Antihydrogen coda

The many-Ps systems being studied by Mills and company may, in time, be useful to antihydrogen researchers. Within the past few years, two independent groups located at CERN—the ATHENA and ATRAP collaborations—have succeeded in producing and characterizing slowly moving antihydrogen atoms (see PHYSICS TODAY, November 2002, page 17, and January 2003, page 14). Rolf Landua, a member of the ATHENA group, notes that colliding a dense gas of Ps with cold antiprotons could be an efficient way to produce cold antihydrogen. And with that antihydrogen, the CERN groups might ultimately test the equivalence principle of general relativity and the *CPT* theorem, which asserts physics is invariant under the combined operations of charge conjugation *C*, spatial inversion *P*, and time reversal *T*. Ironically, in addition to being an aid to antihydrogen researchers working to test the equivalence principle, Ps is also a competitor: The neutral electron–positron system might itself serve to test equivalence. **Steven K. Blau**

References

1. E. A. Hylleraas, A. Ore, *Phys. Rev.* **71**, 493 (1947).
2. D. B. Cassidy et al., *Phys. Rev. Lett.* **95**, 195006 (2005).
3. F. Anderegg, E. M. Hollmann, C. F. Driscoll, *Phys. Rev. Lett.* **81**, 4875 (1998); R. G. Greaves, C. M. Surko, *Phys. Rev. Lett.* **85**, 1883 (2000).

Optical Trap Resolves the Stepwise Transfer of Genetic Information from DNA to RNA

DNA encodes the amino acid sequences of each protein in our bodies, but carries no instructions for how much of each protein to make. Instead, a cell's protein factories, its ribosomes, are set spinning by RNA, DNA's single-stranded relative. By controlling when and which genes are transcribed from DNA to RNA, a cell regulates its protein production.

Transcription is carried out by an enzyme called RNA polymerase. RNAP wraps around DNA like a collar. As it proceeds along DNA, RNAP pulls the helix apart to expose a short stretch of the bases whose sequence embodies the genetic code. Then, from the surrounding solution, RNAP grabs free-floating bases and adds them in the proper, complementary sequence to the end of a growing chain of RNA.

Now, Steven Block of Stanford University in California and his collaborators have used an innovative optical trap to track the progress of a single RNAP molecule along a single DNA molecule. Their results, which shrink the resolution of optical traps from nanometers to angstroms, confirm what biochemists expected: RNAP advances along DNA and assembles RNA one base at a time.[1]

The assembly of RNA can now be tracked with a precision finer than the distance between its bases.

Optical trap

If you could watch a movie of transcription, you'd see a long floppy molecule, the DNA, waving like a leaf of kelp in seawater as a bulky blob, the RNAP, advances along its length and extrudes a floppy molecule of freshly made RNA.

DNA and RNA undulate on scales of microns, yet their constituent bases are just 3.4 angstroms apart. To observe RNAP move along DNA, the Stanford team had to stretch a DNA molecule between two tethers: one attached to RNAP, the other attached to the DNA upstream of RNAP's advance. Gently and continually pulling the tethers apart straightens the DNA. As RNAP carries out transcription, the distance between the tethers increases by a tiny and potentially measurable amount.

That, in outline, is how Block and his colleagues did their experiment. To put the scheme into practice, they had to make several innovative improvements to the construction and operation of optical traps.

Devised in the 1970s by Arthur Ashkin, optical traps work by illuminating a micron-sized transparent bead, typically polystyrene, with a tightly focused laser beam. The bead is trapped and suspended because the convergent beam creates a strong electric field gradient. The dielectric molecules that make up the bead act like dipoles in the electric field and are drawn to the region of strongest field intensity: the focus of the laser beam.

The laser not only traps the bead, but also, through lenses, mirrors, and other optical components, provides the means to change and measure the bead's position.

In a typical biological application, one end of the molecule of interest is fixed to a bead while the other is fixed to the surface of a coverslip or other stationary object. The bead, molecule, and surrounding solution occupy a tiny glass vessel. The laser and other optics sit on an optical bench.

To attain angstrom resolution, the Stanford team had to quell two of the biggest sources of noise in optical traps: the small, jittery vibrations of the fixed tether and the "twinkling" or fluctuations of the laser beam as it makes its way through the optical system.

