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.

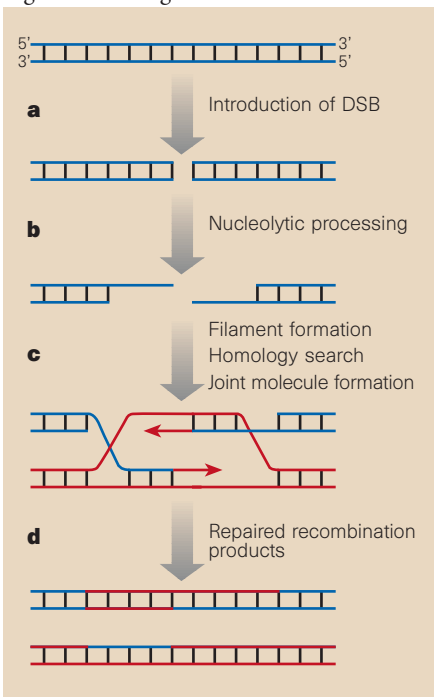

Figure 1 **The function of Rad52 in genetic recombination.** a, **Recombination can be initiated by a double-strand break (DSB) that may be caused by an endonuclease or a DNA-damaging agent.** b, **The DNA is processed at the site of the break to yield regions of single-stranded DNA.** c, **Rad51, assisted 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

Table 1 DNA strand exchange: the difference in the details

Recombination protein	Bacteriophage T4	*E. coli*	*S. cerevisiae* & *H. sapiens*	Homologues in *S. cerevisiae*
Strand exchange	UvsX	RecA	Rad51	Rad55, Rad57, DMC1
Single-strand DNA binding	Gene 32 protein	SSB	RPA	None
Mediator	UvsY	Not required	Rad52	Rad59

binding to ssDNA, thereby converting discontinuous stretches of Rad51 on ssDNA into one functional contiguous filament.

These new results reveal an interesting parallel between eukaryotic and prokaryotic genetic recombination. Bacteriophage T4 also uses a mediator, the UvsY protein, to stimulate strand exchange by UvsX and the T4 ssDNA-binding protein (see Table 1)[8]. The requirement for a mediator, however, is not universal because the *Escherichia coli* RecA protein, the bacterial homologue of Rad51, does not need one. So even though strand-exchange proteins are structurally and functionally highly conserved, the details of their actions differ (see Table 1). Yeast and human Rad51, and T4 UvsX, have no clear preference for binding to ssDNA or dsDNA, whereas *E. coli* RecA strongly prefers ssDNA. This property can eliminate competition on two fronts — RecA can itself displace the *E. coli* ssDNA-binding protein without the help of a mediator, and can overcome the competition by dsDNA for filament formation.

The ramifications of the four papers[1–4] go further, for *S. cerevisiae* contains a second *RAD52* homologue, *RAD59*, which is required for Rad51-independent recombination between intra-chromosomal inverted repeats[9]. If *RAD52* homologues also exist in other species, it would help explain the dramatically different effects of *RAD52* mutations in *S. cerevisiae*, the fission yeast *Schizosaccharomyces pombe* and mouse cells. Although the efficiency of recombination is reduced by more than three orders of magnitude in the *S. cerevisiae RAD52* mutant, it is only twofold lower in the corresponding *S. pombe* mutant[10], and only slightly affected in mouse *RAD52* knockout embryonic stem cells (T. Rijkers and A. Pastink, personal communication).

The explanation could be that some functions of *S. cerevisiae* Rad52 can also be assumed by Rad59 in *S. pombe* and mammals. Another possibility is that different Rad52 homologues act as mediators for different Rad51 homologues, for eukaryotes express multiple versions of *RAD51*. In *S. cerevisiae*, these variations on the Rad51 theme appear to assist Rad51-promoted strand exchange or to be involved in meiosis-specific processes (see Table 1). In mammals their functions are less clear. But, among other things[11], they could be important at the filament ends, which might have different properties to those of the filament body; in this respect, their role would be somewhat analogous to that of the *E. coli* RecF and RecR proteins in post-replication repair[12].

