## news and views

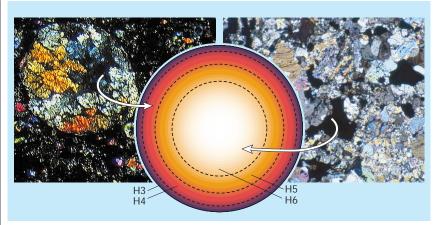


Figure 1 The onion-shell model of an asteroid interior. A suite of meteorites known as the H-chondrites are believed to have originated from a single asteroid. Trieloff *et al.*<sup>1</sup> have quantified the cooling histories of these meteorites and confirmed the validity of the onion-shell model: the H6 chondrites that show evidence of the most severe metamorphism were the most deeply buried; H5, H4 and H3 chondrites, which were less affected by thermal metamorphism, came from shallower levels. The different textures of the chondrites are seen in the micrographs of thin sections of H4 (left) and H6 (right) chondrites.

minerals were not able to heal radiation damage. The minimum annealing temperature for orthorhombic pyroxene is higher, about 550 K (although the pyroxene did not contain plutonium, tracks were created in it where it butted against phosphate minerals). As some <sup>244</sup>Pu decay occurred between the time when a meteorite cooled to 550 K and when it cooled to 390 K, the fission track density is smaller in phosphate minerals than in pyroxene. This difference in track density means that the cooling time between 550 K and 390 K can be calculated<sup>5</sup>.

Trieloff *et al.*<sup>1</sup> studied a chemically distinct suite of meteorites, known as H-group chondrites, that are believed to derive from the same asteroid. The samples they studied show different degrees of thermal metamorphism, which are denoted by their classification, ranging from H6 (most metamorphosed) to H3 (least so)<sup>6</sup>. The planetesimal model that accounts most straightforwardly for these degrees of metamorphism would have the H6 chondrites near its centre, where an internal heat source would heat the rock most and where it would stay hot the longest. At progressively shallower depths the H5, H4 and H3 rock was heated less and cooling occurred more quickly7. This is the 'onion-shell' model of meteorite parent bodies (Fig. 1).

Evidence that chemically distinctive subsets of meteorites are derived from onion-shell parent bodies has been sought for decades without success. Thermochronometric analysis produced inconsistent, conflicting results, calling into question the validity of the onion-shell model. Perhaps, instead, a collision between asteroids caused the H-chondrite parent body to break up while it was still hot, and thereafter the fragments had diverse cooling histories<sup>8</sup>. Maybe there was more than one H-chondrite parent body, and the suite of H-chondrites in fact represents samples of several planetesimals, each with a different thermal history<sup>9</sup>. Or could the heat source have been external rather than internal<sup>10</sup>?

Trieloff *et al.* now dispel these doubts by showing that the thermochronometric data for H6, H5 and H4 chondrites can be fitted into a straightforward model of a planetesimal with a radius of about 100 kilometres and an onion-shell structure, which was internally heated by <sup>26</sup>Al decay and cooled over about 100 million years. (H3 chondrites are too fine-grained and poorly equilibrated to yield useful data.) This advance was made possible by three factors. First, the authors carefully selected the samples that they studied, excluding any chondrites that showed mineralogical evidence of shock — the damage produced in some meteorites by asteroid collisions, which can confuse the thermochronometric record. Second, they included high-quality measurements of potassium– argon ages in their analysis. Third, the fission-track technique was refined by finding a way to remove extraneous tracks caused by cosmic rays, and by correcting for differences in the track-registration efficiencies between phosphate and pyroxene minerals.

This paper represents a posthumous triumph for co-author Paul Pellas, a highly respected and charismatic physicist at the Muséum National d'Histoire Naturelle in Paris, whose principal life's work was the development of the fission-track technique of thermochronometry.

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Cell motility

## Making streams

Richard H. Kessin

Cells of the slime mould *Dictyostelium discoideum* can move in a kind of close-order drill. New evidence suggests that they do this by secreting a chemical attractant specifically from their rear, luring the cells that follow.

n 1944, the microbiologist Ernest Runyon put amoebae of the then little studied slime mould *Dictyostelium discoideum* on both sides of a piece of porous cellophane<sup>1</sup>. Over the next few hours, the amoebae on one side started to gather at a central point, moving at first individually and then, tail to head, in streams. Astonishingly, so did the amoebae on the other side of the cellophane, forming mirror-image streams. Runyon presumed that this was due to a molecule, secreted through the cellophane, that attracted cells on the other side. This turned out to be the first observation that a diffusible attractant molecule is involved in guiding aggregation. It would be more than two decades before John Bonner and his colleagues<sup>2</sup> discovered that this molecule was cyclic AMP, secreted by the migrating amoebae. Carole Parent and colleagues have continued with this line of research, and now show in *Cell*<sup>3</sup> that the *D. discoideum* enzyme that produces cAMP is located specifically at the rear of the migrating cells — perhaps explaining how they move in a stream.

Many different cell types undergo chemotaxis — movement up a gradient of an attractive chemical towards its central source. The ability of *D. discoideum* amoebae to do this, and consequently to

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form aggregates (Fig. 1), is crucial to their survival in harsh environmental conditions. Failure to enter the aggregate, which later differentiates into an elaborate fruiting body producing tough, resistant spores, is a distinct disadvantage to a cell. Amoebae cannot form spores alone: they move or they die. There might also be particular advantages to marching in close-order files, such as the ability to lay down extracellular matrix as a group. This matrix, called the slime sheath, appears at about the time of stream formation and could help the cells to move over rugged surfaces — *D. discoideum* amoebae can clamber efficiently over dirt and most other substrates.

