by the authors, corresponding to human embryonic day 47, focused on the hand and foot plates; at this stage, Cotney *et al.* identified 16% of promoters with human-lineage gains. These results are in accordance with the intuitive idea that later developmental stages will demonstrate more human-specific morphological features (Fig. 1a). In total, more than 2,000 promoters and nearly 3,000 enhancers showed significant human-lineage gains at at least one assayed time point, demonstrating the dramatic orchestration of gene expression that is required for human limb development.

In their comparisons between species, the authors classified enhancer regions into three categories: orthologous (an enhancer sequence that simply exists in all three species); those that exist and are stably marked with a consistent level of H3K27ac in all three species; and those that exist in all three species but that show a gain of H3K27ac in the human lineage.

The characteristics of the sequences that fit into these classes, including their evolutionary age and conservation, provide some seemingly surprising results. First, the majority of human-lineage gains do not occur in highly conserved elements, although they do not seem to be completely unconstrained; rather, the greatest sequence conservation is seen in the stably marked regions. The stably marked and orthologous regions are also significantly older, in evolutionary terms, than those in which activity arises in the human lineage, with many also being present in non-mammalian vertebrates (Fig. 1b). Human-lineage gains, on the other hand, tend to be found in sequences that arose between the time that marsupials and placental mammals shared a common ancestor and the divergence of the placental lineage. A few of the sequences identified as human-lineage gains also overlap with regions previously identified as showing significant change since the divergence of the human lineage from chimpanzees[5]. Cotney and colleagues' findings provide clues to the roles of 16 of these 'human acceler-ated regions', and these may now be attractive candidates for further analysis.

Exactly what is going on in the regions with enhanced regulatory activity in the human lineage is still not known. The sites had no obvious enrichments for specific transcription-factor-binding motifs. Also absent were specific repetitive elements, which have been shown to contribute to the regulatory rewiring of multiple mammalian lineages[6] and to be a contributing factor to the evolution of pregnancy[7]. Understanding the molecular drivers at these and other certain-to-be-discovered regions of human regulatory change is both a formidable and an exciting challenge.

There are limitations to Cotney and colleagues' analysis. For example, the quality of the genome sequences varies between the species, which may have contributed to the authors' inability to find orthologous regions in macaques for some human sites. Alternative explanations

for this lack of orthologues, based on changes in copy number or human-lineage duplications[8], are also complicated by the absence or possible misassembly of these regions in the human genome sequence. Moreover, there are problems associated with mapping and analysis of the short DNA sequences resulting from the ChIP-seq analysis used by the authors to sequence regions containing H3K27ac marks. However, the study provides clear insight into the regulatory changes that help to make us human, and the authors have presented an extremely valuable map, connecting regulatory regions and gene-expression changes involved in human limb development. ∎

Paul Flicek *is in the European Molecular Biology Laboratory, European Bioinformatics Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge CB10 1SD, UK.*
e-mail: flicek@ebi.ac.uk

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CLIMATE SCIENCE

Solution proposed for ice–age mystery

The ice sheets retreated 10,000 years ago during a peak in solar radiation, but this peak was no larger than previous ones. A modelling study suggests why the ice sheets were unusually vulnerable to melting at that time. SEE LETTER P.190

SHAWN J. MARSHALL

I first encountered *Ice Ages: Solving the Mystery*[1], the seminal book by John and Katherine Imbrie, as an undergraduate student, and it played no small part in drawing me in to graduate studies on ice-age climate dynamics. Imbrie *père et fille* describe the various strands of evidence establishing that Earth–Sun orbital variations are the main driver of glacial cycles: the recurring flow and ebb of ice sheets over the continents during an ice age. About 40 such glacial cycles have shaped our planet over the past 2.6 million years (the Quaternary period), representing the most dramatic example of climate variability in Earth's recent history.

