

chalcogenide device is that both show incremental changes in their structure, cumulative over time, when they are operated below their threshold voltages. These changes give rise to controllable intermediate conductivities and are in effect precursors to the binary memory effects that make chalcogenides useful as storage materials. In PC-RAM, this cumulative behaviour is readily explained by crystal growth; in the electrolytic variant, it is explained by electrodeposition.

Both chalcogenide technologies present exciting opportunities that are not restricted to memory, but include cognitive computing<sup>5,8</sup> (E\*PCOS 05: S. R. Ovshinsky, ECD Ovonic) and reconfigurable logic circuits<sup>9</sup>. It is too early to tell which technology will be selected for which niche, but scientific interest alone should motivate a closer look at chalcogenide materials to investigate correlations between phase-change and electrolytic behaviour. To take one example, the migration of dissolved ions is required in the electrolytic case, but could degrade the performance of a phase-change device. Fluxes of both electrons and

ions participate in electromigration — widely studied as a degradation mechanism of the electrically conducting lines for integrated circuits. Thus, a unified approach to the study of chalcogenides, assessing the roles of atoms, ions and electrons, may prove crucial for both device performance and reliability. ■

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## CELL BIOLOGY

# Helices sculpt membrane

Guillaume Drin and Bruno Antony

**Many proteins are carried within cells in bubble-like sacs. These are pinched off from membranes inside the cell, and it seems that the Sar1p protein is key in both starting and finishing this budding process.**

The cell contains a network of membrane-bound compartments that exchange proteins with each other and with the cell surface thanks to several haulage systems, each providing a specific link between one station and another. At the departure point, specialized 'coat' proteins wrap up a small area of the lipid membrane, shaping it into a bulging 'bud' and gathering up proteins due to be transported inside it<sup>1</sup>. The bud detaches from the membrane — a stage called fission — to form a bubble-like 'vesicle' loaded with cargo. Lee et al.<sup>2</sup> report in *Cell* that a coat protein called Sar1p, whose structure contains several  $\alpha$ -helices, initiates buds for one type of vesicle by thrusting one of its helices into the membrane, causing it to balloon outwards<sup>2</sup>.

We knew that Sar1p begins the formation of so-called COPII vesicles, but quite how was unclear. These vesicles transfer proteins from a membrane-bound structure called the endoplasmic reticulum, where they are made, to another such structure, the Golgi apparatus, where they are processed into their final form. A common cellular fuel called guanosine triphosphate (GTP) activates Sar1p. When Sar1p binds to GTP, it exposes a short  $\alpha$ -helix

at its amino (or N) terminus that anchors the protein to the membrane of the endoplasmic reticulum. There, Sar1p recruits two large COPII protein complexes, Sec23/24p and Sec13/31p, which polymerize into a curved lattice. Studies using artificial lipid vesicles called liposomes show that adding all these components is sufficient to generate coated buds on the liposome and, less efficiently, free coated vesicles<sup>3</sup>. Now Lee et al.<sup>2</sup> report how Sar1p contributes to the initial moulding of the membrane and, less expectedly, to membrane fission.

Using electron microscopy, the authors first show that Sar1p alone can deform liposomes into long, narrow tubules, but only when it is bound to GTP, suggesting an involvement of the N-terminal helix. To demonstrate this, they swap this helix for a peptide that binds to an artificial lipid. As expected, the Sar1p mutant still binds to liposomes containing the artificial lipid but no longer deforms them.

Both normal Sar1p and the domain-swapped mutant can interact with the other COPII complexes, so the next step was to compare incubations conducted with the complete set of COPII proteins. Puzzlingly, though, buds do form in the presence of the



## 50 YEARS AGO

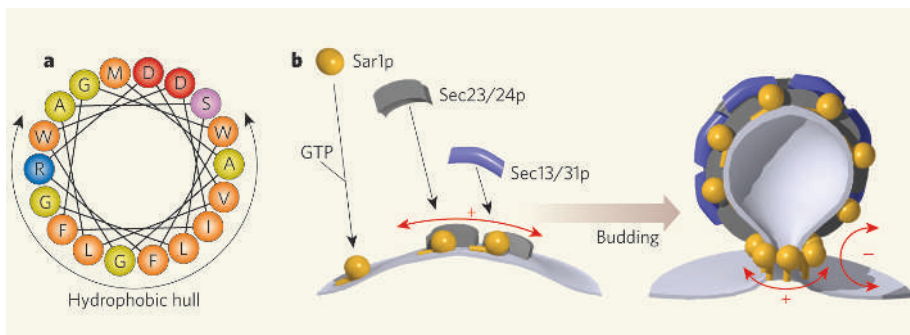
For some time past, the B.B.C. Research Department has been studying the technique of colour television, and recently a programme of experimental transmissions was started outside normal broadcasting hours. On October 20, Sir Harold Bishop, director of technical services, presented a special demonstration for the Press. This comprised the transmission over a closed circuit at the Alexandra Palace station, of still pictures, a short travel film and a number of 'live' camera shots, all of which were reproduced at the receiving end as attractive colour pictures. From *Nature* 29 October 1955.

