Clemens *et al.* see Milankovitch cycles embedded in the past half-million years. (Milankovitch identified a correlation between climate cycles and the periodic variations in the Earth's orbit about the Sun.) Their $^{87}Sr/^{86}Sr$ record is punctuated by deglacial rises and glacial falls that are coherent (the amplitude variations match) and in phase (no leads or lags) with oxgyen isotope fluctuations (growth and decay of glacial ice). This implies strong and fast connections between the continental component of climate change and the forces driving the seawater $^{87}Sr/^{86}Sr$ changes.

Clemens *et al.* recognize that their data are difficult to reconcile with the present paradigm. First, strontium has a residence time in the sea of several million years, too long to accommodate the apparent rates of these isotope changes. Even worse, the systematics of present-day strontium weathering and river $^{87}Sr/^{86}Sr$ ratios[6], including those draining the Himalayas and ^{87}Sr-rich continental shields (glaciated during the ice ages), preclude the requisite changes in the river flux or ratio needed to drive the amplitudes of their observed changes. Turning rivers off altogether during glacials hardly seems reasonable.

The second, more substantial stumbling block is that the measured changes in the ocean ratio are minuscule, all contained within their 2σ error limits. The maximum glacial-to-interglacial changes in $^{87}Sr/^{86}Sr$ (0.000020, or 20 p.p.m.) are at the edge of the best mass spectrometer reproducibility (8 p.p.m.). Alas, the standard deviation of the entire data set is 8 p.p.m. The reported glacial-to-interglacial differences are thus supportable only in the statistical sense. Spectral comparison of the authors' $^{87}Sr/^{86}Sr$ record with the global ocean oxygen isotope record indicates significant covariation for the 100,000 year Milankovitch cycle (less so for the 41,000-year cycle). Their statistical case is robust, based on almost two decades of matching Late Pleistocene climate records to Earth-orbital rhythms[7]. So what could possibly be wrong?

The simplest answer is to dismiss the spectral analysis as analytically unresolvable, that the devil is in the details of the tiny changes in the measurements. Clemens *et al.* have partially answered this problem by analysing all 77 data points in duplicate or triplicate, and by 'supercleaning' a subset of their foraminifera and rerunning them. The 17 samples of the subset have no non-calcite contamination phases that might carry non-seawater ratios and offset the measured ratios. But the ghosts of mass spectrometry hide in mysterious places. Those who wish upon fast ocean variations see signal; those who do not, see noise.

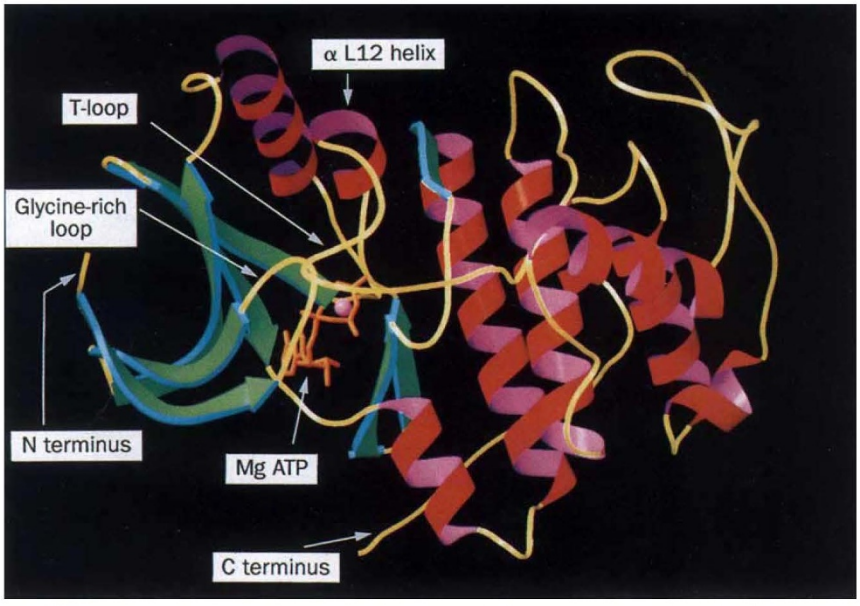
Another possibility is that ocean $^{87}Sr/^{86}Sr$ was not homogeneous during glacial periods as it is today. The foraminifera come from an Ocean Drilling Program site in the equatorial Indian Ocean, only 1,900 kilometres south of the mouths of the great Himalayan rivers that could raise the ratio locally but not globally. Climate-induced fluctuations in the Indian monsoon, which modulate rainfall and thus the ^{87}Sr-rich Himalayan river flows, might impart the Milankovitch precessional (23,000-year) cyclicity to their $^{87}Sr/^{86}Sr$ signal. Yet the cross-spectral analysis shows no evidence of such forcing, confounding the search for a direct local link to the Himalayas. In addition, an earlier less-detailed $^{87}Sr/^{86}Sr$ record from a piston core in the western equatorial Pacific[8] contains similar changes over the past 250,000 years, so the effect is apparently global. (Although the Cambridge team that produced the record is now itself uncertain about its validity[9].)

