

DNA as a Molecular Engineering Platform for Defense Applications



PRESENTED BY:

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2020-12-01



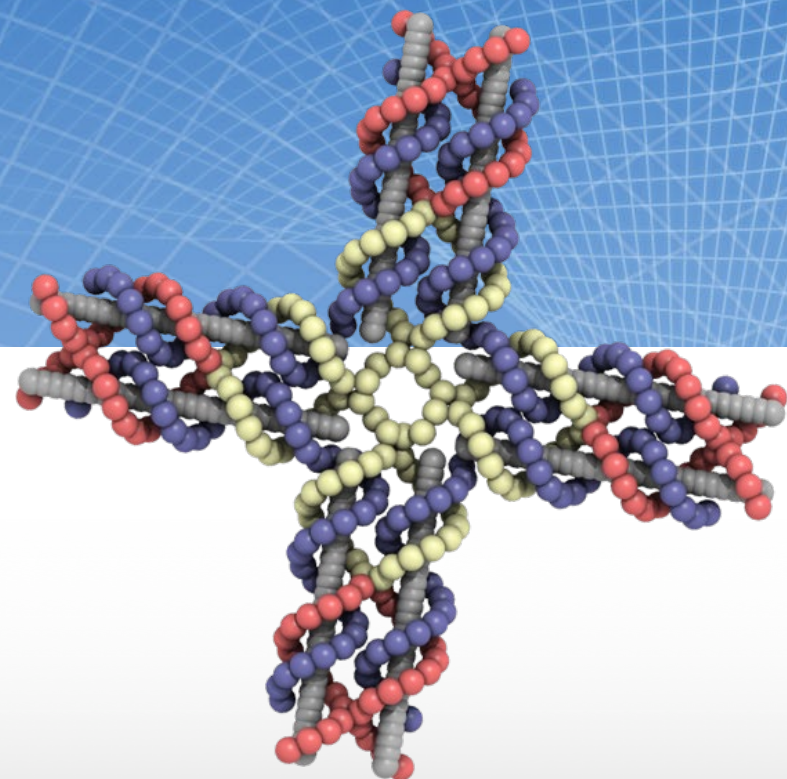
*Homeland Defense & Security
Information Analysis Center*

DNA as a Molecular Engineering Platform for Defense Applications

HDIAC

1 Dec 2020

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Co-Founder & CEO

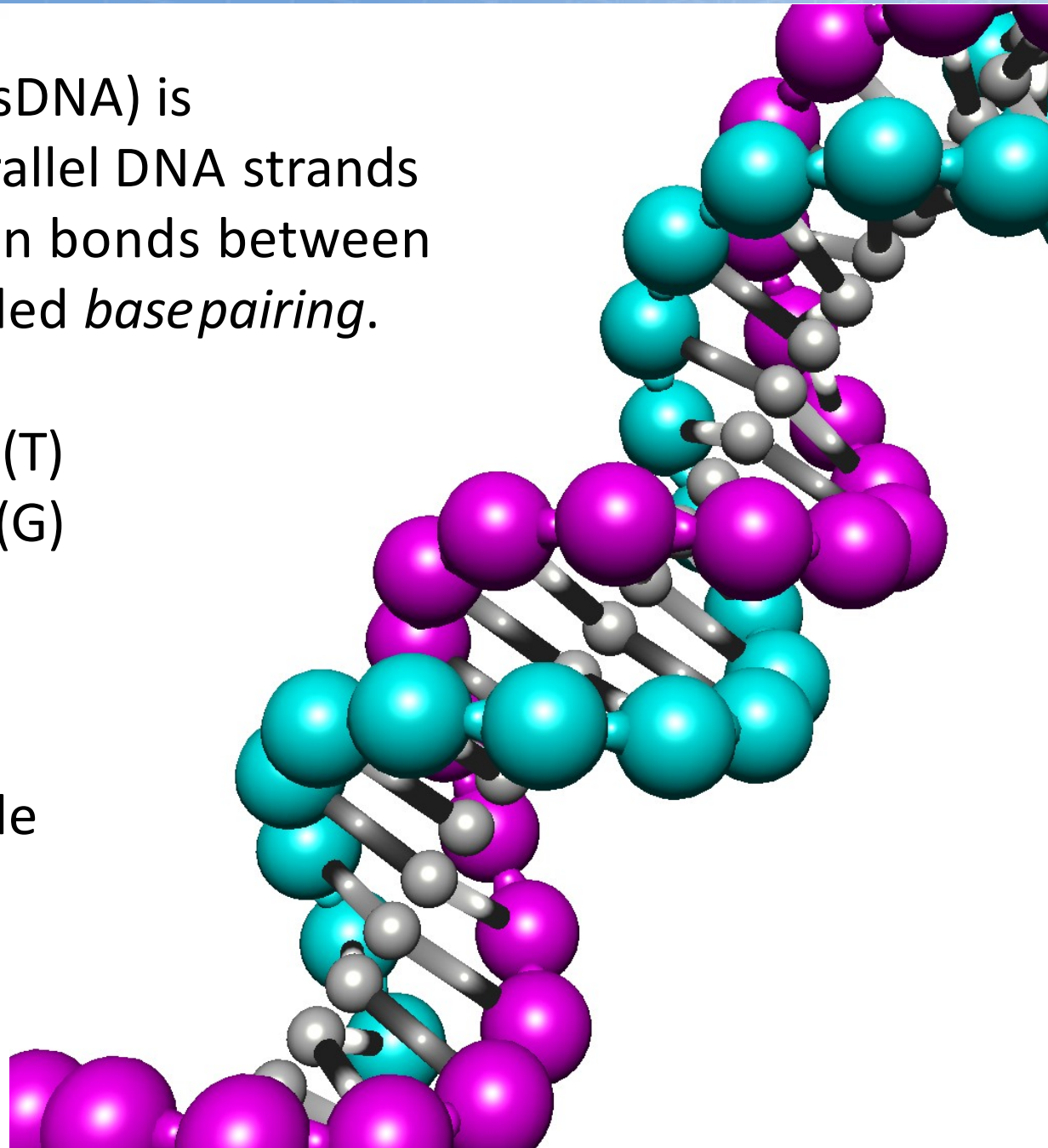


DNA Basics

Double-stranded DNA (dsDNA) is comprised of two antiparallel DNA strands held together by hydrogen bonds between nucleobases, which is called *base pairing*.

adenine (A) \leftrightarrow thymine (T)
cytosine (C) \leftrightarrow guanine (G)

