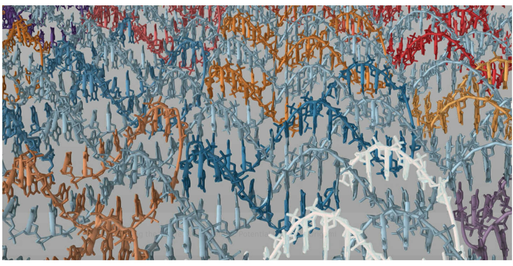
Folding the Future: New Scientific Potential With DNA Origami

BY MATT ALDERTON · MANUFACTURING · JAN 12 2016 · 6 MIN READ



Until his death in 2005, Akira Yoshizawa was known as the grandmaster of origami, the Japanese art of paper folding.

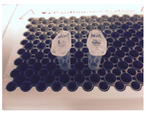
Widely credited with transforming origami from a humble craft into a respected art form, Yoshizawa was a self-taught doyen whose body of work included an estimated 50,000 origami models. Among his most famous folded creations were lumbering gorillas with drooping limbs and sunken faces, elegant butterflies with delicate wings, and lifelike elephants with flappy ears and serpentine trunks. He even made a stunning self-portrait so realistic that the folds in his paper perfectly matched the folds in his skin. Made with neither a single cut of scissors nor a single dab of glue, each piece of paper perfection was a masterpiece stunningly simple yet remarkably complex.

"The possibility of creation from paper is infinite," declared Yoshizawa, who insisted that his work was not just artistic in nature, but also scientific, relying on the laws of geometry, physics, and even biochemistry.

What Is DNA Origami? As impressive as Yoshizawa's work was, modern science has developed a brand of origami even more astonishing. Like the traditional variety, it uses the art of folding to transform raw materials into dynamic three-dimensional objects. The medium isn't paper, however. Instead, it's DNA.

DNA, short for "deoxyribonucleic acid," contains the biological instructions for the development of living organisms. Even though a DNA strand's width is 50,000 times smaller than the width of a human hair and too small to see with most normal light microscopes, it can be easily manipulated because of its chemical composition.

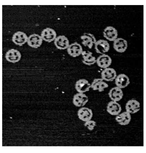
Here's how it works: A single strand of DNA is a polymer composed of small chemical units called "nucleotides." Like magnets, each of the four types of nucleotides has a complementary "other half" nucleotide that it's attracted to. When two strands of DNA are in proximity to one another, the nucleotides automatically attract and bind with their complementary units, forming what are called "base pairs." A typical molecule of double-stranded DNA—the kind found in humans, animals, and even bacteria—consists of two strands whose nucleotides bind to form base pairs in such a way that the strands wrap around each other to form a single long double helix, or "twisted ladder."



When they practice DNA origami, scientists leverage this natural base-pairing process by mixing multiple short strands of synthetic DNA, called "staples," with a single long strand of viral DNA, the "scaffold." These DNA strands are combined in solution inside a test tube, then heated up and cooled back down to initiate the base-pairing process, which causes them to assemble in double helices. Instead of a single long double helix, however, the staples are designed to form a latticework of many connected double helices, which form the desired structure.

Simply put: When they bind with it, the short strands "fold" the long strand and lock it into a preprogrammed shape. "Our hands don't work very well for folding something at the nanoscale—they'd just crush it—so we use small strands of DNA as our hands to fold the long strand," explains Joseph Schaeffer, principal research scientist in the Bio/Nano Research Group at Autodesk.

Small Structures Have Big Promise. The idea of using DNA to create structures dates back to the early 1980s, when New York University Professor Nadrian Seeman pioneered the concept of structural DNA nanotechnology. By utilizing the nucleotide complementarity rules and the ability to synthesize arbitrary sequences of DNA, it could be used as a nanoscale building material. California Institute of Technology Senior Research Fellow Paul W.K. Rothemund evolved Seeman's work in 2006 when he invented DNA origami, using the "stapling" process to fold a single long strand, which he illustrated by creating 50 billion DNA smiley faces visible under an atomic force microscope.



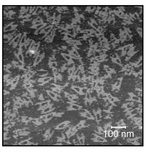
Since then, scientists have used DNA origami to create structures that have not only form, but also function. Potential applications for DNA origami range from self-assembly of materials to "nanorobots" that deliver drugs to targeted areas of the body to help fight disease.

A common challenge is to be able to position material with atomic precision. "Think of it as creating a nanometer-scale assembly line," Schaeffer says. By extending the same "staple" strands that fold the DNA origami, proteins and other molecules can be attached in precise locations on the origami surface. Scientists have also built DNA-based devices that can move along the DNA origami surfaces, allowing the transport of molecules to specific locations.

Designing DNA. Despite enormous promise, DNA origami as a discipline is still in an early phase. To help it mature, DNA nanotechnologists need better tools to assist in designing their origami. Just like the paper variety, DNA origami relies on carefully designed patterns that show what will be folded and how to achieve the desired final shape.

"There are three essential phases in order to build an origami device," Schaeffer says. "First is the design and determining which DNA strands are required to build it. Then you procure those specific strands from a company that sells synthetic DNA. Once this arrives, you combine the strands in a test tube, heat it, and then cool it back down. During this final phase of heating and cooling, the DNA origami folds and assembles itself."

Engineering a DNA nanostructure requires keeping track of hundreds of DNA strands and their interactions with one another—which is extremely complex, and will become even more so as scientists evolve DNA origami to the point where it can support larger, more complicated structures. To make it easier, better design software is needed, according to Schaeffer, who says the Bio/Nano Research Group at Autodesk Research is leveraging Autodesk's design-software expertise and technology to develop CAD tools for nanoscale bio design. The group has started out by demonstrating the complete process of design to assembly and verification, and elected to first construct a DNA origami nanostructure of the Autodesk logo.



Currently, DNA origami is designed using the open-source software Cadnano. Users first sketch their origami in Cadnano with 2D schematics, and have the option of viewing a 3D model using either a Cadnano plug-in for Autodesk Maya or the Autodesk Molecule Viewer. Then they can simulate the DNA origami to predict the final physical structure using CanDo or oxDNA. Future iterations and descendants of these tools will simplify the process even further.

"Just like we're seeing 3D printers make it easy for anyone to take a 3D object from CAD and make it real, we're working on software that will make it easier to design and create DNA origami," Schaeffer concludes. "There are so many cool ideas that could be realized using this technology—if only we could solve some of the design challenges it faces. We're getting in on the ground floor by designing the software that's needed for advancing the field."

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