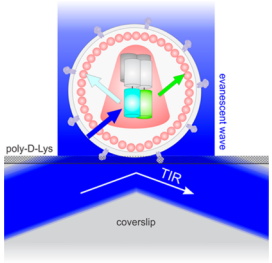
In Virio? HIV Virions as Nanoscopic Test Tubes

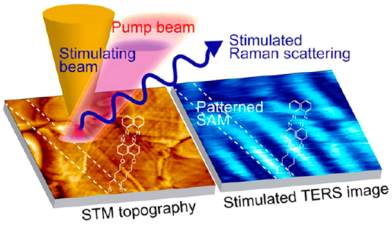
For studying some aspects of HIV pathology, researchers have relied on sensitive single-molecule imaging systems, such as single-molecule fluorescence microscopy. This method provides the ability to track individual viral particles in real time to capture dynamic interactions with cells and to investigate viral infection routes inside cells. Other super-resolution fluorescence methods have offered the possibility to visualize structural features of individual viruses and see the distribution of viral proteins inside a virus. Thus far, no methods exist for quantitatively probing protein–protein interactions (PPIs) inside a single virus or within intracellular viral complexes.

In a new study, Borrenberghs *et al.* (DOI: 10.1021/nn406615v) used individual engineered HIV-1 particles themselves as test tubes for studying PPIs of integrase (IN), one of the three HIV-1 enzymes. The researchers co-transfected a standard human embryonic kidney cell line with DNA plasmids encoding only the necessary HIV-1 structural and catalytic proteins and genomic RNA along with the IN enzyme fused to one of two fluorescent proteins to act as a Förster resonance energy transfer donor or acceptor. Their investigations showed not only that infectious fluorescently labeled viruses can be obtained but that they can be used for quantitatively measuring individual IN proteins and interactions between IN proteins. Their findings suggest that IN forms oligomers inside virions and infected cells, interactions that can be promoted or inhibited by drugs. The authors suggest that this strategy could be used to study other PPIs inside the HIV-1 virus as well as other enveloped viruses.



Bumping Up Raman Signal by a Billion

In the past decade, researchers have become increasingly interested in tip-enhanced Raman spectroscopy (TERS) due to its high spatial resolution and high sensitivity. In this technique, Raman spectroscopy is combined with scanning probe microscopy (SPM), enhancing the Raman signal due to strong electromagnetic field enhancement at the SPM tip in conjunction with localized surface plasmon resonance excitation. Although TERS has become a valuable tool for surface analysis in both physical chemistry and biological studies, its applications have been limited due to the relatively lengthy spectral acquisition times necessary to obtain adequate signal-to-noise ratios. Any technique that can enhance the signal-to-noise ratio would be a boon to the TERS field.

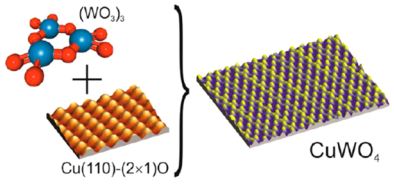


Toward this goal, Wickramasinghe *et al.* (DOI: 10.1021/nn406263m) developed a technique that can substantially increase the Raman signal over that generated by conventional TERS through a stimulated emission mechanism. The researchers introduced a collinear, tunable stimulating beam along with a polarization-modulated pump into a conventional TERS setup. Using this novel method, the researchers used stimulated TERS (sTERS) to analyze an azobenzene thiol monolayer on a gold substrate, using lock-in detection to measure the stimulated signal. The sTERS images clearly revealed the surface distribution of molecules, unlike surface topography images taken at the same time. The experimentally obtained Raman signal from sTERS was about a billion times higher than that from conventional TERS, and the signal-to-noise ratio was 3 orders of magnitude higher. The authors suggest that the better signal from sTERS offers the potential for significantly faster imaging of surfaces compared to normal TERS.