Single bead per nucleotide representation

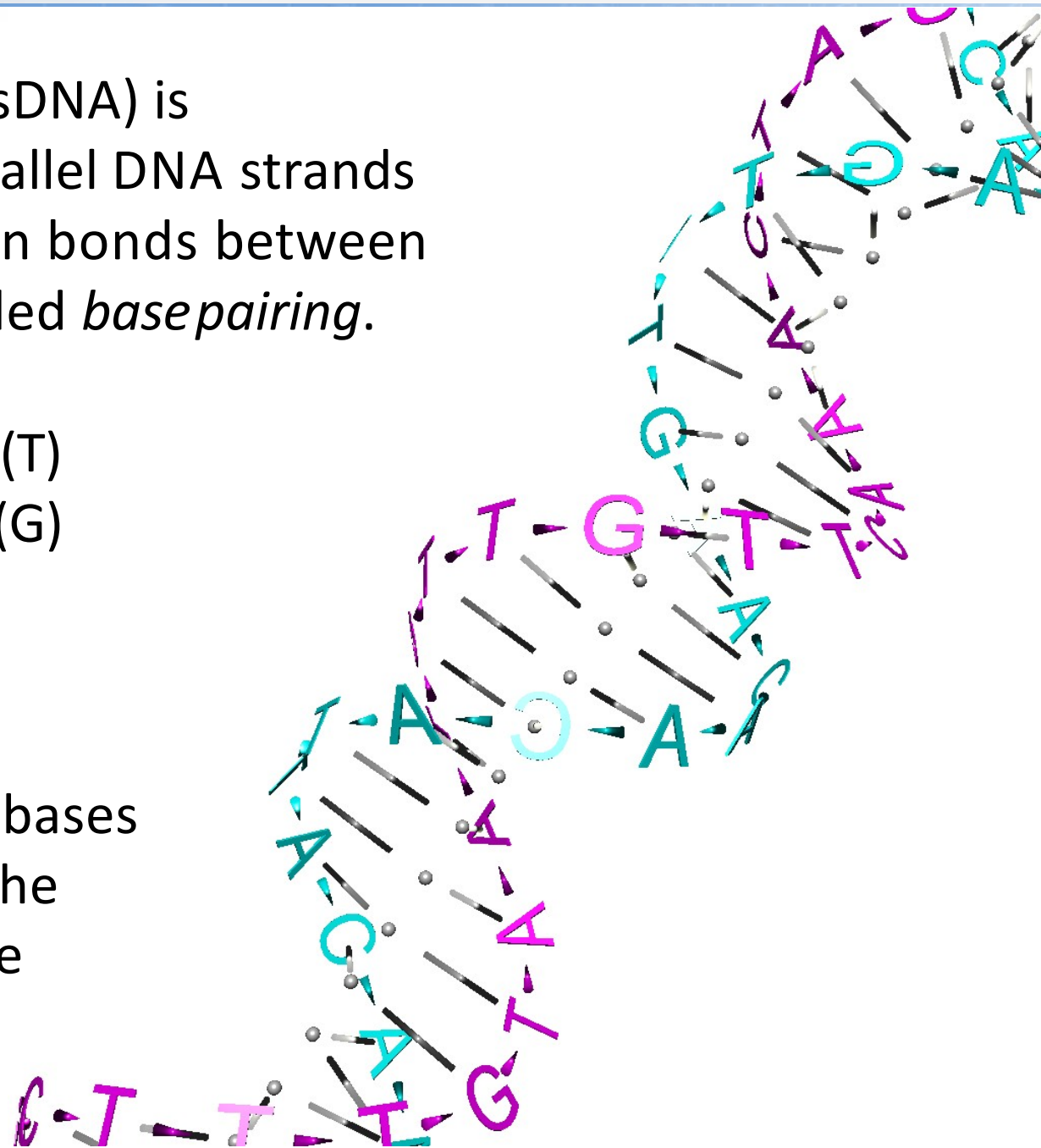


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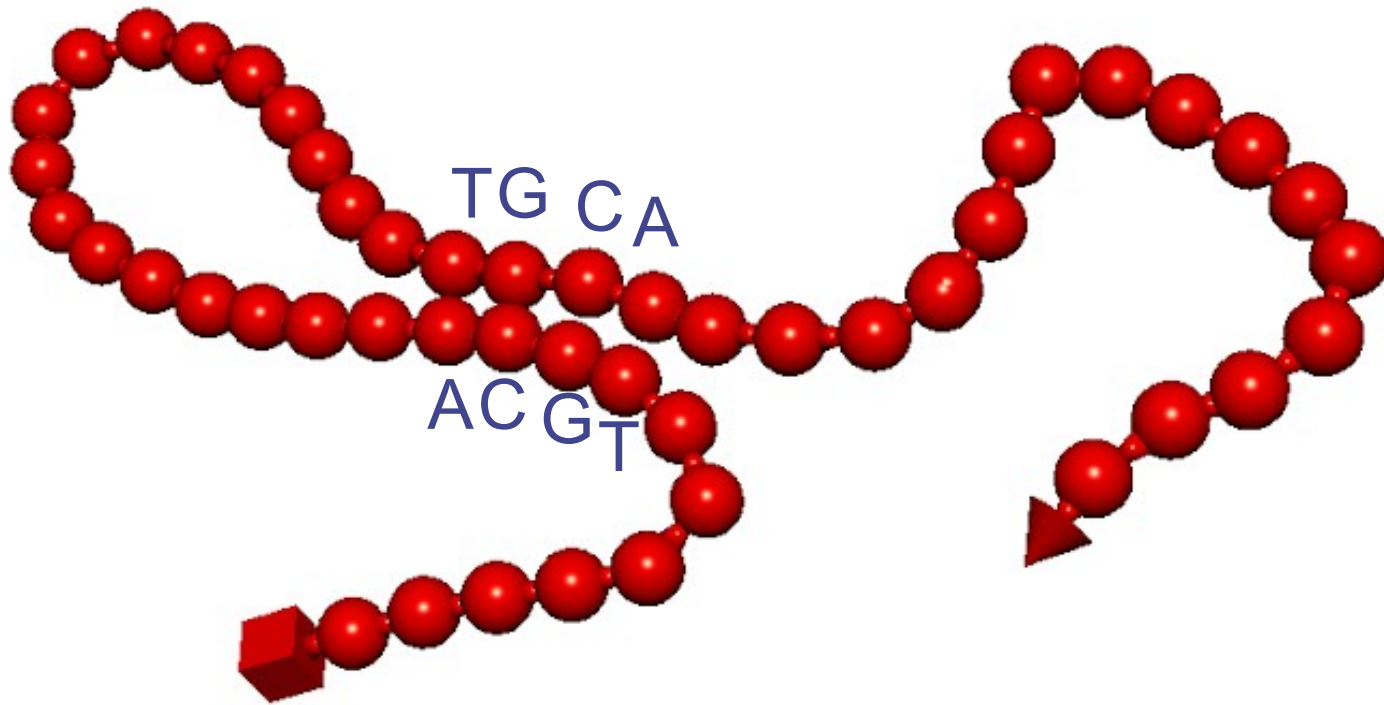
adenine (A) \leftrightarrow thymine (T)
cytosine (C) \leftrightarrow guanine (G)

Segments of consecutive bases that base pair are called the *reverse complement* of one another.



DNA Basics

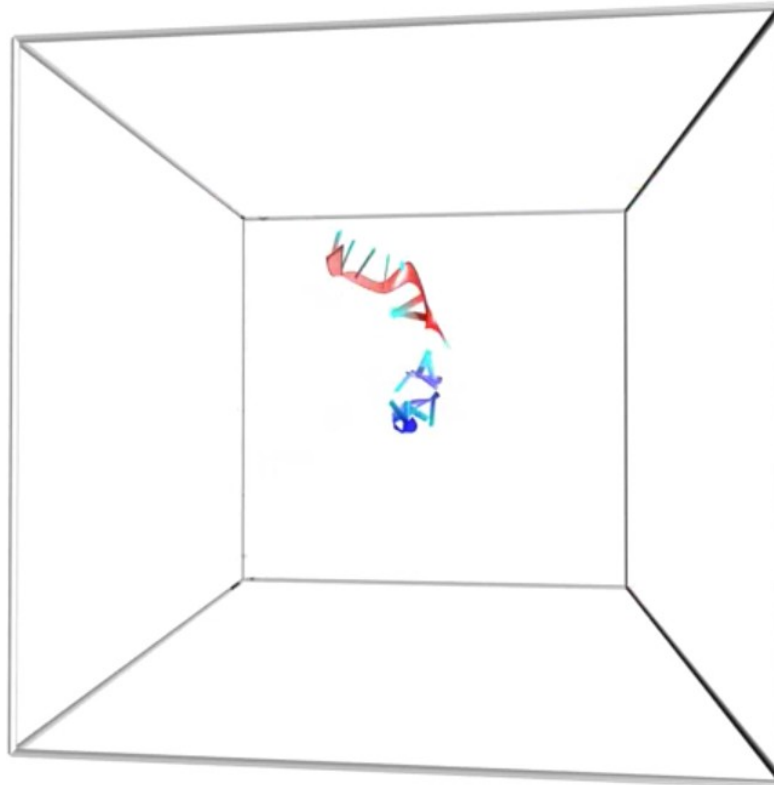
Single-stranded DNA (ssDNA) is not helical and can complement with itself along stretches that are complementary.



ssDNA can be readily synthesized in lengths ranging from short oligonucleotides ("oligos") (<50 bases) to genescale (5000 bases).

Duplex Hybridization (Video 1)