## 100 YEARS AGO

*The Far East.* By Archibald Little. — Of late years the Far East is only far in actual distance; it is very near to our thoughts, while the ignorance regarding these lands is being very rapidly dispelled... China stands now at the parting of the ways; for many years resolute in keeping out foreign inventions so distasteful to the old-fashioned mandarin, circumstances have proved too strong, and railways, the precursors of western life, are now being built or projected throughout the land... Consider the Yangtse Valley... This magnificent river will undoubtedly remain the great high road for commerce into Central China; but railways are and will be built to act as feeders to the main line, much to the profit of the shareholders and of the inhabitants, for Chinese are born traders, and already make use of the pioneer of Chinese railways — the line from Tientsin to Peking — in large numbers.

Finally, we have a vivid description of the southern basin, Canton, Hong Kong, and the provinces bordering on French territory. Yunnan, which adjoins our Burma, has a particular interest to Englishmen; but here, owing to our supineness in days gone by, we have allowed the French to get ahead of us with their railway, which will undoubtedly draw to itself all that is valuable of the trade of the province. From *Nature* 26 October 1905.

50 & 100 YEARS AGO



**Figure 1 | Sar1p in budding and fission.** **a**, The N-terminal 18 amino acids of Sar1p form an amphipathic helix, seen here as though looking along the central axis with each amino acid identified by a one-letter code. The highly hydrophobic amino acids (orange) constitute a wide side, whereas polar amino acids (red, negatively charged; blue, positively charged; purple, hydroxylated) make up a smaller one. Other amino acids are in yellow. **b**, On activation by GTP, Sar1p inserts its N-terminal helix into the membrane. Lee *et al.*<sup>2</sup> show that, once there, it bends the membrane outwards (+) and recruits the Sec23/24p complex, which polymerizes into a coat with Sec13/31p. Eventually, the coated bud is attached to the membrane by a small neck, with a negative curvature (–) in one direction and a positive curvature (+) in the other. Several Sar1p N-terminal helices may orientate parallel to the main neck axis, where they might further constrict the membrane and help fission and release of the bud.

swapped Sar1p mutant, yet free vesicles are scarce. In line with this, follow-up experiments conducted on membranes derived from endoplasmic reticulum show that an intact N terminus in Sar1p is key to the efficient release of COPII vesicles. So, if there is no doubt that the spherical shell formed by Sec23/24p and Sec13/31p is central to the sculpting of the membrane, Lee and colleagues' study<sup>2</sup> implies that the N terminus of Sar1p is not merely a simple piece of tape that sticks the COPII coat to the membrane, but that it has an active role in membrane deformation and fission.

The N-terminal helix of Sar1p is amphipathic — that is, it has a hydrophobic face and a hydrophilic face. The wide hydrophobic 'hull' should insert between the lipid acyl chains of the membrane, while the polar hydrophilic side interacts with the lipid heads and the watery environment of the cytoplasm (Fig. 1a). From model studies, we know that this kind of helix is designed to float on

biological membranes, with the axis lying at the interface between the polar and nonpolar lipid regions<sup>4</sup>. The membrane is a tightly packed bilayer of lipids, so when the N-terminal helices from numerous Sar1p proteins adsorb on its surface, they will expand the outer layer and, because the bilayer has a finite area, compress the inner layer. As a result, the membrane will bend and dome. Indeed, when Lee *et al.* replaced bulky amino acids in the hydrophobic side of the helix with smaller ones, Sar1p was less able to make tubules from the liposomes and to generate transport vesicles from isolated membranes *in vitro*.

Because Sar1p recruits Sec23/24p, which has a three-dimensional structure that is adapted to a convex surface, it is easy to imagine how the two proteins work in concert to bend the membrane at early stages of coat assembly<sup>5</sup> (Fig. 1b). However, the role of Sar1p at the fission step is less intuitive. The curvature of the bud neck resembles that of a horse saddle,

being negative in one direction and positive in the other. If the N-terminal helix of Sar1p invades the neck, its most plausible orientation is to align along the neck axis (Fig. 1b). A ring of parallel helices emerging from the coat edge may further constrict the neck and help membrane fission. Notably, COPII-coated buds on liposomes show a wider neck with N-terminal Sar1p mutants than with the unmutated form (Figs 3 and 8 in ref. 2).

