duschek of the University of California, San Diego, describes the achievement as "extraordinary." Not only does it give cell biologists their first clear view of yeast pol II in action, but it also opens the door to seeing exactly how the enzyme interacts with the many other proteins that regulate its activity. And that, adds Geiduschek, will "transform the analysis of transcription and transcription mechanisms in a fundamental way."

Kornberg and his colleagues have been on the path to the pol II structure for nearly 20 years. The first 10, he recalls, were devoted to isolating the myriad proteins involved in gene transcription. During that time, his team and others found that the pol II machinery of higher organisms is very large. The enzyme alone contains 12 different proteins bound together in a complex that has a molecular weight of about 500,000.

That, combined with the fact that the enzyme is present in cells in very low concentrations, meant that determining the enzyme's three-dimensional structure by x-ray crystallography would be extremely difficult. But by early last year, the Kornberg team, including postdocs Patrick Cramer and Averell Gnatt, the lead authors on the current papers, had determined the structure of a complex containing 10 of the enzyme's 12 proteins to a resolution of about 3.5 angstroms—good enough to see the backbones of the protein chains but not of the side chains of the individual amino acids (*Science*, 28 April 2000, p. 640). (The other two proteins, which aren't needed for RNA elongation, kept pol II from crystallizing.)

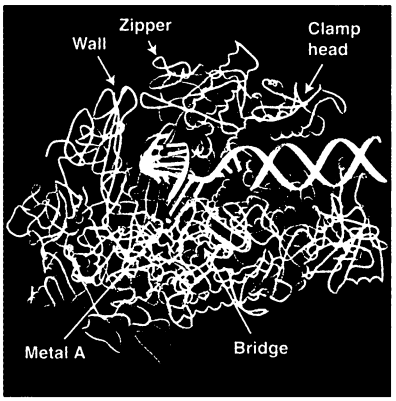
In the current work, the team has solved the pol II structure to a resolution of 2.8 angstroms. Now, Cramer says, "we can see where every amino acid goes." The new structure largely confirms what the earlier one had suggested. For example, the enzyme has a pair of "jaws" that enable it to attach to the DNA to be copied. And because the growing RNA chain is enclosed within pol II's active site, the bottom of the enzyme has a large pore through which the nucleotide building blocks of RNA can enter.

These features are quite similar to those seen in the only other multisubunit RNA polymerase whose structure has been determined, the enzyme from the bacterium *Thermus aquaticus*. Seth Darst, a former Kornberg postdoc now at New York City's Rockefeller University, and his colleagues solved that structure. And even though the bacterial enzyme is less complicated than yeast pol II, having just five subunits rather than 12, Darst says, "the central cores of the structures are identical. ... These enzymes are highly conserved." However, they vary around the periphery, which carries important contact points for regulatory proteins. Researchers will now be able to see those of the yeast enzyme clearly.

And the structure of human pol II should be very similar. Kornberg notes that 53% of the amino acids in the yeast and human enzymes are the same and that the identical amino acids are distributed similarly throughout the proteins of the two enzymes. "To all intents and purposes, the structures are the same," Kornberg says.

Once they had nailed down pol II itself, Kornberg's team was able to take the next step: solving the structure of the enzyme in a complex with DNA and an elongating piece of RNA. The researchers couldn't have done that with last year's lower resolution structure, Cramer says. But with the new one, "the elongation complex [structure] just pops out."

Among other things, that structure provides an answer to a long-standing puzzle in gene transcription. When pol II transcribes a gene, it has to latch onto the DNA and then move long distances—sometimes millions of nucleotides—without falling off. But when it reaches the end of the gene, it needs to let go. What this second structure shows, Kornberg says, is that one segment of the enzyme forms a "clamp," which is open in the free enzyme but swings shut once RNA synthesis begins and the active site contains a DNA-RNA hybrid. RNA synthesis stops at the gene's termination site, however, and with no hybrid there, the clamp swings open, releasing the enzyme.



In the loop. The pol II "clamp" (orange) holds onto the DNA while it's being transcribed into RNA (red).

