Physicists plunder life's tool chest

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Physicists plunder life's tool chest

DNA is both bricks and blueprint - an engineer's dream. John Whitfield speaks to the scientists turning biology into technology.
24 April 2003

JOHN WHITFIELD

Molecular computers can solve mathematical problems.
© GettyImages

DNA might be biologists' favourite molecule, but more and more physicists are joining in the fun. They hope to harness the cell's machinery to build individual molecules into electronic circuits, mechanical machines and drug delivery systems.

"If we look inside the cell, we see extraordinary machines that we couldn't make ourselves, says Len Adleman of the University of Southern California in Los Angeles. "It's a great tool chest - and we want to see what can we build with it."

In 1994, Adleman created the first computer to use

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problems.
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In 1994, Adleman created the first computer to use DNA to solve a mathematical problem[1]. Reading a biology textbook, he was struck by the parallels between DNA, with its long ribbon of information, and the theoretical computer known as the Turing Machine.

The Turing Machine, conceived in 1936 by the British mathematician Alan Turing performs any mathematical operation by working up and down a line of characters, guided by a set of rules.

Adleman tackled the famous 'travelling salesman' problem -finding the shortest route between scattered cities. Such problems rapidly become mind-boggling, because the only way to solve them is to examine every possible option. With many cities, this number is astronomical.

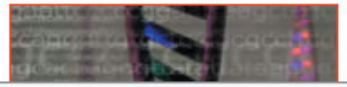
But DNA excels at getting an astronomical amount of data into a tiny space. "One gram of DNA can store as much information as a trillion compact discs," says Adleman. What's more, myriad DNA molecules can examine every possible route at once, rather than one at a time, as in a conventional computer.

The DNA computer used a sequence to represent each city, and another for the route between each city. These sequences then reacted in a test tube. The best route could be found by looking for the DNA sequence that contains all the routes and all the cities in the right combination.

No substitute for silicon

DNA seemed to offer an immense source of computing power. But most experts now doubt that it will ever challenge silicon. Although the reactions happen in a flash, setting them up is laborious, as is getting at the results.

"There are many practical hurdles. Even with the best techniques of today, DNA still lags behind silicon computers," says Ehud Shapiro of the Weizmann Institute in Rehovot, Israel. Instead, Shapiro advocates creating DNA devices that can do things, and go to places, that silicon can't - such as inside our cells, to make and control **drugs**.



Unlike early DNA computers, the devices built in Shapiro's lab can

- **Len Adleman**
- **Ehud Shapiro**
- **Ned Seeman**

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DNA can be programmed to build itself into structures.
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Unlike early DNA computers, the devices built in Shapiro's lab can run through all of the stages of simple calculations without human intervention. Using the right combination of DNA molecules and enzymes, the computer chomps through a sequence until it reaches an answer[2]. In February, the team unveiled a DNA computer that is powered by the energy from the breaking of chemical bonds within the DNA itself[3].

Shapiro has already patented some of his inventions. But to build a biological Turing Machine, he lusts after something that nature has not provided: a molecule that can recognize, cut and join DNA sequences in specific ways. "To go for broke we will have to wait a decade until scientists can synthesize designer enzymes," he says.

Molecular Hardware

The first DNA computers inspired many physicists to become acquainted with molecular biology. Some have now branched out into using the molecule as hardware.

Physicists are bending DNA into shapes that nature never intended. They have already made rugs of interlocking sequences, as well as cubes and more complex three-dimensional solids.

Many of these have been built in Ned Seeman's lab at New York University[4]. "We've had a series of successes with the making of shapes and devices," he says. Now it's time to start advancing to the point where we have applications."

