tion in primates at the National Institute on Aging in Baltimore, says Guarente's idea is "consistent with what one might expect." Still, he cautions, "it's a big stretch to go from that observation in yeast to mammals."

When the Guarente team began its work, the researchers were investigating another theory about how Sir2 might silence DNA. Results from bacterial and mammalian proteins that resemble yeast Sir2 suggested that it might transfer part of NAD, containing the sugar ribose attached to the nucleotide adenosine diphosphate (ADP), to other proteins. They wanted to see if Sir2 would add the ADP-ribose to a synthetic histone segment, and it did. But when they further analyzed the reaction mixture, they got a surprise. Addition of ADP-ribose should increase the histone peptide's weight by 541 daltons. Instead, the researchers found a major product that weighed 42 daltons *less* than the original peptide. "That was an astounding thing," says Guarente. "It was getting smaller, not bigger."

Fortunately, Guarente knew his numbers: 42 is exactly the size of an acetyl group. "So we thought, 'Oh my goodness, it's deacetylating the peptide,' " he recalls. Other researchers hadn't been able to detect that reaction with Sir2 before, he postulated, because they hadn't added NAD. When he and his colleagues then repeated the experiments with and without NAD, they found that indeed, it is required for deacetylation by Sir2. They also showed that a related protein in the mouse performs a similar function, suggesting that Sir2 carries out the same reaction in mammals.

Although the work provides the first direct evidence that Sir2 can deacetylate, it does not prove that deacetylation is responsible for the protein's silencing activity. The problem is Sir2's ADP-ribosyl transferase activity. Last year, Danesh Moazed, a molecular biologist at Harvard University, and his colleagues showed that a particular mutation could obliterate both it and Sir2-mediated silencing. This raises the possibility that the transferase, rather than the deacetylase, is what's necessary for silencing. Guarente has shown, however, that the same mutation also curbs Sir2's ability to deacetylate histones, so it's not clear which activity is more important for silencing.

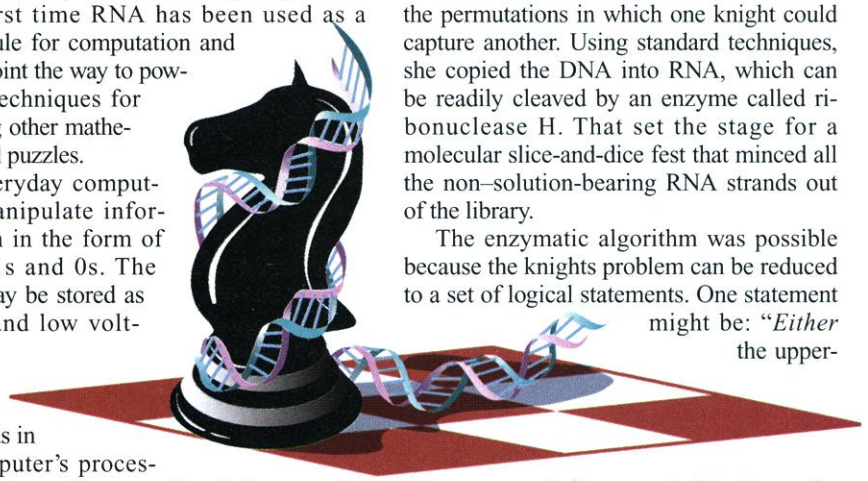
He and his colleagues tried to find out by creating a modified version of Sir2 that lacks most of its ADP-ribose transferase activity, but retains deacetylase activity. This protein performed many of the usual silencing feats, but the experiment wasn't conclusive because the protein was still a weak transferase. "I'm very excited about the new result," Moazed says. "But until we get mutations that cleanly separate the activities, the issue won't be settled." Either way, NAD seems to be involved and could thus serve as a biochemical link between Sir2-mediated silencing, caloric restriction, and aging. If so, Guarente's hypothesis may help us take a step toward living, well, happily ever after.

–EVELYN STRAUSS

MOLECULAR COMPUTING

RNA Works Out Knight Moves

Silicon upstarts aside, the best chess computers are biological—the brain of grand master Gary Kasparov, for example. Now a team of scientists at Princeton University has used a different sort of biological computer—beakers full of organic glop—to solve a chess problem. The feat, the most difficult problem ever solved by molecular computing, marks the first time RNA has been used as a molecule for computation and may point the way to powerful techniques for solving other mathematical puzzles.