CREDIT: A. L. GNATT *ET AL.*

Although researchers are thrilled by the new work, Geiduschek and others point out that "this is really more of a beginning, rather than an end, to the story." The next big step is solving the structure of pol II complexed to the many transcription factors and other proteins that regulate gene transcription. Then, "people can really begin to understand how those factors interact with the polymerase. That will have a huge impact on the field," says Robert Landick of the University of Wisconsin, Madison.

ScienceScope

Dioxin Dilemma The Environmental Protection Agency (EPA) is facing a tough decision over whether to back away from calling dioxin a human carcinogen. In a 13 March draft summary to EPA chief Christine Whitman, a subpanel of EPA's Scientific Advisory Board approved a long-debated draft report that includes the classification (*Science*, 10 November, p. 1071). But the group slammed some of the agency's conclusions. In particular, "most" members of the 21-person panel disagreed with the label.

EPA scientists are hoping for a stronger endorsement from the full science board, due to meet next month. And they vow to resist pressure from industry to downgrade dioxin's dangers. "We're sticking by our guns," says one, noting that the National Institutes of Health and other bodies agree that dioxin causes cancer. But some observers—including *The Washington Post* last week—say Whitman may put the report on ice and order more study.

IT Anyone? It's spring in Canada, and multimillion-dollar national science initiatives are popping up like crocuses. The latest to bloom is a $325 million, 5-year proposal from industry to rejuvenate university information technology departments through research in microelectronics, photonics, and other fields. The initiative, which would be run by a nonprofit entity dubbed eMPOWR Canada, hopes to follow the path taken by a national genomics initiative (*Science*, 13 April, p. 186). Although advocates say it would triple the estimated 350 faculty members in the field, produce skilled workers, and lead to marketable products, the proposal is only one of several that the government is being asked to weigh to bolster academic research.

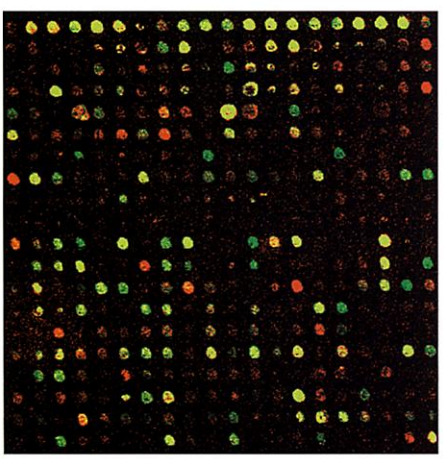
Get-Out-of-Jail-Free Card Geologist Martin Pickford may no longer have to worry about being thrown into a Nairobi jail. Last year, Pickford, a geologist at the Collège de France in Paris who studies human evolution, was arrested by Kenyan authorities and imprisoned for 5 days on charges of fossil hunting without a permit. The charges are linked to a paleontology turf war between Pickford's research group and rivals (*Science*, 13 April, p. 198).

Pickford insists that he had a valid permit, and the charges weren't prosecuted. But just to be safe, the Community Museums of Kenya (CMK)—which sponsors Pickford—has procured him a new license that is good for the entire country through April 2004. Addy Kaaria, head of Kenya's permitting department, confirms that Pickford can now work "with no problem."

labs. But right now there is no standard format for transferring microarray data between scientists and no rules for how a microarray experiment should be described in a publication. In 1999 a group of bioinformaticists and biologists met in Cambridge, U.K., and formed five working groups to tackle the problem. Last month, at the third such meeting,* two of those groups announced that they are close to submitting recommendations on defining what data should be recorded and the format for transferring and archiving them. "It now has a momentum of its own," says Alvis Brazma of the European Bioinformatics Institute, who convened the first meeting and has seen attendance more than triple, to 300 participants.

The Minimal Information About a Microarray Experiment (MIAME) working group presented a final draft of a document that defines how to describe not only the gene expression data, but also the sample and experimental conditions under which the data were collected. The working group hopes to submit the MIAME document for publication in the next 2 to 3 months in what Brazma calls "MIAME version 1.0."

A second challenge involves creating a tagged-text computer format for transferring and archiving microarray data. One proposal comes from a working group led by Paul Spellman of the University of California, Berkeley. Two biotech firms have also individually crafted proposals for a software standard: microarray developer Rosetta Inpharmatics Inc. of Kirkland, Washington, and NetGenics Inc., a bioinformatics software company in Cleveland, Ohio. The three have agreed to submit a revised consensus proposal to a software standards organization by 18 June. "People are putting aside their egos" in the quest for a single standard, says Doug Bassett, senior director of biosoftware products and services for Rosetta.