oxDNA Simulation

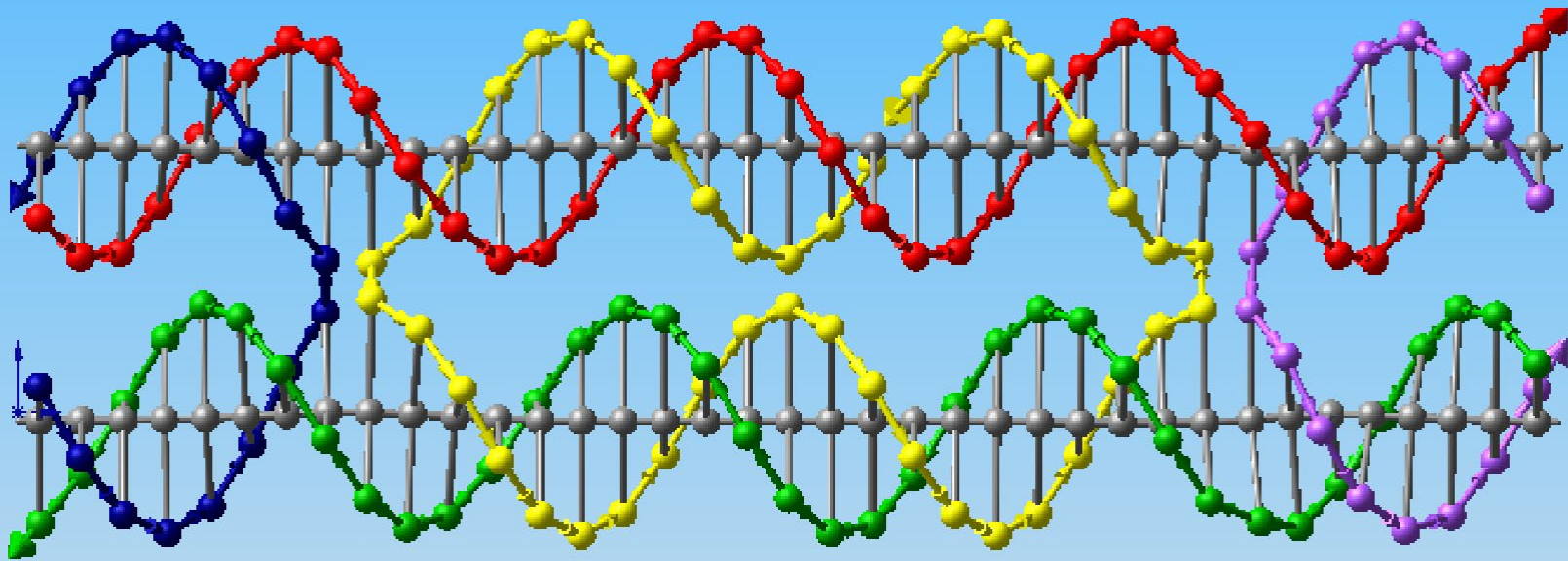


P. Šulc, F. Romano, T. E. Ouldridge, L. Rovigatti, J. P. K. Doye, A. A. Louis, J. Chem. Phys. 137, 135101 (2012)

https://dna.physics.ox.ac.uk/index.php/Screenshots_and_movies#double-stranded_DNA

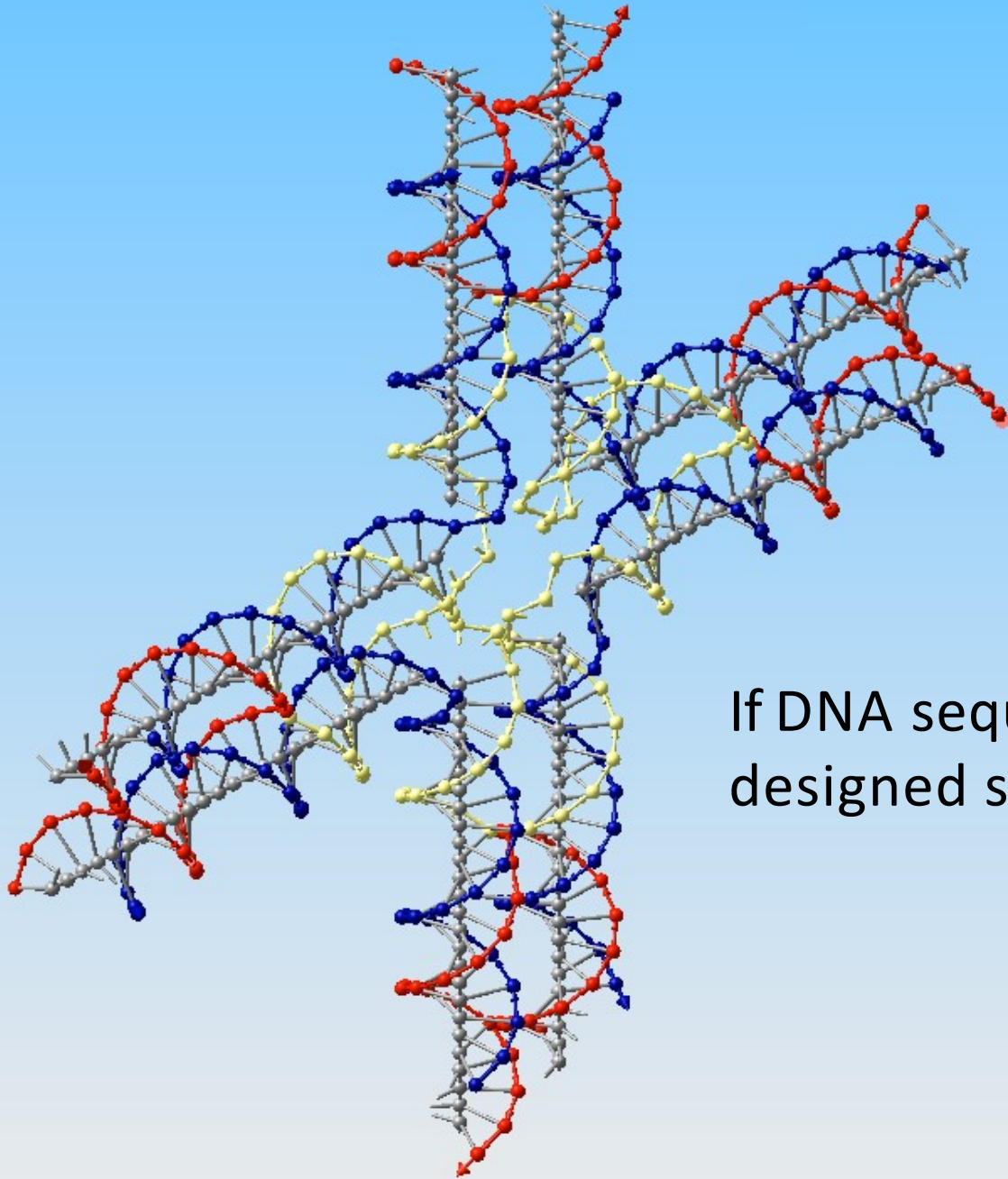
Structural DNA

Single-stranded synthetic DNA can be used as a nanoscale construction material and woven into molecular designs



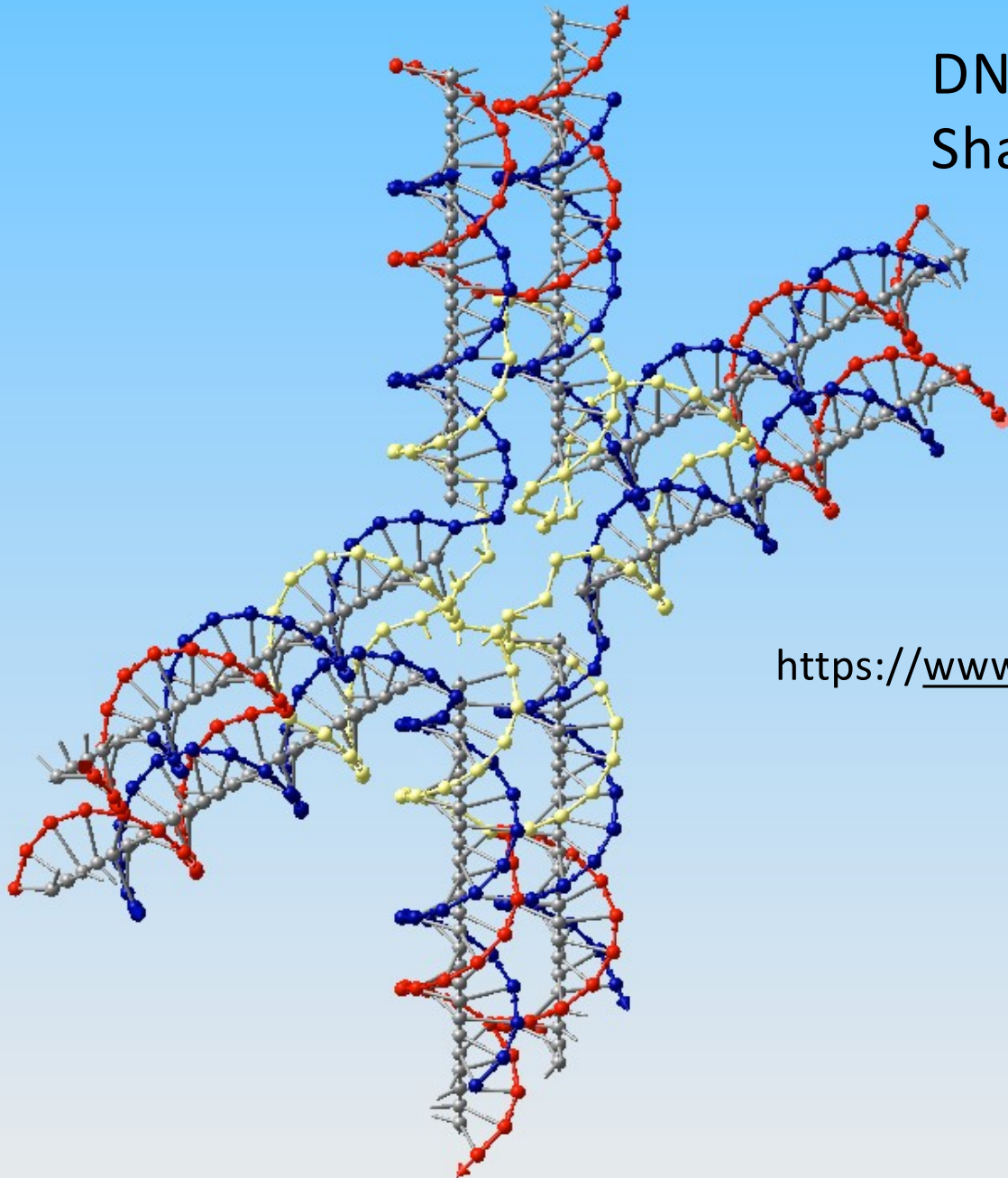
Notice how the blue, yellow and lavender strands participate in both the upper and lower helices.

