

within an advancing cell sheet, Trepap and colleagues have analysed the radial expansion of cell colonies as a function of time. Surprisingly, they find that large traction forces are observed many cell rows behind the leading edge, suggesting a mechanical cooperation from cell to cell over large distances within the cell sheet. As their results indicate long-range force transmission, this finding will undoubtedly fuel debates in the field, especially on the question of the push or pull mechanism that could drive collective migration (Fig. 1b).

When thinking about cells moving as a cohesive tissue, an important issue is the extent to which mechanical stress propagates within multicellular cohorts to control migration behaviour. Various *in vivo* and *in vitro* situations^{7,8} suggest that extrinsic cues can drive the movement of tissues, not by acting directly on all members of the group, but rather by instructing smaller numbers of peripheral leader cells that in turn seem to be responsible for the guidance of naive followers. But it remains an open question whether the global motion is coordinated by 'leader' cells pulling on cells behind or by internal pressure due to cell division and proliferation that would expand cell sheets outwards. Additionally, other mechanisms could involve submarginal cells that extend 'cryptic' lamellipodia several rows behind the wound margin of epithelial cell monolayers and thus could collectively drive cell-sheet movement⁹.

The direct measurement of physical forces within advancing epithelial cell monolayers provides some evidence to discriminate between these various plausible mechanisms. First, mapping the traction forces in directions normal to and parallel to the front edge at different locations

underlines that large traction forces exerted by cells on the substrate are observed far away from the leading edge. Moreover, both traction distributions show non-Gaussian behaviours with exponential tails, independent of the distance from the edge. It further suggests that cells within the sheet share a common mechanical behaviour with a long-range force transmission. The idea of leader cells moving outwards, normal to the free boundary, 'dragging' passive followers behind them, is not sufficient to explain this complex mechanical process.

The propagation of physical forces depends on cell interactions not only with the substrate but also with neighbouring cells. This implies a 'tug of war' between both types of adhesion¹⁰. Physical signals from the substrates tend to induce a migration of cells away from each other, whereas a stronger mechanical input from cell-cell interactions would drive them towards each other. Thus the importance of cell-cell junctions in the force transmission requires a cell sheet to transmit physical forces in a cooperative way. Consistent with these arguments, Trepap *et al.*⁶ show that the average traction stress exerted by cells on the substrate in the direction perpendicular to the edge is not concentrated at the leading edge but decays slowly with the distance from the edge over several cell diameters, keeping values larger than zero. By applying Newton's third law at various distances from the leading edge of the cell sheet, they are able to use the mechanical force balance to calculate the accumulated stress within the cell sheet. They show that this stress transmitted through cell-cell junctions increases as a function of the distance from the edge. These combined findings clearly demonstrate that guidance within tissues is due to a cohesive

and coordinated movement, and that the growth of the epithelial cell sheet is induced by a global state of tensile stress (Fig. 1c). Interestingly, such a tensile stress rules out the possibility of the build-up of an internal pressure due to cell proliferation that would push neighbouring cells outwards.

A remaining question is how such a tensile state is modulated by external cues, such as the stiffness of the environment. As collective cell migration and traction forces are affected by substrate rigidity^{10,11}, one would expect to observe changes in the value of the tensile stress with the stiffness, providing important information about the reciprocal modulation of tension induced by cell-cell and cell-ECM adhesions. The study by Trepap *et al.* opens a promising possibility of testing the impact of mechanical stress on tissue remodelling and repair by dissecting the respective contributions of local and global forces. □

Benoit Ladoux is at the Laboratoire Matière et Systèmes Complexes (MSC), Université Paris Diderot, and CNRS, UMR 7057, Paris, France. e-mail: benoit.ladoux@univ-paris-diderot.fr

References

1. Thomson, D. A. W. *On Growth and Form* 2nd edn (Cambridge Univ. Press, 1942).
2. Vogel, V. & Sheetz, M. *Nature Rev. Mol. Cell Biol.* **7**, 265–275 (2006).
3. Lauffenburger, D. A. & Horwitz, A. F. *Cell* **84**, 359–369 (1996).
4. Munevar, S., Wang, Y.-L. & Dembo, M. *Biophys. J.* **80**, 1744–1757 (2001).
5. Friedl, P., Hegerfeldt, Y. & Tusch, M. *Int. J. Dev. Biol.* **48**, 441–449 (2004).
6. Trepap, X. *et al. Nature Phys.* **5**, 426–430 (2009).
7. Lecaudey, V. & Gilmour, D. *Curr. Opin. Cell Biol.* **18**, 102–107 (2006).
8. Poujade, M. *et al. Proc. Natl Acad. Sci. USA* **104**, 15988–15993 (2007).
9. Faroouqi, R. & Fenteany, G. *J. Cell. Sci.* **118**, 51–63 (2005).
10. De Rooij, J. *et al. J. Cell Biol.* **171**, 153–164 (2005).
11. Saez, A. *et al. Proc. Natl Acad. Sci. USA* **104**, 8281–8286 (2007).

