Closing the loop on the end of a chromosome

Photographs that reveal unsuspected genetic lariats at the ends of chromosomes have added a scientific spin to an old cliché. A picture can be worth a thousand experiments.

One of the hottest topics in biology, telomeres are stretches of repetitive DNA at the ends of chromosomes (SN: 11/25/95, p. 362). Telomeres prevent chromosome ends from sticking to each other and may play crucial roles in aging and cancer. They also somehow help cells avoid treating a normal chromosome tip as evidence of a broken chromosome. Such breaks normally prompt a cell to launch DNA-repair efforts or commit suicide.

Scientists had thought that telomeres consist of a linear DNA molecule, with one of the DNA's usually paired strands slightly longer than the other. This telomeric overhang posed a dilemma. Cells don't tolerate single-stranded DNA.

Some microscopic creatures called ciliates have proteins that bind to their telomeric overhangs and mask them. Yet attempts to find similar proteins in mammals, which have much longer overhangs, have so far proved fruitless.

During such searches, Titia de Lange of the Rockefeller University in New York and her colleagues did identify two proteins, TRF1 and TRF2, that bind to the double-stranded portion of mammalian telomeres. The scientists then joined forces with Jack D. Griffith of the University of North Carolina at Chapel Hill, who heads a research group that studies DNA-protein interactions.

The investigators synthesized telomeric DNA and mixed it with TRF1 or TRF2. Viewed under an electron microscope, telomeres exposed to TRF2 often displayed large circles, which the researchers named t loops, but no single-stranded ends. The overhang somehow had integrated itself into the double-stranded part of the telomere, they concluded. Telomeres isolated from mouse and human cells had the same loops, the scientists report in the May 14 CELL.

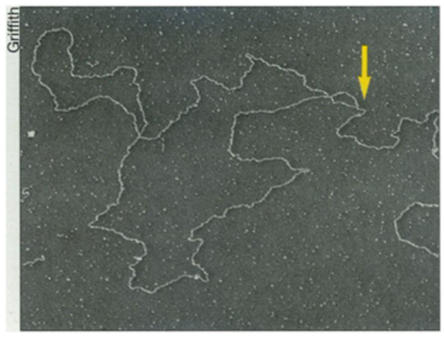
Cells lacking TRF2 activate DNA-repair machinery and sometimes even commit suicide, suggesting that telomeres require TRF2 to form loops, says de Lange. Such cells, as expected, seem to interpret unlooped telomeres as damaged DNA.

Why haven't biologists observed t loops before? Telomeres are only a small portion of a chromosome's DNA. "Unless someone had been looking for [a loop], it would be easy to miss," says Griffith.

Future studies will explore how t loops form and what tricks other organisms employ to mask telomeric overhangs. "It may be that each creature has come up with its own solution," speculates Griffith.

Some researchers suspect that the wear and tear of aging results, in part, from telomeres dwindling. "Perhaps as a part of aging, a few telomeres get so short that they can no longer form t loops," says Jerry W. Shay of the University of Texas Southwestern Medical Center at Dallas.

Since t loops seem to hide the tips of telomeres, scientists now wonder how the enzyme called telomerase acts on telomeres' ends to maintain or extend their length. "The discovery of t loops solves some long-standing problems, makes others moot, and raises some new ones," notes Carol W. Greider of Johns Hopkins Medical Institutions in Baltimore in a commentary in CELL. —*J. Travis*



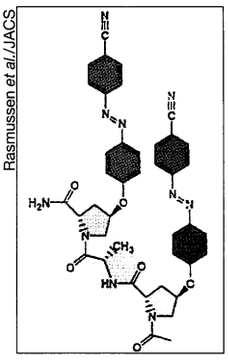
This telomere forms a large loop (left of arrow) that crisscrosses itself.

Peptide packs in holographic data

Holography can do more than make pretty pictures. It can cram thousands of pages of information into a tiny volume of light-sensitive material, a storage density that far surpasses the capacity of traditional computer drives and CD-ROMs.

Now, researchers have improved one such material so that it records holographic data encoded in light-interference patterns in less than 1 second. This is 350 times the recording speed of earlier versions of the material.

Rolf H. Berg, Søren Hvilsted, and P.S. Ramanujam of the Risø National Laboratory in Roskilde, Denmark, first designed such compounds 3 years ago. They consist of short protein molecules, or peptides, with azobenzene dye molecules attached.



Films of a two-unit peptide made up of copies of the dye azobenzene (orange) attached to proline amino acids (blue) can be used as a medium for storing data holographically.

The original azobenzene peptides appeared promising, but "one of the major drawbacks was the response time," says Bernard Kippelen of the University of Arizona's Optical Sciences Center in Tucson. It took several minutes for films of the peptides to record a hologram—too slow for practical applications.

A new version of the peptide synthesized by Palle H. Rasmussen of Risø and the original group has azobenzene attached to the amino acid proline. That amino acid gives the peptide a more rigid polymer backbone, which allows the dye molecules to react to light in a more coordinated way, says Berg. This improves the speed at which the material records and reads out information.

The team reported its findings May 11 in the online version of the JOURNAL OF THE AMERICAN CHEMICAL SOCIETY.

Conventional magnetic disks store data in bits on the surface. In holograms, however, blocks of information are distributed throughout the material's volume (SN: 8/20/94, p. 127).

Because a page of data is recorded like a single snapshot, it can be read all at once. "This gives an extremely fast data rate—as much as 1 gigabit per second," says Glenn T. Sincerbox, director of Arizona's Optical Data Storage Center. In contrast, information on a magnetic disk is retrieved bit by bit by spinning the disk. "The only ways to get higher data rates are to spin it faster or put the bits closer together," he explains.

Although azobenzene peptides are among several promising potential holographic materials, many issues must be resolved before they can become practical for data storage. The film would have to be at least 1 millimeter thick to store the desired amount of data. So far, the researchers have tested only 13-micrometer-thick films. The Risø group's peptide can store 25 megabits of data in 1 square millimeter.

Also, the team used a green laser to record data and a red beam to retrieve them because the color difference protects information from corruption during readout. A practical, compact device would have to operate with a single wavelength of light. Kippelen says that his group is studying other types of light-sensitive polymers to find ways to accomplish this. "Some of these concepts could be extended to peptidelike materials," he notes.

Holographic storage will have to progress quickly to compete with existing technologies. "Traditional magnetic storage is advancing so fast that the window for holography is shrinking," says Kippelen. However, Sincerbox says that holographic storage applications might make their debut within a year. —*C. Wu*