equivalent doses of caffeine in human terms: the answer will await the ability to use positron emission tomography to study the occupancy of the A_{2A} receptor by caffeine in people's brains. But, from the information available so far, it seems likely that the concentrations of caffeine used by Lindskog *et al.*[1] are similar to those reached in our brains after a few cups of coffee. So the authors have led us to the heart of the matter: DARPP-32 keeps us going till the next coffee break by extending the effects of the last cup. Future efforts will identify the target proteins that are regulated by this signalling cascade. Together with insights gained from mice engineered to lack other intracellular signalling molecules, this knowledge should provide an even better understanding of caffeine's effects. So, wake up, smell the fresh coffee and enjoy its effects for a long time, thanks to your dependable DARPP-32! ■

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Earth science

Breaking plates

J. Huw Davies

Seismic images suggest that oceanic plates in the northwest Pacific broke apart as they descended into Earth's mantle. That might explain the high magma output of some volcanoes in the region, and why others are extinct.

Some of the consequences of the motion of Earth's tectonic plates are quite evident: various mountain chains for instance. Others, such as events occurring deep in subduction zones where one plate plunges beneath another, can be seen only indirectly through seismic imaging techniques. The approach allows the structure of Earth's interior to be reconstructed from observed seismograms, and it continues to pay dividends.

An example appears on page 763 of this issue, where Levin *et al.*[1] argue that they have detected two instances of break-up of a subducting slab at the junction of two oceanic plates. There are indications[2,3] that slab disintegration has occurred where oceanic and continental plates collide. But because earthquake activity is uniformly distributed with depth in subducting oceanic plates, it had seemed that purely oceanic plates maintain their integrity.

Levin *et al.* imaged the structure of the upper 200 km of Earth's mantle in the northwest Pacific, in the complex setting where the Aleutian and Kamchatka subduction zones meet (Fig. 1). South of the junction beneath Kamchatka, they identified a high-velocity feature co-located with earthquakes. This they interpret as cool, rigid subducting oceanic plate. North of the junction, velocities were slower than average, with no evidence of deep earthquakes, the implication being that there is no subducting slab there. This is an unexpected finding. In the past, subduction also occurred further north, the plate concerned being generated by ocean-floor spreading in the Komandorsky basin (Fig. 1a). If oceanic plates are rigid, the previously subducted plate north of the junction should still be attached to the Komandorsky basin, which has remained at the surface.

Levin and colleagues' conclusion is that the missing plate has broken off and descended deep into the mantle (Fig. 1b). Subduction zones are regions where Earth's surface returns to cool the hot interior. Counterintuitively, they are also the site of volcanism. The melting of rocks in Earth's interior that is required for this volcanism is thought to result from the entry of hydrous fluids into the hot overlying mantle from the descending oceanic crust[4–6]. North of the junction lie volcanoes that are now extinct, and the inferred absence of oceanic crust there is taken by Levin *et al.* as an explanation: there is now no source of water to promote magmatism. The volcanoes have been extinct for at least five million years, so the plate must have become detached before then, taking oceanic crust away with it. If the plate continued its descent at the velocity of the Kamchatka slab (about 9 cm yr^{-1}), and assuming a dip of 45° or so, then in five million years it would have travelled 450 km and reached a depth of at least 300 km — beneath the region surveyed by Levin and colleagues.

Where oceanic and continental plates meet, the force that breaks a subducting slab is generated by the tendency of the buoyant continent to remain at the surface and that of dense oceanic plate to continue its descent. In the case studied by Levin *et al.*, if the fragment that was broken off was joined along its southern side to the subducting Pacific plate, then the driving force for detachment is clear: the much larger Pacific plate would have pulled the fragment down. Joining of the plates is not required, though, especially