The formation of clathrin-coated vesicles, which transport cargoes from the cell surface, follows an analogous process to that of COPII vesicles in that a short N-terminal helix of the protein epsin allows the plasma membrane to deform<sup>6</sup>. However, the epsin helix is shorter and has a smaller hydrophobic hull. Moreover, its polar side contains several electrically charged residues that bind specifically to PIP<sub>2</sub>, a negatively charged lipid that is a hallmark of the plasma membrane. So if the insertion of hydrophobic residues from amphipathic helices seems to be a common mechanism for inducing membrane curvature, subtle changes in the sequence may govern the ability to deform specific cellular membranes.

Hydrophobic and polar residues form the two broad classes of the amino-acid alphabet, and their segregation is the basis of the amphipathic helix. Yet hydrophobic amino acids vary in size, and this should influence the helix 'footprint' on the membrane. Likewise, the polar amino acids (such as hydroxylated, basic or acidic residues) in the other side do not interact to the same extent with the lipid polar heads<sup>7,8</sup>. No doubt, the language of membrane-deforming helices at the complex membrane–water interface is very rich and remains to be translated.

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## MYCOLOGY

### The whiff of danger

You don't take the death cap (*Amanita phalloides*) home for tea. This species, pictured here, is infamously poisonous, with many other mushrooms being toxic to a greater or lesser degree.

Thomas N. Sherratt, David M. Wilkinson and Roderick S. Bain have addressed two issues raised by the existence of poisonous mushrooms (*Am. Nat.* doi:10.1086/497399). The first question was what purposes possession of poisons might serve in mushrooms. One possibility is that toxins are simply a metabolic by-product. Another that has

been suggested by several authors is that they act as a deterrent to predators, which might otherwise destroy the mushroom before its spores have matured and dispersed. Fungus-loving vertebrates could in particular be highly destructive.

An evolutionary principle is that if you as an organism go to the bother of being unpalatable, you might as well signal that fact. Does this apply in mushrooms? To investigate this second issue, Sherratt *et al.* turned to data compilation and neural-network analysis. They made use of

modern evolutionary trees to judge the incidence of poisonousness in mushrooms, then analysed data sets, culled from field guides, to see whether poisonous species tend to have particular ecological correlates — whether, for instance, they are more colourful, more aggregated or have a more noticeable odour.

Overall odour (and not cap colour) came out as the best predictor of toxicity, a result that was supported by pairwise comparisons of related poisonous and edible forms. Given that many animals forage by night, and that nocturnal mammals tend to have relatively poor colour vision, the authors suspect that odour provides the more effective signal.



Sherratt *et al.* make plain that their study is correlative only, and that — for them and others — this is a work in progress. There is rich scope for further investigation of the hypothesis that poisonous mushrooms use odours as warning signals, and of the likely exceptions.  
**Tim Lincoln**

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## SOLID-STATE PHYSICS

## Spin in the slow lane

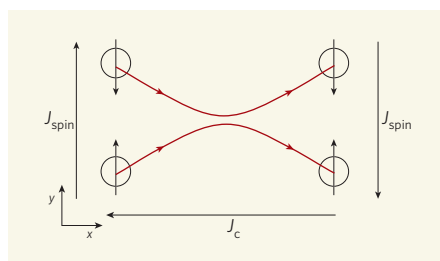
Bart van Wees

Electrons were until recently thought to transport their charge and spin equally freely through metals and semiconductors. Now it seems that spin can lag considerably behind charge.

The recognition that electrons can transport through a solid not just charge, but also spin (the intrinsic ‘rotation’ of electrons, which gives rise to their magnetic moment), sowed the now burgeoning field of spintronics. As charge and spin are properties of individual electrons, it is tempting to conclude that both will be transported equally efficiently. But Weber *et al.*<sup>1</sup>, writing on page 1330 of this issue, show that the diffusion of electron spin can be substantially slower than that of electron charge. This could have important implications for spin-based electronics.

