a human vaccine for Ebola virus? The short answer is no, not yet. For example, Sullivan *et al.* infected the monkeys with relatively small amounts of virus, equivalent in human terms to only a few nanolitres of blood from an infected person[7,8]. True, this amount of virus did lead to the deaths of the unvaccinated monkeys, but previous studies have shown that antibody preparations that protect against low doses of virus may be ineffective against higher doses[9,10]. It will be crucial to know whether the vaccine strategy can protect against more substantial challenge. Also, Sullivan *et al.* did not identify the immune mechanism of protection (antibody, cellular or both), and this may be important in guiding further vaccine development. Nevertheless, coupled with earlier findings that monkeys can be protected against high doses of Marburg virus by a vaccine based on a modified alphavirus construct[11], it seems hopeful that human vaccination against filoviruses will be achieved.

Who will benefit from a vaccine for Ebola or Marburg viruses? The obvious answer is the local population in an outbreak area, and the medical and support personnel travelling there. In reality, however, funds are likely in the first instance to be directed towards surveillance, hygiene and barrier-nursing methods, which can be highly effective in containing an outbreak[6]. An immediate benefit of a vaccine will be to increase the margin of safety for those studying the viruses, permitting more research into the control of infection. One such aspect of research is the search for the natural reservoirs of the filoviruses.

Finally, some have rightly raised concerns about the amount of effort spent studying Ebola and Marburg viruses, given that they affect relatively few people compared with the major pathogens in Africa, such as HIV and malaria. But our ability to predict developments in our struggle with microbes is limited. We may yet encounter more dangerous versions of the existing filoviruses, or even new ones. To be prepared, by learning how to control those viruses that are here now, is only prudent. ■

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Superconductivity

C_{60} — the hole story

Olle Gunnarsson

Superconductivity has been demonstrated at a surprisingly high temperature in a C_{60} solid, raising questions about its electronic properties and hopes of even higher temperatures to come.

The sudden drop in electrical resistivity at low temperatures that characterizes superconductivity was first seen in fullerenes such as C_{60} nearly a decade ago. By introducing electrons into the carbon lattice, fullerenes can become superconducting at temperatures up to 40 K. As reported by Schön *et al.* on page 549 of this issue[1], it turns out that superconductivity can be achieved at even higher temperatures if positively charged 'holes' are introduced instead of electrons.

Almost a century has passed since Kamerlingh Onnes unexpectedly discovered superconductivity when he noticed that mercury's resistivity abruptly dropped to zero at 4 K. Ever since then, this field has been an active area of research, resulting in two Nobel prizes in 1972 and 1987. Early ideas about conventional superconductivity culminated in a theory put forward by Bardeen, Cooper and Schrieffer (BCS) in 1957. In the BCS theory, the interaction of conduction electrons with tiny vibrations of the crystal lattice (phonons) leads to an attraction between the normally repulsive electrons so that they can pair up and flow without resistance.

Over the same period, experimentalists were searching for superconducting materials with higher transition temperatures, T_c, below which a material is superconducting. But progress was slow, and after a T_c of 23 K was reached in 1973, no further increase was achieved for 13 years (Fig. 1). This led to a lively discussion[2,3] about whether 23 K was close to some theoretical upper limit to T_c.

This all changed in 1986, when superconducting copper-oxide materials were discovered[4]. The maximum T_c was quickly pushed up to well over 100 K. Unlike most earlier superconductors, the copper oxides are normally insulators rather than conductors, and charge carriers have to be introduced into the material by chemical doping before they can become superconducting. It was soon accepted that superconductivity in the copper oxides is not primarily due to a phonon mechanism, as in conventional superconductors, but to an electronic mechanism, the nature of which is still under debate. So the high transition temperatures found for the copper oxides do not rule out the possibility of a maximum T_c for phonon-driven superconductors.

Coincidentally, in 1985, chemists discovered a new form of carbon[5] — known today as buckyballs or fullerenes. Like the copper oxides, crystalline C_{60} is normally an insulator, but can be made metallic by chemical doping. In normal C_{60} there are no charge carriers because the energy bands in its electronic structure are either completely filled or completely empty. To create a metal, the conduction band has to be partly filled with electrons (electron doping) or the valence band has to be partly emptied (hole doping). In 1991 it was found that adding alkali atoms to C_{60} crystals leads to charge transfer from the alkali atoms to C_{60} — that is, electron doping. Such alkali-doped compounds (A_3C_{60}) can become 'metallic'[6] and, at low temperatures, superconducting[7,8].

The superconductivity in A_3C_{60} is thought to be due to an interaction between electrons and phonons. The strength of this interaction is one of the factors that determine the value of T_c. Modifying the crystal

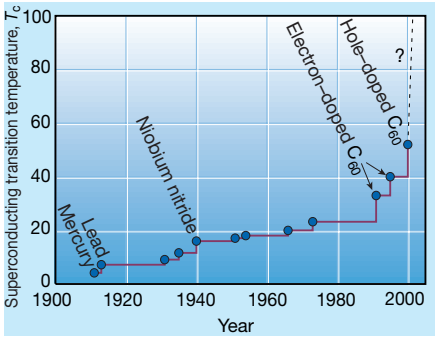

Figure 1 **The maximum transition temperature, T_c, for which superconductivity has been found in conventional superconductors over the past century. It is assumed that C_{60} superconductivity conforms to this standard phonon-driven mechanism, in which tiny lattice vibrations (phonons) provide the glue that binds electrons into superconducting pairs. Electron doping of C_{60} crystals, and now hole doping of C_{60} by Schön *et al.*[1], have allowed phonon-driven superconductors to reach much higher transition temperatures.**