Since Bonner's discovery that cAMP is needed for streaming in D. discoideum, many of the elements and mechanisms involved have been worked out. (In experiments, cAMP is generally used as the central source of chemoattractant, as well as being released naturally by the migrating amoebae.) We now know that this organism has at least four types of cAMP receptor, as well as several unusual molecules that regulate adenylyl cyclase — the enzyme that synthesizes cAMP from ATP (reviewed in refs 4-6). An extracellular signal of cAMP is detected by the receptors, which are distributed over the entire periphery of the cell. Specific lipids then accumulate in the membrane at the front edge of the cell, and recruit certain molecules, including CRAC (for 'cytosolic regulator of adenylyl cyclase') and AKT/PKB, an enzyme involved in organizing cellular movement<sup>7,8</sup>. This series of events ensures that the cell moves towards the source of cAMP, and also leads to the activation of adenylyl cyclase and the further production

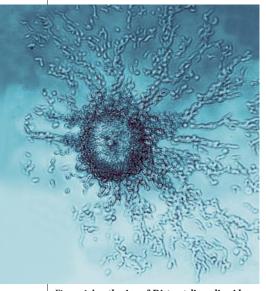


Figure 1 A gathering of *Dictyostelium discoideum* amoebae. Cells can be seen migrating — some individually, and some in streams — towards a central point. Aggregation territories can be as much as a centimetre in diameter.

of cAMP, a large proportion of which is duly secreted. And so the process continues in the next cell in line.

The expectation has always been that adenylyl cyclase itself would be located everywhere along the cell membrane, much like the cAMP receptors. But that turns out not to be the case. Parent and colleagues<sup>3</sup> have found that during chemotaxis, streaming D. discoideum amoebae localize adenylyl cyclase at their rear (in their 'uropod'), putting the enzyme in close contact with the leading edge of the following cell, but quite far from the receptors that first detect cAMP. Deleting the adenvlyl cyclase still permits chemotaxis towards a central — natural or artificial — source of cAMP, but not the extensive head-to-tail line-up of cells that is normally seen. The authors reasoned that if, as these results suggest, the position of adenylyl cyclase in the rear is essential for creating streams, then mixing cells that lack adenylyl cyclase with wild-type cells should terminate the chains. That proved to be the case (Fig. 2). It has been known for decades<sup>9</sup> that amoebae enter a stream behind a cell that is already in the queue. This behaviour could be explained if the moving cells secreted cAMP specifically from their uropods, as suggested by the location of adenylyl cyclase — this remains to be shown definitively.

Parent and colleagues also found that the localization of adenylyl cyclase to the uropod requires that the cell be polarized. This happens gradually as D. discoideum starts to starve in harsh conditions — a prelude to migration into an aggregate. Moreover, localization does not depend on protein kinase A, which is the main target of cAMP within the cell and a central regulator of events during Dictyostelium development, but it does require an intact internal 'skeleton' made up of the actin protein. Membrane-bounded intracellular sacks (vesicles) containing adenylyl cyclase also seem to be needed. The authors showed that a permanently active form of adenylyl cyclase did not become as enriched as normal in the uropod, and so, as predicted, amoebae that had this mutant enzyme did not form streams during chemotaxis. Wild-type cells could insert adenylyl cyclase in the uropod on chemotactic stimulation. But in mutant cells the enzyme seemed to be trapped in vesicles that did not reach their proper destination.

All of this leaves open the question of how events at the leading edge of a migrating cell — increasingly well worked out by the groups of Parent, Devreotes, Firtel and others — lead to the activation of adenylyl cyclase in the rear. Whatever the answer, Parent and colleagues' data<sup>3</sup> provide a mechanism by which cells can increase the efficiency of chemotaxis. Presumably, the close contact between the adenylyl cyclase in the rear of one cell and the front of the cell behind provides some of the advantages of

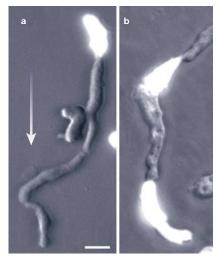


Figure 2 The importance of proper molecular positioning to streaming in Dicytostelium discoideum. Parent and colleagues<sup>3</sup> have found that the enzyme adenylyl cyclase must be located at the rear of migrating D. discoideum amoebae for streaming to occur. Presumably, this localization enables the attractant chemical cAMP, produced by adenylyl cyclase, to be released specifically from the rear and thereby recruit another cell directly to it. a, Cells with mutant adenylyl cyclase were labelled with green fluorescent protein (GFP), and appear white here. They were then mixed with unlabelled wild-type cells and allowed to form streams. Usually, the mutant cells terminate a stream. b, Wild-type cells labelled with GFP were allowed to form a stream with other wild-type cells. Wild-type cells can enter a stream and attract other cells. The large arrow indicates the direction of migration. Scale bar. 10 µm. (Reproduced from ref. 3 with permission from Elsevier.)

a neurological synapse, restricting the signal and keeping the amoebae heading in the right direction as quickly as possible. Perhaps mammalian cells can do the same, whether they are white blood cells moving to sites of inflammation, skin cells participating in wound healing, or embryonic cells during the heroic voyages of development. ■ *Richard H. Kessin is in the Department of Anatomy and Cell Biology, Columbia University, 630 West 168th Street, New York, New York 10032, USA. e-mail: rhks@columbia.edu* 

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