comes from Stevens *et al.*[1]. The authors loaded all the muscle cells in intact guinea pig bowel preparations with a fluorescent dye, to measure the internal concentration of Ca^{2+}. On a cellular scale they detected discrete Ca^{2+} waves, which spread through the longitudinal muscle layer. By tracking the sites of origin and spread of the internal Ca^{2+} waves, Stevens *et al.* could describe their behaviour. They found that Ca^{2+} waves in the longitudinal layer result from neuronal activity, because these waves can be suppressed by drugs that block the effects of neurally released excitatory transmitter. The waves spread readily along the axis of the colon, but poorly around the circumference. Such uneven, or anisotropic, conduction reflects the ease with which ionic currents spread along and across the cells that make up this longitudinal layer.

Stevens and colleagues also found that the firing of inhibitory nerves produces local barriers of inhibition, which limit the spread of the excitatory wave and allow an increase in the internal concentration of Ca^{2+}. This, in turn, triggers local contractions, which mix the contents of the gut. When this peristaltic reflex is activated, descending inhibitory waves abolish the discharge of Ca^{2+} waves, allowing the region to relax. After the period of inhibition, Ca^{2+} waves are again detected and the ensuing contraction moves the gut contents onward in an ordered way. So, the intrinsic nervous system acts not only to initiate localized movements, but also as a command system that oversees the movement of gut contents over longer distances.

An exciting aspect of Stevens and colleagues' work is that it brings together information obtained from a molecular approach with a more integrated physiological problem. Over the past decade there have been dazzling advances in our knowledge of membrane channels, intracellular messengers, control of the internal Ca^{2+} concentration and genetic profiles. But many of these advances have overlooked the fact that we often do not know what the elements involved do in the body. It will be very productive to apply the knowledge base from more reductionist approaches to physiological problems. One example is the use of gene manipulation to identify the role of the ICC in gastrointestinal motility[6]. Measuring changes in the internal concentration of Ca^{2+} during peristalsis is another step in this direction. ☐

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Mesoscopic vortex physics

From vortices to genomics

Terence Hwa

A basic property of superconductors, besides their lack of electrical resistance, is the ability to exclude magnetic fields from their interior so long as the applied field does not exceed a critical value H_c. In the case of type-II superconductors, which include the high-T_c materials, screening of external fields is only partial, with magnetic flux penetrating the interior in the form of vortex lines below a lower critical field H_{c1}. Previous research in this area has focused on the collective behaviour of large numbers of vortex lines. Now, on page 43 of this issue, Bolle *et al.*[1] report observations of the kinetics and thermodynamics of *individual* vortex lines threaded through a planar type-II superconductor. A series of fascinating discrete 'events' is observed close to the lower critical field H_{c1}, where a small number of vortex lines are present in the sample. The findings are comparable to 'mesoscopic' electronic systems (typically a micrometre or less in size), where interesting effects such as Coulomb blockade and universal conductance fluctuation occur when the quantization of electronic charge becomes important in a small volume.

The events observed by Bolle *et al.* are sharp responses to small changes in the ambient conditions, such as the applied field and temperature. Amazingly, the noisy-looking response curves are mostly reproducible (see their Fig. 2 on page 44). These intermittent, staircase-like curves depend on the details of the sample under study, and can be regarded as its fingerprint. The intermittent responses reflect an intricate balance of the different forces acting on the vortex lines: the attraction of the vortex lines to the material defects that are distributed randomly in the sample; a 'line tension', which aligns the average orientation of the vortex lines to the applied field; and the magnetic repulsion, which prevents different vortex lines from going to the same defects.

