



reservoir that is refilled with a syringe—a design similar to some CEDs.

The device is made up of two parylene sheets that are held together with medical-grade, double-sided adhesive tape, forming the microfluidic channel. The bottom parylene sheet layer contains a poly(3,4-ethylenedioxythiophene):poly(styrene sulfonate) (PEDOT:PSS) electrode that traces the bottom of the microfluidic channel. The team created this part of the device by depositing a 3- $\mu\text{m}$ -thick parylene film onto a 1-inch by 3-inch glass slide, then depositing a 10-nm-thick layer of Cr and 100-nm-thick layer of Au, and finally patterning the interconnects using a metal liftoff process with acetone. The slide was then patterned with PEDOT:PSS to form electrodes. The top half of the device required depositing a 1.7- $\mu\text{m}$ -thick parylene film onto a glass slide, followed by patterning with Cr/Au, depositing a second 1.8- $\mu\text{m}$ -thick parylene film layer, etching with AZ9260 photoresist to define the outline of the ion bridge pattern (300 through-holes for the *in vivo* version of the device), and patterning the ion bridge material (chemically bleached PEDOT:PSS). They sandwiched the layers with the adhesive, which was cut to the shape of the fluidic channel.

The researchers conducted a number of *in vitro* tests on their device using GABA, a neurotransmitter that scientists have used to control epileptic activity in *in vitro* models using OEIPs. The researchers measured the current flow through the ion bridge material and found that GABA accounted for 91% of the (cation) charge transport. The rest of the ions transported came from the solution, Malliaras says, adding that the amount of these ions is too low to cause any ill effects in real-world applications. The device showed a nearly 20-fold increase in the flux for GABA at only 1/20th of the voltage of previous reports of traditional OEIPs. And its on-off ratio was exceptionally high—nearly five orders of magnitude between 1 V and 0 V. In *in vivo* tests, which were done mostly to prove the device could be implanted, Malliaras and his team placed the device on the surface of a rat's cortex and filled the microfluidic channel with KCl solution to deliver potassium ions. They found that they could induce hyperactivity within a matter of seconds.

Daniel Simon, a materials scientist at Linköping University in Sweden who researches cortical drug delivery using OEIPs, was impressed with the work,

particularly the team's successful merging of the mixed ionic and electric conduction of organic electronics and the easy long-range liquid transport of fluidics. "Indeed, I see their system as a great addition to the organic bioelectronics toolbox, showing the potential of hybrid solutions to the drug delivery challenge," he says. But Simon, who was not involved in the work, doubts the electrolysis danger of traditional OEIPs, as well as the ability of the new microfluidic platform to sustain drug delivery for more than a couple seconds. Still, he looks forward to the team's follow-up research. "And possibly combining their work with our own to overcome the last remaining hurdles in fast, efficient, sustainable, and leak-proof drug delivery components," he says.

Malliaras and his colleagues are now using the platform in animal models of epilepsy to examine whether the microfluidic device can safely and effectively treat seizures. Other potential applications include subcutaneous implantation in diabetics to deliver insulin and microdialysis of the brain, a technique to separate and quantify neurotransmitters, hormones, and other biomolecules from fluid in the brain.

**Joseph Bennington-Castro**

## Bio Focus

### Structure of natural materials informs design of graphene-based composites

Numerous ongoing efforts strive to exploit the full potential of graphene—the most fashionable current material in materials science—and rely on its exceptional tensile strength for various structural applications. However, this two-dimensional carbon structure still faces challenging scalability and mass production roadblocks. More importantly, bulk composites cannot seamlessly integrate graphene into their structure without sacrificing many of the beneficial properties of this material. Graphene oxide (GO), which includes various epoxy and hydroxyl groups, is easier to mass-produce and combine with other materials. However, stacked

GO sheets are held together by intermolecular hydrogen bonds of adjacent oxygen-containing groups. On their own, without additional reinforcement, these networks stand up poorly to shear stresses and cannot generate composites that are both strong and tough.

In order to solve this challenge, researchers from the Laboratory for Atomistic and Molecular Mechanics at the Massachusetts Institute of Technology turned to mussels for inspiration. They found that the feet of these mollusks contain adhesive proteins with a structure that closely resembles polydopamine (PDA), which is a dopamine molecule that is polymerized under alkaline conditions. The research team, led by Markus J. Buehler, chemically bonded this material with graphene oxide layers and used a combination of experimental and computational approaches to describe the

