RÉSUMÉ

Notes from underground

THE search for cosmological dark matter has taken Japanese physicists into caves in a stone quarry 100 km north of Tokyo. There, S. Orito *et al.* (*Phys. Rev. Lett.* **66**, 1951-1954; 1991) installed plastic sheets, covering 2,000 m^2, and left them for 2 years, shielded from cosmic rays and solar flares. Their hope was that any passing superheavy elementary particles, if such things exist, would leave in the sheets tracks of atomic damage that could be revealed later by chemical etching. The method is sensitive to slow-moving particles weighing at least 10^{12} proton masses. Orito *et al.* found no sign of any superheavy particle and conclude that their abundance must be less than one for every 10^{29} photons in the Universe — a result which pushes the cosmological limit but does not yet rule out this putative form of dark matter.

Tail tales

COMPETITION in the female reproductive tract between sperm of different males is a matter not only of sperm numbers, as is recognized, but of their length (*Proc. R. Soc.* B**243**, 181-185; 1991). M. Gomendio and E. R. S. Roldan looked at the sperm of certain primates and rodents, dividing the animals into two groups — polyandrous species, in which females mate with several males in the course of an oestrus cycle, and in which sperm competition occurs, and the singular monandrous species. The sperm of polyandrous species, it turns out, are significantly larger, by virtue of the length of their tails. The authors also report that longer sperm can indeed swim faster than their shorter brethren, and may also be able to penetrate the egg more easily — that is, size does matter.

Gender gap

R. C. GUR and colleagues, writing in *Proceedings of the National Academy of Sciences* (**88**, 2845-2849; 1991), show that men are more prone to certain age-related changes of the brain than are women. Gur *et al.* studied the crania of 69 healthy adults between the ages of 18 and 80 years using magnetic resonance imaging, and found support for the idea that ageing is, as previous work has shown, associated with a decrease in brain volume and increase in that of the cerebrospinal fluid. But they also observed that the rate of increase in volume of the cerebrospinal fluid is greater with age in men than it is in women. Moreover, men display an asymmetric effect, not seen in women, atrophy of the left hemisphere being more pronounced than that of the right. Choosing a judiciously conditional turn of phrase, the authors say that their study "may help us to understand neural substrates of behavioral changes associated with aging".

any features that might form at continental margins. A final question involves the long-term persistence of the upwelling zones. The distance of the paired upwelling from the mid-ocean ridge must change as new plate is created at the mid-ocean ridge. Thus, to persist, the upwelling must be very strongly tied to the thermal contrasts between continental and oceanic lithosphere.

The final, perhaps semantic, question is: when does a hotspot cease to be a hotspot?; or, what is the difference between hotspot convective upwelling and other forms of convective upwelling? If hotspots are limited to narrow upwelling zones moving slowly, at best, with respect to one another, then the distinction is rather straightforward. Vogt's upwelling has a long horizontal axis parallel to the continental margin and is tied to the continent rather than to other hotspots. How does this differ from a weak hotspot that gets smeared out horizontally? Is the distinction important?

Vogt's interesting argument may help explain features parallel to the continental margin, and further define hotspots. Vogt is correct in saying that one of the most important problems is the post-mountain building uplift history of the Appalachians, and that it will be hard to test his model. □

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BIOPOLYMERS

Light on molecular recognition

Robert Kaiser, Tim Hunkapiller and Leroy Hood

WRITING in *Science*[1], Fodor *et al.* describe an exciting strategy for the light-directed, spatially addressable parallel synthesis of a large number of chemically related yet distinct species on a glass surface — thus producing molecular diversity through combinatorial chemical synthesis. The technique provides a fresh way of tackling one of the fundamental problems of modern biology, namely molecular recognition, or how nucleic acids and proteins interact in a highly specific manner.

Interactions between nucleic acids generally arise from one-dimensional complementarity through the ability of nucleotides to form classic Watson–Crick base pairs. Molecular recognition at the DNA level, therefore, is often assayed by determining whether a DNA probe and target sequence hybridize. In contrast, proteins interact with other molecules by three-dimensional complementarity, the matching of shapes that give rise to optimal interatomic interactions.

Because the rules for protein folding are unknown, studies of molecular recognition at the protein–protein or protein–nucleic acid levels often centre around the testing of many diverse forms of one component for specific binding to the second component. In general the process can be broken into two parts: first, the generation of numerous forms in which a limited set of elements are combined in all possible ways to generate a potentially very large and diverse set of candidates for testing; second, the selective enrichment of one or a few high-affinity forms from this test set. In the past, investigators have tended to employ biological strategies for both combinatorial diversification and selection[2,3]. More recently chemical synthesis has been used to generate combinatorial diversification followed by biological selection[4]. Fodor's approach provides a massively multiplexed assay system that is no longer dependent on the limitations of competitive selection.

The power of combinatorial strategies for generating molecular diversity is best illustrated by the vertebrate immune system[5]. The cells of the immune system must be able specifically to detect and bind a pool of foreign molecular species (antigens) of potentially unlimited structural diversity. The genome of a single organism cannot hope to encode a unique receptor for every possible antigen, so the limited diversity of the germline genetic information must be amplified. This is accomplished by randomly selecting and combining elements from limited pools of gene segments (V, D and J) to construct a pair of unique rearranged genes for each immune cell that encodes the immune receptors (antibodies and T-cell receptors). Thus, the potential receptor diversity of an individual organism is proportional to the product of the sizes of the germline repertoires of the various gene-segment groups[5]. It is estimated that the human immune system has the potential to generate some 10^{11} unique antibodies by this and other combinatorial and/or mutational mechanisms[6]. Selection is then accomplished through clonal amplification of only those cells displaying a single type of receptor that complements an inducing antigen.

One particularly productive area of research that rests upon the antibody model has been the design and generation of antibody structures which mimic enzymes as selective catalysts[2,3]. Better understanding of enzymic catalysis has allowed the generation of specific antibodies displaying a wide variety of catalytic capabilities, including hydrolysis or formation of ester and amide