(gamma stimulation) can clear protein plaques (a hallmark of neurodegeneration) in mouse models of Alzheimer's disease[6,7]. Gamma stimulation has been heralded as a non-invasive treatment for neurodegeneration and has already moved into clinical trials[8–10]. The cellular mechanisms that underpin the effects of this therapy are unclear, although there are some links to activation of microglia – the immune cells of the central nervous system[7]. In the latest study[2], the authors show that gamma stimulation enhances glymphatic clearance, most noticeably in the brain's cerebral cortex. Gamma stimulation increases aquaporin-4 localization along the vascular endfeet of astrocytes and widens the diameter of meningeal lymphatic vessels, driving increased fluid flow through the tissue and clearance from the brain to the lymphatic system.

The flow of cerebrospinal fluid through perivascular spaces seems to be driven, at least in part, by the pulsing of arteries and larger changes in the diameter of blood vessels initiated by sensory stimulation or the slow contraction and relaxation of smooth muscle in the blood-vessel wall (vasomotion)[11–14]. The exact signals that trigger changes in blood-vessel diameter and vasomotion, and therefore increase glymphatic clearance, have not been identified.

Murdock and colleagues bring a new aspect of glymphatic regulation into play: the control of vasomotion by neuropeptide molecules. By monitoring the release of a neuropeptide by active neurons in real time, the authors find that gamma stimulation upregulates neuropeptide signalling in the interstitial fluid. Neuropeptides can act on the vasculature and astrocytes, both of which are crucial components of the perivascular space. The main question now is: how does synchronized neuronal activity trigger neuropeptide signalling and, ultimately, upregulate fluid flow?

Both papers raise several further questions. For example, how might burst firing of neurons – fast, sequential pulses of electrical activity (action potentials), rather than sparse firing of a single action potential at a time – affect interstitial fluid flow and clearance? Are neurons the main cell responsible for the changes to glymphatic flow? Additional signalling pathways might exist: the signalling molecule adenosine is a potent dilator of blood vessels and is released by neurons after visual stimulation at 40 Hz (ref. 15). Also, astrocytes buffer large potassium-ion gradients at the synapse, wrap the perivascular space, can sense neuropeptides and are connected by intercellular 'gap junctions'[16]. Yet, the way in which astrocytes might buffer ionic gradients in the interstitial fluid, potentially driving 'rivers' of flow around neurons, has yet to be investigated.

Furthermore, does the cellular shape (morphology) of neurons and astrocytes matter? How might interstitial flow in highly organized spaces such as the cortex and hippocampus differ from that in regions of the hypothalamus, which are less organized but have enriched neuropeptide signalling? Currently, there are no good ways to answer these questions, but they should be the focus of the next stages of glymphatics research.

Jiang-Xie and colleagues suggest that, as long as neurons fire in synchrony, the frequency of firing is not that important. At first glance, this contrasts with Murdock and colleagues' findings, which suggest that neuronal oscillations at 40 Hz are required for clearance. But both studies could be correct if a provocative alternative hypothesis is true: each brain region might have a 'tuning frequency', in which a defined pattern of neuronal firing drives efficient clearance. If that is the case, perhaps it is possible to harness this knowledge for the treatment of brain disorders in which the loss of cell populations is a contributing factor, such as Parkinson's disease, in which dopamine-releasing neurons are lost. Understanding the physiology and drivers of localized waste clearance in the brain could be the key that unlocks the therapeutic potential of the glymphatic system.

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Condensed-matter physics

Quantum sensor settles debate about hydrides

Kin On Ho & Sen Yang

By adapting a device designed to create extremely high pressures into one that can sense magnetic fields, researchers have obtained evidence that a hydrogen-rich material is a superconductor, eliminating long-standing doubts. **See p.73**

Superconductors are materials with no electrical resistance below a critical temperature – a tantalizing prospect for efficient power transmission. The lack of resistance is usually the first clue that a material can superconduct, but its candidacy must be supported by other properties, including a tendency to expel magnetic fields through a phenomenon known as the Meissner effect. On page 73, Bhattacharyya *et al.*[1] report evidence of the Meissner effect in cerium superhydride, a material belonging to a series of hydrogen-rich materials having a maximum critical temperature close to room temperature. The authors' feat was made possible by the clever use of a quantum device that can apply the pressure required to make cerium superhydride superconducting, and that can simultaneously sense magnetic fields.

Superconductivity was first discovered in 1911 in mercury, a material that superconducts at temperatures around 4.2 kelvin, which can be achieved only with cryogenic cooling[2]. A milestone was reached in the late 1980s, when a series of copper oxides was shown to display superconductivity up to 93 kelvin, a temperature that is higher than the boiling point of liquid nitrogen[3,4]. But the quest continues for a material that superconducts at close to room temperature, which would broaden the technological potential of this extraordinary state.

