Crystallography

Some are less equal than others

Alan Mackay

Why is it dark at night? This is Olber's Paradox. The modern explanation for it is that the Universe is expanding; but in 1922 C. V. L. Charlier suggested another, ingenious solution: the Universe might be infinite and hierarchical, with galaxies of galaxies of galaxies. There would be no privileged centre and all viewpoints would be quasi-equivalent, yet the density of this Universe would tend to zero with increasing scale. A similar idea might apply to the microcosmos of atomic arrangements: clusters of clusters are an alternative to strict crystalline arrangements, and could form a new type of condensed matter. On page 376 of this issue[1], Hubert *et al.* report a structure with this theme — clustered icosahedral particles of boron suboxide.

The mathematical simplicity of infinite crystal lattices has beguiled crystallographers, with its absolute identity of lattice points. The classification system of crystals is based on the 230 symmetries allowed by that assumption — that an infinite number of asymmetric units are to be arranged so that their surroundings are absolutely identical. The assumption of crystallinity is necessary for the recovery of phase information in single-crystal X-ray diffraction, which is the principal tool of crystallography, so sharp diffraction patterns can be interpreted in terms of infinite crystals. But hierarchy could offer an alternative to lattice repetition, in providing an assembly of atoms with an infinite number of almost identical, or quasi-equivalent, sites.

This principle of quasi-equivalence was formulated by Caspar and Klug[2] when they considered how polio virus (icosahedral particles of 60 subunits) could form crystals of cubic symmetry[3] — as indicated by their diffraction pattern. The solution found by nature for polio is surprisingly like Linus Pauling's structure of $Mg_{32}(Al,Zn)_{49}$: the units are locally icosahedral clusters arranged on a translation lattice.

Perhaps this should not be surprising: identical units do not have to have identical surroundings, and natural materials are physical and not mathematical objects. Biological structures such as collagen are predominantly hierarchical in the same way as rope: fibres are twisted into strands, which are then twisted into bigger strands, and so on for several levels.

Hierarchy has now also appeared as a building principle in a class of inorganic materials, the quasicrystals. These are solids with fivefold symmetry (as betrayed by their diffraction patterns) — a symmetry impossible for a conventional crystal.

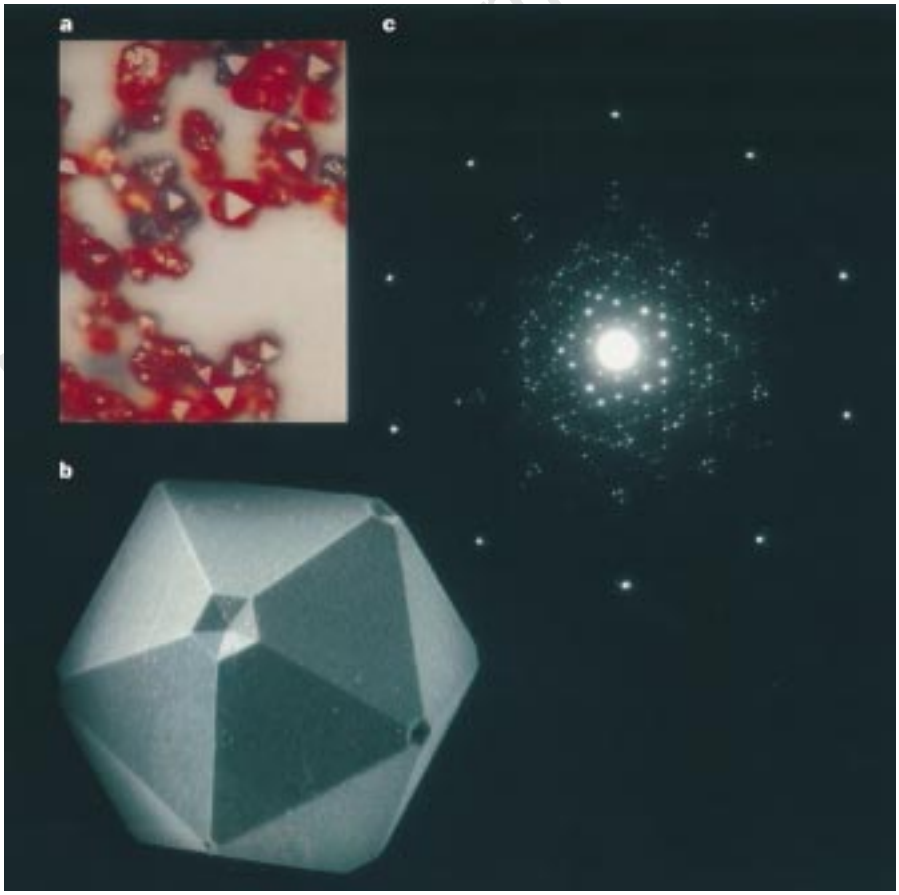
F. C. Frank noted that the densest packing of 12 spheres around a central sphere is icosahedral, and J. D. Bernal, following Charlier, asked whether this rule could be continued hierarchically. The problem is to find further rules to fill in the gaps so as to keep the overall density finite. Model-building experiments produced an icosahedral shell packing[4] which, for the first few layers, was close to a packing of 13 icosahedral clusters, each of 13 spheres — and indeed β-rhombohedral boron was found in 1970 to contain such $B_{12}(B_{12})_{12}$ units.

