50 Years Ago

It has been reliably demonstrated that rats can discriminate between the presence or absence of X-rays … The process by which X-rays elicit arousal and orienting reactions in mammals has not yet been determined. However, for simplicity we assume this mechanism operates via a 'radiation receptor'. Attempts to locate this hypothetical radiation receptor have yielded conflicting results … We used a narrow 3/16-in. X-ray beam as a signal or conditioned stimulus to warn the animal of a subsequent shock to the paws. The beam was most effective when it was directed at the olfactory region of the head … In an attempt to clarify this issue, we conducted a study of the effectiveness of X-ray as an arousing stimulus in rats the olfactory bulbs of which had been removed … The results indicate a distinct loss of sensitivity when the olfactory bulbs are removed.

From *Nature* 6 February 1965

100 Years Ago

In *Popular Astronomy* Prof. E. C. Pickering quotes some interesting letters from Profs. Backlund, of Pulkovo, and Schwarzchild, of Potsdam, with reference to astronomers and the war. None of the Pulkovo astronomers have been called to serve, but Prof. Backlund's son is in the Russian ranks, and of French astronomers, M. Croze, astrophysicist of the Paris Observatory, has been summoned, as well as the son of the director, M. Baillaud, who has six sons and sons-in-law in the war. On the German side, many young astronomers are in the field. Dr. Zurhellen and Dr. Kühl, who were with the eclipse expedition, have been interned in Russia; Dr. Münch, of Potsdam, is wounded and a prisoner in France.

From *Nature* 4 February 1915

Finally, Zhao *et al*. tested the function of another enzyme in the lincomycin pathway, LmbT, which they thought might attach EGT to a biosynthetic intermediate. LmbT is a homologue of glycosyltransferase enzymes, which attach sugars to other molecules. The researchers performed a series of gene-disruption and *in vitro* biochemical experiments, establishing that LmbT must act before installation of the 4-propyl-L-proline (PPL) moiety, which forms part of the structure of lincomycin A. In the process, they also proved that three more enzymes — LmbC (ref. 8), LmbN and LmbD — collectively incorporate PPL into the antibiotic.

Zhao and colleagues went on to isolate the suspected product of LmbT and to demonstrate the enzyme's function using *in vitro* assays. They discovered that LmbT catalyses the transfer of lincomycin A's sugar (for which the biosynthetic pathway has previously been reported[9]) to EGT, thus chemically activating the sugar in readiness for its reaction with MSH later in the pathway. Such a role is completely unprecedented: EGT was known to exist as a metabolite, but not as a substrate for an enzyme-catalysed reaction.

A particularly impressive aspect of this work is the authors' use of an intricate series of *in vivo* and *in vitro* experiments that relied on intermediates obtained from mutant cultures and from both enzymatic and chemical syntheses, guided by comparative gene analysis and genome mining. More generally, the study demonstrates that integration of primary metabolites (those that are essential for an organism's survival, such as MSH and EGT) and secondary metabolites (non-essential compounds, such as the products of the Lmb enzymes) is crucial for the biosynthesis of complex molecules. It also highlights the ingenious ways in which nature repurposes enzymes — in this case, using homologues of MSH-dependent detoxification enzymes for biosynthesis. And the establishment of functions for LmbE, LmbV and LmbT will no doubt help researchers to work out the functions of the enzymes' numerous homologues in the ever-growing roster of sequenced genomes. ■

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PALAEOCLIMATE

Climate sensitivity in a warmer world

Comparison of climate records from the Pliocene and Pleistocene geological epochs of the past five million years suggests that positive climate feedbacks are not strengthened during warm climate intervals. SEE ARTICLE P.49

DAVID W. LEA

A major concern in projecting future climate change using models is that positive climate feedbacks might become enhanced in a warm climate, accelerating future warming in response to rising greenhouse-gas levels. Climate feedbacks are changes in atmospheric or surface properties induced by climate change that magnify or diminish the overall temperature response. Their aggregate strength is represented by the climate sensitivity, which is the ratio of observed warming to climate forcing, such as increasing atmospheric carbon dioxide levels. Warm intervals of Earth's recent geological past, which can be studied through climate proxies, provide a basis for testing the response of climate sensitivity to warming. On page 49 of this issue, Martínez-Botí *et al.*[1] use improved proxy atmospheric CO_2 data to compare climate-sensitivity determinations from the warm Pliocene epoch, 5.3 million to 2.6 million years (Myr) ago, to those from the cold, extensively glaciated Pleistocene epoch, 2.6 to 0.012 Myr ago. They find that climate sensitivity differs little between these vastly dissimilar times, once the influence of ice sheets is removed.

