channels are validated drug targets for conditions ranging from high blood pressure to anxiety and epilepsy. However, rational drug design has been difficult until recently because of a lack of structures in different conformations, and because researchers typically want to target one of several similar channels[19]. Thanks to high-resolution structures, it's now possible to assign functional states to different channel conformations. As a result, drugs can be designed to target specific channels in specific states, at particular interfaces between channels and accessory subunits. Structure-based virtual and experimental drug screening and design are now in full swing.

Looking ahead, it will be exciting to follow developments in our understanding of how ion channels assemble into large supramolecular complexes, and how they interact with membranes to modulate diverse forms of signalling. In particular, visualizing how ion channels associate or segregate along neuronal projections, and at nodes of Ranvier (gaps in neurons' insulating sheaths) should yield unprecedented insights into the propagation of nerve impulses in the brain.

It is awe-inspiring to see what a lasting influence the cloning of *Shaker* has had. The Jan and Tanouye groups' crucial decision to share their precious *Shaker* clones has left a decades-long legacy of scientific achievements.

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Materials chemistry

Suspended pores boost gas solubility in water

Margarida Costa Gomes

Porous solids have been dispersed in water to produce suspensions that can carry much more oxygen than blood can. Such 'porous water' opens the way to water-based formulations for biomedical use. **See p.712**

All gases interact, to some extent, with water. Nevertheless, with the exception of reactive gases, their concentration in water is low — often much lower than in organic solvents. If the concentration of aqueous solutions of gases could be increased, this would greatly improve the sustainability of many chemical processes and energy-storage strategies. Most notably, developing the ability to dissolve large amounts of gases such as oxygen or carbon dioxide in aqueous solution would be a major advance for biomedical applications. On page 712, Erdosy *et al.*[1] report a way of creating permanent pores in water, thereby substantially increasing its capacity to dissolve gases.

The dissolution of a gas in water can be regarded conceptually as a two-step process. The first conceptual step is the formation of a cavity in liquid water large enough to accommodate a gas molecule that could then be dissolved in the second step. The effort needed to form a cavity depends only on the structure and molecular interactions of pure liquid water, whereas the accommodation of a gas molecule in a cavity depends both on the interactions between the gas and the water, and on the way in which water molecules become arranged around the gas molecule. If the thermodynamic benefit of bringing the gas molecule into the cavity is lower than the effort required to form a cavity, then the dissolution is not favourable and the solubility of the gas is low; this is the case for non-reactive gases in water. Erdosy *et al.* set out to increase the capacity of water to dissolve gases by introducing permanent cavities into the liquid.

Liquids that contain permanent cavities constitute a new family of materials known as porous liquids. Such liquids share the ability of porous solids to absorb large amounts of gases, but have several advantages for continuous applications: they can be pumped around as a fluid; and their pores are more easily accessible, which aids the absorption of large quantities of solutes and their subsequent removal from the pores. Porous liquids were proposed[2] in 2007 and were first prepared[3] in 2015. They can be made of molecules that have permanent and stable internal cavities and that do not interpenetrate. However, the

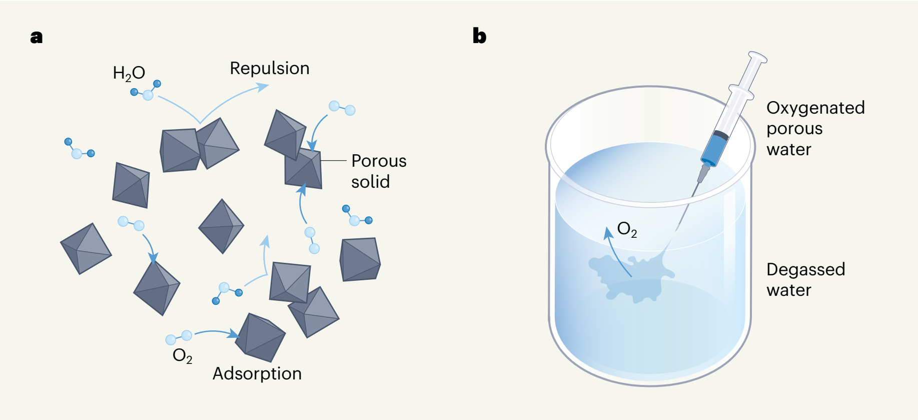

Figure 1 | Porous water. a, Erdosy *et al.*[1] suspended particles of porous solids in water. The pores in the solids repel water molecules, which therefore are not adsorbed by the particles. By contrast, oxygen molecules dissolved in the water rapidly occupy the empty pores. The resulting suspension can thus absorb much more oxygen than can pure water. **b**, When the oxygenated suspensions are injected into water that contains no dissolved gases (degassed water), the oxygen molecules spontaneously exit the particles, entering the water.

synthesis of such 'cage' molecules is challenging, and the resulting compounds can turn out to be solids, or liquids that are too viscous for most applications.

