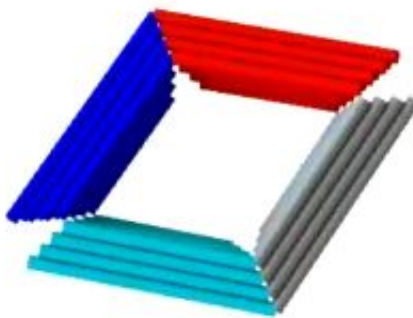
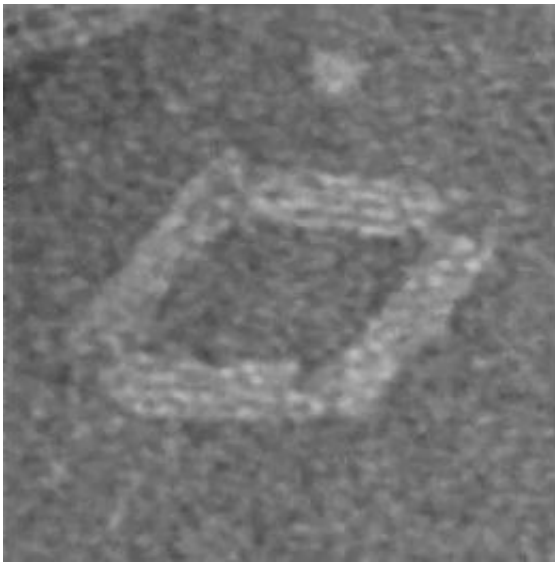


DNA origami could lead to nano 'transformers' for biomedical applications

January 5 2015, by Pam Frost Gorder



If the new nano-machines built at The Ohio State University look familiar, it's because they were designed with full-size mechanical parts such as hinges and pistons in mind.

The project is the first to prove that the same basic design principles that apply to typical full-size machine parts can also be applied to DNA—and can produce complex, controllable components for future nano-robots.

In a paper published this week in the *Proceedings of the National*

Academy of Sciences, Ohio State mechanical engineers describe how they used a combination of natural and synthetic DNA in a process called "DNA origami" to build machines that can perform tasks repeatedly.

"Nature has produced incredibly complex molecular machines at the nanoscale, and a major goal of bio-nanotechnology is to reproduce their function synthetically," said project leader Carlos Castro, assistant professor of mechanical and aerospace engineering. "Where most research groups approach this problem from a biomimetic standpoint—mimicking the structure of a biological system—we decided to tap into the well-established field of macroscopic machine design for inspiration."

"In essence, we are using a bio-molecular system to mimic large-scale engineering systems to achieve the same goal of developing molecular machines," he said.

Ultimately, the technology could create complex nano-robots to deliver medicine inside the body or perform nanoscale biological measurements, among many other applications. Like the fictional "Transformers," a DNA origami machine could change shape for different tasks.

"I'm pretty excited by this idea," Castro said. "I do think we can ultimately build something like a Transformer system, though maybe not quite like in the movies. I think of it more as a nano-machine that can detect signals such as the binding of a biomolecule, process information based on those signals, and then respond accordingly—maybe by generating a force or changing shape."

The DNA origami method for making nano-structures has been widely used since 2006, and is now a standard procedure for many labs that are developing future drug delivery systems and electronics. It involves

taking long strands of DNA and coaxing them to fold into different shapes, then securing certain parts together with "staples" made from shorter DNA strands. The resulting structure is stable enough to perform a basic task, such as carrying a small amount of medicine inside a container-like DNA structure and opening the container to release it.

To create more complex nano-machines that could perform such tasks repeatedly, Castro joined with Haijun Su, also an assistant professor of mechanical and aerospace engineering at Ohio State. Combined, the two research teams have expertise in nanotechnology, biomechanics, machine engineering and robotics.

Castro said there are two keys to their unique approach for designing and controlling the machines' motion. The first involves making certain parts of the structure flexible. They make flexible parts from single-stranded DNA, and stiffer parts from double-stranded DNA.

The second key involves "tuning" the DNA structures so that the machines' movements are reversible and repeatable. The researchers dot their structures with synthetic DNA strands that hang off the edges like the awning of a roof. Rather than join portions of the machine together permanently, these strands are designed to act like strips of hook and loop fasteners—they stick together or unstick depending on chemical cues from the machine's surroundings.

In the lab, doctoral students Alexander Marras and Lifeng Zhou took long strands of DNA from a bacteriophage—a virus that infects bacteria and is harmless to humans—and "stapled" them together with short strands of synthetic DNA.

First, they joined two stiff DNA "planks" with flexible staples along one edge to create a simple hinge. Castro likened the process to "connecting two wooden 2x4's with very short pieces of string along the 4-inch edge

at one end."

They also built a system that moved a piston inside a cylinder. That machine used five planks, three hinges and two tubes of different diameters—all made from pieces of double-stranded and single-stranded DNA.

To test whether the machines were moving properly, they imaged them with transmission electron microscopy. They also labeled the DNA with fluorescent tags, so that they could observe the shape changes with a spectrofluorometer. Tests confirmed that the hinges opened and closed and the piston moved back and forth—and that researchers could control the motion with the addition of chemical cues to the solution, such as additional strands of DNA.

This approach of designing simple joints and connecting them together to make more complex working systems is common in macroscopic machine design, but this is the first time it's been done with DNA—and the first time anyone has tuned the DNA to produce reversible actuation of a complex mechanism.

The research team is now working to expand the design of mechanisms for tuning the machines, and they will also attempt to scale up production of the machines for further development.

More information: Programmable motion of DNA origami mechanisms, *PNAS*, www.pnas.org/cgi/doi/10.1073/pnas.1408869112

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