DNA Strand Displacement driven Molecular Additive Manufacturing (DSD-MAM)

Contract Number: EE0008310
Dana-Farber Cancer Institute/University of Oxford
Project Period: 2018 June 1 – 2021 November 30

William Shih, PhD, Dana-Farber Cancer Institute (Prime)
Andrew Turberfield, PhD, University of Oxford (Sub-contract)

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Overview

Timeline

- Projected Issue date June 2018 June
- Projected End date 2022 November
- Project 0% complete

Barriers

- No existing baseline technology exists for self-assembly-based Atomically Precise Manufacturing (APM). However, living cells are an existence proof that this is physically possible.

Budget

	FY 16 Costs	FY 17 Costs	FY 18 Costs	Total Planned Funding (FY 18-Project End Date)
DOE Funded	_	_	87K	1215K
Project Cost Share	_	_	21K	313K

Partners

- Sub-award to Andrew Turberfield at University of Oxford, Dept. of Physics

Project Objectives

PROBLEM Develop a pathway to scalable integrated nanosystems for atomically precise manufacturing (APM).

RELEVANCE Assembly to atomic-level specification will deliver qualitatively new functionalities and low-variability, ultra-high performance, and will enable tools and processes that dramatically reduce the energy and materials costs of manufacture.

PROJECT GOAL Self-assemble molecular 2D printers from DNA.

POTENTIAL BENEFITS Success will initiate a bootstrapping cascade that will lead to APM as a practical manufacturing technology.

Technical Innovation

CURRENT PRACTICE No baseline technology exists for atomically precise manufacturing (APM) via massively parallel operation of synthetic molecular machinery.

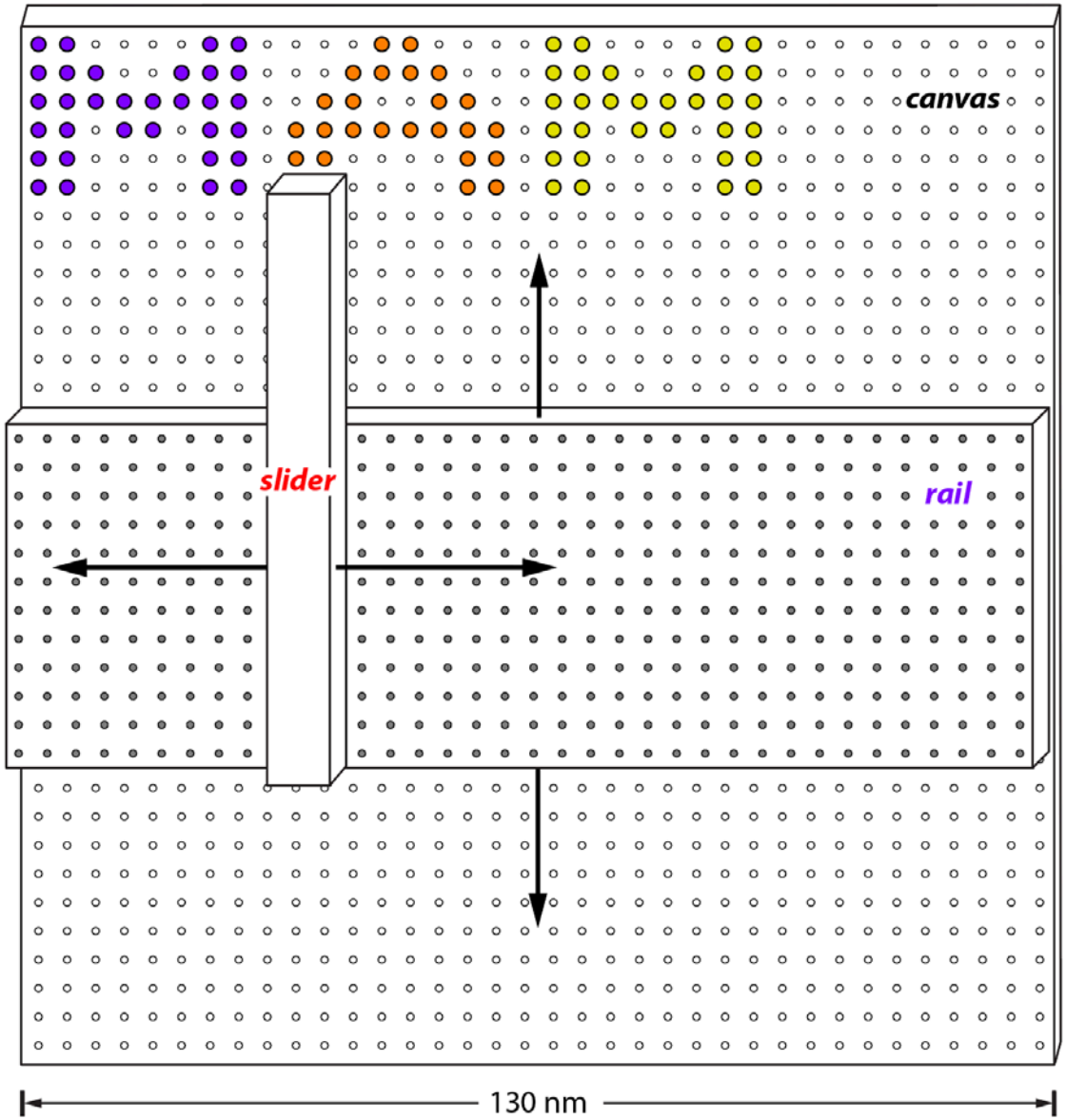
INNOVATION World's first integrated nanosystem for Atomically Precise Manufacturing. And not just one nanosystem, but trillions of copies. . . .

