

recognizable, but they are only pseudogenes (genes that are not transcribed). They might have lost their function at different points in the evolution of fish, because *HoxC3*, at least, is still present in the zebrafish.

The apparent acceleration of genomic evolution along the pufferfish lineage might be correlated with accelerated morphological evolution. Pufferfish belong to one of the most morphologically derived groups of fish, and they lack ribs, pelvic fins and the pelvic girdle. Are the missing genes those that are no longer necessary because these structures have been lost during evolution? If so, the missing Hox genes in the pufferfish might also be absent in the other groups of fish which have secondary loss of pelvic fins (such as eels) or even tail fins (for example, the ocean sunfish *Mola mola*). Moreover, the loss of Hox genes might also be accompanied by the secondary loss (or simplification) of appendages in land vertebrates, such as in limbless amphibians, reptiles and whales.

What selective forces maintain or modify genomic organizations? The observation that Hox genes are clustered, and that the architecture of these clusters is highly conserved in evolution, has led to the suggestion that the regulatory elements that control expression of the Hox genes cannot be separated from these genes without jeopardizing their proper functioning and, possibly, determination of morphology along the antero-posterior axis. For vertebrates^{13,14} these ideas have been partially confirmed experimentally¹⁵, and this tight functional linkage might be particularly strong along the lineage that leads to reptiles and mammals (Fig. 1).

The long-standing question of whether

the evolution of genes or networks of interactions through regulatory elements drives most morphological diversification might, then, have different answers in different evolutionary lineages. In the most species-rich group of vertebrates — fish — organization of the Hox genes might not be completely constrained by interwoven regulatory networks, and differentiation might be driven by gene evolution. However, in the lineage that leads to reptiles and mammals, the driving force behind morphological diversification might have been newly evolving interactions in networks of regulatory elements¹⁶. □

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stable isobars, in which more than one stable nucleus exists at a given mass number.

There are three basic nuclear processes that produce heavy elements: the s-, r- and p-processes, standing for slow, rapid and proton-rich. The abundances produced by each of these³ are shown in Fig. 1.

The s-process probably takes place in red giant stars that are burning helium, with a given nucleus capturing a neutron perhaps every few thousand years. But only fractions of a second separate successive photodisintegrations in the p-process or neutron captures in the r-process, implying that these processes must occur in supernova explosions. So some details of supernova explosions can be deduced from isotopic analysis of meteoritic material — in particular, interstellar grains that have undergone relatively little thermal processing during and since the formation of the Solar System.

One important recent discovery was that there are two different r-processes⁶: one responsible for the r-process nuclides up to about $A = 140$ (where A is the mass number), the other for nuclides above $A = 140$. The discovery stemmed from extinct radionuclides, which lived long enough to survive with measurable abundances from the time of their production to their injection into the forming Solar System, but not long enough to be measurably present now. They are detected through excesses of the daughter elements that result from their decay.

The abundance of ¹⁸²Hf in the early Solar System is consistent⁶ with the continuous production of the actinides in the Galaxy, with mixing to maintain a roughly constant abundance level on a timescale consistent with the mean life of ¹⁸²Hf — about 10⁷ years. But trouble arises from two lighter radionuclides, ¹⁰⁷Pd and ¹²⁹I. If these were made by the same r-process that produced the

Isotope astrophysics

Two cradles for the heavy elements

A. G. W. Cameron

Where do the Solar System's heavy elements come from? We know that many of the elements heavier than iron must have been formed in supernovae; but exactly how? Taken together, three new papers (one on page 261 of this issue¹, and two to appear in the *Astrophysical Journal*^{2,3}) imply that two different types of supernova are responsible for elements in different mass regimes.

It is now some four decades since Suess and Urey⁴, largely working from analyses of meteorites, assembled a table of abundances of the elements that enabled nuclear physicists to identify the principal processes in stellar interiors that had produced those elements. The actual nuclear physics of those processes became reasonably well understood within the following few years. However, it has taken considerably longer for us to understand the astrophysical environ-

ments within stellar interiors in which many of those processes take place. The process whose environment has proved most elusive has been the r-process, in which neutron capture takes place on a very rapid timescale.