Metal Tungstates Go Two-Dimensional

Ternary tungstate oxides, such as metal tungstates, have fascinating properties that have attracted attention not only for fundamental study but also for their potential applications in fields including optics, optoelectronics, low-dimensional magnetism, photochemistry, and photocatalysis. However, with the advance of nanotechnologies that require shrinking dimensions of materials, the ability to create thin films of metal tungstates with atomic control as well as a better understanding of these materials will be necessary.

Addressing these issues in a new study, Denk *et al.* (DOI: 10.1021/nn500867y) developed a novel approach to synthesize two-dimensional (2D) $CuWO_4$ and characterized this material structurally and spectroscopically. The researchers covered a single-crystalline Cu(110) surface oxide with a monolayer of $(WO_3)_3$ clusters deposited in the gas phase in a monodisperse cluster beam. At low temperature, individual clusters were deposited onto the Cu oxide surface. After the surface temperature was increased to 600 K, the $(WO_3)_3$ clusters reacted with the Cu–O surface oxide to create a morphologically flat, well-ordered overlayer of $CuWO_4$. Using a variety of characterization methods, the researchers determined the atomic structure of this ultrathin ternary oxide, showing that it corresponds to a $CuWO_4$ monolayer arranged in three sublayers, with O–W–O/Cu stacking from the interface and localized regions of anisotroic flexibility. Further investigation showed that this material displayed a reduced band gap and increased density of states close to the Fermi level compared to bulk $CuWO_4$. The authors suggest that this novel synthesis method and the knowledge gleaned from characterization could offer new insights for using this material in photo- and electrocatalysis.

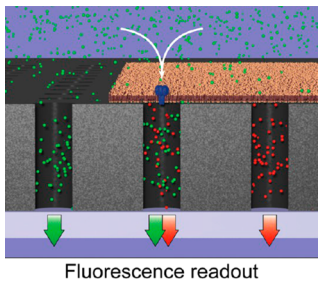


Published online April 22, 2014
10.1021/nn502030g

Making a Membrane-on-a-Chip

Studying transport processes across biological membranes remains challenging because researchers have yet to establish protocols to handle and to immobilize fragile supported lipid bilayers and to determine on which side of the membrane reactants reside. Although researchers have had some success in overcoming these obstacles with surface-supported planar lipid bilayers, in which both sides of the membrane can be monitored separately, these methods have suffered from high production costs and the need to immerse microscope components in the aqueous environment above the membrane, hindering high-throughput screening.

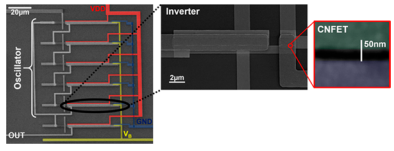
Seeking a better way to study biological membranes, Kusters *et al.* (DOI: 10.1021/nn405884a) developed microstructured Si/SiO_2 chips that support suspended biological membranes, enabling high-throughput study using an air objective. Their platform relies on commercially available chips that contain arrays of thousands of cylindrical measurement chambers. By rupturing giant unilamellar vesicles across these cavities, the researchers generated suspended lipid bilayers. Tests with an endosomal lipid mimic showed that the bacterial toxin α-hemolysin's (αHL) ability to form pores in this membrane was dependent on the ionic strength of the aqueous environment, with high salt solutions leading to low pore formation and low salt solution resulting in more pores. This scenario was reversed for membranes composed of saturated lipids. Further investigation revealed significant heterogeneity between individual pores, with some easily passing fluorphores and others delaying their passage. Other experiments confirmed the feasibility of this platform for drug screening against pore-forming bacterial toxins and for studying viral membrane fusion. The authors suggest that this protocol could significantly ease the *in vitro* study of biological membranes.



