protease opens up to allow the products to escape. The findings of Shen *et al.*[1] suggest that this final enzyme-opening step limits the rate of the overall reaction, so that mutations that facilitate this opening process activate IDE.

Shen and colleagues' results[1] excitingly suggest that drug molecules might also be able to activate IDE by mimicking the latch-disrupting mutations. Of course, designing a molecule that targets the latch system may prove challenging. On the other hand, the new structures of IDE will undoubtedly facilitate the development of inhibitors targeting IDE's active site. The potential use of IDE inhibitors for the treatment of diabetes should not be dismissed out of hand, because transient pharmacological inhibition of IDE might yield different results from the life-long, pan-cellular defects present in the genetically altered rodent models discussed above. Moreover, any risk of exacerbating Alzheimer's disease (by elevating amyloid-β-protein levels) might be avoided by using compounds that do not cross into the brain. Whether inhibition or activation of IDE is ultimately prescribed, Shen and colleagues' crystal structures herald the dawn of a rational, structure-based approach to the pharmacology of this ubiquitous protease. ■

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PALAEOANTHROPOLOGY

Return of the last Neanderthal

Eric Delson and Katerina Harvati

New finds from Gibraltar date Mousterian tools to as recently as 28,000 years ago. By inference, their Neanderthal makers survived in southern Iberia long after all other well-dated occurrences of the species.

The last Neanderthals were participants in one of the most dramatic events in the story of human evolution. At a time of increasing climatic instability and environmental deterioration, they would have had to have survived in ever-smaller groups, confined to less environmentally hostile refugia on the coast of the Mediterranean, and competing for access to resources with modern humans pressing on their territory.

These conditions are widely thought to have led to the Neanderthals' extinction within a relatively short time after the colonization of Europe by modern humans[1]. But in a paper[2] on page 850 of this issue, Finlayson *et al.* revise that model considerably*. They produce dating results from Gorham's Cave, Gibraltar, that might indicate that a group of Neanderthals survived extinction in this part of southern Iberia until at least 28,000 years ago — thousands of years after anatomically modern humans had firmly established themselves as the inheritors of the European continent.

Neanderthals inhabited western Eurasia from a time in the Middle Pleistocene between 500,000 and 160,000 years ago (depending on the definition of the earliest members of the Neanderthal group[3,4]) until approximately 30,000 years ago (Fig. 1). They were characterized by a suite of specialized morphological features, many of them unique to the group, that together make them highly distinct from modern humans. Their skeletal remains are often found associated with 'Mousterian' stone tools, named after the Le Moustier site in France. In Europe — but not in northwest Africa or southwest Asia — such tools are exclusively found with Neanderthals, and are presumed to have been made by them.

Neanderthal remains discovered from times near the end of their existence are sometimes found with tool assemblages resembling those produced by early modern humans. This is possibly a result of acculturation or imitation of modern human technology[5]. Although there is still some discussion over the Neanderthals' taxonomic status and their relationship to modern humans, it is now widely recognized that they represent a distinct, Eurasian evolutionary lineage. They shared a common ancestor with modern humans in the early Middle Pleistocene or before[3,6,7], but became isolated thereafter from the rest of the Old World. Glacial climatic conditions are considered at least in part responsible for this isolation and for the evolution of some distinctive features of Neanderthal morphology, especially their short limbs and heavy trunks. These are similar to, but more extreme than, features of cold-adapted modern populations such as the Inuit[8,9].

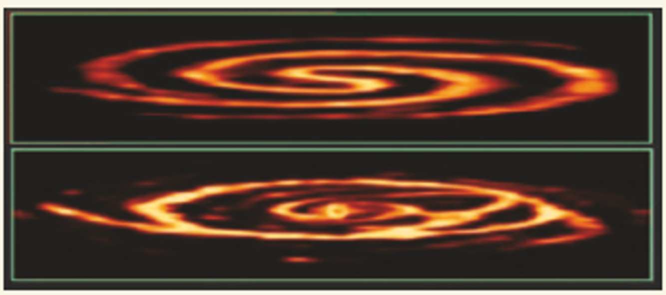
The interaction between Neanderthals and modern humans after the arrival of the latter in Europe around 40,000 years ago is among the most interesting topics in European palaeoanthropology. Did they meet? Did they compete? If so, in what ways? Did they interbreed? If they did, did the Neanderthals become assimilated into the modern-human gene pool, or was theirs a union without issue[4]?

Until recently, the interval of coexistence of the two groups in Europe was thought to be as long as 8,000 to 10,000 years. Although it has

*This article and the paper concerned[2] were published online on 13 September 2006.

ASTRONOMY

Andromeda's troubled past



It would have been quite a collision. Around 210 million years ago, galaxy M31 — better known as Andromeda — and its smaller neighbour M32 met almost head-on, leaving the battered structure of M31 seen today. This striking proposal is made by D. L. Block *et al.* on page 832 of this issue (*Nature* **443,** 832–834; 2006).

The story is summed up by the two snapshots, each roughly 120,000 light years across, included here. They show the results of Block and colleagues' numerical simulations, with (top) a serene M31 some 35 million years before the collision, and (below) the dishevelled M31 of today.

The simulations offer telling support for the authors' scheme of events, which hinges on two dust rings in the galaxy's disk (see Fig. 1 on page 832). One, at a radius of about 33,000 light years, is well known; the other, much closer in, was identified only recently with NASA's Spitzer Space Telescope. The two rings emerge from the simulations — precise in both position and orientation — as a consequence of a head-on galaxy–galaxy impact, with M32 being the likely culprit.
Tim Lincoln