The new reports[1–4] show that mediation by Rad52 is required during the critical, early steps in genetic recombination. But another question remains — because Rad51 binds with similar efficiencies to ssDNA and dsDNA, how is the inhibitory effect of dsDNA on filament formation overcome? The answer might lie in the requirement for additional protein factors. A candidate is Rad54, whose function is still unknown, but it interacts with Rad51 and genetically it is in the same epistasis group as Rad51 and Rad52. Moreover, there must be much more to come in the Rad52 story because it also features in Rad51-independent recombination. □

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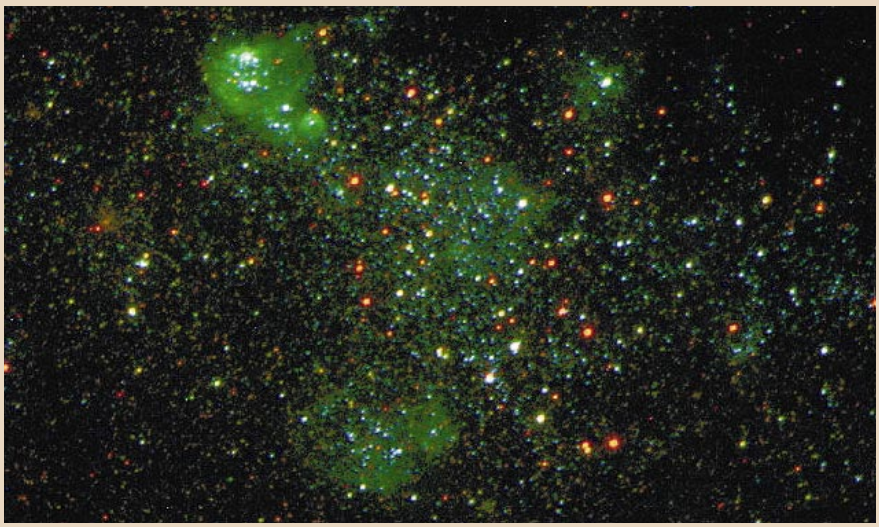
Galaxy evolution

Red giants in blue dwarfs

Are all galaxies old? Most that we observe certainly are, as they contain some stars almost as old as the Universe. But blue compact dwarf galaxies (BCDs) had been thought younger — rare baby galaxies in among the adults. Now that is called into doubt by one BCD that contains old red giant stars.

The first generation of stars in a galaxy forms from primordial gas produced in the Big Bang, mostly hydrogen and helium. They burn this by nuclear fusion, and some explode, sending out heavier elements that end up in younger stars such as the Sun. But the BCDs contain few heavy elements (as determined from their spectra), and so there is little evidence for an early generation of stars in these galaxies — they appear, in this respect, to be truly new galaxies.

On the right is a small galaxy called VII Zw 403, about fifteen million light years away — close in cosmological terms, but until now too far away for telescopes to resolve the tell-tale red giants. So R. E. Schulte-Ladbeck, M. M. Crone and U. Hopp delved into the data archives of the Hubble Space Telescope (*Astrophys. J.* 493, **L23–L26; 1998). The blue stars and the bright red supergiants are young; but the fainter, ordinary red giants, dotted about over the whole image, are old, in a late stage of stellar evolution that our Sun will also undergo.**



There is no doubt that BCDs are undergoing rapid star formation now; and their lack of heavy elements suggests that star formation may have paused between formation of the earliest and the new generation of stars.

So one BCD has admitted its age. Will the others follow suit? Schulte-Ladbeck and Crone have now won time with Hubble to look closely at four more galaxies, so we may soon know.

Stephen Battersby

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Palaeoclimatology

A glimpse of the glacial

Thomas F. Stocker

During most of the past 100,000 years, temperatures on Earth were much colder than they are now and climate was very unstable. About 21,000 years ago that climatic period culminated in the Last Glacial Maximum (LGM), when about 50 million km^3 of water was locked in huge ice sheets, lowering sea level by more than 120 metres. Climate during the LGM was clearly very different from what it is today. But how different? This is the subject of the paper by Ganopolski *et al.* on page 351 of this issue[1].

Using a properly tuned, simplified, coupled ocean–atmosphere climate model, they first verify the model's ability to simulate modern climate on the global scale. After adapting insolation, concentrations of atmospheric greenhouse gases and ice-sheet distribution to values typical for the LGM, they find that the same model yields a stable climatic state with other atmospheric and oceanic characteristics that are reminiscent of the LGM. The simulated changes are broadly consistent with what we know from decades of invaluable analyses of marine sediments, polar and tropical ice cores, tree rings and groundwater — all of which are archives that record past climatic changes.

Why should we be interested in simulating the climate of the LGM, when that state is unlikely to return for another 50,000 years[2] and Earth's climate will instead most probably warm considerably? There are four reasons. First, climate models must be able to simulate the full range of dynamical behaviour of the climate system, and so the LGM or transient and extreme climatic periods are the most critical tests they can be exposed to. Second, models that estimate future changes must be consistent with the sensitivity of the climate system to altered forcing parameters. Third, these models, if correct, can provide a more detailed picture of past changes for regions or parameters for which no suitable palaeoclimate archives are available. Finally, this will eventually contribute to a quantitative, model-based interpretation of palaeoclimatic proxy data.