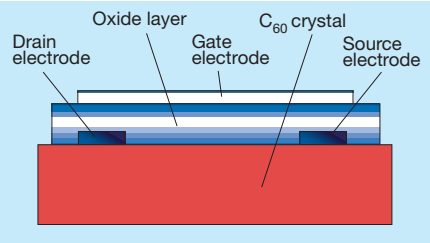

Figure 2 **The field-effect transistor configuration used by Schön *et al.*[1,11] to induce charge carriers into C_{60} crystals, changing them from insulators into superconductors.**

lattice by introducing larger alkali atoms increases the electron–phonon coupling as the lattice expands. In an expanded lattice, such as Cs_3C_{60} under pressure[9], T_c can reach 40 K. Surprisingly, Cs_3C_{60} at normal pressure is not superconducting, perhaps because of structural distortions or the closeness to a metal–insulator transition. Either way, it indicates that T_c cannot be increased further by expanding the lattice. In view of their success with electron-doped C_{60}, researchers are interested in hole-doping C_{60}, in particular because T_c is then predicted to be even higher[10]. But adding holes to C_{60} is very difficult, because C_{60} is strongly electronegative, so it has not yet been achieved by chemical doping.

Schön *et al.*[1] take a completely different approach to hole-doping C_{60}. They grow an oxide layer on the surface of a C_{60} crystal and place a gate electrode on top. By adding source and drain electrodes to the underlying crystal they create a field-effect transistor[11] (Fig. 2). Applying a voltage to the gate electrode induces charge in the surface layer of the crystal, doping the C_{60}. If the applied voltage is positive, electrons are induced; if the voltage is negative, holes are induced. An essential aspect of this approach is the authors' ability to make devices that can take electric fields large enough to induce several electrons or holes per C_{60} molecule. They can also vary the amount of doping by simply changing the gate voltage, thereby finding the optimal level of doping for a high T_c. In earlier work they induced superconductivity at a T_c of 10 K in an electron-doped C_{60} crystal[11]. In the present paper[1], they report a T_c of 52 K for hole-doped C_{60}.

A T_c of 52 K is very high for phonon-driven superconductivity — well above what had usually been thought possible. And with this technique, T_c may be increased even more. For electron-doped C_{60}, expansion of the crystal lattice increases T_c. With hole doping, however, T_c is already very large for the unaltered lattice structure, and its expansion, perhaps by incorporating inert molecules, could increase T_c substantially. Just as with electron-doped C_{60}, this approach would probably also fail for hole-doped systems if the lattice is expanded too much — for instance, the system could then become an insulator. But the ability to continuously change the doping, even to fractional numbers of charges per molecule, may allow T_c to be increased substantially before this happens.

This work opens up several interesting avenues. The possibility of comparing electron- and hole-doped C_{60}, and of varying the doping continuously, should improve our understanding of the electronic structure in C_{60} in general, and of superconductivity in C_{60} in particular. With Schön *et al.*'s field-effect transistor, only the outermost layer of C_{60} molecules is thought to be doped — the system is said to be quasi two-dimensional (2D). It will be interesting to compare this situation with chemically doped 3D systems, both in terms of the electronic behaviour and in terms of 2D versus 3D superconductivity. There may also be potential for making practical devices, because with this system it is possible to switch C_{60} between insulating and superconducting behaviour. For instance, one can imagine it being used as an ideal switch[11]. ■

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Evolutionary biology

The problem of variation

David L. Stern

One genetic source of the sex-specific variation in pigmentation patterns of different fruitfly species has been identified. This study illustrates the power of bringing together developmental and evolutionary biology.

Put simply, evolution is the result of natural selection promoting or eliminating particular heritable 'phenotypic' differences in a population, such as a behaviour or a physical characteristic. Over the past 150 years, many aspects of this process have been explored. But one factor in the equation has remained enigmatic — the source of the heritable phenotypic variation itself.

On page 553 of this issue[1], Kopp and colleagues illustrate how developmental genetics can help to solve this problem. Their first finding is interesting enough: they have identified a key genetic regulator of sex-specific differences in abdominal pigmentation in the fruitfly *Drosophila melanogaster*. Even more impressive, they show that changes in the regulation of this gene may have contributed to the variety of pigmentation patterns seen among different fruitfly species. Finally, they investigate how these findings relate to mating behaviour.

Nowadays it is thought that mutations in DNA sequences cause changes in phenotype. But it has proved difficult to identify evolutionarily relevant mutations — those that alter phenotypes and persist in natural populations. There are three core difficulties. First, the DNA regions that encode genes contain vast quantities of so-called neutral variations, which have no effect on either the phenotype or the fitness — the ability to survive and reproduce — of an organism.

Second, many evolutionarily relevant mutations may occur outside the protein-coding regions of genes. Genes can be divided roughly into the DNA sequence that codes for RNA, which may in turn be translated into protein, and regulatory regions, which encode instructions for regulating gene expression. These instructions are deciphered by DNA-binding proteins called transcription factors, which recognize specific DNA motifs and enhance or repress transcription. In doing so, they switch genes on or off in specific spatial and temporal patterns throughout development[2]. Although regulatory regions have a critical role in development, we still have a poor understanding of how their structure relates to their function. The third difficulty is that even dramatic evolutionary alterations in the DNA of regulatory regions can result in no change in function[3,4].

The upshot of all this is that many evolutionarily relevant changes in DNA sequences are probably buried within vast quantities of neutral variation, within both protein-coding sequences and poorly understood regulatory regions. Another obstacle to identifying evolutionarily relevant mutations is the paucity of experimental systems that allow physical variations to be related to DNA variations.

The new discipline of evolutionary developmental biology is ideally poised to tackle these problems, by applying the experimen-