

Figure 1 | Dietary restriction and longevity in *C. elegans*. Two studies^{1,2} show that, in response to dietary restriction, the activities of SKN-1 and PHA-4 gene-transcription factors increase (black arrows). Neuronal, but not intestinal, SKN-1 mediates longevity in response to reduced dietary intake, where it triggers the release of unidentified hormones (stars) from the pair of ASI neurons to increase mitochondrial activity throughout the body. The PHA-4 transcription factor may also induce hormonal production in the tissues where it is expressed — neurons, intestine and gonad.

mediating dietary restriction was unknown.

Bishop and Guarente (page 545)² discovered that a lack of SKN-1 abolishes dietary-restriction-induced longevity over a wide range of food concentrations. Again, the role of SKN-1 in mediating longevity through dietary restriction was specific, because its removal had little effect on lifespan enhanced through a reduction of insulin/IGF signalling. In adult worms, a different form of SKN-1 resides in the intestine from that found in the single pair of neurons known as the ASIs¹⁰. The authors found that the SKN-1 from the ASI neurons, and not from the intestine, was required for dietary-restriction-induced longevity (Fig. 1), and that restriction of dietary intake promoted increased SKN-1 expression specifically in these two cells. The ASIs are neurosensory cells that integrate cues from the environment and produce various hormones that are relayed to the whole body^{12,13}. This indicates that SKN-1-dependent hormonal signals that are released from the ASIs coordinate organism-wide physiological responses to dietary restriction.

Indeed, Bishop and Guarente² observed global metabolic changes in response to dietary-restriction-induced activation of *skn-1*, indicative of an organismal response. In particular, restricting dietary intake increased the rate of oxygen consumption — a marker of mitochondrial respiration — in a SKN-1-dependent manner. Mitochondria are the powerhouses of the cell, deriving cellular energy from various metabolites and consuming oxygen in the process. The authors found that, when mitochondrial activity was chemically inhibited, the beneficial effects of dietary restriction on survival were also abolished. Evidently, dietary restriction seems to increase mitochondrial activity, presumably to efficiently extract energy from a limited amount of food. How increased mitochondrial activity might promote longevity is not known. Conceivably, it may trigger mechanisms that protect cells against oxidative stress, or stimulate turnover of damaged cellular components.

Together, these findings^{1,2} indicate that dietary restriction activates a highly regulated process, rather than passive metabolic changes. A role for PHA-4 and SKN-1

transcription factors in mediating the effects of dietary restriction on longevity is exciting because, so far, only a handful of molecules have been described that regulate physiological responses to dietary restriction. Moreover, because *pha-4* and *skn-1* genes are evolutionarily conserved, similar mechanisms may hold in higher organisms.

These findings also raise a host of other questions. Although both PHA-4 and SKN-1 are required for dietary-restriction-induced longevity, neither is truly sufficient. Are other

factors involved? Must PHA-4 and SKN-1 work together? Moreover, what is the nature of the hormonal pathway that coordinates the effects of dietary restriction? Do the vertebrate counterparts of these transcription factors also have a role in regulating survival? Potentially, the answers to these questions may illuminate the path to increased human health and longevity.

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1. Panowski, S. H., Wolff, S., Aguilaniu, H., Durieux, J. & Dillin, A. *Nature* **447**, 550–555 (2007).
2. Bishop, N. A. & Guarente, L. *Nature* **447**, 545–549 (2007).
3. Horner, M. A. et al. *Genes Dev.* **12**, 1947–1952 (1998).
4. Kalb, J. M. et al. *Development* **125**, 2171–2180 (1998).
5. Friedman, J. R. & Kaestner, K. H. *Cell. Mol. Life Sci.* **63**, 2317–2328 (2006).
6. Kenyon, C. *Cell* **120**, 449–460 (2005).
7. Wolff, S. et al. *Cell* **124**, 1039–1053 (2006).
8. Zhang, L., Rubins, N. E., Ahima, R. S., Greenbaum, L. E. & Kaestner, K. H. *Cell Metab.* **2**, 141–148 (2005).
9. Bowerman, B., Eaton, B. A. & Priess, J. R. *Cell* **68**, 1061–1075 (1992).
10. An, J. H. & Blackwell, T. K. *Genes Dev.* **17**, 1882–1893 (2003).
11. Zhang, D. D. *Drug Metab. Rev.* **38**, 769–789 (2006).
12. Bargmann, C. I. & Horvitz, H. R. *Neuron* **7**, 729–742 (1991).
13. Li, C. *Parasitology* **131** (Suppl.), S109–S127 (2005).