Building a Better Carbon Nanotube Field-Effect Transistor

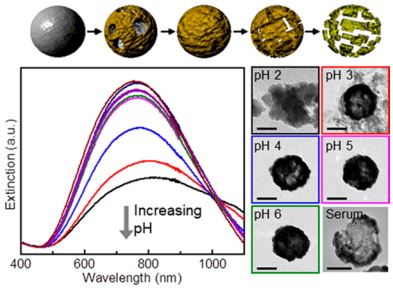
Silicon-based metal-oxide-semiconductor field-effect transistors (MOSFETs) have long formed the basis of the semiconductor industry. While size decreases have traditionally improved performance, silicon MOSFETs are becoming increasingly difficult to scale because electrostatic control of current and mobility diminishes as the channel length decreases. Seeking an alternative semiconductor for shrinking field-effect transistor dimensions, researchers have looked to single-wall carbon nanotubes (CNTs). However, early attempts to create carbon nanotube field-effect transistors (CNFETs) were plagued with mispositioned and metallic CNTs that harmed circuit performance. Techniques to overcome these glitches have shown promise but thus far only in devices at least 1 μm in size.

In a new study, Shulaker *et al.* (DOI: 10.1021/nn406301r) show that it is possible to apply similar techniques to create highly scaled CNFETs, with sub-20 nm devices. Their method relied on a very large scale integration (VLSI)-compatible approach that modified an earlier imperfection-immune design paradigm. In this technique, any mispositioned CNTs are removed by etching out predefined regions of a wafer on which highly aligned CNTs were grown by chemical vapor deposition, and metallic CNTs are removed by electrical breakdown. The researchers used this method to produce CNFET with channel lengths ranging from 90 to sub-20 nm. Tests showed that these CNFETs could be incorporated into inverters that operate at speeds up to 1 MHz. Additionally, the researchers created a fully integrated CNFET-based infrared light sensor and interface circuit at the 32 nm technology node. The authors suggest that these advances bring technologies based on highly scaled CNFET circuits closer to fruition.



Medical Promise for Hollow Au–Ag Nanoshells Could Fall Apart

Nanoparticles have shown substantial promise for photothermal therapy, a cancer ablation method already being tested in multiple clinical trials. In this technique, nanoparticles taken up into tumors through the enhanced permeability and retention (EPR) effect are irradiated with near-infrared (NIR) light, which selectively heats and kills tumor cells while sparing surrounding healthy tissue. Recently, several groups have reported that hollow Au nanoshells can be made successfully in the sub-100 nm range, the necessary size to promote the EPR effect, through a galvanic replacement reaction between Au and Ag. Although these nanoparticles could be useful for biomedical applications, their *in vivo* stability has not been well-studied, and published research in this area has focused only on the fate of the Au shell while ignoring that of the sacrificial Ag core.

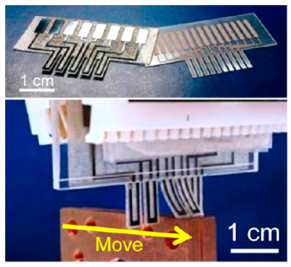


To fill this gap, Goodman *et al.* (DOI: 10.1021/nn405663h) investigated the effects of physiological conditions on hollow gold nanoshells (HGNS) of three different sizes (43, 62, and 82 nm) synthesized through a galvanic replacement reaction that left remnants of a Ag core. All three sizes of the HGNS had virtually identical NIR resonances of about 800 nm. Tests showed that, while functionalizing the nanoshells with PEG kept them stable under irradiation in solution, *in vivo* tests in mice showed a strongly disparate separation of the two metals in organs throughout the body. Further investigation showed avid fragmentation in acidic pH solution as well as in human and bovine serum. The authors suggest that further study of nanoshells formed through galvanic replacement is critical before these materials are used for biomedical applications.

Temperature and Strain Sensors: A Whisker Away?

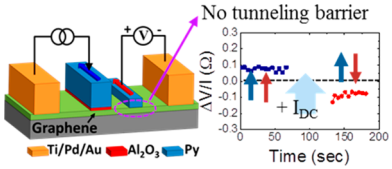
Researchers have long used nature as an inspiration for designing new materials and devices. For example, recent developments include electronic eyes, skin, and noses. For ease of practical use and economical manufacture, these devices must be fabricated on macroscale, flexible substrates. Although researchers have amassed significant experience with printing transistors on flexible substrates, fully printed macroscale sensors have yet to be realized thus far.

