large experiment was only possible within the gates of a genome factory; however, adaptation of the microsatellite markers to semi-automated reading on sequencing machines has generalized the technology[7,8].

Armed with these new tools, many groups are attempting to analyse the genetic contribution to complex diseases and phenotypes. The results of Davies *et al.*[1] and Hashimoto *et al.*[2] on IDDM are among the first of the flood. Type 1 diabetes is a good choice for pioneering these methods: not only is it a very important disease but two genes have already been implicated. Reassuringly, the new studies confirm the importance of *IDDM1*, a gene of the major histocompatibility complex (MHC)[9], and provide more support for a small contribution from *IDDM2*, believed to be the insulin locus itself[10,11]. Both groups agree on the identification of a new susceptibility locus, in the vicinity of the *FGF3* gene on the long arm of chromosome 11. In a more limited study using a candidate gene approach[12], the same gene association has been detected. It should be stressed that these studies do not imply that *FGF3* is the susceptibility gene; finding this gene and the several others implicated by these studies[1,2,12] will be the next problem. In simple genetic diseases, *de novo* mutations and gene-inactivating mutations frequently prove the identity between candidate gene loci and disease loci. The gene variants contributing to complex diseases are likely to be common polymorphisms which, in the absence of the other risk factors, do not cause disease. Saturating the region with more polymorphic markers and looking for linkage disequilibrium will help, but genetic approaches will eventually fail because of the complex genetics. Direct tests of the biological effects of the candidate genes will be required to confirm the identity of the susceptibility genes.

One of the most important outcomes of a genome scan is that it can exclude the existence of major contributing genes. The experiments on IDDM rule out other genes with effects as large as the MHC gene and identify several candidate regions for relatively minor genes. In most complex diseases, treatment has been limited to amelioration of the symptoms rather than tackling the underlying causes. Identification of the new disease-related genes may suggest new therapeutic and preventive strategies and enable environmental influences to be assessed. In the absence of genetic differences predisposing to the disease, environmental differences affecting the development of the disease can be pinpointed, so individuals at risk would have the option of modifying their exposure to the environmental risk factors. Genome scans may also help to resolve other arguments on nature versus nurture. ☐

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GEOPHYSICS

Anisotropy and rift systems

Martha Kane Savage

THE theory of plate tectonics, which holds that continents and oceans have been torn apart and huge oceanic plates thrust under other oceans or continents, is well supported and has become a standard principle on which studies of the Earth are based. Yet some of the underpinnings of the theory, such as the relationship between the flow of the asthenosphere and the movement of the overlying lithospheric plates, remain incompletely understood. Numerical models of flow within the asthenosphere have been calculated, but direct observation of the flow is impossible. Measurements of seismic anisotropy, together with assumptions about the relationship between anisotropy and the deformation of the olivine crystals which make up the bulk of the upper mantle, allow us to begin to map deformation of the lithospheric mantle and flow of the underlying asthenosphere. Using the shear-wave splitting technique, S. Gao and others (page 149 of this issue[1]) present some of the best evidence to date for the direction of asthenospheric flow beneath a continental rift.

Seismic anisotropy is the property that propagation of seismic waves in one direction through a medium may be faster than that in another direction. Shear-wave splitting results because shear waves have particle motion perpendicular to the direction of wave propagation. When a shear wave enters a simple anisotropic medium, the component that is polarized parallel to the fast axis will begin to lead the orthogonal component, so that the wave becomes 'split' with time. The difference in time between the fast and slow waves is called the delay time, and is proportional both to the length of the anisotropic path and the degree of anisotropy. These measurements yield high-lateral-resolution estimates of the orientation of the fast axis of anisotropy.

