This could be achieved by a reduction of the per locus mutation rate and/or the number of genes in the genome (possibly, as with mitochondria and chloroplasts in eukaryotic cells, losing some to the nuclear genome).

Comparisons of the synonymous substitution rates in free-living and endosymbiotic bacteria so far tentatively suggest that the per locus mutation rate is no different[3]. And, unlike eukaryotic organelles, *Buchnera* seem to have lost only a few genes[8]. Most notably, however, they have lost the gene (*recF*) encoding a repair enzyme[12]. At first sight this seems remarkable, for this would surely seem to be one of the most important genes to hang on to. But again the observation is consistent with theory[7] — a good way for a clonal lineage to minimize the rate of accumulation of mutations is to ensure that most of them are not slightly deleterious but very harmful, so removing them immediately rather than allowing them to accumulate. Such a strategy is only viable, however, if dead bacteria can be replaced by non-mutated clone members and if bacteria with heavily deleterious genes can never take over a population (for example by fast replication). So symbionts are particularly likely to develop this strategy, being restricted to host cells and surrounded by clonal relatives.

So that is one compensatory trick that *Buchnera* has came up with to avoid mutational meltdown. Another, as Moran points out, is that a few endosymbionts, *Buchnera* included[13], contain very high concentrations of the chaperone protein GroEL. In free-living forms, chaperones are produced at high temperatures to stabilize proteins that might otherwise denature. Perhaps, Moran conjectures, the endosymbionts employ GroEL during normal existence to stabilize mutationally decayed proteins.

If this is so, the question arises as to whether compensatory mechanisms are peculiar to endosymbionts or are a general characteristic of asexual lineages. If they are widely found, then mutational meltdown need never be a problem. But there are several arguments as to why these mechanisms are likely to be endosymbiont-specific. These bacteria live in a location where energetically expensive compensation is possible (that is, the host can afford to give the symbionts excess nutrients so that they can produce large quantities of chaperone); where mutations can be easily eliminated by host inter-cell selection; where the host may be able to compensate for some of the symbionts' failings; and where kin selection between members of a clone could favour inter-symbiont synergism.

All in all, then, the fact that long-lasting lineages of endosymbionts are asexual and exist in small populations is not evidence uniquely favouring the parasite hypothesis, and is consistent with both of the main hypotheses for the maintenance of sex found in most taxa. Moreover, Moran's finding of accelerated evolution lends considerable weight to the importance of mutational decay. But it is not known whether *Buchnera* has reached an equilibrium with respect to the number of deleterious mutations or whether decay is continuing. Perhaps when GroEL itself decays beyond a certain point, the whole system will collapse — for all we know, endosymbionts (and Y chromosomes) may be doomed to extinction. □

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CONDENSED-MATTER PHYSICS

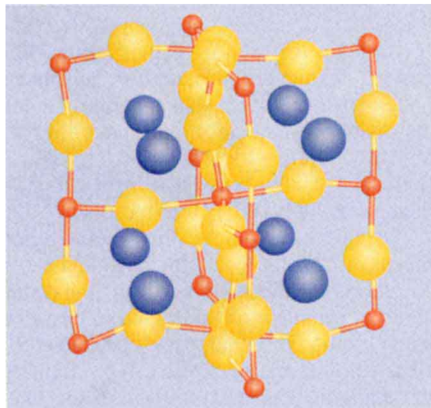
Heavy oxygen tips the balance

Warren Pickett

In most materials, magnetic phenomena at room temperature and below are essentially independent of the masses of the nuclei of the constituent atoms. The atoms can usually be considered as infinitely heavy and static in theoretical descriptions of such phenomena, although there are exceptions. Over a decade ago, Kim[1] showed how atomic motion could result in small but measurable changes in the properties of 'itinerant' ferromagnets. It is therefore not so surprising that atomic motion might have a measurable effect on the temperature below which lanthanum-based manganites become ferromagnetic (the Curie temperature, T_c). But the magnitude of the effect, as reported by Zhao *et al.* on page 676 of this issue[2], is alarming.

