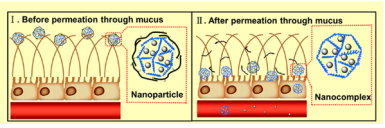
## An Upshot for Diabetics

Protein therapeutics have proven their worth in the clinic, showing high efficacy and selectivity for a variety of conditions. However, these biomolecules typically have low permeability across epithelial tissue and are rapidly degraded when not absorbed, leading to low oral bioavailability that currently necessitates parenteral administration. Many recent studies have shown promise toward advancing oral administration using nanotechnology. However, the pivotal challenge of improving absorption of these drugs is getting them past the mucus barrier that covers and protects the epithelium, which requires significantly different surface properties than simply getting nanocarriers into cells.

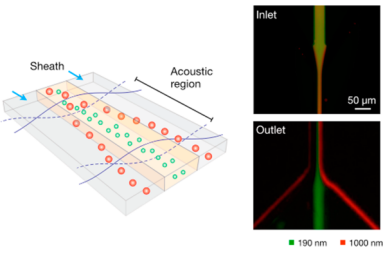
In a new study, Shan *et al.* (DOI: 10.1021/acsnano.5b00028) report the development of self-assembled nanoparticles with an outer coating that facilitates mucus permeability and slowly diffuses, revealing an inner core formulated to penetrate cell membranes and release its protein cargo. Using insulin as a model protein therapeutic, the researchers mixed this drug with the cell-penetrating peptide penetratin. They then added these nanocomplexes to a solution of *N*-(2-hydroxypropyl) methacrylamine polymer (pHPMA), which acts as a negatively charged mucus-inert coating. Tests with a mucus-secreting epithelial cell line show that nanoparticles with slightly negative charges slipped past the mucus barrier and were able to enter cells at rates up to 20-fold higher than free insulin. *In vivo* experiments found that oral administration of these nanoparticles successfully cut blood sugar by up to half in diabetic rats, with nanocomplexes missing the pHPMA coating causing only a negligible hypoglycemic response. The authors suggest that their multistep strategy can successfully overcome the multiple barriers to oral administration of protein therapeutics.




## Sounding Off: Purifying Microvesicles with Acoustics

Microvesicles (MVs), membrane-bound phospholipid vesicles secreted by mammalian cells into the bloodstream, have been recognized in recent years as partial surrogates of parental cells that have diagnostic potential. Thus, being able to separate and to enrich these cells from biofluids are important goals. Although MVs are abundant in blood, isolating these tiny particles from their complex media has proven challenging. Conventional batch processes, such as multiple filtration and ultracentrifugation, often require large sample volumes and can also damage MVs, making these techniques less than ideal. Although acoustic-based microfluidic techniques have been shown to exert differential forces on particles by size using ultrasound waves, this method has yet to be demonstrated on MVs.

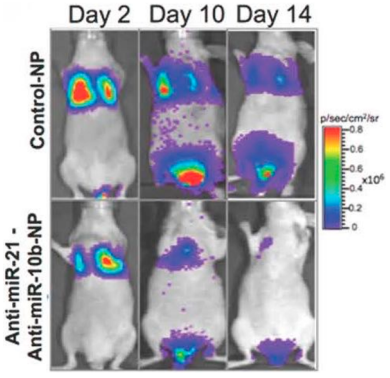
In a new study, Lee *et al.* (DOI: 10.1021/nn506538f) use acoustic microfluidics to separate MVs from other contents in biological samples. The researchers developed a microfluidic device in which a central channel passes through a pair of interdigitated transducer electrodes, which generate a symmetric standing surface acoustic wave field across the channel direction. The end of the channel splits into three outlets. Because larger particles tend to migrate toward the pressure nodes, the researchers hypothesized that smaller particles would continue down through the center channel and large particles would get shunted toward the side outlets. Tests showed that this scenario indeed occurred, allowing the researchers to separate polystyrene beads by size, as well as exosomes from other types of MVs and MVs from red blood cells. The authors suggest that this technique could offer a quick and gentle method for isolating MVs that is compatible with small sample sizes.




