melt and saline fluid. At high pressures (>15 kbar) the main effect of adding chlorine is simply to increase the solubility of silicate melt in fluid. Perhaps it is not chloride complexes but total solute content that controls element partitioning. Whether the differences between the two salt-water studies are due to the different pressure ranges explored or to experimental or analytical problems remains to be tested, but linking element partitioning to total solute content provides one explanation for some of the similarities between the saline and salt-free results.

A final word of caution — all of these experiments were conducted at 900 °C or more. Most slab dehydration is thought to occur at much lower temperatures[11], where silicate solubility and fluid partitioning may be considerably depressed. Also, at slab temperatures greater than 900 °C silicate melting might become important .

This sudden wealth of fluid/crystal partitioning data has provided welcome laboratory confirmation of the role of recycled sea water in the creation of arc magmas and the continental crust. Many issues remain outstanding, in particular the role of different fluid solutes. Studies of arc magmas where chlorine and water are combined with trace elements may be needed to identify the importance of salty water in subduction recycling. ☐

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HAEMOGLOBIN

Root cause of fish buoyancy

Rory Howlett

FISH have a problem — because their body tissues are denser than water they have a tendency to sink. Those that have solved the problem with a swim bladder face the complication that, to retain neutral buoyancy, they must secrete gas into the bladder against a pressure gradient; the deeper they swim, the bigger the gradient. A study by Mylvaganam *et al.*, published in the March issue of *Nature Structural Biology*[1], in part reveals how they do it. The authors show that certain fish haemoglobins have structural characteristics that make them efficient proton-driven oxygen pumps, able to drive the gas into a swim bladder.

Cartilaginous and bony fish retain buoyancy in different ways. Cartilaginous fish such as sharks never cease swimming, using their pectoral fins as hydrofoils and their asymmetrically shaped tail fins to generate lift, and also accumulate low-density oils and the hydrocarbon squalene in their tissues. Most pelagic and surface-living bony fish have a swim bladder which is essentially an extensible sack of gases, mostly nitrogen and oxygen, and which acts as a kind of portable float.

Gas has clear advantages over squalene, but its use in an aqueous environment also presents challenges. As a fish swims deeper it experiences higher water pressure and its swim bladder is compressed, while the opposite occurs as the fish moves towards the surface. To compensate for these changes, as well as diffusional losses, the fish has continually to regulate the amount of gas in the swim bladder, and here things can become tricky. Some species replenish gas supplies simply by gulping air at the water surface which is then passed through a duct to the swim bladder. But others, such as those living in deeper water or lacking a bladder duct, must secrete gases from the blood to the swim bladder against a pressure gradient. This is generally achieved through the ingenious design of the so-called gas gland, which secretes lactic acid. One effect of the acid is to force nitrogen out of solution, but the most striking consequence is a marked reduction in the oxygen affinity of blood haemoglobin — a phenomenon known as the Root effect.

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Spot the difference — blue marlin, like the subject of Mylvaganam and colleagues' studies, has Root-effect haemoglobin.

It is this pH-dependent release of oxygen from Root-effect haemoglobin, as well as some fancy plumbing in the gas gland itself, that largely accounts for the ability of fish to compress oxygen and force it into the swim bladder when extra buoyancy is needed. But exactly why is the oxygen affinity of fish haemoglobin so exquisitely sensitive to pH? The oxygen binding and release characteristics of haemoglobins involve allosteric changes, and it seems reasonable to assume that the Root effect is driven by proton-induced conformational changes in fish haemoglobins, although the precise mechanism has remained unclear.

To address this issue, Mylvaganam and colleagues studied the structure and function of a representative Root-effect haemoglobin from *Leiostomus xanthurus*, commonly known as the spot, a bony fish that lives along the eastern seaboard of the United States. Using X-ray crystallography, they have determined the structure of the ligand-bound protein at 2 Å resolution, and have identified several key amino-acid residues that assemble into two positive-charge clusters across the interface of two β-chains in the high-affinity R-state haemoglobin. Binding of a proton flips an electrostatically based switch, pushing apart the two positive-charge clusters, and inducing a profound conformational change. This effectively locks the Root-effect haemoglobin in the low-affinity T-state even at high pressures of pure oxygen, which would account for the remarkable effectiveness of Root-effect haemoglobins as proton-driven oxygen pumps.

Aspects of the proposed mechanism will have to be confirmed by mutagenesis studies, to assess the effect of specific amino-acid substitutions in the two positive-charge clusters. Meantime, comparisons of the sequences of various fish haemoglobins should provide pointers as to how the magnitude of the Root effect has been fine-tuned by natural selection to suit the specific needs of fish with different life histories and ecology. More generally, the new work opens the way to the rational engineering of haemoglobins with defined oxygen-binding characteristics that could be of importance in medicine and elsewhere.

This is just one of the latest of a series of findings unveiling the marvellous properties of haemoglobin: one only has to turn the page to find discussion of another. And last year, for instance, Komiyama *et al.*[2] showed that the allosteric characteristics of crocodile haemoglobin are determined by a few key amino-acid residues; these give rise to the adaptive oxygen-binding characteristics of haemoglobin suited to the respiratory needs of crocodiles, which often remain submerged for long periods when drowning large prey. ☐

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