output? This fascinating problem in signal transduction must be solved before we can fully appreciate how morphogens pattern fields of cells. ■

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Earth science

Mantle cookbook calibration

Craig R. Bina

Doubts about a fundamental model of the chemistry of Earth's deep interior have now been transmuted into doubts about a standard used to calibrate these studies — gold's equation of state.

The properties of the Earth's mantle change abruptly 660 km below the surface, with sharp rises in both density and the transmission speed of seismic waves created by earthquakes. But in 1998 it was announced that highly sophisticated laboratory experiments[1] had failed to confirm this 660 km transition — instead, seeming to place the mineral transformation concerned at 600 km. Elsewhere in this issue, Chudinovskikh and Boehler[2], and Shim *et al.*[3], describe how they have revisited the question. The news they report is both reassuring and disturbing.

For decades, the global 660-km seismic discontinuity has been thought to coincide with the chemical reaction $\gamma \rightarrow pv + mw$, in which the mineral γ-$(Mg,Fe)_2SiO_4$ (also called ringwoodite or silicate spinel) breaks down to a mixture of pv-$(Mg,Fe)SiO_3$ (silicate perovskite) and mw-$(Mg,Fe)O$ (magnesiowüstite, also called ferropericlase) at high pressures. This view was supported by experiments in which the reaction occurred at pressures and temperatures believed to be appropriate to 660 km depth[4–6]. In these experiments, samples were subjected to high pressures and temperatures inside diamond-anvil and multi-anvil devices, and were then cooled quickly and removed for analysis — a bit like looking at one's baking after removing it from the oven and allowing it to cool.

In 1998 Irifune *et al.*[1] used synchrotron X-rays to peer through the oven door and observe the baking *in situ*. But consternation greeted their report that the $\gamma \rightarrow pv + mw$ transition took place at pressures about 2 gigapascals (GPa) lower than expected, equivalent to a depth of 600 km rather than 660 km. Irifune *et al.* gave two possible explanations for this result: either their state-of-the-art pressure measurements were in error, or the common model of Earth's deep chemistry was wrong.

The two new papers[2,3] describe experiments aimed at resolving the equilibrium pressure of the $\gamma \rightarrow pv + mw$ reaction. Using diamond-anvil devices, Chudinovskikh and Boehler[2] (page 574) subjected samples of Mg_2SiO_4 to high pressures and temperatures, swiftly cooled them to room temperature, and examined them using Raman spectroscopy while still at high pressures. Shim *et al.*[3] (page 571) do precisely what Chudinovskikh and Boehler suggest in their closing sentence: they examined such samples *in situ*, at high pressures and temperatures, using synchrotron X-rays. The two groups used different methods of pressure calibration,

Behavioural ecology

Down on fungal farm

MATTHEW KWESKIN

Leaf-cutting ants of the tribe Attini do not eat the vegetation they gather. Rather they use it to grow fungi, and then feed off the fungi. The ants' vast nests, containing up to eight million individuals, have chambers devoted to fungus cultivation. But like all farmers, the ants face competition for the crop in the form of pathogens — in this case other fungi, which threaten to destroy the fruits of their labours.

A couple of years ago, Cameron Currie and colleagues showed how the ants use antibiotic-producing bacteria for pest control. From observations of the species *Atta colombica* (pictured), he and Alison Stuart now describe other strategies to that end (*Proc. R. Soc. Lond. B* **268,** 1033–1039; 2001). One is simple cleanliness: the ants lick the surfaces of both the nest itself and new leaf material to keep them clear of contaminants.

The authors also sprayed fungal-cultivation chambers with spores of two pest fungi, *Trichoderma viride* and *Escovopsis*, to see the reaction. When rogue spores were found by the inhabitants, large numbers of workers congregated at the infected site to gather up spores in their mouthparts and cart them away. If the spores reached the stage of germination, the ants turned to weeding by removing chunks of leaf along with crop and pest fungi.

The ants seem to be able to tell the difference between the two invading fungi. The specialist pathogen *Escovopsis* triggered more ants to take up cleaning duties, and their efforts went on much longer, than those directed against *Trichoderma*. But the ant farmers don't have everything their own way. Although *Trichoderma* was eliminated rapidly, *Escovopsis* hung on in the nests. It may be that this pathogen grows too quickly for the ants to keep up, or that the stickiness of the spores makes it impossible for the ants to remove 100% of them from a nest. **John Whitfield** but both conclude that the $\gamma\rightarrow$pv + mw transition occurs at pressures and temperatures (about 24 GPa and 1,800–1,900 K) appropriate to 660 km depth. This points to problems in experimental pressure calibration, rather than to a fundamental misunderstanding of the chemistry of Earth's interior. More specifically, it seems that the source of the 2-GPa discrepancy may lie largely in the equation of state (EOS) of gold.