Everyday computers manipulate information in the form of bits: 1s and 0s. The bits may be stored as high and low voltages (as in a computer's processor) or as north- or south-pointing magnetic fields (as in a hard drive). But they may also take more exotic forms. For example, the chemical bases that make up molecules of DNA and its cousin RNA are ideal for storing digital information. In 1994, computer scientist Leonard Adleman of the University of Southern California in Los Angeles showed that jugs of DNA could be turned into computers (*Science*, 11 November 1994, p. 1021). Since then, scientists have been using DNA to solve small mathematical problems such as adding two numbers together. Now, in the 15 February *Proceedings of the National Academy of Sciences*, evolutionary biologist Laura Landweber and her colleagues at Princeton University describe how they used RNA to solve the "knights problem" on a 3 × 3 chessboard: finding all the ways to place a collection of knight pieces (which move in an L-shaped pattern) so that no knight can attack another.

To solve this problem with a regular computer, you could start by assigning one bit to each of the nine squares on the board. Each bit represents whether a knight is sitting in that position (1) or if that position is empty (0). Then you could simply crank through all the possible combinations of 1s and 0s for the nine positions and eliminate the ones where knights are able to attack each other.

Landweber took a similar "brute force" approach. First, she synthesized 18 different stretches of DNA, each consisting of 15 base pairs. Each stretch represented a bit for a particular space—a "knight" or a "blank" for each of the nine positions on the board. (For instance, CTCTTACTCAATTCT meant that the upper left-hand corner is blank, while ACCTTACTTTCCATA meant there's a knight in the center square.) She then created a "library" of millions of DNA strands representing all possible configurations of the board—that is, every possible permutation of knights and blanks.

Landweber then methodically eliminated the permutations in which one knight could capture another. Using standard techniques, she copied the DNA into RNA, which can be readily cleaved by an enzyme called ribonuclease H. That set the stage for a molecular slice-and-dice fest that minced all the non–solution-bearing RNA strands out of the library.

The enzymatic algorithm was possible because the knights problem can be reduced to a set of logical statements. One statement might be: "*Either* the upper-left corner is blank, *or* the two squares that a knight threatens from that position must be blank." To satisfy that statement, Landweber split the library into two. Into one jug, she poured an enzyme that targeted the sequence that meant "there is a knight in the upper-left corner." To the other jug she added two enzymes that targeted the sequence that signaled the presence of a knight in the two threatened positions. After the broken fragments were all weeded out, neither jug contained an RNA strand that included sequences that had both a knight in the upper-left corner and a knight in one of the two squares threatened from that position.

Landweber then mixed the jugs together, converted the RNA back to DNA, amplified the DNA, and started all over again with another logical statement. After repeating the process for each logical statement that describes the knights process, she was left with a flask full of strands corresponding to every valid solution to the knights problem—plus a few rogues that escaped the cleaving enzymes by a fortuitous mutation. "We pulled out 42 correct solutions and one incorrect solution out of 43 clones that we tested,"

ILLUSTRATION BY C. CAIN

says Landweber.

"It is the world champion so far," says Adleman, who, along with other biochemists and computer scientists, is trying to make a molecular computer do a problem that a human can't do in a reasonable amount of time. "[Landweber] has got the inside track for trying to reach that milestone first."

To develop practical nucleic-acid computers, however, scientists will have to clear some major hurdles, such as figuring out how to correct errors and how to produce and handle large volumes of nucleic acid. Kasparov has no reason yet to feel threatened by beakers of glop, but Adleman is hopeful that nucleic-acid computers will be more than mere curiosities. "Here's nature's toolbox, a bunch of little tools that are dirt cheap; you can buy a DNA strand for 100 femtocents," he says. "Here's a great set of tools, we know they can do lots—let's build cool things!" **–CHARLES SEIFE**

SCIENTIFIC MISCONDUCT

Fired Researcher Is Rehired and Refired

A bitter and long-running dispute at the University of Arizona (UA) over the firing of a senior biomedical researcher for scientific misconduct has taken a strange new turn. On 4 February, UA president Peter Likins reinstated the researcher he had fired 19 months ago—former Regents Professor Marguerite Kay, an expert on the immune system and Alzheimer's disease. But, on the same day, Likins notified Kay that she was being dismissed again and he barred her from the campus, citing a policy that permits him to exile a faculty member whose presence is deemed "likely to constitute a substantial interference with the orderly functioning of the university. ..." Likins gave the same reasons as before: A faculty panel ruled in 1998 that Kay had engaged in scientific misconduct and neglected her duties as a professor (*Science*, 5 November 1999, p. 1076).