## A Double Attack on Triple Negative Breast Cancer

The origins of cancer often lie in dysregulation of key microRNAs (miRs). Thus, inhibiting the function of oncogenic miRs could be an effective strategy in fighting some forms of cancer. Studies have already shown the potential of antisense-miRs in cancer treatment. For example, inhibiting miR-10b using antisense-miR-10b in a mouse model carrying human breast cancer tumors inhibited metastatic spread to the lungs. Similarly, other studies using antisense-miR-21 have shown impaired tumor cell growth, induced apoptosis, and a reduction of migration and invasion of cancer cells expressing miR-21 at high levels. Although these findings are promising, delivering antisense-miRs effectively remains challenging due to their degradation by serum nucleases, off-target effects, poor cellular uptake, and rapid renal clearance.

Testing a new strategy, Devulapally *et al.* (DOI: 10.1021/nn507465d) loaded polymer nanoparticles with both antisense-miR-10b and antisense-miR-21 to deliver a two-way




attack on triple negative breast cancer (TNBC), a form of the disease in which cells lack receptors to estrogen, progesterone, and Her2, which can complicate treatment. The researchers used a water-in-oil-in-water double emulsion method to create copolymer nanoparticles made of poly(lactic-*co*-glycolic acid) and poly(ethylene glycol), polymers already in use for human therapeutics, which were loaded with the antisense-miRs. Tests showed that these nanoparticles were effectively taken up in cultured TNBC cells, inhibiting their growth and invasion. In TNBC tumor xenografts in animal models, injections of these loaded nanoparticles significantly reduced tumor size. By targeting delivery with the urokinase plasminogen activator receptor, the researchers were able to increase tumor cell apoptosis by 40%. The authors suggest that this multipronged approach could represent a potential new therapeutic option for TNBC.

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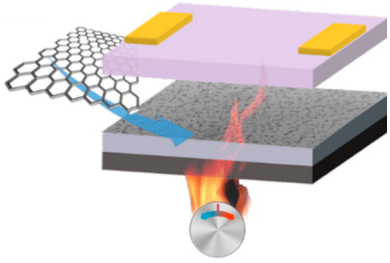
## Tuning Thin Film Transistors with Graphene

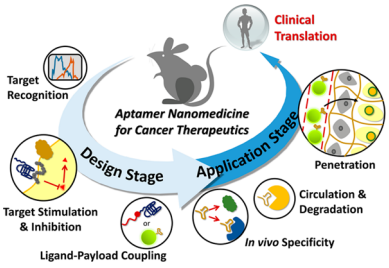
Graphene has attracted significant attention in the electronics industry for its extraordinary electronic properties. However, for this material to reach its potential, researchers need to develop methods to mass produce high-quality graphene and to open a band gap in this material so that it can be used for logic applications. Although researchers have made headway in addressing the first challenge, the second has yet to be effectively addressed.

In a step toward reaching this goal, Mosciatti *et al.* (DOI: 10.1021/acsnano.5b00050) have developed hybrid polymer–graphene thin-film transistors (PG-TFTs) that use solution-processed polymers on top of solution-processed graphene nanoscale patches. By applying liquid-phase exfoliated graphene dispersions on $SiO_2$, then annealing in air, the researchers discovered that the ionization energy (IE) of this material could be tuned from 4.8 to 5.7 eV. Then, by applying either a p- or an n-type semiconducting polymer on top, they were able to fabricate devices where the output current could be tuned from either completely off or modulable, displaying characteristics that ranged from semiconducting to truly conductive with varying graphene coverage. When the IE of the graphene was outside the polymer band gap, these devices could act either as a multifunctional three-terminal switch or a memory device with stable performance through multiple read-write cycles. The authors suggest that this method for tuning graphene's band gap could lead to developments in materials science, physics, and chemistry.



