affinity for methylated histone tails is a general feature of PHD fingers, because Shi *et al.* (page 96)[2] observe that the PHD fingers of the tumour-suppressor protein ING2 (for 'inhibitor of growth') and those of related proteins interact preferentially with methylated lysine 4 of histone H3. However, whereas the recruitment of NURF or CHD1 leads to gene activation, when ING2 is recruited it brings with it a histone deacetylase (HDAC) that removes nearby acetylation marks, triggering a closed chromatin structure in which the genes are repressed. ING2 inhibits cell proliferation when genomic DNA is damaged, so Shi *et al.* examined the effects of DNA damage on the interaction of ING2 with chromatin. Experimental DNA damage led to binding of the ING2–HDAC complex to the regulatory region of the gene encoding cyclin D1, a major inducer of cell proliferation, and the expression of this gene was repressed.

BPTF and ING2 interact preferentially with nucleosomes methylated at lysine 4 *in vitro* and will not bind to nucleosomes methylated at lysine 9. The molecular basis for this selectivity is clearly illustrated by the structures of the PHD fingers of these proteins in complex with the methylated peptides. These structures have been determined by Li *et al.* (page 91)[3] and Peña *et al.* (page 100)[4]. The PHD fingers form surface pockets that precisely accommodate a short region of the H3 tail, including methylated lysine 4, but not an analogous segment surrounding methylated lysine 9. A common principle of all methyl recognition events is the presence of two to four aromatic amino acids that form a hydrophobic environment[3,4,10]. Variations in PHD finger structure allow other methylated peptides to be accommodated. For example, the PHD finger of the nucleosome remodeller Mi2 interacts preferentially with H3 tails methylated at lysine 36 (ref. 2).

Those who had hoped for a clear-cut set of rules governing the recognition and interpretation of methyl marks — a 'histone code' — will be disappointed by the embarrassment of riches uncovered by the latest reports. Given the multitude of potential interactors that bring about diverse functional consequences, and the relative weakness of histone-tail interactions, it is clear that histone methylation alone cannot specify the selectivity of nucleosome interactions observed *in vivo*. Additional specificity could be provided by combinations of histone modifications that may be recognized by corresponding combinations of interacting domains. For example, the PHD finger of BPTF may cooperate with a neighbouring bromodomain in docking with a combined methyl–acetyl mark[3] (Fig. 1c). On the other hand, alternative recruitment strategies involving sequence-specific DNA-binding proteins are known for all the regulators mentioned here. So it is likely that histone methylation marks are not the primary targeting determinants, but rather contribute to the stabilization or concentration of factors once they have been targeted to a certain chromatin neighbourhood (Fig. 1a, b).

We have only just begun to unravel the pathways towards chromatin opening that integrate the various writers and interpreters of histone modification marks[10,12]. Decoding the information hidden in the chromatin wrapping promises to reveal the instructions for how the packaged genetic information is to be used. ■

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1. Wysocka, J. *et al. Nature* **442,** 86–90 (2006).
2. Shi, X. *et al. Nature* **442,** 96–99 (2006).
3. Li, H. *et al. Nature* **442,** 91–95 (2006).
4. Peña, P. V. *et al. Nature* **442,** 100–103 (2006).
5. Schreiber, S. L. & Bernstein, B. E. *Cell* **111,** 771–778 (2002).
6. Turner, B. M. *Cell* **111,** 285–291 (2002).
7. Sims, R. J. III *et al. J. Biol. Chem.* **280,** 41789–41792 (2005).
8. Pray-Grant, M. G., Daniel, J. A., Schieltz, D., Yates, J. R. III & Grant, P. A. *Nature* **433,** 434–438 (2005).
9. Flanagan, J. F. *et al. Nature* **438,** 1181–1185 (2005).
10. Huang, Y., Fang, J., Bedford, M. T., Zhang, Y. & Xu, R. M. *Science* **312,** 748–751 (2006).
11. Bienz, M. *Trends Biochem. Sci.* **31,** 35–40 (2006).
12. Wysocka, J. *et al. Cell* **121,** 859–872 (2005).

CONDENSED-MATTER PHYSICS

Superfluidity in the picture

J. E. Thomas

Strongly interacting atomic Fermi gases — useful models for many other exotic forms of matter — enter a superfluid state at low temperatures. The first direct observation of that transition has been made.

Fermions are the building-blocks of the Universe. Strongly interacting gases of these particles make up atomic nuclei, the matter in neutron stars and the quark–gluon plasma of the Big Bang. These systems differ greatly in size and energy but have a lot in common; knowledge of one system therefore illuminates our understanding of the others.

On page 54 of this issue, Zwierlein *et al.*[1] present direct observations of a superfluid phase in one such system — a gas of strongly interacting Fermi atoms — and also determine the temperature of the gas directly. Such atomic gases have been the subject of intensive study[2–5], as they are particularly easy to create and control in a laboratory environment. Although it is accepted that these atoms have been cooled down to an intriguing type of superfluid state, a direct observation of this transition, similar to the formation of ice from freezing water, has been elusive.