HIGH-TEMPERATURE SUPERCONDUCTIVITY

Local pairs and small surfaces

Stephen R. Julian and Michael R. Norman

Mapping out the strange territory of high-temperature superconductors has proved a challenge. In the latest tour de force, two experiments take big steps forward, in complementary directions, to chart the lie of the land.

More than 20 years after they were first discovered, high-temperature superconductors remain fundamentally baffling. In superconductors, conduction without electrical resistance arises through the pairing of electrons so as to overcome obstacles to current flow. But whereas the better-understood 'conventional' superconductors confine their superconducting behaviour to temperatures within a few degrees of absolute zero, certain metallic oxides of copper conduct without electrical resistance at temperatures up to 150 kelvin. Two papers in this issue^{1,2} substantially advance our understanding of these bizarre materials. First, in a beautiful study, Doiron-Leyraud et al. (page 565)¹ describe the emergence of the classic signature of a metal, a Fermi surface, in a high-temperature superconductor. Second, Gomes et al. (page 569)² take the most probing look yet at what happens to the electron pairs at temperatures above the transition from the high-temperature superconducting state (Box 1, overleaf).

Doiron-Leyraud and colleagues' measurements¹ have an echo of the old-fashioned physics of metals; however, the small size of the Fermi surface they observe strongly suggests that entirely new physics is in play.

The Fermi surface is named after the Italian physicist Enrico Fermi, who in 1926 suggested that current-carrying electrons fill up available energy states in a metal rather like water fills a lake. The Fermi surface — a strange, often geometrically beautiful, structure that separates filled states from unfilled states in an abstract energy space known as *k*-space — is the shoreline of this lake. For simple metals, its size and shape depend only on the electron density and the crystal structure of the metal.

In the 1960s, the combination of measurements in high magnetic fields and computer-aided calculations allowed the Fermi surfaces of many metals to be mapped out. It became apparent that the existence of the Fermi surface explains more than just the universal features of metals, such as the dependence of their electrical resistance on temperature. Its detailed

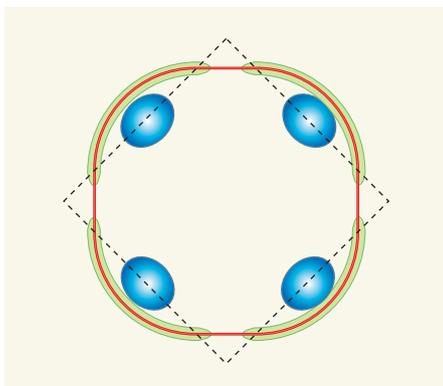


Figure 1 | Search for the Fermi surface. The Fermi surface is depicted in an abstract energy space known as *k*-space (here, a two-dimensional projection of the actual three-dimensional space), and maps out the areas of occupied electron energy states in a metal. The conventional theory of metals demands a large Fermi surface for high-temperature superconductors (red line), as indeed is found in overdoped cuprate samples, which have large numbers of charge carriers. For underdoped samples, the picture is more complex, with photoemission measurements indicating a Fermi surface of truncated 'arcs' (green). Alternatively, smaller 'pockets' (blue) might be centred along special lines in *k*-space (dotted black line). These pockets could emerge from hidden order that introduces an additional periodicity in the material's crystal structure. The enclosed areas of the arcs and the pockets have been adjusted to match the measurements of Doiron-Leyraud *et al.*¹ on their extremely pure yttrium barium copper oxide sample.

