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NEWS & VIEWS

CONDENSED-MATTER PHYSICS

Great moments in disorder

Steven T. Bramwell

An array of nanomagnets has been designed to resemble the disordered magnetic state known as 'spin ice'. This could transform our understanding of disordered matter and, potentially, lead to new technologies.

How can we understand disordered states of matter such as liquids, glasses and disordered magnets? First, we must know how they are organized; second, we must know how that organization responds to changes in external constraints such as temperature, pressure or magnetic field. This knowledge is beyond our reach in most cases: disordered states are intrinsically complicated and do not reveal themselves clearly to experiment. But thankfully, there are exceptions. One of them is a magnetic state known as spin ice in which the magnetic moments of ions — their 'spins', in analogy to the property of electron spin — remain disordered even at low temperatures, revealing much about the basic physics of disorder.

On page 303 of this issue, Schiffer and colleagues (Wang *et al.*)[1] report the creation of spin-ice behaviour in an array of nanoscale magnets. Such 'artificial' spin ice, which is stable at room temperature and possesses magnetic moments large enough to be observed directly, offers a new approach to understanding and exploiting the properties of disordered systems.

In conventional spin ice[2,3], magnetic ions form a network of linked tetrahedra (for example, ions of the lanthanide element holmium in the compound holmium titanate). The spins of these ions point either in or out of the tetrahedra (Fig. 1a). The dipolar interaction with their neighbours' magnetic fields favours an in–out arrangement of neighbouring moments, but not all pairs of neighbours can be satisfied simultaneously: the system is 'frustrated'. The best compromise — two moments pointing in, two pointing out, in any one tetrahedron — constitutes the local organizing principle. The same rule controls the hydrogen structure of ice[4] (Fig. 1b), and is fully satisfied by a huge number of equivalent arrangements of spins (or hydrogen atoms). This means that the chance of achieving an ordered structure is effectively nil. So spin ice, just like normal ice, remains disordered, with a non-zero entropy (a key measure of disorder) as its temperature approaches absolute zero.

Schiffer and colleagues' artificial spin ice[1] consists of a two-dimensional array of 80,000 elongated magnetic islands, each a few hundred nanometres long. The magnetic moment of every island is aligned parallel to its long axis, as in a bar magnet, and is coupled to its neighbours by the ubiquitous dipolar interaction. For a square geometry, the two in, two out rule is approximately satisfied ('square ice'[5], Fig. 1c). But because the magnetic moments involved are about three million times bigger than those of holmium ions, they interact more strongly and have less tendency to flip. The artificial spin-ice state is therefore stable at room temperature; for conventional spin ice, this is only the case at temperatures below 1 kelvin. Schiffer and colleagues encouraged their system to settle into a minimum energy state by cycling the applied magnetic field, and