The classification of fundamental particles into fermions and bosons depends on their internal rotation, or spin. Spin is a quantized property; that is, it can only take on certain discrete values. If a particle's spin is a half-integer multiple of Planck's constant *h* divided by 2π, it is a fermion. The familiar atomic building-blocks — the electron, neutron and proton — are all fermions. Spin can point 'up' or 'down', and fermions obey the Pauli exclusion principle, which permits at most one spin-up and one spin-down particle in each quantum energy level. This explains the way in which electrons are observed to fill up the energy levels in atoms, two by two.

Bosons, on the other hand — particles of whole-integer spin — experience no such restriction. Composite particles (atoms, for example) that are built out of an even number of fermions are bosons, while those containing an odd number of fermions are fermions. So whereas a gas of atomic fermions stacks up in the energy levels in a ladder-like fashion, with at most one spin-up and one spin-down atom on each rung, all the atoms in an ultracold gas of bosons can condense into the lowest quantum energy state: the superfluid state of matter

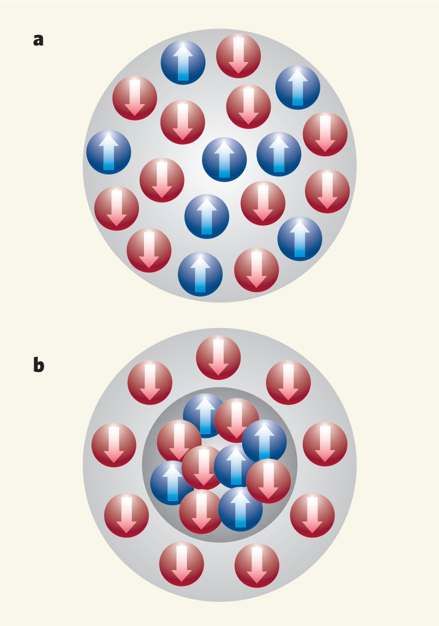

Figure 1 | Changing shape. a, A homogeneous state of an unequal number of spin-up and spin-down atoms, such as that prepared by Zwierlein *et al.*[1]. **b,** As the gas temperature is lowered past a critical value, a phase transition occurs. A superfluid state forms in the centre of the gas with spin-up and spin-down atoms paired and equal in number, and the excess unpaired atoms move to outside the central core.

known as a Bose–Einstein condensate. For fermions, this is generally not possible, but this situation changes dramatically when spin-up and spin-down particles attract each other. Then, at sufficiently low temperature, fermions of opposite spin can pair to form composite bosonic objects, and a superfluid that flows without friction is also produced in this case.

In metals, the pairing of spin-up and spin-down electrons produces a superconducting superfluid, in which electric current can flow without resistance. If the strength of the pairing between the electrons is weak, and the pairing energy is a small fraction of the electrons' total energy, this superconducting transition occurs at very low temperatures (below the boiling point of helium at 4.22 K), and thus is useful only in a laboratory environment. A strong pairing, by contrast, can produce a transition at high temperature. Super-high-temperature superconductors that would operate at temperatures well above room temperature would enable lossless power transmission, magnetic levitation and more efficient communication. The interest in developing such materials is understandably great.

Remarkably, certain atomic Fermi gases at temperatures of a fraction of a millionth of a degree above absolute zero provide a model system for testing the theory of such high-temperature superconductors, because the pairing energy of their atoms is a large fraction of the fluid's total energy — in fact larger than that in any existing superconductor. Such gases have a feature known as a Feshbach resonance, near which the strength of the interactions between spin-up and spin-down atoms can be tuned over a wide range simply by applying a magnetic field. At resonance, the attractive interaction between atoms is so strong that the gas flows like a high-temperature superfluid, modelling the movement of electrons in a superconductor that would work even at temperatures of thousands of degrees. Many experiments, including measurements of pair condensation[6,7], collective oscillation modes[8,9], pairing energy[10], heat capacity[11] and, most recently, vortices that signal superfluid flow[12] have established that the transition to a superfluid phase occurs. But until now, the direct signature of the transition that would be given by a change in shape of the atomic cloud had not been observed.

Zwierlein and colleagues' proof[1] of that change comes from a mixture of fermionic lithium-6 atoms in which the number of spin-up and spin-down atoms is unequal[13,14]. At temperatures above a critical value, the trapped mixture remains homogeneous, with a uniform distribution of both spin-up and spin-down particles across the trapped mixture (Fig. 1a). As the temperature is lowered, however, the gas cloud suddenly makes a transition to an energetically more favourable shape. A higher-density central 'bump' forms that contains nominally equal numbers of paired spin-up and spin-down atoms, while the excess of the majority spin component moves to the outside (Fig. 1b).

