ment unit if asked—some for the care that is offered, some to protect their families, and some because of social pressure. But many will flee or hide, and if they become ill, they will shed virus somewhere that is not under surveillance, possibly infect those around them, and perpetuate the outbreak.

Perhaps outbreaks would be easier to control if contacts could be offered something other than watchful waiting. Patients treated with the monoclonal antibody (mAb) therapies approved by the US Food and Drug Administration (FDA) for EVD had a CFR of ~35%, whereas the overall CFR was 66% during the 2018–2020 outbreak in the Democratic Republic of the Congo, where these therapies were studied (*5*). During EVD outbreaks, therapeutic mAbs could be used as postexposure prophylaxis (PEP) for contacts. Unfortunately, these therapies are expensive to manufacture and available only in limited quantities, and so they are presently reserved for the treatment of patients with confirmed disease or, rarely, as PEP for very high-risk exposures—for example, health care workers exposed to ebolavirus during patient care. The rVSV-EBOV vaccine appears to have some efficacy as PEP, at least in attenuating disease. A recent study showed that rVSV-EBOV reduced the likelihood of death in EVD patients by 44% when given two or fewer days before illness onset (*6*). Although achieving attenuated disease is promising, uptake of unfamiliar vaccines can be limited (*7*).

Obeldesivir is an oral prodrug that shares the same active metabolite as remdesivir—a broad-spectrum antiviral with preclinical efficacy against filoviruses that is also used to treat COVID-19 patients—and so it should have similar antiviral activity. Obeldesivir is now being studied for efficacy in treating COVID-19 (clinical trial NCT05715528). Cross *et al.* demonstrate that, like remdesivir, obeldesivir has in vitro efficacy against species of both *Ebolavirus* and *Marburgvirus*. It also fully protected cynomolgus macaques against a 100% lethal challenge with Sudan virus when a 10-day course was started 24 hours after challenge. Although other therapeutics, such as mAb treatments and remdesivir, are similarly protective against filovirus challenge (*8*, *9*), they are delivered intravenously, and this difference is where the potential value of obeldesivir lies.

The simplified administration of obeldesivir as an oral medication could increase the uptake of contact-tracing strategies. Additionally, as a small-molecule drug, it should be much less expensive to produce and be available in greater quantities than mAb therapies. These features could allow for the systematic delivery of PEP to all persons exposed to filovirus (see the figure). However, efficacy in nonhuman primate studies does not guarantee efficacy in exposed humans, so clinical trials will need to be carried out during future outbreaks. If the results of Cross *et al.* hold true for use in humans and can be replicated for other filoviruses, obeldesivir may be a solution to improving contact-tracing efforts and outbreak control. By offering preventive treatment to contacts, daily visits can be a more positive experience that is centered around their well-being, monitoring the effectiveness of PEP, and—for now, only in EVD outbreaks—a readiness to escalate to mAb treatment if needed. It is too soon to know whether obeldesivir PEP will change the relationship between the contacts and the follow-up teams, but it provides hope.

There are other reasons to be hopeful about the potential of obeldesivir. It could be a treatment for FVD survivors to eliminate virus from immune-privileged sites and thereby reduce the likelihood of sexual transmission, given that there is reason to believe that remdesivir does this (*10*). However, the advent of an effective vaccine and treatments for EVD has not brought about the change in outbreak control that was expected, at least not yet. Perhaps the benefit that obeldesivir may provide will not be entirely evident to the communities experiencing the outbreaks, and thus things may not change as much as hoped. Still, by addressing the needs of the people with whom follow-up teams must stay in contact and by offering them some hope, perhaps obeldesivir will prove to be what was needed to improve outbreak control. ■