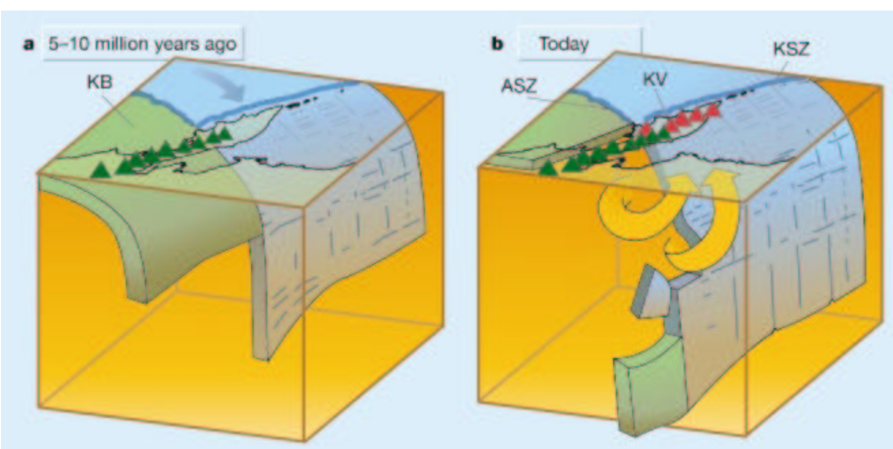

Figure 1 **Tectonics in the northwest Pacific.** a, **A view from Siberia looking towards the Pacific, and interpretation of events 5–10 million years ago. The Pacific oceanic plate descends beneath south and central Kamchatka (blue), whereas plate produced by spreading in the Komandorsky basin descends beneath north Kamchatka (green). The green triangles show volcanoes then active.** b, **The Aleutian–Kamchatka junction today, interpreted from the work of Levin *et al.*[1]. The plate beneath north Kamchatka seems to have broken off and fallen deep into the mantle. Volcanism usually occurs above subduction zones, the likely cause being water released from descended oceanic crust which enters the mantle and promotes melting. Levin *et al.* regard the lack of oceanic crust in the region above this detached segment as an explanation for the now-extinct overlying volcanoes (green triangles). The authors[1] also argue that a second segment of plate detached at depth beneath central Kamchatka, leading to stronger mantle upflow and the exceptional magma output of the Klyuchevskoy volcano. The red triangles indicate active volcanoes. KB, Komandorsky basin; KSZ, Kamchatka subduction zone; ASZ, Aleutian subduction zone; KV, Klyuchevskoy volcano.**

as the two pieces of oceanic plate are of such different age. It might instead be that the Komandorsky basin plate is too buoyant to subduct, because it is young and hot, and that it pulled away from the subducted older plate. This process would have been enhanced if plates are weakest near the surface, at a region of maximum curvature that becomes cut by large faults just before subduction occurs[7].

A further conclusion of Levin and colleagues is that a second piece of slab became detached at depth about two million years ago. The authors argue that the ensuing vigorous upflow of hot mantle, fed by water from the remaining ocean crust, explains the world-record magma output of the overlying Klyuchevskoy volcano (Fig. 1b). This is a plausible interpretation. But the mantle imaging is not good enough to be certain, and it is not the only explanation for the increased magmatic activity. Hot rock flowing around the side of the plate, which Levin *et al.* also predict is occurring, or increased hydrous-fluid input from subduction of part of the nearby Emperor seamount chain, are also possible causes. Other volcanoes with a high magma output also occur near junctions in subduction zones. Examples are Mount Fuji, where there is no evidence of underlying slab disintegration, and Mount Etna, where the activity is also attributed to enhanced upwelling flow[8].

Tasks for the future are to identify the forces driving ocean-slab disintegration and to image the broken pieces deep in the mantle beneath the northwest Pacific, and also to investigate similar places where Earth might have been negligent with its plates. Furthermore, the new work[1] has implications for researchers trying to model the dynamics and explain the geochemistry of Earth's mantle[9]. The break-up of subducting plates could introduce blobs[10] — rather than sheets — of geochemically distinct material into the mantle mix that is being stirred by convection. Detailed observations such as those of Levin *et al.* should lead to more accurate estimates of both the geometry and the geochemical consequences of plate subduction — and so to better simulations of mantle convection and improved definition of the geochemical reservoirs. ■

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Developmental biology

Signalling legacies

Richard S. Mann and Fernando Casares

Until now, the signals that control the development of the legs in insects and vertebrates have been thought to be different. But new work reveals similarities, which might have evolutionary implications.

