100 YEARS AGO

It is reported in some of the daily papers that Dr. Otto Schmidt, of Cologne, has succeeded in isolating and cultivating a parasite from cancer and in preparing an antiserum for the disease. So many positive statements of the isolation of a cancer-parasite have been made during the last few years, and have subsequently proved to be incorrect, and so many capable men have been investigating cancer without result, that reports of this kind cannot be accepted without further proof. The publicity given to matters of this kind is much to be deprecated; in the majority of instances false hopes are raised which must end in disappointment for many sufferers.

From *Nature* 12 November 1903.

50 YEARS AGO

It was a famous moment in the history of science when, during the discussion of Darwin's theory of evolution at the British Association meeting at Oxford in 1860, Bishop Wilberforce turned to T. H. Huxley and asked him whether he claimed descent from an ape on his father's or his mother's side. The actual words of Huxley's reply are not known… The main source of our information, his son Leonard Huxley, wrote "most unluckily, no contemporary account of his own exists of the encounter". Such an account does, however, exist in a letter written to Dr. Dyster within a few months of the meeting, on September 9, 1860, and now preserved in the collection of Huxley Papers at the Imperial College of Science and Technology, London… "When I got up I spoke pretty much to the effect — that I had listened with great attention to the Lord Bishop's speech but had been unable to discover either a new fact or a new argument in it — except indeed the question raised as to my personal predilections in the matter of ancestry… If then, said I, the question is put to me would I rather have a miserable ape for a grandfather or a man highly endowed by nature and possessing great means and influence and yet who employs those faculties and that influence for the mere purpose of introducing ridicule into a grave scientific discussion — I unhesitatingly affirm my preference for the ape. Whereupon there was unextinguishable laughter among the people, and they listened to the rest of my argument with the greatest attention."

From *Nature* 14 November 1953.

critical value are allowed to detach, thereby enabling fracture to occur.

The calculations show how significant the effects of hyperelasticity can be, even when the hyperelastic zone is only a few hundred atoms in size and the remainder of the material is behaving elastically. Buehler *et al.*[1] suggest that, under the right conditions, the properties of this tiny hyperelastic region entirely control the fracture process. Supersonic propagation of cracks — far surpassing the limiting velocity allowed by linear elastic theory[10] — becomes possible, and as a result shock fronts may be emitted from the hyperelastic region.

As every crack is surrounded by a nonlinear region, hyperelastic effects should be commonplace. On the other hand, laboratory experiments[11] have indicated that linear elastic theory provides an excellent description of the dynamics of rapidly moving cracks. So when would the more exotic behaviour induced by hyperelastic effects be seen? Buehler *et al.*[1] predict that the key to this question is the ratio of the size of the hyperelastic region marking the onset of hyperelasticity, to an 'energy' length scale, defined as the size of the region around the tip that encompasses enough energy to drive the fracture process. When the hyperelastic region is much smaller than the energy length scale, hyperelastic effects are negligible; but if the two are similar, these effects could dominate the fracture process. We might then expect to observe the effects of hyperelastic behaviour when fracture occurs in a highly strained material, or if a material suffers a high rate of strain, such as caused by the impact of a projectile.

The process of rapid fracture is strongly influenced by the interplay of physical effects on many different scales. Simulations, such as these by Buehler *et al.*[1], should enable us to bridge the gap between the laboratory scales where fracture is observed and the near-atomic scale where fracture germinates. Describing the detailed motion of millions of atoms involved in the fracture process is an impressive technical feat, but it is still important to be able to see the wood for the trees — to identify the key features relating the delicate interplay between the myriad dancing atoms at a crack tip and the macroscopic effects that they generate. This work, together with other studies[7–9], is a step towards both a fundamental understanding of these processes and, possibly, a powerful tool for the design of new materials. ■

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Plant development

An axis of auxin

Stefan Kepinski and Ottoline Leyser

Embryos have two distinct ends, which become apparent early on. Quite how this initial polarity is sustained in plant embryos has been unclear. Step forward the *agent provocateur* of plant development — auxin.