Structural DNA



If DNA sequences are chosen correctly, designed structures will self-assemble.

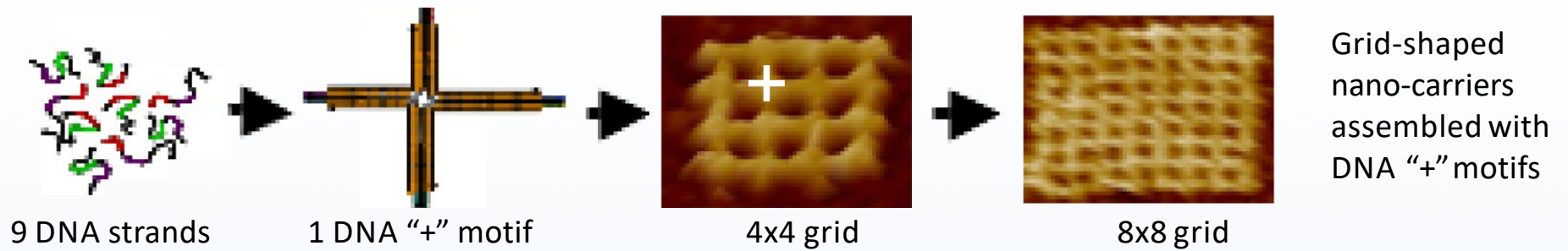
Origami Hybridization (Video 2)



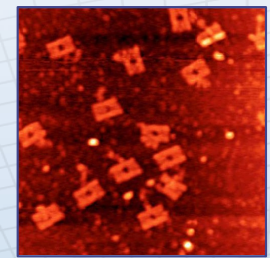
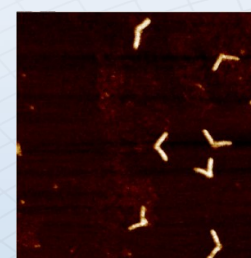
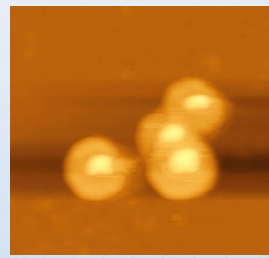
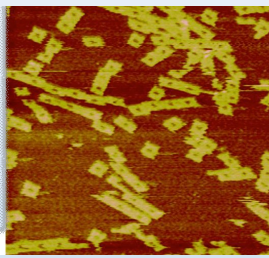
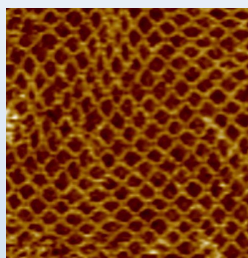
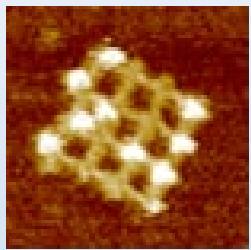
DNA origami folding animation
Shawn Douglas

https://www.youtube.com/watch?v=p4C_aFlyhfl

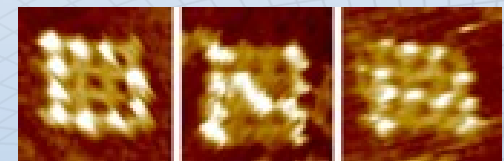
Example DNA Nanostructures



With properly ordered DNA sequences, arbitrarily shaped nano-carriers can be produced en masse via self-assembly and functionalized with a rich assortment of subcomponents to create custom, even personalized, pharmaceuticals, vaccines and reagents.



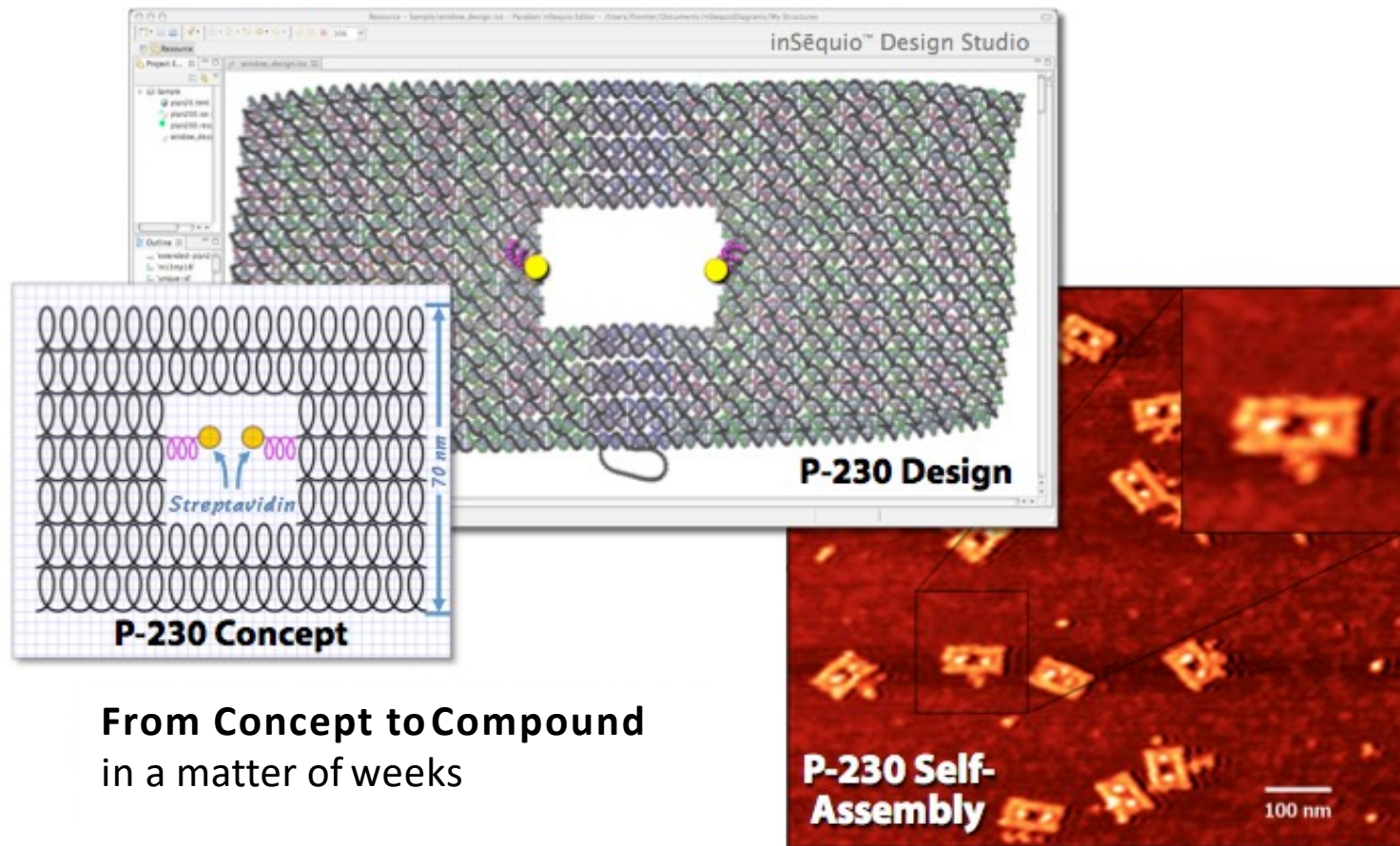
AFM images showing just a few of the types of nanostructures that can be produced with Essemblix.



D-N-A "written" in streptavidin on a nano-carrier surface

inSēquoio Design Studio

Parabon's **inSēquoio™ Design Studio** software, the development of which has been partially funded by the DoD, provides a powerful suite of computer-aided design (CAD) capabilities that enable design of sophisticated DNA nanostructures.