Anisotropy in the Earth's crust can be caused by preferred orientation of minerals, or by preferred orientation of cracks[2]. But within the mantle, high overburden pressure and high ductility suggest that few cracks are present, and it is thought that lattice-preferred orientation of the highly anisotropic olivine mineral is the dominant cause of anisotropy[3,4]. One response of olivine crystals to strain is that of 'dislocation creep', in which the fast axes begin to point towards the direction of maximum strain. Within flowing material, the maximum strain is parallel to the flow direction. For finite strain, such as that caused by large differential motions between two plate boundaries, the maximum strain is parallel to the plate boundaries[5]. For this reason anisotropy has increasingly been used to study deformation of the lithosphere and the flow of the asthenosphere[6–8].

Asthenospheric flow on a worldwide scale has been associated with the 'absolute' motion of the lithosphere above a relatively stable mantle below the asthenosphere through anisotropy determined by global surface-wave inversions[9]. Anisotropy has also been invoked in more detailed studies of asthenospheric flow near oceanic and continental rifts. As Gao *et al.* summarize for oceanic rifts, under the rift axis itself the fast axis of anisotropy may be vertical, whereas on either side of the rift the fast axis is oriented perpendicular to the rifts. Sandvol *et al.*[10] found fast axes along the axis of the Rio Grande (continental) rift to be subparallel to the rift axis. The study by Gao and colleagues is the first to examine anisotropy across a tight array of seismometers laid out in a profile across a continental rift.

The authors have deployed an array of 28 seismometers at 50-kilometre intervals across the 30-million-year-old Baikal rift zone (see Fig. 1 of their paper, page 149). They have come up with a remarkably consistent pattern of shear-wave splitting measurements, in which the orientation of the inferred fast axis is perpendicular to the rift axis. This orientation continues from at least 500 km northwest of the rift, through the rift axis, to about 250 km southwest of the edge of the rift, where the orientation abruptly changes direction. This orientation of the fast axis perpendicular to the rift axis is similar to that observed at mid-ocean rifts. The orientation of the fast axis beyond the abrupt change is consistent with nearby measurements, and Gao *et al.* suggest that it is caused by Cenozoic deformation of the lithosphere associated with the collision of India and Asia.

The shear-wave splitting technique cannot directly yield the depth at which the anisotropy is present, yet several arguments suggest an asthenospheric source. The abrupt transition in directions at the surface requires the transition at depth to occur in the upper 250 km. The authors further point out that, in the centre of the rift where the lithosphere is thinnest, the magnitude of the signal they receive is too high to be explained by reasonable compositions of material if they are within a thin lithosphere. So they conclude that much of the anisotropy must be attributed to the asthenosphere.

The shear-wave splitting study suggests that the Baikal rift is similar to the oceanic rifts in that the asthenosphere is moving in a direction consistent with movement away from the rift that is being pulled apart. An alternative model, in which the rift is a response to offset in a shear zone, is ruled out because the fast axis of anisotropy does not reflect that expected in response to a shear field.

This first detailed study[1] of asthenospheric flow across a continental rift is an initial step in understanding the relationship between the asthenosphere and lithosphere in continental rifting. Some intriguing questions remain to be explored. The new results suggest that continental rifting may behave like oceanic rifting, in that the sense of motions of the asthenosphere at a distance from the central axis are the same. But how similar are the two phenomena in other respects? Does the anisotropy in the centre of the rift also have a component of vertical motion that might be related to the upward motion of the rifting asthenosphere? Why does the Rio Grande rift exhibit anisotropy that is subparallel rather than perpendicular to the rift direction? Do continental rifts behave similarly in different areas? These questions will be solved only by more careful, detailed studies such as those described by Gao *et al.* □

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MACROMOLECULES

Architectural delights

Harry W. Gibson

LITTLE by little, designer molecules are becoming a reality. Molecular boxes, Olympic rings and novel molecular building blocks were just some of the molecular architectures to be unveiled at the recent IUPAC conference in Akron*.

