under the strong leadership of the gnomAD consortium, which has made it clear that the priority is to continually expand the database to be more representative of the global population. In doing so, it will equip scientists with ever-more tools with which to reveal the hidden secrets of our genome.

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Condensed-matter physics

Tailoring graphene for electronics beyond silicon

Francesca Iacopi & Andrea C. Ferrari

The integration of non-silicon semiconductors into systems on chips is needed for advanced power and sensing technologies. A semiconducting graphene 'buffer' layer grown on silicon carbide is a step on this path. **See p.60**

Electronics relies on the use of switching devices made from semiconducting materials, in which an electric current can be controlled, ideally down to the movement of single charges. Semiconductors achieve this because the allowed energies of their electrons leave a gap between a low-energy and a high-energy band, and electrons can be excited to cross this 'bandgap'. Materials with different-sized bandgaps can have complementary functions, such as performing logic operations, supplying power or acting as a sensor. But integrating these materials into a single device is challenging. On page 60, Zhao *et al.*[1] report a way of growing a graphene-like layer with a narrow bandgap on a material with a wide bandgap.

Graphene is a material that is gapless because its electronic bands touch at one point, called the Dirac point, and then diverge. This peculiar behaviour makes it ideal for applications in photonics and optoelectronics[2,3]. Although its gapless nature means that it is not the material of choice for electronic devices, it can be used in components that operate in the terahertz portion of the electromagnetic spectrum (1 THz is 10^{12} Hz), where it fills a role that very few other materials can[4].

There has nevertheless been a constant effort over the past 20 years to 'open a bandgap' in graphene, to convert this versatile material into a semiconductor. One way of doing so involves cutting or shaping graphene into nanoribbons[5,6], which can now be achieved with atomic precision[7]. In this case, the bandgap opens because the electrons are further confined to a single dimension. However, nanoribbons are subject to sample-to-sample variations, and it is currently difficult to produce them at the scale required for consumer electronics. Another way to create a bandgap involves leveraging how graphene interacts with the substrate on which it is grown[8]. This is the route that Zhao *et al.* took.

Graphene is a single layer of carbon atoms arranged in a honeycomb lattice. It can be grown by heating the semiconducting material silicon carbide (SiC) until the silicon atoms on its surface sublimate, leaving a carbon-rich layer that can recrystallize[9]. The resulting layer has a hexagonal structure, similar to that of SiC, with some carbon atoms covalently bonded to the substrate. Subsequent layers form as normal graphene, but the partial bonding makes this first 'buffer' layer a semiconductor[10]. A bandgap opens not through dimensional confinement, as for nanoribbons, but as a result of the bonding constraints that SiC imposes[11].

Graphite (of which graphene is a single layer) has been produced from SiC since at least 1896 (ref. 12), and the growth mechanism has been investigated since the 1960s (ref. 13). Over the past 20 years, this approach has been refined and used systematically to obtain graphene at the scale of a wafer (that is, the typical size used for mass production of electronic devices)[9].

It was known as early as 2008 that the graphene buffer layer that forms on SiC could be a semiconductor[14], but achieving wafer-scale samples has been a challenge. Zhao *et al.* succeeded in creating a controlled environment by sandwiching two SiC chips so that the silicon surface of the top chip was opposite the carbon surface of the bottom one. When the system was heated at ambient pressure, carbon atoms were transported from the carbon surface to the silicon surface to form the buffer layer. This differs from other routes, in which atoms are depleted from the silicon surface and lost to the system's surroundings[14].

The authors' technique allowed them to

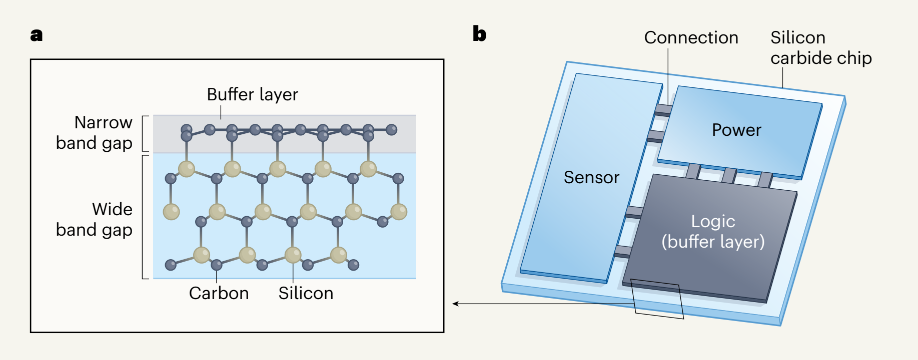

Figure 1 | Combining 'beyond-silicon' materials to make an integrated system on a chip. Graphene (a single layer of carbon atoms arranged in a honeycomb pattern) can be grown on silicon carbide (SiC), which has a wide 'bandgap' between the allowed energies of its electrons. **a**, Graphene is 'gapless', but Zhao *et al.*[1] devised a way of tailoring a graphene 'buffer' layer on SiC, such that the layer has a bandgap (albeit a narrow one) and is therefore semiconducting. **b**, This approach could be used to integrate materials with wide and narrow bandgaps into the same chip, where they could serve as sensing, logic and power components, to create integrated systems on chips. The conducting graphene layers (not shown in **a**) that grow on top of the buffer layer could be used as connections between chip components.

maintain the silicon–carbon stoichiometry and limit growth to the buffer layer only, suppressing the formation of subsequent graphene layers (Fig. 1a). The controlled environment enabled the generation of large flat terraces on the SiC surface, which gave rise to long-range order in the buffer layer.