We will use the rapidly developing 'DNA origami' self-assembly technique to create the required molecular machine tools. Novel functionalities of these nanomachines will include the following: nanometer-precision 'stepper' positioning mechanisms based on multivalent interactions for high cooperativity and greater robustness; integration of three independently moving layers of DNA origami to achieve 2D controllable motion; integration of spatial positioning with deposition functionality.

IMPACT ON FUTURE MANUFACTURING Potential applications: photovoltaics; photosynthetic and fuel cells; thermoelectrics and anisotropic heat spreaders; solid-state lighting; molecular electronic and plasmonic circuits; selectively permeable membranes; self-repairing materials with high strength-to-weight and fracture resistance.

Technical Approach

'stack' architecture to be developed by Dana-Farber Cancer Institute



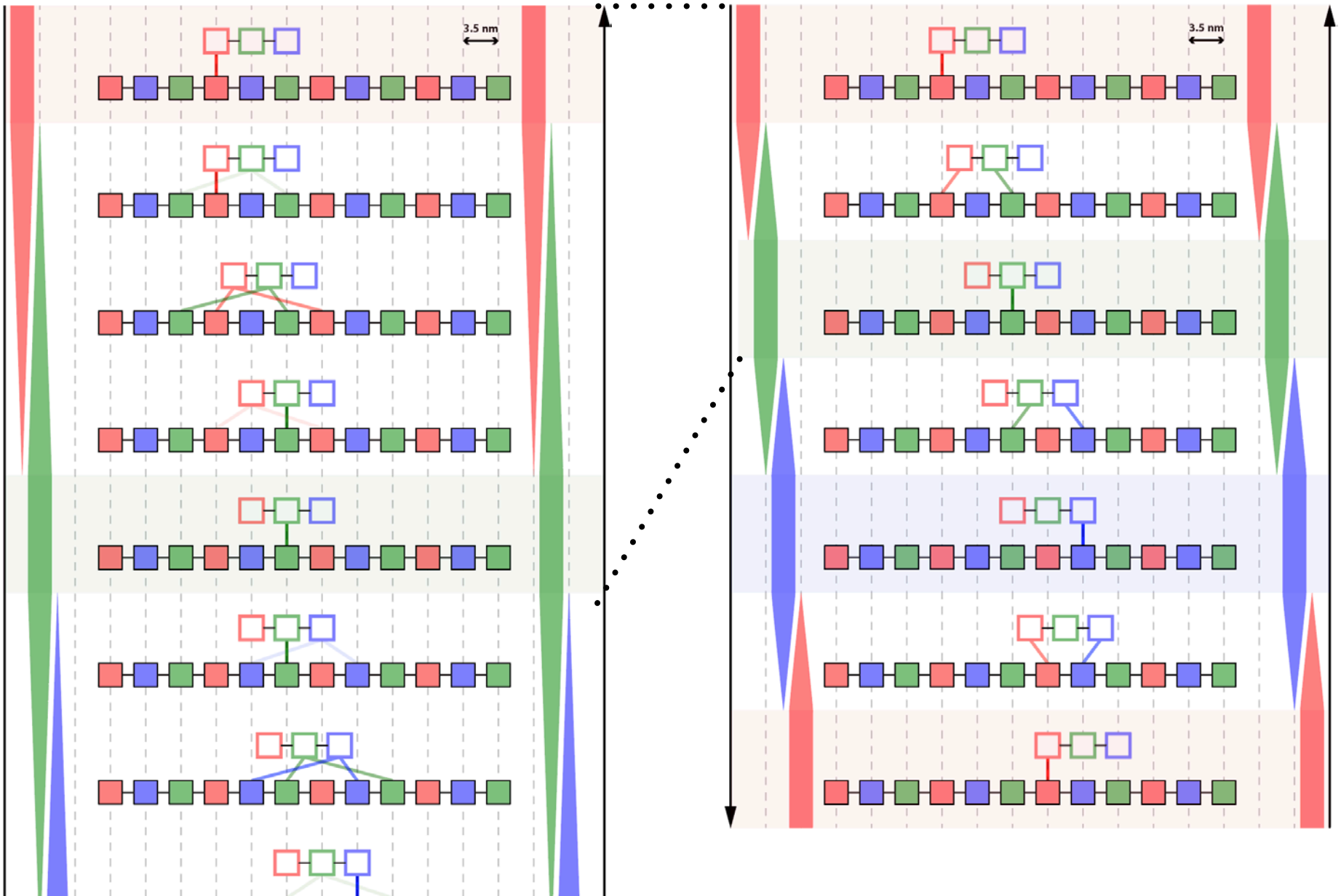
Stepper motors move **3.5 nm** per transition in response to externally triggered pulses of short DNA strands.

DNA-origami **slider** steps to the left and right on DNA-origami **rail**.