An underlying physical picture has emerged from detailed theoretical studies referred to by Bolle *et al.*: in equilibrium, the vortex lines find a special configuration of trajectories that minimizes the overall free energy for the specific arrangement of random defects in the sample. In such a minimal state, a small change in the ambient conditions is not likely to produce any significant response by the already-optimized vortex configuration. However, when the system is forced to change, for example when an extra vortex line is added, a major rearrangement of vortex trajectories takes place, leading to the intermittent, large responses observed in the experiment. This phenomenon can be thought of as the equilibrium analogue of avalanches studied in the context of self-organized criticality (for a review, see ref. 2).

Much of the above picture has been speculated qualitatively in one form or another in studies of the spin-glass model, which has been taken as a paradigm of disorder-dominated systems in the past 25 years[3]. However, it is only for vortex systems that quantitative theoretical studies have become possible. Such studies are performed in the context of a class of models known as 'directed polymers'. Figure 1 (overleaf) shows an example of a single directed polymer in a '1+1' dimensional random medium. The term '1+1' (as opposed to '2') is used to emphasize the fact that the directions *r* and *z* that span the embedding space of the polymer are not equivalent, as the polymer is oriented on average in the *z* direction. Theorists have also used the '2+1' dimensional model to describe a vortex line in a three-dimensional superconductor, and the '1+2' dimensional model to describe the interface separating two bulk phases of a three-dimensional ferromagnet.

The directed polymer in a '1+1' dimensional random medium is a rare case of a disorder-dominated system whose statistical properties can be solved in great detail analytically, far beyond the mean-field analysis to which most other systems (including the spin-glasses) are limited. Also, the thermodynamics of individual samples can be computed much more quickly using a transfer-matrix method, when compared with the exponentially long computational time needed for spin-glass-type problems. The combined analytical and numerical approach has yielded a great deal of information concerning the exotic properties of randomly pinned directed polymers. Many of these properties are believed to be generic to disorder-dominated systems. This development is analogous to how exact solutions of one-dimensional quantum systems have shaped our understanding of strongly correlated, many-body quantum systems in general.

Despite the theoretical progress made, experimental studies have been hampered by problems with probing the fluctuations of individual lines in a macroscopic sample. Bolle *et al.*[1] overcame this difficulty by

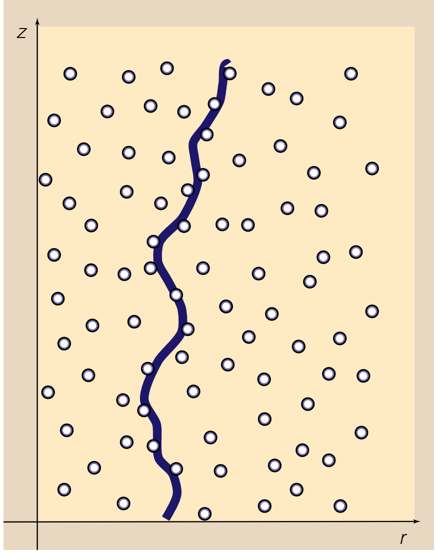

Figure 1 **A directed polymer (solid line) in a '1+1' dimensional random medium. The polymer dimensions are described as '1+1' (rather than the usual '2') because the *r* and *z* directions that span the embedding space of the polymer are not equivalent, as the polymer is oriented on average in the *z* direction. The circles represent random disorders that the directed polymer is attracted to. This model has been used to describe the behaviour of individual vortex lines in a planar superconductor, such as that studied in the experiment by Bolle *et al.*[1]. The directed polymer model has also been used in a variety of other contexts, ranging from non-Hermitian quantum mechanics to sequence matching in genomics.**

attaching a small sample (1.6-μm thick) to a novel micro-mechanical oscillator. The magnetic response of the system was obtained by monitoring small changes in the resonance frequency of the oscillator due to the few vortex lines trapped in the sample. Interaction of these few lines was then used to deduce the properties of a single line. This work is the first quantitative experimental study of this fundamental and fascinating problem of statistical physics. The results obtained are consistent with theoretical predictions, although more detailed experiments are still necessary to make point-to-point comparisons.