Another way to make icosahedra is found in multiply-twinned particles of silver and gold, where 20 face-centred-cubic regions are joined, with slight distortion, into icosahedra. These have been observed[5] by electron microscopy from about 1964, and many other icosahedral clusters have since been found. Their size is limited by the increasing strain as successive layers are added, the spacing of spheres in the layers being some 5% greater than in close packing, so a transition from icosahedron to cuboctahedron will probably occur at a certain size.

The first theory of hierarchical packing came from the tiling of pentagons in two dimensions. Consideration of how the gaps were to be filled led to Penrose tiling[6] in two and three dimensions — a mathematical pattern that has the geometrical properties required of a quasicrystal. In three dimensions, Penrose tiles are obtuse and acute rhombohedra with angles of 116.6° and 63.4°.

Significantly, the 20 tetrahedra making up the multiple twin in gold and silver must have inter-edge angles at the centre of the cluster of 63.43° (instead of 60° for regular tetrahedra). And now Hubert *et al.*[1] have found that boron suboxide crystals (B_6O) are rhombohedral, with an inter-edge angle of 63.1°, and that these crystals occur as icosahedral twins. Twenty rhombohedral unit cells fit together snugly at a common vertex without dislocations at the interfaces, and the structure can continue outwards indefinitely, particles of some 10^{12} atoms being observed (Fig. 1).

Without dislocated grain boundaries, glide planes in this boron suboxide are locked and so the particles are very hard, promising technical applications. And these aggregates are far larger (up to 20 μm) than those observed hitherto for multiply-twinned particles. B_6O and various other



H. HUBERT *ET AL.*

Figure 1 **Clusters of boron suboxide, B_6O** (a, **photograph;** b, **electron micrograph**) **and its X-ray diffraction pattern** (c). **These icosahedral shapes, up to about 15 μm across in the photograph, are not crystals, but hierarchical clusters with a fivefold symmetry forbidden to crystals. B_6O may also be a useful engineering material, because of its hardness.**

boron compounds show marked tendencies towards icosahedral packing and it was thought, before quasicrystals of Al_6Mn were reported, that boron would be the best candidate for forming a three-dimensional Penrose tiling, as the unit cell of B_6O is the Penrose acute rhombohedron.

These boron suboxide particles are not quasicrystals, but they are an important step away from the 230 space groups towards a more general type of structure.

True quasicrystals can probably also be described as icosahedral clusters, themselves clustered icosahedrally in hierarchical levels, the gaps being filled by the overlapping of these clusters[7]. Quasicrystals are a further step away from conventional crystals, because they have many centres of local icosahedral symmetry, whereas a boron suboxide particle has only one.

As more varied structures appear — especially to the electron microscope, which does not depend on the assumption that many copies of the same unit can form only crystals — we can escape from the preconceptions engendered by the immense success of X-ray single-crystal structure analysis. We must expect many still more varied structures to lie outside the austere dominion of classical crystallography. □

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Genetic recombination

From competition to collaboration

Roland Kanaar and Jan H. J. Hoeijmakers

Politics and science furnish many examples of the dramatically different effects of competition and collaboration. Similar phenomena occur at the molecular level in nature, and four reports[1–4] (three of them in this issue[2–4], beginning on page 401) demonstrate the point. They show that competition between two proteins required for genetic recombination is turned into fruitful collaboration by a third participant, the Rad52 protein.

