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

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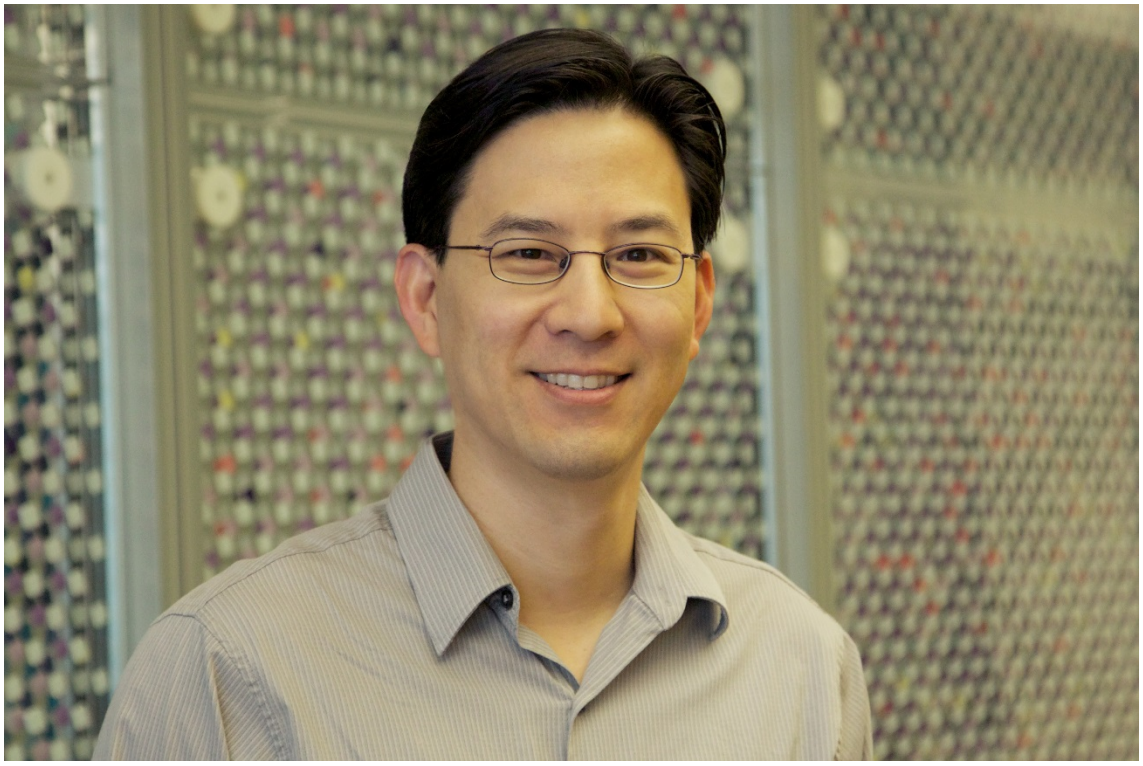
Abstract: Atomically precise manufacturing (APM) seeks to produce materials and devices with each atom in its designated position. Here we are developing self-assembling molecular printers as prototypes of integrated nanosystems for APM. In doing so, we will establish a baseline technology where none currently exists. Our three-year goal is to demonstrate two architectures for DNA-based 2D printers, validate their performances in patterning on a DNA-origami canvas with <5-nm-pitch grid spacing, and characterize the error and failure rates of these prescribed functional behaviors. We envision first-generation MAM nanosystems implemented as DNA-origami frameworks constructed with sub-nanometer precision by self-assembly. These prototypes will be actuated by cycles of DNA strand displacement and will achieve positioning accuracies on the order of a nanometer; the performance of the systems will be validated using electron microscopy and super-resolution fluorescence microscopy. DSD-MAM nanosystems will operate at low speeds and with high failure rates, and will be restricted to mild aqueous environments. Nonetheless, they will allow exploration of the potential of APM and will initiate a bootstrapping cascade of molecular machine-tool development. When they become sufficiently robust, first-generation devices will direct the assembly of next-generation MAM nanosystems from highly crosslinked, multi-nanometer-scale building blocks synthesized by bulk chemistry (e.g. spiroligomers). The improved materials properties, including enhanced rigidity, of these and subsequent generations of printers will advance manufacturing precision, driving parallel improvements in the local control of chemical-bond formation. This bootstrapping evolution – which parallels the development of machine tools during the first industrial revolution – will continue until APM becomes a practical manufacturing technology.

Bio Note: William Shih is a Professor in the Department of Biological Chemistry and Molecular Pharmacology at Harvard Medical School and the Department of Cancer Biology at the Dana-Farber Cancer Institute and a Core Faculty member at the Wyss Institute for Biologically Inspired Engineering at Harvard. William studied Biochemical Sciences at Harvard for his A.B. (1990–1994) and Biochemistry at Stanford for his Ph.D. (1994–2000) He did a postdoctoral fellowship at The Scripps Research Institute (2001–2004) and has since been back at Harvard as a faculty member. William was a 2008 NIH Director's New Innovator Awardee, a 2013 Blavatnik National Award Finalist in the Physical Sciences, and the 2017 Foresight Prize Awardee in Experimental Nanotechnology.

William is overseeing an effort to apply Synthetic Biology approaches to the development of self-assembling DNA nanostructures and devices for use in biomedical applications. In addition to carrying genetic information, DNA is increasingly being explored for its use as a building material. This new process is called DNA origami because a long strand of DNA can be programmed to fold in on itself to create specific shapes, much as a single sheet of paper is folded to create a variety of designs in the traditional Japanese art. Using long biologically produced DNA strands to construct particles with precisely specified shapes, William is able to approximate a level of complexity that rivals that of the molecular machinery found in cells. To

achieve structures of even greater complexity, his laboratory is pioneering methods for hierarchical assembly of these particles into three-dimensional networks with site-specific control over chemical functionalization and mechanical actuation. This work could lead to breakthroughs in manufacturing and medicine. For example, these incredibly tiny forms could be used as cogs in a machine for molecular manufacturing, optical reporters for bioimaging, and carriers for delivery of cancer drugs deep inside the body.



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