TOPOLOGICAL INSULATORS

The next generation

Spin-orbit coupling in some materials leads to the formation of surface states that are topologically protected from scattering. Theory and experiments have found an important new family of such materials.

Joel Moore

Topological insulators are materials with a bulk insulating gap, exhibiting quantum-Hall-like behaviour in the absence of a magnetic field. Such systems are thought to provide an avenue for the realization of fault-tolerant quantum computing because they contain surface

states that are topologically protected against scattering by time-reversal symmetry. However, topological phases in condensed matter generally behave like 'hothouse flowers'; they are beautiful but fragile and, until now, were thought to be impossible to create without extremes of temperature and

magnetic field. This conventional wisdom may be overturned by a pair of papers in this issue^{1,2}, which show that a certain class of three-dimensional topological insulator material can have protected surface states and display other topological behaviour potentially up to room temperature without

magnetic fields. On page 398, Zahid Hasan and colleagues¹ report the observation of characteristic signatures of a topological insulator in the band structure of Bi_2Se_3 studied using angle-resolved photoemission spectroscopy (ARPES) and first-principles calculations. In contrast with previously studied materials, Bi_2Se_3 is shown to have a large bandgap and a single surface Dirac cone associated with the topologically protected state in the material. Concurrent theoretical work using electronic structure calculations, reported by Shou-Cheng Zhang and co-workers² on page 438, shows that Bi_2Se_3 is in fact only one of an emerging class of new large-bandgap topological insulators, providing a simple tight-binding model to capture their physical properties. These results pave the way for the experimental realization and potential application of robust topological phases in a variety of materials.

What makes topological insulators different from ordinary band insulators? In a topological insulator, spin-orbit coupling causes an insulating material to acquire protected edge or surface states that are similar in nature to edge states in the quantum Hall effect. For example, the three-dimensional topological insulator phase^{3,4} recently discovered in BiSb alloys⁵ has surface states that are predicted to remain metallic even under quite strong disorder, as long as no magnetic fields or magnetic impurities break the time-reversal symmetry that protects the phase. Such a surface state in a three-dimensional topological insulator is a higher-dimensional analogue of one-dimensional current-carrying edge states in the quantum spin Hall effect⁶. In its simplest form, it can be viewed as a Dirac fermion metal, similar to that in graphene but without the twofold valley and spin degeneracies (Fig. 1).

Although the phase observed in BiSb alloys is theoretically the same as the one now observed in Bi_2Se_3 , there are three crucial differences that suggest that Bi_2Se_3 may become the reference material for future experiments on this phase. First, access to the topologically protected surface state in BiSb is complicated by the presence of several other surface bands. In contrast, ARPES measurements and theory show that only a single surface state is present in Bi_2Se_3 , and that it has an electronic dispersion almost the same as an idealized Dirac cone (Fig. 1). Second, Bi_2Se_3 is stoichiometric — it is a pure compound rather than an alloy like $\text{Bi}_x\text{Sb}_{1-x}$ — and, hence, can in principle be prepared with higher purity and less disorder. This is important because although the topological insulator phase is predicted to be quite robust to disorder, many

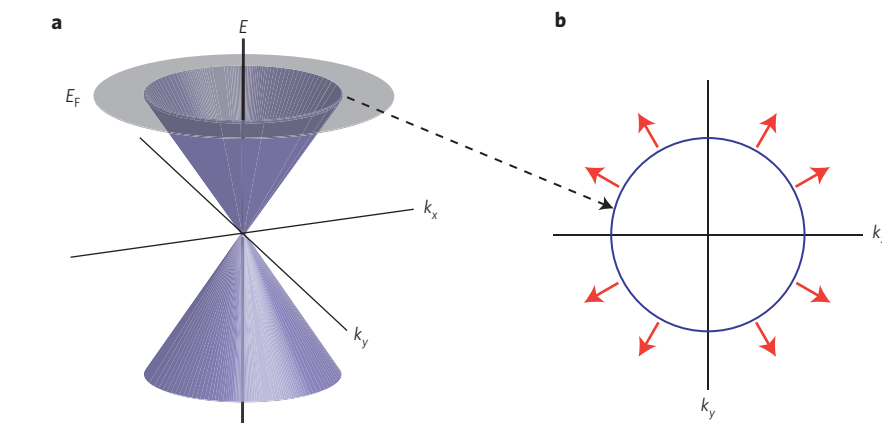


Figure 1 | ‘Light-like’ electrons, protected by time-reversal symmetry, in topological insulators. **a**, A simple model of the surface band structure of a topological insulator with a single Dirac cone. We note that the Fermi level (E_F) does not, in general, pass through the Dirac point. **b**, A distinguishing feature of the topological insulator surface is that there is a single electron spin state at each surface wavevector \mathbf{k} , and that states with opposite wavevector, $-\mathbf{k}$, have opposite spin ‘orientation’.

experimental probes of the phase, including ARPES measurements of the surface band structure, are clearer in high-purity samples. Third, and perhaps most important for applications, Bi_2Se_3 is found to have a large bandgap, of approximately 0.3 eV (equivalent to 3,600 K), which agrees well with theoretical estimates of this quantity.