Are the present river $^{87}Sr/^{86}Sr$ systematics poor analogues for the glacial past? Were glacial continental drainage patterns and $^{87}Sr/^{86}Sr$ ratios so dramatically different that we are missing some subtlety? There might be a case for this view if built on a geochemical proxy other than $^{87}Sr/^{86}Sr$, but the well-established ^{87}Rb–^{87}Sr dating method and the concomitant large data set for $^{87}Sr/^{86}Sr$ in rocks and fluids virtually precludes oversight in this instance.

So we are left with one of the choices that Clemens *et al.* mention last — pulsations of the seafloor hydrothermal fluxes with the ice ages. Fluxes would need to relax on deglaciations, driving up seawater $^{87}Sr/^{86}Sr$ in steps. What mechanisms might be responsible? Tectonic flexure of the upper mantle, by loading and unloading the enormous masses of water-ice between ocean basins and continents, might be considered, but is too slow to produce phase lock with climate change. Changes in the hydrothermal isotope ratio (0.703) also seem unlikely.

But there is one unexpected possibility. The 130-m rise and fall of sea level (by

The phosphate's tale



THIS illustration is not a pasta cook's nightmare but the structure of cyclin-dependent kinase 2 (CDK2), as reported on page 595 of this issue. Like other protein kinases, CDK2 catalyses the transfer of γ-phosphate from Mg ATP to a protein substrate, this particular enzyme being implicated in control of the G1- and S-phase events of the human cell cycle. It is the catalytic subunit of human CDK2 that is shown here. It consists of two domains: an amino-terminal lobe (mainly green β-sheet, left) and a larger carboxy-terminal lobe (mainly red α-helix, right). The Mg ATP sits at the bottom of the substrate-binding cleft between the two lobes. Unlike other protein kinases, where the catalytic subunit is fully active, the CDK2 apoenzyme is unable to phosphorylate its substrate. It seems that the glycine-rich loop, and indirectly the α L12 helix, force the Mg ATP into an unfavourable conformation for γ-phosphate transfer; also, a large loop — the T-loop — blocks the substrate-binding cleft. Yet for the cell cycle to proceed CDK2 must be activated, albeit transiently. The initial step is thought to involve the binding of cyclin A to the enzyme's amino-terminal lobe. This may destabilize the α L12 helix, allowing the Mg ATP to assume a conformation for phosphate transfer and loosening up the T-loop. Full activation of CDK2 requires the phosphorylation (by another kinase) of threonine 160, at the tip of the T-loop. This phosphate could pin the loop back against the carboxy-terminal lobe, through ionic interactions, allowing the substrate access to the active site. G. R.