of a chromosome remained to determine the arrangement of sequence variations for each chromosome haplotype. This allowed them to use sequence data to calculate the copy number of each haplotype in each cell and thereby identify the putative micronuclear chromosome.

The authors' sequence data further showed that micronuclear chromosomes had significantly more structural rearrangements than other chromosomes. Most of the rearrangements seemingly arose through a breakage and rejoining mechanism, which could be secondary to faulty DNA replication in the micronucleus. The transient lifespans of micronuclei and their tendency to contain only one or two chromosomes thus elegantly account for the focal nature of chromothripsis. Presumably, once the cell proceeds into the next division and the micronucleus reincorporates into the main nucleus, the damaged chromosomes are exposed to appropriate levels of replication and repair factors, and the rearrangements could become stabilized over subsequent generations. The discovery of mitotic defects as an origin of chromothripsis provides further evidence that chromosome mis-segregation and DNA rearrangements, both of which are observed in tumour cells, can be mechanistically linked[6].

Zhang *et al.* identified extensive rearrangements in nearly all micronuclear chromosomes, indicating that ruptured micronuclei lead to extensive mutation. Examining micronucleated cells before DNA replication, and cells in which micronuclei do not rupture, could reveal whether DNA replication is required for chromothripsis, and determine whether chromothripsis is but one of many possible outcomes for micronuclear chromosomes. LookSeq is a powerful method to address these and many other questions, providing knowledge on both the history of a cell and the architecture of its genome. ■

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CLIMATE SCIENCE

Timing is everything during deglaciations

Links between various climate records for the North Atlantic Ocean and the Mediterranean Sea have helped to identify a potential mechanism that enhanced sea-level rise during the last interglacial time interval. SEE LETTER P.197

KATHARINA BILLUPS

As everyone who enjoys a good murder mystery knows, establishing the *modus operandi* of the villain is crucial to solving the crime. Similarly, understanding the forces that drive climate change requires an unambiguous reconstruction of the sequence of events involved. In this vein, Marino *et al.*[1] (page 197) have unravelled a chain of events characterizing the melting of the large polar ice sheets that existed about 140,000 years ago. This deglaciation led to the last interglacial interval — the last time that Earth underwent an interval of peak warmth between glacial periods, and at which the sea level was similar to or perhaps slightly higher than it is today[2]. The findings reveal fundamental differences between the two most recent glacial-to-interglacial transitions.

Numerous publications[3,4] have provided a comprehensive picture of the timings of events that make up the most recent glacial-to-interglacial transition, which began 20,000 years ago. These events culminated in our current interglacial epoch, the Holocene. But such a detailed picture is more difficult to assemble further back in time, given the inherent difficulties in dating older geological materials.

The problem is that the availability of radiometrically dated materials needed to determine an accurate sequence of events decreases the further back in time one goes. Other means of establishing ages must therefore be used. But ages derived from, for example, astrochronology (which allows sediments to be dated using timescales calibrated by astronomical events), are more often than not further apart than the events of interest. This plagues all studies trying to resolve rapid climate changes occurring on timescales of about 10,000 years or less, which includes the timescale over which major deglaciations take place.

In their search for the chain of climatic events leading up to the last interglacial interval, Marino and colleagues have provided a solution to the age-model problem. They adjusted individual climate proxy records for the ocean (oxygen-isotope records from the fossilized remains of unicellular marine organisms called foraminifera) to oxygen-isotope records derived from speleothems — inorganic

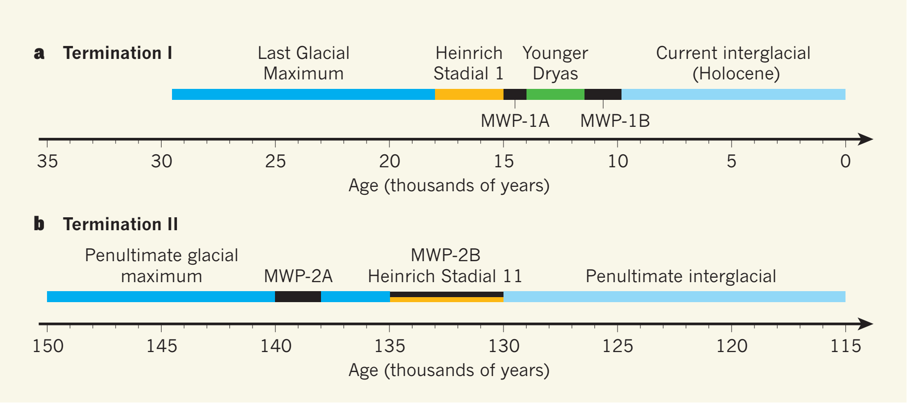

Figure 1 | Glacial-to-interglacial transitions. a, Termination I (TI) was the most recent time during which Earth passed from a glacial to an interglacial period. The Last Glacial Maximum represents the period when ice sheets were at their maximum extent. This was followed by a cooling event (Heinrich Stadial 1) and then the main phase of deglaciation, meltwater pulse 1A (MWP-1A). Deglaciation was interrupted by a return to almost full glacial conditions — the Younger Dryas — before the final deglaciation phase, MWP-1B. Ages for individual events in TI are taken from refs 4 and 9. **b**, Marino *et al.*[1] report the sequence of events for Termination II, the penultimate glacial-to-interglacial transition. In contrast to TI, the cooling event (Heinrich Stadial 11) coincided with the main deglaciation phase (MWP-2B). MWP-2A represents a relatively minor meltwater pulse earlier in the transition.