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10.1126/science.ado6257

MATERIALS SCIENCE

Accelerating 2D materials discovery

A large-scale theory-driven approach predicts many new 2D materials

By **Anupma Thakur[1]** *and* **Babak Anasori[1,2]**

Two-dimensional (2D) materials are a class of nanomaterials that are sheets of one or a few atoms thick. They can be used in electronics, optics, energy storage, sensing, catalysis, biomedical, and environmental applications (*1*–*4*). Many 2D materials are made by slicing (exfoliating) bulk-layered structures to their thinnest layer of only a few atoms in thickness (*1*, *2*). However, without a full understanding of the interactions between the layers of atoms, simple trial-and-error experiments lead to slow progress in 2D materials discovery and substantial waste of resources from failed attempts. To circumvent these issues, a shift toward theory-driven experimental synthesis is essential. On page 1210 of this issue, Björk *et al.* (*5*) report high-throughput computational strategies with chemical exfoliation for synthesizing 2D materials. They used models to predict and guide the exfoliation process, which enhances efficiency and expands the family of 2D materials.

2D materials have intriguing properties, including high surface area, charge mobility, tunable bandgap, optical transparency, mechanical strength, and flexibility (*1*–*4*). Exfoliation leads to the confinement of charge carriers, heat, and phonon transport, resulting in distinct physical behavior in 2D materials (*1*, *3*). Additionally, the intrinsic properties of 2D materials can be modulated by the addition or removal of a few atoms within the 2D sheets and stacking different 2D materials, facilitating the development of precisely engineered devices (*1*).

2D materials are synthesized either by adding atoms one by one to make an atomically thin 2D sheet (bottom-up methods) or by exfoliation of a bulk layered material

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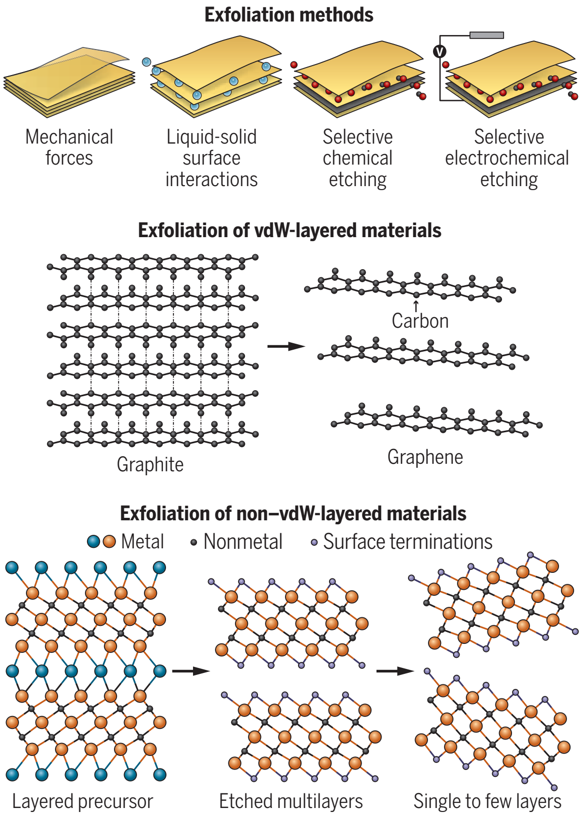
into ultrathin atomic 2D sheets (top-down methods). Although bottom-up synthesis allows high precision, top-down exfoliation methods are scalable (*2*). The feasibility of exfoliating layered materials depends on the type of bonds between atomic layers. Weak bonds [for example, van der Waals (vdW)] make mechanical exfoliation possible (*1*, *6*). Graphite is an example of a vdW-layered material that has weak bonds between the carbon layers, whereas the in-plane carbons have ultrastrong covalent bonds (*1*, *6*). This difference in bonding within the layered graphite allows the layers to be exfoliated (*6*) (see the figure).

To date, various approaches have been used to exfoliate graphite, including mechanical exfoliation through the application of shear forces and liquid exfoliation, which uses liquid-solid interactions (*1*, *6*). Beyond graphene, hexagonal boron nitride (h-BN); single-element 2Ds (Xenes); mono-, di-, or tri-chalcogenides; metal oxides and hydroxides; metal halides; metal oxyhalides; and metal nitride halides have been explored as 2D materials (*7*). The recent addition of 2D rare-earth metal oxyhalides further diversifies this growing family of 2D vdW materials (*8*) and suggests that rare-earth metal oxyfluorides, metal nitride halides, metal carbide halides, and naturally occurring vdW minerals could have potential as vdW 2D materials (*9*).