Genetic recombination, the exchange of information between DNA chains, accomplishes two seemingly conflicting tasks — generation of genetic diversity within species, and maintenance of genetic stability by repairing DNA damage. Whether recombination results in diversity or stability depends on whether the exchanges occur between homologous chromosomes during meiosis or between identical sister chromatids. Clinically, genetic recombination has attracted attention because of possible cross-talk between the breast-cancer-susceptibility genes, *BRCA1* and *BRCA2*, and the recombination machinery[5]; biologically, its importance is underscored by the conservation of its salient features from fungi to humans.

At the core of recombination is the search for homologous DNA followed by exchange of DNA strands (Fig. 1). A common initiator is a DNA double-strand break that is processed to expose regions of single-stranded DNA (ssDNA). In eukaryotes, the Rad51 protein coats the ssDNA to form a filament that scans the genome for a homologous double-stranded DNA (dsDNA) sequence (in a mammalian nucleus, which contains about 6×10^9 base pairs, this must be an especially arduous task). On completing this quest, the ssDNA-containing filament and the intact dsDNA form a joint molecule before strand exchange can occur.

But how, *in vivo*, does the filament assemble despite being subject to many competing reactions? An ssDNA-binding protein known as RPA (replication protein A) is required, presumably to remove secondary structure from the ssDNA to allow for efficient filament formation by Rad51, but it also competes with Rad51 for ssDNA binding. And although dsDNA is a substrate for the reaction, it binds Rad51, thereby inhibiting filament formation. From genetic studies it was clear that another protein, Rad52, was a major player in these events, but unlike Rad51 and RPA its molecular function remained elusive. The new, biochemical, studies reveal the effect of Rad52.

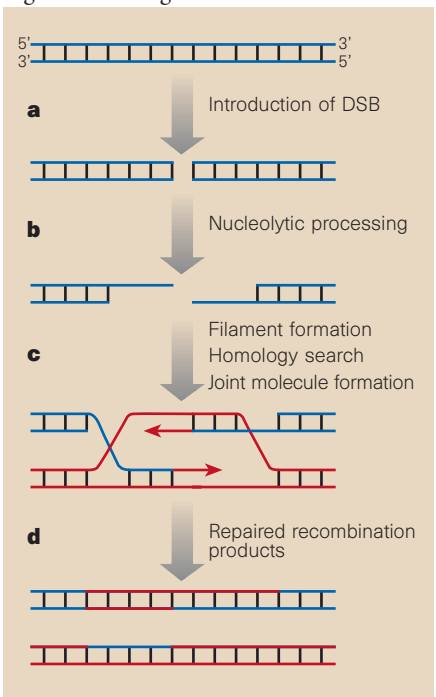

Figure 1 **The function of Rad52 in genetic recombination.** a, **Recombination can be initiated by a double-strand break (DSB) that may be caused by an endonuclease or a DNA-damaging agent.** b, **The DNA is processed at the site of the break to yield regions of single-stranded DNA.** c, **Rad51, assisted by replication protein A (RPA), coats the single-stranded DNA to form a filament that searches for homologous sequences (on the homologous chromosome or the sister chromatid) and, when it finds them, initiates the formation of a joint molecule. Four studies[1–4] now show that Rad52 stimulates homologous pairing by Rad51.** d, **The break is repaired by DNA synthesis (arrows in** c**) using the intact strands as templates. Following branch migration and resolution, repaired recombination products are released.**

Three of the reports[1–3] deal with the budding yeast *Saccharomyces cerevisiae*. They show that although RPA is required for Rad51-promoted strand exchange, it inhibits exchange when incubated simultaneously with Rad51 and ssDNA. Inhibition is overcome when Rad52 is incubated together with Rad51, RPA and ssDNA, followed by the addition of homologous dsDNA.

Rad52 is ideally suited for this job as mediator between Rad51 and RPA, because it interacts with both proteins[1,6] and binds ssDNA[4,7]. The mechanism is not yet clear, but Rad52 could function in several, not mutually exclusive, ways. First, it could increase the cooperativity of Rad51 binding to ssDNA. Second, it could enhance the dissociation of RPA from ssDNA and promote RPA transfer to the displaced strand, preventing reversion of strand exchange. Third, the ability of Rad52 to increase the annealing rate of complementary ssDNAs (ref. 7) could help Rad51 initiate joint molecule formation.

The other report[4] in this issue concerns human Rad52. The authors show that joint molecule formation does not occur when human Rad51 is present at subsaturating amounts. But when ssDNA is preincubated with human Rad52, followed by the sequential addition of subsaturating amounts of human Rad51 and dsDNA, joint molecule formation proceeds efficiently. These observations support the idea that human Rad52 increases the cooperativity of human Rad51