the lattice, to provide a slight bias that caused buckling to occur in a particular direction. Such imperfections would generally be undesirable in other contexts.

One of the current limitations of Xia and colleagues' work is that it takes a long time to make a tiny amount of the architected material — we estimate that it would take about a day to produce 1 cubic millimetre of material, although the exact timing will vary depending on the printing conditions and the geometries of the material involved. A new 3D-printing approach known as volumetric additive manufacturing[7] might help to accelerate and scale up the process, but it currently has limited spatial resolution and works with only a small range of materials.

Xia and colleagues' findings have a variety of potential applications. For example, in micrometre-scale robots, which have limited room for components, the use of materials that can change shape to perform multiple functions would be most helpful. The technology might also find uses in autonomous micro-devices that perform desired functions by changing shape in response to stimuli such as changes in ion concentration, or in devices known as microactuators[8] that 'snap'[9] between two configurations in response to electrical signals or electrochemical stimuli.

The study also demonstrates a means of releasing the stress that builds up in silicon anodes of lithium batteries as they change volume during discharge, to prevent failure of the anodes — which is one of the key challenges in the development of next-generation silicon–lithium batteries. Moreover, the work opens up opportunities for controlling the propagation of high-frequency vibrations (known as phonons) using electricity, which might enable the development of potentially useful microelectromechanical systems.

Future research into electrochemically reconfigurable materials could benefit from the use of computational methods, such as machine learning, to optimize the topology of architected materials and the shapes produced for different applications. Such methods might increase the lifetime and/or the number of possible lithium loading–unloading cycles of architected materials by decreasing the strains required to induce buckling. They might also reduce the time taken for materials to respond to an electrochemical stimulus (currently 5 to 10 minutes), by increasing the surface area at which electrochemical reactions can occur, for example by using hierarchical substructures.

Finally, if the material systems that are compatible with this approach can be expanded, it would open the way for sensors and smart actuators to be used in many other applications, including medical devices. Given that our bodies contain various ion-containing, water-based fluids, it might be possible to devise micro-devices that sense physiological variables without external power, or to make smart implants that adapt to local conditions by modulating their shapes. ■

Seung-Yeol Jeon *and* **Sung Hoon Kang** *are in the Department of Mechanical Engineering and the Hopkins Extreme Materials Institute, Johns Hopkins University, Baltimore, Maryland 21218, USA.*
e-mail: shkang@jhu.edu

1. Xia, X. *et al. Nature* **573**, 205–213 (2019).
2. Jung, G. S. & Buehler M. J. *Nature* **565**, 303–304 (2019).
3. Mullin, T., Deschanel, S., Bertoldi, K. & Boyce, M. C. *Phys. Rev. Lett.* **99**, 084301 (2007).
4. Kang, S. H. *et al. Adv. Mater.* **25**, 3380–3385 (2013).
5. McDowell, M. T., Lee, S. W., Nix, W. D. & Cui, Y. *Adv. Mater.* **25**, 4966–4985 (2013).
6. Baggetto, L., Danilov, D. & Notten, P. H. L. *Adv. Mater.* **23**, 1563–1566 (2011).
7. Kelly, B. E. *et al. Science* **363**, 1075–1079 (2019).
8. Jiang, Y., Korpas, L. M., & Raney, J. R. *Nature Commun.* **10**, 128 (2019).
9. Shan, S. *et al. Adv. Mater.* **27**, 4296–4301 (2015).

STRUCTURAL BIOLOGY

A mechanism for touch

Piezo proteins mediate the sense of touch. A near-complete structure of one such protein has been obtained, and the mechanism for converting mechanical signals into electrical ones has been probed in another. SEE ARTICLES P.225 & P.230

EDWIN W. MCCLESKEY

Our bodies can sense a wide array of mechanical stimuli: our sense of touch can distinguish between a soft breeze floating over the skin and a painful pinch, and other systems can detect the stretch of a muscle or even blood pressure. Our ability to sense these things requires an applied force to be turned into an electrical signal in the tiny endings of sensory neuronal cells that suffuse different tissues. Two related proteins, the Piezo1 and Piezo2 ion channels, mediate many of the mechanically stimulated processes in animals, by allowing positive ions to flow across the surface membrane of cells in response to force applied to the membrane[1]. Such mechano-electric transduction is mediated by Piezo2 in sensory neurons and by Piezo1 in non-neuronal cells that respond to forces such as shear and osmotic force[2]. On page 225, Wang *et al.*[3] report a remarkable, almost complete structure of Piezo2, and on page 230, Lin *et al.*[4] describe experiments that test how transduction occurs in Piezo1.