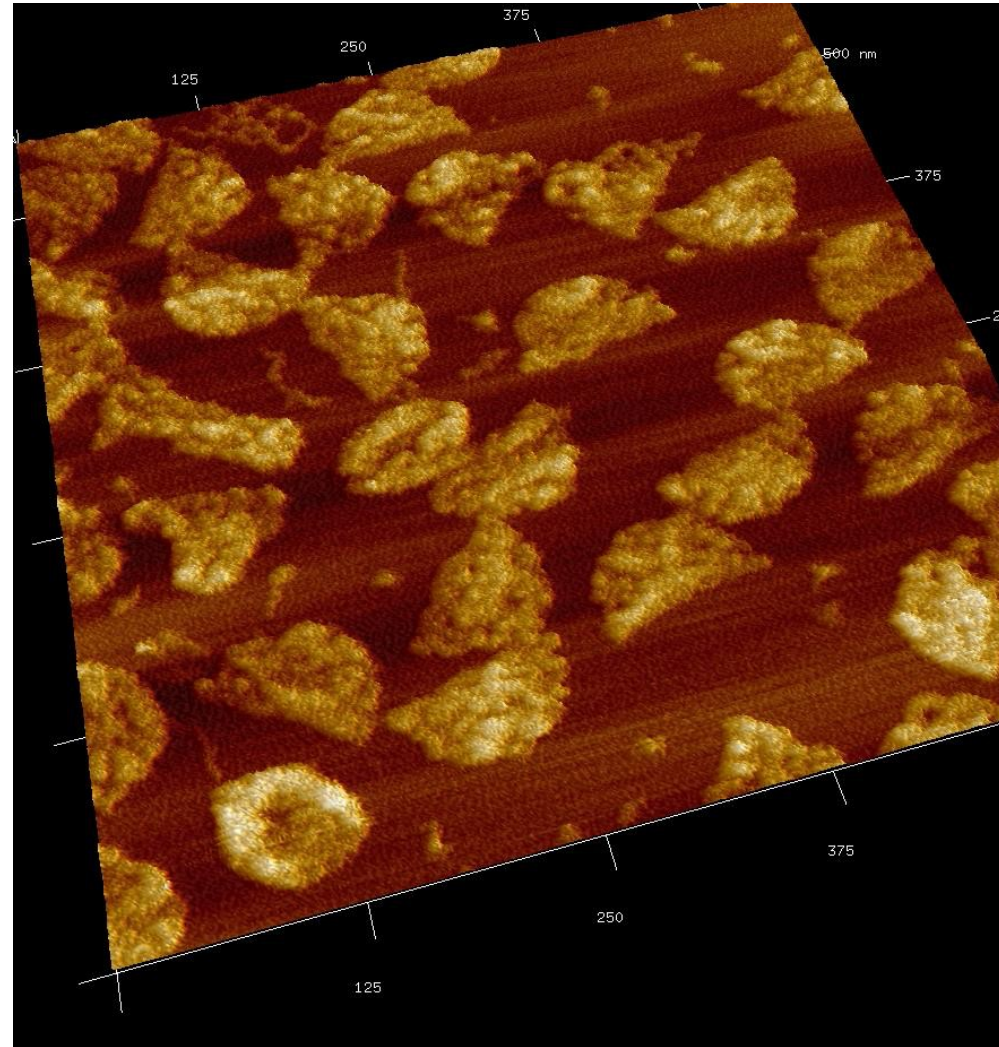
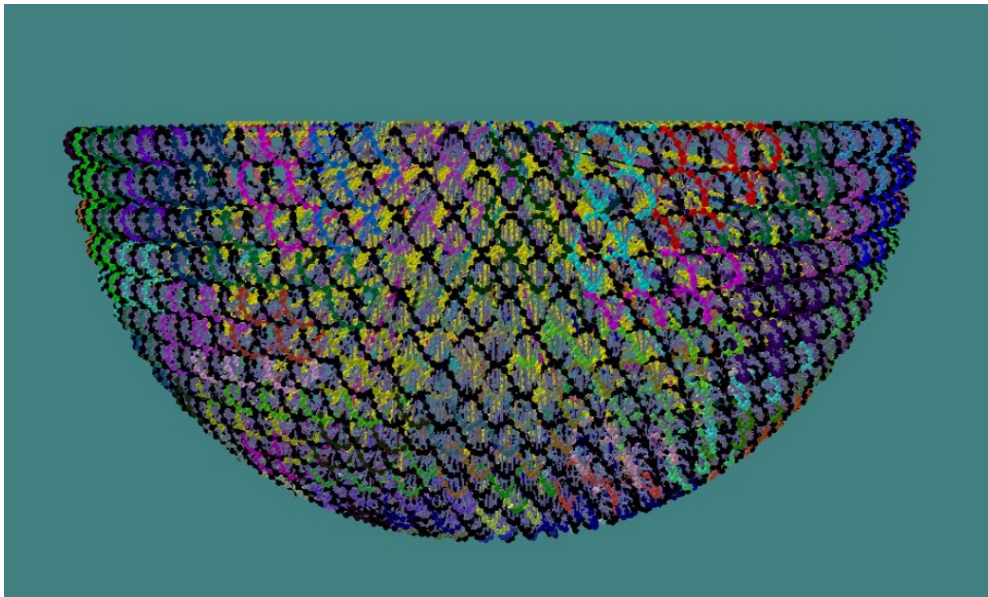
From Concept to Compound
in a matter of weeks

inSēquio3D (Videos 3-5)

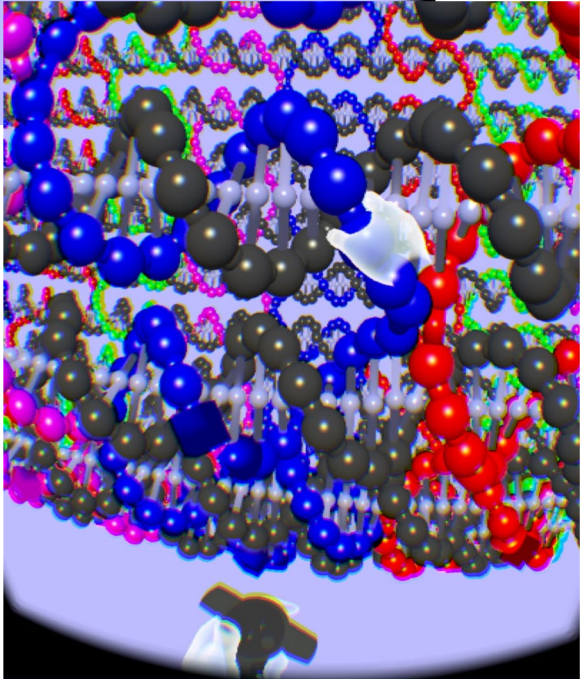
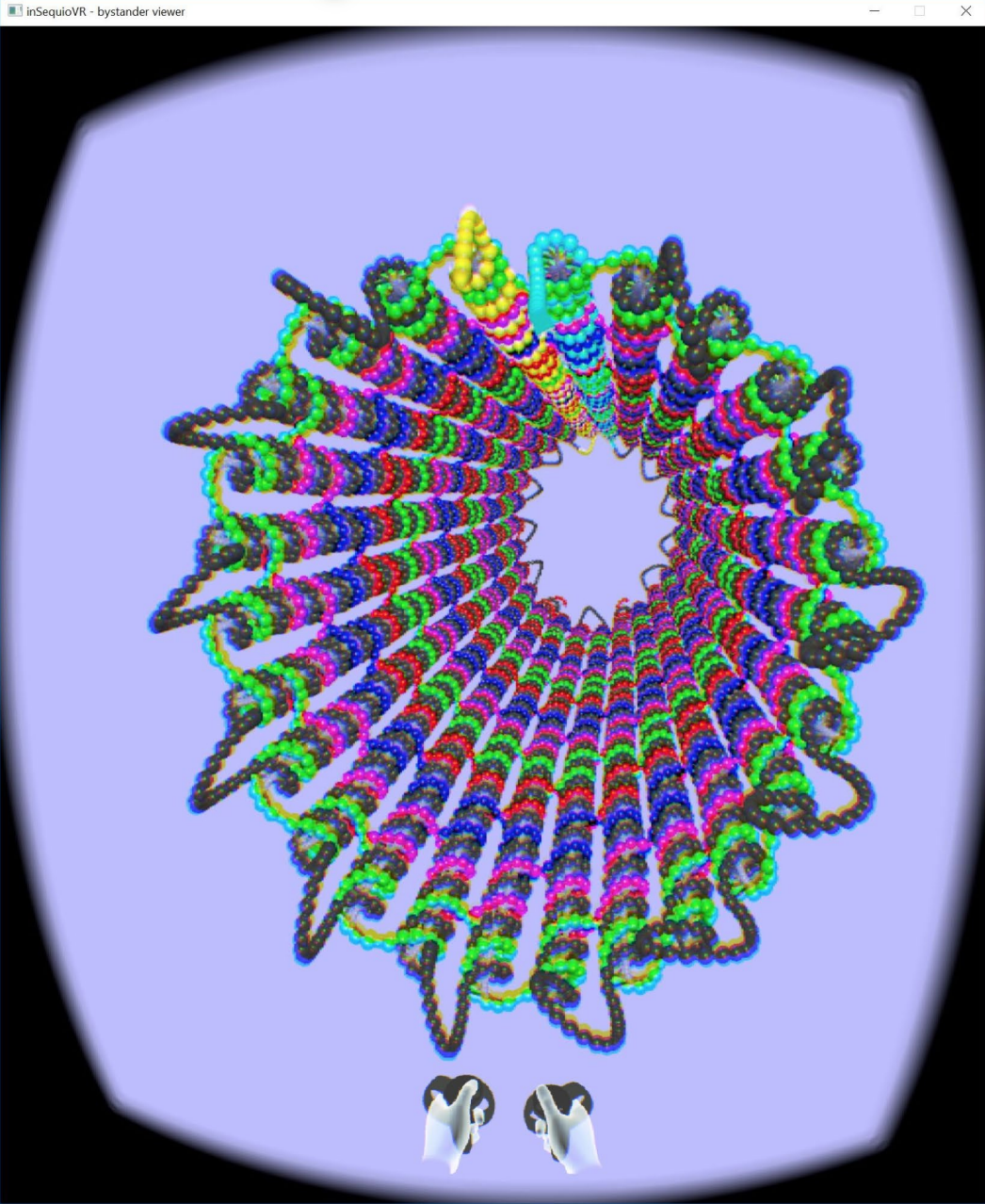
The screenshot displays the inSēquio3D software interface. The top menu bar includes File, Edit, Selection, Draw, Topology, Geometry View, Find, Analyze, Experimental, Windows, and Help. The toolbar contains various tools for editing and visualization, such as Nick, Splice, Crossover, Double Crossover, Remove Crossover, Pair Bases, Pair Bases Irregular, Unpair, Delete, Measure Distance, Move, Rotate, Rotate Axis, Copy, Fit All, Fit Selected, Home, Spin, Pick, Lasso Box, Clear Selections, ssDNA as Line, ssDNA as Circle, ssDNA as Polyline, dsDNA as Line, dsDNA as Circle, dsDNA as Interpolated Spline, Linker, Peptide as Line, Peptide as Circle, Peptide as Polyline, Global XY CP, Global YZ CP, and Global ZX CP. The main workspace is split into two views: a 2D Schematic (left) and a 3D Design (right). The 2D schematic shows several parallel DNA strands represented as lines with small rectangular boxes representing base pairs. The 3D design shows a detailed ball-and-stick model of the DNA structure, with atoms represented by spheres of different colors (black, green, red, yellow) and bonds as sticks. The background is a light blue gradient. On the right side, there are two panels: Properties and Strands. The Properties panel shows details for a selected strand, including Color (#ffff), Count (58), Name (staple_r10_002), Sequence (AGGATTAGAGATAACCCACAAGA...), Type (Strand), and Attributes (Linear). The Strands panel shows a table of strands with columns for Name, Length, and Sequence.

