Materials science

A platform for making and transferring oxide films

Atsushi Tsukazaki

Crystalline films of technologically useful oxide materials have been grown by a method based on surface-modified substrates. Unlike usual oxide films, these can be easily transferred to any material. **See p.75**

Inorganic compounds that contain oxygen and at least two other elements are known as complex oxides. Crystalline films of these compounds have desirable properties such as superconductivity, magnetism and ferroelectricity (spontaneous electric polarization), and could be used in next-generation devices[1–3] if they can be integrated with mature device technologies. Integration is typically achieved by growing films on compatible substrates using a method called epitaxy, but this approach works only for relatively limited material systems. In the past few years, free-standing membranes of certain oxides have been made[4,5] by removing epitaxial films from substrates using a process dubbed chemical lift-off. Now, on page 75, Kum *et al.*[6] report a versatile method for producing a wide variety of complex-oxide films that can be easily transferred to any material.

The authors' approach uses a technique known as remote epitaxy[7–9], in which the epitaxial film and the substrate are separated by a few sheets of the two-dimensional material graphene (Fig. 1a). Potential-energy fields produced by atoms in the substrate can penetrate the graphene and transmit information about the substrate's crystal lattice, enabling the epitaxial growth of high-quality films. The field penetrability is proportional to the strength of ionic bonds in the substrate material[8]. A film grown in this way can be easily removed (exfoliated) from the graphene because the two materials are coupled by only weak van der Waals forces (Fig. 1b). Remote epitaxy therefore combines outstanding epitaxial growth and exfoliation.

The fabrication of high-quality oxide films requires a well-regulated growth scheme and atomic-level control over the material interfaces and substrate surfaces[1–3]. In the past few decades, single-crystal oxide substrates of various crystal structures have become commercially available. These include substrates of strontium titanate, aluminium oxide and magnesium aluminate, which have perovskite, corundum and spinel crystal structures, respectively.

For the epitaxial growth of a particular film, the substrate should be appropriately selected in terms of its crystal structure, lattice dimensions and coefficient of thermal expansion – a quantity that describes how the size of a material is affected by a change in temperature. Consequently, growth conditions, such as temperature, oxygen pressure and growth rate, need to be optimized to stabilize the desired crystalline phase and obtain high crystallinity.

In their remote-epitaxy work, Kum and colleagues carefully optimized the growth conditions of oxide films on graphene-coated substrates. In general, control over the degree of oxidation is crucial for making high-quality oxide films, so the background oxygen pressure should be well regulated during film growth. However, when the authors used a growth method called pulsed-laser deposition and supplied oxygen to their set-up at the required high temperature, they found that the graphene was etched from the substrate. To prevent this etching, they grew the initial part of the oxide film (a thickness of about 5–10 nanometres, compared with a final thickness of the order of 100 nm) in a vacuum. The crystallinity of this part was still high owing to oxidation of the film during the growth of the remaining part. Finally, the authors exfoliated the oxide film from the graphene to produce a free-standing oxide membrane.

In other experiments, Kum *et al.* found that strontium ruthenate could be used instead of graphene to grow an oxide film by a process known as sputtering. The film could then be exfoliated from the strontium ruthenate by depositing a layer of nickel on top of the film. The nickel acts as a stressor – it provides

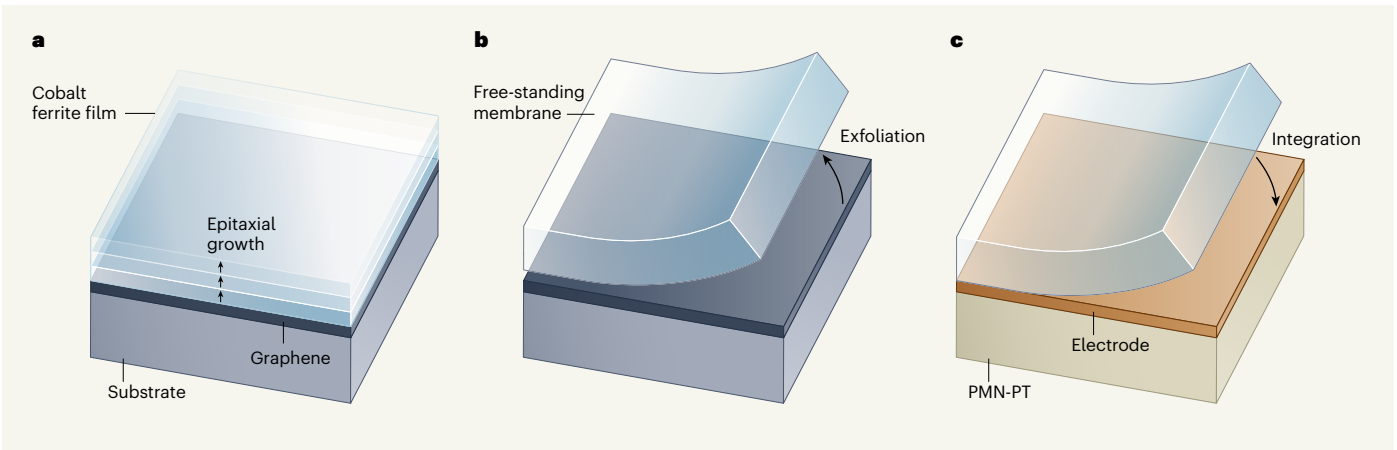

Figure 1 | Growth and integration of complex-oxide films. a, Kum *et al.*[6] report a versatile approach for making high-quality films of technologically useful compounds called complex oxides and transferring these films to other materials. As a demonstration, the authors grew a film of the complex oxide cobalt ferrite using a technique known as remote epitaxy, whereby the film and the underlying substrate are separated by a few sheets of the material graphene. **b**, They then exfoliated (removed) the film from the graphene to produce a free-standing membrane. **c**, Finally, the authors integrated the membrane with an electrode and a membrane of another complex oxide, lead magnesium niobate–lead titanate (PMN-PT), which had also been made using remote epitaxy (but replacing graphene with strontium ruthenate). Such integration is difficult to achieve using the conventional scheme for growing oxide films because cobalt ferrite and PMN-PT have different crystal structures.

enough strain energy to overcome the weak bonds between the film and the strontium ruthenate.

