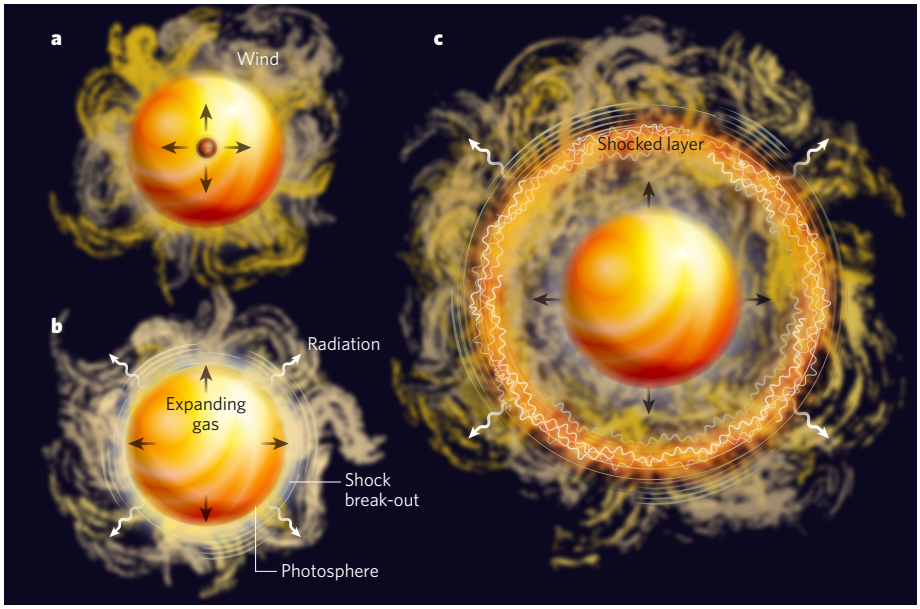

Figure 1 | Shock break-out. Soderberg and colleagues' observations[1] of an X-ray outburst preceding a type-Ibc supernova provide sterling support for prevalent models of how these cosmic explosions occur. **a**, Once its nuclear fuel is exhausted, the core of a massive star collapses in on itself, generating a huge explosion that propagates outwards as a shock wave. The progenitor star is surrounded by a 'wind' of gas previously lost from the star. **b**, After a matter of minutes, the shock wave reaches the surface of the star (the photosphere) and radiation from the explosion that is trailing in its wake escapes, accelerating the surrounding gas outwards. The moment of this 'shock break-out' is what the authors succeeded in capturing. **c**, Days later, a layer of hot gas has developed where the rapidly expanding, but cool, supernova gas impacts on the surrounding wind. This shocked layer is the site of electrons moving close to the speed of light that are responsible for radio and X-ray emission, typical supernova signatures.

hydrodynamic simulations that allow for the effects of a radiation field that is out of equilibrium will be needed before we can properly model the niceties of the transition.

Is there any other possible interpretation of the X-ray outburst, other than the emergence of a supernova shock? Might the outburst simply be a lower-energy cousin of a γ-ray burst? These bursts are thought to be produced by the same type of progenitor as type-Ibc supernovae, albeit less than 100 times as frequently. Their pathology is very different: rather than being the result of a spherical shock wave rippling through the star, they are assumed to be caused by directed, relativistic jets of particles and magnetic fields that are generated by a central black hole or neutron star and then burrow through their surrounds.

The X-ray outburst from SN 2008D was much weaker than a γ-ray burst, although that might simply represent a downwards extension of the permissible intensity range[3,4]. It has also recently been suggested[4] that the outburst shares with γ-ray bursts certain relationships between the amount of energy radiated isotropically (that is, equally in all directions), its peak spectral energy and the peak luminosity of the ensuing supernova. But speaking against the γ-ray-burst interpretation is not only the weight of post-burst observations seeming to indicate a normal supernova, but also the lack of firm evidence for the relativistic motions that are a signature of γ-ray bursts.

The observations[1] of SN 2008D would thus seem to be the earliest of light emanating from a supernova, just minutes after core collapse. NASA's Galaxy Evolution Explorer (GALEX) has recently seen the rising ultraviolet emission associated with shock break-out from type-II supernovae[5,6]. The progenitors of these supernovae are surrounded by an envelope of hydrogen gas, and the shock wave takes close to a day to traverse them.

As well as telling us more about the types of star that produce supernovae, such observations of shock break-out, by helping to tie down the time of core collapse, could provide useful auxiliary information in terrestrial hunts for exotic citizens of the cosmos thought to be produced in these cosmic cataclysms. The benefits could be felt by neutrino detectors, and by detectors searching for evidence of the elusive ripples in space-time known as gravitational waves. ■

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STRUCTURAL BIOLOGY

Snapshots of DNA repair

Stephen C. Kowalczykowski

In recombinational DNA repair, nearly identical sequences in chromosomes are found and swapped. Structures of the RecA–DNA complexes involved provide insight into the mechanism and energetics of this universal process.