row:	Name	Length	Sequence
43	staple_r08_008	38	AAATAGCGATA...
44	staple_r08_009	32	CACCCACGAG...
45	staple_r08_010	42	AGCGGCTTTCA...
46	staple_r09_000	36	TCAGAAAACGC...
47	staple_r09_001	42	GCGACATCAG...
48	staple_r09_002	32	AGCAAGCTTT...
49	staple_r09_003	63	CATCGAAGITT...
50	staple_r09_004	42	GAAGCCCGAAA...
51	staple_r09_005	32	TCAAAAACGGA...
52	staple_r09_006	36	GATAGGCTCCA...
53	staple_r09_007	48	AAAGCTTTTAC...
54	staple_r09_008	36	TTAAGGTGAAT...
55	staple_r09_009	32	TCAGGTCTAAT...
56	staple_r09_010	37	TTACCATTACAT...
57	staple_r10_000	51	ATTTCGAATAT...
58	staple_r10_001	47	TCTTCGGAACCTG...
59	staple_r10_002	58	AGGATTAGAGA...
60	staple_r10_003	32	TACCGAGTAIAA...
61	staple_r10_004	54	CTTCTATGATAT...

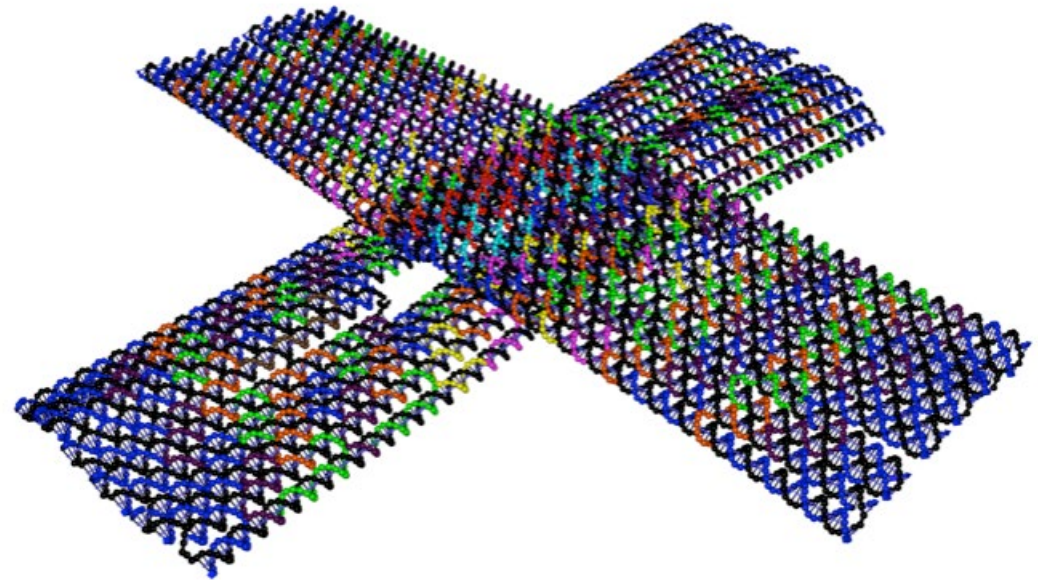
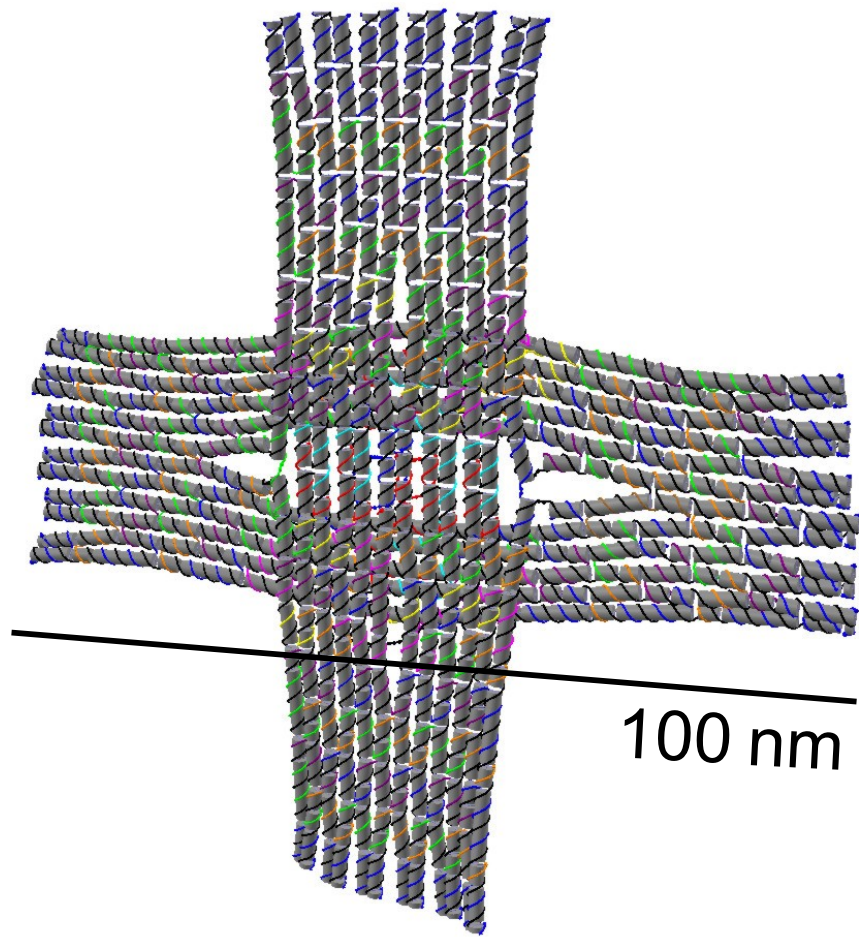
inSēquioVR