Ganopolski *et al.* abandon the classical approach of using comprehensive three-dimensional general circulation models of one of the two main components of the climate system (the atmosphere or the ocean), while using a simplified representation of the other. Instead, they build on the progress made in developing zonally averaged climate models[3,4], which have become important tools in palaeoclimatic research, and combine it with a new atmospheric model component. Such models permit the numbers of runs required for optimal tuning. This means that loosely constrained model parameters or incompletely known boundary conditions can be varied in such a way that the relevant atmosphere–ocean exchange fluxes of momentum, heat and fresh water, simulated by the respective model components, are brought into adequate agreement.

Because of limitations on computer time, such systematic fine-tuning is not yet possible for coupled three-dimensional models. So most of these models drift to unrealistic states, and flux corrections must be applied. This remedy is undesirable but permissible for small and linear excursions from a well-defined climate state. But caution is called for when modelling climates as different from today's as the LGM.

The crucial component for a successful simulation is the hydrological cycle, which is notoriously difficult to simulate. Water vapour is the most important greenhouse gas, and its reduction in level contributes significantly to the global cooling of 6.2 °C in Ganopolski and colleagues' model. This is colder than the usually accepted estimates of about 4 °C, but it is consistent with recent reconstructions of significantly lower temperatures for the LGM at high and low latitudes[5–7].

The hydrological cycle also influences the circulation of the deep ocean. Changes in patterns of evaporation and precipitation determine the location of deep-water formation and the mix of waters from northern and southern origin in the North Atlantic[8]. Reduction in high-latitude precipitation, and an even bigger decrease in evaporation due to a larger extent of the ice cover in the northern North Atlantic (the ice margin moves from 75° N to 55° N in the model), mean that a surface freshwater anomaly can develop; in consequence, the area of deep-water formation in the North Atlantic also moves about 20° south. The density of the sinking waters is reduced, with the consequence that they penetrate less deeply. In this way, water masses of southern origin can extend far north in the Atlantic basin and fill much of the deep Atlantic. This meridional shift in the distribution of water mass below 1,000 m, seen in the model, is consistent with palaeoceanographic evidence from stable carbon isotope measurements on benthic foraminifera[9].

As well as strengthening our confidence in reconstruction of proxy data, coupled climate models are also crucial in assessing hypotheses on which less complete models are based. Ganopolski *et al.* find that, during the LGM, the oceanic meridional heat flux in the Atlantic was very different from today. Although this is not surprising (sea-surface temperatures were lower[10], and sites of deep-water formation and sea-ice margins moved south), it contradicts recent assumptions used for atmosphere-only models[11]. The reduction of heat delivery into the North Atlantic by northward-flowing waters is also expected, given the extremely cold temperatures on Greenland during the LGM (ref. 5). This leads to a pronounced asymmetry in cooling for the LGM, with a fall of more than

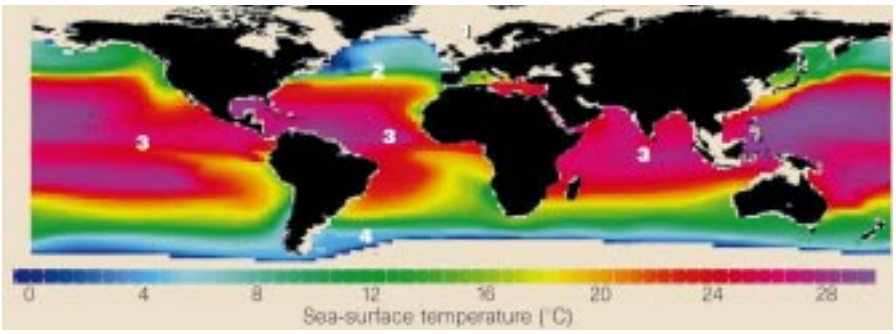

Figure 1 **CLIMAP[10] reconstruction of sea-surface temperature in August at the Last Glacial Maximum (LGM), 21,000 years ago. Four areas that pose crucial questions for climate reconstruction by numerical models are indicated as follows. 1, Are the Nordic Seas ice-free during the summer[15]? 2, What are the sea-surface salinities in the area of LGM deep-water formation[16,17]? 3, What is the reduction of sea-surface temperature in the tropical ocean[7,18]? 4, What are the surface-water characteristics in the Southern Ocean during the LGM? Other questions concern how the atmospheric temperature gradient changes with time, continental temperatures, the distribution of tracers and isotopes in the ocean, the water-mass mix, and the location of areas of deep-water formation and their seasonality. (Reproduced from ref. 19.)**