findings offer fresh insight into the consequences of the increased aridity that is projected to occur because of human-driven global climate change[10]. Specifically, they reveal that, for dryland ecosystems worldwide, the balance between carbon, nitrogen and phosphorus will become increasingly disrupted as ecosystems become drier. This will occur through widespread losses of soil organic matter (and therefore of biologically available pools of carbon and nitrogen), and through an increased role of abiotic factors (and therefore of available phosphorus). Of particular concern are the authors' data showing that this decoupling of elemental cycles accelerates in a nonlinear manner as aridity increases, suggesting that, as global climate change progresses, the ecosystem properties of many drylands could pass a tipping point that will be difficult or impossible to reverse.

The study highlights the fact that, as aridity increases, adverse ecological consequences will arise not only through the direct effects of moisture limitation, but also through the indirect effects of decoupled elemental cycling and reduced organic matter in soil. This could have far-reaching consequences. For example, dryland ecosystems will be able to store less carbon both above and below ground, thus compromising their ability to mitigate increased levels of atmospheric carbon dioxide and climate change. More immediately, reduced soil carbon and nitrogen may impair the supply of nutrients from the soil and therefore the productivity of crops and livestock, with potentially dire consequences for many of the more than 2 billion people who inhabit dryland regions. This study underscores the fact that increased aridity associated with global change, and its effects on soil nutrient balances, could greatly affect the capacity of drylands to deliver key ecosystem services upon which human well-being depends. ■

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STRUCTURAL BIOLOGY

Pivotal findings for a transcription machine

Crystal structures of the complete RNA polymerase I complex are now revealed. The structures link the opening and closing of this enzyme's DNA-binding cleft to the control of transcription. SEE ARTICLES P.644 & P.650

JOOST ZOMERDIJK

RNA polymerases are intricate molecular machines that transcribe DNA into RNA, combining RNA synthesis with the precise movement of a DNA template across their active site. Eukaryotic cells (those of animals, plants and fungi) have several RNA polymerases, each dedicated to the production of specific RNAs. RNA polymerase I (Pol I) synthesizes the ribosomal RNA component of the cell's protein-producing factories and so is crucial for cell survival, growth and proliferation; malfunction of Pol I can cause cell death or support the unrestrained proliferation characteristic of cancer cells[1]. In two groundbreaking papers in this issue, Fernández-Tornero *et al.*[2] (page 644) and Engel *et al.*[3] (page 650) present the first crystal structures of the complete 14-subunit yeast Pol I at 3.0 and 2.8 ångströms resolution, respectively. The structures provide unprecedented insight into Pol I-specific features, potential mechanisms in transcription, and evolutionary conservation of the structures and functions of Pol enzymes*.

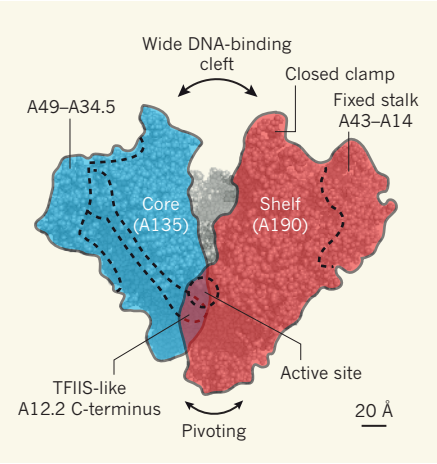

Figure 1 | Structure of RNA polymerase I. Front view of the 14-subunit, 590-kilodalton polymerase I complex with approximate locations of the core and shelf modules, which broadly overlap the cleft sides formed by subunits A135 and A190, respectively, as well as the DNA-binding cleft. The open and closed states of the cleft are determined by relative pivoting of the core and shelf modules at the cleft base near the active site, where RNA synthesis occurs. Also indicated are the locations of: the permanently closed clamp; the fixed stalk, which consists of the A43–A14 subcomplex and contributes to permanent closure of the clamp; the TFIIS-like C-terminal domain of A12.2, which is integral to the active site; and the A49–A34.5 subcomplex, which stabilizes A12.2.

