CLAUDIO VARGAS/AFP/GETTY

Respite from the storm

It's clear that the devastation inflicted by tropical cyclones will increase as the planet warms. But socio-economic models that predict changes in the human population could be used to markedly reduce the number of people exposed, as Geiger *et al.* report in *Nature Climate Change* (T. Geiger *et al. Nature Clim. Change* https://doi.org/gxsj; 2021).

The authors conducted a regionally specific analysis of tropical-cyclone simulations, and combined it with conservative predictions for how population patterns will change over the course of the century. They compared their estimates with the number of people expected to be exposed to tropical cyclones in a world warmed 1°C above pre-industrial temperatures with population patterns fixed at 2015 values.

The global population is generally expected to peak around 2050 and then to fall. Using such estimates, the authors predicted an increase of 41% in people affected if the global mean surface temperature instead increases by 2°C before 2050. But a more moderate 20% increase is expected if the 2°C rise can be delayed until 2100, when population decreases in susceptible areas might compensate for the risks associated with warming. **Abigail Klopper**

Materials chemistry

Platinum catalysts strained controllably

Sylvain Brimaud

The distance between the surface atoms of noble metals, such as platinum, affects the catalytic activity of these elements. An experimental approach using nanoparticles enables this effect to be systematically controlled and measured. **See p.76**

Devices known as electrocatalytic converters, such as water electrolysers and hydrogen fuel cells, act as interfaces for chemical energy and electrical energy. These technologies are starting to be adopted in efforts to develop hydrogen as a storage medium for energy produced by intermittent renewable sources: solar energy, for example, could be used to power electrolysis of water to produce hydrogen; and hydrogen can be used in fuel cells to produce electricity for powering electric vehicles. Platinum is often used as a catalyst for the electrochemical reactions that occur in these devices. The reactions take place at the surface of the metal, and so nanoscale platinum particles are used, to optimize the surface-to-mass ratio of this expensive and scarce element.

Nevertheless, improvements in the catalytic activity of the particles, and in the selectivity with which the electrochemical reactions generate the desired reaction products, are needed to improve the efficiency of the devices and thereby reduce the amount of platinum used. On page 76, He *et al.*[1] report a method that enables systematic tuning of the distance between platinum atoms in a thin film of the metal deposited on the surface of cubic nanoparticles. This allows the relationship between the interatomic distance and the catalytic activity of the film to be investigated for selected electrocatalytic reactions.

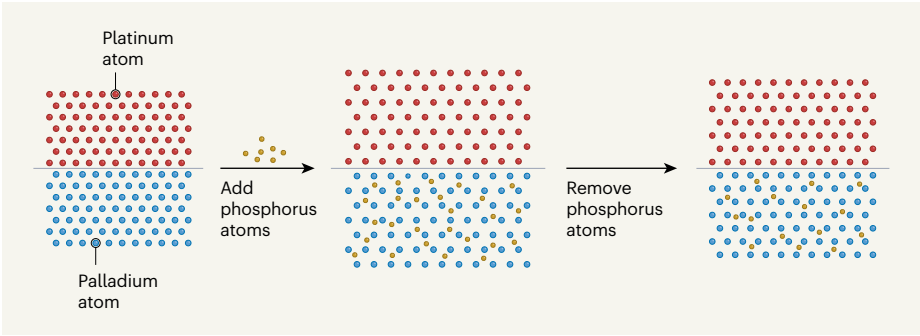

Figure 1 | Size-changing nanocubes control catalytic activity of platinum surfaces. He *et al.*[1] prepared nanocubes of palladium coated with a few layers of platinum atoms. The crystal lattices of the two metals are very similar, and so the interatomic distances between the platinum atoms match those of the palladium atoms. However, subsequent addition of phosphorus atoms to the palladium core increases the distance between palladium atoms, which in turn increases the distance between platinum atoms. Removal of phosphorus atoms decreases the interatomic distances. The addition and removal of specific amounts of phosphorus therefore provides a controllable way to alter the distances between platinum atoms, so that the effects of interatomic distance on the catalytic activity of the platinum shell in certain electrochemical reactions can be investigated systematically. The positions of the phosphorus atoms in the palladium lattice are illustrative, and were not determined experimentally.

The electronic characteristics of the surface atoms of the late transition metals (such as platinum) affect how strongly chemical species can adsorb to these atoms[2,3]. This, in turn, affects the rate of subsequent reactions of the adsorbed chemical species. The electronic properties of the metal atoms can therefore be tuned to alter the rates of electrochemical reactions catalysed by these elements, and the effects on reaction rates can be predicted computationally following a set of theoretical principles and approximations[4].