Lanthanum-based manganites, such as $La_{1-x}Ca_xMnO_{3+y}$, have recently become the subject of much attention by virtue of their unusual — and potentially useful — magnetic properties. At high temperatures they are insulating; at low temperatures they are metallic. But the temperature at which the insulator-to-metal transition occurs can be increased by applying a (large) magnetic field. As a result, if the temperature is held in the region of the transition and a magnetic field is applied, the electrical resistance of the material can be decreased by a factor of 1,000 or more. This phenomenon is now known as 'colossal magnetoresistance' (CMR), and researchers are energetically pursuing its cause. The subsequent observations of structural phase transitions[3] and charge order–disorder transitions[4] driven by an applied magnetic field have only added more questions. The observation by Zhao *et al.*, that simply increasing the mass of the oxygen atoms (by replacing ^{16}O with ^{18}O) decreases T_c by >20 K, now brings some focus to the fundamental description of these perplexing materials. In particular, it is the first experiment to establish what many have suspected — that atomic motion must be included in any viable description of the manganites.

An interesting complication in the manganites is that T_c coincides with the electronic transition temperature; as the electronic properties switch from insulating to metallic, the manganites transform from being magnetically disordered to magnetically ordered (ferromagnetic).



Structure of the unit cell of $LaMnO_3$: the La (blue), Mn (red) and O (yellow) spheres are proportional to their ionic radii. Note that the distortion from a simple cubic perovskite structure is substantial.

This coincidence indicates that the magnetic and electronic properties are strongly coupled. An applied magnetic field, H, will couple mainly to the spin magnetic moment of the electrons (coupling to orbital motion is usually a smaller effect). This coupling is $2S\mu_B H$ (where μ_B is the Bohr magneton). For an $S=3/2$ spin moment in a magnetic field of 5 tesla, the coupling energy is 1 meV or, in temperature equivalent, 10 K. Although this is a relatively small energy scale, it makes its presence felt through the strong magneto-electronic coupling — a flip of a spin in an applied magnetic field can change the local electronic structure from insulating to metallic, so affecting the energy balance on a (larger) electronic scale.

Another potentially important contributor to the properties of the manganites is a Jahn–Teller structural instability; the lattice surrounding the Mn^{3+} ions distorts to lift a degeneracy in the energy levels of the electronic ground state of these ions, and so lowers the energy of the entire (electronic+lattice) system. The electronic configuration of the Mn^{3+} ions is d^4 with all spins aligned, with all three t_{2g} orbitals fully occupied, but only single occupation of the two degenerate e_g orbitals (which point directly at the neighbouring oxygen ions).

The ideal structure of these compounds is simple cubic perovskite. But the parent compound of the CMR materials, $LaMnO_3$, has a complex structure (see figure), which can be described as a series of distortions from the simple cubic structure: rotation of the MnO_6 octahedra around the z axis; tilting of the octahedra about an axis in the x–y plane; distortion of MnO_6 octahedra resulting in three unequal Mn–O bond lengths; and relaxation of the entire structure to give three unequal lattice constants. The rotational motions result from a misfit of ionic sizes whereas the distortion of the MnO_6 octahedron is widely believed to be the manifestation of the Jahn–Teller instability. As Ca is substituted for La, the distortion of the MnO_6 octahedra nearly vanishes according to diffraction experiments that measure the average structure. But there has been speculation that the Jahn–Teller distortion nevertheless remains, either as an incoherent local distortion (fluctuations in space) or, more exotically, as dynamical Jahn–Teller fluctuations.

Although invoking the Jahn–Teller mechanism to account for data has been common, all phenomena up to this point could in principle be addressed in terms of static atoms. The new result of Zhao *et al.* clearly points to the strong involvement of the dynamic (thermal) motion of the oxygen ions: an increase of the oxygen mass by about 10% drives down T_c by roughly 10%. One of the prime proponents of the importance of Jahn–Teller effects in manganites has been theorist Andrew Millis. His classical model[5] concentrates on a structural ('Jahn–Teller') transition, rather than on electronic transport and magnetic ordering; as such it does not incorporate the oxygen mass explicitly and therefore does not address the current data.

A simple, and perhaps simplistic, guess at the isotope shift of T_c might go as follows: neglecting lattice fluctuations and their coupling to the electronic and magnetic properties, the transition temperature is $T_{c,O}$; accounting for the fluctuations will depress T_c below $T_{c,O}$; a heavier mass allows smaller fluctuations and will result in less depression of T_c. Thus, T_c increases with mass. Zhao *et al.*, however, report that the heavier mass (M) decreases T_c, so that the isotope shift $\alpha = \mathrm{dlog}(T_c)/\mathrm{dlog}M$ is negative.

