

the absence of a functional VNO (as in *Trpc2*-deficient females), even low, female-typical levels of testosterone may suffice to permit high levels of male-typical behaviour.

Regardless of the mechanism involved, however, it seems that one or more male pheromones inhibit mice from mounting other male mice, and elicit aggressive behaviour in males. So when male or female mice cannot distinguish between the sexes, they initiate male-typical mating routines towards all conspecifics, presumably using pheromonal cues sensed by the MOE<sup>5-8</sup> (Fig. 1).

What does the work of Kimchi *et al.*, taken together with previous findings, tell us about the functional role of structural differences in the brain? As females can display male-type mating patterns, it seems unlikely that gender-specific effectors of mating patterns lie in neural structures that differ between the sexes, such as the medial amygdala, which integrates olfactory and pheromonal information, and the medial preoptic nucleus in the hypothalamus<sup>11,10</sup>. It is more likely that these sexually dimorphic regions are responsible for sex-specific changes in neural activity evoked by pheromones (Fig. 1). Such areas could also be where steroid hormones modulate the strength of male- or female-specific routines of sexual behaviour. Indeed most, if not all, of the sexually dimorphic structures in the brain express receptors for gonadal steroid hormones<sup>10</sup>. Perhaps such structures influence only those behavioural patterns, such as inter-male aggression and female sexual receptivity, that seem to be more robustly limited to one sex. Whatever the answer, the latest results suggest that sexual differentiation of neural circuits engaged by the VNO are crucial for the gender-typical display of behaviour in rodents.

Do Kimchi and colleagues' findings hold true for other organisms? Studies in the fruitfly *Drosophila* have shown that female flies genetically modified to express a male-specific messenger RNA — *fruitless<sup>M</sup>* (*fru<sup>M</sup>*) — engage in male-type courtship rituals with flies of either sex<sup>11-13</sup>. It is not known, however, whether the *fru<sup>M</sup>* protein confers male courtship capacity on a female when it is present only in adulthood. This protein is expressed in several sensory structures and neuronal groups in the fruitfly brain, and probably influences male courtship behaviour at many levels. Nevertheless, as Kimchi *et al.* have found in mice, sexual behaviour in fruitflies seems to be governed by simple rules, with sensory information activating either male- or female-typical mating circuits<sup>14,15</sup>. Whether such simple rules dictate affairs of the human heart remains to be seen. ■

Nirao M. Shah is in the Department of Anatomy, University of California, San Francisco, 1550 4th Street, MC2722, San Francisco, California 94158, USA. S. Marc Breedlove is in the Neuroscience Program, Michigan State University, 108 Giltner Hall, East Lansing, Michigan 48824, USA.

e-mails: nms@ucsf.edu; breedsms@msu.edu

- Morris, J. A., Jordan, C. L. & Breedlove S. M. *Nature Neurosci.* **7**, 1034-1039 (2004).
- Kimchi, T., Xu, J. & Dulac, C. *Nature* **488**, 1009-1014 (2007).
- Edwards, D. A. & Burge, K. G. *Horm. Behav.* **2**, 49-58 (1971).
- Axel, R. *Sci. Am.* **273**, 154-159 (1995).
- Mandiyani, V. S., Coats, J. K. & Shah, N. M. *Nature Neurosci.* **8**, 1660-1662 (2005).
- Yoon, H., Enquist, L. W. & Dulac, C. *Cell* **123**, 669-682 (2005).
- Leypold, B. G. *et al. Proc. Natl Acad. Sci. USA* **99**, 6376-6381 (2002).
- Stowers, L., Holy, T. E., Meister, M., Dulac, C. & Koentges, G. *Science* **295**, 1493-1500 (2002).
- Phoenix, C. H., Goy, R. W., Gerall, A. A. & Young, W. C. *Endocrinology* **65**, 369-382 (1959).
- Shah, N. M. *et al. Neuron* **43**, 313-319 (2004).
- Demir, E. & Dickson, B. J. *Cell* **121**, 785-794 (2005).
- Stockinger, P. *et al. Cell* **121**, 795-807 (2005).
- Manoli, D. S. *et al. Nature* **436**, 395-400 (2005).
- Ejima, A. *et al. Curr. Biol.* **17**, 599-605 (2007).
- Kurtovic, A., Widmer, A. & Dickson, B. J. *Nature* **446**, 542-546 (2007).

## THEORETICAL PHYSICS

# A black hole full of answers

Jan Zaanen

**A facet of string theory, the currently favoured route to a 'theory of everything', might help to explain some properties of exotic matter phases — such as some peculiarities of high-temperature superconductors.**

How are heat and charge transported within a high-temperature superconductor? And what happens when heavy nuclei are torn apart to make the soup of elementary particles known as a quark-gluon plasma? In a paper published on the *arXiv* preprint server, Hartnoll *et al.*<sup>1</sup> show convincingly that the easiest insight into the superconductor problem, just as into the quark-gluon plasma<sup>2,3</sup>, is to be had by looking at a black hole. Not any old black hole, of course, but a black hole in a negatively curved space-time with an extra dimension (Fig. 1).