The bandgap of this layer is about 0.6 electronvolts, around half that of silicon (1.1 eV), close to that of germanium (0.65 eV), and much narrower than that of SiC, which can be more than 3 eV. At room temperature, Zhao and colleagues' buffer layer has a hole mobility (a measure of the performance of a semiconductor) nearly three times that of germanium, and about ten times that of silicon (see go.nature.com/4anxwnk). Layered semiconducting materials, such as those comprising stacked sheets of molybdenum disulfide, have mobilities much lower than that of silicon[15].

Although several challenges remain, both fundamental and technical in nature, work on combining layered materials in 'beyond-silicon' technologies should be intensified. This is particularly true for devices based on semiconductors with wide and ultra-wide bandgaps (ranging from around 2 eV to more than 6 eV), for which techniques must be developed to integrate layered materials into hybrid systems on chips. Such research could be key to developing photonics and quantum technologies, and for applications that aid the transition to renewable energy, such as solar cells and power electronics for electric vehicles.

However, when Zhao *et al.* incorporated their buffer layer into a transistor structure, they found that its mobility was 200 times less than it was when isolated. The authors attribute this drop to the fact that the dielectric material used for the transistor gate was not optimized. Determining whether a better dielectric could improve mobility is the first of many challenges ahead. Others include obtaining consistent control over the type and amount of charge induced in the buffer layer, as well as regulating how this layer interacts with other nearby materials in an integrated structure, such as a transistor.

Zhao and colleagues' material is not intended to replace silicon-based electronics, but it could be promising for fabricating logic gates on SiC. Substrates made from SiC are not directly compatible with silicon technologies, but they are increasingly being used in power electronics and are attracting interest for spacecraft electronics and micro-electromechanical systems[16], as well as biomedical devices. This is thanks to the material's wide bandgap and its ability to withstand harsh conditions, such as high temperatures and pressures, radiation and corrosive environments, all of which compromise silicon's performance[17].

A key advantage of Zhao and co-workers' approach is that it naturally pairs SiC with a material that has a narrow bandgap (the graphene buffer layer). The resulting hybrid structure could be used, for example, to integrate devices with different functions into the same SiC chip[18] (Fig. 1b). This would enable improved efficiency for systems that combine sensing with computing logic components. These could benefit renewable-energy generation, which can experience irregular input owing to changing weather conditions.

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Physiology

Muscle immune cells alleviate exercise woes

Gerald Coulis & S. Armando Villalta

A suppressive type of immune cell called a regulatory T cell has a key role in helping muscles to adapt to exercise – guarding muscle mitochondrial organelles against damage mediated by proinflammatory factors generated during physical activity.

Although the health benefits of exercise are associated with immune-system activation, dysregulation of immunity with overtraining is often linked to detrimental effects on human health and exercise performance[1]. However, the immunological factors that regulate beneficial and damaging inflammation during exercise are not fully understood. Writing in *Science Immunology*, Langston *et al.*[2] report a previously unknown role for immune cells called regulatory T (T_{reg}) cells in exercise adaptation and demonstrate that T_{reg} cells dampen inflammation to protect mitochondrial organelles from destructive proinflammatory molecules called cytokines.

T_{reg} cells are a specialized subset of immune cells, called T cells, that suppress other immune cells to dampen inflammation and autoimmune targeting of the body's own proteins (self-antigens). If T_{reg} cells are absent or have functional defects, this can cause the catastrophic failure of immune regulation and death owing to the immunological attack of the host's own organs. T_{reg} cells are already known[3] to orchestrate muscle repair through a protein called amphiregulin that stimulates the function of muscle stem cells. Adding to the list of complex physiological functions carried out by these cells, Langston and colleagues now show that exercise increases the number of T_{reg} cells in skeletal muscle to curb inflammation and promote metabolic and functional adaptation.

The authors provide compelling evidence that T_{reg} cells inhibit immune cells that produce a proinflammatory cytokine called interferon-γ (IFN-γ). Langston *et al.* studied resting (sedentary) and exercising mice that were genetically modified to enable the specific deletion of T_{reg} cells. Using this system, the authors demonstrate that various immune cell types in exercised muscle that produce IFN-γ increased in number in the absence of T_{reg} cells (Fig. 1). The rise in the expression of IFN-γ in these T_{reg}-depleted mice, compared with that in animals with T_{reg} cells, stimulated IFN-γ-mediated signalling pathways over metabolic and blood-vessel-forming