shape also accounts very precisely for other, decidedly non-universal, features, such as the dependence of the resistance on the magnetic field. This dependence can be upwards, downwards, oscillatory and even — in the so-called Hall effect — sideways, where a voltage arises at right angles to the direction of the current flow. In particular, the oscillatory Hall signal directly reflects the size of the Fermi surface.

Attempts in the early 1990s to see the Fermi surface in high-temperature superconductors by such means produced controversial sightings. As a consequence, newer techniques such as photoemission spectroscopy, in which light is used to 'knock' out the electrons, and so sketch out the Fermi surface, were drafted into the hunt. As these studies progressed, the supposed Fermi surface seemed to melt away. Gradually, the feeling emerged that perhaps there was no Fermi surface at all in high-temperature superconductors — a truly novel situation for metallic materials.

Doiron-Leyraud *et al.*¹ have dramatically changed the story with 'smoking gun' evidence for a Fermi surface in a high-temperature superconductor: the observation of a Hall resistance that oscillates up and down with increasing magnetic field. Such oscillations are quantum-mechanical in origin, and arise from the circular motion of a metal's electrons in a magnetic field. Observing them requires very pure samples. The sample used by

Doiron-Leyraud *et al.* is the result of 19 years' work on one family of cuprate superconductors, yttrium barium copper oxide³. This particular sample is special even by the standards of those efforts: it has what is known as an ortho-II structure, in which all the oxygen atoms in the crystal are found in a well-ordered superstructure.

So what can we learn from the appearance, after all this time, of a Fermi surface in a high-temperature superconductor? That depends on its origin, which is a debate likely to dominate the physics of cuprate superconductors in the immediate future. It cannot be the 'large' Fermi surface predicted by the conventional theory of metals: that would produce a much higher frequency of resistance oscillation with increasing magnetic field than is observed. Interestingly, such a large surface has been inferred from photoemission spectroscopy⁴ and magneto-transport measurements⁵, but only in 'overdoped' cuprates, which have much higher densities of charge carriers and seem to behave more like conventional metals. Owing to its peculiar crystal structure, an underdoped ortho-II sample such as that investigated by Doiron-Leyraud and colleagues¹ wouldn't necessarily have a simple, large Fermi surface. But even the more complicated Fermi surface predicted for the ortho-II cuprate⁶ doesn't seem to fit these new experimental observations.

The authors' oscillation measurements tell us the size of the Fermi surface, but not where it is in *k*-space. Because of that, there is a degree of latitude in the physical interpretations of the results. Photoemission results⁷ indicate

that, in underdoped cuprates, the large Fermi surface found in overdoped samples breaks up into 'arcs' — one of the many novel features of underdoped cuprates that are associated with the presence of a so-called 'pseudogap'. One suggestion made by the authors is that these arcs form small pockets that constitute an enclosed Fermi surface of the observed size (Fig. 1). Alternatively, 'hidden order' associated with the pseudogap might introduce an additional periodicity in the material and cause the large Fermi surface to break up into smaller pockets⁸. A further suggestion is that these small pockets might be a natural consequence of underdoped cuprates also being lightly doped insulators. Finally, a small surface could arise from some unknown physical mechanism in which the magnetic field quenches the long-range order, but local superconductivity persists.