inSēquioVR



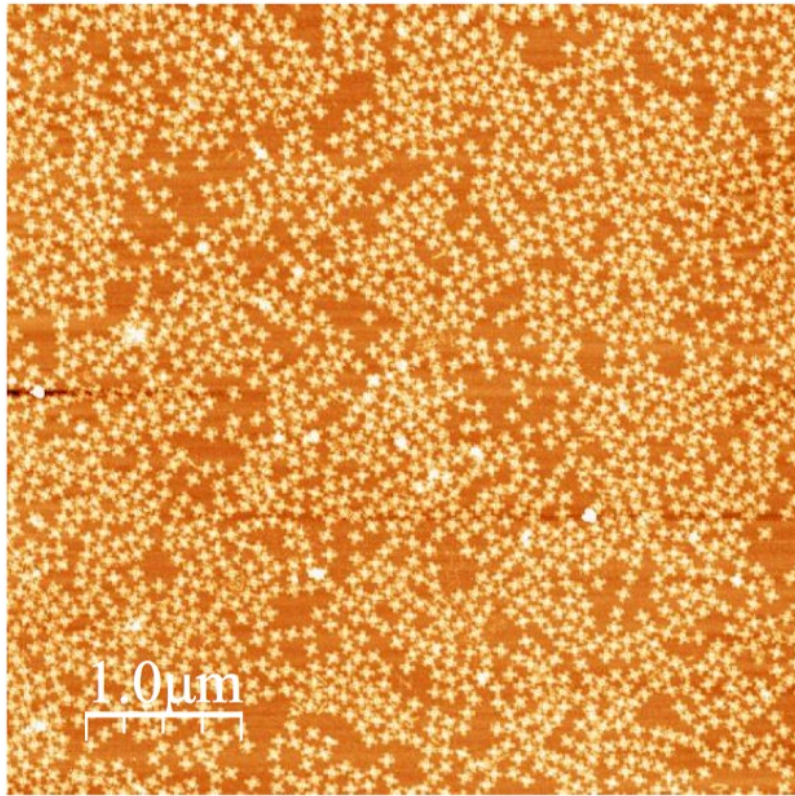
Cross-Tile Origami



Circumscribing a Human Hair

Avg diameter (d) of human hair (μm)	75
Avg circumference (πd) of human hair (μm)	235.6
Nanostructure width (nm)	100
Nanostructure width (μm)	0.1
Number of nanostructures required to circumscribe an average human hair	2356

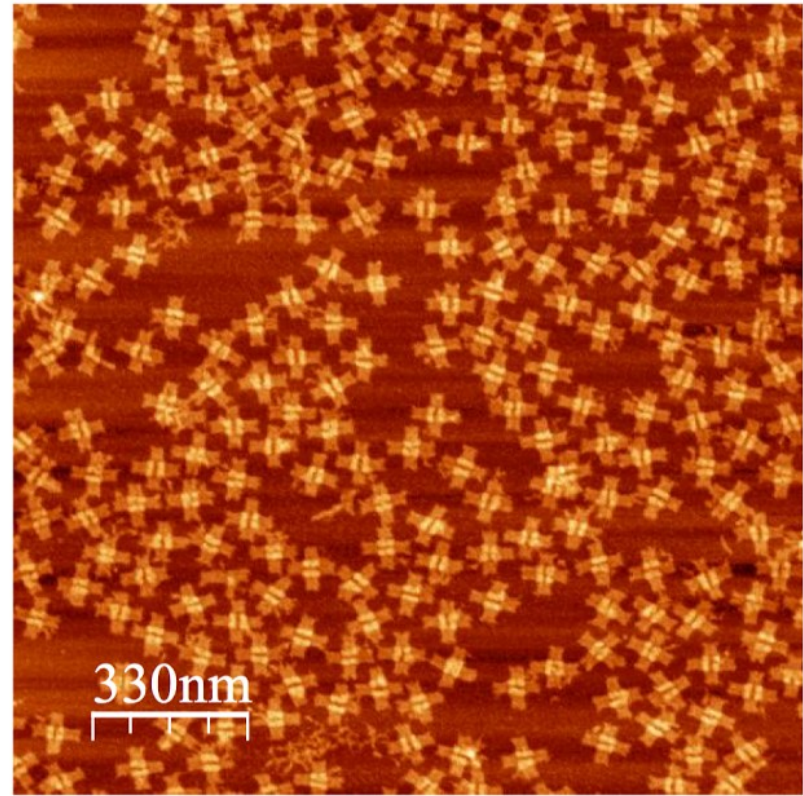
Cross-Tile Origami



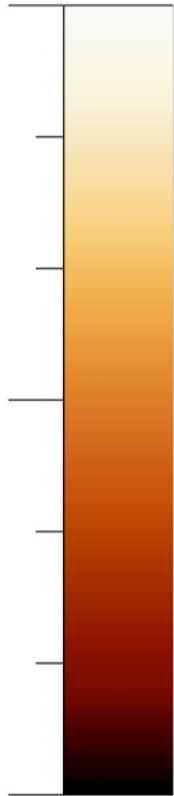
Scale: 5 X 5 μm^2



0.00 nm



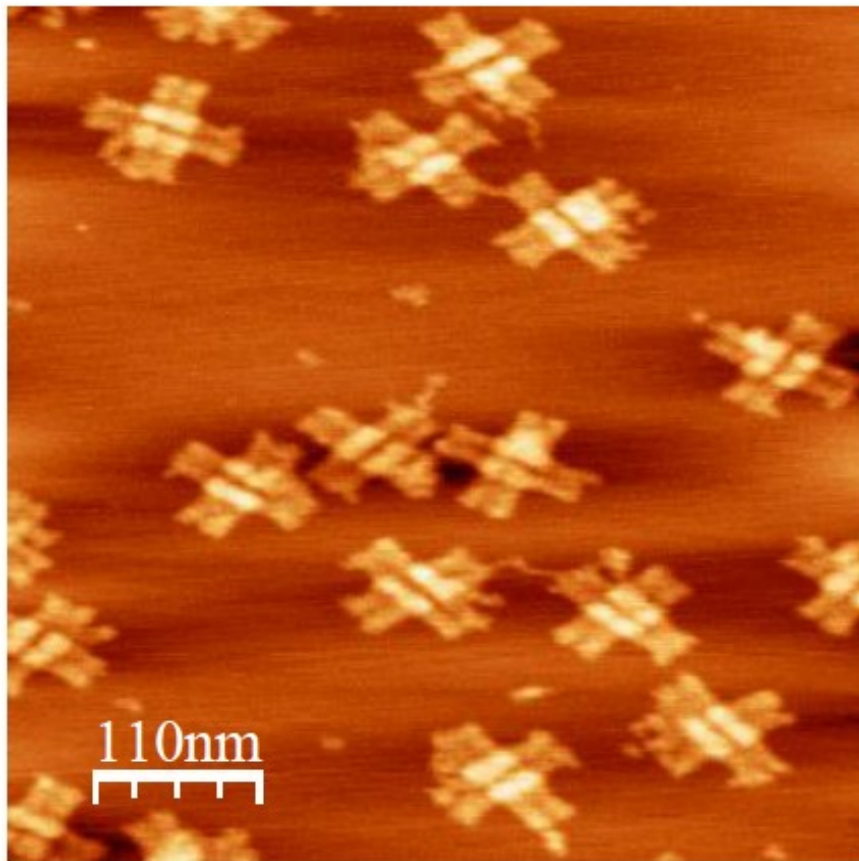
Scale: 1.7 X 1.7 μm^2



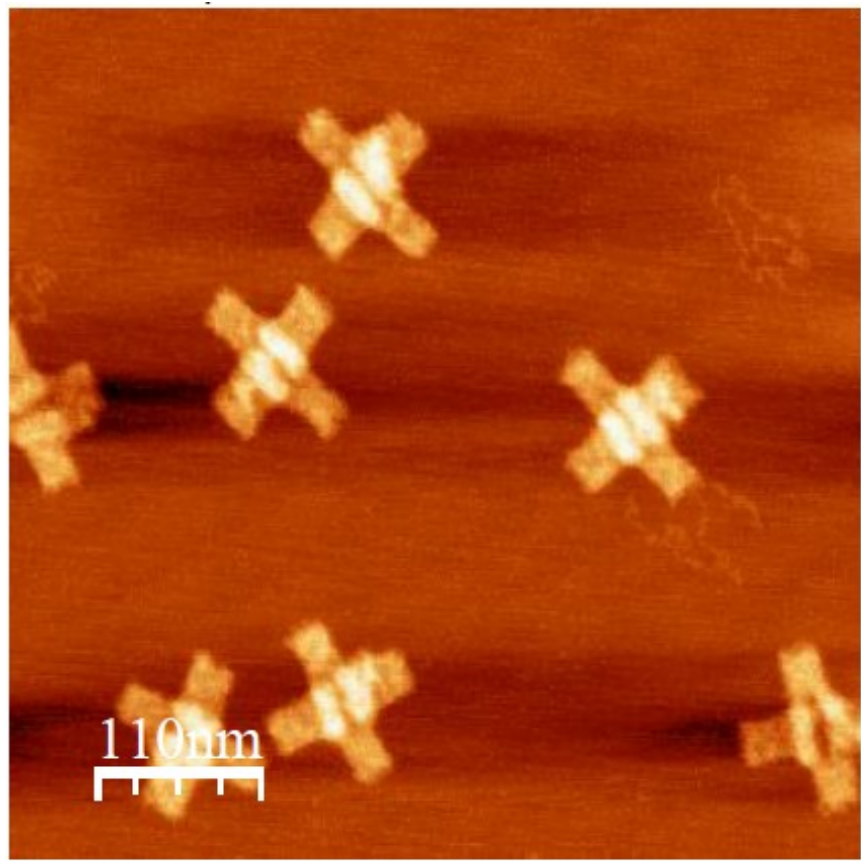
0.00 nm

Rahman M, Neff D, and Norton M. "Rapid, high yield, directed addition of quantum dots onto surface bound linear DNA origami arrays." *Chemical Communications* 50.26 (2014): 3413-3416.