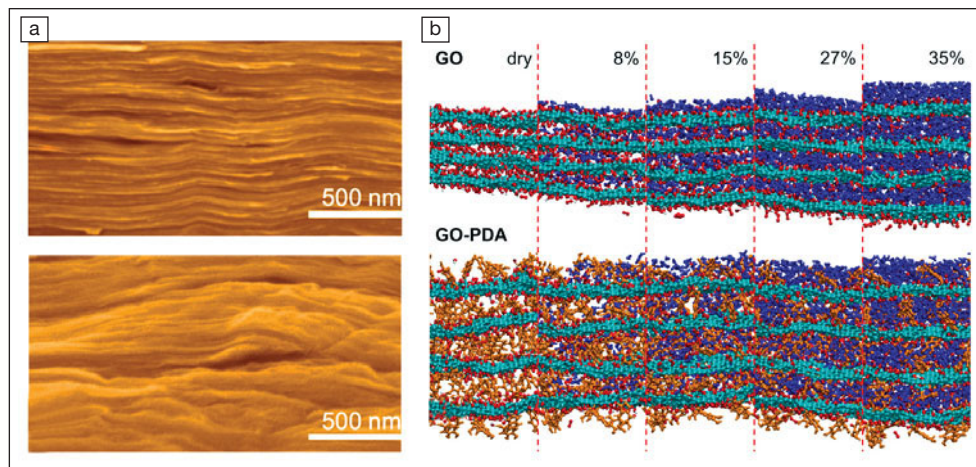
structure and properties of the resulting composites. The team published their results in a recent issue of *Nano Futures* (doi:10.1088/2399-1984/aa6aed).

Buehler says, "We were excited about the opportunities that arise when combining distinct biological material platforms into a new system, such as done here by taking advantage of the great adhesion properties of mussel threads, the intriguing layered geometry of nacre, combined with graphene oxide to realize a synthetic analog of the layered minerals. These concepts allowed us to construct a *de novo* designer material that offers exceptional mechanical properties combined with other useful traits."

The research group assembled the composites into stacks that were modeled after the structure of nacre shells. Much like their biological counterpart, the materials drew their superior strength from the

interwoven polymer. Density functional theory calculations showed that, instead of oxygen-to-oxygen functional group bonding, the polymer found reactive epoxy groups and formed carbon-to-carbon bonds, which are significantly stronger. Since the reaction simultaneously defunctionalized graphene oxide, the resulting graphene (with a 130 GPa tensile strength) was much stronger than its oxidized version (63 GPa tensile strength).

The chemical bonds were the first important element of the structure. The hydrophilic nature of the material intercalated different amounts of water in between the layers, and the researchers relied on x-ray diffraction and molecular dynamics simulations to assess the effects of this process on layer-to-layer stacking. The “dry” GO-PDA composites featured large interlayer spacings, and small amounts of water that intercalated between the sheets without pushing them apart. In contrast, water molecules used strong hydrogen bonding to bridge adjacent laminates, which pulled them together and shrunk the composite.



(a) Scanning electron microscope images of the graphene oxide-polydopamine (GO-PDA) material; (b) a snapshot of a molecular dynamics simulation for GO and GO-PDA with different water content. Credit: Chun-Teh Chen and Shengjie Ling.

Intercalated water molecules, and the resulting additional bonding reinforcement, yielded greater strength and toughness of the resulting GO-PDA composites. The researchers subjected these materials to different air moisture content levels, and an increase in relative humidity from 33% to 75% increased the toughness by 123%. The strength of the resulting composites, which had reached 170 MPa, exceeded the level of their natural nacre counterparts.

Bioinspired nanomaterials inherit designs that are the product of millions of

years of evolution, and the resulting properties offer numerous improved capabilities. The work by Buehler’s group shows that composite structures and laboratory-engineering materials, such as graphene composites, stand to benefit by drawing inspiration from living organisms. This work also shows the benefits of a combined approach that relies on both computational simulations and experimental results in an effort to design high-performing, commercially viable materials and composites.

**Boris Dyatkin**

### Intermolecular forces for self-assembly identified through simulations

The patterns that form upon molecular self-assembly are a direct consequence of interaction forces among the entities constituting the structure. Thus, the study of different intermolecular forces and the resulting self-assembled pattern is of extreme importance. Corresponding mathematical modeling has its roots in statistical mechanics. The usual practice is to modify the interparticle interaction and simulate the resulting self-assembly. A recent study led by Thomas Truskett and co-workers at The University of Texas at Austin asks an

inverse question: “Can one know what sort of intermolecular forces are required to produce a desired structure upon self-assembly?” The findings were published recently in the *Journal of Chemical Physics* (doi:10.1063/1.4981796).

The simulations begin with an initial estimate of the interaction potential and a target structure. Other inputs such as number of particles ( $N$ ), volume of the ensemble ( $V$ ), and temperature ( $T$ ) are specified and kept constant (for an NVT ensemble). First, molecular dynamics simulations are used to compute the equilibrium structure from the initial guess for intermolecular forces. Then based upon the difference between the current and target structures, optimization calculations are used to iteratively improve the interaction potentials

(“difference of two self-assembled structures” is defined by the Kullback–Leibler measure in the present calculations). At every iteration, the researchers find a new equilibrium structure based on the most recent estimate for interaction potential. Calculations are terminated once a prescribed accuracy is achieved; in other words, when the structure based on the force field is close to the target structure.

The research team also demonstrated the applicability of the formulation by applying it to three distinct system types: cluster fluids (fluid-like particle aggregates that are roughly spherical in shape and monodisperse in size); porous mesophases (self-assembly of the conjugate inverse cluster phase); and crystals, with multiple examples of each.