The ability to generate, study and use phenomena such as spin injection, spin currents and spin accumulation, in metals as well as semiconductors, has made it imperative to discover how similar — or different — spin and charge transport are. In metals, no substantial differences have been observed<sup>2</sup>; but in semiconductors, experiments in the past decade have already indicated that charge and spin diffusion act differently<sup>3</sup>. The comparison of the two transport mechanisms is simplified by assuming that the electron spin (or its associated magnetic moment) can point only up or down along a specific axis. In conventional charge currents, these spin-up and spin-down electrons move in the same direction. But when, in the absence of a charge current, spin-up electrons move in one direction, and an equal number of spin-down electrons move in the opposite direction, a spin current is established, with magnetic moment effectively being transported in one direction.

Usually, electron motion is diffusive: scattering on impurities, lattice defects and lattice vibrations will, after some time, randomize the direction of an electron’s movement. The more scattering that takes place, the slower the electron diffusion will be. As this effect applies equally to spin-up and spin-down electrons, the naive expectation is that the effective rates of charge and spin diffusion should be the same. But this neglects the electrostatic repulsion, or Coulomb interaction, that exists between electrons. The Coulomb interaction does not affect the diffusion of charge, as it does not change the total momentum of the



**Figure 1 | Spin drag.** Two electrons are moving in the  $x$ - $y$  plane with opposite directions of spin. In this particular case, they initially contribute to a charge current  $J_c$  in the negative  $x$ -direction (conventionally, electric current is depicted as a flow of positive charges, in the opposite direction to the actual electron flow). Because the spin-up electron is moving upwards and the spin-down electron downwards, there is also a net spin-up current  $J_{\text{spin}}$  in the positive  $y$ -direction. Because of Coulomb repulsion as the electrons near each other, and the resulting exchange of momentum, their direction of motion in the  $y$ -direction, and so their contribution to the spin current, is reversed. Their contribution to the charge current, however, is unaffected. Thus, unlike the diffusion of charge, the diffusion of spin is slowed down — the spin Coulomb drag demonstrated by Weber *et al.*<sup>1</sup>. (Modified from ref. 1.)

electrons. But it does reduce the diffusion rate of spin through scattering between spin-up and spin-down electrons (Fig. 1) — the effect known as spin Coulomb drag that has now been demonstrated experimentally by Weber and colleagues<sup>1</sup>.

Measuring the relevant experimental parameter, the spin diffusion constant  $D_s$ , necessitated a clever technique based on a so-called spin grating<sup>4</sup>. The authors first used<sup>1</sup> the interference between two laser beams polarized linearly, but at right angles to each other, to ‘pump’ their sample — a crystal of the semiconductor gallium arsenide — with a very short light pulse. The two beams met in the plane of the semiconductor at an angle, so their relative phase changed linearly along its surface. This induces a periodic variation in spin density — the spin grating — in the quantum wells in which the electrons are confined. Here, regions of excess spin-up and excess

spin-down electrons alternate with a spatial period  $L$  that is dependent on the angle of incidence of the two beams. This spin grating decays with time, partially through intrinsic relaxation of the spin, and partially as a result of diffusion between the excess spin-up and spin-down regions (on a typical timescale  $T = L^2/D_s$ , given by the laws of diffusion).

The authors then applied a further linearly polarized, ‘probe’ laser pulse to their crystal. This brought the Faraday effect into play, which dictates that the interaction of a beam of light with a magnetic field — in this case, that induced by the electron spins — will bring about a (slight) rotation of the polarization of the reflected beam. The angle of rotation depends on the induced magnetization (and thus the spin density), so the decay of the spin grating can be investigated by varying the delay between the pump and probe pulses. By ascertaining the effective decay time as a function of the spatial period  $L$ , the authors determined the relative importance of diffusion and relaxation, and obtained values for both  $D_s$  and the intrinsic spin relaxation time. They found that the rate of spin diffusion indicated by  $D_s$  was considerably slower than the charge diffusion rates obtained from conventional electronic measurements.

In theoretical calculations<sup>5,6</sup>, spin Coulomb drag is expressed by a parameter known as the spin-drag transresistivity; this relates the current in each of the spin channels (spin up or spin down) to the effective electric field in the opposite spin channel. The significance of the transresistivity depends on the number of spatial dimensions considered, the strength of the various interactions between the electrons, and the conventional electronic resistivity. If this last quantity is small, as it is in good conductors such as metals, the effect of spin drag will be relatively small<sup>2</sup>. In the two-dimensional system used by Weber *et al.*<sup>1</sup>, however, the effect of spin Coulomb drag turns out to be considerable. Reducing further to a one-dimensional system has revealed that spin and charge can even separate<sup>7</sup>, with the two intrinsic electron properties developing their own distinctive transport modes. These findings are bound to stimulate further research. What is already abundantly clear, however, is that spin and charge both move at their own pace. ■

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