We live in a three-dimensional world and, not surprisingly, the development of many animals — including ourselves — depends on the establishment of three body axes. Two of these, the head-to-tail (anterior–posterior) and back-to-front (dorsal–ventral) axes, are established in the egg before fertilization or, in some cases, as an immediate result of fertilization. In contrast, the proximal–distal axis, which extends from the base of each appendage (where it attaches to the body) to its tip, must be generated from scratch every time an animal grows a leg, arm or wing. How this axis is established has been the subject of debate for several decades, and work on leg and wing development in the fruitfly, *Drosophila melanogaster*, has provided many insights, at least for insects. Papers on page 781 of this issue[1] and in a recent issue of *Science*[2] take our understanding a step further, by demonstrating an unexpected role for signalling through a protein called the epidermal-growth-factor receptor in fruitfly leg development.

Fly legs emerge from flat discs of tissue that are set aside during embryonic development[3]. At this stage two secreted signalling molecules, Wingless (Wg) and Decapentaplegic (Dpp), are needed to set up the proximal–distal axis[3]. These molecules are expressed as two opposing wedges in the disc, one ventral and the other dorsal (Fig. 1a, page 739). Where they meet, at the centre of the disc, will become the distal tip of the leg.

Not only are both signals required in the formation of the proximal–distal axis[3], but additional axes can be generated experimentally by creating new sites at which Wg and Dpp intersect. For example, bifurcated legs (which have an additional proximal–distal axis) can be generated by forcing just a few ventral cells, which normally express just Wg, to express Dpp as well[4]. Importantly, the additional legs generated in this way are composed mainly of wild-type cells, suggesting that the fates of these cells were changed by the Dpp- and Wg-expressing cells. Without this new source of Dpp and Wg, the wild-type cells would have contributed only to the normal legs.

Two models have been proposed to explain this result. The first is based on an analogy with Spemann and Mangold's classic demonstration[5] of the existence of an 'organizer' — a group of cells that influence the behaviour of neighbouring cells — during amphibian development. According to this view, the intersection between the Wg and Dpp signals creates a distal 'organizer' in the leg disc[4]. It was proposed that this organizer is the source of a third signal that causes neighbouring cells to become distal; the farther a cell is from the organizer, the more 'proximal' its fate would be.

The alternative model posits that Wg and Dpp cause nearby cells to become distal directly, without inducing a third signal[6]. So, cells that receive the highest levels of both Dpp and Wg, such as those at the centre of the disc, would become distal, whereas cells receiving successively lower levels of both signals would take on successively more proximal fates.

Either model could account for the generation of bifurcated legs: a new source of Dpp and Wg would be expected to create a new proximal–distal axis whether indirectly (by creating an organizer) or directly. However, one limitation of the organizer model when it was originally suggested was that there was no candidate for the signal from the hypothesized organizer. By contrast, significant experimental support for the direct model came from showing that Dpp and Wg activate two genes along the proximal–distal axis directly, without inducing a third signal[6]. These genes, *Distal-less* (*Dll*) and *dachshund* (*dac*), are required for the generation of distal and intermediate regions, respectively[3] (Fig. 1b). Thus, largely because of this work[6], the prevailing theory has been that the combined and graded activities of Wg and Dpp directly produce the leg's proximal–distal axis.

But it takes more than *Dll* and *dac* to make a leg. After these genes have been turned on, several others, also required for distal leg fates, begin to be activated in subsets of the *Dll*-expressing leg region[3]. Although these genes cross-regulate each other[7], it was not known whether they, too, would be targets for Wg and Dpp. Campbell[1] and Galindo *et al.*[2] now show that Wg and Dpp are not required at the time when these genes are first turned on. Accordingly, whereas removing either Dpp or Wg function early in development truncates the legs, later removal has only minor effects on leg development[2]. ▸