Lowering the threshold for bioelectronics

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superconductors⁷. In turn, intercalated layers do modify the properties of epigraphene. Separated from the substrate by hydrogen intercalation, the epigraphene layer that was previously in direct contact with SiC (buffer layer) turns from semiconducting to conducting⁸; the epigraphene layer above the buffer layer changes from heavily negatively doped to charge neutral with Sn intercalation⁹, or to *p*-doped, controlled by the H intercalation¹⁰.

Atom intercalation opens possibilities even beyond the stabilization of new 2D structures and the study of unknown phenomena at this scale. Epigraphene, this single- or multilayer graphene that forms epitaxially on SiC crystals when they are heated¹¹ has been developed as a platform for 2D nanoelectronics since 2001^{4,5}, taking advantage of the perfectly defined interfaces resulting from the SiC/graphene heteroepitaxy, and the transferless

wafer-size scalability provided by the industrial grade single-crystal substrate. Having all-epitaxial 2D heterostructures that can be grown controllably and that can be studied in ambient condition is a formidable playground. One can only imagine the possibilities opened by combining epigraphene properties (room-temperature ballistic conductance, long spin diffusion, sturdy QHE plateaus and so on) with that of magnetic or superconducting 2D metals or other topological materials for investigating topological phenomena, as well as developing spintronics or advanced optoelectronics.

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ORGANIC ELECTROCHEMICAL TRANSISTORS

Lowering the threshold for bioelectronics

A high-speed, high-gain enhancement-mode ion-gated transistor shows promise for low-power chronically implanted bioelectronic systems.

Scott Keene and Yoei van de Burgt

Bioelectronic applications aim to link the biological environment with conventional electronic systems. But due to the vastly different nature of both worlds (hard versus soft, electrons/holes versus ions, dielectrics versus liquids), finding optimal materials has proven difficult and has been the focus of the field of bioelectronics for many years. Recently, organic electrochemical transistors — or ion-gated transistors — based on soft and biocompatible materials have been developed to bridge this gap. These devices convert ionic currents from biological media to electronic signals and at the same time reduce the mechanical mismatch with biological tissues. There have been significant demonstrations of IGTs for biosensing and electrophysiological recordings¹, yet they are still limited by their relatively slow speeds (about 1–10 kHz) and high power consumption. Now, writing in *Nature Materials*, Claudia Cea, George Spyropoulos and colleagues have found a straightforward way to modify an ion-gated transistor material to connect electronic

devices with biological environments in a fast, stable and low-power manner².

Poly(3,4-ethylenedioxythiophene) polystyrene sulfonate (PEDOT:PSS) has been the basis for a wide variety of applications and is generally considered the most ubiquitous mixed ionic/electronic conducting polymer blend, resulting from its wide commercial availability, biocompatibility and straightforward processing. However, when implemented in ion-gated transistors, PEDOT:PSS has two key drawbacks. First, it is intrinsically doped with positive charges (holes) due to the negatively charged PSS backbone. As a result, transistors based on this material operate by default in the ON state unless they are switched to the OFF state with an applied gate potential V_G (this is the so-called depletion-mode operation of a transistor, whose transfer characteristic is shown in Fig. 1b, red curve). A default ON state leads to both relatively high power consumption as well as device-to-device crosstalk due to the transmission of signals when $V_G = 0$ V. Second, the high areal

capacitance of PEDOT:PSS leads to slow charging times, limiting the operating speed of the transistors.

The authors have overcome both problems by combining an internal ion-gated organic electrochemical transistor (IGT) architecture, based on previous work³, with a common de-doping reagent for PEDOT:PSS, polyethylene-imine. The IGT architecture results in a faster device response due to the inclusion of the electrolyte in the device channel to avoid diffusion-limited ionic transport, as well as the use of a low-capacitance gate that reduces the total RC charging time of the device (Fig. 1a). The de-doping reagent lowers the threshold potential to effectively tune the device to its OFF state when no gate voltage is applied — the device thus operates in enhancement mode, and its transfer characteristic is shifted with respect to V_G (as shown in Fig. 1b, green curve). This means that the IGT channel has high intrinsic resistance when $V_G = 0$ V, ensuring that stray signals are blocked from the surrounding circuitry.

