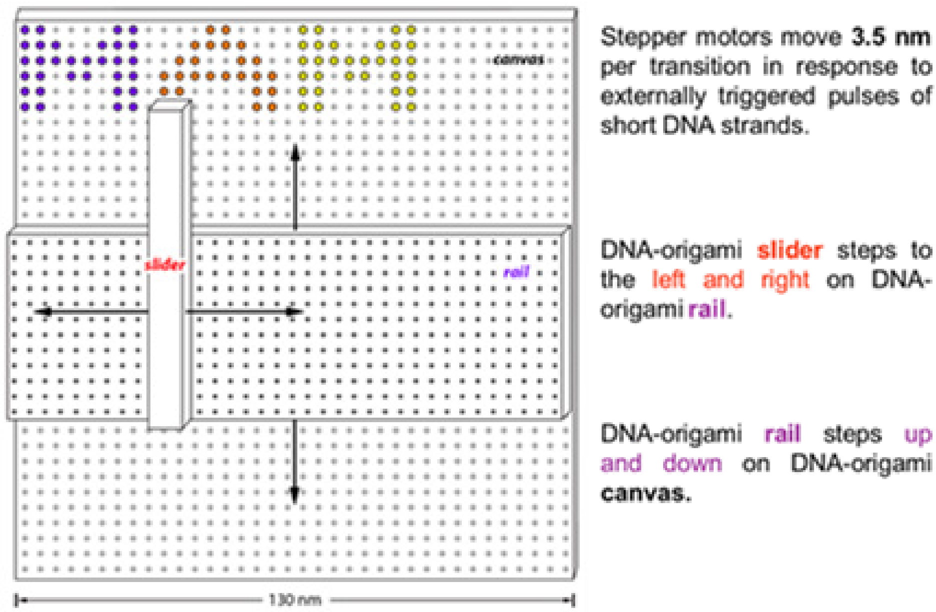
U.S. DEPARTMENT OF
ENERGY

Office of
ENERGY EFFICIENCY &
RENEWABLE ENERGY

DNA Strand Displacement-Driven DNA Origami Tools and Materials

Atomically precise manufacturing (APM) is an emerging disruptive technology that could dramatically reduce energy use and increase performance of materials, structures, devices, and finished goods. APM does this by manufacturing so that every atom is at its specified location relative to the other atoms—there are no defects, missing atoms, extra atoms, or incorrect (impurity) atoms. Like other disruptive technologies, APM will first be commercialized in early premium markets, such as research and medicine.

All molecules, including strands of deoxyribonucleic acid (DNA) are, by definition, atomically precise (AP). In this type of APM project, AP DNA strands are used as construction material and as construction equipment. The initial development of the tools and systems, to manipulate and assemble trillions of systems involving DNA structures, will open up a wide variety of DNA-molecule scale manufacturing possibilities—including semiconductor-DNA hybrids for computing and data storage. This project leverages recent progress being made in two rapidly developing fields. First, self-assembly and programmed movement of DNA origami (conventional 'origami' is made by folding long strands of DNA, aided by shorter 'staple' DNA), to create scaffolds of wide variety of molecular structures with nanometer (nm) level precision, has been achieved. Recently, DNA origami has been programmed to move using other DNA strands. Second, additive manufacturing (AM)—also known as 3D printing—is a manufacturing technique that progressively adds layers of material to build up products with more refined geometries while avoiding material waste. Based on these breakthroughs, this molecular additive manufacturing project aims to demonstrate design and control for a first-of-its-kind APM molecular printer and canvas.



Schematic of a printer made from self-assembled DNA origami. This technology will use DNA strand displacement to spatially position and activate trillions of print heads simultaneously for additive manufacturing.
Graphic courtesy of Dana-Farber Cancer Institute.

The project begins with DNA origami self-assembly. The origami self assembles because of the quaternary logic of Watson-Crick based pairing. Software based on this logic assists the researchers in design of DNA strands with sequences that fold into the desired shape, and additional DNA strands with sequences that induce the desired motion upon their introduction. One early application of these origami frameworks is a stepping motor. Once the stepper is demonstrated, the next step will be to control it with respect to the DNA origami 'canvas.' In the short term, this massively parallel DNA actuated and controlled technology makes DNA prototyping faster and more robust.