Exfoliation methods for 2D materials

Exfoliation methods to produce two-dimensional (2D) materials that are single to few atoms thick include applying mechanical forces, liquid-assisted sonication, and chemical and electrochemical etching. The precursor material can be layered, bonded by van der Waals (vdW) forces, as in the case of graphite, which allows simple exfoliation to produce graphene. Non-vdW materials, such as MXenes, require selective etching of certain layers of atoms from the precursors to produce 2D materials.



Non-vdW materials (layered or nonlayered), with chemical bonds in three dimensions, are difficult to isolate directly because they lack readily cleavable bonds. Bottom-up approaches seem to be the only route to synthesizing 2D materials of non-vdW structures. However, because the chemical reactivity and bond strength are dissimilar between different layers of atoms, selective chemical etching of relatively weakly bonded layers can lead to artificially constructing weakly bonded layered structures with vdW bonds between certain atomic planes, which can be cleaved to make 2D sheets. 2D transition-metal carbides, nitrides, and carbonitrides, together called MXenes, were among the first 2D materials synthesized by means of top-down selective chemical etching of their non–vdW-layered precursors (*10*–*12*).

MXene precursors are made of 2D layers of transition-metal carbides [for example, titanium carbide (Ti_3C_2)] with covalent and ionic bonds. These carbide layers are "glued" together by a layer of another element (usually aluminum) with metallic bonds. The metallic bonds are strong enough that the typical mechanical exfoliation methods cannot break them. However, because the metallic bonds are weaker than the covalent and ionic bonds, the aluminum layers can be selectively etched with wet-chemical etching and converting the non–vdW-layered structure into a vdW-layered structure, which can be further exfoliated into 2D sheets through similar routes to the naturally occurring vdW materials (*12*, *13*).

MXenes are 2D materials with five or more atomic layers, which adds to their tunability by changing the number of layers or the layer compositions for desired properties. For example, Ti_3C_2 and titanium carbonitride (Ti_3CN) MXenes outperform all other materials in blocking electromagnetic waves (*14*). The scalable production of MXenes as nanoinks allows their immediate use in industry—for example, in electromagnetic interference shielding, wireless communications, and printable electronics. However, technological advancement and high demand for smarter and smaller devices call for more materials discovery at the smallest scales with desired properties.

Björk *et al.* used a large-scale and theory-driven methodology to identify 2D materials that can be synthesized through chemical exfoliation of bulk non–vdW-layered materials under acidic conditions. They investigated an extensive dataset of 66,643 layered materials and predicted 42 distinct 2D materials derived from 119 different bulk layered precursors. A 2D compositional space comprising 2D metal silicides; phosphides; and a range of chalcogenides, carbides, borides, and oxides was computationally predicted, and 2D $Ru_2Si_xO_y$ was experimentally synthesized.

These 42 new 2D materials were predicted only from ternary layered compositions and one selective chemical etching. When the vast materials space with four or more elements is considered, as well as more complex structures and other selective etching routes (for example, molten salt), the advanced theory-driven 2D material design techniques demonstrated by Björk *et al.* could have a substantial impact in deciphering the complexities of the chemical exfoliation processes of bulk precursors and facilitate the development of new materials. The evolution from bulk materials to 2D materials does not just represent a change in dimensionality; it denotes a leap toward the future of material innovation. Using high-throughput computational screening and machine learning further accelerates the expansion of the nanomaterials space by designing 2D materials with targeted properties for their use in electronics, energy devices, sensors, catalysis, and biomedical engineering. ■

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ACKNOWLEDGMENTS

The authors acknowledge the support by the US National Science Foundation (award 2419026).

10.1126/science.ado4113

GRAPHIC: K. HOLOSKI/*SCIENCE*