Why should climate sensitivity be stronger in a warm world? A warmer world is likely to have less snow and ice, thereby reducing their

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MARTIN LIPMAN

Figure 1 | Then and now. Comparison of Strahcona Fjord, Ellesmere Island, in the high Canadian Arctic during the Pliocene epoch (illustration on the left) and today (photograph on the right). The changes illustrate the extreme polar amplification of warming during the Pliocene. Martínez-Botí *et al.*[1] use climate reconstructions from the Pliocene to determine whether positive climate feedbacks were stronger during warm intervals.

amplifying effect on climate change[2,3]. But how other feedbacks, such as water vapour and clouds, respond to warming is less certain. Simulations with climate models suggest that the positive feedback due to water vapour may strengthen in warmer climates[4], but uncertainties about how cloud feedbacks respond to warming confuse our understanding of the overall dependence of climate sensitivity on climate state.

Ancient climate records provide an alternative approach to assessing climate sensitivity, through the analysis of proxies, which reveal both the forcing (for example, atmospheric CO_2 levels or ice extent) and response (the temperature change). This approach offers the tremendous advantage of relying on natural equilibrium climate states rather than on synthetic ones simulated in models. Past climates were also influenced by various slow feedbacks such as ice sheets, vegetation and dust — factors typically not included in climate simulations. However, the method hinges on proxy reconstructions that have associated uncertainties, especially for marine-based atmospheric CO_2 reconstructions used in studies reaching beyond 0.8 Myr ago, the age of the oldest ice cores[5].

Palaeoclimate researchers have targeted the Pliocene epoch because it is the most recent time interval in which conditions were substantially warmer, about 2–3 °C warmer globally, than pre-industrial conditions[6]. Proxy reconstructions indicate that the Arctic climate during the Pliocene was much warmer than it is today, about 8–19 °C warmer, depending on location and season[7] (Fig. 1). But this extreme Arctic warmth seems to have coexisted, paradoxically, with atmospheric CO_2 levels that are similar to the present ones, implying an extreme amplification of positive climate feedbacks in the Pliocene[8].

Martínez-Botí and colleagues challenge this existing hypothesis using a well-validated technique to reconstruct Pliocene atmospheric CO_2 between 3.3 and 2.3 Myr ago at higher temporal resolution and with less variability than previous proxy reconstructions[5]. Their reconstruction clearly indicates for the first time that mid-Pliocene atmospheric CO_2 was up to 60% higher than pre-industrial values (450 parts per million (p.p.m.), compared with 280 p.p.m. before the Industrial Revolution and 400 p.p.m. today). The new record also indicates clear transitions in atmospheric CO_2 that are coherent with known climate events, including a drop in atmospheric CO_2 between 2.9 and 2.7 Myr ago that precedes global cooling and the onset of Northern Hemisphere glaciation 2.6 Myr ago — remarkable findings in themselves.

The researchers go a step further, applying their results to climate sensitivity for the warm Pliocene state by developing averaged reconstructions of land and ocean temperature and comparing them directly to their atmospheric CO_2 reconstruction. The slope relating the forcing (atmospheric CO_2) and response (temperature) at each time slice yields a tight constraint on climate sensitivity that is specific to the Pliocene. The authors find Pliocene climate sensitivity to be half as strong as that found for the cold Pleistocene. A repeat of the analysis after removing the forcing associated with glacial–interglacial changes in ice sheets reveals that Pliocene and Pleistocene climate sensitivities to atmospheric CO_2 changes alone were essentially the same.

In a broader context, these results also relate to attempts to use the instrumental temperature record to narrow the range of equilibrium climate sensitivity, which is the equilibrium temperature change caused by a doubling of atmospheric CO_2 allowing for 'fast' feedback processes only. Some studies have argued[9] that the slightly weaker rate of global warming since 2001 reduces the lower boundary of equilibrium climate sensitivity to well below 2 °C. Although Martínez-Botí and colleagues' derived Earth-system sensitivity[10] includes slow feedbacks, which complicates direct comparison to results from climate models, their results are likely to translate[10] to an equilibrium climate sensitivity of between 2 and 3 °C, well within the generally accepted range.

Despite the significant advance Martínez-Botí and co-workers' study represents, several challenges remain. First, given the wide range of proxy atmospheric CO_2 data for the Pliocene[5], it will be essential to validate the new results and assess why earlier reconstructions and methodologies differ from this one. Second, the extreme Pliocene warming in the terrestrial Arctic (Fig. 1) still requires enhanced polar climate feedbacks that remain unexplained[7]. Finally, for climate modellers, there remains the substantial challenge of reconciling emerging palaeoclimate-based sensitivity results with simulations of both past and future climate states. ■

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