

body. The core body mediates dimerization and forms a cystine knot; this is a characteristic structure of disulphide-bonded cysteines that is also found in BMP-7 and numerous other secreted proteins⁸. The knot takes the general shape of a ring of intramolecular disulphide bonds, through which passes a single intermolecular disulphide linkage that stabilizes the dimeric structure.

The BMP-7 dimer has wings that are structurally similar to but more compact than those of Noggin. In the complex¹, the Noggin and BMP-7 butterflies are arranged back-to-back with the wings touching (Fig. 1c) and Noggin's wings extending out to embrace those of BMP-7. This overall structure provides an essential spatial arrangement that allows an amino-terminal extension of each Noggin monomer to snake around BMP-7 and form a 'clip' that occludes the surfaces of the growth factor that make contact with its receptor. Indeed, one of the amino acids in the amino-terminal half of the Noggin clip (proline 35) extends into a hydrophobic pocket on BMP-7 that normally⁴ makes a key contact with a phenylalanine residue on the type I receptor. At the other end of the clip, hydrophobic amino acids cooperate with others to mask the hydrophobic patch on BMP-7 that makes contact with the type II receptor. These extensive contacts and the occlusion of both receptor-binding sites on BMP-7 probably explain both the high affinity of Noggin for BMP-7 and its potent antagonistic activity.

So just how important are these contacts to Noggin's antagonism of BMP-7 and, ultimately, to its physiological functions? To answer this question, Groppe *et al.* produced versions of Noggin that had different mutations in each of the interaction surfaces, and used them in tests of limb-bud development in the chick. In normal limb development, BMPs are essential for formation of the cartilage that presages where bones will form⁹. They are also needed to sculpt the fingers, by inducing cell death between the digits. So, treating developing limb buds with Noggin leads to a loss of cartilage formation and a block in cell death between digits. But Groppe *et al.* found that mutations in Noggin's second interaction surface strongly reduced its ability to bind BMP-7 and to antagonize BMPs *in vivo*. In contrast, mutation of the first interaction surface had a less dramatic effect on binding to BMP-7, and weak effects on limb development. Nevertheless, this latter mutation does cause joint fusions in a number of human skeletal dysplasias, so the affected surface is biologically important¹.

This Noggin-BMP-7 structure¹ provides the first glimpse of how a secreted antagonist blocks BMP function. It remains to be seen whether BMP antagonists from another, larger protein family — the DAN family — have similar overall structures. But at least

one such antagonist, Cerberus, can inhibit BMPs as well as members of another, structurally unrelated family of secreted factors, the Wnt proteins¹⁰. It will be interesting to see how the DANs can block multiple pathways. Furthermore, Noggin and DAN genes are rarely found in invertebrate genomes, but are conserved in diverse vertebrate species. The finding that Noggin and BMP-7 share considerable structural similarity, despite having opposite biological functions, suggests that the demands of patterning vertebrate organisms may have driven the evolution of a BMP antagonist from an ancient BMP-like gene. ■

Jeffrey L. Wrana is in the Department of Medical

Genetics and Microbiology, University of Toronto, and the Program in Molecular Biology and Cancer, Samuel Lunenfeld Research Institute, Mount Sinai Hospital, 600 University Avenue, Toronto M5G 1X5, Canada.

e-mail: wrana@mshri.on.ca

1. Groppe, J. *et al. Nature* **420**, 636–642 (2002).
2. Urist, M. R. *Science* **150**, 893–899 (1965).
3. Hogan, B. L. M. *Genes Dev.* **10**, 1580–1594 (1996).
4. Kirsch, T., Sebald, W. & Dreyer, M. K. *Nature Struct. Biol.* **7**, 492–496 (2000).
5. Hart, P. J. *et al. Nature Struct. Biol.* **9**, 203–208 (2002).
6. Smith, W. C. & Harland, R. M. *Cell* **70**, 829–840 (1992).
7. Gong, Y. *et al. Nature Genet.* **21**, 302–304 (1999).
8. Vitt, U. A., Hsu, S. Y. & Hsueh, A. J. *Mol. Endocrinol.* **15**, 681–694 (2001).
9. Capdevila, J. & Izpisua Belmonte, J. C. *Annu. Rev. Cell Dev. Biol.* **17**, 87–132 (2001).
10. Piccolo, S. *et al. Nature* **397**, 707–709 (1999).

Nuclear physics

A triple point in nuclei

David Warner

Triple points describe states of matter in which three phases exist at the same time — such as solid, liquid and gas. The same phenomenon has now been found to occur between three different shapes of atomic nuclei.