What might sound like a theoretical physicist's idea of a bad joke could, in fact, be history in the making. The context is a highlight of string theory known as the anti-de-Sitter space/conformal field theory correspondence<sup>4</sup> — AdS/CFT for short — which demonstrates an intimate connection between Einstein's general theory of relativity and quantum physics. That it might also find use in such far-flung fields as superconductivity and the quark-gluon plasma is the stuff of physicists' dreams — the unifying power of physical laws as formulated in the language of mathematics.

Viewed as a whole, string theory amounts to a head-on attack on the incompatibility of general relativity and quantum theory, the two greatest accomplishments of twentieth-century physics. According to general relativity, space and time are dynamic entities, linked to matter and energy. By contrast, quantum physics tells us how matter and energy behave, but can only be formulated in a frozen space-time.

String theory is a collection of mathematical discoveries that might just offer a solution to this puzzle. But it has had a bad press of late. This is in part because its 40-year history is littered with claims that, if only we would stick to its true path of enlightenment, the answers to the big questions of physics would be just around the corner. Its failure to deliver on those promises and produce, so far, anything of con-

sequence to experiment has become rather an embarrassment.

The AdS/CFT correspondence is a case in point. It is a fascinating mathematical result, uncovered by the Argentinian physicist Juan Martín Maldacena in 1997, but had seemed unrelated to anything that happens in or outside the laboratory. The correspondence predicts a universe governed solely by gravity, being in this regard rather like ours, with stars, black holes and all the other familiar trappings. The difference is that it has an extra, fourth spatial dimension (plus the normal one time dimension) and a negative (anti-de-Sitter) overall curvature, so forming a universe closed in on itself.

As it turns out, this world corresponds precisely to a non-gravitating universe of just three spatial dimensions filled with something similar to the quantum fields that describe the elementary particles in the standard model of particle physics. Thus, general relativity and quantum-field theory seem to be embedded deep inside the same structure. But try as they might, string theorists have not been able to find an AdS/CFT-like theory that impinges directly on the world we live in. Until now, that is.

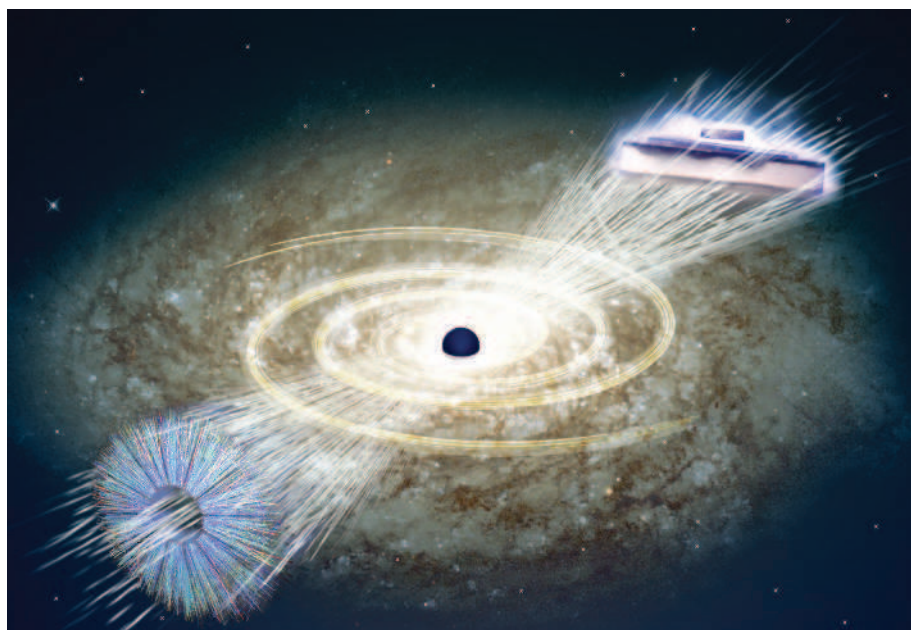
Hartnoll *et al.*<sup>1</sup> use the AdS/CFT correspondence to illuminate the real-life problem of how heat and charge currents flow in a 'quantum liquid' of electrons. These quantum liquids are found in the metallic state of copper oxide (cuprate) superconductors above the transition temperature ( $T_c$ ) below which they become superconducting (which is generally around 100 kelvin). In terms of quantum mechanics, these liquids are strange beasts. Somehow, the electrons manage to organize themselves in a quantum critical state, meaning that their collective quantum physics becomes scale-invariant — it looks the same, regardless of the time- and length-scales over which one observes the system<sup>5</sup>. High-temperature

superconductivity below the transition temperature is commonly believed to have something to do with this enigmatic, normally conducting state, in which quantum and thermal fluctuations merge.