Fig. 1 | High-performance rectifying circuits based on enhancement and depletion mode internal ion-gated transistors (e-IGT and d-IGT, respectively). **a**, Schematic showing the gate structure of an IGT, where the metallic gate contact (G) is coated with a ion membrane interfacing the device channel made of PEDOT:PSS (dark green spheres represent the negative charges of the PSS backbone, light green spheres represent positive ions). By applying a negative V_G , holes (represented by white +) injected from the source contact (S) induce ions to move rapidly towards the gate due to the short drift distance (D_{ion}) travelled compared to an IGT without ions in the channel. Fast response of the IGT is thus due to fast ion transport through the channel as well as its low gate capacitance (C_{EDL}), resulting from the formation of an electronic double layer (EDL) at the metal–electrolyte interface. **b**, Comparison of transfer characteristics of e-IGT (green curve) and d-IGT (red curve) highlighting for each device the subthreshold region that is optimal for amplification of electrophysiological signals. **c**, Combining both devices, circuits can be designed that amplify voltages near 0 V (green area in **b**) as well as higher potentials (red area in **b**). **d**, These circuits are used to process electrophysiological recordings in implanted bioelectronic systems. Scale bars 5 s, 0.5 μ A. Figure adapted with permission from ref. ², Springer Nature Ltd (**a,c**).

Modifying the doping state to optimize the properties of PEDOT:PSS according to the application targeted has already proven to be successful in solar cells⁴, batteries⁵ and neuromorphic devices⁶. Now, this same technique improves the performance of PEDOT:PSS-based IGTs too; importantly, the biocompatibility of the dopant chosen, polyethylene-imine, enables the use of these devices for high-fidelity electrophysiological recordings and in situ signal filtering. In fact, Cea and colleagues showed that their IGTs were fast and sensitive enough to record action potentials from single neurons when implanted in rats' brains. Moreover, they combined enhancement-mode and depletion-mode IGTs to realize implantable electrical filters working in a wide voltage range (Fig. 1b–d). Each of the IGTs have a different optimal operating voltage range

given by the subthreshold region of their transfer curves (Fig. 1b). Interestingly, by combining the two devices in a rectifying amplification circuit (Fig. 1c), both small (near 0 V) and large amplitude signals in hippocampal recordings are rectified efficiently by the enhancement-mode and depletion-mode IGTs, respectively (Fig. 1d). By efficiently detecting both small and large amplitude hippocampal activity, the demonstrated circuit could be used to accurately detect epileptic discharges, outperforming traditional signal filtering approaches.

Modification of bioelectronic device properties can thus open up further applications by building systems that can sense and locally process complex electrophysiological signals, and even diagnose health problems. Local

computation at the point of recording is in itself particularly interesting as it reduces the need for high-bandwidth data communication in and out of the biological system (for instance, the brain). Adaptable circuits could be trained to identify a particular seizure and react to it by releasing drugs to suppress epileptic activity⁷. Other exciting applications can be envisioned, such as advanced prosthetics in which signalling from the biological environment can be used to modify the electrical or chemical properties of the material to dynamically tune and close a feedback loop. The tuning of electrical properties of IGTs is therefore an essential step forward in the field of adaptable, chronically implanted bioelectronic interfaces.

Yet, despite the great performance already demonstrated by doped organic electronic materials, the electronic and structural effects of doping and de-doping are still poorly understood. Better understanding of the mechanism behind modification of the doping state will further enhance the design and manufacturability of specific materials and allow for a larger range of tunability and optimization. At present, most organic devices used in bioelectronics employ positively charged polymers (p-type) like PEDOT:PSS, yet progress is being made to develop negatively charged (n-type) materials⁸, where the electronic carriers are electrons rather than holes, compatible with these applications. Combining p- and n-type transistors can enable more advanced complementary circuits, which are the basis for almost all conventional computational circuits.