This abrupt change is interpreted as a phase transition, analogous to the formation of ice in water when cooled to below its freezing point. When the gas is rotated, vortices form in the central region. Such vortices require perfect hydrodynamic flow, so their appearance is a sure sign that this region is a superfluid.

The majority spin component in the outside region brings an added benefit: it functions as a thermometer for the gas. When the trap initially confining the atoms is turned off, this pure component expands ballistically. That enables precise measurement of the velocity distribution of the atoms, which in turn is a measure of the temperature of the gas. As most thermodynamic quantities depend on temperature, this provides a valuable experimental check on theoretical models.

With precise control of spin populations and precision thermometry, the experiments open up new territory for modelling some of the most fundamental processes in the Universe, including superfluidity in neutron stars, hydrodynamics in a quark–gluon plasma and string-theory predictions of minimum viscosity in any generalized system. ■

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1. Zwierlein, M. W., Schunck, C. H., Schirotzek, A. & Ketterle, W. *Nature* **442,** 54–58 (2006).
2. O'Hara, K. M., Hemmer, S. L., Gehm, M. E., Granade, S. R. & Thomas, J. E. *Science* **298,** 2179–2182 (2002).
3. Thomas, J. E. & Gehm, M. E. *Am. Sci.* **92,** 238–245 (2004).
4. Kinast, J., Turlapov, A. & Thomas, J. E. *Opt. Phot. News* **16,** 21 (2005).
5. Chevy, F. & Salomon, C. *Phys. World* **18,** 43–47 (2005).
6. Regal, C. A., Greiner, M. & Jin, D. S. *Phys. Rev. Lett.* **92,** 040403 (2004).
7. Zwierlein, M. W. *et al. Phys. Rev. Lett.* **92,** 120403 (2004).
8. Kinast, J., Hemmer, S. L., Gehm, M. E., Turlapov, A. & Thomas, J. E. *Phys. Rev. Lett.* **92,** 150402 (2004).
9. Bartenstein, M. *et al. Phys. Rev. Lett.* **92,** 203201 (2004).
10. Chin, C. *et al. Science* **305,** 1128–1130 (2004).
11. Kinast, J. *et al. Science* **307,** 1296–1299 (2005).
12. Zwierlein, M. W., Abo-Shaeer, J. R., Schirotzek, A., Schunck, C. H. & Ketterle, W. *Nature* **435,** 1047–1051 (2005).
13. Partridge, G. B., Li, W., Kamar, R. I., Liao, Y. & Hulet, R. G. *Science* **311,** 503–505 (2006).
14. Zwierlein, M. W., Schunck, C. H., Stan, C. A., Raupach, S. M. F. & Ketterle, W. *Science* **311,** 492–496 (2006).

VIROLOGY

Micro mystery solution

Bill Sugden

A particular talent of herpes simplex virus-1 is that it can lurk unseen in the cells of an infected person for long periods. It turns out that the virus achieves this feat through the agency of a microRNA.

Herpes simplex virus-1 (HSV-1) infects most of us but then stays hidden for most of our lives. When it does re-emerge, the virus usually causes cold sores; its close cousin, HSV-2, can likewise hide, then re-emerge to cause distressing and painful genital sores. How these viruses stay hidden in the face of a vigorous immune response is a mystery that has yielded only fitfully to investigation. Nigel Fraser and his colleagues (page 82 of this issue)[1] have now identified a small HSV-1 gene that helps infected neurons to survive, and thereby enables the virus to remain hidden in them.

The genome of HSV-1 contains about 100 genes. The virus expresses most of them in cells in oral sores. Infection leads to amplification of its DNA, formation of viral particles that encapsulate the new viral DNA (Fig. 1, overleaf), death of the host cells, and release of progeny viral particles. This 'productive phase' of infection is common in viruses. What is unusual about herpes viruses is that they also have a latent phase, during which they reside in some cells of an infected organism without supporting a productive infection.

HSV-1 infects people. But learning how this pathogen co-habits with us has required the use of animal hosts as models for experimental analysis. Two decades ago, mice that survived an initial infection with HSV-1 were found to harbour HSV-1 DNA in their trigeminal ganglia, as we do[2]. The trigeminal ganglia are the clusters of neurons that innervate our face, with some neurons terminating near the lips. It turned out that these infected neurons predominantly or solely express just one transcript of the viral genome — a very unexpected result[3]. That transcript was also identified in latently infected neurons in humans, and was called the latency-associated transcript, or LAT. As it was the sole viral participant in latency, LAT was assumed to have a pivotal role in the phenomenon.

The ensuing analyses yielded perplexing findings, however. The *LAT* gene is initially transcribed to yield an RNA that is 8.5 kilobases long but lacks the hallmarks of being a precursor to a messenger RNA[4]. It is processed, or spliced, as are precursors to mRNAs, but surprisingly a 2-kilobase stretch derived from the splicing is long-lived and tends to remain in the host cell's nucleus[4]. No protein encoded by *LAT* has been consistently detected *in vivo*.