In multicellular organisms, different kinds of cell are specialized for different tasks — reproduction, say, or light perception. Clearly, the proper functioning of these organisms requires that the various cell types are positioned correctly relative to one another. Hence, common to the development of all multicellular organisms is the formation of axes along which the body plan is organized. Such axes are usually manifest very early in development, and indeed it is often impossible to identify an apolar stage[1]. This is certainly the case in many higher plants, including the experimental organism *Arabidopsis thaliana*, where a developmental decision that ultimately gives rise to a shoot at one end and a root at the other can be traced back to the first, asymmetric division of the fertilized egg cell[2]. But how is this initial asymmetry maintained and translated into the polar root–shoot axis? On page 147 of this issue[3], Friml and co-workers strikingly demonstrate that such 'elaboration' depends on the movement to and fro of the plant hormone auxin.

As Fig. 1 shows, the initial division of the fertilized *Arabidopsis* egg cell produces two daughter cells: a small upper cell (the apical cell) and a larger basal cell. The apical cell generates the 'proembryo', which develops through a series of stereotypic divisions to give rise to the upper, central and mid-lower

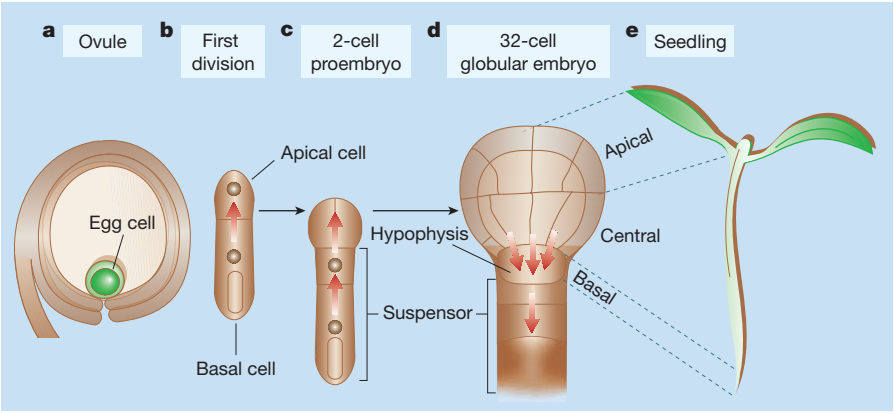

Figure 1 **The basics of early *Arabidopsis* development.** a, **The egg cell lies deep in the female parts of the flower, within the ovule.** b, **Once fertilized, the egg undergoes an asymmetric division, producing a larger basal cell and a smaller apical cell. Friml *et al.*[3] have found that the basal cell exports the hormone auxin (red arrow) and that the apical cell responds to it.** c, **The basal cell divides horizontally to form the suspensor, while the auxin-receiving apical cell divides vertically to form the 2-cell proembryo.** d, **Around the stage of the 32-cell globular embryo, the flow of auxin is suddenly reversed[3] and now accumulates in the hypophysis, the founder of the basal regions of the embryonic root. At this stage, one can begin to distinguish the regions that give rise to the apical, central and basal parts of the seedling** (e).

regions of the seedling. Meanwhile, the basal cell produces the suspensor — a stack of cells that attaches the proembryo to maternal tissue. Initially, all of the suspensor cells lie outside the embryo proper, but later the uppermost cell is recruited by the proembryo to form the hypophysis, the founder of the lowest regions of the embryonic root[2].

It has been difficult to pin down how the initial asymmetry is translated into this suspensor–root–shoot axis. One contender for the role is auxin. A truly multi-talented signalling molecule, auxin has a finger in virtually every plant-developmental pie, from the control of branching in both shoot and root to the patterning of the root tip[4]. All of these processes depend on the cellular responses to local auxin concentrations, and on the generation of patterns of auxin accumulation. The responses to auxin involve changes in gene expression, which are mediated by families of positive and negative gene regulators whose relative abundance is tightly controlled by auxin[5]. The accumulation of auxin, meanwhile, is directed by two protein families: the AUX influx carriers, which pass auxin into cells, and the PIN efflux carriers, which pass it out[6]. Directionality of auxin transport is provided by the asymmetric localization of the PIN proteins[6].

A role for auxin in elaborating the embryonic axis has been suspected for many years, not least because polarity defects can be induced in embryos by blocking auxin movement[7]. More recent molecular genetic evidence comes from the analysis of mutations in three *Arabidopsis* genes, *MONOPTEROUS* (*MP*), *BODENLOS* (*BDL*) and *GNOM* (*GN*), all of which cause defects in axis elaboration. *MP* encodes a positive and *BDL* a negative regulator of auxin-inducible genes[8,9], whereas *GN* encodes a protein needed for the proper subcellular targeting of the PIN proteins[10,11]. What is exciting about the work of Friml *et al.*[3] is that it ties these strands together definitively.

