

Condensed-matter physics

Vortices weave a tangled web

David R. Nelson

In high-temperature superconductors, quantized vortex filaments can be twisted up into a DNA-like double helix. An experiment is proposed to test how easily these vortex lines cut through each other.

in which the parasite lodges generates toxic, carbon-centred free radicals^{8,9}. Theoretically, these highly reactive molecules can modify key parasite proteins, disabling essential biological targets and killing the parasite. Using a technique known as spin-trapping, Vennerstrom and colleagues provide evidence that trioxolanes can indeed generate a carbon-centred free radical in a manner reminiscent of the artemisinins. There are several proposed protein targets for the noxious free radicals produced by artemisinin, one of which is an enzyme known as PfATP6 (ref. 10). Future studies should reveal whether OZ277 and its chemical siblings target the same proteins as the artemisinin derivatives.

The development of OZ277 is a flagship project for the Medicines for Malaria Venture^{11,12}. It is an excellent example of how a well-managed partnership between academia and major pharmaceutical companies can have a significant impact on antimalarial product research and development.

Basing the drug development process on a chemically unstable entity such as a secondary ozonide was a daring move. And the research that enabled ozonides to be redesigned, not only to increase the chemical and metabolic stability, but also to provide phenomenal antimalarial properties, is impressive. The subsequent tailoring of the 'ozonide' molecule to enhance its availability to the body was hugely successful — the new synthetic analogues are more potent and act for longer *in vivo* than artemether and artesunate by some margin. As such, when combined with a second antimalarial, this new class could offer the best solution to date for destroying drug-resistant malaria parasites. ■

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1. Winstanley, P. A., Ward, S. A. & Snow, R. W. *Microbes Infect.* **4**, 157–164 (2002).
2. Vennerstrom, J. L. *et al.* *Nature* **430**, 900–904 (2004).
3. Klayman, D. L. *Science* **228**, 1049–1055 (1985).
4. Borstnik, K., Paik, I. H., Shapiro, T. A. & Posner, G. H. *Int. J. Parasitol.* **32**, 1661–1667 (2002).
5. O'Neill, P. M. & Posner, G. H. *J. Medicin. Chem.* **47**, 2945–2964 (2004).
6. Vroman, J. A., Alvim-Gaston, M. & Avery, M. A. *Curr. Pharm. Design* **5**, 101–138 (1999).
7. Haynes, R. K. *Curr. Opin. Infect. Dis.* **14**, 719–726 (2001).
8. Posner, G. H. & Oh, C. H. *J. Am. Chem. Soc.* **114**, 8328–8329 (1992).
9. Wu, Y. K. *Acc. Chem. Res.* **35**, 255–259 (2002).
10. Eckstein-Ludwig, U. *et al.* *Nature* **424**, 957–961 (2003).
11. Vennerstrom, J. L., Dong, Y., Chollet, J. & Matile, H. *US Patent* 6,486,199 (2002).
12. www.mmv.org/pages/page_main.htm

Nature Outlook: Malaria

More about the challenges posed by malaria appears in the collection of articles published as a *Nature Outlook* supplement, beginning on page 923 of this issue. The articles cover scientific, social and political problems, with the emphasis on Africa.

Inside a superconductor, electrical currents flow without resistance. Almost as remarkable as this electron flow without dissipation are the quantized, thread-like vortices of charge that swirl like miniature tornadoes around lines of magnetic field. Last year, Alexei Abrikosov shared the Nobel Prize in Physics for his brilliant 1957 prediction (made well before similar developments in high-energy theory and astrophysics) that, in a class of materials called 'type II' superconductors, a regular lattice of parallel vortex filaments, aligned with an external magnetic field, would form¹. In high-temperature copper-oxide superconductors, discovered 30 years later, Abrikosov's vortex lattice actually 'melts' over an appreciable range of magnetic field and temperature^{2,3}. Olson Reichhardt and Hastings⁴, writing in *Physical Review Letters*, now propose a key experiment that could unravel the physics of these vortices as they become entangled in the melted state.

A typical phase diagram for a high-temperature superconductor is shown in Fig. 1, overleaf, as a function of temperature and of the magnetic field induced in the material⁵. The Meissner phase of the diagram, in which surface currents completely exclude an applied magnetic field, follows the horizontal axis (where there is no magnetic induction in the superconductor) and terminates at the temperature at which the material ceases to be a superconductor — its transition temperature. According to Abrikosov's original theory, an applied magnetic field would penetrate the material as a regular lattice of quantized vortex filaments when the magnetic induction is greater than zero and below some critical field line (Fig. 1). But thermal fluctuations melt this lattice above the 'coexistence region' — where liquid and solid phases coexist at slightly different densities⁶.

