sive dissociation, an absorbing layer that removes the kinetic energy of the ion, no charge transfer, and no chemisorption that could lead to dissociation. The group at Purdue has reached this goal in a remarkable way (*2*): The ion energy is kept low, which is experimentally very tedious, and to avoid chemisorption, the ions are trapped in a fluorocarbon self-assembled monolayer (F-SAM) on an Au substrate. To make sure that the molecules are stopped without hitting the substrate, bulky groups at the end of the molecules act as parachutes (see figure). The F-SAM monolayers have been demonstrated to be remarkably inert. Only when a molecule is locked between the molecules of the F-SAM is it trapped. No molecular deformation and no charge transfer occur. This combination makes it possible to softly land molecules intact at a surface. It is remarkable that the molecule retains even its charge in the layer. The only price one has to pay is that only molecules that are properly oriented can penetrate the chains of the F-SAM. This technique may indeed allow for an entirely novel way of storing information at the nanoscopic level.

References and Notes

1. J. F. VanDerVeen, *Surf. Sci. Rep.* **5**, 199 (1985).
2. S. Miller *et al.*, *Science* **275**, 1447 (1997).
3. B. L. Bentz and W. Odom, Eds., *Int. J. Mass Spectrom. Ion Processes* **143**, 1 (1995).
4. A. W. Kleyn and T. C. M. Horn, *Phys. Rep.* **199**, 191 (1991).
5. W. Heiland, in *Low Energy Ion-Surface Interactions*, J. W. Rabalais, Ed. (Wiley, Chichester, UK, 1994), pp. 313–354.
6. R. G. Cooks, T. Ast, T. Pradeep, V. H. Wysocki, *Acc. Chem. Res.* **27**, 314 (1994).
7. K. Bromann *et al.*, *Science* **274**, 956 (1996).
8. H.-P. Cheng and U. Landman, *ibid.* **260**, 1304 (1993).
9. ———, *J. Phys. Chem.* **98**, 3527 (1994).
10. J. W. Weaver and G. D. Waddill, *Science* **251**, 1444 (1991).

11. The author thanks T. Weeding for her critical reading of the manuscript. This work is part of the research program of the Stichting voor Fundamenteel Onderzoek der Materie (FOM), which is financially supported by the Nederlandse Organisatie voor Wetenschappelijk Onderzoek (NWO).

CELL BIOLOGY

Unresolvable Endings: Defective Telomeres and Failed Separation

R. Scott Hawley

In chess games and mystery novels, the focus is always on the end. A similar captivation with endings has directed the attention of generations of geneticists and cytologists to the ends of chromosomes, the telomeres. The question has always been, Just how are telomeres special, and what are their functions? Two reports (*1*, *2*), one on page 1478 of this issue (*1*), suggest a surprising new significance of telomeres in the processes of meiotic and mitotic chromosome segregation. Both reports point to an unexpected conclusion: Although telomeres themselves may not mediate chromosome segregation, the separation of telomeres during cell division creates a special problem for the segregational system.

The discovery of the structure of DNA, together with our understanding of how DNA replicates during the production of daughter cells, pointed to the first clear function for telomeres (*3*). Somehow, telomeres must facilitate the replication of the ends of the DNA molecule such that the chromosome does not shorten with each round of replication. Recall that DNA polymerase can only move in one direction (5′ to 3′). Thus, once the RNA primer on the leading strand at the end is removed, there is no way to "back-fill" the missing base pairs. Left unaltered, the next replication event will result in a daughter chromatid that has been shortened by a few base pairs (*4*).

Telomeres exist in at least two general forms, each of which appears to solve the problem of replicating chromosome ends in a different manner. In most organisms the telomere consists of tandemly repeated copies of a G-rich simple repeat sequence (for example, TTGGGG in *Tetrahymena thermophila*). The ends of the chromosome are prevented from shortening at each replication by the ability of an enzyme, called telomerase, to synthesize more such repeats at each end (*3*). This de novo synthesis of new telomeric repeats is mediated by a corresponding RNA template within the telomerase holoenzyme.

