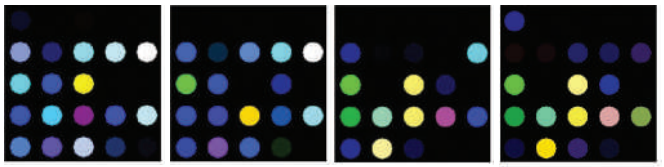
ORGANIC CHEMISTRY

Dotty solutions

What are you drinking? One answer to this frequently asked question might be found by a sensor that uses an array of chemically sensitive dyes to identify organic compounds dissolved in water.

The innovative array developed by Chen Zhang and Kenneth S. Suslick (see *J. Am. Chem. Soc.* doi:10.1021/ja052606z; 2005) uses 36 dots of dyes that change colour in response to pH, molecular polarity and Lewis basicity (how readily a molecule donates an electron pair). These properties are strongly influenced by water, making it tricky to identify trace molecules in solution. So Zhang and Suslick dampen the effects of water by using hydrophobic dyes on a hydrophobic membrane.

The combination of colour changes in the dye dots when they are dunked in solution forms a 'fingerprint' of the compounds present. The authors confirm this using a variety of common organic molecules at concentrations as low as one micromol per litre. And, although a breakdown of components is not possible with the array, complex mixtures of organic molecules do excite a unique response — as the authors show by testing a number of similar aqueous solutions found in their refrigerators (see images).



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Zhang and Suslick concede that the recognition of flavours is still some way off. That would require the incorporation into the array of hydrophobic dyes that are sensitive to salt or sugar, for instance. For now, answers to questions of taste, at least, will remain on the tip of the human tongue.

Richard Webb

activated only by wild-type MYC. The mutants' failure to activate BIM seems to contribute to their enhanced tumorigenicity, because both wild-type and mutant MYC were equally oncogenic when HSC lacking BIM were used. This implies that BIM normally constrains the carcinogenic potential of wild-type MYC, consistent with previous observations[3].

Activation of BIM by wild-type MYC does not require p53 signalling, as BIM levels were elevated in p53-deficient cells overexpressing wild-type MYC. Therefore, the oncogene activates BIM through an independent route. The authors' model predicts that BIM expression is not induced in Burkitt's lymphoma cells carrying MYC mutations. Indeed, high levels of BIM were found in all seven human Burkitt's lymphoma samples examined that carried a wild-type MYC gene, but in only one of seven Burkitt's lymphoma samples carrying a mutant gene.

Although the MYC mutants seemed to have little effect on p53 itself, they did activate one of its downstream effectors, an inhibitor of cell division called p21. How does this effect on p21 occur, and does it contribute to MYC-driven signals? Wild-type MYC inhibits p21 production by binding to the p21 gene promoter in a complex with the protein Miz-1 and recruiting further repressor proteins[4,5]. Perhaps the mutations disrupt MYC's interaction with the repressors. Or, as overexpression of mutant MYC also suppresses its own promoter, perhaps there is no wild-type MYC to form complexes with Miz-1, thereby relieving the suppression of p21. Consistent with this notion, overexpression of wild-type MYC reduced p21 levels.

BIM and p21 levels seem to be inversely regulated in this system, but it remains unclear whether wild-type MYC directly activates BIM or does so through p21. In the latter case, an interesting scenario emerges in which p21 acts upstream of BIM[6], serving as a switch to determine whether a cell will stop dividing or undergo apoptosis.

Both wild-type and mutant MYC have similar activating effects on three components of the p53-controlled apoptotic pathway — Bax, PUMA and NOXA. However, activation of these apoptosis-promoting factors does not trigger apoptosis if BIM activation is compromised (Fig. 1). Similarly, BIM activation by wild-type MYC does not induce apoptosis if the p53 pathway is disabled. The picture that emerges suggests that impairment of either the p53 or the BIM signalling route is enough to make wild-type MYC as oncogenic as the MYC mutants. The apoptotic signals conveyed by either pathway seem to be similar and additive. In mouse models, loss of one copy of the BIM gene confers strong resistance to apoptosis[3], and it will be interesting to learn whether such a loss is sufficient to abolish the difference between wild-type and mutant MYC in inducing lymphomas.

