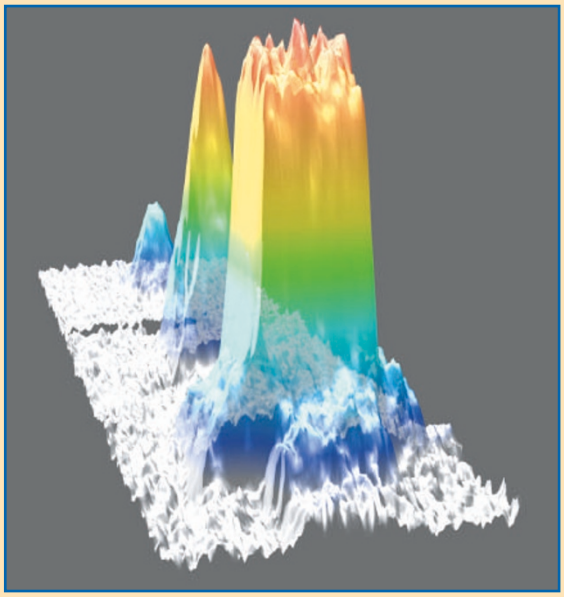
Condensed-matter physics

Lab in a trap



A collection of fermions — sub-atomic particles with half-integer spin — will not all crowd into one energy state. Rather, two by two, they will populate the lowest-available states up to some cut-off energy, beyond which no ground-state fermions may stray. These populated states are bounded by the so-called Fermi surface. All fermionic systems have a Fermi surface, and an ultracold gas of potassium atoms trapped in an optical lattice is no exception, observe Michael Köhl and co-workers (*Phys. Rev. Lett.* **94,** 080403; 2005).

The lattice is composed of three standing waves of laser light held at right angles to each other. By controlling the depth of the lattice and the particle number, the underlying physics of quantum many-body systems — the interactions between atoms and their dynamics — can be investigated directly.

Köhl *et al.* show that they can 'switch on' interactions between the particles in a Fermi gas. This results in a Fermi surface that, as more fermions are added to the trap, evolves from the smaller, rounded shape seen at the back of the image shown here to the larger, sharp-edged, square pillar in the foreground. Moreover, the interaction between two atoms in different spin states leads to the higher-energy bands becoming populated, although the number of atoms involved is smaller than expected. This strongly interacting regime is not well understood, but Köhl and colleagues' results clearly demonstrate that optical lattices provide another approach to solving outstanding problems in condensed-matter physics. **May Chiao**

that oestrogen may be pivotal to the ability of the sympathetic nervous system to regulate bone formation. Moreover, if the sympathetic nervous system sets bone mass through β-adrenergic receptors, treatment with β-blockers (which are used to treat hypertension, for example) should improve bone mass. Whether this intriguing prediction is correct has not been settled by retrospective studies[9–11] and will require carefully designed clinical trials.

Bone continuously renews itself by a process called remodelling: old bone is eaten away (resorbed) by cells called osteoclasts, and new bone is laid down by cells called osteoblasts. It has been known for some time that the hypothalamus integrates inputs from the body and transmits signals that alter bone remodelling. This was previously thought to be mediated by altering the secretion of hormones, especially gonadal steroids. Elefteriou *et al.*[7] report that the sympathetic nervous system is also involved, and they provide a molecular mechanism linking leptin, the sympathetic nervous system and decreased bone mass.

Hormones that control bone resorption often act indirectly, by stimulating osteoblasts to promote the formation of osteoclasts, rather than directly on osteoclasts themselves. For example, Elefteriou *et al.* report that adrenergic signals cause osteoblasts to secrete RANK ligand, the principal physiological inducer of osteoclast formation (Fig. 1). This effect requires protein kinase A, an enzyme that activates its target proteins by adding a phosphate group to them. In this case, the target is ATF4, a factor that is essential for osteoblast development and function. Once activated, ATF4 stimulates the production of RANK ligand.

Collectively, the results suggest that leptin induces bone loss via actions on the CNS and by regulating input from the sympathetic nervous system to bone. This is confirmed by the absence of leptin effects in mice lacking β2-AR. However, leptin-deficient *ob/ob* mice have high rates of bone resorption (previously attributed to oestrogen deficiency), despite a reduction in β-adrenergic signalling that should lead to decreased resorption.

A final interesting component of the work by Elefteriou and colleagues may help to explain this apparent paradox. They report that mice lacking the leptin-regulated neuropeptide CART (for 'cocaine- and amphetamine-regulated transcript'), have a low bone mass at baseline. Because levels of the RNA encoding CART are very low in leptin-deficient mice, one might predict that CART mediates the effects of leptin. By contrast, the authors find that mice without CART have increased bone resorption in response to leptin. These observations suggest that neurons expressing CART act to inhibit bone loss, including that mediated by leptin.

The CART neurons involved in bone loss have yet to be identified. One obvious target is the CART neurons in a region of the hypothalamus called the arcuate nucleus[12]. These neurons are stimulated by leptin and also express POMC, the prototypic CNS target of leptin. Interestingly, these neurons directly target sympathetic preganglionic neurons (the first neurons in the autonomic neuron chain)[13]. However, it is unclear whether they mediate leptin's effects on bone, as mice that lack leptin receptors only in POMC/CART neurons do not seem to have bone abnormalities[14].

CART expression is widespread in the brain and spinal cord, including sympathetic preganglionic neurons themselves, and in several other regions of the hypothalamus including the 'ventral premammilary nucleus', which has neurons that express high levels of receptors for sex steroids[15]. Given the proposed interaction of oestrogen and the autonomic nervous system, it is intriguing to speculate that hypothalamic cell groups (including CART neurons) might integrate a number of signals, including leptin and oestrogen, to coordinate the CNS control of bone mass through its output to sympathetic preganglionic neurons.

Several points remain to be reconciled with this model of the regulation of bone mass. For example, obese women have high leptin levels and high bone mass; lean women with very low leptin levels (such as marathon runners) have low bone mass. In addition, whether leptin has direct effects on bone cells remains to be settled[5,16]. Nonetheless, Elefteriou and colleagues' findings provide support for the notion that the hypothalamus and its control of the autonomic nervous system are key to the regulation of bone homeostasis. ■

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