A surprising feature of Doiron-Leyraud and colleagues' measurements¹ is that the oscillatory signal occurred in a Hall resistance that had a negative sign. This is 'wrong' according to conventional ideas: the Hall coefficient is expected to be positive, because carriers are induced in the cuprates by removing electrons. The negative Hall coefficient might be associated with local superconducting vortices that persist in magnetic fields far above that where the resistance becomes finite⁹. But perhaps, as with so many other aspects of cuprate physics, there is something really novel going on that we haven't yet imagined. Certainly, the understanding of how the quantum oscillations of the newly discovered Fermi surface arise will

Box 1 | Breaking up is hard to do

The idea that matter changes phase with rising temperature is familiar: we all know how a solid melts to a liquid when its temperature increases. A similar 'melting' process occurs in superconductors and magnets. One of the many conundrums posed by high-temperature superconductors is how exactly the phase transition out of the superconducting state occurs.

In one important respect, the conventional superconducting and magnetic phases represent opposite ends of a spectrum of phase transitions. When the temperature of a material goes above that at which the macroscopic consequences of magnetism disappear, the atomic moments do not disappear, but are just no longer aligned with one another. The individual moments disappear only at a much higher temperature. In virtually all

superconductors, by contrast, the electron pairs thought to be responsible for superconductivity break up at the same critical temperature at which the macroscopic behaviour of zero resistance disappears.

But high-temperature superconductors, it seems, are intermediate between these two limits of phase-transition behaviour. The persistence of pairs in such superconductors above the superconducting transition temperature has been inferred using various probes. But most of these probes are spatially averaged, and how the pairs break up on a local scale as the temperature rises was unknown.

In a novel experiment reported in this issue, Gomes *et al.* (page 569)² used a scanning tunnelling probe to follow the pairing process in a cuprate high-temperature superconductor. This proved

a challenge, because the thermal vibrations of the probe tip make it difficult for it to remain focused on a single atom. The authors found that the local gap in the superconductor's allowed energy states caused by electron pairing disappeared at a temperature at which the thermal energy was equivalent to a quarter of the size of the local energy gap at absolute zero temperature.

The larger the gap, therefore, the higher the temperature at which the gap persists — in many cases, well above the temperature at which the superconducting behaviour of the bulk material ceases. These measurements clearly imply that at least some of the unusual normal-state properties of the cuprates above their superconducting transition temperature are due to the survival of pairs. Indeed, breaking up is never easy. **S.R.J. & M.R.N.**

be pivotal to solving the mystery of high-temperature superconductivity. ■

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1. Doiron-Leyraud, N. *et al. Nature* **447**, 565–568 (2007).
2. Gomes, K. K. *et al. Nature* **447**, 569–572 (2007).
3. Liang, R., Bonn, D. A. & Hardy, W. N. *Physica C* **336**, 57–62 (2000).
4. Damescelli, A., Hussain, Z. & Shen, Z.-X. *Rev. Mod. Phys.* **75**, 473–541 (2003).
5. Hussey, N. E. *et al. Nature* **425**, 814–817 (2003).
6. Bascones, E. *et al. Phys. Rev. B* **71**, 012505 (2005).
7. Norman, M. R. *et al. Nature* **392**, 157–160 (1998).
8. Chakravarty, S. *et al. Phys. Rev. B* **63**, 094503 (2001).
9. Xu, Z. A. *et al. Nature* **406**, 486–488 (2000).

EVOLUTIONARY BIOLOGY

Animal personalities

Alison M. Bell

That different people differ in their readiness to take risks is an obvious feature of human personality. Theoretical advances now help in making sense of observations of analogous behaviour in animals.

Personality might seem to require a complexity and subtlety that is unique to humans. But evidence for individual variation in traits that we would recognize as personality, for example aggressiveness in fighting or boldness in the face of a predator, has cropped up in animals ranging from fish to monkeys to squid. Even an individual spider behaves differently from other spiders, through time and in different situations¹. Wolf *et al.* (page 581 of this issue²) now show how such variation in behaviour can make evolutionary sense.

