6. Schramm, A. C. *et al. Biophys. J.* **112**, 2624–2633 (2017).
7. Chou, S. Z. & Pollard, T. D. *Proc. Natl Acad. Sci. USA* **116**, 4265–4274 (2019).
8. Zhong, E. D., Bepler, T., Berger, B. & Davis, J. H. *Nature Methods* **18**, 176–185 (2021).
9. Zivanov, J. *et al. eLife* **7**, e42166 (2018).
10. Punjani, A., Rubinstein, J. L., Fleet, D. J. & Brubaker, M. A. *Nature Methods* **14**, 290–296 (2017).
11. Zimmermann, D., Santos, A., Kovar, D. R. & Rock, R. S. *Curr. Biol.* **25**, 2057–2062 (2015).
12. Gomez, D., Peña Ccoa, W. J., Singh, Y., Rojas, E. & Hocky, G. M. *J. Phys. Chem. B* **125**, 12115–12124 (2021).
13. Giraldo-Barreto, J. *et al. Sci. Rep.* **11**, 13657 (2021).

The authors declare no competing interests.

Materials chemistry

A molecular flip-flop for separating heavy water

Thomas Heine & Randall Q. Snurr

Molecules of heavy water contain the deuterium isotope of hydrogen and have been impossible to separate from ordinary water. Nanoporous materials with flexible apertures in their structures point the way to a solution. **See p.289**

Isotopes are atoms that have the same atomic number but different numbers of neutrons in their nuclei. For example, protium (H) and deuterium (D) are isotopes of hydrogen that have 0 and 1 neutrons, respectively. Water molecules that contain deuterium atoms instead of protium atoms are known as heavy water. The physical properties of heavy water differ only slightly from those of ordinary water, which makes it extremely difficult to separate D_2O from H_2O. On page 289, Su *et al.*[1] report two nanoporous materials that take up H_2O in preference to D_2O – a property that can be used to separate these highly similar molecules.

Deuterium was discovered by the physical chemist Harold Urey in 1931, after which heavy water quickly became an essential material for nuclear research. Indeed, during the Second World War, the Allies sabotaged and eventually destroyed the first sizeable facility for producing heavy water after it was seized by German troops, to slow down the German development of nuclear weapons[2]. Today, besides its applications in the nuclear industry, heavy water is used in isotopic labelling techniques (such as those used to work out chemical-reaction mechanisms) and as a source of deuterium for making advanced drug candidates[3] (see also go.nature.com/3gwsvbz).

An obstacle for any direct separation of heavy water from ordinary water, apart from the similar physico-chemical properties of these compounds, is that D_2O quickly transforms into HDO when mixed with H_2O, owing to rapid exchange of hydrogen atoms between molecules. This is a problem because HDO is even more similar to H_2O than is D_2O.

Methods for producing heavy water therefore often involve separations of other small molecules that contain different hydrogen isotopes. The state-of-the-art techniques for D_2O production are the Girdler sulfide process[4], which involves the exchange of hydrogen isotopes between water and hydrogen sulfide (H_2S); and the oxidation of D_2 that has been separated by cryogenic distillation from a liquefied mixture of isotopic analogues of dihydrogen (H_2, HD and D_2). But these separation procedures suffer from low selectivity and have high energy demands.

Nanotechnology offers options that go beyond these conventional approaches. In 1995, it was suggested[5] that quantum effects at about 77 kelvin (the boiling temperature of liquid nitrogen at ambient pressure) would allow heavier D_2 molecules to diffuse more easily through subnanometre-scale pores than can lighter H_2 molecules. Various porous materials have since been shown[6] to effect such 'quantum sieving', including compounds known as metal–organic frameworks (MOFs; also called porous coordination polymers). An extension of this separation strategy, called chemical-affinity quantum sieving, has also been reported[6], in which D_2 is adsorbed by porous materials preferentially to H_2. A breakthrough[7] in this area, reported this year, is a process involving the selective pore opening of a flexible MOF. This material remains in a stable, closed-pore form when exposed to H_2, but adopts an open-pore structure in the presence of D_2.

A method has also been developed for separating mixtures of protons (H^+ ions) and deuterons (D^+ ions). This is achieved by electrochemically pumping these ions through 2D crystals[8] – the separation occurs as a result of selective diffusion of the protons through the crystals[9]. It has also been reported[10] that deuterons, rather than protons, can be selectively transported between the sheets of atoms in layered materials, because the energetic barrier to entering the spaces between the sheets is lower for deuterons.

Su *et al.* report two new MOFs that selectively adsorb H_2O over D_2O (Fig. 1). The nanoporous crystalline structures of MOFs consist of organic molecules stitched together with strong bonds at metal nodes. Su and colleagues' MOFs both have copper nodes but have different organic linkers, and form molecule-sized cages connected by