Seeing spots. Standards would help scientists share and interpret microarray data.

It will then be up to journal editors to enforce the standards. Brazma hopes that eventually authors will be required to deposit data in a public database—but not until it's clear to everyone that the standards capture the right information and don't present a burden to researchers submitting the data, he and others say. Establishing standards is "something everyone realizes needs to happen," says Mike Cherry of Stanford University, who organized this year's meeting, "There'll be a lot of complaints if it's not done well." –R. JOHN DAVENPORT

* The Third International Meeting on Microarray Data Standards, Annotations, Ontologies, and Databases, 29–31 March, Stanford University, Palo Alto, California (www.mged.org).

STEM CELLS

NIH Pulls Plug on Ethics Review

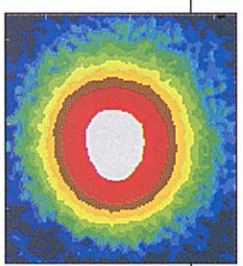
Advocates for research with human embryonic stem (ES) cells are worried by the latest twist in the cells' political story. Last week the National Institutes of Health cancelled its planned meeting of the panel that is supposed to determine whether a given stem cell line complies with NIH's ethical guidelines (*Science*, 6 April, p. 27). Because the NIH can't fund projects until their cell lines have been approved by the panel, the cancellation delays indefinitely federal funding of human ES cell research.

ES cells have the potential to develop into any cell type in the body, and many scientists would like to discover how to use them to treat intractable diseases such as diabetes or Parkinson's. However, the work is controversial because the cells are derived from week-old human embryos. Although a clause in the law that funds NIH prevents the agency from funding research that would harm or destroy an embryo, a lawyer at the Department of Health and Human Services (HHS) ruled in 1999 that because ES cells—which can grow ad infinitum in culture—are not themselves embryos, the NIH could fund work with cells that were derived by privately funded researchers or researchers overseas. The Bush Administration is reviewing that ruling.

Meanwhile, the Human Pluripotent Stem Cell Review Group was to meet on 25 April to review at least one cell line, derived with private funds by Australian researchers Martin Pera and Alan Trounson and their colleagues. However, NIH said last week that the meeting had been cancelled. "The [HHS] department told us inasmuch as they're conducting a review, it was premature for the review group to meet to assess compliance" with the guidelines, said NIH spokesperson Anne Thomas.

ScienceScope

Life Sentence X-ray astronomers are cheering a decision to give BeppoSAX, an Italian-Dutch x-ray satellite, a new lease on life. The Italian space agency ASI last week extended operation of the spacecraft, which was due to die at the end of the month, to 1 May 2002. The reprieve is "just marvelous," says astronomer Stan Woosley of the University of California, Santa Cruz.



BeppoSAX, launched 5 years ago, hit the headlines in 1997 when its wide-field x-ray cameras enabled astronomers to pin down gamma ray bursts (right), the most violent explosions in the universe (*Science*, 23 May 1997, p. 1194). Keeping it alive gives astronomers access to two gamma ray trackers, as NASA launched its HETE-2 orbiter last year.

BeppoSAX is down to just one working navigational gyroscope, but even if it fails officials expect the craft to remain operable due to an upcoming software fix. And if BeppoSAX stays healthy, its mission could be prolonged even further.

How Big? Would a larger, longer grant improve the quality of YOUR research? Principal investigators and their institutions will be able to take a swing at that softball question this year as part of a survey designed to improve grants management at the National Science Foundation (NSF). The survey is intended to help the government "determine the 'right' grant size for the various types of research [NSF] funds," according to the president's recent 2002 budget request to Congress.

NSF officials hope it also will lead to double-digit budget increases in 2003 and beyond. NSF director Rita Colwell has already calculated that National Institutes of Health–sized awards would require a doubled budget, but White House officials have complained that such calculations are based on anecdotal rather than hard evidence.

The community stands ready to pitch in. At last week's NSF budget briefing, Alan Kraut, executive director of the American Psychological Society, asked Colwell: "What can we do to help you convince [the White House]?"

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