In combination with the absence of impurity states in the gap, this large bandgap indicates that topological insulator behaviour may be seen at room temperature and greatly increases the potential for applications. To understand the probable impact of these new materials, an analogy can be drawn with the early days of high-temperature superconductivity in the copper oxides: the original cuprate superconductor, lanthanum barium copper oxide, was quickly superseded by second-generation materials such as yttrium barium copper oxide and bismuth strontium copper oxide for most scientific and applications-related purposes. For three-dimensional topological insulators, Bi_2Se_3 is likely to become part of such a second-generation class of material, superseding the first-generation BiSb. Another possible second-generation topological insulator is Bi_2Te_3 . One of the topological insulator materials discussed by Zhang and colleagues², Bi_2Te_3 is already well known to materials scientists working on thermoelectricity — it is a commonly used thermoelectric material in the crucial engineering regime near room temperature.

This second generation of topological insulators is likely to pave the way for a variety of experiments and potential applications. One class of proposed experiment is based on the observation that a weak time-reversal-breaking perturbation

applied to a topological insulator opens a surface bandgap. This results in a quantized magnetoelectric coupling (an applied electrical field induces a magnetic dipole and vice versa, with a proportionality constant of fixed magnitude) resulting from a quantum Hall effect carried by the surfaces⁷. Although some effects resulting from this magnetoelectric coupling — labelled ‘axion electrodynamics’ because of an analogous interaction between the proposed axion particle and electromagnetic fields — were discussed in the 1980s⁸, it was then not clearly understood how such effects may be realized in realistic materials. The improved understanding of magnetoelectric coupling that may result from experiments on topological insulators is also relevant to multiferroic materials, in which axion electrodynamics is a part of the full magnetoelectric response⁹. Consequently, the observation of such a quantized magnetoelectric coupling in the topological insulator is a high priority for experiments, as this emergent property would complement the microscopic band structure observed in photoemission¹.

An even more ambitious experimental direction enabled by these new materials is the study of how correlated-electron physics such as superconductivity is modified in a topological insulator. One particularly intriguing example is the prospect of creating local Majorana fermion excitations, which could be realized through the proximity effect between a topological insulator and an ordinary (fully gapped) superconductor¹⁰. A defining characteristic of a Majorana fermion is that it is its own antiparticle and therefore only has half as many degrees of freedom as a conventional

Dirac fermion such as the electron. So far, Majorana fermions have not been observed clearly in experiment, but it has been predicted that in some situations an electron may split into two Majorana fermions¹⁰, and that several interesting condensed-matter phases are believed to support them as emergent excitations. A direct observation of a Majorana fermion would be a key step on the path to quantum computation using topological phases.

There are important open problems for theory as well. The topological insulator phase can be defined at the single-electron level, manifesting excitations having the quantum numbers (spin and charge) of the

electron, similar to the integer quantum Hall effect. In contrast, the fractional quantum Hall effect is a topological phase displaying excitations with fractional charges and statistics. Our developing understanding of topological insulators may lead us to discover new 'fractionalized' phases of this sort. The two papers in this issue demonstrate that rapid experimental and theoretical progress in the research on topological insulators is both answering and raising fundamental questions pertaining to possible exotic phases of electrons in solids. □

Joel Moore is in the Department of Physics, University of California, and the Materials Sciences

Division, Lawrence Berkeley National Laboratory, Berkeley, California 94720, USA.

e-mail: jemoore@berkeley.edu

References

1. Xia, Y.-Q. *et al.* *Nature Phys.* **5**, 398–402 (2009).
2. Zhang, H. *et al.* *Nature Phys.* **5**, 438–442 (2009).
3. Fu, L., Kane, C. L. & Mele, E. J. *Phys. Rev. Lett.* **98**, 106803 (2007).
4. Moore, J. E. & Balents, L. *Phys. Rev. B* **75**, 121306 (2007).
5. Hsieh, D. *et al.* *Nature* **452**, 970–974 (2008).
6. König, M. *et al.* *Science* **318**, 766–770 (2007).
7. Qi, X.-L., Hughes, T. L. & Zhang, S.-C. *Phys. Rev. B* **78**, 195424 (2008).
8. Wilczek, F. *Phys. Rev. Lett.* **58**, 1799–1802 (1987).
9. Essin, A. M., Moore, J. E. & Vanderbilt, D. *Phys. Rev. Lett.* **102**, 146805 (2009).
10. Fu, L. & Kane, C. L. *Phys. Rev. Lett.* **100**, 096407 (2008).