Kum and co-workers demonstrated the transferral of oxide membranes to other materials for: strontium titanate, yttrium iron garnet and magnetic cobalt ferrite, produced by pulsed-laser deposition; lead magnesium niobate–lead titanate (PMN-PT), formed by sputtering; and ferroelectric barium titanate, made by a process called molecular-beam epitaxy. One example of a stacked structure produced by such transferral consists of a 300-nm-thick layer of cobalt ferrite, an electrode and a 500-nm-thick layer of PMN-PT (Fig. 1c).

The authors found that this structure displays high magnetostriction (coupling between magnetic and mechanical behaviour) and piezoelectricity (coupling between electric and mechanical behaviour), because it is free-standing rather than being clamped by a substrate. Cobalt ferrite, PMN-PT and yttrium iron garnet have different crystal structures, making it difficult to stack these materials by the usual growth scheme without such clamping.

Kum *et al.* also stacked graphene and oxide membranes to examine the electrical coupling between these materials. The density of electric charge in graphene can be inferred from the positions of peaks in Raman spectra — spectra generated through the scattering of incident light. The authors found that these positions depend on the stacked structure, indicating that charge is transferred across graphene–membrane interfaces. These results suggest that stacks of other combinations of materials will offer ways to integrate the various functions of oxides with mature device technologies.

The authors' exfoliation technique enables complex-oxide films to be easily transferred from an epitaxial interface to any material. Because the thickness and stacking of films can be controlled, ultrathin membranes and stacks of various membranes could be possible. Such a simple way of transferring the functions of oxides might advance the field of oxide-based electronics through integration with emerging quantum material systems[10]. However, the availability of graphene-coated substrates could be a key issue for developing the method.

This technique will probably be extended beyond the transferral of complex-oxide films. For example, it might provide an innovative strategy for engineering interfaces, by allowing 2D or 3D films and membranes to be integrated with each other through effects associated with multiple couplings between them. An understanding of the chemical or physical bonds at the interface between membranes in stacked structures is crucial and will reveal how such an interface differs from the epitaxial one. Finally, unusual material combinations (in which, for example, the size and orientation of crystal lattices of membranes are mismatched) could enable useful interface functions that are difficult to achieve or control at the epitaxial interface.

Atsushi Tsukazaki is at the Institute for Materials Research, Tohoku University, Sendai 980-8577, Japan.
e-mail: tsukazaki@imr.tohoku.ac.jp

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Virology

Latent HIV-1 gets a shock

Mathias Lichterfeld

HIV-1 can evade the immune system by hiding out in a dormant form. Two studies describe interventions that can effectively reactivate the latent virus in animals, potentially rendering it vulnerable to immune-mediated death. **See p.154 & p.160**

'Shock and kill' might sound like a military strategy, but in fact it describes the dominant model currently used in the search for a cure for HIV-1 infection. Although antiretroviral therapy (ART) is highly effective at limiting the extent of the infection, the virus can hide out in a 'latent' form in immune cells called $CD4^+$ T cells, undergoing little or no transcription and thus remaining undetected by the immune system[1,2]. When ART is stopped, these viral-reservoir cells can rapidly fuel HIV rebound. The theory behind 'shock and kill' involves the use of drugs that reverse this latency and could increase viral gene expression (shock), rendering the viral-reservoir cells vulnerable to elimination (kill) by other cells of the immune system. Two groups[3,4] now describe distinct interventions in animal models that cause what seem to be the most robust and reproducible disruptions of viral latency reported so far.

"The current studies showcase some of the conceptual and technical challenges intrinsically associated with pharmacological latency reversal."

In the first study, Nixon *et al.*[3] (page 160) focus on a drug called AZD5582, which can activate the transcription factor NF-κB — a major instigator of HIV-1-gene expression. AZD5582 was originally developed to treat cancer, and activates the 'non-canonical' NF-κB pathway, which results in an atypical type of NF-κB-driven transcription that is slow but persistent. The authors tested AZD5582 in two animal models: 'humanized' mice (which carry human-derived liver, bone-marrow and thymus cells) that were infected with HIV; and rhesus macaques infected with the HIV-related simian immunodeficiency virus (SIV). Both groups of animals were already receiving ART.

The authors demonstrated that AZD5582 treatment led to marked increases in the levels of viral RNA in $CD4^+$ T cells in a range of tissues in both species, indicating that transcription of the virus had been activated. This was combined with a substantial rise in virus levels in the blood. AZD5582 is not optimized for use in humans; nonetheless, these results suggest that pharmacological activation of the non-canonical NF-κB pathway could be an attractive way to trigger HIV-1-gene expression as part of a shock-and-kill approach (Fig. 1).

In the second study, McBrien *et al.*[4] (page 154) used an entirely different, though complementary, approach to disrupting viral latency. Again, the authors used both ART-treated humanized mice infected with HIV-1 and ART-treated, SIV-infected rhesus macaques. They combined two immunological interventions. The first involves antibody-mediated depletion of $CD8^+$ T cells — immune cells previously shown to act in concert with ART to reduce levels of viral transcription[5]. The second, administered concurrently, involves treatment with a drug called N-803, which strongly activates the signalling