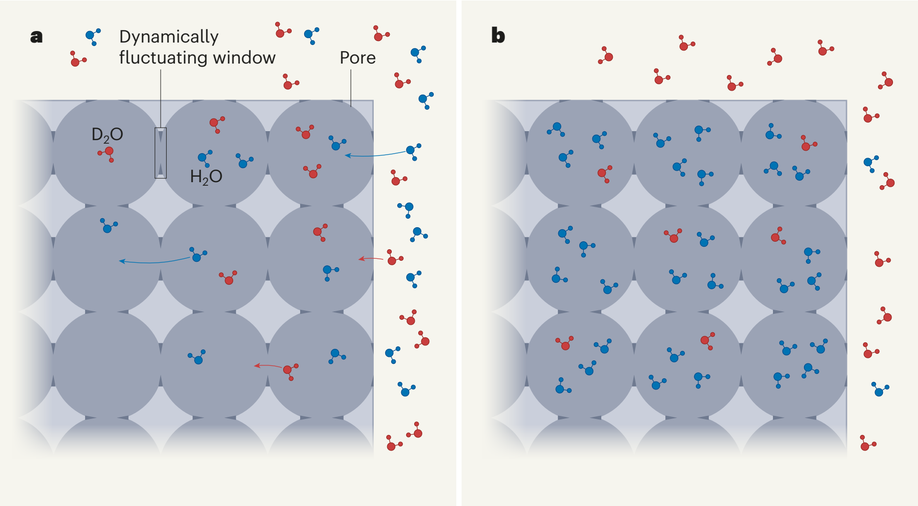

Figure 1 | A porous solid that selectively adsorbs one isotopic analogue of water. a, Su *et al.*[1] prepared a porous material whose cage-like molecular structure consists of pores connected by locally flexible windows. When immersed in a mixture of ordinary water and heavy water (the molecules of which contain deuterium, an isotope of hydrogen), dynamic fluctuations in the window sizes cause ordinary water to diffuse more rapidly through the material than does heavy water (indicated by longer arrows). **b**, After seven days, the difference in diffusion rates causes the liquid trapped in the pores to be enriched in ordinary water, compared with the original composition. This might lead to the development of methods for separating heavy water from ordinary water, for use in applications such as some in the nuclear industry.

triangular windows. The windows in the two materials have similar diameters (2.2 and 2.0 ångströms), both of which are narrower than the kinetic diameter of water (a measure of the size of water molecules, which is 2.65 Å). The materials do not undergo major structural changes, as some MOFs do, but have some flexibility, especially around the windows. In Su and colleagues' words, they are "globally robust but locally flexible".

The authors show that the two MOFs adsorb H_2O and D_2O at different rates. For example, one of the materials takes 2.5 times longer to adsorb the same amount of D_2O as H_2O. Importantly for potential applications, these differences were observed at room temperature.

Su *et al.* went on to show that the MOFs selectively adsorb H_2O from a mixture of H_2O, HDO and D_2O. When one of the MOFs was immersed for seven days in a mixture in which the ratio of H_2O:HDO:D_2O was 49.3:41.4:9.3, the liquid adsorbed by the material was enriched in H_2O, producing a composition of 69.6:27.8:2.6. It should be noted that these co-adsorption experiments were static – the MOF was simply left to stand in the liquid mixture. Dynamic co-adsorption experiments in which the liquid mixture is passed through a column of the MOF under pressure would also be helpful in showing whether the reported selectivity can be exploited for practical separations.

The authors suggest that the observed faster adsorption of H_2O is due to the local dynamics of the MOFs, which produce a 'flip-flopping' motion that causes differences in the rates at which the isotopic analogues of water molecules hop through the narrow windows. The authors characterize their materials with a variety of techniques and using quantum chemical modelling in support of their proposal, but the precise mechanism remains elusive. Water molecules are too heavy for quantum tunnelling – a phenomenon of quantum mechanics in which tiny objects have a certain probability of passing through barriers – to have a role, and quantum sieving is unlikely because D_2O would be expected to diffuse more easily than H_2O. Further investigations to better explain the current observations are a fascinating area for future research.

This work opens up a new strategy for separating heavy water from ordinary water, and potentially for separations of other small molecules. For example, it might pave the way to an efficient method for removing tritiated water (T_2O; T is the hydrogen isotope tritium), a radioactive and toxic by-product of the nuclear industry, from wastewater streams. Extension of this concept to other separations will require a better fundamental understanding of the mechanism that produces selective diffusion of H_2O, so that the relevant pore characteristics can be customized to capture other molecules. For now, the work clearly demonstrates that MOFs and related materials with narrow, locally flexible pores are intriguing materials for advanced, energy-efficient separations.

Thomas Heine is in the Faculty of Chemistry and Food Chemistry, Technical University of Dresden, 01062 Dresden, Germany.
Randall Q. Snurr is in the Department of Chemical and Biological Engineering, Northwestern University, Evanston, Illinois 60208, USA.
e-mails: thomas.heine@tu-dresden.de; snurr@northwestern.edu

1. Su, Y. *et al. Nature* **611**, 289–294 (2022).
2. Dahl, P. F. *Heavy Water and the Wartime Race for Nuclear Energy* (Inst. Phys. Publishing, 1999).
3. DeWitt, S. H. & Maryanoff, B. E. *Biochemistry* **57**, 472–473 (2018).
4. Miller, A. *CNS Bull.* **22**, 18–24 (2001).
5. Beenakker, J. J. M., Borman, V. D. & Krylov, S. Y. *Chem. Phys. Lett.* **232**, 379–382 (1995).
6. Kim, J. Y., Oh, H. & Moon, H. R. *Adv. Mater.* **31**, 1805293 (2018).
7. Bondorf, L. *et al. Sci. Adv.* **8**, eabn7035 (2022).
8. Lozada-Hidalgo, M. *et al. Nature Commun.* **8**, 15215 (2017).
9. Lozada-Hidalgo, M. *et al. Science* **351**, 68–70 (2016).
10. Hu, S. *et al. Nature Nanotechnol.* **13**, 468–472 (2018).

R.Q.S. declares competing interests. See go.nature.com/3nbipn8 for details.