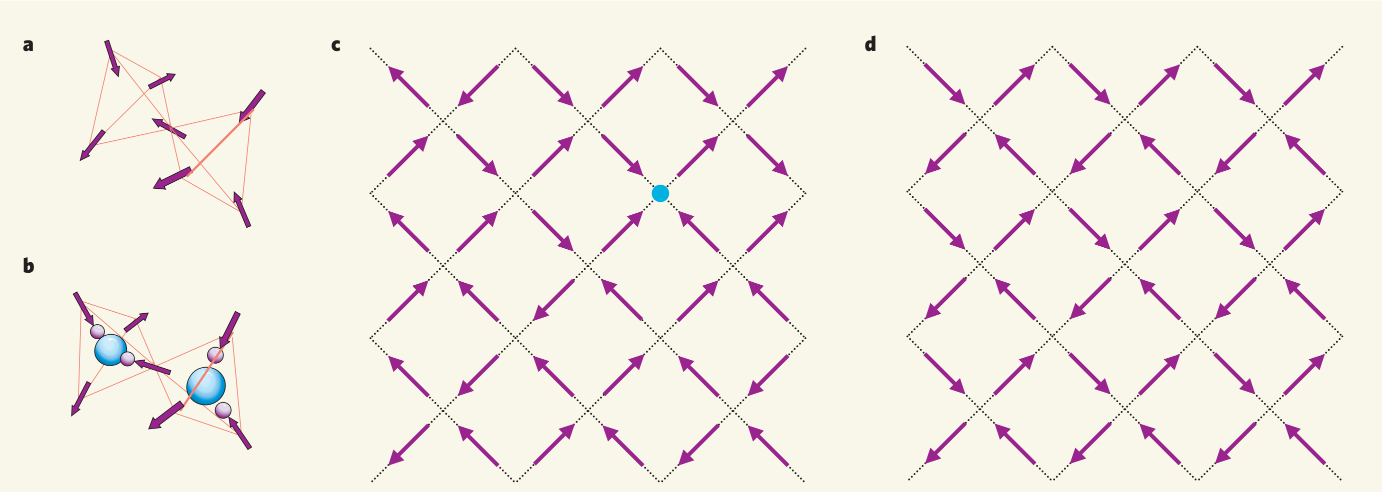

Figure 1 | Organized disorder. **a**, Part of the disordered arrangement of ionic magnetic moments (spins) in spin ice, holmium titanate ($Ho_2Ti_2O_7$): a network of linked tetrahedra with two spins in, two spins out per tetrahedron. **b**, Put a hydrogen atom on the end of every spin of spin ice, and you represent the low-temperature disordered hydrogen structure of (cubic) water ice, H_2O: each hydrogen atom lies on the line connecting two neighbouring oxygen atoms, but is shifted away from the mid-point of that line to ensure that the whole structure is a hydrogen-bonded network of v-shaped water molecules (oxygen atoms, large circles; hydrogen atoms, small circles). **c**, Here arrows represent the magnetic moments of nanoscale magnetic islands in the disordered state of the artificial 'square' spin ice created by Wang *et al.*[1]. Each corner has two arrows pointing in, and two pointing out, but within this constraint the direction of the arrows on any one corner is arbitrary: the two in, two out condition is not sufficient to define an ordered state. The blue circle marks a defect where the two in, two out configuration is not maintained. **d**, An ordered pattern in which the arrows of alternate squares have the same configuration. This is possibly the true minimum energy state of artificial spin ice.

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then determined the directions of individual magnetic moments using a technique known as magnetic force microscopy. Statistical analysis of these directions confirmed that a spin-ice state, characterized by a preponderance of the two in, two out configuration, had indeed been created.

Conventional spin ice lends itself well to experimentation. Its disordered spin arrangements have been imaged by neutron scattering, and applying magnetic fields to it has revealed disordered phases that respond to neutron scattering and bulk measurements as if they consisted of stacks of independent chains or sheets — so as if they have only one or two dimensions, rather than three. Phase transitions that, like the liquid–liquid or liquid–gas transitions in more complex matter, involve no change in structural symmetry have also been observed[6]. In such 'symmetry-sustaining' transitions, what is ordered remains ordered, and what is disordered remains disordered.

But experiments on conventional spin ice raise interesting questions. First, what is the true origin of the two in, two out rule? The dipolar interaction between magnetic moments is long-range, so any explanation that considers only near neighbours must be incomplete. This question has largely been answered: remarkably, the standard model of spin ice predicts that the two in, two out rule emerges from the many-bodied dipolar interaction of some 10^{23} magnetic moments[7,8]. Second, is there a 'true' ordered ground state (Fig. 1d)? The question is also pertinent to normal ice[9], as such a minimum-energy state is required by the third law of thermodynamics, which states that entropy approaches zero as temperature tends to absolute zero. An ordered ground state is also predicted by the standard model of spin ice, but is not observed experimentally. Finally, what microscopic factors drive phase transitions in an applied magnetic field? This question, too, remains essentially open.

Artificial spin ice could, in principle, help to supply further insight into these problems. It could, for example, be engineered to have different, controllable interactions and then be subjected to temperature changes or magnetic fields to mimic the behaviour of conventional spin ice. Direct imaging with magnetic force microscopy could be used to identify and understand individual defects in the spin-ice state. Such defects (Fig. 1c) cannot be imaged by neutron scattering on conventional spin ice, but might be crucial in determining its properties.