Personality has been difficult to explain from an evolutionary perspective because, at first glance, it could seem maladaptive³. An individual that is consistently uninhibited and bold is going to end up eaten by a predator. The optimal animal should be bold only when it makes sense to be bold, and adjust its behaviour when the situation changes. Although animals are legendary for their remarkable 'behavioural plasticity' (think migration or camouflage, for example), there is growing evidence that animals do not always change their behaviour as much as they should. In other words, behavioural plasticity is limited³.

One possible explanation for this is that individuals should behave consistently if it's simply too hard to undergo a personality transformation. If turning off a general tendency to be aggressive requires time and energy to entirely rewire neural machinery, or to build a physiology that can support a different metabolism, then individuals might be better off sticking to an intermediate strategy⁴. Similarly, if information about the immediate environment is uncertain, then it makes sense just to behave the same way and avoid the risk of making a mistake⁵.

This line of reasoning can help to explain why a given individual behaves consistently, but not, for example, why some individuals are always more aggressive than others. Such

variation is puzzling, because natural selection will favour individuals with characteristics that perform the best, and less 'fit' individuals will be removed from the population. If a trait is heritable and linked to survival or reproductive success, then evolutionary theory tells us that variation will eventually disappear from the population. But, empirically, we know that personality traits are heritable⁶, are linked to fitness⁷ and are quite variable.

So how is all this behavioural variation maintained? One way is if the fitness of one strategy depends on the frequency of other strategies in the population^{8,9}. Imagine, for example, a group composed entirely of individuals that accumulate resources by guarding them — territorial male birds, for example. An individual using a different strategy — say, dashing in to sneak the resource while a guard is otherwise occupied — would do well in that situation (so long as it is rare), because it would effectively occupy an 'open niche', devoid of competitors.

Alternatively, behavioural variation can be maintained if the best strategy depends on an individual's 'state', which effectively anchors a personality type⁸. This state can be anything from sex or health to body size, and the idea is that an individual should behave consistently so long as its state does not change. This explanation leaves the question of what maintains variation in state.

Wolf *et al.*² offer an answer by proposing that an individual's strategy for survival and reproduction — its life-history strategy — is a relatively unchanging state (unlike hunger level, for example), and that individuals adopt different life-history strategies because of fitness trade-offs. Any behaviour that is related to a life-history strategy will be stable through time and differ between individuals with different strategies.

The authors' model starts by assuming that an individual can either reproduce now, but



50 YEARS AGO

"Incorporation of radioactive amino-acids in the proteins of bull spermatozoa" — It is widely held that ribonucleic acid is directly involved in protein synthesis, and there have been several recent demonstrations of the necessity for the presence of ribonucleic acid during synthesis of proteins. In view of this, it seemed to be of interest to examine protein turnover in mature, ejaculated spermatozoa, which apparently contain at most only traces of ribonucleic acid... The absence of the acid from bull semen has been confirmed in the present investigation... It is possible that in this case deoxyribonucleic acid may be involved in the synthesis of proteins... The other possibility would be to regard protein synthesis in spermatozoa as an enzymatic process independent of nucleic acids.

From *Nature* 1 June 1957.

100 YEARS AGO

Mr. Walter Wellman, who proposes to make another attempt to reach the North Pole by means of his airship *America*, has left for Norway, on the way to Spitsbergen, where the balloon will be inflated. In the first week of July there will be trials of the airship until it is demonstrated that it is ready for the voyage... Mr. Wellman has given Reuter's representative the following particulars of his plans:— The airship has been made 18 feet longer and its lifting power increased by 3000 lb., giving a total lifting force of 19,500 lb. The balloon is 184 feet long and 52 feet in its greatest diameter, its cubic volume being 265,000 cubic feet. With the single exception of Count Zeppelin's airship, this is the largest ever built... The total radius of action is believed to be 2500 miles, or double the distance from the base to the Pole and back again. The balloon will not ascend more than 300 feet to 500 feet, and a guide-rope will trail over the surface of the earth.

From *Nature* 30 May 1907.

50 & 100 YEARS AGO