The electronic interactions between the atoms in a catalytic site on a platinum surface can be modified by changing the interatomic distance (strain effects), or by replacing a neighbouring atom with an atom of a different chemical element (electronic effects). In principle, both types of effect will alter the binding strength of chemical species adsorbed to the catalytic site in a predictable and quantifiable way. But it has been difficult to control and measure these effects in experiments.

The most straightforward experimental verifications of the theoretical frameworks and associated approximations have been obtained with model surface systems in which layers of platinum atoms are grown under ultra-high vacuum conditions on a single crystal of another metal, so that the platinum atoms adopt the crystal lattice of the substrate (epitaxial growth). Because the platinum atoms adopt the interatomic distances of the substrate lattice, rather than the atoms' preferred interatomic distances, the thin film of platinum is subjected to strain – either compressive or tensile strain, depending on the mismatch between the normal lattices of the two metals. The electronic effects of the substrate on the adsorption properties of the platinum film vanish beyond three atomic layers, so that only strain effects remain for thicker films[5–7].

He *et al.* now report a variation of the thin-film approach (Fig. 1). They prepared palladium nanocubes (edge lengths 20 nanometres) covered by about seven layers of platinum atoms. The dimensions and geometries of the crystal lattices of platinum and palladium match each other closely. However, the authors were able to reversibly expand and shrink the palladium lattice by adding and removing phosphorus atoms in the core – the degree of expansion or shrinkage depends on the amount of phosphorus that is added or removed. The distances between platinum atoms in the thin shell therefore follow the interatomic distances in the lattice of the palladium core lattice, thus providing a controllable way to strain the shell.

"The authors were able to reversibly expand and shrink the palladium lattice."

The authors carefully controlled the temperature when expanding or contracting the palladium core, to prevent alloying of the two metals or phosphorization of the platinum shell, and used a wide array of analytical techniques to characterize the resulting core–shell nanoparticles. He *et al.* thus produced 12 batches of nanoparticles, each of which contained platinum shells with a specific amount of tensile or compressive strain – an experimental tour de force.

The authors then probed the effects of strain on the catalytic activity of the platinum shells in two model electrochemical reactions – the methanol oxidation reaction and the hydrogen-evolution reaction, which are of practical interest in methanol fuel cells and in water electrolysis, respectively. He *et al.* observed large variations in catalytic activity as a function of strain: the strain–activity relationship follows an M-shaped curve for methanol oxidation, and a volcano-shaped curve for the hydrogen-evolution reaction. This allowed the authors to determine the platinum–platinum distances that optimize the catalytic activity per mass of platinum for the core–shell particles in the two reactions.

A limitation of He and co-workers' approach is that it cannot exclude the possibility that the observed reaction rates are driven by a small number of lattice heterogeneities or defect sites at the platinum surface[8] that are not representative of the atomic structure of the majority of the shell. Nevertheless, the authors' thorough characterization of a large number of sample batches, taken together with the qualitative matching of the experimentally derived strain–activity relationships with the trends expected computationally from theory, strongly support their claims. The mechanistic aspects of the phosphorization–dephosphorization of the platinum-covered palladium core also need to be better resolved, but this does not detract from the merits of He and colleagues' remarkable achievement.

It should be noted that materials that are highly catalytically active in model systems are not always suitable for practical application in the electrodes of electrocatalytic converters. Many aspects of the material and the electrode architecture need to be considered, of which the activity per mass of the active material is just one. He and colleagues' electrocatalyst materials will probably not be useful in electrocatalytic converters, for several reasons – for example, smaller particle sizes will be required. The authors have made a first attempt to address this problem by preparing optimum-strained particles with a 6-nanometre palladium core. Above all, a much cheaper material than palladium is needed as a core for the platinum shell. This should stimulate a search for a low-cost core material whose lattice dimensions can be easily tuned by the inclusion and removal of another element, and onto which a thin platinum film can grow epitaxially.

However, the value of the new work is that it provides a general framework, combining nanomaterial preparation and extensive characterizations, for verifying computational predictions of properties of catalytic materials for complex, multistep electrochemical reactions. This approach is much more affordable than the previous methods in which ultra-high-vacuum techniques were used to prepare samples.

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Cancer

Tumours block protective muscle and nerve signals

Teresa A. Zimmers

Certain cancers cause people to weaken and waste away. A mouse model of this points to tumour-induced blockade of molecules that normally protect muscle innervation and mass. Will the discovery lead to therapies for this deadly condition?