As chemotherapy usually activates the p53 pathway, these observations prompt a comparison of the response to chemotherapy between lymphoma patients carrying a translocated mutant MYC gene and normal p53 and patients carrying a translocated wild-type MYC and mutant p53. For patients with a mutant MYC, one might argue that, despite the reduced apoptosis resulting from suppression of BIM, forceful activation of the p53 pathway might potently induce apoptosis. However, it is possible that p21 would divert the signal towards cell-cycle arrest rather than death[6]. This comparison would also show whether the resistance to chemotherapy observed in mouse models of Burkitt's lymphoma[7] that overexpress MYC and are deficient in p53 faithfully mimics the response of human lymphomas with similar characteristics. If this is the case, it will offer the opportunity to refine the treatment of Burkitt's lymphoma. ■

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MANTLE GEOCHEMISTRY

Big lessons from little droplets

Claude Herzberg

How does Hawaii look deep below the surface? Like viewing an object at a different magnification, studies of minuscule inclusions in volcanic rocks on the surface provide a fresh perspective on the question.

Mantle plumes are thought to be roughly elongate cylinders of rock that buoyantly rise up from deep within the Earth, manifesting themselves at the surface in features such as the Hawaiian islands and Iceland. Much attention has centred on Hawaii, because it is constructed from Earth's largest volcanoes distributed along two geochemically distinct alignments, and there is considerable debate about what these distinctions reveal about the underlying plume that feeds them. On page 837 of this issue[1], Ren *et al.* add to that

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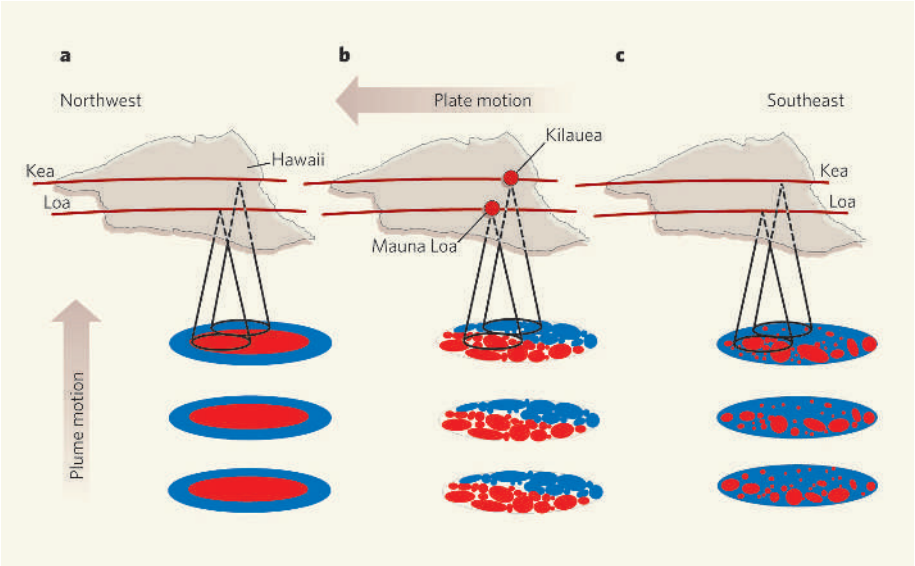

Figure 1 | Models of the geochemical structure of the Hawaiian mantle plume. The diagram depicts three possible plume structures below the two alignments (Kea and Loa) of Hawaiian volcanoes, which are surface expressions of the tectonic plate on which they sit. **a**, A concentrically zoned and vertically continuous plume[6]. **b**, A bilateral bundle of filaments vertically continuous on the 50–500-kilometre scale[7], with undefined spaces between filaments. Mauna Loa and Kilauea are two volcanoes on the Loa and Kea trends, respectively. **c**, A partly ordered structure, with streaks of red in a matrix of blue (modified from ref. 8). Red, average geochemical properties of volcanoes along the Loa track[3–8]; blue, average geochemical properties of volcanoes along the Kea track[3–8]. Ren *et al.*[1] favour the partly ordered structure (**c**), which they believe is defined by streaks of pyroxenite (red, pyroxene-rich rocks) in a heterogeneous peridotite matrix (blue, olivine-rich rocks).

debate: they show that interpretations depend on the size of the material that is subject to chemical analysis.