Another way to produce porous liquids is to dissolve cage molecules in solvents that consist of bulky molecules (or in ionic liquids that consist of bulky ion pairs), so that the solvent cannot enter the cages[3]. Taking this idea further, porous liquids have also been prepared by dispersing porous solids in liquids whose molecules are too large to enter the pores[4]. This strategy has opened up countless opportunities for preparing porous fluids based on ionic liquids[5] and other organic solvents that have bulky molecules[6], with potential applications in any area that uses liquid solvents. The design of a porous liquid therefore comes down to choosing a porous solid and an appropriate bulky liquid – the choices made determine the properties of the final material.

However, this strategy cannot be used to prepare porous water, because almost all the cavities in porous solids are large enough to accommodate water molecules. Erdosy *et al.* therefore used a different approach. They were inspired by biomolecules with cavities that are big enough to host water, but which remain empty because hydrophobic groups in the pores repel water molecules. The authors decided to disperse hydrophobic porous solids in water to form stable dispersions (colloidal suspensions) that act as porous liquids. Their hypothesis was that the low affinity of water molecules for the pores would be sufficient to maintain voids in the aqueous suspension (Fig. 1).

Erdosy and colleagues did indeed obtain stable suspensions using uniformly sized nanocrystals of a hydrophobic porous solid known as silicalite-1 (a member of the zeolite family of porous solids, which are widely used in industrial applications). The authors also obtained stable colloidal suspensions using ZIF-8 and ZIF-67 – which belong to a group of porous solids known as zeolitic imidazolate frameworks (ZIFs). The ZIF compounds required their external surfaces to be modified by the non-covalent association of water-soluble proteins, or by the covalent attachment of small organic ligand molecules, to stabilize the suspensions.

The authors found that their colloids have a lower density than that of pure liquid water, indicating that the pores in the solids do not fill with water molecules in the aqueous suspensions. Further proof of this was obtained from molecular simulations, which showed that water molecules forced into the pores are spontaneously expelled. Moreover, the simulations showed that oxygen is rapidly adsorbed from aqueous solution by the suspended porous solids.

Erdosy *et al.* report that oxygen can be reversibly adsorbed by porous water prepared using only 4.0% by volume of silicalite-1 nanocrystals (90 nanometres in size), reaching oxygen levels higher than that of blood. When the concentration of porous solid is increased to 12.7% by volume, the oxygen-carrying capacity increases to values similar to the density of pure oxygen gas. The porosity of the suspensions could be increased still further using the hydrophobic zeolite ZSM-5. This forms stable colloids at concentrations as high as 40% by volume – and has an extremely high oxygen-carrying capacity that, to the best of the authors' knowledge, far exceeds the capacity of any other aqueous oxygen carriers.

> **"The pores in the solids do not fill with water molecules in the aqueous suspensions."**

Not all porous aqueous fluids could be used for sustainable applications that require high gas concentrations. Many factors, other than gas capacities, have to be taken into account when designing porous water for a given application. For example, the stability of the suspensions could affect their use in energy storage devices, and the toxicity of the porous solids needs to be considered in medical oxygenating fluids. But given that myriad solids with hydrophobic pores could be designed to be biocompatible and sustainable, I am confident that stable aqueous colloidal suspensions will be used to considerably improve any technology that requires large concentrations of gases in water.

Porous water could, in principle, be used in blood substitutes, and to replace polluting organic solvents that have high gas capacities in the high-throughput synthesis of chemicals, in gas separations and in the capture and use of CO_2. It could also help to lower the energy demands of many chemical processes, because it would enable high gas concentrations to be attained in water under ambient conditions. It seems that porous water is here to stay.

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Metabolism

Long-sought mediator of vitamin K recycling

Nathan P. Ward & Gina M. DeNicola

The identity of the enzyme that enables vitamin K to combat the adverse side effects of a drug called warfarin has been long sought. Analysis of a type of cell death called ferroptosis has now unexpectedly solved the mystery. **See p.778**

Vitamin K was discovered by the biochemist Henrik Dam in 1936, and named after its role in promoting blood clotting, or *koagulation*, in Dam's native Danish[1]. The vitamin is a type of molecule called a naphthoquinone. It can exist in multiple forms, but only one supports clotting – the 'reduced hydroquinone' form, known as VKH2. Levels of VKH2 are maintained in the body by the enzyme vitamin K epoxide reductase (VKOR), which is part of the major (canonical) vitamin K recycling pathway. On page 778, Mishima *et al.*[2] pin down the identity of a different reductase enzyme that has a role in another crucial vitamin K recycling pathway.

When blood clotting needs to be treated – for example, in response to a stroke – the anticoagulant warfarin is used to inhibit VKOR, thus lowering levels of clot-promoting VKH2 in the blood (Fig. 1a). Although effective, warfarin therapy can easily lead to warfarin poisoning[3], in which life-threatening bleeding arises owing to a lack of clotting. The standard clinical treatment for warfarin poisoning is administration of a high dose of vitamin K, which is reduced to VKH2 by a warfarin-resistant reductase, thereby enabling clotting[3]. Until now, the identity of this 'non-canonical' reductase has been unknown.

The group that performed the current study was already familiar with one candidate reductase, the enzyme FSP1. The researchers had previously shown FSP1 to be a suppressor