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UNIVERSITY OF ILLINOIS

Researchers turn DNA into a tool

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Nature uses DNA molecules to store information. For example, about making proteins our body needs to function properly.

But University of Illinois researchers are using DNA in a different way — as a construction tool.

UI chemistry Professor Scott Silverman and colleagues employ the tendency of the ribbonlike DNA molecules to take a certain shape to control the shapes of other large macromolecules well over 100 atoms in size.

Moreover, they can tell going in whether the DNA will affect the shape of the target molecule to which they attach it.

"In order to use it we have to have a reasonably firm predictive ability," Silverman said recently.

Their method, published in the Journal of the American Chemical Society by Silverman and UI graduate student Chandrasekhar Miduturu, is the result of five years of work that will end up as Miduturu's doctoral dissertation. The work has been supported by the UI and the David and Lucile Packard Foundation.

At this point, the UI-developed technique is a good basic science tool for understanding

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DNA

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how molecules such as DNA, RNA and proteins fold and take on structures, a process that's biologically essential and on the cutting edge of biotechnology.

"Here, we're trying to understand nature," Silverman said. "The utility of all this is still to be proven."

But if scientists can understand the process, they also may be able to use the tool to control it "in ways that could be potentially useful," he said.

"The shapes of molecules affect how they function," Silverman said. "By controlling the shape we have a way to control, eventually, the function."

At least some diseases are apparently rooted in breakdowns when molecules fold. The technique might, at some point in the future, be used to fix that, although Silverman thinks it's a stretch at this point to say it will lead to medical treatments.

Likewise, molecules often get together to create tiny molecular machines with various functions. The tool could be used to shape components in such machines and assemble them.

The technique might be useful in nanotechnology with nonbiological macromolecules, as well, for instance the polymers that make up plastics.

"I think nonbiological applications are more likely," Silverman said. "But who knows what people are going to be able to come up with if we have control ... in such a detailed manner."

Other scientists have used DNA as a static "scaffold" on which to hang molecules in an array, typically two-dimensional.

But using it dynamically, and particularly with predictable results, to control the shape of individual molecules in three dimensions is a breakthrough for Silverman's lab, which emphasizes the study of nucleic acids like DNA and RNA.

RNA macromolecules, which the body uses to transform the information stored by DNA into things like proteins, are the test subject on which the UI researchers have applied DNA as a shape controller governed by chemical reactions.

To do that, they chemically attach two strands of DNA to an unfolded RNA molecule. The DNA strands resemble two sides of a ladder cut down the middle through its rungs. Those sides naturally join to create the classic "double helix" shape of DNA molecules.

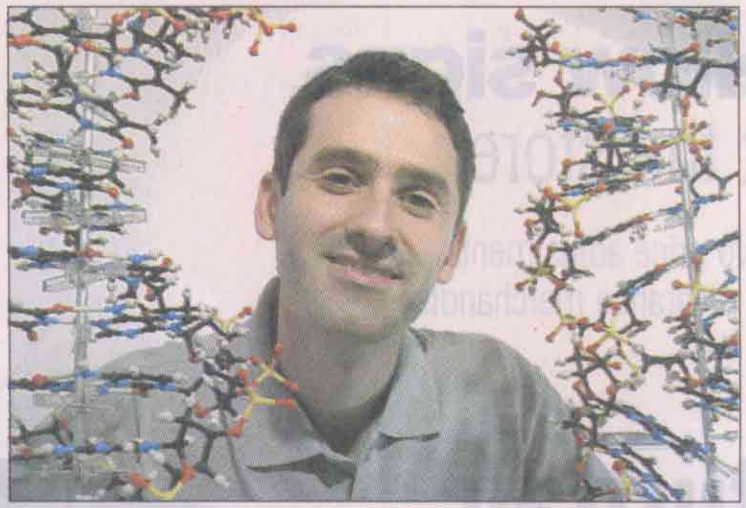
The researchers then prompt the RNA molecule to fold as much as it can. The DNA, depending on its position, length and the chemistry used, either does nothing, like a barnacle stuck to a boat hull, or influences the structure of the RNA, Silverman said.

"Something's got to give, either the structure of the macromolecule or the DNA double helix," he said. "You can have cake. You can have ice cream. But you can't have both. We can predict and control" which.

Silverman and colleagues are working on attaching more than one DNA constraint to RNA and other large molecules, which might give them, in essence, two switches that could be turned on and off to orchestrate the folding process at various stages.

"That's some place that we'd like to go," Silverman said, "to see how much control we can have."

They also plan to work on shaping molecules in ways that could potentially allow them to assemble into molecular machines.



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University of Illinois chemistry Professor Scott Silverman, posing with models of DNA, left, and RNA, is using DNA as a molecular-scale construction tool to control the shapes of other molecules, in order to study the process by which molecules take shapes.