The Hawaiian plume is roughly 100 kilometres in diameter, and rises from the lower mantle below a depth of 660 kilometres[2]. It begins to partly melt in the final stages of its upward journey, and lava erupts at the surface to make the Hawaiian volcanoes. These are heterogeneous in that each volcano has its own geochemical identity, which can vary with time[3–5]. However, lavas from Kilauea, currently the most active volcano, have a geochemistry similar to that of older lavas that erupted along the 'Kea' alignment of volcanoes[4,5], which include Mauna Kea, Kohala and Haleakala to the northwest. The geochemistry of Kea volcanoes differs from that of the 'Loa' volcanoes[4,5], which include Loihi, Mauna Loa, Kahoolawe and Koolau, a parallel alignment displaced to the west (see Fig. 1 on page 837).

These differences, expressed in radiogenic isotopes, and trace and major elements, have been interpreted to reflect the three-dimensional spatial organization of the chemical constituents in the plume before melting took place. This is referred to as the geochemical structure of the Hawaiian plume[1,6–8]. But there is no consensus about the form of this structure; different models are summarized in Figure 1.

One model has geochemical heterogeneities ordered in a concentric and vertically continuous structure[6] (Fig. 1a); Loa volcanoes sample the centre, Kea volcanoes sample the periphery. Another model has geochemical heterogeneities ordered in filaments clustered together like spaghetti[7] (Fig. 1b), which is consistent with the expectation of stretching and shearing of heterogeneities in a plume[9]; Loa and Kea volcanoes sample a bilateral distribution of filaments[7]. A third model has a more random but partly ordered distribution of geochemical heterogeneities both vertically and laterally[8] (Fig. 1c). The origin of these heterogeneities is a separate issue. However, there is a consensus that it has something to do with near-surface magmatism, crust production and sediment accumulation in the early Earth, subduction of this outer unit into the deep mantle, and an upward return in a hot plume that melts to make Hawaii.

All three models are interpretations of the geochemistry of whole-rock samples — 'hand specimens' — of centimetre scale. The approach taken by Ren and co-workers[1] differs: using microanalytical techniques, they have acquired geochemical data on melt inclusions, about 10–100 micrometres in size, contained in millimetre-sized crystals of olivine, a common mineral in some volcanic rocks. They show that major-element and trace-element compositions of olivine-hosted inclusions from a single rock extracted from a single volcano can have the properties of both Loa and Kea volcanoes. They suggest that either the Loa or the Kea component is represented by whole rocks, but both are represented in olivine-hosted inclusions regardless of the specific geographical location of the volcano. This study supports the more random model[8], although some hybrid of the ordered models (Fig. 1a, b) is still required to yield the Loa and Kea trends (Fig. 1c).

How is it possible that whole-rock samples from an individual volcano support either a Loa or a Kea source, but the inclusions support both sources? Why does the scale of the geochemical observation yield different interpretations? The answers lie in an understanding of how rock melts. The Hawaiian plume melts by forming millimetre-sized liquid droplets that inherit the geochemical properties of their source rock. Each drop of melt usually mixes with other drops during transport to the surface. Although it is not clear exactly where mixing takes place, it is known to homogenize the geochemistry on the centimetre scale of the hand specimen and the kilometre scale of an individual volcano. A rock from Kilauea can be thought of as a blend of one melt drop from a Loa source and 100 melt drops from a Kea source. However, even a well-mixed rock can contain olivines that crystallized from melt droplets before mixing took place. In this way, crystal growth can entomb the drops as tiny inclusions before they become part of the blend.

The large geochemical heterogeneities reported by Ren and co-workers for Hawaii are similar to those of inclusion studies for lavas from Iceland[10]. However, the Iceland case has been interpreted somewhat differently, as being the result of the continuous removal of small melt fractions from a single source composition[10], a process called fractional melting. The authors of that study[10] acknowledge that some of their data might also be explained by variable source compositions, as do Ren *et al.* for Hawaii. And it is likely that some of the geochemical variability reported by Ren *et al.* can be explained by fractional melting.

Further studies are evidently called for. What is becoming clear is that complementary inclusion and whole-rock geochemical studies expand the scale of observation in a way that is comparable to viewing an object with variable magnification. ■

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