## Update on Aptamers

Aptamers, short oligonucleotides engineered to bind to specific targets such as small molecules, proteins, other nucleic acids, and even cells and tissues, have shown considerable promise in biomedicine as both diagnostic agents and therapeutics. Although aptamers act in a similar manner to antibodies, they have a host of advantages, including fewer off-target effects when delivered systemically, better tumor uptake kinetics, higher stability, and lower production costs. Eleven aptamers are currently under clinical trials for treatments related to macular degeneration, coagulation, oncology, and inflammation, and one has been approved in the United States and European Union for treating age-related macular degeneration. However, despite these successes, several challenges need to be addressed before this tool can advance in the clinic.

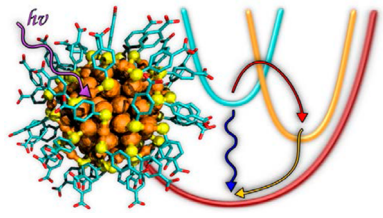



In a new Review article, Lao *et al.* (DOI: 10.1021/nn507494p) summarize the current state of aptamers for cancer therapeutics, including hurdles in design and delivery that must be overcome for aptamers to become viable therapeutics. For example, the authors point out that the current systematic evolution of ligands by exponential enrichment (SELEX) method for aptamer design may not result in products capable of recognizing and then stimulating or inhibiting the desired targets. Thus, they say, conjugating aptamers to a therapeutic payload may be a more suitable option. They add that researchers may be able to achieve dual aims by combining therapeutic and diagnostic payloads. At the application stage, the authors further note that aptamers face problems with immunogenicity and nuclease degradation, achieving systemic circulation, and penetrating tumors. By addressing these challenges, aptamers may achieve therapeutic goals that other ligands for targeted oncology treatments have yet to reach.

## Pinning Down the Molecular–Metallic Transition

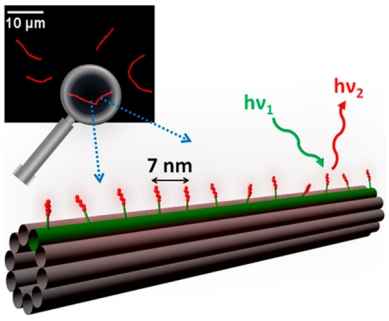
To predict the behavior of nanoclusters with metal particles, researchers understand that, generally, clusters with just a few metal atoms tend to behave like molecules, and those that are tens or hundreds of nanometers in size tend to be more metal-like. However, the behavior of clusters just a few nanometers in size, with *ca.* 100 metal atoms, can be difficult to predict. A key property for determining molecular *versus* metal behavior is the electronic energy level structure of the material, particularly the presence or absence of an energy gap or highest occupied molecular orbital/lowest unoccupied molecular orbital (HOMO/LUMO) gap. Optical spectroscopy can be a useful tool for evaluating this property, particularly in compositionally precise samples. Researchers have thus been able to study thiolate-protected gold clusters, with recent studies showing that $Au_{25}(SR)_8$ clusters seem to display molecule-like behavior, but $Au_{144}(SC_2H_4Ph)_{60}$ clusters seem to act as metals. However, there have been no studies of relaxation dynamics between these two species to understand when the transition from molecular to metallic relaxation behavior occurs.

In a new study, Mustalahti *et al.* (DOI: 10.1021/nn506711a) used ultrafast time-resolved mid-IR spectroscopy and density functional theory calculations to evaluate this behavior in $Au_{102}(p\text{MBA})_{44}$ clusters. Their detailed energy relaxation dynamics findings show that this water-soluble cluster exhibits a well-defined molecule-like relaxation behavior with a long relaxation time component, in contrast to the clear metallic relaxation behavior shown by $Au_{144}$ in previous studies. The authors suggest that the transition from molecular to metallic relaxation behavior occurs somewhere between $Au_{102}$ and $Au_{144}$ species.