Piezo ion channels assemble from three identical Piezo proteins, each containing more than 2,500 amino-acid residues[5]. Solving such large structures — finding the location of each atom — is a great technical challenge. Nevertheless, studies in the past couple of years have described partial structures of Piezo1 at near-atomic resolution[6–8].

Wang and colleagues now take things further with their near-atomic-resolution structure of Piezo2, resolving each of its 38 transmembrane helices. This is yet another achievement of the 'resolution revolution' in single-particle cryo-electron microscopy

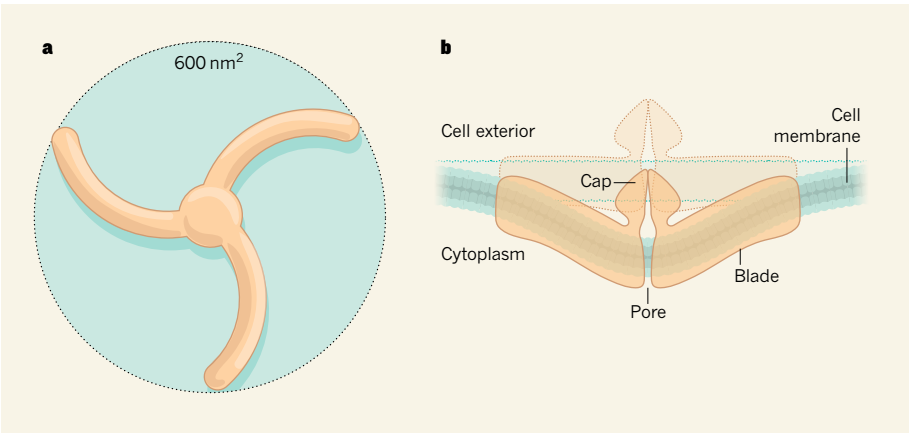

Figure 1 | The structure of Piezo ion channels and their response to forces. Wang *et al.*[3] report the near-complete structure of Piezo2, a membrane ion channel that converts mechanical stimuli into electrical signals. Viewed from above or below the membrane, the trimeric channel looks like a three-bladed propeller and defines an extensive membrane area of about 600 square nanometres — in line with the idea that it responds to stretching of the membrane. **b**, Lin *et al.*[4] report that the bowl-like shape of the Piezo1 channel, viewed here from the side, creates a dimple in the surrounding membrane. The protein and dimple flatten reversibly when a force (not shown) of the size that could cause the channel's pore to open is applied to Piezo1, perpendicular to the membrane.

(cryo-EM)[9]. Cryo-EM obtains molecular structures by analysing thousands of images of individual protein molecules that have been frozen randomly throughout a thin layer of non-crystalline ice. It has proved particularly powerful for solving the structures of large membrane proteins, such as ion channels, that do not readily form the crystals required for X-ray crystallography.

A model of the target protein is often required as a template for cryo-EM analysis. Wang *et al.* used the previously reported structures of Piezo1 as the model for Piezo2. The resulting enormous structure of Piezo2 can therefore be viewed as the culmination of multi-year efforts from multiple labs.

These efforts have revealed that Piezo channels have four key features, which have been given helpfully descriptive names: the propeller, the cap, the pore and the nano-bowl (sometimes also called the dome). The propeller has three blades, one from each of the constituent proteins, equally spaced around the centre and each casting an arc roughly 200 ångströms in length. Each blade contains 36 α-helices, which have the correct lengths to fit across a lipid bilayer, and the correct hydrophobicity to be embedded in one. The string of helices therefore probably weaves back and forth across the membrane. Together, the three spring-like blades define an area of membrane of about 600 square nanometres — a sound arrangement for a sensor of membrane stretch (Fig. 1a).

The cap is a large, extracellular domain that sits outside the pore, similar to the caps that have been implicated in the gating of other trimeric ion channels[10]. The pore region is composed of six α-helices (two from each protein), and it has the internal surface charge expected of channels that allow the passage of positive ions rather than negative ones[6]. The pores of Piezo1 and Piezo2 are both clamped shut in the solved structures, with one constriction site in Piezo1 and two in Piezo2.

So, what is the transduction mechanism by which force opens the pore? There are two general ways in which a membrane protein might detect an external force: it could simply sense the stretch of the lipid membrane itself, or it might be pulled or pushed by other proteins that are attached to it in the regions either side of the membrane (the extracellular matrix or the cytoplasm). Both types of Piezo channel have a curved geometry, like a bowl open to the outside of the cell, and this unusual shape suggests a simple mechanism for force transduction[8]: if the curve of the protein causes local distortion of the membrane, then a lateral stretch could flatten both the membrane and the protein. If this flattening of the protein structure is somehow linked to the gates that open the channel's pore, no accessory proteins would be needed for transduction.