Bringing spin ice to room temperature could also inspire technological applications. In magnetic-memory media, information is encoded into the magnetic moments of ferromagnetic grains. The drive to increase the density of memory bits in such media will mean smaller, more strongly magnetized elements that are more closely spaced[10]. This trend will amplify the dipolar interaction and its consequences[11]. Experiments with spin ice, however, show how to create a dense array of magnetic elements, which, although they interact, retain many states in which information could potentially be encoded.

This is for the future. As a replica of conventional spin ice, artificial spin ice is not perfect: the two in, two out configuration is maintained only approximately, and the system should actually prefer an alternative, ordered state[12] (Fig. 1d). Its failure to find this state might reflect the inefficiency of the energy-minimization protocol involving magnetic field cycling. Despite its limitations, however, Schiffer and colleagues' invention[1] does emphasize the potential of designed magnetic arrays, not only as model systems for the study of disorder, but also as the basis of technological applications. ■

Steven T. Bramwell is in the Department of Chemistry, University College London, 20 Gordon Street, London WC1H OAJ, UK, and the London Centre for Nanotechnology, 2–16 Torrington Place, London WC1E 7HN, UK.
e-mail: s.t.bramwell@ucl.ac.uk

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CANCER BIOLOGY

Signatures guide drug choice

Julian Downward

Cancer drugs are increasingly designed to target specific cell-signalling pathways. When, and in what combination, these drugs should be used might be judged by analysing the gene expression signature of the tumour.

Current approaches to the design of drugs against cancer assume that almost all tumours escape normal growth regulation by usurping a few of the dozen or so key cell-signalling pathways. However, pathways can be activated at different points, so it is not always easy to tell which signalling mechanism has been activated by looking for mutations in known cancer-associated genes (oncogenes, or tumour-suppressor genes). If the gene at the top of a signalling cascade is unaffected, for instance, one cannot assume that the pathway is not involved, as a factor further downstream might have been activated. It can thus be hard to predict the best treatment for a particular tumour. Two papers in this issue[1,2] address this problem in different ways, and provide a potential strategy for choosing the most effective combination of therapies based on the gene expression signature of a tumour.

Tumour cells seem to rely heavily on the continued activation of one or two pathways — a phenomenon termed oncogene addiction — whereas normal cells use a broader range of signals[3]. This, combined with the damage accrued through the reckless lifestyle of the cancer cell, provides an Achilles' heel that might be exploited therapeutically by targeting pathways activated by oncogenes such as RAS, SRC and MYC. The RAS pathway (Fig. 1), for example, can be activated in many different ways in tumours, including mutation of the RAS oncogene itself (seen in 40% of lung cancers) and of the BRAF oncogene, the next factor in the pathway (mutated in some 60% of melanomas)[4]. Thus, looking for evidence of an initiating mutation can make it hard to identify all tumours in which this pathway has been activated.

Equally, looking for a single downstream indicator of pathway activation, such as phosphorylation of the enzyme ERK (one of the final steps in the RAS pathway), can also be problematic. Negative feedback loops, such as the induction of phosphate-removing enzymes that target ERK, can attenuate the steady-state phosphorylation of ERK. In addition, branching of the pathway can mean that other targets might be more important in certain circumstances (Fig. 1).

One step in the RAS pathway that is being targeted by candidate drugs is MEK, an enzyme that is directly activated by BRAF, and that is thought to be responsible for much of the downstream signalling from RAS (Fig. 1). To see whether MEK inhibitors could be useful for treating all tumours with aberrant RAS signalling, Solit *et al.* (page 358)[1] tested human tumour cell lines carrying mutations in BRAF or RAS for sensitivity to these drugs. Cells bearing an activating BRAF mutation were extremely sensitive to MEK inhibitors, both *in vitro* and when transplanted into immunodeficient mice. By contrast, cells with an activating RAS mutation showed much lower and more variable sensitivity to these inhibitors.