The most familiar example of a triple point is in water: on a graph of pressure and temperature, the three lines separating the vapour–liquid, liquid–solid and solid–vapour phases all cross at a temperature of 273.15 K, that value being set to define the Kelvin scale of temperature. Phase transitions such as these are normally associated with temperature, but on the quantum scale they can occur at zero temperature through other mechanisms. In the lowest energy (ground) states of atomic nuclei, different phases exist which correspond to different geometrical shapes. According to Jan Jolie and colleagues¹, writing in *Physical Review Letters*, these phases come together at a triple point, validating a prediction made by the Russian physicist Lev Landau in a classic

paper on the theory of second-order phase transitions². Writing in 1937, Landau could not have expected his theory to apply in the nuclear domain.

When ice melts, it does so at a particular temperature and with a sudden change in its state, as the crystal structure is destroyed by the thermal motion of the water molecules. This is an example of a first-order phase transition: at the transition temperature, the two phases — solid and liquid — coexist and latent heat is required to effect the transformation from one to the other. Landau's theory deals with second-order phase transitions in which the state of the system changes in a continuous way with no coexistence of phases. Instead, at the transition point, the two phases become

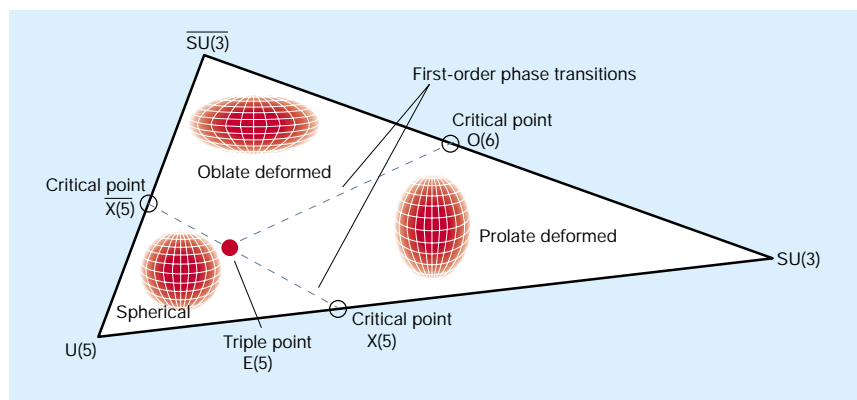


Figure 1 The extended Casten triangle. Each apex denotes a mathematical symmetry corresponding to one of the three shapes shown. Transition points and their associated critical symmetries are indicated, as are first-order phase transitions. Jolie *et al.*¹ propose that there is a nuclear triple point that marks the second-order transition between a spherical nuclear shape and a prolate or oblate deformed one. Existing data for the barium nucleus support this hypothesis.

indistinguishable. A familiar example is the magnetic transition in iron, in which the magnetization associated with the ferromagnetic state vanishes at the Curie temperature and the system becomes paramagnetic.

The phase transitions in these classical systems arise from a competition between order and thermal fluctuations. In quantum systems, however, phase transitions can take place at zero temperature and the change in order is invoked by some other parameter. In its ground state, an atomic nucleus has a stable geometrical shape that results from the interaction between its constituent neutrons and protons (known collectively as nucleons). As the number of nucleons changes from nucleus to nucleus, shape phase transitions occur, in which the geometrical configuration changes, for example, from spherical to 'prolate quadrupole deformed', or cigar-shaped. (Strictly speaking, phase transitions in finite systems can only be defined in the classical limit in which the number of constituents tends to infinity. In practical terms, this means that the discontinuity associated with the transition is smoothed out in the finite system.) Quantum phase transitions involving changes in geometrical configurations occur in other finite many-body systems as well, such as molecules.

Interest in nuclear-shape phase transitions has been galvanized over the past two years by a new interpretation of the behaviour of the nuclei ^{152}Sm (samarium) and ^{134}Ba (barium). In nuclear physics, quantum phase transitions can be studied most easily using algebraic techniques that associate a specific mathematical symmetry with the different nuclear shapes. In particular, in the framework of the 'interacting boson model'³, three such shapes exist corresponding to spherical symmetry, a deformed shape with axial symmetry and a deformed shape without axial symmetry (described mathematically by the groups $U(5)$, $SU(3)$ and $O(6)$, respectively). The transition between the first two of these is represented by a line of first-order transitions on the phase diagram, and the transition between $U(5)$ and $O(6)$ is a second-order point.

New experimental data^{4,5} and a fresh examination⁶ of both data and theory for ^{152}Sm and ^{134}Ba have demonstrated the relevance of the concept of quantum shape phase transitions in the nuclear domain. Moreover, Francesco Iachello has developed 'critical' symmetries that provide an analytical way to describe the structure of nuclei at the critical points of the second-order transition⁷ and in the coexistence region of the first-order transition⁸ ($E(5)$ and $X(5)$, respectively) — predictions that are again matched by the behaviour of ^{152}Sm and ^{134}Ba .