Benefits for Our Industry and Our Nation

The DNA-based molecular manufacturing tools developed in this project will enable tools and processes that have the potential to dramatically reduce the energy and materials costs of manufacture. The AM replaces processes that require highly refined starting materials, high-energy casting processes, and/or substantial subtractive processing. APM can potentially offer zero material waste by building materials from liquid or soluble feedstocks rather than carving them from solids. This prototype could additively manufacture more robust molecular (AP) tools to atomic-level specifications. The tools could become assemblers of new materials with extremely high functionalities (e.g., strength or conductivity) and other ultra-high performance features, such as energy storage or DNA computing capabilities that are sufficiently robust for a wide range of manufacturing applications.

Applications in Our Nation's Industry

This type of molecular manufacturing—technology bootstrapped from AP DNA tools—has the potential to be broadly applicable and further the development of APM. As the technology progresses, potential applications may include: photovoltaics; photosynthetic and fuel cells; thermoelectrics and anisotropic heat spreaders; solid-state lighting; molecular electronic and plasmonic circuits; selectively permeable membranes; and self-repairing materials with high strength-to-weight ratio and fracture resistance.

Project Description

The project objective is to demonstrate self-assembly of three independently moving layers of DNA origami and control motion in two dimensions (2D) with stepper motor positioning while printing a pattern at multiple sites simultaneously.

Barriers

- Ability to control multisite interactions at interfaces between DNA origami surfaces in the 'stack' and 'wrap' designs
- Overcoming failure and low-performance modes for the sliders (e.g., sliders that fail to move for one or more cycles, or sliders that fall off the rails)
- Overcoming high positional variance of sliders at each register
- Overcoming pixel-writing failures (e.g., missing pixels and unwanted pixels) at multiple print heads through better control of chemical reactions

Pathways

The project will develop DNA-based 2D printers using two architecture designs: 'stack' and 'wrap.' Initially, the project team will be focused on actuating a self-assembled stepper nanomotor in one dimension (1D). Subsequently, efforts will focus on validating actuation in 2D.

Following successful 2D actuation, the project will work to advance a self-assembled, programmed, and externally controlled 2D printer that can write a pattern on a DNA origami canvas (the workpiece) with high levels of patterning and site occupancy on the canvas. While external control of DNA origami has been shown previously, this project aims to demonstrate control over printing with three independently moving DNA origami, with parallelism in the trillions.

Milestones

This three-year project began in June 2018.

- Demonstrate assembly and transmission electron microscopy (TEM) validation of 1D stepper nanomotors with two different architectures ('stack' and 'wrap'), with the expectation that at least one architecture can be actuated in 1D with >50% yield per driven step (completed)
- Demonstrate assembly and TEM validation of 2D stepper nanomotors with 'stack' and 'wrap' architectures, with the expectation that at least one architecture can be actuated in 2D with >50% yield per driven step (2020)
- Demonstrate 2D printing on the canvases, catalyzed by positional control of the write head, with the expectation that at least one architecture can be patterned with >80% occupancy per designed site, as assessed by TEM (2021)
- Demonstrate surface immobilization and microfluidic actuation of 1D and 2D stepper nanomotors using super-resolution fluorescence microscopy to monitor stepping of the nanomotors in real time (2021)

Technology Transition

This proof-of-concept project will develop a prototype programmable nanoscale printer capable of writing a pattern on a DNA origami canvas. This DNA-based molecular additive manufacturing process demonstrates massively parallel operation of synthetic molecular machinery. The use of self-assembly based methods makes this a highly scalable approach. In early premium research markets, these first-generation molecular 2D printers will offer many advantages over conventional DNA origami construction techniques, such as faster prototyping, higher throughput, faster dynamic rearrangement of patterns, and the ability to respond with feedback.

First-generation molecular printers may prove popular in the research community where related methods, such as single-molecule optical trapping and atomic force microscopy, already have gained traction. Once the concept is experimentally validated, it is envisioned that funds will be raised for a start-up company to assist with subsequent commercialization, with supplemental support provided by Harvard. Initially, molecular printers may be distributed to a set of selected pilot users for testing. Later, distribution may ramp up through a web-based sales interface. Distribution may also be considered through licensing to existing companies in the U.S. that already offer DNA origami as a product.

Project Partners

Dana-Farber Cancer Institute
Harvard University
Boston, MA
Principal Investigator: Dr. William Shih
Email: *William_Shih@dfci.harvard.edu*

University of Oxford
Oxford, United Kingdom

For additional information, please contact

Tina Kaarsberg, PhD
Technology Manager
U.S. Department of Energy
Advanced Manufacturing Office
Phone: (202) 586-5112
Email: *Tina.Kaarsberg@ee.doe.gov*■

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