Curiously, *Drosophila melanogaster*, the organism in which telomeres were first discovered, possesses a very noncanonical telo-

The author is in the Department of Genetics, Section of Molecular and Cellular Biology, University of California at Davis, Davis, CA 95616, USA. E-mail: shawley@netcom.com

WEBWATCH

Electronic eruptions

http://volcano.und.nodak.edu/

At any one moment, dozens of volcanoes are active around the world. Volcano World is a prototype Web site supported by NASA to provide remote sensing data on volcanoes to a wide group of users. Data from a variety of sources are available, along with updates on currently active volcanoes, images of eruptions, and maps of volcanic regions. Educational material is the primary offering, with opportunities to learn how volcanoes work and submit questions to the volcanologists on the Web team. Links are also provided to the top volcano observatories and research centers.

Population ecology

http://www.gypsymoth.ento.vt.edu/~sharov/popechome/welcome.html

Groups of organisms that interact give rise to complex dynamical structures, and this is the domain of population ecology. Drawing together many resources, this site at Virginia Polytechnic Institute offers paths to computational models, journals, and online research papers. Extensive links to large data sets useful in ecological modeling are available, along with pointers to important simulations such as SmartForest at the University of Illinois. Links to related areas such as pest management and mathematics are also listed.

Material matters

http://vims.ncsu.edu/cgi/index.acgi

Hypertext is ideal for online textbooks. One of the best in materials science is ViMS, short for Visualizations in Materials Science, created at North Carolina State University. The site is a highly polished presentation of the syllabus of NCSU's introductory materials science course and is supplemented by more than 700 megabytes of downloadable movies, computer graphics, and simulations. Exercises for the student are available in Adobe PDF format and the contents of the site are available on CD-ROM.

Edited by David Voss

Readers are invited to suggest excellent scientific Web sites by e-mail to editors@aaas.org.

mere. *Drosophila* appears to have solved the problem of ending its chromosomes by co-opting transposons, pieces of DNA that can move around the genome (5). These transposons, HeT-A and TART elements, are found in multiple copies at the end of each chromosome. Presumably, the gradual shortening of chromosomes that occurs at each cycle of replication in *Drosophila* is counteracted by the stochastic transposition of new transposon repeats to the ends. The current model for this telomeric transposition invokes a mechanism by which the RNA transposition intermediate is converted into end DNA by reverse transcriptase. As noted by Pardue (5), both mechanisms of telomere extension are similar in that telomerase is also a reverse transcriptase, and thus in both cases ends are extended by copying from an RNA template.

An enhanced version of this Perspective, with live links, can be seen in *Science* Online on the Web at http://www.sciencemag.org/

Beyond their role in replication, telomeres have also been proposed to participate in meiotic pairing, in meiotic and mitotic chromosome segregation, and in the organi-

UPDATE: CHEMISTRY

Biological Nitrogen Fixation and Model Chemistry

G. J. Leigh

Nitrogenases are well known as the enzymes that biological systems such as plants and bacteria use to process N_2, yet the mechanism of their action continues to be a puzzle. In a previous Perspective (*1*), I discussed the finding that a mononuclear metal complex could split the unreactive N_2 molecule under mild conditions to give a nitrido complex (*2*) but speculated that this had no direct relevance to the way that nitrogenases fix nitrogen. Nevertheless, the discovery showed a kind of reactivity of N_2 with coordination compounds that was unexpected, if not completely unprecedented with species such as metal surfaces.

The chemistry of N_2 complexes effectively began about 30 years ago, principally with mononuclear complexes, and proceeded with the general belief (*3*) that these molecules would show us the kind of chemistry that must be used by nitrogenases. This chemistry is still the best-explored area of N_2 reactivity, although there has been a steady trickle of generally unrelated and often accidental discoveries suggesting that the protonation of N_2 in mononuclear molybdenum complexes may not represent the only reaction pathway available to nitrogenases.