In a step toward this goal, Harada *et al.* (DOI: 10.1021/nn500845a) developed fully printed highly sensitive electronic whisker arrays that incorporate sensors to measure not only strain but also temperature, exceeding the function of natural whiskers. The two functionalities were printed on separate substrates, then laminated together. For the strain sensors, the researchers used a carbon nanotube (CNT)−Ag nanoparticle (AgNP) film composed of AgNP ink mixed with a CNT paste held together with a binding polymer. When a high strain is applied to the film, the entangled CNTs connect the AgNPs, decreasing resistance. Resistance can be further modified by changing the AgNP ratio, tuning the response to strain. For the temperature sensor, the researchers used a poly(3,4-ethylenedioxythiophene)-poly(styrenesulfonate)-CNT composite film that changes resistance with temperature. Tests showed that the strain sensor on its own could detect raised letters and a stair-like formation when dragged overtop. Combined with the temperature sensor, the whiskers measured not only the strain of being swept over a heated copper object but also its temperature. The authors suggest that this device could open the door to more fully printed electronic sensors.



A New Spin on Graphene Spin Devices

Among its many other interesting and useful qualities, graphene has been suggested as an ideal channel material for spin conduction. Graphene devices have already demonstrated spin transport over 20 μm and spin diffusion lengths up to 5 μm at room temperature. Yet, to develop spin-based logic further, researchers must demonstrate spin transfer torque in these devices to show that spin information can be delivered to outputs. In typical graphene lateral nonlocal spin valve devices, tunneling barriers are inserted at both injector and detector contacts to reduce the conductance mismatch between the magnets and graphene channels as well as contact-induced spin relaxation. However,



the barrier at the receiving magnet limits spin angular momentum transfer because of its high resistance.

In a new study, Lin *et al.* (DOI: 10.1021/nn500533b) found a way around this challenge by designing a new graphene spin device without a tunneling barrier at the receiving magnet. To compare this new device with a conventional one, the researchers constructed two lateral spin valve devices with five electrodes on the same peeled graphene flake, one with tunneling barriers at the injector and detector contacts and the other missing the tunneling barrier at the detector contact. Tests showed that the devices delivered comparable spin valve signals, but the one with a single tunneling barrier had lower noise and lower contact resistance at the detector interface. In the asymmetrical device, the researchers also demonstrated a significant reduction in critical charge current density. The authors suggest that these findings advance the design of graphene spin devices.

Growing van der Waals Solids

To capitalize on graphene's unique properties, recent research has sought to combine it with other materials. In one example, investigators have theorized that stacking two-dimensional (2D) materials, such as semiconducting transition metal dichalcogenides (TMDs), insulating hexagonal boron nitride, and semimetallic graphene could produce materials with tunable electronic and optoelectronic properties. Thus far, several groups have reported van der Waals (vdW) structures made of these stacked materials that demonstrate a variety of new phenomena. However, they have been primarily fabricated using mechanical exfoliation to stack individual 2D crystals, a method that can lead to interface contamination.

Seeking a new way to synthesize these unique heterostructures, Lin *et al.* (DOI: 10.1021/nn5003858) directly grew MoS_2, WSe_2, and hexagonal boron nitride (hBN) on epitaxial graphene, forming large-area van der Waals solids. The researchers synthesized the TMDs on graphene by a gas-phase reaction of either MoO_3 and S or WO_3 and Se, and they synthesized the hBN on graphene using ammonia borane as the precursor in a tube chemical vapor deposition chamber. They found that the properties of the underlying graphene largely dictate properties of the combined materials, showing in several different experiments that strain, wrinkling, and defects on the graphene's surface act as nucleation centers for growing the other material on top. Further investigation showed that growing MoS_2 on graphene significantly improved its photoresponse compared to MoS_2 alone. The authors suggest that using epitaxial graphene as a substrate to directly grow vdW solids could lead to even more materials with unusual and useful qualities.