In the evolution of a star considerably more massive than the Sun, nuclear fusion reactions build toward products in which the binding energy per nucleon becomes maximized. This produces an abundance peak at ⁵⁶Fe. Making nuclides much heavier than this involves neutron capture, which generally produces nuclides on the neutron-rich side of the region of stable elements, known as the valley of beta stability. Only in the violence of a supernova explosion can the nuclides on the neutron-deficient side be produced, primarily by losing nucleons in photodisintegration. It is possible to distinguish these processes by examining the abundances of nuclei in the Solar System, particularly of

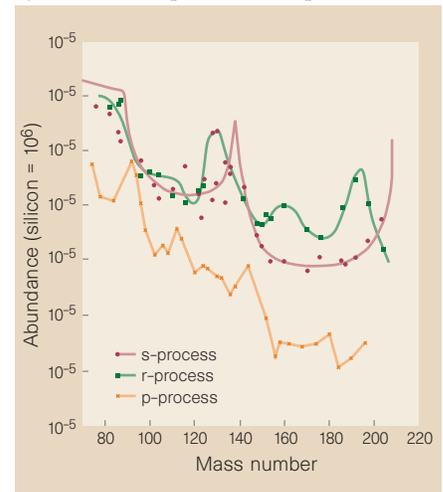


Figure 1 The solar abundances of the nuclides, as a function of mass number, showing the p-, s- and r-process contributions. For the s- and r-processes, average smooth lines have been drawn through the characteristic zig-zag patterns of the odd and even mass numbers. (From ref. 5.)

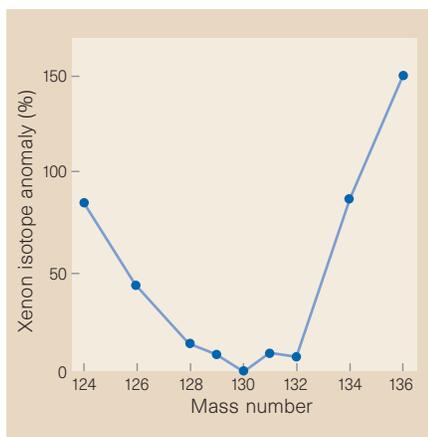


Figure 2 Overabundances of xenon from pre-solar diamonds, relative to solar values. (After Ott⁸.)

actinides, then they would be some two orders of magnitude more abundant than they are. So there must have been an interval of $\sim 10^8$ years between the last r-process production of ^{107}Pd and ^{129}I and their injection into the forming Solar System.

This is the basis for the claim that there are two distinct r-processes, with yields confined above and below about $A = 140$. The high-mass r-process must operate more frequently; a typical point in the interstellar medium receives products from it at roughly 10^7 -year intervals, but the low-mass-number r-process is much rarer, giving that point a contribution only every 10^8 years or so.

The newest results, which both confirm this idea and suggest how the two processes arise, come from interstellar diamond grains extracted from meteorites, and the anomalous isotopic abundances of their xenon and tellurium. These diamonds are tiny — only about one in a million contains a xenon atom, so the measurements must be made on bulk samples.

Figure 2 shows the overabundances in the principal xenon component contained in the diamonds (called XeHL). This pattern persists over a wide range of conditions of gas extraction from different samples at different temperatures⁷, indicating a common astrophysical source. Most striking are the high abundances of mass numbers 134 and 136 (r-process products), and 124 and 126 (p-process products). It has been suggested⁸ that this XeHL pattern is produced in a supernova environment by some kind of separation between those xenon isotopes with shorter-lived precursors and those with longer-lived precursors. But a new paper contradicts this idea.

Instead of xenon, Richter *et al.*¹ look at the tellurium in interstellar diamonds. It has large overabundances *only* at mass numbers 128 and 130, both r-process isotopes whose precursors live about an hour. The tiny overabundance ($<4 \times 10^{-5}$) for the $A = 120$ p-process product, for example, is in striking

contrast to the xenon p-process products shown in Fig. 2. The time delay in forming $A = 120$ is also only about an hour, and the supernova p-process should⁹ have a yield at $A = 120$ comparable to those at $A = 124$ and 126 for xenon. So a separation based on precursor lifetimes can't explain the tellurium data. What can? To address this, we will have to look more closely at the extreme physical conditions occurring in supernovae.

The r-process is thought to involve neutrino-driven winds in the surface layers of a newly formed neutron star. A neutron star must be formed during the collapse process that produces a supernova, to supply the observed amount of energy. Enough energy is released so that the thermal energy, $E = kT$ (where k is Boltzmann's constant, and the temperature T is usually measured in MeV) is large compared with the rest-mass energy of the electron, and enough to fill the available phase space of quantum states with neutrinos. Inside the neutron star, the six flavours of neutrino — electron, muon and tau, and their corresponding antiparticles — interchange rapidly among themselves and with the radiation field.

The neutrinos leak out of the neutron star in seconds. Even when they are near the surface layers of the neutron star, however, the neutrinos continue to interchange with one another and with electrons, positrons and photons. This heats the surface matter, blow-

ing it off as a dense, neutron-rich wind. As it expands and cools, nuclear reactions take place that build up seed nuclei, and the r-process takes place on these seed nuclei as they cool further.