The establishment of the structures of two molybdenum nitrogenases with the unusual iron-molybdenum clusters apparently containing the site of N_2 reduction (*4*) left us with the problem of identifying exactly what it might be. It is still quite feasible that mononuclear chemistry does indeed provide the key to nitrogenase reactivity, but the reports by Shan *et al.* on page 1460 (*5*) and Fryzuk *et al.* on page 1445 (*6*) in this issue open the question even wider.

Although there is disagreement as to whether the nitrogenase cluster can or cannot accommodate a N_2 molecule (*7*), this has not prevented speculations that place N_2 inside the cluster, on the surface of the cluster, or even partly inside and partly outside. Now Shan *et al.* (*5*) show us that N_2 molecules can be accommodated by six gold atoms that constitute a kind of cage. This kind of binding has little precedent in nitrogen chemistry other than a single example of a disamarium-tetralithium cage (*8*). The cluster assembles spontaneously from two trinuclear gold species and hydrazine (not N_2), and it decomposes in acids with partial or complete protonation of the N_2, depending on the supporting phosphine.

Whether the nitrogenase cluster can allow a N_2 molecule to enter it and then to be protonated inside is still a completely open question. The N-N separation in the new cluster is 1.457(14) Å (numbers in parentheses indicate error in the last digits), which should denote a single bond, and the Au-Au separations across the opposing triangles of gold atoms are greater than 3.6 Å, probably nonbonding distances. Apparently the N_2 holds the whole hexanuclear gold assemblage together. Might it not be described better as two trinuclear clusters bridged by N_2? In the nitrogenase clusters, the corresponding Fe-Fe separations, supported by bridging sulfide ions, are about 2.5 Å, and direct Fe-Fe interaction is not excluded (*4*).

The report by Fryzuk *et al.* (*6*) suggests a hitherto unrecognized possibility for nitrogenase reactivity. It has long been a mystery why all nitrogenases are apparently such prolific hydrogenases. Even in the best circumstances, they "waste" about 25% of their expensive reducing electrons as H_2. The usual rationalization is that N_2 displaces H_2 when it binds to the active site, although why that displacement should be necessary is not obvious (*9*). To date, coordinated N_2 has been shown to react with electrophiles, principally the proton, and with organic radicals (*3*). Now side-on bridging N_2 in a dinuclear zirconium complex has been shown to react with silanes and dihydrogen.

It might be argued that the final attack on the coordinated N_2 generating the coordinated N_2H is indeed electrophilic, but that is not really the point. Here we have a new class of reactions of N_2, and one that would appear to be feasible in nitrogenases and, superficially at least, analogous to the Haber process reactions used in the industrial processing of dinitrogen.

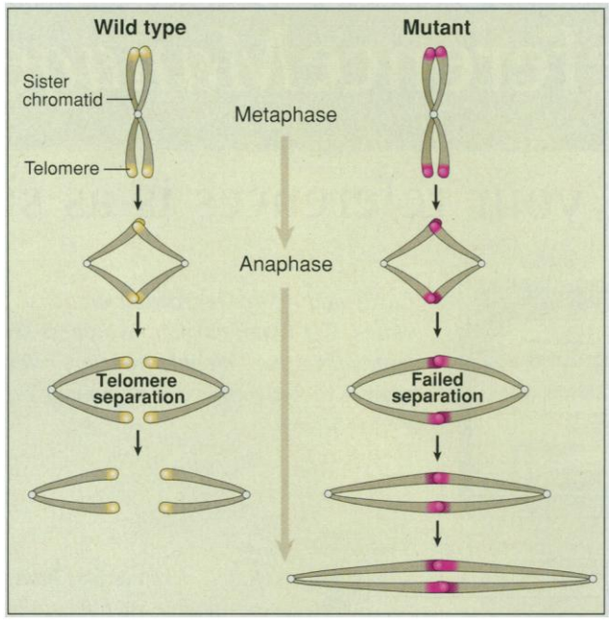
Rather than clarifying the reaction modes of nitrogenase, these reports add to the list of possibilities. Nitrogenase does indeed move in mysterious ways, and possibly in ways that we cannot yet imagine.

