be predicted, the average motion of a large number of electrons can, resulting in well-defined transistor operation.

How do electrons flow through a single-molecule transistor? The answer is by a simple fundamental process. The repulsive Coulomb interaction between electrons means that there is an energy cost in adding an extra electron to any object of small dimensions (this same energy cost is in part responsible for the ionization and affinity energies in an atom). In a molecular transistor, this energy cost can be tuned to zero by applying a voltage to the gate electrode. At a particular gate voltage, the electrostatic potential is such that an extra electron can hop from the source onto the molecule. However, Coulomb repulsion forbids a second, extra, electron hopping on at the same time — the first electron must leave the molecule, moving into the drain, to make way for the next electron. This one-by-one electron motion, governed by the quantum of electron charge, is known as single-electron tunnelling.

But there is another quantum property important for electron transport through small objects — the electron spin. Electrons each carry one half-unit of spin in one of two configurations, defined as 'up' or 'down'. As there is no preference for the direction of the spin, the lowest-energy (ground) state of the system is a combination of up and down spins. To reach this ground state, an electron spin must flip between up and down, and this can be arranged by replacing an up-spin electron on the molecule by a down-spin electron from one of the electrodes. This spin-flipping, driven by the desire of the system to be in its ground state, enforces an exchange of electrons between molecule and electrodes through a process called the Kondo effect[8].

In the experiments by Park *et al.*[3] and Liang *et al.*[4], the molecule is tuned between two states that differ by one charge and one spin unit. In one state, the conduction mechanism is single-electron tunnelling. In the next state, with an odd number of electrons on the molecule, electron transport is mediated by the Kondo effect. Remarkably, when the Kondo effect dominates, the conductance reaches values close to the quantum limit (which is $2e^2/h$, where $e$ is the electron charge and $h$ is Planck's constant) for a perfectly conducting one-dimensional wire. This result is quite remarkable, considering the intrinsic difficulty of establishing good electrical connection between a molecule and a metal electrode.

Do these realizations of a single-atom transistor mean that molecular electronics is just around the corner? That goal may be a little closer, but there is still a long road ahead before atomic or molecular transistors can be assembled into viable, dense, fast logic-circuits. Right now, these single-molecule or single-atom transistors are no competition for silicon transistors. But they will serve both scientifically, for studying electron motion through nanoscale objects, and technologically, for developing chemical techniques with which to fabricate electronic devices on single molecules. ■

*Silvano De Franceschi and Leo Kouwenhoven are in the ERATO Mesoscopic Correlations Project, Department of NanoScience, Delft University of Technology, PO Box 5046, 2600 GA Delft, The Netherlands.*
*e-mail: leo@qt.tn.tudelft.nl*

1. Joachim, C., Gimzewski, J. K. & Aviram, A. *Nature* **408,** 541–548 (2000).
2. Dekker, C. *Physics Today* **52,** 22–28 (1999).
3. Park, J. *et al. Nature* **417,** 722–725 (2002).
4. Liang, W., Shores, M. P., Bockrath, M., Long, J. R. & Park, H. *Nature* **417,** 725–729 (2002).
5. Park, H. *et al. Nature* **407,** 57–60 (2000).
6. Reichert, J. *et al. Phys. Rev. Lett.* **88,** 176804 (2002).
7. Zhitenev, N. B., Meng, H. & Bao, Z. *Phys. Rev. Lett.* **88,** 226801 (2002).
8. Kouwenhoven, L. & Glazman, L. *Physics World* 14, 33–37 (2001).

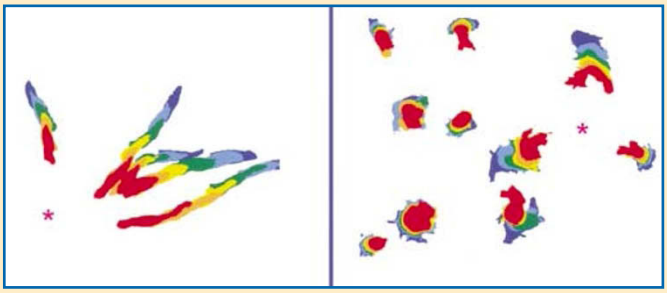
Cell motility

## The attraction of lipids

The pictures reproduced here aren't just pretty — they reveal something fundamental about how cells move towards the source of an attractant chemical. The left image shows the behaviour of normal cells of *Dictyostelium discoideum*, a type of slime mould. The cells on the right lack an enzyme called PTEN. The colour scale, from blue to red, indicates how each cell moves over time. The normal cells are clearly moving towards a chemical source (asterisk), but the mutant cells seem less sure where they're going.

The images are taken from a paper by Miho Iijima and Peter Devreotes (*Cell* **109,** 599–610; 2002). Together with work by Satoru Funamoto *et al.* (*Cell* **109,** 611–623; 2002), this study reveals the importance to motility of enzymes — including PTEN — that alter the lipid content of cell membranes.

Many cells need to move up a concentration gradient of a given chemical ('chemoattractant'); in humans, for instance, immune cells migrate towards signals emitted by invading microorganisms. Cells



must sense the gradient and then extend protrusions ('pseudopodia') in the direction of movement. Filaments of the protein actin form the skeleton of pseudopodia.

Studies with lipid-binding proteins suggested that the lipid content of cell membranes forms a gradient during chemoattraction, with 3-phosphoinositides being concentrated at the front edge. These are thought to bind signalling proteins, leading to the changes needed for movement. But how does the lipid imbalance come about? This question is tackled in the new papers.

Funamoto *et al.* started by studying phosphatidylinositol-3-OH kinases (PI(3)Ks), enzymes that produce 3-phosphoinositides, in *D. discoideum*. When cells were placed in a chemoattractant gradient, two different PI(3)Ks moved to the membrane at the leading edge, with similar kinetics to 3-phosphoinositide-binding proteins. Membrane-bound PI(3)Ks seemed to trigger the formation of pseudopodia.

So the localization of PI(3)Ks could explain the generation of 3-phosphoinositides at the leading edge. But the concentration of these lipids tails off sharply towards the rear of a cell, hinting that an enzyme that degrades them might be at work there. Both groups investigated a possible candidate — PTEN. When Funamoto *et al.* overexpressed this enzyme in *D. discoideum*, the cells moved more slowly and became less polarized in response to a chemoattractant. Iijima and Devreotes engineered *D. discoideum* lacking PTEN, and again the cells moved abnormally, taking a circuitous route to the chemoattractant. The cells also produced pseudopodia more erratically, sometimes at the back, and had more actin filaments than normal. Finally, both groups found that PTEN is usually located at the rear of moving cells.

This suggests that PTEN and PI(3)Ks help to produce a gradient of 3-phosphoinositides, which is much steeper than the chemoattractant gradient. The lipid gradient translates into the correct localization of key signalling proteins and actin filaments, and so into directed movement. But how these enzymes are moved about the cell, and how they interact with other chemoattractant-sensing pathways, remains to be seen. **Amanda Tromans**