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WHAT'S NEXT

A Self-Powered DNA Computer Redefines Small

By IAN AUSTEN

EXPERIMENTAL computers that calculate using DNA rather than electronics have many promising properties. To start with, they are exceptionally tiny. About one trillion DNA computers would fit in a single drop of water. Yet their storage capacity is potentially vast. A single gram of DNA holds about as much information as one trillion compact discs.

Now a research group at Weizmann Institute of Science in Rehovot, Israel, has added another twist. Its latest creation makes data function as the computer's power source.

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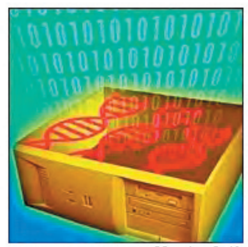

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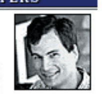

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Now a research group at Weizmann Institute of Science in Rehovot, Israel, has added another twist. Its latest creation makes data function as the computer's power source.

"It's not like we're going to save the energy store of the world with this," said Ehud Shapiro, a computer scientist and the lead researcher of the Weizmann project. "But lo and behold, we have been able to compute without using energy."

Like all current DNA computers, Dr. Shapiro's frugal model is mostly a laboratory curiosity. And there is skepticism, even from some DNA computer researchers, that today's demonstrations can be transformed into practical tools. But if that happens, Dr. Shapiro isn't hoping to create a rival to electronic computers. Instead he foresees new biological devices, including what he calls "a doctor in the cell."

Dr. Shapiro said it might be possible to program a DNA computer with medical knowledge and insert it into cells. Once there, it could track its host's condition and synthesize molecules to create drugs. "But this is the ultimate vision," he added. "The 50-year vision."

Dr. Shapiro's interest in biology was prompted by "questions about the origins of life," he recalled. But like other scientists, he noticed that there were many similarities between computing and the action of DNA.

Dr. Shapiro was struck by the way DNA's transformation within cells resembled the operation of a Turing machine. Developed in 1936 by the British mathematician Alan Turing, the conceptual device used a mechanism that worked with two strips of paper divided into cells. The machine would move along both tapes at the same time - reading symbols written within the input tape cells, comparing them with instructions stored its memory and then writing symbols on the output tape. At the end, it would provide a yes-or-no answer about the list of input-table symbols. For example, it could say whether an input tape marked with the letters A and B had an even number of B's.

With the Turing machine as its model, in late 2001 Dr. Shapiro's group produced the first DNA computer that could produce results without having humans guide its molecular reactions (the computer's method of calculation). For the input tape in their machine, the Weizmann researchers used specially engineered strands of DNA. It became the computer's software.

Much like the symbols on the tape in the Turing machine, DNA strands store genetic information in a four-letter alphabet. The researchers used two of those letters to represent the input data in the form of 0 or 1 symbols. The

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Much like the symbols on the tape in the Turing machine, DNA strands store genetic information in a four-letter alphabet. The researchers used two of those letters to represent the input data in the form of 0 or 1 symbols. The other two letters were used to simulate the operational state of the computer. In the Turing machine, those states include scanning and printing. The DNA computer, however, simply had the states 0 or 1. For the DNA computer's hardware, the Weizmann researchers employed two enzymes that cells use to reproduce their DNA before they divide.

In the first Weizmann computer, the string of DNA the researchers wanted to analyze -the input data - was created with one of its two strands left incomplete. Floating in the same test tube was the computer's software DNA, also created with a free-ended molecule. The software strands were designed to include all of the possible symbol and state combinations on their open strands. Like two halves of a zipper with mismatched teeth, not all the open input-software DNA sections could mesh with the open sections of all the software DNA. But when the open string of the input DNA encountered a software string with an open end that was complementary to its own, the two joined and were sealed by an enzyme. Spacers engineered into the resulting DNA string then attracted another enzyme. It made another ragged cut, starting the matching process over again.

This matching, cutting and sealing continued until a special output detector DNA molecule fit the open end of the strand. The final molecule that was created provided the answer to the researchers' question.

The second computer, described in a paper published last month in the Proceedings of the National Academy of Sciences, eliminated the sealing of the input DNA with the software DNA. That process, Dr. Shapiro said, made it impossible to recycle the first computer's software DNA because the sealing enzyme acquired the energy for its task by taking molecules from its strands.

In the second computer, all the energy needed to push the process forward comes from a small amount of heat released from the input DNA after it is snipped by the reading and cutting enzyme. "It provides both information and fuel," Dr. Shapiro said.

Of course, no DNA computer produces its results on a conventional monitor. Instead, results must be divined by using a electrophoretic gel to create the kind of black-and-white DNA charts that are displayed by expert witnesses at criminal trials.

The lack of an easy method for displaying DNA computing results is one reason that they are better suited to performing biological tasks rather than

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at criminal trials.

The lack of an easy method for displaying DNA computing results is one reason that they are better suited to performing biological tasks rather than being developed as a rival to electronic computers, Dr. Shapiro said. While he acknowledged that his "doctor in a cell" scenario is a distant dream, he said it might be possible to develop some way to use the process for DNA sequencing.

Lloyd M. Smith, a professor of chemistry at the University of Wisconsin who has helped develop other DNA computers, agreed that they are unlikely to replace electronic models. But he is just as skeptical of their potential in cell-based medicine.

"It's basically pretty cool that you can solve such big problems with molecules," Dr. Smith said. "But it's not practical. For me the utility in DNA computing has been in getting me to think differently about what computations are."

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