Theory predicts that, below the critical temperature, electrons start to form pairs (called Cooper pairs) with the help of crystal-lattice vibrations known as phonons[5]. The condensation of these pairs leads to superconductivity, so inducing Cooper pair formation can increase the critical temperature at which superconductivity appears. Metallic hydrogen is expected to superconduct close to room temperature because its low atomic mass

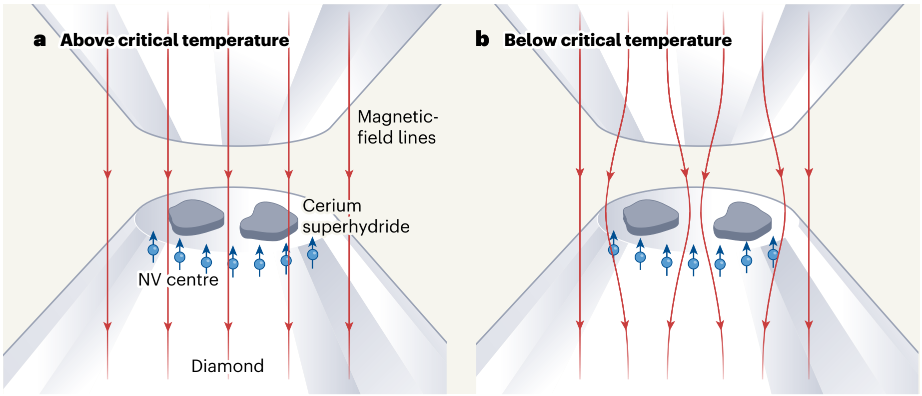

Figure 1 | A test of superconductivity at high pressures. Bhattacharyya *et al.*[1] devised a way of testing the prediction that cerium superhydride shows superconductivity at high pressures below a critical temperature. They used a device called a diamond anvil cell, which comprises two diamonds that can generate extreme pressures by compressing a sample between their tips. Defects called nitrogen vacancy (NV) centres can be created in the diamond crystal structure, and the intrinsic angular momentum (arrows) of these defects makes them sensitive to changes in magnetic fields. **a**, Above the critical temperature, cerium superhydride does not alter the external magnetic field. **b**, The authors showed that, below the critical temperature, cerium superhydride repels magnetic fields — a clear sign of superconductivity.

allows for high-frequency phonons and strong electron–phonon coupling[6]. Yet it is challenging to confirm this prediction in experiments owing to the ultra-high pressures needed to form this phase of hydrogen.

In the past two decades, focus has shifted to hydrogen-rich systems, for which a comparably lower pressure is required[7,8]. For example, in 2015, sulfur hydride was synthesized with a relatively high critical temperature of 203 kelvin, moving it squarely into the superconductivity spotlight[9]. However, the pressures required to confirm superconductivity in these systems are still high, and this can lead to results with poor sensitivity and huge uncertainty, creating intense debate about the veracity of claims. Some hydride systems also contain elements that prevent them from having zero resistance, so evidence of the Meissner effect is increasingly being regarded as crucial for proving that a hydride is indeed a superconductor.

However, such evidence is hard to come by because it is difficult to sense magnetic fields in a robust way at the pressures above which these materials are expected to superconduct. Remarkably, this obstacle can be overcome by leveraging a feature of the very device that is used to generate these extreme pressures: the diamond anvil cell (Fig. 1). This cell comprises two diamonds with hard, polished tips that can compress a sample to pressures of hundreds of gigapascals (GPa; one million times atmospheric pressure). These diamonds can be modified to include a point defect known as a nitrogen vacancy (NV) centre, which consists of a vacancy in the lattice and a nearby nitrogen impurity. This combination makes the quantum energy levels of the NV centre particularly sensitive to changes in magnetic fields.

NV centres were first used as high-pressure magnetic sensors in 2019 (refs 10–12), and they were also used to probe Meissner effects in materials under pressures of up to 7 GPa (refs 11,12). However, superconductivity in hydride systems is expected to occur at pressures of more than 100 GPa, which poses several experimental challenges. Perhaps the most pressing issue is that, under high pressure, mechanical stress causes the field sensitivity of the NV centres to deteriorate, so that the way in which superconductivity changes magnetic fields might not be detected.

Bhattacharyya *et al.* overcame this problem by cutting the diamond in a way that protected the NV centres along one axis of the crystal lattice, while suppressing the effect of NV centres along other axes. This technique heightened the sensitivity of the device and provided submicrometre-scale resolution, even above 100 GPa, a feat that has also been achieved by others using a similar approach[13]. The authors were able to track electric current (and therefore resistance) and sense magnetic fields simultaneously by embedding measurement devices in the same cell.

"The quest continues for a material that superconducts at close to room temperature."

Using this method, Bhattacharyya *et al.* first showed that their NV centres could sense magnetic fields at up to 140 GPa. They then measured the magnetic field at different positions in a cerium superhydride sample, and showed that the results were consistent with behaviour characteristic of the Meissner effect: the sample repels magnetic fields. The authors' data are strongly supported by their simultaneous measurements of almost-zero resistance in the same hydride. These findings settle a long debate by showing that cerium superhydride displays superconductivity at a critical temperature of 91 kelvin and pressure of 137 GPa, which can be achieved by cooling with liquid nitrogen.

Bhattacharyya and colleagues' NV sensing scheme can immediately be extended to further studies of this system, as well as to investigations of other materials. There is room for improvement through a better understanding of why superhydride synthesis results in samples that are small and inhomogeneous. A technique called wide-field imaging could contribute to this endeavour by shedding light on the reactions involved in the synthesis. This information could, in turn, be helpful in elucidating details of the superconducting phase.

The magnetic-field measurements could also enable estimation of the fundamental length scales associated with the Meissner effect in superhydrides, which could help to verify that the behaviour of cerium superhydride is consistent with the theory of conventional superconductors. Future research using the technique of Bhattacharyya and colleagues could well revolutionize our understanding of high-temperature superconductivity. In the short term, their findings allow superconductivity researchers to move forwards after a period marked by retractions and uncertainty.

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