Fixed tethers jitter because the objects they are attached to can move very slightly with respect to the optical trap. To address the problem, Block and his team applied a tech-

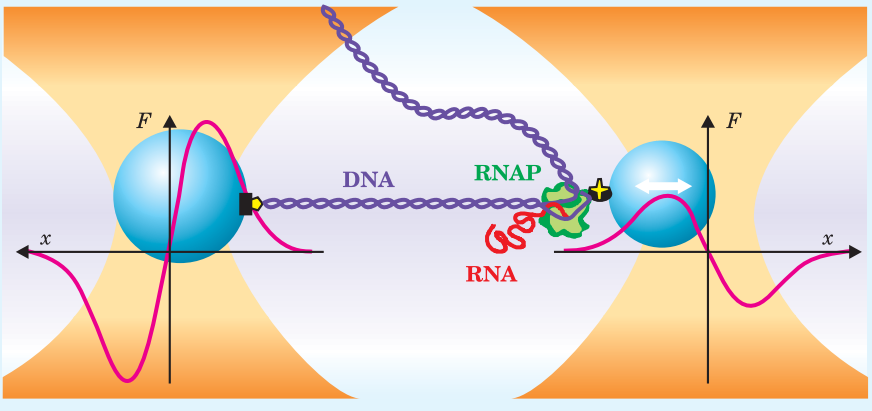


Figure 1. Pulling apart two trapped beads under constant force yields the size of the steps RNA polymerase makes along DNA as it produces RNA. Constant force is maintained because the trapped bead on the right is in a regime where force does not depend on position. (Courtesy of Steven Block.)

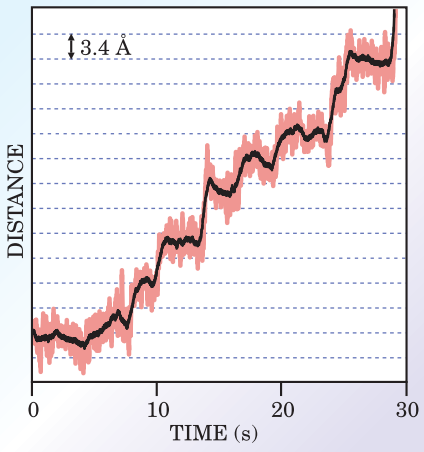


Figure 2. RNAP advances along DNA in steps comparable in size to the mean 3.4-Å separation of nucleotides (dotted grid lines). (Courtesy of William Greenleaf and Elio Abbondanzieri.)

nique they had demonstrated three years ago.[2] They attached both ends of the DNA tether to separate, optically trapped beads, in effect levitating the DNA and RNAP molecules. Figure 1 shows the arrangement.

Stars twinkle in the night sky because atmospheric density fluctuations refract starlight in and out of an observer's line of site. Atmospheric fluctuations can also perturb the path of a laser beam in a lab. To remove their effect, one could put the laser and other optical components inside an airtight box and pump out all the air. But working in vacuum is troublesome.

Instead, the Stanford group surrounded their optical equipment with helium at ambient temperature and pressure. The gas density still fluctuates, but because helium's refractive index is lower than air's, the twinkling deflects the beams far less.

Close to the edge

Conceptually, the simplest way to measure the progress of RNAP along DNA is to apply a constant force between the beads attached to the two molecules. Then, because the tension is constant, the molecules don't stretch any further and the measured extension is due solely to RNAP's advance.

The usual way to maintain tension is to monitor and adjust the stretch with a sophisticated feedback system. But William Greenleaf, a graduate student in Block's lab, devised a simpler method.[3] Around the center of the optical trap, the force on the bead is proportional to the distance the bead is pulled out of the trap. But near the trap's edge, the restoring force reaches a peak then wanes. For a small range of extension around that maximum, the force is invariant. If one of the beads is trapped in this region, RNAP advances under constant force.

Figure 2 shows a typical data set. Applying a constant force of 18 piconewtons and recording the transcription at an average rate of 1 base per second produces a trace with distinct steps. Combining several traces and analyzing the distribution yields a clear peak with a mean step of 3.7 ± 0.6 Å, comparable to the mean separation between bases. Evidently, evolution picks the simplest transcription scheme: transferring the smallest units of genetic information, the bases, one by one, rather than in bunches.