No reprieve. Marguerite Kay has been barred from the UA campus.

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This bizarre twist is the result of a judge's rulings last year that the university had acted in an "arbitrary and capricious" manner in firing Kay without a regular personnel hearing, and that she was wrongly denied full legal representation in a misconduct hearing. Likins informed Kay she had a right to appeal the redismissal, which would presumably trigger a personnel hearing.

Kay's supporters on the faculty were outraged by these moves. Two lawyers on the faculty senate immediately objected that Likins had violated Kay's rights and, thereby, the rights of all tenured faculty members. Attorneys Roy Spece Jr. and Andrew Silverman read a protest note during a senate meeting on 7 February in which they urged Likins to redo the entire investigation against Kay. The findings of misconduct against her, they argued, were rendered "null and void" by the court rulings. Judge Stephen Villarreal of the state court for Pima County found that the faculty-run hearing that investigated and condemned Kay's research in 1998 was deficient because Kay's attorney was not permitted to speak during the proceedings (*Science*, 26 November 1999, p. 1657). As a result, "the only proper way to proceed is to return to the very beginning and to do it right this time," said Spece and Silverman.

Likins clearly isn't interested in doing that. In a memo to department heads on 4 February, he noted that the court "did not make any determination regarding the substantive basis for the decision to dismiss Dr. Kay." And he said that the work of several faculty committees that investigated the case "will be respected." Likins declined to comment, according to university spokesperson Sharon Kha, because university rules forbid public discussion of personnel matters. Kha said she was limited to stating that Kay is once again on the faculty—nothing more.

Kay also could not be reached for comment. But her attorney in Tucson, Don Awerkamp, predicted that the decision not to redo the investigation from the top but to rely on the disputed misconduct investigation of 1998 will waste time and "cost hundreds of thousands of dollars more in litigation expenses."

On Kay's behalf, Awerkamp filed suit against the university in December, demanding $3 million for breach of contract. The suit also seeks additional damages for violation of Kay's rights to due process in job termination, and for pain and suffering and other harms. Included in the list of defendants are the university's board of regents, Likins, the chief counsel, the former research administrator, the oncologist who chaired the panel that investigated Kay, and two other faculty members who stepped for-

ScienceScope

Do It Again Expanding overcrowded labs and replacing aging equipment are likely to top the list of priorities in Japan's next 5-year science plan. This month a subgroup of the Council for Science and Technology, the nation's highest science advisory body, is finishing up reports on the nation's research needs, in anticipation of a formal request from the prime minister for a detailed plan covering the 5-year period beginning in April 2001.

Lab overcrowding has become "a big problem" as science funding has boomed, says Hiroo Imura, a former president of Kyoto University. Imura chairs the policy committee, whose panels also highlighted the need to attract more non-Japanese researchers and award more competitive grants.

The previous plan, Japan's first, included an ambitious 17 trillion yen ($162 billion) spending goal that the government achieved through a combination of regular and supplemental budgets. A sluggish economy may preclude repeating that sharp increase, says Hiroyuki Yoshikawa, a former University of Tokyo president and council member. But political support for science is so strong, he believes, that "even if the economy worsens, [budgets] won't decrease."

Quantum Leap The U.S. military plans to spend $15 million to nurture the fledgling field of quantum teleportation, which seeks to harness the bizarre behavior of atomic particles to process information at breathtaking speeds (*Science*, 23 October 1998, p. 637). The technique allows scientists to transfer a quantum-mechanical property, such as spin or polarization, from one particle—a photon or an atom, for instance—to another, even if the two are separated by millions of kilometers.

Three academic teams—based at the California Institute of Technology, the Massachusetts Institute of Technology, and the University of California, Los Angeles—will each get about $1 million a year over the next 5 years from a coalition of defense funders to work on different aspects of quantum communication. The Caltech team, for instance, will work on error correction methods, while MIT and UCLA will tackle optical fiber and memory problems.

The teams "fit very nicely together," says physicist Henry Everitt, who heads the effort for the Army Research Organization.

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