The picture was not complete, however, without the new work published by Jolie *et al.*¹. Until now, the nuclear phase diagram, known as the Casten triangle (Fig. 1), had

shown a line of first-order phase coexistence between the $U(5)$ and $SU(3)$ symmetries that culminated in a second-order point defining the $U(5)$ – $O(6)$ transition. But where was the transition in the third leg of the triangle, between $SU(3)$ and $O(6)$? In earlier work, Jolie *et al.*⁹ showed that part of the triangle was missing: it should be extended to incorporate $SU(3)$ symmetry. This corresponds to axially symmetric, oblate deformation, instead of the prolate shapes represented by $SU(3)$ — a flattening rather than a stretching, essentially a change in sign of the relevant shape variable. The previously established $O(6)$ symmetry then also plays the role of a critical symmetry, describing the first-order phase transition from a prolate to oblate shape.

Armed with this extended version of the Casten triangle, Jolie *et al.*¹ have now completed the story by analysing the nuclear-shape phase diagram in terms of the Landau theory of continuous (second-order) phase transitions. The authors show that, in the nuclear case, a second-order transition can only occur as an isolated point that coincides with a junction of two lines of first-order transitions (Fig. 1). This is the triple point of nuclear deformation. In agreement with Landau's theory, the phase transitions occur between symmetries of higher and lower order (spherical and deformed) and between symmetries characterized by opposite signs

of the order parameter (corresponding to prolate and oblate deformation). At the triple point, all three phases exist and, looking back to earlier experimental studies, the ^{134}Ba nucleus has provided the first experimental proof that this is so.

The study by Jolie *et al.*¹ shows, in a straightforward and elegant way, how the classical theory of phase transitions can be applied to describe the shapes of atomic nuclei in their ground states. The theory describes the nature of the transition from one shape to another as a function of the appropriate parameters — a unified picture that offers a new perspective on the changing shape of nuclei. It also emphasizes how basic theoretical concepts can span a multitude of physical systems. ■

David Warner is in the Surface and Nuclear Division, Daresbury Laboratory, Daresbury, Warrington, Cheshire WA4 4AD, UK.
e-mail: d.warner@dl.ac.uk

1. Jolie, J. *et al. Phys. Rev. Lett.* **89**, 182502 (2002).
2. Landau, L. *Collected Papers of L. D. Landau* (ed. ter Haar, D.) 193–216 (Pergamon, Oxford, 1965).
3. Iachello, F. & Arima, A. *The Interacting Boson Model* (Cambridge Univ. Press, 1987).
4. Casten, R. F. & Zamfir, N. V. *Phys. Rev. Lett.* **87**, 052503 (2001).
5. Casten, R. F. & Zamfir, N. V. *Phys. Rev. Lett.* **85**, 3584–3586 (2000).
6. Iachello, F., Zamfir, N. V. & Casten, R. F. *Phys. Rev. Lett.* **81**, 1191–1194 (1998).
7. Iachello, F. *Phys. Rev. Lett.* **85**, 3580–3583 (2000).
8. Iachello, F. *Phys. Rev. Lett.* **87**, 052502 (2001).
9. Jolie, J. *et al. Phys. Rev. Lett.* **87**, 162501 (2001).

Aerodynamics

Red admiral agility

Rafał Żbikowski

Our understanding of insect flight is hampered by the difficulty of obtaining data when the insects are flying freely. But such experiments can be carried out and show butterflies to be masters of flight control.

Over the past ten years there has been much progress in understanding insect flight^{1–3}. The news keeps coming, and the latest instalment appears on page 660 of this issue⁴, where Srygley and Thomas describe aerodynamic observations made on free-flying red admiral butterflies. By injecting wisps of smoke into a wind tunnel, through which the butterflies flew towards an artificial flower, the authors were able to record airflow features around the wings using high-speed cameras. From the ensuing analysis, they conclude that the butterflies possess an impressive repertoire of aerodynamic mechanisms, which they employ in different circumstances and with great virtuosity.

We evidently still have much to learn about insect flight, which has been refined over an evolutionary history of 300 million years or more⁵. There are plenty of reasons for such studies. This is a subject of fundamental importance in biomechanics⁶, and

more generally in biology, because of the abundance and ubiquity of insects, and their importance in many ecosystems⁷.

Insects are also masters of manoeuvrability at low speeds, in hovering and flying backwards and sideways, skills that are of great interest to engineers in two respects. One is the lessons to be learned in designing flapping-wing 'micro air vehicles' (defined as being no more than 15 centimetres in length, width or height). Another is the prospect of reverse-engineering insect flight control, by finding out how insects steer in the air. Man-made flying vehicles are controlled by software commands, but the software design requires many man-years of work and powerful computer chips for its implementation. By contrast, in flies for instance, flight control probably originates from a central complex in the fly brain consisting of about 3,000 neurons⁸. This gives the insect less computational power than a toaster, yet insects are more agile than aircraft equipped