The Stanford experiment also sheds light on how RNAP, a molecular motor, consumes and converts energy to do its job. Within DNA and RNA, each base is bound to a single phosphate group. But in solution, the bases come with two additional phosphate groups. In grabbing free-floating bases to make RNA, RNAP catalyzes the hydrolysis of the extra phosphate groups, thereby releasing energy. In principle, the energy released by hydrolysis could be enough both to add a base to the RNA and to power RNAP's advance. Biophysicists call such cycles power strokes.

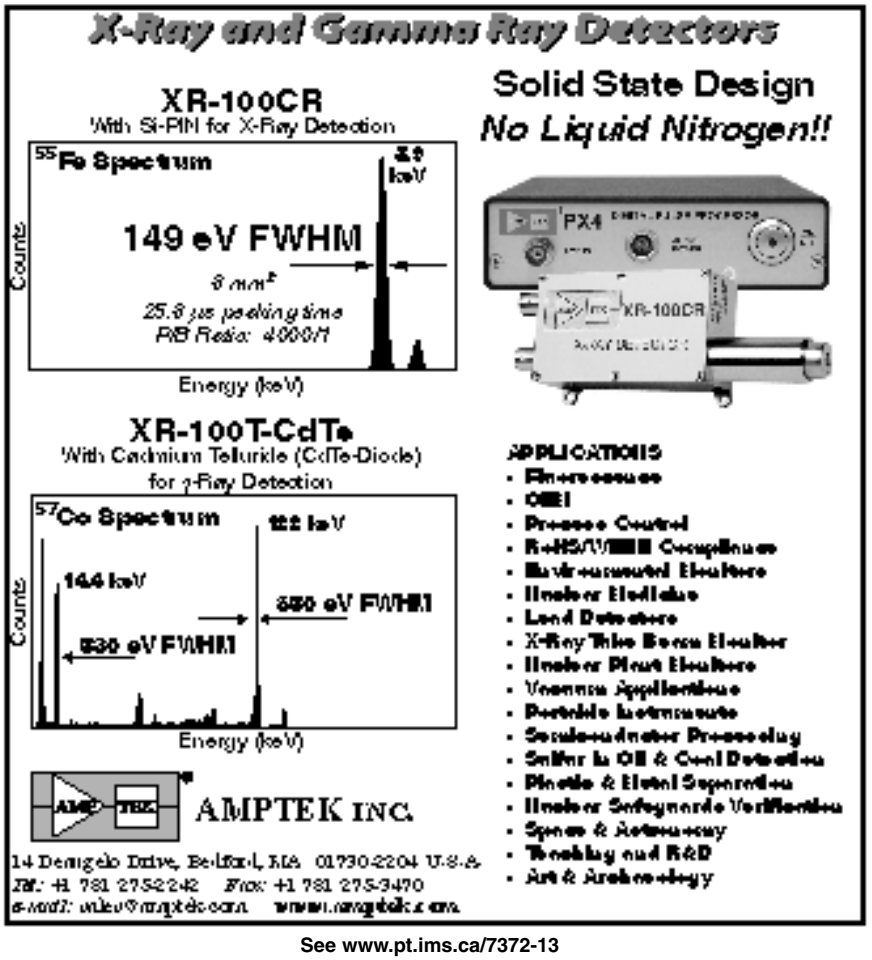
But there's another source of energy: heat. Molecular motors, like other proteins, are in a state of constant thermal fluctuation. In the case of RNAP, those fluctuations can, in principle, encompass the motor's current, previous, and subsequent positions along its DNA track. If chemical energy is added at the right moment to hold the motor in its forward position, the motor will advance in one direction like a ratchet.

To determine whether RNAP operates as a power stroke or a ratchet, the Stanford researchers varied both the force that helps pull RNAP along and the concentration of free-floating bases. Increasing the assisting force will always ease a ratchet's advance. By contrast, a power stroke will accelerate only if its fuel delivery rate can keep up. RNAP, it turns out, is more like a ratchet.

Charles Day

References

1. E. A. Abbondanzieri et al., *Nature* **438**, 460 (2005).
2. J. W. Shaevitz, E. A. Abbondanzieri, R. Landick, S. M. Block, *Nature* **426**, 684 (2003).
3. W. J. Greenleaf, M. T. Woodside, E. A. Abbondanzieri, S. M. Block, *Phys. Rev. Lett.* **95**, 208102 (2005). ■



See www.pt.ims.ca/7372-13