The author is at the School of Chemistry, Physics, and Environmental Science, University of Sussex, Brighton BN1 9QJ, UK. E-mail: g.j.leigh@sussex.ac.uk

References

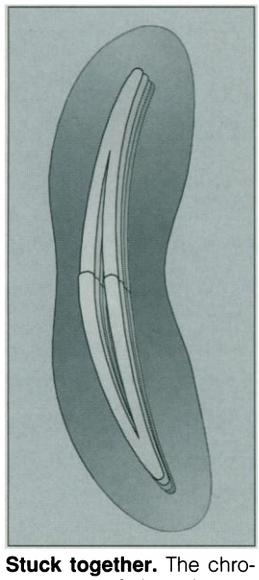
1. G. J. Leigh, *Science* **268**, 827 (1995).
2. C. E. Laplaza and C. C. Cummins, *ibid.*, p. 861.
3. See, for example, R. A. Henderson, G. J. Leigh, C. J. Pickett, *Adv. Inorg. Chem. Radiochem.* **27**, 197 (1983).
4. M. K. Chan, J. Kim, D. C. Rees, *Science* **260**, 792 (1993); J. T. Bolin *et al.*, in *New Horizons in Nitrogen Fixation*, R. Palacios, J. Mora, W. E. Newton, Eds. (Kluwer, Dordrecht, 1993), p. 89.
5. H. Shan, Y. Yang, A. J. James, P. R. Sharp, *Science* **275**, 1460 (1997).
6. M. D. Fryzuk, J. B. Love, S. J. Rettig, V. G. Young, *ibid.*, p. 1445.
7. J. Christiansen, R. C. Titsworth, B. J. Hales, S. P. Cramer, *J. Am. Chem. Soc.* **117**, 10017 (1995); K. K. Stavrev and M. C. Zerner, *Chem. Eur. J.* **2**, 83 (1996).
8. J. Jubb and S. Gambarotta, *J. Am. Chem. Soc.* **116**, 4477 (1994).
9. G. J. Leigh, *Eur. J. Biochem.* **229**,14 (1995).

zation of the nuclear architecture. But in fact telomeres are not needed for replication: Ring chromosomes, which have no telomeres because the DNA molecule exists as a closed circle, can recombine with circular and linear homologs, are transmitted normally, and support gene expression appropriately. Moreover, elegant studies in *Drosophila* have clearly shown that linear, telomere-deficient chromosomes can be transmitted both in meiosis and mitosis, albeit with shortening at each generation (*6*). Similar findings have also been reported for the mitotic chromosome transmission of telomere-deficient chromosomes in the budding yeast (*7*): Many cells were capable of replicating and segregating a telomere-deficient yeast chromosome for as many as 10 divisions before the eventual loss of that chromosome. Because these "endless" chromosomes seemed to pair, recombine, segregate, and express their genes normally, whatever special functions telomeres possessed beyond replication are not essential for these processes. So, do telomeres participate in segregation beyond replicating the ends of the DNA molecule?



Separation anxiety. With a mutation in the RNA template of telomerase that causes errors in the telomere sequences, *Tetrahymena* sister chromatids cannot separate effectively at mitotic anaphase.

The report in this issue by Kirk *et al.* (*1*) provides the first evidence that a telomere defect can impair mitotic chromosome segregation. These authors have shown that altering the telomerase RNA template in *Tetrahymena* can create a block in anaphase chromosome separation in the germ line. Detailed cytological analysis of nuclei in which the altered RNA template had presumably directed the corresponding change in telomere DNA sequence revealed a failure of telomere separation of sister chromatids at anaphase. The chromatids with altered telomeres did not appear to separate from each other even in late anaphase, but rather the stretched chromosomes were often seen as one continuous fiber passing through the midzone of the spindle (see figures). In some instances, the chromosome stretched to twice the length of a separated chromatid. The authors conclude that wild-type telomeres are normally associated on sister chromatids until metaphase and that the defective telomeres prevent a critical process in telomere separation. Thus, a specific element of the telomere repeat is required in cis to either mediate chromatid separation or to prevent persistent associations.