## Fluorescent Silver Clusters Go Totally Tubular

Researchers have exploited the versatile self-assembly properties of DNA for a variety of nanotechnologies, including for nanoscale arrangement of optical elements such as organic fluorophores, noble metal nanoparticles, and colloidal quantum dots. When a single-stranded DNA oligomer is attached onto the desired molecule or nanoparticle, it is possible to position it precisely at selected sites on DNA scaffolds using complementary hybridization. This method can be used to elicit a variety of interesting optical phenomena. Achieving these effects often requires stringent control over the size, shape, and surface morphology of individual optical elements. Although this can be difficult to achieve for nanoparticles, ligand-protected metal clusters offer a route toward achieving these goals with atomic precision. However, these nanoparticles have yet to be combined



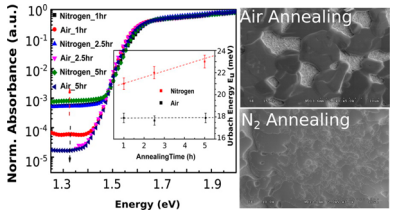

with DNA scaffolds for controlled nanoscale placement.

In a new study, Copp *et al.* (DOI: 10.1021/nn506322q) used DNA-stabilized fluorescent silver clusters with either 14 or 15 silver atoms as optical elements on 10-helix tiled DNA nanotubes to create linear arrays of these optical elements. The researchers first synthesized these clusters on a single-stranded DNA "host" with a linker that extended outward. They then attached these linkers to complementary docking sites extending from the DNA nanotubes. Fluorescent microscopy and spectroscopy confirmed decoration of the DNA nanotubes and that this attachment did not affect the cluster geometry. The authors suggest that this study demonstrates atomically precise metal clusters arranged at programmed positions on a nanoscale scaffold and offers a method that could be generalized to other types of DNA scaffolds and metal clusters.

## Something in the Air for Perovskite Solar Cells

Renewable energy that is cost-effective and environmentally friendly continues to draw considerable research attention. Solution-processed photovoltaic cells including organic photovoltaics, dye-sensitized solar cells, chalcogenide quantum dots, and semiconductor-sensitized extremely thin absorber solar cells have shown particular promise. However, the performance of these devices has been limited because of their complex design and limited exciton and charge carrier diffusion lengths. Organic–inorganic metal halide perovskite-based solar cells have the potential to overcome these hurdles, however, with power conversion efficiencies exceeding 17%. These devices' extraordinary optical and electronic properties mainly stem from their highly crystalline frameworks with a precise, high-symmetry crystal structure. However, researchers know little about how processing conditions can affect this crystal structure, which could be used to help optimize device performance.

In a new study, Pathak *et al.* (DOI: 10.1021/nn506465n) studied how annealing conditions affect the crystal structure of perovskite films and the resulting performance of corresponding solar cells. By testing different annealing atmospheres, air and nitrogen, and annealing times ranging from 1 to 5 h, the researchers found that the performance of solar cells that incorporate these films was significantly higher for those annealed in air, regardless of the annealing time. Further investigation showed that this better performance was strongly linked to improved crystal order and larger, more defined grain domains. The authors suggest that this knowledge may help investigators enhance these qualities to develop even higher performing perovskite film-based photovoltaic devices.




## Reverse-Engineering Structures from Voronoi Particles

The assembly of nanoparticle superlattices and colloidal crystals has gradually progressed from basic research into a growing industry. However, maintaining momentum in this field will require better understanding of how targeted crystal structures can be assembled with high quality and yield from inexpensive and easily synthesized building blocks. Although researchers are making significant strides toward this goal, it is still difficult to predict the resulting crystal that building blocks might form as well as the complementary question of what building blocks are the best choice to construct a target structure.

In a new study, Schultz *et al.* (DOI: 10.1021/nn507490j) examined this puzzle using Voronoi particles: hard, space-filling particles in the shape of Voronoi cells of desired structures. The researchers ran simulations with 46 target atomic crystal structures and Bravais lattices whose Voronoi tessellations yielded a single shape for nanoparticle building blocks. Results showed that under high pressure, most of these nanoparticles assembled into their target structures. However, under moderate pressure, results varied significantly, with only the most symmetric Voronoi particles assembling into target structures at moderate densities. The majority of the building blocks tested assembled into orientationally degenerate structures, rather than space-filling ones. Particles with multiple types of large facets were more likely to suffer from non-selective entropic bonds than those with a single type of large facet, making them poor assemblers. The authors suggest that these findings can help aid in the design of nanoscale building blocks so that their level of degeneracy will not destabilize the target structure.