift-off. By varying the deposition angles, the researchers controlled the nanoparticle

spacing. Characterization by electron energy-loss spectroscopy revealed distinct plasmon modes on these dimers. The authors suggest that this method confers the desirable ability to pattern plasmonic noble metal nanodimers over large areas, which is key to many practical applications.

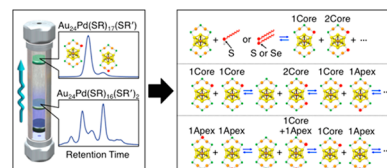


Probing the Products of Ligand-Exchange Reactions

Thiolate-protected gold clusters have attracted increasing attention because these nanomaterials are highly stable in solution, can be assembled with precision at the atomic level, and exhibit size-specific physical and chemical properties, including photoluminescence, electrochemical activity, and catalytic activity. They are also highly functionalizable using ligand-exchange reactions, which allows clusters with targeted chemical compositions to be synthesized with high yield. Although the mechanism of this reaction has been well studied with a variety of methods, the rates of the reactions, the chemical distributions of their products, the geometric structures of the products, and the distributions of the generated isomers remain unclear.

To investigate, Niihori *et al.* (DOI: 10.1021/acsnano.5b03435) probed the products from ligand-exchange reactions of phenylethanedithiolate-protected Au₂₄Pd clusters (Au₂₄Pd(SC₂H₄Ph)₁₈) with thiol, disulfide, or diselenide using reverse-phase high-performance liquid chromatography. This method separated out each coordination isomer from the reaction with high resolution, enabling them to be evaluated quantitatively, and provided more information about the nature of the reaction. The researchers found that the reactions appear to begin preferentially at thiolates that are bound directly to the metal core. Because the reaction occurred between clusters in the cluster solution, this led to variations in coordination isomer distribution of the clusters

in solution. Controlling the coordination isomer distribution of the reactant clusters enabled control of the distribution of the products. The authors suggest that these results could help optimize the creation of desired metal clusters in other ligand-exchange reactions.

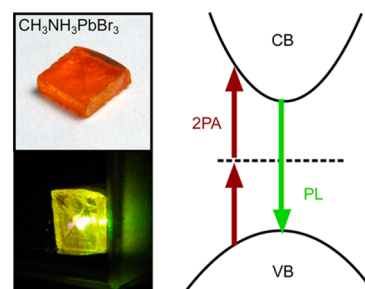


Shedding Light on Two-Photon Absorption

Although organometallic halide perovskites can be produced readily under low temperatures from the solution phase, they possess exceptional properties that rival those of materials with more complicated syntheses, such as low trap-state densities, long and balanced diffusion lengths, large carrier mobilities, and high linear absorption coefficients. These properties have driven perovskite thin-film absorbers to record conversion efficiencies up to a certified 20.1%. These materials have also found uses in light-emitting devices, such as low-threshold optically pumped lasers and high-brightness light-emitting diodes. Recently, researchers have developed methods allowing the solution-processed growth of large perovskite single crystals. Their large dimensions, clean band gap, and solid-state order provide a medium for investigating two-photon absorption in these materials.

In a new study, Walters *et al.* (DOI: 10.1021/acsnano.5b03308) probe two-photon absorption in CH₃NH₃PbBr₃ perovskite crystals. After pumping single crystals with intense light from a high-power mode-locked titanium sapphire laser operating at 800 nm to provide below-band-gap excitation, the researchers observed the emission of strikingly bright green light. This photoluminescence provided direct evidence of two-photon absorption, showing that the perovskite crystals acted as an effective upconverter for near-infrared radiation. Repeated measurements on several samples yielded a nonlinear absorption coefficient of 8.6 cm GW⁻¹ at 800 nm, a value comparable to epitaxial single-crystal semiconductors with similar band gaps. The researchers took advantage of this nonlinear process to correlate a 100 fs pulsed laser electrically using a photodetector fashioned from a CH₃NH₃PbBr₃ perovskite

crystal. The authors suggest that future studies could build on this work to investigate the nonlinear optical properties of these materials.



The Attraction of Room Temperature Multiferroicity

The weak hyperfine interaction and low spin-orbit coupling of organic donor and acceptor charge-transfer complexes have positioned these materials as a means to develop all-organic ferroelectrics and spintronics. The Curie temperatures and switchable polarization of organic ferroelectrics have improved over the last decade due to better control of molecular stacking and understanding of organic electronic structures. However, researchers still lack direct observations of room temperature magnetic spin ordering and room temperature magnetoelectric coupling effects, also known as multiferroics. One way to design organic multiferroics would be to use ordered charge-transfer crystals composed of electron donors and acceptors, in which the collective transfer of electrons from donor to acceptor, or *vice versa*, leads to the formation of simultaneous spin order.

Pursuing this goal, Qin *et al.* (DOI: 10.1021/acsnano.5b03558) assembled thiophene donors and well-ordered fullerene acceptors into prototypical charge-transfer crystals. Using 10% acetonitrile as the polar solvent, these materials self-assembled into ribbon-like, three-dimensional charge-transfer networks. Stimulating this material with an external magnetic field at room temperature, the researchers discovered that the dielectric constant differed depending on the applied frequency. Magnetoconductance studies confirmed these spin-dependent magnetic field effects. Electron spin resonance measurements further confirmed the existence of charge transfer. Additional experiments showed that charge-lattice coupling within the crystallized thiophene nanowire chain produces a spin density wave, which causes spontaneous magnetization of the crystals. The orientation of the spin cone further

contributes to this effect. The authors suggest that a better understanding of these materials could lead to a new class of all-organic nanoferronics.