DNA-origami **rail** steps up and down on DNA-origami **canvas.**

Technical Approach

Three-phase stepper motor
actuated by pulses of short DNA strands



Technical Approach

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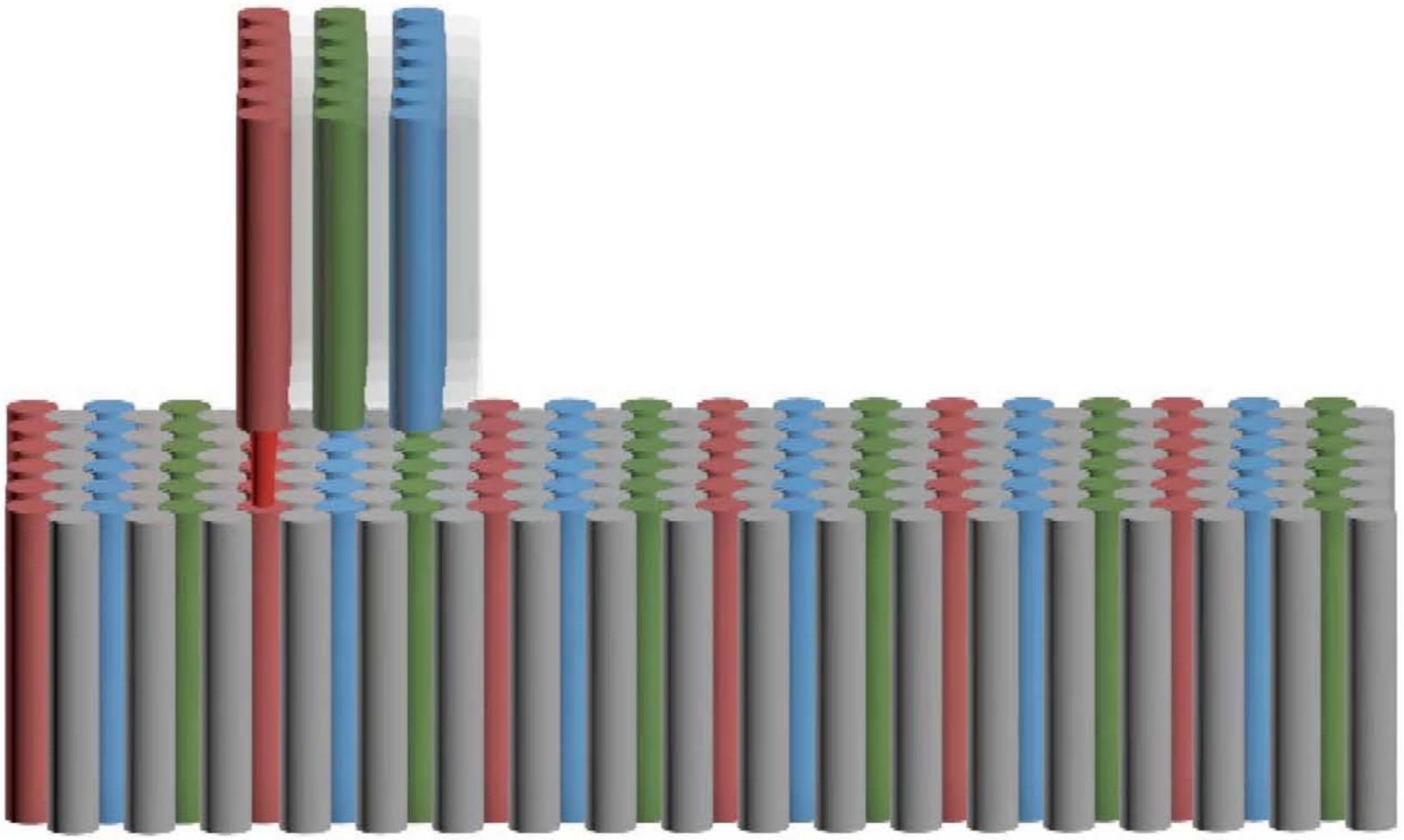
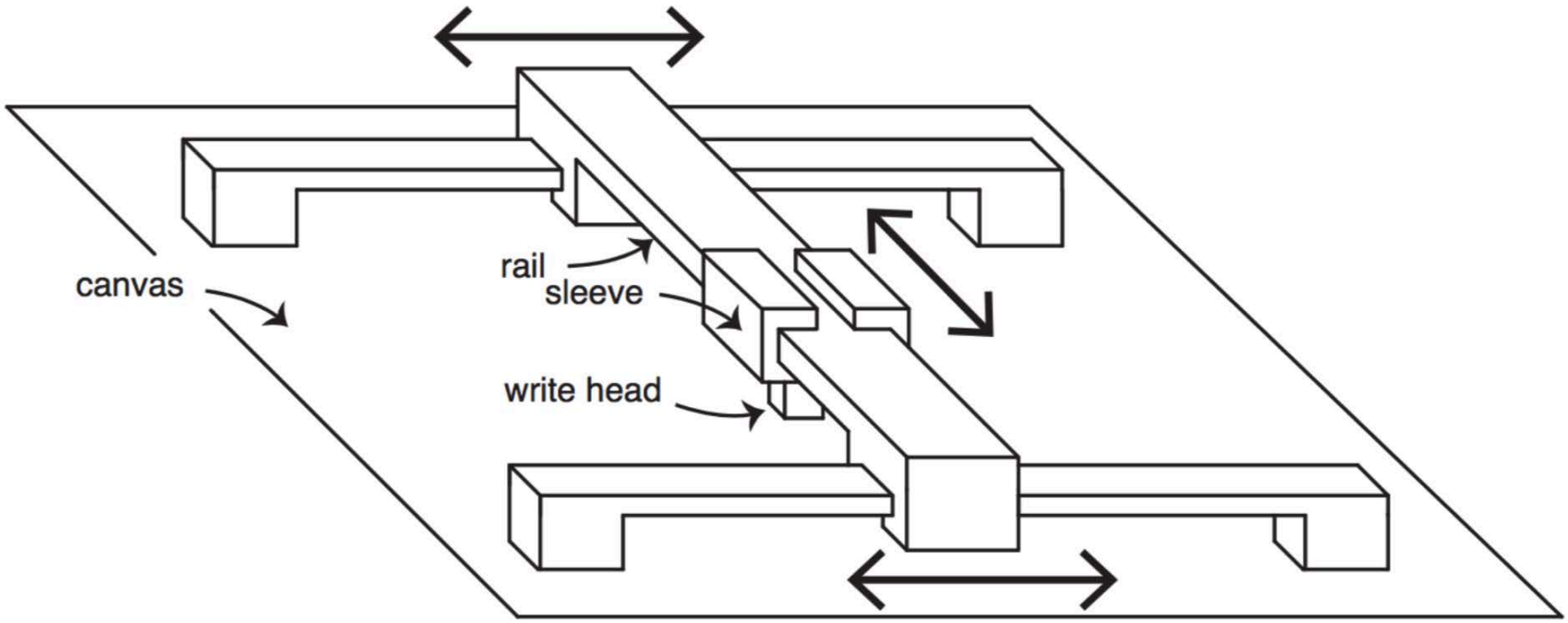