Although they are in all other regards vastly different, the quantum fields that pop up in the AdS/CFT correspondence share the quantum-critical (or 'conformal'; the C in CFT) property with this quantum-thermal brew. The scale invariance they share is a mighty principle; in fact, it is so powerful that the many differences between the two types of field don't matter. It was thus shown in 2001 that at energies small compared with the temperature, the transport properties of a substance containing a conformal quantum field relate mathematically through the AdS/CFT correspondence to the geometry of a black hole in anti-de-Sitter space<sup>2</sup>. This makes it possible to derive the equations describing transport in the quantum-thermal critical brew in a few easy lines, instead of the pages of algebra that one encounters in the direct evaluation of quantum field theory of the type that one finds, for example, in superconductivity<sup>6</sup>.

Hartnoll *et al.*<sup>1</sup> push what one might term the 'AdS-to-high- $T_c$  correspondence' to its logical conclusion. They study its application to a particular, rather recondite transport phenomenon known as the Nernst effect — the crosswise flow of heat and charge currents in the presence of a magnetic field<sup>7</sup> — in the nearly quantum-critical matter of a two-dimensional cuprate system. In a theoretical *tour de force*, they use the physics of a black hole in a three-dimensional anti-de-Sitter space that carries both electrical and magnetic charge to guide them in the very complex derivation of the relevant transport equations directly from quantum field theory. They show that these theoretical results are seemingly consistent with a number of hitherto unexplained features of the Nernst effect in a high-temperature superconductor<sup>7</sup>.

So where does the quark-gluon plasma fit in? Here, the AdS/CFT correspondence



**Figure 1 | The answer's out there.** The easiest path to enlightenment on the mysterious phenomena of superconduction (levitating magnets; top right) and the quark-gluon plasma (bottom left; an event display from the Relativistic Heavy-Ion Collider at Brookhaven National Laboratory) leads through a black hole, say Hartnoll and colleagues<sup>1</sup>.

comes to the aid of the experimentalists in a similar way<sup>3</sup>. The background is the observation that quark-gluon fireballs, as have been created in the Relativistic Heavy-Ion Collider at Brookhaven National Laboratory on Long Island, behave in a remarkably simple way, but one that current theories find difficult to explain — they are governed by normal hydrodynamics, but have extremely low viscosity. Quite simply, the AdS/CFT correspondence tells us that when the quantum physics is scale invariant, the viscosity of such a system can be as small as it is. This result is far from obvious given our current understanding of quantum chromodynamics, the standard-model quantum-field theory of the strong nuclear force that governs interactions in the quark-gluon plasma.

So what does this mean for the greater ambition of using string theory to unite gravity and

quantum physics? I personally take the discovery that black holes are so useful for sorting out the behaviour of real-life quantum systems as a signal that string theory might somehow be on the right track. But only further work like that of Hartnoll *et al.*<sup>1</sup> will confirm that hunch. ■

Jan Zaanen is at the Instituut-Lorentz, Universiteit Leiden, PO Box 9506, 2300 RA Leiden, the Netherlands.

e-mail: jan@lorentz.leidenuniv.nl

- Hartnoll, S. A., Kovtun, P. K., Mueller, M. & Sachdev, S. Preprint at <<http://arxiv.org/abs/0706.3215>> (2007).
- Policastro, G., Son, D. T. & Starinets, A. O. *Phys. Rev. Lett.* **87**, 081601 (2001).
- Riordan, M. & Zajc, W. A. *Sci. Am.* **294** (5), 24–31 (2006).
- Maldacena, J. *Sci. Am.* **293** (5), 33–39 (2005).
- van der Marel, D. *et al. Nature* **425**, 271–274 (2003).
- Herzog, C. P., Kovtun, P., Sachdev, S. & Son, D. T. *Phys. Rev. D* **75**, 085020 (2007).
- Wang, Y., Li, L. & Ong, N. P. *Phys. Rev. B* **73**, 024510 (2006).

## MOLECULAR BIOLOGY

# Damage control

Claus M. Azzalin and Joachim Lingner

**The chemical composition of normal DNA at the end of chromosomes does not differ from that of damaged and broken DNA within chromosomes. New findings hint at how the DNA-repair machinery distinguishes the two.**

The maintenance of genome integrity is crucial for the survival of every organism. So even a single break along a chromosome triggers a molecular signalling cascade that leads to an appropriate DNA-damage response (DDR). This response allows recognition of the damage site and decelerates cell-cycle

progression, giving the cell a chance to repair the damage<sup>1</sup>. Theoretically, the two free ends of each eukaryotic linear chromosome — telomeres — should evoke a similar cellular response. However, as long as they are intact, telomeres activate DDR only transiently, if at all, at defined stages of the cell cycle. In a paper

published on page 1068 of this issue, Lazzarini Denchi and de Lange<sup>2</sup> provide clues on how this is achieved at a molecular level.

Telomeres consist of serial repeats of nucleotides terminating in a 3' protruding, single-stranded sequence. Telomeric DNA associates with a six-protein complex known as shelterin<sup>3</sup>, which shelters the DNA from recognition by the DDR pathways as sites of damage. Lazzarini Denchi and de Lange show<sup>2</sup> that two of the shelterin proteins, TRF2 and POT1, independently repress the two main DDR pathways, which are normally induced by damage to DNA sequences within chromosomes.

In most cells, telomeres progressively erode as cells go through successive cycles of division; this is because of incomplete replication