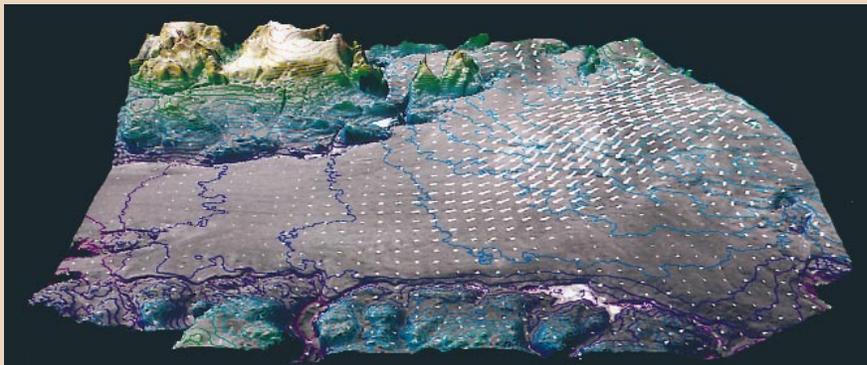
But this general description of the r-process can be applied to two very different cases involving high and low entropy — corresponding to high and low thermal energy.

In the hot, high-entropy case, the core of a massive star collapses to form a neutron star (and possibly further to form a black hole). For several years this has been the standard setting for the r-process, but simulations show that to match Solar System r-process abundances demands very high entropies indeed, corresponding to entropies of at least 400 (in units of Boltzmann's constant per baryon). Theory balks at this: it appears to be impossible^{10,11} to reach an entropy as high as 200. Perhaps the theorists should concentrate less on increasing the numbers of neutrons and look at reducing the numbers of seed nuclei, so that the existing neutrons can carry the r-process build-up to higher mass number.

Nevertheless, neutron stars with massive stellar precursors seem essential to understand both the r-process and the p-process that produced the XeHL in Fig. 2. The p-process is thought to operate mainly in the oxygen–neon envelope of such a massive star⁹. Can the high-entropy picture then be

Satellite mapping

3-D glacial flow



Most satellite maps are only two-dimensional. But in the past few years, synthetic-aperture-radar (SAR) images from artificial satellites have been combined into interferograms, to produce high-resolution topographic maps of the Earth's surface and spectacular maps of surface deformation over active faults, volcanoes and glaciers. On page 273 of this issue, Johan Mohr and colleagues present a further improvement of this technique (Mohr, J. J., Reeh, N. & Madsen, S. N. *Nature* 391, 273–276; 1998).

Instead of mapping only the radar line-of-sight component of ice flow, as in

conventional SAR interferometry, they have taken advantage of the differing angles afforded by ascending and descending satellite orbits to map the full three-dimensional flow pattern of Storstrømmen, a large outlet glacier in northeastern Greenland. Above is a perspective view of this flow field looking from the east, with white arrows representing the glacial flow. The slowing near the end of the glacier (left of figure) is unusual, but expected for a glacier that has recently surged. This method can be used to assess the volume changes of land ice masses.

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adapted to provide two distinct r-processes? One suggestion² is that the formation of a neutron star as an end point might generate enough neutrons to drive the r-process up into the actinide region, whereas if the end-point is instead a black hole, then the neutrons would be prematurely cut off and only the low-mass-number range of products would be produced. Although this is an attractive idea, it doesn't predict the tellurium results, in which there is no trace of a p-process yield. As the supernova shock would be launched before the black hole ended neutron production, the p-process products should be there.

But a low-entropy r-process has now been discovered³ that could give products primarily in the lower range of mass numbers. Many stars of 6–12 solar masses exist in binary systems. At some point, these stars expand, transfer most of their hydrogen to their companions, and become white dwarfs. Eventually they accrete material back from their companions, and some of them grow in mass until the Chandrasekhar limit is reached, at which point the star collapses to form a neutron star. This is accretion-induced collapse (AIC), and results in so-called type-1a supernovae.

The entropy per particle in AIC is only about 3–5. As an entropy of at least 8 would be needed to completely break up the nuclei into nucleons, the star must retain very large numbers of seed nuclei. So the ratio of neutrons to seed nuclei would be relatively small, and this would favour a final distribution of r-process products in the lower range of mass numbers.

Further, the lack of a massive envelope means that AIC events do not lead to a p-process, and so could fit the tellurium results.

How were these isotopes implanted in the interstellar diamonds? Industrial diamonds are often produced by chemical vapour deposition in a cooling flow; and presumably something similar happens when a supernova shock wave encounters a carbonaceous layer. In a massive supernova, such a layer would be in the outer envelope of the star, whereas in an AIC supernova the carbon is likely to be in the material from the companion star flowing onto the white dwarf in the binary pair. But this requires further exploration.