To follow the responses of embryos to auxin, the authors introduced a gene for green fluorescent protein (GFP), attached to a synthetic control region that is activated by auxin. They found that the first signs of a response (that is, the first signs of GFP production and hence auxin activity) occur at a very early stage, in the apical daughter cell of the asymmetrically divided egg. As the proembryo develops, the auxin-response signal persists, remaining absent from the suspensor cells beneath. This pattern continues until the proembryo consists of about 32 cells, when a remarkable thing happens. The axis of auxin response is suddenly reversed, becoming undetectable in the apical regions, with a new maximum in the developing hypophysis beneath. The authors find that these response patterns reflect actual gradients of auxin concentration, with maximal responses occurring at maximal concentrations.

To find out how these gradients arise, Friml *et al.* investigated the expression patterns of the PIN auxin-efflux proteins. They show that, within the two-cell proembryo, a previously uncharacterized PIN-family member — PIN7 — is expressed in the basal cell at the boundary facing the cell's apical sister. This is consistent with the auxin maximum in the apical cell. Later, the cells of the suspensor continue to express PIN7 at their apical side, while in the proembryo another protein, PIN1, is expressed without apparent polarity[10].

But at the 32-cell stage, it's all change. Both PIN1 and PIN7 become localized to the basal membranes of the cells in which they are expressed (proembryo and suspensor cells, respectively) — an event that coincides with the reversal of the auxin gradient and, presumably, with the onset of auxin production in the proembryo. This new direction of auxin flow is apparently reinforced by the expression of two other PIN-family members, so that, although PIN7 is positioned to transport auxin down the suspensor and out of the embryo, the net effect is the accumulation of auxin, and a maximal response to it, in the embryonic root.

Do these auxin fluxes help to maintain the embryonic axis of polarity? The authors' studies of mutant plants show that they do. Embryos with mutations in PIN7 have trouble establishing the initial auxin-response maximum in the apical cell and its daughters, and this coincides with a confused apical/basal identity in the proembryo. The effects of mutations in other PIN proteins are milder and affect later stages of basal embryo development. But matters are not entirely predictable. Knowing the PINs' expression patterns, if you were going to put money on any of these mutants not making it out of embryogenesis it would be on those with PIN7 defects — yet these plants recuperate to produce relatively normal seedlings. Interestingly, the recovered axis is always in the correct orientation, hinting that the polarizing influence of the suspensor is maintained into these later stages. It is not clear how polarity is restored, but it does require auxin efflux, as plants with mutations in all four embryonically expressed PINs fail to recover. These data, together with the requirement for an embryonic response to auxin implicit in the defects caused by *MP* and *BDL* mutations, underline the relevance of asymmetric auxin transport and responses in maintaining polarity.

So does auxin do it all? Is the initial polarizing signal from maternal tissue — the signal that directs the first, asymmetric cell division — also auxin? And can auxin itself direct the polar localization of PIN proteins? It is certainly possible that the initial asymmetry is directed by a low level of auxin flow from maternal tissues that passes beneath the radar of current techniques, and that maternal auxin, channelled up the suspensor, could continue to provide axial information later on. Furthermore, auxin has for many years been proposed to act in feedback loops to regulate its own flux[6]. But it is harder to envisage a mechanism whereby auxin could trigger the dynamic changes in its direction of flow that are observed here.

Are there then other signals, and, if so, what is their relationship to auxin? Is auxin instructive or permissive? If the former, auxin must first instruct apical, and then, almost immediately, basal fates. As this would require that auxin concentration is

maintained and interpreted with the utmost rigour, auxin might instead permit development, within an apical or basal context set by additional input. At least we are now in a position to muse on these possibilities, thanks to the work of Friml and colleagues. ■

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Condensed-matter physics

The quest for imperfection

Thomas F. Rosenbaum

The electrical properties of silver chalcogenides are unusually affected by magnetic fields. A simulation suggests how this might arise from tiny imperfections and could facilitate the design of new materials.