But there is one nagging problem: as much as Earth's orbital wobbles seem to pace the advance and retreat of ice sheets, many aspects of ice-age climate dynamics remain a mystery. For one thing, those who model climate and ice sheets have not yet been able to simulate glacial cycles in a realistic way. Glacier advance into mid-latitudes requires severe cooling and increased snowfall compared with present-day conditions, to an extent that far exceeds the predicted response of the Earth system to 'cold' orbital configurations in climate models. It is even more difficult to get rid of continental ice sheets once they gain a foothold on the landscape. The modelling results reported by Abe-Ouchi *et al.*[2] in this issue may provide a solution to these problems.

The crux of the challenge in modelling glacial cycles is that Earth's response to orbital

forcing is entirely out of proportion. Changes in Earth's tilt axis and the eccentricity of its orbit around the Sun give rise to geographical and seasonal changes in incoming solar radiation. The global annual impact of these variations is negligible, but what really matters to the ice sheets is the amount of sunlight at high northern latitudes during the summer melt season. Peak radiation in this region varies by up to 100 watts per square metre because of orbital variations (Fig. 1a); this would certainly affect Arctic ice cover. However, integrated summer radiation, which is what counts in ice-sheet melting[3], has deviated by less than 10% from present-day values over the most recent glacial cycle (Fig. 1b), and it is not obvious why this has elicited such a large shift in global climate.

In fact, a host of positive feedbacks — cooling influences associated with increases in snow and ice cover — conspire to amplify the orbital signal and send the world careering into glaciations. It is difficult to overcome these cooling influences, and so orbital changes alone are not enough to trigger deglaciation. The most recent glaciation persisted for roughly 100,000 years, and the ice sheets survived several periods of orbital warming before they finally destabilized and withdrew, starting about 20,000 years ago (Fig. 1c). At that time, summer solar radiation in the Northern Hemisphere increased, eventually peaking at about 6% above modern levels 10,000 years ago. But similar peaks occurred earlier during this period of glaciation, so what was different about this one?
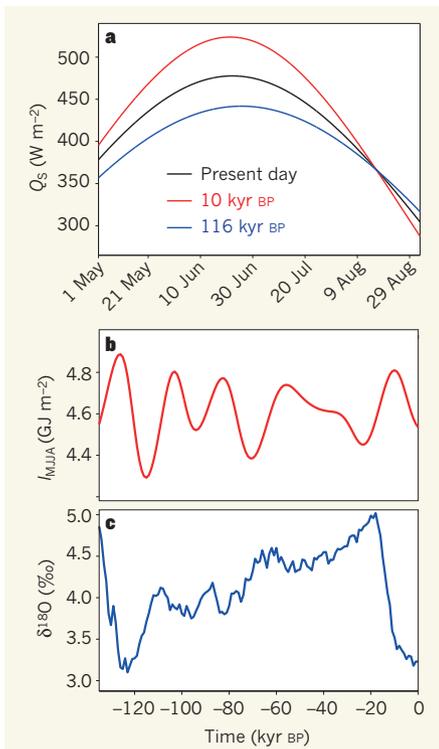
Figure 1 | Solar radiation and ice-sheet coverage.
a, The average daily incoming solar radiation (Q_s) at 60° N from May to September varies as a result of fluctuations in Earth's orbit around the Sun, as revealed by these data for 116,000 years before present (116 kyr BP; the inception of the last glacial period), 10 kyr BP (the period of maximum insolation during the most recent deglaciation) and the present day[3]. **b**, The integrated summer insolation (I_{MJJA}) at 60° N during the last glacial cycle reveals several peaks. **c**, Stacked benthic stable isotope ratios ($\delta^{18}O$) from the global ocean are a proxy for global ice-sheet volume during the glacial–interglacial cycle[7]. Comparison of **b** with **c** reveals that the insolation peak that triggered deglaciation was only as large as other insolation peaks that did not induce deglaciation. Abe-Ouchi et al.[2] report that the geometry of North America and the time taken for bedrock to sink beneath ice sheets explain why deglaciation occurred when it did.