The special feature of the directed polymer problem that makes it analytically tractable is the transfer-matrix approach, which expresses the free energy of the polymer recursively in terms of the free energy of a shorter polymer. Huse *et al.*[4] observed that the 'evolution' of the free energy under successive application of the transfer matrix is equivalent to the dynamics of a randomly forced Burgers' equation, developed in the mid-1970s[5] in an attempt to understand the hydrodynamics of strongly driven fluids. Much of the knowledge of '1+1'-dimensional directed polymers is derived from exact results of the corresponding Burgers' equation.

The surprising connection between the directed polymer and the hydrodynamics of the Burgers' equation is just the beginning of a long list of problems the directed polymer is related to. Best known is the kinetic roughening of driven interfaces[6]. Other examples include the stick–slip motion between two sliding surfaces[7], the complex eigenvalue distribution in non-Hermitian quantum mechanics[8], and — perhaps most surprisingly — the relation[9] to a 'sequence-alignment' algorithm, which is routinely used by molecular biologists to search for homology between genes and proteins[10]. In fact, the sequence alignment problem was formulated as a minimal directed-path problem in the bioinformatics literature as early as 1970[11]. The transfer-matrix method was proposed back then as a means to find the optimal trajectory of the directed path on a special '1+1' dimensional lattice, with a 'random potential' derived from the composition of sequences being aligned. Today, special-purpose computers and chips have been constructed to satisfy the high demand for such transfer-matrix calculations.

The insight gained from understanding the statistical physics of the directed polymer has already led to very efficient ways of computing the statistical significance of alignment results[12], the lack of which has limited applications of these powerful tools. It is conceivable that the experimental investigation of mesoscopic vortex physics initiated by Bolle *et al.* may one day lead to ultra-fast physical devices capable of aligning a vast number of sequences in parallel. ☐

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Neurobiology

A spine to remember

Per Andersen

How can we remember some information for many years, even after only a short experience of it? On page 66 of this issue, Engert and Bonhoeffer[1] present evidence that when nerve cells receive an intense stream of impulses, they may form new structural and, perhaps, functional connections. Such new couplings may be the substrate for the long-term storage of information in the brain.

For about 100 years, neuroscientists have been guided by two proposals. The first, by Tanzi[2], states that the nervous substrate for learning and memory could be a "thickening of the nerve fibres". But Ramón y Cajal[3] postulated that this substrate is a strengthening of the connections — or even a building of new connections — between the nerve cells that are most actively engaged in the learning task. Although there is experimental support for these ideas, conclusive evidence has been extraordinarily difficult to find.

A popular cellular model to explain how nervous transmission may be enhanced is long-term potentiation (LTP). This phenomenon is thought to occur either after the synapses to a cell are activated by a train of high-frequency impulses[4], or by a situation in which the cell receives two simultaneous influences (activation of excitatory synapses, and an artificially reduced membrane potential, or depolarization), a pairing that is repeated a number of times[5]. Engert and Bonhoeffer[1] have now observed that new sites for communication between neurons — dendritic spines — emerge in a highly restricted part of the dendritic tree of hippocampal cells after LTP in the same region. Because these dendritic spines are the only known postsynaptic partners for the presynaptic boutons in excitatory hippocampal pathways[6], the findings indicate that new excitatory synapses are formed.

Engert and Bonhoeffer used an organotypic preparation, in which a thin slice of the hippocampus is cultured for several days, and many of the neurons and their connections are preserved. These cells can then be impaled and fluorescently labelled. A group of excitatory synapses on a small dendrite of each neuron was allowed to function inside a tiny sphere, 30 μm in diameter, by superfusion with a fluid similar to that normally found in the brain. The release of neurotransmitters from all other synapses, on this and surrounding cells, was blocked by a solution containing high levels of cadmium and a low concentration of calcium. Local synaptic activation was then paired with depolarizing pulses through an intracellular electrode,