Homologous recombination is one of the many processes used by cells to repair damaged DNA and to diversify their genomes. A central step in recombination involves the exchange of DNA strands between identical, or nearly identical, segments of chromosomes. This crucial reaction is catalysed by the RecA family of DNA-strand-exchange proteins, which include the founding member in bacteria, Rad51 in eukaryotes and RadA in archaeans. On page 489 of this issue, Chen *et al.*[1] describe structures of both the substrate (RecA complexed with single-stranded DNA) and the product (RecA complexed with double-stranded DNA) of DNA strand exchange. The structures reveal non-uniform DNA stretching, and suggest a mechanism for strand exchange.

On the face of it, DNA strand exchange is a simple reaction: one strand of double-stranded DNA (dsDNA) is replaced with an identical single strand of DNA (Fig. 1a). This reaction would be simple, were it not for the stability of dsDNA, which resists strand separation, and the need to accurately align DNA sequences. Thus, although the stability is useful for the storage of genetic information, it is an impediment to DNA repair and recombination.

The RecA-like proteins do not deal with this problem by unwinding dsDNA, as helicase enzymes do. Instead, they first assemble on a single strand of DNA, which was generated in the preceding step of recombination, to form a helical nucleoprotein (protein–DNA) filament. When formed with ATP, this filament (termed the presynaptic complex) is the active

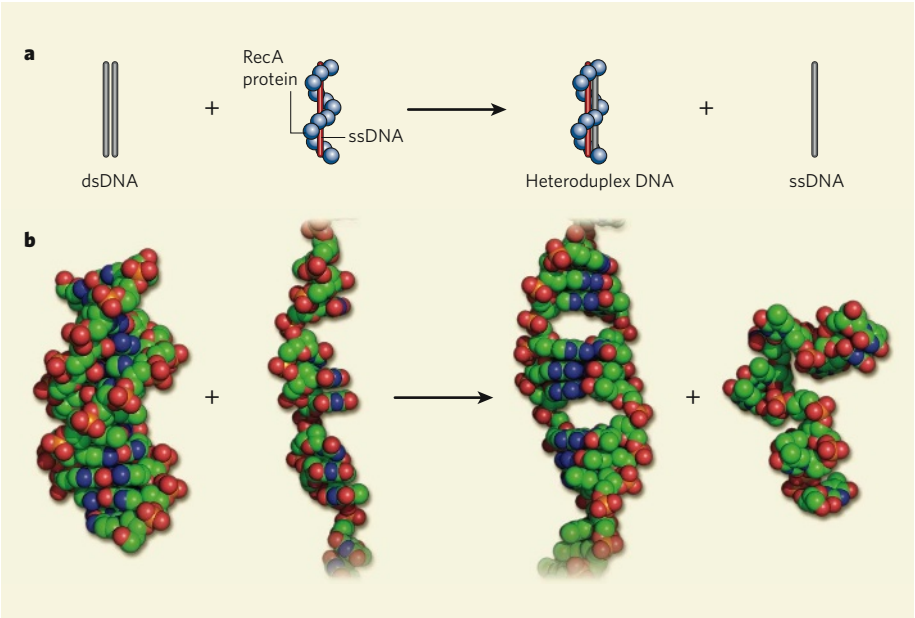

Figure 1 | DNA strand exchange promoted by RecA protein. **a**, The prototypical DNA-strand-exchange reaction. Double-stranded DNA (dsDNA) pairs with the RecA presynaptic filament, which consists of RecA protein and single-stranded DNA (ssDNA), to produce heteroduplex DNA bound by RecA and the exchanged ssDNA. **b**, Structures of the participating DNA molecules: B-form dsDNA; ssDNA within the presynaptic filament (as determined by Chen and colleagues[1], protein not shown); dsDNA within the filament[1] (protein not shown); and randomly coiled ssDNA.

species in DNA strand exchange that searches for a homologous sequence within the dsDNA. Once found, DNA strand exchange occurs as a concerted swap of DNA strands. The hydrolysis of ATP inactivates the filament, and permits disassembly of the complexes[2].

Herein lie the mysteries of DNA strand exchange. How does the RecA nucleoprotein filament recognize DNA sequence identity? And, on finding it, how does the exchange occur? How is the stability of dsDNA overcome? Partial answers to these questions emerged from biochemical studies. The homology search is a 'simple' collisional process because ATP hydrolysis is not essential, only ATP binding. In fact, ATP binding by the RecA nucleoprotein filament is sufficient for DNA strand exchange[3]. The free energy of ATP hydrolysis is not directly involved in the exchange of DNA strands; rather, the free energy of presynaptic-filament binding to the dsDNA 'activates' it by extending and untwisting it, making the duplex DNA a willing participant in the exchange process[4]. ATP hydrolysis then allows dissociation of all participants: a classic case of 'credit card' energetics (expend now, pay later …).