What is this melted liquid of fluctuating, randomly braided vortex filaments like? An important property is its shear viscosity, which determines the ease with which point-like, linear or planar defects can pin the vortices in place. These defects might be missing atoms (for example, oxygen vacancies), columnar damage tracks from heavy-ion radiation, or more extended objects such as grain boundaries or globules of a different atomic phase. The pinning of vortex lines, thereby immobilizing them relative to the host material, is crucial in many high-field

applications. Indeed, if vortices are allowed to move in response to an applied current (which exerts a force on them), their motion dissipates energy, and resistanceless flow in a magnetic field is impossible. A vortex crystal resists shear deformations, so that pinning the Abrikosov flux lattice is relatively easy, like tacking a carpet to a slippery floor. However, pinning the melted lattice in a vortex liquid is much more difficult — this requires a high viscosity, similar to the property that allows us (temporarily, at least) to nail a pancake of 'silly putty' to a wall. Silly putty is composed of long, tangled polymer chains, and it is tempting to think of a melted liquid of Abrikosov vortices (Fig. 1) as a related 'directed polymer melt' of entangled vortex filaments. Crucial to the high viscosity of real polymer melts, however, are large energy barriers to the polymer chains crossing each other.

Do vortices, which are singularities in the underlying superconducting order, behave as impenetrable lines, or do they cut freely through one another? The answer depends on field and temperature. The energy barriers against flux cutting are very small near the critical field line (Fig. 1), where quantized vortices first form. However, when nearly parallel vortex lines cross, the 'quantum of vorticity' effectively doubles. The quantum of vorticity is a universal combination of Planck's constant, the speed of light and the electron charge, and determines the strength of the swirling supercurrents around a vortex. Well below the critical field line, this doubling leads to a very large crossing energy. Two entangled vortices can always cut each other easily if the lines deform so as to cross each other at a large angle, but this is resisted by the line tension. Although there is some experimental evidence for a large viscosity in a vortex liquid, theoretical estimates of the ratio of the melting temperature and the crossing energy at that temperature vary widely^{6,7}.

Olson Reichhardt and Hastings⁴ propose an elegant way to probe that all-important vortex crossing energy, using a magnetic force microscope (MFM). An MFM is similar to an atomic force microscope, except that it has a magnetized tip that pulls on the end of an individual vortex line⁸. It should be possible to pin the entry points of two vortex lines in place, and then use the MFM to wind one vortex around another into a double helix (Fig. 1). If the energy barriers to

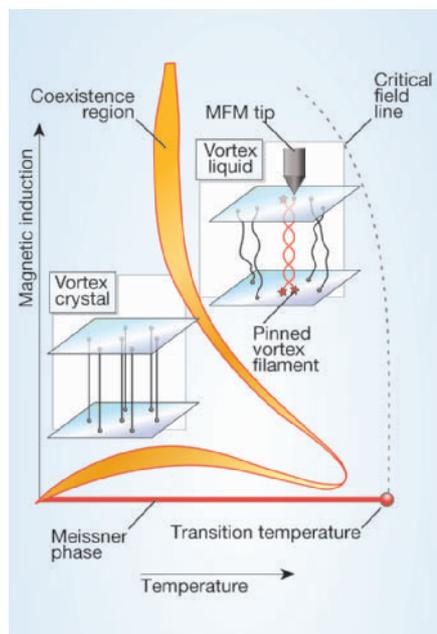


Figure 1 Equilibrium phase diagram for a high-temperature superconductor. The axes represent temperature and the induced magnetic field in the superconductor. For zero magnetic induction, the superconductor is in the Meissner phase up to its transition temperature. But when there is magnetic induction, vortex filaments appear in the material, represented here as lines around which supercurrents swirl. Superconducting order, interrupted by vortex lines, exists below the critical field line. At low temperature and below the coexistence region (in which both liquid and solid phases are possible), the vortex lines form an ordered Abrikosov vortex lattice; at higher temperatures above the coexistence region, the lattice melts to become an entangled vortex liquid. Olson Reichhardt and Hastings⁴ propose that the vortices in this phase could be manipulated, even wound up into double helices, using a magnetic force microscope (MFM).

flux-cutting are large, the vortex pair will twist up like a rubber band attached to the propeller of an old-fashioned model airplane. Both the applied force and the net displacement of the vortex tip can be monitored and compared with theoretical predictions⁴. In practice, flux-cutting will eventually occur, causing a highly twisted pair to relax and thus limit the build-up of stored energy. The mechanical braiding of a vortex pair would create additional supercurrents; these would occur in a pattern resembling a compressed version of the field lines generated by a solenoidal, or barrel-like, electromagnet. By monitoring the twist and subsequent relaxation with an MFM, the dynamical cutting of vortex lines could be probed in some detail.