Stuck together. The chromosomes of the micronuclei of *Tetrahymena* become stretched when the telomeres are defective.

That specific proteins are also required in trans to mediate chromatid separation is suggested by the work of Cenci *et al.* (*2*). These authors demonstrate that in *Drosophila*, the organism with the noncanonical telomere, mutations in the UbcD1 gene also impede or prevent telomere separation at metaphase and even anaphase. The UbcD1 gene encodes a *Drosophila* ubiquitin-conjugating enzyme. In contrast to the *Tetrahymena* mutants studied by Kirk *et al.*, flies that carry mutations in the UbcD1 gene have telomeres that associate inappropriately with the telomeres of their sister chromatids and with the telomeres of both homologous and nonhomologous chromosomes. In a few instances, most of the *Drosophila* chromosome complement was observed to be linked end-to-end as a huge polycentric chromosome. Thus, the problem of resolving persistent telomere associations is not limited to sister telomeres, but may include telomeres of nonhomologous or homologous chromosomes as well.

Although this problem of nonsister telomere associations may be most acute in organisms like *Drosophila*, where intimate somatic pairing is the rule rather than the exception, the clustering of telomeres at one point in the nucleus has been observed in a variety of organisms (*8*). The mechanisms that resolve these telomeric associations may differ even within an organism. Cenci *et al.* (*2*) noted that metaphase telomere linkages and anaphase bridges seen in UbcD1 mutant cells are often resolved before the end of anaphase in mitotic cells, whereas in male meiotic cells they are apparently often unresolvable, leading to chromosome bridging and subsequent breakage. Thus, this study, like that of Kirk *et al.* (*1*), indicates that a specific function is required to mediate telomere separation. But in this case the defect is not due to an altered DNA sequence acting in cis, but to an absence of the UbcD1 ubiquitin-conjugating enzyme, which presumably acts in trans.

The common theme in both studies—that specific functions are required for telomere separation or to prevent telomere association—is all the more interesting because *Drosophila* has such noncanonical telomere whereas *Tetrahymena* has defined the canonical telomere. Kirk *et al.* (*1*) also record the existence of mutants in *Schizosaccharomyces pombe* that produce phenotypes similar to those observed in the mutant *Tetrahymena* cells, but which appear to define genes encoding trans-acting proteins (*9*). The requirement for a special function to control telomere association and separation may well be a general one. In this sense, the construction of telomeres created a solution to the problem of DNA replication, while creating a problem for chromatid and chromosome separation. The solution to that problem appears to require both the telomeric DNA sequences themselves and the proteins acting at the telomere.

References

1. K. E. Kirk, B. P. Harmon, I. K. Reichardt, J. W. Sedat, E. H. Blackburn, *Science* **275**, 1478 (1997).
2. G. Cenci *et al.*, *Genes Dev.*, in press.
3. E. H. Blackburn and C. W. Greider, Eds., *Telomeres* (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1996).
4. J. D. Watson, *Nature* **239**, 197 (1972).
5. M.-L. Pardue, in (*3*), pp. 339–370.
6. J. M. Mason, E. Strobel, M. M. Green, *Proc. Natl. Acad Sci. U.S.A.* **81**, 6090 (1984); H. Biessmann and J. M. Mason, *EMBO J.* **7**, 1081 (1988); H. Biessmann, S. B. Carter, J. M. Mason, *Proc. Natl. Acad Sci. U.S.A.* **87**, 1758 (1990).
7. L. L. Sandell and V. A. Zakian, *Cell* **75**, 729 (1993).
8. A. F. Dernburg, J. W. Sedat, W. Z. Cande, H. W. Bass, in (*3*), pp. 295–338.
9. H. Funabiki, I. Hagan, S. Uzawa, M. Yanagida, *J. Cell Biol.* **121**, 961 (1993); H. Funabiki *et al.*, *Nature* **381**, 438 (1966); T. Hirano, S.-I. Funahashi, T. Uemura, M. Yanagida, *EMBO J.* **5**, 2973 (1986).
10. I thank A. H. Dernburg and K. E. Koehler for helpful comments on the manuscript.