Structural information derived from electron microscopy was particularly revealing with respect to these questions. The ATP-bound form of the RecA nucleoprotein filament is extended by about 50% relative to standard B-form DNA, with around 6.2 RecA monomers and 18 DNA base pairs per turn[5]; this extended filament is also seen for all RecA homologues[6]. In contrast, the DNA in the inactive ADP-bound nucleoprotein filament is less extended. Thus, the RecA nucleoprotein filament undergoes ligand-induced structural transitions between an active, extended filament and an inactive, compact filament[5]. The electron microscopy studies also revealed that the RecA nucleoprotein filaments are structurally polymorphic, varying in pitch, width and extension[5], highlighting the challenge facing higher-resolution structural analysis.

Nonetheless, in 1992 the crystal structure of a RecA filament was solved[7], but the structure lacked DNA and was of the inactive ADP-bound compact form[8]. For many years, the absence of a structure of the active form confounded molecular and mechanistic interpretation[9].

However, Chen and colleagues[1] now elucidate structures of RecA assembled on single-stranded DNA (ssDNA) and on dsDNA, defining both the substrate and product forms of the reaction, respectively. How did they succeed? The authors recognized that the intrinsic conformational flexibility of the RecA nucleoprotein filaments and their capacity to self-assemble indefinitely might hinder crystallization in the active state. Their solution to these problems was ingenious, and is applicable to other self-assembling systems.

First, they created 'pre–polymerized' assemblies of RecA protein by fusing four, five or six monomers of RecA into a single polypeptide chain. To prevent indefinite polymerization of the resulting 'mini-filaments', the sites for monomer–monomer interactions were deleted from the first and last monomers in the chain. Despite the many potential pitfalls, this approach worked splendidly, producing functional proteins. When assembled in the presence of an ATP analogue on DNA that exactly accommodated these fusion proteins (15 and

50 YEARS AGO

The launching of *Sputnik* 3 (Satellite 1958 δ) was announced from Moscow on May 15. The satellite was stated to be conical in shape, with a length of 12.3 ft. excluding aerials, a base diameter of 5.7 ft. and a weight of 2,926 lb., including 2,134 lb. of apparatus. The experiments for which the satellite is designed include studies of cosmic rays, geomagnetism, solar radiation and micrometeorites, and the results are to be telemetered back to the Earth. The satellite is equipped with solar batteries and carries a radio transmitter with a frequency of 20.005 Mc./sec. There are two other objects in orbit with the satellite, namely, the rocket which performed the last stage of propulsion and a nose cone which protected the instruments during the climb through the atmosphere.
From *Nature* 24 May 1958.

100 YEARS AGO

The last half-yearly number of the Journal of the Royal Anthropological Institute contains an important memoir, prepared by two enthusiastic Scotch anthropologists, Messrs. Gray and Tocher, on the pigmentation of hair and eyes among the school children of Scotland ... The highest density of fair hair is to be found in the great river valleys opening on the German Ocean and in the Western Isles. In the former case, this probably points to invasions of a blonde race into those regions. Similarly, the higher percentage of fair hair in the Spey valley and in the Western Isles implies inroads of the Vikings or Norsemen. It is perhaps pushing the evidence too far when the writers suggest that the high percentage of fair-haired girls in the neighbourhood of Dunfermline is due to the train of blonde damsels who are supposed to have accompanied the Saxon princess Margaret, who about the time of the Norman Conquest became Queen of Malcolm Canmore.
From *Nature* 21 May 1908.

50 & 100 YEARS AGO

18 nucleotides, respectively), these mini-filaments formed ordered crystals.

The structures reveal an ordered filament with 6.2 monomeric units per turn and a pitch of 92–95 ångstroms. The DNA is close to the filament axis, is extended relative to B-form DNA, and has global features compatible with the electron microscopy. The ATP is completely buried at an interface between monomers. Each RecA monomer interacts with three nucleotides of the DNA (a triplet) adjacent to itself in the structure, as well as with two more nucleotides, one from each of the preceding and following triplets. As a result, each nucleotide triplet is bound by three monomers.

Perhaps the most remarkable feature of the nucleoprotein filament is the DNA structure (Fig. 1b). The 50% extension is not manifest as an isotropic extension at the nucleotide level; instead, the DNA is seen to comprise a three-nucleotide segment with a nearly normal B-form distance between bases (an axial rise of 3.5–4.2 Å for ssDNA and 3.2–3.5 Å for dsDNA), followed by a long untwisted internucleotide stretch (approximately 7.1–7.8 Å in ssDNA and 8.4 Å in dsDNA) before the next three-nucleotide element, and so on. This was a surprising result, because most people assumed that the DNA within the RecA–DNA complexes was uniformly stretched to an average of about 5.2 Å between bases.