Nevertheless, a consistent picture has emerged in which rare, low-entropy AIC supernovae inject the lighter r-process isotopes, and more common core-collapse supernovae take over for isotopes heavier than about $A = 134$. □

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Structural biology

A mechanism for all polymerases

Thomas A. Steitz

Possibly the earliest enzymatic activity to appear in evolution was that of the polynucleotide polymerases — the ability to replicate the genome accurately being a prerequisite for evolution itself. Thus, one might anticipate that the mechanism by which polymerases work would be both simple and universal. Further, these enzymatic scribes must faithfully copy the sequences of the genome into daughter nucleic acid, or the information contained within will be lost for ever. Finally, replicative DNA polymerases are highly processive, traversing the whole genome of a virus DNA without falling off.

On pages 251 and 304 of this issue, Doublé *et al.*¹ and Kiefer *et al.*² provide significant insights into the catalytic mechanism, fidelity and processivity of DNA polymerases. In a detailed crystal structure at 2.2 Å resolution, Doublé *et al.* have captured the DNA polymerase that replicates bacteriophage T7 DNA, along with the *Escherichia coli* thioredoxin in the act of adding a

deoxynucleoside triphosphate (dNTP) to a primer–template DNA. The incoming dNTP (actually dideoxy here) is accompanied by two magnesium ions, which are bound to the phosphates of the nucleotide and to two aspartic-acid residues that are widely conserved among DNA and RNA polymerases. To prevent the reaction from occurring in the crystal, the authors used a dideoxynucleotide at the primer terminus whose 3' OH, when present, would interact with one of the two metal ions.

This structure supports a 'two-metal-ion' mechanism of nucleotide addition, which was proposed³ by analogy to the nearly identical mechanism of the 3'–5' exonuclease of DNA polymerase I (Fig. 1). In this mechanism, metal ion A lowers the affinity of the 3' OH for the hydrogen, facilitating the 3' O⁻ attack on the α -phosphate. Metal ion B assists the leaving of the pyrophosphate, and both metal ions stabilize the structure and charge of the expected pentacovalent transition state. This two-metal-ion-catalysed

mechanism could act in an RNA or DNA polymerase made from RNA rather than protein and, thus, could function in an all-RNA world.

An identical two-metal-ion polymerase mechanism seems to be used by another, non-homologous DNA polymerase — mammalian DNA polymerase β (Pol β) — presumably as a consequence of convergent evolution. Kraut and co-workers⁴ found a similar arrangement of primer–template DNA, ddNTP and magnesium ions in Pol β . Indeed, when Doublé *et al.*¹ superimposed the primer–template DNAs as bound to these two polymerases, they found that the nucleotide, the two magnesium ions and their two aspartic-acid ligands superimpose likewise, in spite of the differences between the two protein structures. The conservation of catalytic-domain structure and liganding of the metal ions by two aspartic-acid residues, in structures of the B (Pol α)-family DNA polymerases⁵, T7 RNA polymerase⁶, human immunodeficiency virus reverse transcriptase⁷ and poliovirus RNA-dependent RNA polymerase⁸, implies that all families of polynucleotide polymerases may use the same, two-metal-ion mechanism.

One source of the impressive fidelity with which polymerases copy DNA is uncovered in the co-crystal structure of *Bacillus stearothermophilus* DNA polymerase large fragment with primer template, solved by Kiefer *et al.*², and that of the T7 polymerase complex¹. Both provide details of a sequence-independent molecular recognition of correctly formed base pairs. Protein side-chains interact, in the minor groove,

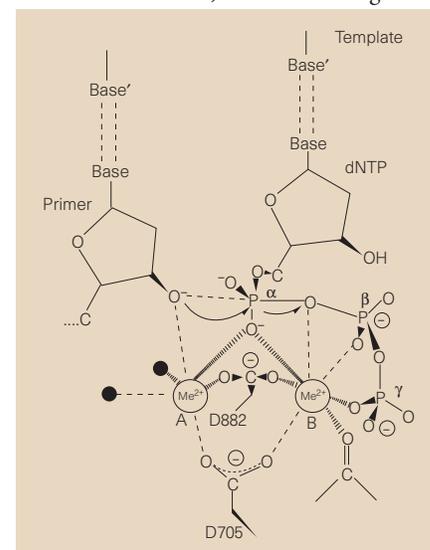


Figure 1 The two-metal-ion mechanism of polynucleotide polymerases³ in the context of the T7 DNA polymerase–substrate complex solved by Doublé *et al.*¹. Two divalent metal ions, A and B, are ligated to enzymes of the *Escherichia coli* DNA polymerase I family by aspartic-acid residues 705 and 882. The black circles are water molecules bound to metal ion A. (Modified from ref. 12.)