People who have certain types of cancer, particularly gastrointestinal and lung tumours, frequently experience what is called cachexia[1] – a progressive and often severe weight loss, irrespective of the level of food intake. This condition arises when tumours rewire the body's neural, immune and metabolic systems to trigger the breakdown (catabolism) of adipose tissue and skeletal muscle[2,3]. As their muscles grow weaker and smaller, affected individuals lose their ability to function normally. They become vulnerable to injury, infections and treatment toxicities, and then ultimately fail to respond to cancer treatment.

Even though cachexia causes more than 30% of all cancer deaths[4], and is prevalent and deadly in many other conditions, including organ failure, there are no effective approved therapies. Pre-clinical animal studies demonstrate that blocking muscle wasting preserves function and lengthens life, with or without anti-tumour therapy[5] – which suggests that the same might also be true for people with cancer who are at risk of cachexia. Writing in *Science Translational Medicine*, Sartori *et al.*[6] identify a targetable pathway for cancer-associated cachexia (Fig. 1), bringing us closer to developing a treatment.

To counter disease and injury, animals have evolved mechanisms that include inflammatory signals alerting the central nervous system to reduce appetite and food-seeking behaviours – an adaptation that limits vulnerability to predators. The same signals drive the process of catabolism, which liberates stores of fatty acids and amino acids to repair tissue, fight infection and protect brain and organ function. Once tissues are repaired and infections cleared, inflammation subsides and normal feeding resumes, allowing replenishment of the body's reserves. However, cancer co-opts these survival mechanisms, turning these useful adaptations into a source of harm. Tumours, which can be considered both a type of regenerative tissue and a non-healing wound, do not subside over time in the way that a typical injury or infection does. So the catabolism of fat and muscle proceeds unabated, often leading to emaciation and death.

How tumours trigger these changes is beginning to be unravelled. Signals, yet to be fully identified, that emanate from the tumour (or arise from the host response to the tumour) are received by muscle cells. In the muscle, these signals activate the catabolism of proteins. In part, this happens through a process of destruction known as the ubiquitin-proteasome system, which depends on specific enzymes that tag proteins for degradation. This leads to the characteristic shrinking of muscle fibres and wasting of muscle throughout the body seen in cachexia.

> **"No treatments exist for cachexia, which can be fatal."**

A decrease in the size of muscles and muscle fibres (atrophy) can also be triggered for other reasons. They include reduced quality, activity or number of the neurons that innervate muscle to control voluntary motor movement (a condition referred to as denervation), as occurs in motor neuron diseases such as amyotrophic lateral sclerosis. Each of these mechanisms is also proposed to contribute to muscle wasting in cancer[7].

Sartori and colleagues' study is a collaboration between research groups that previously identified[8,9] a series of molecular interactions known as the BMP pathway as a positive regulator of muscle function and mass. BMPs are secreted proteins that signal among cells and between tissues[10]. During development, these proteins specify the pattern and fate of tissues in the embryo. In adults, BMPs have essential roles in musculoskeletal health. They act on cells by binding receptors called BMPRs. This leads to the activation of SMAD proteins, which move to the nucleus to alter gene expression and, ultimately, cellular characteristics.

It was previously shown that a rise in BMP7 or BMPR activity promotes an increase in muscle size (hypertrophy) through SMAD1/5/8 proteins, and that BMP signalling is protective of muscle size in conditions of reduced innervation[8]. Earlier work has also established that BMP signalling through SMAD4 promotes muscle growth, and that the BMP inhibitor protein, Noggin, which blocks BMPR activation, induces muscle wasting[9]. These studies established BMP signalling as an important growth-promoting pathway in muscle. Sartori and colleagues have now investigated this pathway in the context of cancer-associated cachexia.

Studying a commonly used mouse model in which colon tumours inserted into an animal's flank lead to rapid and lethal muscle wasting, Sartori *et al.* document the activation of the ubiquitin-proteasome system and decreased BMP activity compared with the systems in mice without such tumours. The use of genetic approaches to increase BMP activity or to block Noggin blunted the activation of the ubiquitin-proteasome system and spared muscle in the mice with tumours. This evidence therefore indicates that tumour-induced Noggin impairs BMP signalling, leading to protein catabolism and muscle wasting.

Beyond the effects on muscle size, the investigators identify defective muscle innervation as preceding the loss of muscle mass, suggesting a causal role for denervation in cachexia. Using a combination of experimental approaches, the authors demonstrate that this defect was a loss of functional interaction between motor neurons and muscle cells (myofibres). This misalignment and degeneration of the neuron–myofibre connection could be mimicked by exposure to excess Noggin. Providing BMP or blocking Noggin were protective in this context.

What triggers this Noggin expression in muscle? Sartori *et al.* propose that it is the pro-inflammatory molecule IL-6. This protein helps to orchestrate the immune response and is tightly linked to cancer cachexia. Excess IL-6 induces cachexia, whereas IL-6