The results presented by Cea, Spyropoulos and co-workers provide a compelling demonstration of how biocompatible additives can be used straightforwardly to tune the properties of bioelectronic devices. This will certainly encourage further work to tune doping in wider ranges and will possibly suggest strategies to realize stable n-type devices with similar tunability. High-performance-integrated complementary logic circuits embedded in flexible and implantable bioelectronic systems may be within reach soon. □

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CRYSTALS

Ice goes fully cubic

Two independent studies describe the discovery of structurally pure cubic ice Ic made from either ice XVII or a high-pressure hydrogen hydrate.

Christoph G. Salzmann and Benjamin J. Murray

In March 1629, the cleric and scholar Christoph Scheiner witnessed a rare 28° halo from the sun over the ancient city of Rome. More than three centuries later, this observation was suggested to have arisen from the presence of octahedral crystals consisting of cubic ice (ice Ic) rather than the familiar hexagonal ice (ice Ih)¹. However, despite tremendous research efforts, the preparation of pure ice Ic has remained unsuccessful so far². Now, writing in *Nature Materials*, Leonardo del Rosso and colleagues³ report the formation of ice Ic by simply heating ice XVII, an unusual low-density form of ice. Simultaneously, Kazuki Komatsu and co-workers⁴ show that ice Ic can also be made by degassing hydrogen from a high-pressure hydrate. The discovery of design principles for making ice Ic opens up a route to the accurate determination of its physical properties and more complex forms of ice I, and it will stimulate new research with respect to a wide range of structurally related materials such as diamond and semiconducting chalcogenides.

Eighteen phases of ice have been discovered so far at a wide range of temperature and pressure conditions⁵. Hexagonal ice Ih is the low-pressure form of ice that we are all familiar with. Its structure and that of its cubic counterpart, ice Ic, are shown in Fig. 1a,b. Both members of the ice I family contain identical layers of hydrogen-bonded water molecules. The structural difference between the two arises from the way in which these layers are stacked. In ice Ih, each layer is the mirror image of the previous one, whereas ice Ic is built up by shifting the layers upon stacking.

For the best part of the twentieth century, it was claimed that ice Ic could be made by, for example, water-vapour deposition onto cold substrates⁶. However, a major leap in our understanding came with the realization

Fig. 1 | Crystal structures and X-ray diffraction of the ice I family. **a–c**, Structures of ice Ih, ice Ic and ice Isd. Oxygen and hydrogen atoms are shown as red and white spheres, respectively. The dashed blue line in **a** shows a mirror plane and the arrow in **b** is a displacement vector. Hexagonal and cubic stacking is indicated by ‘h’ and ‘c’, respectively. **d**, Calculated X-ray diffraction patterns ($\lambda = 1.5406 \text{ \AA}$) of various ice I structures as indicated by the Ramsdell notation and stacking sequences.

that the so-called ice Ic samples were not actually fully cubic but contained hexagonal stacking faults⁷. The structure of such a stacking-disordered ice I (ice Isd) is shown in Fig. 1c. In contrast to ice Ih, which shows sharp X-ray diffraction peaks, the irregular stacking in ice Isd leads to diffuse diffraction features mainly around $2\theta = 24^\circ$ (Fig. 1d). Computational fitting of such diffraction patterns provides the percentage of cubic stacking, the ‘cubicity’, for a given sample^{8–10}. Up until now, the highest cubicity on record was 78%, a long way from ice Ic, for which the cubicity is 100%².

Now two independent studies have described robust means to obtain fully cubic

ice Ic. Del Rosso and co-workers show that heating ice XVII under vacuum to 160 K leads to the formation of ice Ic³. In addition to diffraction data, the Raman spectrum of the newly discovered ice Ic is presented, which may prove useful for its identification in future studies. Ice Ic was also shown to be slightly lower in density compared to ice Ih. This finding could provide an explanation as to why only ice XVII transforms to ice Ic whereas other ice phases yield ice Isd under similar conditions. Because the density of ice XVII is significantly lower than that of ice Ic, this may enable a mechanistic pathway to ice Ic that is not accessible from denser starting materials. In a separate study, Komatsu