The change in the electrical resistance of a material with magnetic field — its magnetoresistance — lies at the heart of many applications, from storing information in a computer to measuring the speed of a car. The resistance of two materials in particular, silver selenide and silver telluride, can be made to increase linearly as the applied magnetic field increases, up to field values at least one million times that of the Earth's magnetic field[1,2]. This linear response over such a large range makes these semiconductor materials attractive as magnetic-field sensors, although their performance is unusual in terms of basic physics. Parish and Littlewood[3] have tackled the question, as they report on page 162 of this issue, using a combination of fundamental theory and computer simulations. They show that it is not material perfection, but macroscopic disorder and inhomogeneity, that are the essential ingredients for such a remarkable magnetoresistive response.

Crystalline perfection and purity is the paradigm for the semiconductor electronics industry, where gowned technicians in dust-free clean rooms prepare crystal wafers of silicon containing impurities controlled to one part in a billion. In contrast, perfectly stoichiometric, homogeneous silver selenide and silver telluride (Ag_2Se and Ag_2Te, respectively, and 'silver chalcogenides' collectively) are useless for applications. It is only when a small amount of excess silver is introduced, ideally at the level of one part in 10,000, that the material becomes interesting. The exact distribution of the excess silver atoms in the 'optimally doped' material is not known, but the atoms presumably group in small clusters or fine wires on nanometre or micrometre scales.

So how do such fluctuations in composition lead to an anomalously large, linear magnetoresistance that also doesn't saturate at high field values? Abrikosov[4] was the first to realize that the problem should be modelled in terms of the creation of an 'effective medium', in which disorder is combined with quantum mechanics in a theory that explains the properties of semiconductors that are almost, but not quite, metals. Parish and Littlewood[3], however, invoke a classical explanation that is applicable over a broad range of temperatures and to a wide variety of compositional irregularities. They construct (conceptually, and on the computer) a two-dimensional, random network of resistors — effectively, an inhomogeneous semiconductor. Usually, a resistor has a single current input and output, but these resistors are special: each disk-like resistor has four terminals around its edge, two for the input and output of current and two additional posts for reading voltages. In this way, the voltage drop across the resistor need not be aligned with the direction of the current. From such a four-terminal device it is possible to construct a matrix of the device's conductivity: diagonal components correspond to the voltage being aligned with the current; off-diagonal components arise because a current in one direction can induce a voltage in a different direction.

There are two key elements to consider — the effect of an applied magnetic field, and the response of the resistor network as a whole. When a magnetic field is applied perpendicular to the direction of current flow, the charge-carrying electrons in each disk are forced into circular trajectories (called cyclotron orbits) and a voltage is induced that is transverse to both the field and the current directions. This transverse voltage is known as the Hall voltage and has the special property of growing linearly with increasing magnetic field. This linear response is obviously necessary for matching theory to experiment, but it is not enough to explain the exact behaviour of the silver chalcogenides. The magnetoresistance would still be expected to saturate at a magnetic-field strength that is almost 100 times lower than that already reached in experiments — experiments that show no evidence of saturation.

It is at this point that the collective behaviour of a random array of resistance disks becomes important. No longer do the cyclotron orbits alone set the definitive scale of the response. Rather, disorder and inhomogeneity, as expressed by fluctuations in the properties of the individual array resistors — for example, whether the Hall voltage is positive or negative — are the appropriate control parameters. The current paths no longer simply follow electric-field lines, but can loop back on themselves and even travel perpendicular to the applied voltage. The net effect in a large array is a linear magnetoresistance that corresponds to that of the silver chalcogenides. Moreover, Parish and Littlewood's approach in essence presents design rules for creating new materials with a tailor-made magnetoresistive response.

The concept of exploiting imperfection can be applied across the field of condensed-matter physics. Heterogeneous systems, from polymers to high-temperature superconductors, organize themselves on microscopic length scales with macroscopic consequences. Eschewing the rigorous demands and expense of perfectly replicated and ordered devices has obvious advantages, but introduces complications in addressability and control. A good example is the nascent field of quantum computation. Here it is feared that disorder will lead to dissipation, disrupting the finely tuned superposition of quantum states that is necessary for processing quantum information. Yet quantum entanglement can, in fact, dominate the magnetic response of a solid-state system[5].

Rather than building gates between components in a conventional sense, it may be possible to take advantage of materials that have different microscopic environments, and which are tuned and addressable electronically, magnetically or optically. Following this strategy, disorder will be sought for its natural mix of physical parameters and length scales, permitting the development of flexible and easily scalable devices. ■

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