MFM experiments on vortex lines might seem reminiscent of recent experiments in biophysics⁹. Among the striking observations are that 'supercoiled' DNA, created through helix crossings, can undergo relax-

ation mediated by a remarkable enzyme called a topoisomerase¹⁰. Using an MFM to detach a vortex line from a columnar pin in the superconductor¹¹ would be like tearing apart the DNA double helix¹². Just as biophysics experiments on single molecules provide an alternative to the averaging over large numbers of molecules that characterizes traditional biochemistry, MFM experiments on individual vortices are an attractive alternative to macroscopic probes of vortex physics.

For instance, the abrupt freezing transition of the vortex liquid that occurs on cooling does not occur in copper-oxide superconductors if the magnetic field is high¹³. One explanation for this puzzling behaviour is that point pinning, resulting from intrinsic disorder such as oxygen vacancies in the material, produces a new, disordered 'vortex glass' ground state at low temperatures¹⁴. Alternatively, if flux-cutting barriers are high, the dense, tangled vortices may simply drop out of equilibrium when cooled and form a 'polymer glass' of high viscosity⁶. Careful macroscopic measurements on samples of different thickness might be

able to distinguish between these scenarios. However, if realized, the MFM experiment of Olson Reichhardt and Hastings could get right to the heart of the matter, by probing individual flux lines directly. ■

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- Tomlin, S. *Nature* **425**, 548 (2003).
- Safar, H. *et al.* *Phys. Rev. Lett.* **69**, 3370–3373 (1992).
- Zeldov, E. *et al.* *Nature* **375**, 373–377 (1995).
- Olson Reichhardt, C. J. & Hastings, M. B. *Phys. Rev. Lett.* **92**, 157002 (2004).
- Crabtree, C. W. & Nelson, D. R. *Physics Today* April, 38–45 (1997).
- Nelson, D. R. *Defects and Geometry in Condensed Matter Physics* Chs 7, 8 (Cambridge Univ. Press, 2002).
- Carraro, C. & Fisher, D. S. *Phys. Rev. B* **51**, 534–538 (1995).
- Wadas, S., Fritz, O., Hug, H. J. & Guentherodt, H.-J. *Z. Phys. B* **88**, 317–320 (1992).
- Bustamante, C., Bryant, Z. & Smither, S. B. *Nature* **421**, 423–427 (2003).
- Strick, T., Croquette, V. & Bensimon, D. *Nature* **404**, 901–904 (2000).
- Hatano, N. & Nelson, D. R. *Phys. Rev. B* **56**, 8651–8673 (1997).
- Essevaz-Roulet, B., Bockelmann, U. & Heslot, F. *Proc. Natl Acad. Sci. USA* **94**, 11935–11939 (1997).
- López, D. *et al.* *Phys. Rev. Lett.* **80**, 1070–1073 (1998).
- Fisher, D. S., Fisher, M. P. A. & Huse, D. *Phys. Rev. B* **43**, 130–159 (1991).

Cell division

Timing the machine

Bruce Bowerman

During cell division everything must happen at the right time, or errors occur. A common cellular control device, protein phosphorylation, is now shown to time the assembly of a key part of the division machinery.

Cells divide and thereby multiply. This fundamental process is central to the development and survival of all organisms, and mistakes in it are responsible for a plethora of human diseases, from Down's syndrome to cancer. Accordingly, cell division — also known as mitosis — has received much attention from biologists. This attention has led to the discovery and analysis of a cycle of events that influences key regulatory proteins¹, but the mechanisms by which these proteins in turn influence the machinery of mitosis are less well understood. Writing on page 908 of this issue, Mishima *et al.*² help to mitigate this disparity, describing direct links between cell-cycle regulators and the cell-division machinery.

The central machine in cell division is the bipolar mitotic spindle, an apparatus that partitions the duplicated genome of a mother cell equally into two daughter cells¹. The spindle is composed largely of microtubules — relatively rigid but highly dynamic tubes formed by the polymerization of tubulin proteins. Microtubules are nucleated by two microtubule-organizing centres (also called centrosomes in animal cells), one at each

spindle pole (Fig. 1). Spindle microtubules, in conjunction with associated proteins, capture and separate the duplicated genome, which comes in the form of long DNA molecules known as sister chromatids.

Spindle assembly begins during genome duplication, when the single centrosome that a cell inherits at birth also duplicates. The resulting two centrosomes migrate apart, grow, and nucleate more microtubules, which radiate out in all directions. The growing, or 'plus', ends of some microtubules capture pairs of sister chromatids, each sister at first remaining bound to its duplicate. Eventually, all sister chromatids are captured, with the two sisters in each pair connected to opposite poles. Subsequently, the protein-based glue between paired sisters is dissolved, and poleward forces move them apart — a stage of mitosis known as anaphase.

During anaphase a remarkable transition in spindle structure occurs. Many of the microtubules projecting from each pole do not capture chromatids, and some instead interdigitate, as their plus ends grow from opposite poles and pass each other. During anaphase, these 'antiparallel' microtubules