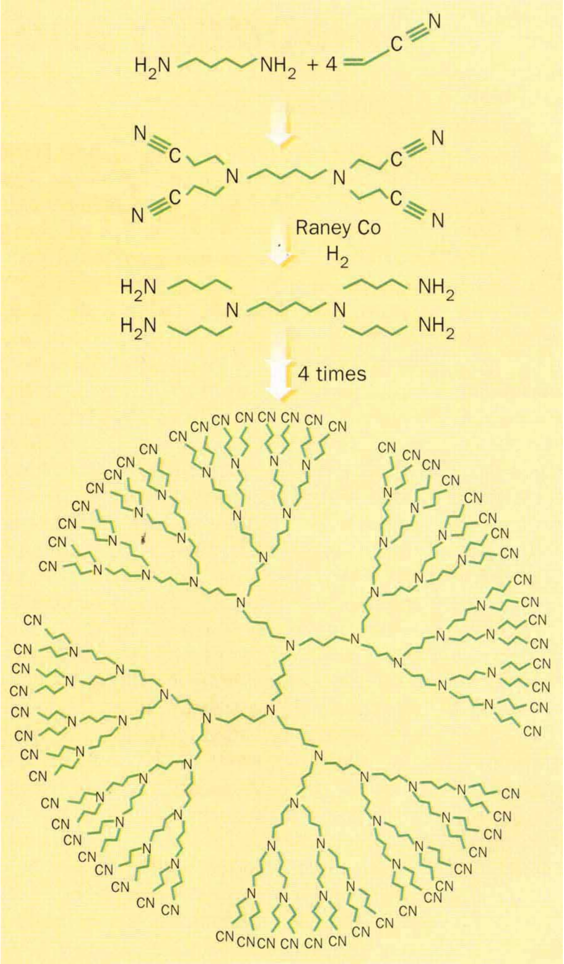

FIG. 1 Synthesis of dendrimer with 64 cyano functional groups; the amino derivative is produced from this by hydrogenation.

It is now possible to entrap molecules of small to medium size in molecular 'boxes' constructed from dendrimers, polymers so branched that they form bushy spheres with sizeable pores between the inner branches. Starting with 1,4-butanediamine and acrylonitrile, dendrimers can be synthesized on large scales[1] (as shown in Fig. 1). Using the higher-generation systems with 32 or 64 surface amino moieties it is possible to entrap molecules by introducing them into the pores and then 'closing the lid' by attaching t-butoxycarbonyl (t-BOC)-protected amino acids, such as phenylalanine, to the surface (E. W. Meijer, Technical Univ. Eindhoven). Among the molecules so imprisoned have been a nitroxyl spin probe, various dyes, the electron acceptor TCNQ and nitrobenzoic acid.

When more than one species is imprisoned, they can be released selectively. For example, when nitrobenzoic acid and rose bengal are entrapped together, hydrolysis of the t-BOC protecting groups from the amino-acid moieties on the surface liberates the aromatic acid, but retains the dye. Subsequent hydrolytic cleavage of the amino acid from the surface of the dendrimer allows the rose bengal dye to escape. The imprisoned molecules in some cases are tightly constrained and in others less so, causing variations in relaxation dynamics, fluorescence and induced circular dichroism relative to the 'free' molecule. Applications such as imaging processes or controlled release of drugs are conceivable for these molecular boxes.

Interlocked rings — catenanes — have long captured the fancy of artists and scientists, but only recently have such structures bowed to the skills of synthetic chemists. By use of carefully designed components that incorporate the necessary structural information for self-assembly, [4]catenanes[2] and [5]catenanes have previously been made; one is dubbed 'olympiadane'[2] from its resemblance to the familiar Olympic symbol. Now a [6]catenane and a [7]catenane (see Fig. 2) have been synthesized (J. F. Stoddart, Univ. Birmingham). These remarkable structures result from molecular recognition between arylene crown ether and bipyridinium-type macrocyclic moieties. The [7]catenane consists of three large interlocked rings with two smaller rings connected with each of the two outer large rings, and produced a molecular ion at a mass-to-charge ratio m/z=7,130 in liquid secondary-ion mass spectrometry. Can true 'molecular chains' be far off?

This sort of self-assembly of linear or dendritic systems of controlled size, shape and function is a goal of many research

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*35th IUPAC Symposium on Macromolecules, Akron, Ohio, 11–15 July 1994.