Structural analyses of bacterial Pol, eukaryotic Pol II and archaeal Pol have detailed the architecture of these enzymes, the interactions between their subunits and their inner workings during transcription[4]. Pol I and Pol III share overall architecture with Pol II[5]. However, each Pol contains specific subcomplexes and features that influence its ability to transcribe a particular subset of genes: whereas Pol I produces rRNAs, Pol II generates messenger RNAs and Pol III synthesizes small non-coding RNAs, including transfer RNAs and 5S rRNA[6].

Pol I is the most productive of the eukaryotic polymerases. To achieve high-throughput transcription, multiple Pol I complexes transcribe the ribosomal DNA, and these are densely packed along each template and are highly processive (likely to traverse the entire template). The Pol I crystal structures reveal various distinguishing features that have the potential to influence the enzyme's output, partly by facilitating its productive association with the DNA template.

The structures confirm that the zinc-ribbon domain at the carboxy terminus of Pol I subunit A12.2 inserts into, and forms an integral part of, the enzyme's active-site region[7] (Fig. 1). (By contrast, TFIIS, the functional counterpart of A12.2 in Pol II, only transiently associates with the active site of paused Pol II.) Within the active site, this zinc ribbon can stimulate the removal of faulty and redundant RNA sequences to prevent Pol I arrest and consequent 'traffic jams' along the template, thus increasing transcription efficiency. The stability of A12.2 in Pol I is influenced by its interaction with the (TFIIF-like) dimerization domain of the Pol I-specific subcomplex A49–A34.5 (ref. 8). The structural data now rationalize this, revealing the contact points between A12.2 and the A49–A34.5 amino-terminal dimerization domain, as well as extensive interactions of the A34.5 C terminus as it wraps around the outer face of the A135

*This article and the papers under discussion[2,3] were published online on 23 October 2013.

subunit, which help to anchor the subcomplex.

Procession of RNA polymerases along a DNA template is facilitated by a closed-clamp component. The structures of Pol I reveal that the A43–A14 subcomplex, which comprises a fixed stalk (Fig. 1), contributes to a permanently closed state of the clamp and, therefore, to the high processivity of Pol I. By contrast, the clamps of other RNA polymerases are mobile elements. In Pol II, for example, attachment of the Rpb4–Rpb7 stalk locks the clamp in a closed state over the complex of RNA and DNA template during transcription, but this stalk is detachable[9,10].

Intriguingly, both teams' crystals are dimers of Pol I, in which the stalk of each Pol I inserts into the DNA-binding cleft of the other Pol I, through the A43 C-terminal 'connector' domain, thus making extensive contacts with the cleft and the coiled-coil motif of the clamp. The dimers have an unusually wide cleft (Fig. 1), perhaps partly because of this A43-connector insertion.

The cleft is too wide to anchor the complex of RNA and DNA template, particularly near the active site. This widening contributes to further rearrangements near the active site. (For example, crucial 'aspartate-loop' interactions are configured differently from those in Pol II; the 'bridge' helix contributing to DNA movement through the active site is unfolded in the middle and kinked; and there is partial blockage of the gate to the exit channel for newly synthesized RNA.) Furthermore, the wide cleft is occupied by a Pol I-specific extended loop of A190, which the authors refer to as the expander[3] or DNA-mimicking loop[2]. Because of its location, this loop would interfere with DNA loading at the active site. In one of the three Pol I structures presented by Fernández-Tornero *et al.*, no loop is detectable at the active site, hinting that it is unlikely to be essential for stabilization of the expanded cleft, although not excluding a role in its establishment.