The joy of building with DNA is that the molecule does much

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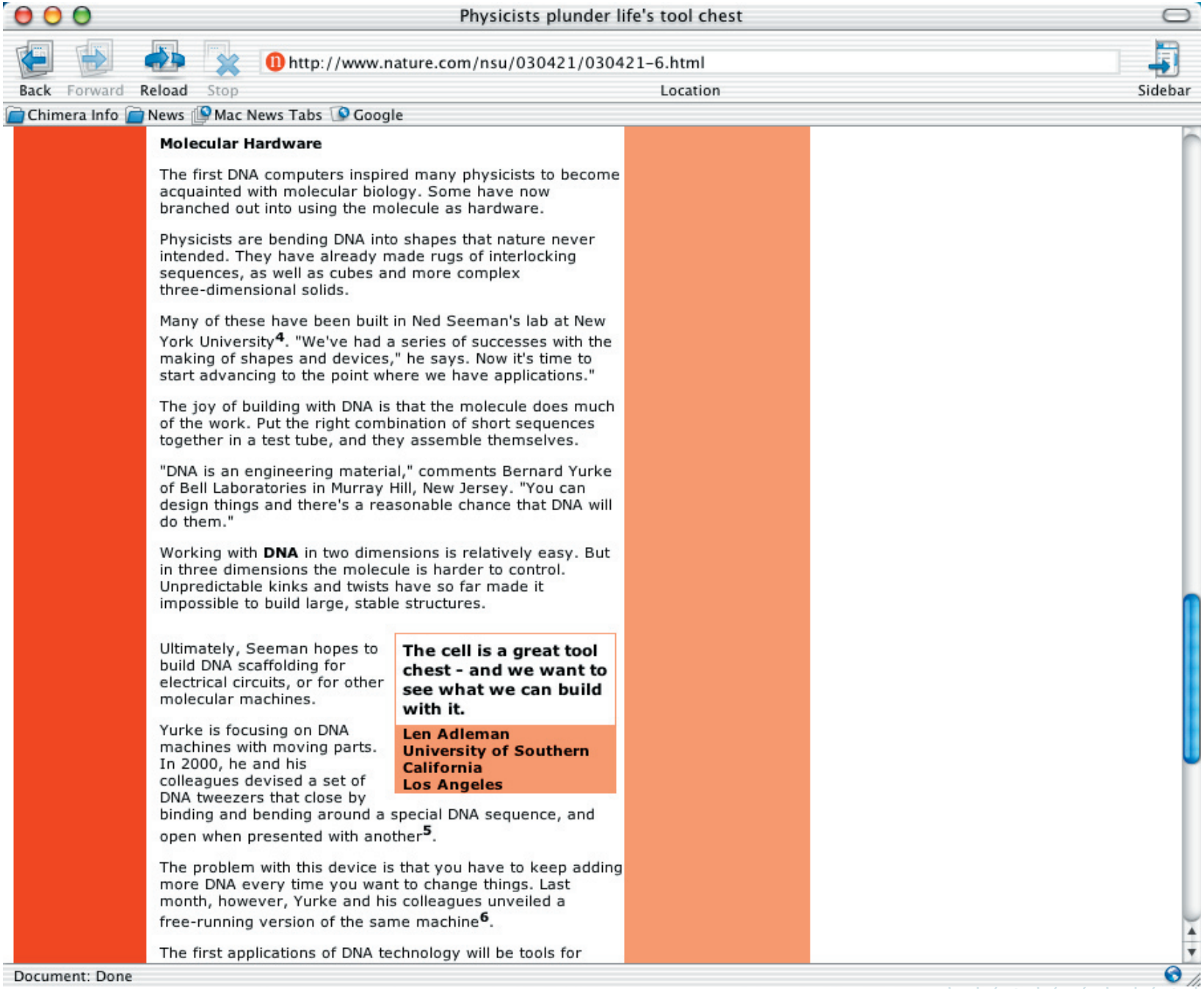
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Molecular Hardware
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The joy of building with DNA is that the molecule does much of the work. Put the right combination of short sequences together in a test tube, and they assemble themselves.
"DNA is an engineering material," comments Bernard Yurke of Bell Laboratories in Murray Hill, New Jersey. "You can design things and there's a reasonable chance that DNA will do them."
Working with DNA in two dimensions is relatively easy. But in three dimensions the molecule is harder to control. Unpredictable kinks and twists have so far made it impossible to build large, stable structures.
Ultimately, Seeman hopes to build DNA scaffolding for electrical circuits, or for other molecular machines.
The cell is a great tool chest - and we want to see what we can build with it.
Len Adleman
University of Southern California
Los Angeles
Yurke is focusing on DNA machines with moving parts. In 2000, he and his colleagues devised a set of DNA tweezers that close by binding and bending around a special DNA sequence, and open when presented with another[5].
The problem with this device is that you have to keep adding more DNA every time you want to change things. Last month, however, Yurke and his colleagues unveiled a free-running version of the same machine[6].
The first applications of DNA technology will be tools for
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The first applications of DNA technology will be tools for scientists, helping them to understand cells and molecules by manipulating them, or sort through libraries of DNA sequences.

The prospect of DNA machines for the rest of us is tantalizing, but still a long way off. "With the right kind of molecular motors we could build things on the nanoscale that are very complex," says Yurke. "I don't know how to carry that out yet."

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