Through asynchronous coupling of sophisticated climate and ice-sheet models, Abe-Ouchi and co-authors make a convincing case that the geometry of North America and the long response time of isostatic compensation — the change in height of Earth's surface in response to ice-sheet formation and retreat —are the main agents that transform 19,000-year (19-kyr), 23-kyr and 41-kyr orbital variations into a 100-kyr Earth-system response[4]. Ice sheets build up and flow southwards in both North America and Eurasia, taking many millennia to thicken and advance to their southern limits. Subglacial bedrock is depressed as underlying mantle material flows slowly outwards. At equilibrium, a 3,000-metre-thick ice sheet undergoes about 1,000 metres of subsidence[5], but achieving equilibrium takes thousands of years. Similarly, land that was underneath the glacial ice

sheets is still springing back.

Isostatic subsidence is one of the few negative feedbacks associated with glaciation: as an ice sheet slowly sinks, its surface lowers into a warmer climate, increasing the amount of melt and the area of the ice sheet exposed to melting. In Abe-Ouchi and colleagues' simulations, this process becomes most effective late in the glacial cycle, when the North American ice sheets are thick and have advanced far enough south; because this takes a long time, North America is set for a 100-kyr response. By contrast, the geography of the Eurasian ice sheets (which are thinner and less extensive, and occur in a warmer climate) gives them less inertia, and so they are more sensitive to 20- and 41-kyr orbital variations.

This idea is not new — earlier modelling studies[5,6] also implicated isostatic rebound as one of the main processes underlying the 100-kyr glacial cycle. However, free-running simulations of the cycle have never before been achieved without invoking 'exotic mechanisms' — such as imposed ocean-circulation changes, dynamic ice-sheet destabilization or 'dusting' of the ice sheets — that force deglaciation at the 'right' time. One innovative technique that helps to capture the glacial cycle in Abe-Ouchi and colleagues' analysis is the use of multiple snapshots from climate models, which provide information about different ice-sheet sizes, carbon dioxide concentrations and orbital configurations. This is necessary because the computational time required to run a sophisticated climate model over tens of millennia is still prohibitively long.

However, some lingering mysteries remain,

such as the effects of the oversimplified treatment (or absence) of ice sheet–ocean interactions, basal flow (ice-sheet sliding and subglacial sediment deformation) and ice-stream processes in the authors' simulations. Furthermore, ice-sheet melt rates are estimated only from air temperature, and are not based on energy-balance physics within the atmospheric model used by the authors. As climate and ice-sheet models become more sophisticated, we will see further refinement of these results.

Moreover, Abe-Ouchi and colleagues' findings do not explain the transition that took place 900,000 years ago, when the world moved from 41-kyr to 100-kyr glacial cycles. Isostatic time scales and North American geography did not change across this boundary, so another factor must have been at work. There are some layers yet to be explored in the mysteries of the ice age. ∎

Shawn J. Marshall is in the Department of Geography, University of Calgary, Calgary, Alberta T2N 1N4, Canada, and at the Canadian Institute for Advanced Research.
e-mail: shawn.marshall@ucalgary.ca

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Jurassic fossils and mammalian antiquity

Two new Jurassic fossils yield conflicting reconstructions of the mammalian tree. These divergent genealogies have profoundly different implications for the origin and early diversification of mammals. SEE ARTICLE P.163 & LETTER P.199

RICHARD L. CIFELLI & BRIAN M. DAVIS

Fossil discoveries and molecular studies in recent decades have greatly advanced our understanding of mammalian relationships and diversification[1]. Yet major points of disagreement remain over some of the basal branches of the family tree. There is little doubt that mammals, strictly defined[2], were widespread and ecologically diverse by the middle of the Jurassic period, about 165 million years ago[3–5]. But when did they originate? A major sticking point is the inclusion (or not)

of certain poorly known early forms. Substantial information is now provided by two separate discoveries, reported in this issue by Zhou et al.[6] (page 163) and Zheng et al.[7] (page 199), of splendidly preserved fossils from China that date to between 160 million and 165 million years ago.

Both fossils, which include evidence of fur but lack complete skulls, have been assigned to the Haramiyida. This enigmatic group includes fossils dating back to the Late Triassic — that is, about 40 million to 50 million years before the appearance of undoubted