Our estimates of pressures and temperatures inside the Earth are indirect. They come from a variety of sources, and the consistency between them gives us confidence in their validity. But reproducing and measuring these conditions inside a device such as a diamond anvil is no easy matter. In multi-anvil devices, temperatures are measured using thermocouples, and pressures are calibrated by extrapolation from reactions at lower pressures[6]. Irifune *et al.*'s great advance[1] was to peer through the multi-anvil oven door using intense X-rays, allowing not only observation of the sample *in situ*, but also direct measurement of pressure by comparing the *in situ* specific volume of a standard material (gold) to an EOS that specifies its volume as a function of pressure and temperature. In diamond-anvil devices, temperatures are measured from radiation spectra, and pressures are determined from shifts in the fluorescence spectrum of ruby[2]. An *in situ* approach using intense X-rays allows pressure to be calibrated from the EOS of a standard material — such as gold, or platinum[3].

Problems arise in choosing an EOS for pressure calibration. As Chudinovskikh and Boehler point out, there are discrepancies between various reference EOS for gold. Indeed, experiments[7] on the ilm$\rightarrow$pv transition (a cousin of the $\gamma\rightarrow$pv + mw transition but occurring in $MgSiO_3$ silicate ilmenite) confirmed that one such EOS[8] (also used by Irifune *et al.* for their pressure standard) places the transition at pressures 2–3 GPa lower than does another EOS for gold[9]. The platinum pressure standard used by Shim *et al.*[3], perhaps chosen to avoid the ambiguities of gold, is consistent with this second gold EOS, hence their higher pressures. In other experiments[10] there has been agreement between the gold- and platinum-based pressure scales, but the group concerned appear to have used a different platinum EOS to that used by Shim *et al.*

The results of all these studies suggest that there are two distinct classes of EOS for pressure calibration — as if there were two different brands of oven thermometers (or rather barometers). One class of EOS yields pressures that place the $\gamma\rightarrow$pv + mw transition at 660 km, whereas the other yields pressures about 2 GPa lower, placing the transition at 600 km. Furthermore, in a sort of EOS contagion, the low transition pressure for the $\gamma\rightarrow$pv + mw reaction reported by Irifune *et al.*[1] has already been used to calibrate pressures in a study[11] of the ilm$\rightarrow$pv transition. Unsurprisingly, this yields transition pressures about 2 GPa lower than in other studies.

So the controversial 2-GPa (60-km) apparent shift of the $\gamma\rightarrow$pv + mw transition appears to signal disagreements about high-pressure EOS of standard reference materials, rather than a misunderstanding of Earth's internal chemistry. This is both reassuring and disturbing.

It is reassuring because continued study of the transition reveals behaviour that provides a remarkably good match with the observed properties (depth, magnitude, sharpness, fine structure and topographic undulations) of the 660-km discontinuity[12]. If the $\gamma\rightarrow$pv + mw transition occurs instead at 600 km, why is no seismic discontinuity observed there, and what causes the observed 660-km discontinuity? Such paradoxes would require a radical change in mantle chemistry somewhere between 410 and 600 km deep, which is not observed geophysically.

The disturbing aspect is that, even with the remarkable ability to look inside the oven while it is baking, there is still confusion about the relative calibrations of different pressure scales. Further interlaboratory comparisons are needed, along with assessments of the EOS from other techniques such as calorimetry, spectroscopy and *ab initio* simulations of material properties. ■

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Human genetics

Tackling common disease

John A. Todd

Crohn's disease is characterized by inflammation and destruction of the bowel. Identification of defective variants of a gene that predispose people to the disease is an encouraging development.

The 1980s saw the identification of the genes which, when mutated, cause rare, inherited diseases such as cystic fibrosis that follow straightforward patterns of inheritance. The 1990s promised similar conquests in understanding the more common diseases (defined as more than one case per 1,000 people) that have a more complex genetic basis. The promises were not delivered.

At last, on pages 599 and 603 of this issue, two groups[1,2] describe the first identification of a gene involved in a common disease, based on a standard approach known as linkage analysis. I predict that a steady stream of such papers will follow. The disease concerned is Crohn's disease, inheritance of which was previously correlated with[3] — linked to, in genetic terminology — chromosome 16. Working independently, Hugot *et al.*[1] and Ogura *et al.*[2] have now pinpointed disease-predisposing variants (alleles) of the *NOD2* gene in the region of chromosome 16 that shows the strongest linkage to the disease. The bonus is that the function of the protein encoded by *NOD2* is partly known: it detects bacteria in the gut, and helps control the inflammatory response to them[4].

Much of the genetic difference between individual people lies in differences known as single-nucleotide polymorphisms (SNPs): these are natural variations in the four bases from which DNA and genes are composed. It is largely these variations that geneticists exploit to track chromosomes from parents to children, and, in linkage analysis, to correlate the presence of certain chromosome sequences with the occurrence of disease. The segment of chromosome 16 identified as containing a gene (or genes) implicated in causing Crohn's disease was large, around 20 million base pairs. This segment contains perhaps 250 genes, variation in any one of which, or combinations thereof, could be responsible for the observed linkage.

The next task was the daunting one of finding the disease-associated gene or genes within this haystack. There are two means to this end: the 'functional candidate gene' and the 'positional' approaches, and both require some luck. In the first approach, which is based on existing knowledge of the causes of a disease, genes are selected that look likely to be involved in causation. To confirm the involvement of the candidate gene, its DNA sequence is determined in patients suffering from the condition concerned to see whether