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carbonate deposits in caves — which have radiometrically constrained chronologies for this interval of time.

This approach is not new. But the novelty of the current work lies in the fact that all records come from the Mediterranean region, and are thus naturally coupled through the local hydrological cycle and through oxygen-isotope fractionation within it, thereby providing a basis for clear correlations. Once the oxygen-isotope records from different Mediterranean sites are placed in a common temporal framework, the relative timing of associated climate parameters emerges. Temporal relationships can then be established between changes in sea surface temperatures, meltwater pulses and the deposition of ice-rafted debris onto the ocean floor.

The revised chronology of the proxy records examined by Marino and co-workers points to a pivotal difference in climate dynamics between the most recent and the penultimate glacial-to-interglacial transitions, which are also known as Terminations I and II, respectively. Both are associated with times when summer insolation (incoming solar radiation) in the Northern Hemisphere and atmospheric carbon dioxide levels were increasing. One would therefore expect the ensuing ice-sheet melt-back behaviour to have been similar as well. But it was not.

It is known that, during Termination I, there was a period of maximum cooling in the North Atlantic called Heinrich Stadial 1, which coincided with peak iceberg discharge (Fig. 1a). This was followed by the major phase of deglaciation, known as meltwater pulse 1A. Deglaciation was subsequently interrupted by a return to almost full glacial conditions — the Younger Dryas — before the final ice retreat during meltwater pulse 1B.

By contrast, Marino and colleagues' chronology shows that the main phase of deglaciation (meltwater pulse 2B) during Termination II occurred during the period of maximum North Atlantic cooling and iceberg discharge (Heinrich Stadial 11). In short, Heinrich Stadial 1 preceded the major phase of ice-sheet retreat, whereas Heinrich Stadial 11 coincided with it (Fig. 1b). This means that not all terminations are equal, making it much more difficult to find an underlying forcing mechanism.

North Atlantic cooling and enhanced iceberg discharge during Heinrich Stadial 11 might seem to be at odds with background climate warming and deglaciation. But as the authors point out, the new chronology also reveals that Heinrich Stadial 11 coincided with warming in the Southern Hemisphere, as recorded by ice cores[5]. Warming in one hemisphere coinciding with cooling in the other is a well-characterized phenomenon called the bipolar see-saw[6]. The term refers to ocean-surface heat transport from the Southern to the Northern Hemisphere as part of a large-scale circulation process (the meridional overturning circulation) in the Atlantic Ocean. During Heinrich Stadial 11, relatively slow ocean circulation allowed heat to build up in the Southern Hemisphere. The authors suggest that this warming stimulated melting of the Antarctic ice sheet, contributing to the enhanced sea-level rise associated with the penultimate deglaciation.

Marino and co-workers' study exemplifies how the nature of the temporal ties between climate records can affect the reconstruction and understanding of climate events. The researchers provide a specific solution to the timing of events during Termination II. However, the generality of their approach is limited by the assumptions that need to be made about climatological links between radiometrically dated speleothem and marine proxy records from dissimilar oceanographic regions.

Rapid deglaciations such as Terminations I and II are part of an asymmetric climate pattern that begins with slow ice-sheet build-up followed by rapid ice-sheet melt-back. This sequence repeats on timescales of about 100,000 years and first appears in the geological record of climate change about 900,000 years ago[7]. There are no obvious direct external forcing mechanisms for this pattern, unlike the shorter climate cycles that occur on timescales of 41,000 to 19,000 years. The evolution of the 100,000-year climate cycle is therefore one of the big unsolved mysteries in palaeoceanographic research[8]. A robust temporal reference frame for the sequence of events defining each deglaciation, such as that assembled by Marino *et al.* for the penultimate one, should help to build a consensus about the *modus operandi* behind this climate pattern. ■

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HUMAN EVOLUTION

Ancient DNA steps into the language debate

Two studies of ancient human DNA reveal expansions of Bronze Age populations that shed light on the long-running debate about the origins and spread of Indo-European languages. SEE ARTICLE P.167 & LETTER P.207

JOHN NOVEMBRE

The archaeological adage that pots are not people expresses the challenge of using cultural artefacts to trace the movement of populations. To surmount this obstacle, archaeologists and population geneticists are joining forces to extract DNA from human remains that are found with archaeological evidence of ancient cultures. In this issue, Haak *et al.*[1] (page 207) and Allentoft *et al.*[2] (page 167) report two of the largest studies of ancient DNA to date. Combined, the studies analyse 170 samples, and each group brings evidence to bear on a long-standing controversy about the origins of the Indo-European language family.

Indo-European languages have been spoken across Europe and in central and southern Asia since the beginning of recorded history. This is a broad language family, including Italic, Germanic, Slavic, Hindi and Tocharian languages, among others. When and where the precursor of these languages began to spread has long been a subject of debate[3]. There are two main theories: the Anatolian and the steppe hypotheses.

The Anatolian hypothesis posits that Proto-Indo-European spread with farming out of Anatolia (a region that lies within modern-day Turkey) during the Neolithic period, approximately 7000 BC. Some archaeological and genetic data support this hypothesis, as does a phylogenetic analysis of linguistic data[4]. By contrast, the steppe hypothesis[3,5] supposes that Proto-Indo-European spread from the Pontic–Caspian steppe (a region of modern-day Russia, Ukraine and Kazakhstan that lies north of the Black Sea and stretches eastwards to the Caspian Sea; Fig. 1a). Recent versions of the hypothesis argue that the language spread during the late Copper Age and early Bronze Age, between 3700 BC and 2000 BC, carried

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