The negative shift, opposing the simple effect of fluctuations, lends credence to Zhao and colleagues' suggestion that the primary effect is of polaronic origin. The Jahn–Teller polaron is a charge carrier accompanied by a local Jahn–Teller distortion; that is, the charge and local distortion effectively move through the material as a single entity (a polaron). It has a kinetic energy W_{eff} that is oxygen-mass dependent, and decreases with increasing mass. Because T_c scales with W_{eff}, the isotope shift is negative. Zhao *et al.* also point out that the variation of the polaronic bandwidth with La/Ca ionic radius can account for the trend to larger isotope shifts for smaller mean ion size on the La–Ca sublattice.

Does this news point to the mechanism of CMR? Not directly, it seems, although it shows that dynamical behaviour is an essential component of the behaviour near T_c. An important question, still open, is this: how can a system with such strong polaronic character near T_c, in which carrier motion is impeded by its strong coupling to atomic motions, become such a good conductor at low temperature? Values of resistivity as low as 10 $\mu\Omega$ cm have been reported, and this amount of resistivity can be accounted for simply by charge scattering from the randomly distributed La^{3+} and Ca^{2+} ions. The excellent conduction is consistent with simple band metal behaviour, but there is no theory to account for how the strong electron–lattice coupling would 'evaporate' at low temperature.

These new isotope shift results allow one to put a new slant on our picture of the CMR materials. Near T_c, there is a huge increase in resistivity resulting from the heavier oxygen isotope — that is, these are also 'colossal isotoporesistance' materials. It is intriguing to note that the effects of the isotopic mass increase (a lowering of T_c) can, at least approximately, be offset by the application of a magnetic field of the proper strength, which will drive T_c back up to its original value. The essential questions about CMR materials are unanswered, but some of the issues are being clarified. □

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DAEDALUS

How desire dies

MANY a woman complains about the short attention span of her lover. After orgasm he suddenly ceases to reiterate his love and passion; instead, he just turns over and goes to sleep. The speed of this orgasmic mental transformation demands explanation. The depletion of a sexual hormone would take far too long. The one thing that changes mood this fast is the sudden injection of a powerful drug. Heroin, nicotine and the adrenaline of our panic syndrome work in seconds. Clearly the male system is flooded at orgasm with some equally fast-acting passion-killing metabolite. Not until this has slowly cleared away can sexual interest return. Women have a different sexual chemistry, and can climax repeatedly.

And this, says Daedalus, explains the failure of the centuries-old search for a true male aphrodisiac. There is no such thing; there is only an anti-aphrodisiac, whose absence from the body allows sexual interest to develop. The brain must have receptors which turn off sexual desire when the compound binds to them.

Some pharmaceuticals can also deaden sexual desire, as an unwelcome side effect. They include antidepressants such as thioridazine and fluoxetine, beta-blockers such as atenolol, and even bromide — the British Army has been suspected of lacing soldiers' tea with bromide to dampen their sexual urges. Presumably these compounds or their metabolites bind more or less strongly to the brain's anti-aphrodisiac receptors.

So DREADCO's biochemists are seeking the male anti-aphrodisiac in donated blood samples. Daedalus suspects that it builds up in the male system with age. The blood of sexually obsessed teenagers should be almost free of it; that of sexually retired elderly gentlemen should be its richest natural source. It should soar dramatically in a volunteer seducer just after a conquest. Compounds whose concentration varies in the right way will be checked for molecular similarity to the sex-sabotaging drugs. Once identified, the anti-aphrodisiac will be synthesized for sale.

DREADCO's 'Passion-Killer' will abolish sexual desire in seconds. As a natural male product, it will be free of the feminizing side effects of previous hormonal anti-aphrodisiacs. Any man in compromising circumstances — a sexual criminal anxious not to re-offend, a diplomat cornered by some Mata Hari, or a politician striving to uphold family values — can simply 'pop' a pill and be released from temptation. Many a sexually reluctant woman will welcome it too, as a crafty additive to her husband's evening meal, or the candle-lit dinner of some unalluring lover. David Jones