NUCLEAR PHYSICS

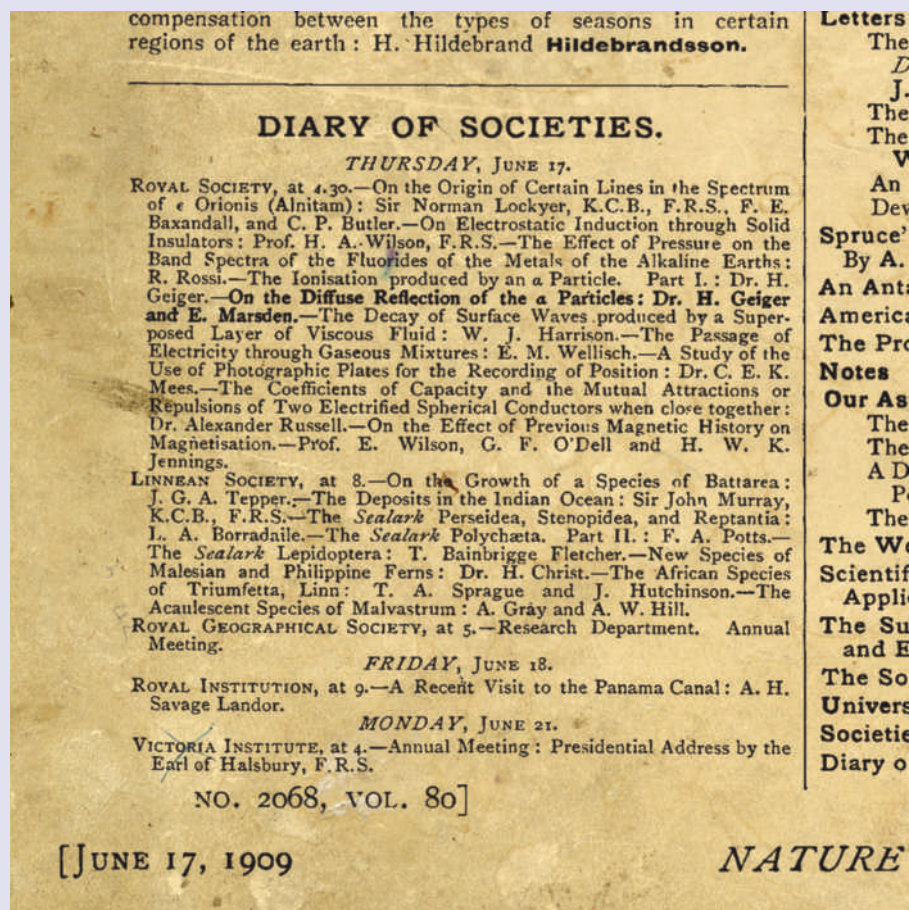
An afternoon's outing

Hidden in the yellowing pages of century-old issues of *Nature* are some scientific gems. They might be fully fledged 'Letters to the Editor', curiosities from 'Notes or nuggets from 'Our Astronomical Column'. Even the simple listings in 'Diary of Societies', at the end of each issue, can be fascinating — as is this entry (pictured) from the issue of 17 June 1909.

At the behest of their boss, Ernest Rutherford, at the University of Manchester, Hans Geiger and Ernest Marsden had been conducting experiments on the scattering of α particles from a thin gold foil. On that June afternoon — a century ago — they were to present to London's Royal Society their data "On the Diffuse Reflection of the α Particles" (*Proc. R. Soc. A* **82**, 495–500; 1909).

The rest really is history. Geiger and Marsden had observed that, although most α particles passed through the foil pretty much undeflected, very occasionally — and contrary to expectation — an α particle could be scattered right back, through a very large angle. Rutherford had the interpretation: "the atom consists of a central charge supposed concentrated at a point", he wrote later (*Phil. Mag.* **21**, 669–688; 1911); the atom, far from being the 'plum pudding' that had been envisaged, had a nucleus.

Rutherford acknowledged that the essence of his nuclear model had been captured in the 'Saturnian atom' of Japanese physicist Hantaro Nagaoka (*Phil. Mag.* **7**, 445–455; 1904), "which he supposed consisted of a central attracting



mass surrounded by rings of rotating electrons". But it was these data from Geiger and Marsden in 1909, and those that followed, that enabled the detail of the structure of the atom to be drawn more

accurately than ever before. The nucleus was revealed, and a century of nuclear physics began.

ALISON WRIGHT