The unusual repeat pattern of DNA extension in the RecA nucleoprotein filament offers a structural basis for understanding the dynamics of filament assembly. Assembly occurs by rate-limiting initiation of polymer formation (nucleation) followed by growth[2]. The structure shows that it would be energetically unfavourable for a single monomer to make the full repertoire of molecular contacts with DNA because of the need to both unstack the bases and extend the DNA to the next nucleotide triplet. Thus, the free energy for binding of the first monomer will be unfavourable relative to the binding of a second protein to an existing monomer, explaining the observed cooperativity of RecA binding to DNA[2]. Binding of a third monomer provides additional net free energy, because now two of the three monomers benefit from the added free energy of cooperative interactions. As more monomers bind, the energetic cost of extending the DNA is 'amortized' over an increasingly greater number of RecA monomers, until the net free energy of nucleus formation is sufficiently negative to permit stable nucleation. Although more complex scenarios can be envisaged, the structures of Chen and colleagues[1] now permit detailed energetic modelling of filament formation.

The results also highlight the physical mismatch between the ssDNA within the filament and the naked duplex DNA target (Fig. 1b). How does RecA align these sequences? The structures[1] offer provocative insights into how the transient three-stranded intermediate might look, and how the fidelity of DNA strand exchange might be enforced. It is easy to imagine the pairing between an ssDNA triplet within the filament and the naked dsDNA, as both have approximately B-form dimensions. However, pairing of the next three base pairs of DNA requires extension of the dsDNA to conform to the observed extension of the ssDNA in the filament. This energetically unfavourable base unstacking and chain extension could be compensated both by the now lower entropic cost (because the next triplet is part of the already paired dsDNA) and by the favourable base-pairing interactions that would form if the next triplet were fully homologous. However, if even one of the base pairs was non-complementary, then the nascent paired molecule might not be sufficiently stable, and homologous pairing with a partially homologous sequence would be aborted.

Furthermore, the structures show that the strand complementary to the ssDNA in the presynaptic filament makes few contacts with the protein. Hence, it is largely stabilized by correct Watson–Crick base-pairing, thereby requiring accurate DNA pairing. Successful DNA pairing requires at least 15 base pairs of homology[10], and the structures suggest how such fidelity is enforced.

Determination of the three-dimensional structure of the active state of RecA nucleoprotein filaments by Chen and colleagues[1] is a watershed in recombination biochemistry and mechanics. Not only do the structures inform us about this central protein, but they also enable the formulation of structural hypotheses that relate to the RecA orthologues and to interacting proteins. Although the eukaryotic and archaeal RecA homologues differ in many functional and mechanistic details, the RecA structures will provide a valuable foundation for understanding them. Also, many proteins interact with the various forms of RecA family members to regulate assembly and disassembly of the filament. Having structures of both the ATP– and ADP–RecA nucleoprotein filaments will help clarify the mechanistic basis of their biological functions. Clearly, more (DNA) partner-swapping experiments will be forthcoming. ■

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CELL BIOLOGY

Viruses in camouflage

Kirsten Sandvig and Bo van Deurs

The vaccinia virus acts like a Trojan Horse to enter its host cells: it envelops itself in the membrane of a dying cell, and is then taken up by healthy cells.

Endocytosis is the process by which cells internalize extracellular material. It is crucial to cell survival and the proper functioning of tissues, being involved in processes as diverse as growth, neural transmission and pathogen clearance. But several opportunistic molecules (bacterial and plant toxins) and pathogens (viruses and bacteria) can exploit the endocytic machinery of a host cell for their own gain[1,2]. Writing in *Science*, Mercer and Helenius[3] report how vaccinia virus (Fig. 1) — a cousin of variola virus, which causes smallpox — deceives host cells into taking it up through endocytosis.

When cells are damaged or dying, for example during programmed cell death (apoptosis), they show several characteristic features. For instance, phosphatidylserine, a lipid that is abundant in the inner (cytoplasmic) layer of the cell membrane, is redistributed to the outer layer. This phospholipid is thus available to bind to receptors on the surface of phagocytic cells that initiate the apoptotic cell's destruction and engulf it[4]. Another sign of apoptosis is membrane blebbing, or the formation of irregular bulges on the cell membrane. Blebbing also occurs during other processes, such as cell migration and division, but its function is unclear.

When enveloped viruses bud off from their host cell, they inherit a lipid coating (envelope) that has the same composition as the host cell membrane. Mercer and Helenius[3] report that the outer layer of the vaccinia virus envelope contains phosphatidylserine and that this is crucial for infection. They propose that the