

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 $A = 134$. □

A. G. W. Cameron is at the Harvard-Smithsonian Center for Astrophysics, 60 Garden Street, Cambridge, Massachusetts 02138, USA.

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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,

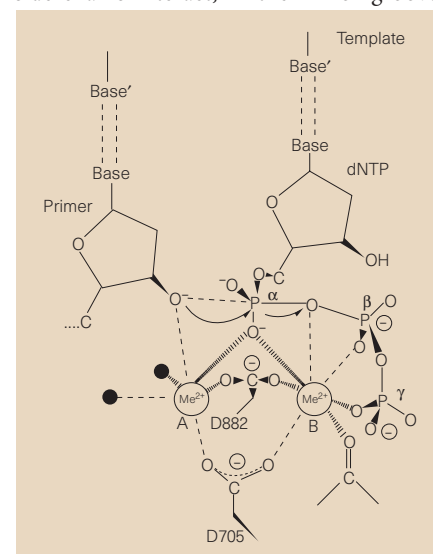


Figure 1 The two-metal-ion mechanism of polynucleotide polymerases³ in the context of the T7 DNA polymerase–substrate complex solved by Doublé *et al.*¹. Two divalent metal ions, A and B, are ligated to enzymes of the *Escherichia coli* DNA polymerase I family by aspartic-acid residues 705 and 882. The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

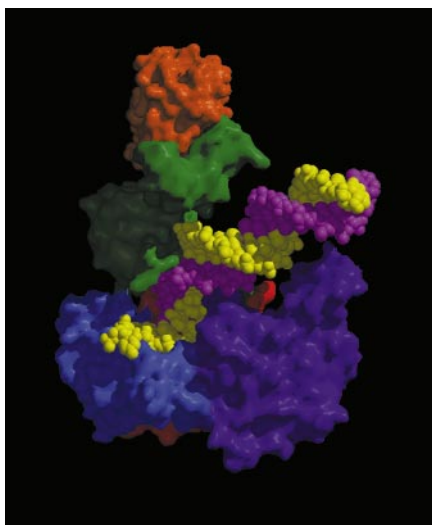


Figure 2 Structure of the T7 DNA polymerase, solved by Doublé *et al.*¹, locked in synthesis mode. The fingers (blue), thumb (green) and palm (red) domains are shown, as well as the exonuclease (purple) and *Escherichia coli* thioredoxin (orange).

with the hydrogen-bond acceptors that lie in identical positions in all four Watson–Crick base pairs. These interactions can occur only with correct Watson–Crick base pairs, and not with mismatches. The DNA near the primer terminus has the widened minor groove of an A-form structure (as observed with other polymerase–DNA complexes^{4,9,10}), and this facilitates access to the minor groove. The base of the incoming dNTP and its template partner fit snugly into a pocket that accommodates only Watson–Crick pairing¹.

The crystal structure of the T7 polymerase complex includes the *E. coli* thioredoxin, which renders the polymerase so processive that it can replicate the entire T7 genome before falling off¹¹. The thioredoxin subunit interacts with a polymerase domain termed the ‘thumb’ (Fig. 2). It is adjacent to the duplex DNA product in a region 12–18 base pairs from the primer terminus, where the DNA in this crystal becomes disordered. Consequently, the mechanism by which thioredoxin confers processivity remains uncertain. The thioredoxin, which is flexibly tethered to a binding loop in the thumb, could swing across the DNA-binding groove to encircle the DNA¹. Or, less likely, it could simply extend the DNA-binding site¹. Kiefer *et al.*² observed that their crystals of *Bacillus* fragment are catalytically active, and can undergo several rounds of nucleotide incorporation. Thus, the processive sliding that is thought to accompany the translocation step in DNA synthesis can occur within the confines of the crystal.

Comparison of the Pol β or T7 DNA polymerase ternary-complex structures with the corresponding binary complexes or apo-enzyme structures shows that binding

of both substrates results in a dramatic change in the orientation of the ‘fingers’ domain. In the T7 enzyme¹, the whole domain rotates about 40° (relative to the primer template), providing the proper binding site for the incoming dNTP and its template partner. In the *Bacillus* fragment binary complex², the template base is not positioned to pair with the incoming dNTP. The relationship of this conformational switch to fidelity and translocation is worth further examination.

These two co-crystal structures^{1,2}, as well as those of *Thermus aquaticus* DNA polymerase⁹ and HIV reverse transcriptase¹², bind primer–template DNA to their catalytic (‘palm’) domains in a similar fashion. But this is not the way that was proposed by Pelletier *et al.*⁴ from their co-crystal structure of Pol β . Because Pol β is not homologous to these enzymes, it can be compared only by alignment of the bound primer–template DNAs. However, striking analogies can then be seen within the non-homologous structures of the ‘fingers’ and ‘thumb’ domains, which bind the dNTP and primer–template. By comparing the functional complexes of

these structurally diverse polymerases we should, therefore, be able to identify those structural elements that are essential for the polymerase reaction. □

Thomas A. Steitz is in the Department of Molecular Biophysics and Biochemistry, and the Howard Hughes Medical Institute, Yale University, 266 Whitney Avenue, New Haven, Connecticut 06520-8114, USA.

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Smart materials

Off and on reflection

Philip Ball

The architect’s palette has been enriched by smart materials, which enable a building to adjust its environment to the prevailing conditions. At a meeting last month*, Peter Duine (Philips Research Labs, Eindhoven) described a tantalizing addition to the palette: windows that can be reversibly switched from a transparent to a mirror state.

The appeal of a switchable mirror might be obvious to gimmick addicts, but are there more practical attractions in such devices? For privacy purposes it beats drawing the curtains, but one can also imagine applications in energy-conscious architectural design — using switchable mirrors as elements of smart systems that control the amount of sunlight admitted through a window. And as a means to influence the path of light beams, the mirrors might be put to good use in display devices and interior lighting systems, particularly when the light sources are hard to reach and adjust.

The new work, which brings these technological goals closer to fruition, stems from a report in 1996 of switchable optical properties in yttrium and lanthanum¹. The underlying principle is a transition between a reflective metallic state and a translucent insulating state, induced by converting a thin film of a metal to its ionic hydride. All of

als form hydrides on exposure to hydrogen gas, whereupon ionization of the metal can empty the conduction band and make the compound insulating. A thin enough (sub-micrometre) film may then be transparent.

For trivalent rare-earth metals like yttrium and lanthanum, however, the situation is slightly more complicated. In particular, the metals can exist in both a divalent and a trivalent state, corresponding to the hydrides MH_2 and MH_3 . Three different phases occur on exposure to hydrogen gas: the α -phase, a solution of a small amount of interstitial hydrogen in the metal; the β -phase (the dihydride); and the γ -phase (the trihydride). The two hydride phases (β and γ) can easily be interconverted by altering the hydrogen pressure, as the gas can readily diffuse in and out of the thin film. The dihydride retains a partially filled conduction band, and so provides the metallic mirror, whereas the trihydride is transparent.

To make a device, the thin metal films deposited on glass are enclosed in a sealed cell after being coated with a 20-nm film of palladium to prevent oxidation. Palladium is a renowned hydrogen ‘sponge’, and so hydrogen gas introduced into the cell has easy access to the rare-earth metal. Graded-diffusion experiments, in which the gas is permitted access to the films from one end only, show the formation of the γ -, β - and α -phases, successively further away from the hydrogen source region.

* Fall Meeting of the Materials Research Society, Boston, 1–5 December 1997.