Fernández-Tornero and colleagues' crystals display varying degrees of cleft widening. Comparative structural modelling of RNA polymerases suggests that the Pol I cleft widens as a result of relative pivoting of 'core' and 'shelf' modules (which are formed mainly by the largest subunits, A135 and A190) at the base of the cleft, near the active site[2,3] (Fig. 1). Engel *et al.* draw parallels to similar domain pivoting in inhibitor-bound or paused bacterial Pol, in which a pivoted or ratcheted state is associated with cleft opening and coupled rearrangements of domains near the active centre, inactivating the polymerase[11,12].

Because the new structures imply that the DNA template must be loaded into Pol I that has a closed clamp, perhaps the open or shut status of the cleft contributes to DNA-loading efficiency. It is possible that binding of the DNA template in the open cleft of a Pol I monomer triggers cleft closure, potentially coupled with relocation of the expander loop, rendering the enzyme active. Cleft closure by pivoting of the core and shelf modules presumably occurs concomitantly with refolding of the bridge helix, opening of the RNA-exit gate and the approach of A135 to anchor the DNA template in the active site. An understanding of the exact rearrangements will hinge on structural analysis of Pol I engaged in transcript elongation and, therefore, in complex with DNA and RNA.

Engel *et al.* propose that regulatory factors binding at the core–shelf interface might facilitate cleft closure. They speculate that Rrn3 (a factor that tethers Pol I to proteins bound specifically to promoter DNA sequences) triggers cleft closure by binding Pol I near the RNA-exit channel[3,13]. This attractive possibility awaits confirmation, perhaps through analysis of a Pol I–Rrn3 co-crystal. Conversely, factors that terminate transcription by Pol I might induce cleft opening. In all probability, the regulation of transcription by modulation of the core–shelf interface, which is seen in bacterial Pol, is also a feature of eukaryotic RNA polymerases[3].

Solving the crystal structure of the complete Pol I complex is a triumph, providing a wealth of information with which to build a picture of the specific mechanisms and control of rRNA-gene transcription in eukaryotes and also to explore the general mechanisms of transcription by all RNA polymerases. Another tour de force will be necessary to solve the structure of Pol I in transcription-elongation mode and, further, that of the complete Pol I pre-initiation complex, incorporating Rrn3, the core promoter-binding factors (Rrn6, Rrn7 and Rrn11 with TBP) and the rDNA promoter sequences. Such structures, together with those presented by Fernández-Tornero *et al.* and Engel *et al.*, will yield information that is vital for establishing when and where crucial protein and DNA contacts are made, disrupted and rearranged as Pol I steps through the transcription cycle. ■

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QUANTUM PHYSICS

Single electrons pop out of the Fermi sea

The ability to control individual electrons in an electronic conductor would pave the way for novel quantum technologies. Single electrons emerging from a sea of their fellows in a nanoscale electrode can now be generated. SEE LETTER P.659

CHRISTIAN FLINDT

Splashing water in the bath usually leads to small waves, splashes and droplets. Similarly, applying a voltage pulse to the sea of electrons in a nanoscale electrode produces a complex quantum state involving several electrons that have been kicked out of the sea, as well as holes — or missing electrons — left behind. On page 659 of this issue, Dubois *et al.*[1] report the first experimental voltage-pulse generation of just a single electron, not several, emerging on top of an electronic sea*.

*This article and the paper under discussion[1] were published online on 23 October 2013.

A nanoscale electrode is a reservoir of electrons, often referred to as a Fermi sea. Applying a voltage to the electrode amounts to changing the sea level by either pouring more electrons into the electrode (thus increasing the sea level) or emptying out electrons (thereby decreasing the sea level). A voltage that varies with time typically stirs up the Fermi sea and causes waves and splashes of electrons. This effect led Levitov and colleagues[2–4] to investigate theoretically how a time-dependent voltage affects a Fermi sea. Surprisingly, and quite remarkably, they found that a particular shape of voltage pulses should excite just a single electron onto the surface of the Fermi