Technical Approach

‘wrap’ architecture to be developed by U. Oxford



Projected Milestones

MONTHS 1–14 We will demonstrate assembly and TEM validation of 1D stepper nanomotors with two different architectures (‘stack’ and versus ‘wrap’). Nanomotors will be controlled in bulk solution by manual pipetting steps. We expect that at least one architecture can be actuated in one dimension with >95% yield per driven step by the end of Period 1.

MONTHS 15–28 We will demonstrate assembly and TEM validation of 2D stepper nanomotors with ‘stack’ and ‘wrap’ architectures. As with the 1D steppers, the 2D nanomotors will be controlled in bulk solution by manual pipetting steps. We expect at least one architecture can be actuated in two dimensions with >95% yield per driven step by the end of Period 2.

MONTHS 29–42 We will demonstrate 2D printing on the canvases, catalyzed by positional control of the writehead. We expect at least one architecture can be patterned with >80% occupancy per designed site by the end of Period 3, as assessed by TEM. We also will demonstrate surface immobilization and microfluidic actuation of 1D and 2D stepper nanomotors. DNA-PAINT super-resolution fluorescence microscopy will be used to monitor stepping of the nanomotors in real-time.

Technical Approach

Participant roles and responsibilities

William Shih, PhD, Dana-Farber Cancer Institute: Principal Investigator; pioneer in 3D DNA origami; responsible for leading the project and implementing the ‘stack’ architecture

Andrew Turberfield, PhD, University of Oxford (sub-contract): co-Investigator; pioneer in DNA walkers; responsible for implementing the ‘wrap’ architecture

Project risks and unknowns

Many of the key technologies required for success of our proposed approach already have been demonstrated. What has never been shown before is the control of multisite interactions at interfaces between DNA-origami surfaces as in the ‘stack’ and ‘wrap’ designs. Anticipated failure/low- performance modes include sliders that don’t move for one or more cycles or else fall off their rails, sliders that exhibit high positional variance at each register, and printheads that exhibit pixel-writing failures (e.g. missing pixels, unwanted pixels) despite positioning within specifications. Our objective is to develop strategies for minimizing the fraction of DSD-MAM nanosystems that exhibit these kinds of suboptimal performances.

Transition (beyond DOE assistance)

Expected strategy for further technology development and eventual transition to the commercial marketplace.

The output of this three-year project will be a programmable printer able to pattern a DNA-origami canvas. Its principal importance is as an essential step in the development of a new technology for atomically precise manufacturing. However, the first-generation molecular 2D printer will offer many advantages over conventional DNA-origami patterning, such as faster prototyping, faster dynamic rearrangement of patterns, and the ability to respond with feedback.

We anticipate that first-generation molecular printers will prove popular in the research community where related methods such as single-molecule optical trapping and atomic force microscopy already have gained traction. Molecular printers will offer far greater throughput than these previous methods. Our plan is, upon experimental validation of the molecular printer concept, to raise funds to start a company in the United States for commercialization, with support from Wyss Institute at Harvard. In our first year, we will distribute molecular printers to a set of selected pilot users for initial testing. Later, we will ramp up distribution to general customers who can order through a web interface. As a backup, we will consider distribution through licensing to existing companies in the United States that already offer DNA-origami as products, such as Guild Biosciences and Parabon Nanolabs.