Lin *et al.* tested this proposal in two ways. First, they studied Piezo1 channels in lipid vesicles. This was crucial because previously reported Piezo structures were obtained in aggregates of detergents (detergent micelles), rather than in lipids, so it has been uncertain how Piezos sit within, and interact with, lipid bilayers. The authors found that Piezo1 does indeed distort the vesicle membrane (Fig. 1b), clearly puckering the vesicles into non-spherical shapes. In the second test, the authors applied force to the Piezo channel using the probe of an atomic force microscope (AFM), and found that the bowl underwent reversible flattening at biologically relevant pressures.

It should be noted that the AFM applies force perpendicular to the membrane, rather than laterally through it, but the experiment still demonstrates the springiness of the bowl at appropriate forces — a crucial requirement of the proposal. However, the experiment does not address whether biological stimuli directly stretch cell membranes or act through an accessory protein (akin to the action of the AFM probe). Also not addressed is how flattening of the bowl would open the pore. The extracellular cap might be important for pore opening because, as Wang *et al.* show[3], mutations that eliminate most of it render the channel insensitive to membrane deformation. However, there are many ways to explain the loss of function of a protein when a large part of it is deleted.

Further effort is now required to verify which transduction mechanism — membrane stretch or protein–protein interaction — operates in cells. The first task is to solve the atomic structure of both Piezo channels isolated in artificial lipid membranes, rather than in detergent micelles. Ideally, this would be achieved using lipid vesicles that have been frozen under different osmotic conditions. Osmotic forces will stretch the membrane and, according to the membrane-stretch model, should bias Piezo towards different gating states. Such states might be detectable using cryo-EM or by measuring ion flux through the pores, thereby demonstrating that Piezo can open without aid from other proteins. The two Piezo channels might behave differently in such experiments.

The protein–protein interaction model could be explored further by electron tomography, a method that can distinguish between and locate different types of membrane protein in nerve cells and identify cytoplasmic proteins with which they interact[11]. The observation of force transduction in real time will also be essential. The activity of ion channels, and conformational changes in them, have been measured simultaneously in real time in live cells[12]. This would be a powerful assay for detecting whether protein–protein interactions affect Piezo transduction, and for investigating how channel flattening might link to gates in the pore. Each of these lines of research presents formidable technical challenges. Nevertheless, such high-risk research seems worth the effort, because our sense of touch is so fundamental to our sense of being. ■

Edwin W. McCleskey *is in the Science Program of the Chan Zuckerberg Initiative, Redwood City, California 94002, USA.*
e-mail: emccleskey@chanzuckerberg.com

1. Coste, B. *et al. Nature* **483**, 176–181 (2012).
2. Murthy, S. E., Dubin, A. E. & Patapoutian, A. *Nature Rev. Mol. Cell Biol.* **18**, 771–783 (2017).
3. Wang, L. *et al. Nature* **573**, 225–229 (2019).
4. Lin, Y.-C. *et al. Nature* **573**, 230–234 (2019).
5. Ge, J. *et al. Nature* **527**, 64–69 (2015).
6. Saotome, K. *et al. Nature* **554**, 481–486 (2018).
7. Zhao, Q. *et al. Nature* **554**, 487–492 (2018).
8. Guo, Y. R. & MacKinnon, R. *eLife* **6**, e33660 (2017).
9. Cheng, Y. *Cell* **161**, 450–457 (2015).
10. Mansoor, S. E. *et al. Nature* **538**, 66–71 (2016).
11. Chen, X. *et al. J. Neurosci.* **31**, 6329–6338 (2011).
12. Sasmal, D. K. & Lu, H. P. *J. Am. Chem. Soc.* **136**, 12998–3005 (2014).

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PALAEOANTHROPOLOGY

Elusive cranium of early hominin found

A 3.8-million-year-old hominin fossil reveals what the cranium of the oldest known *Australopithecus* species looked like, casting doubt on assumptions about how these ancient relatives of humans evolved. SEE ARTICLES P.214 & P.220

FRED SPOOR

Human evolution often captures the imagination, not least because some of our extinct hominin relatives are personified by well-preserved fossils with catchy nicknames. For example, a partial skeleton of *Australopithecus afarensis* is named Lucy, and an *Australopithecus africanus* cranium (the skull without its lower jaw) is called Mrs Ples. However, the oldest known species that is unambiguously part of the human evolutionary tree[1], *Australopithecus anamensis*, has mainly languished away from the limelight because of its small and not particularly glamorous fossil record. Until now,