Cross-Tile Origami

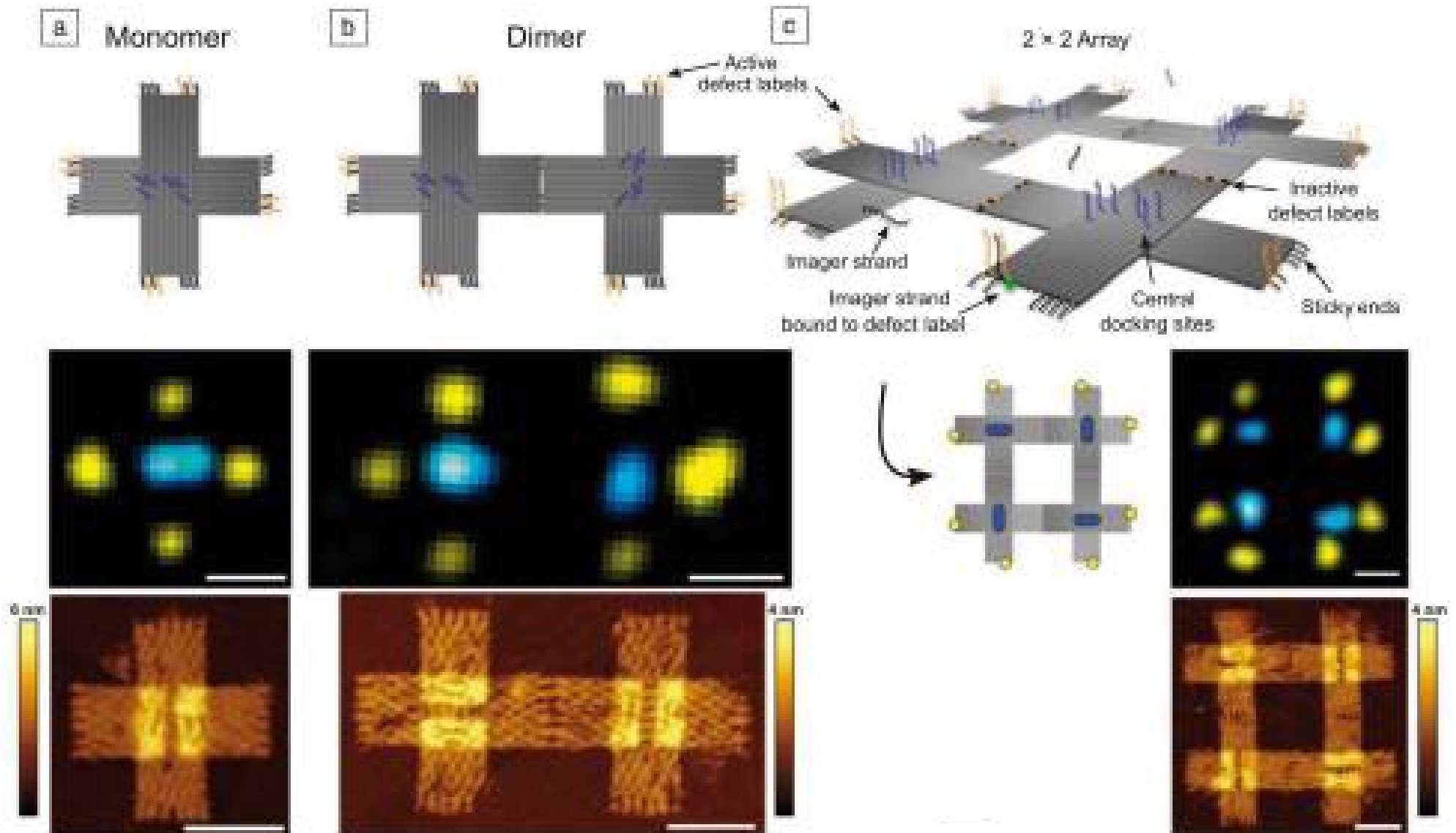


560 nm x 560 nm



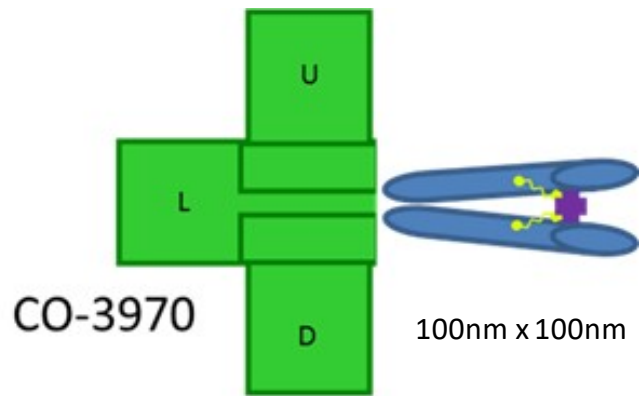
550 nm x 550 nm

Super-resolution Microscopy



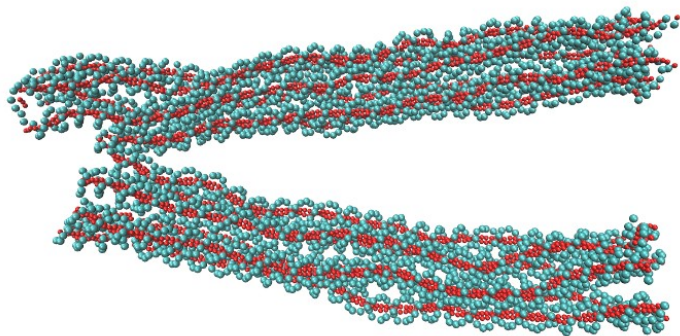
Graugnard, Elton, et al. "Nanometrology and super-resolution imaging with DNA." *MRS bulletin* 42.12 (2017): 951.

Artificial Antibodies

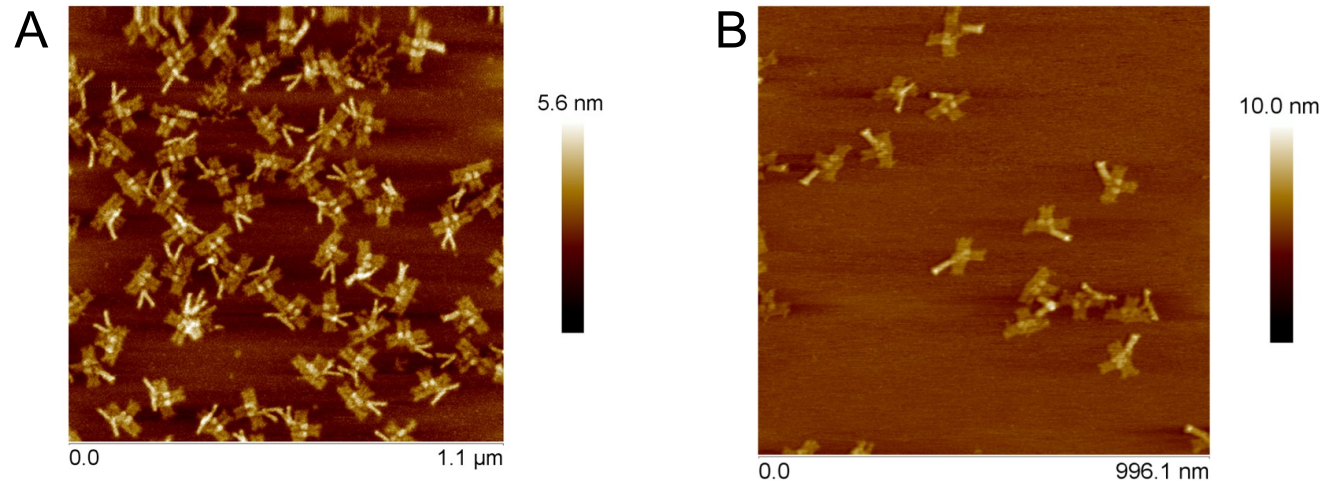


Single molecule nanosensor

Objective: Develop a general purpose, single-molecule nanosensor that can capture and report molecular binding of a target species.

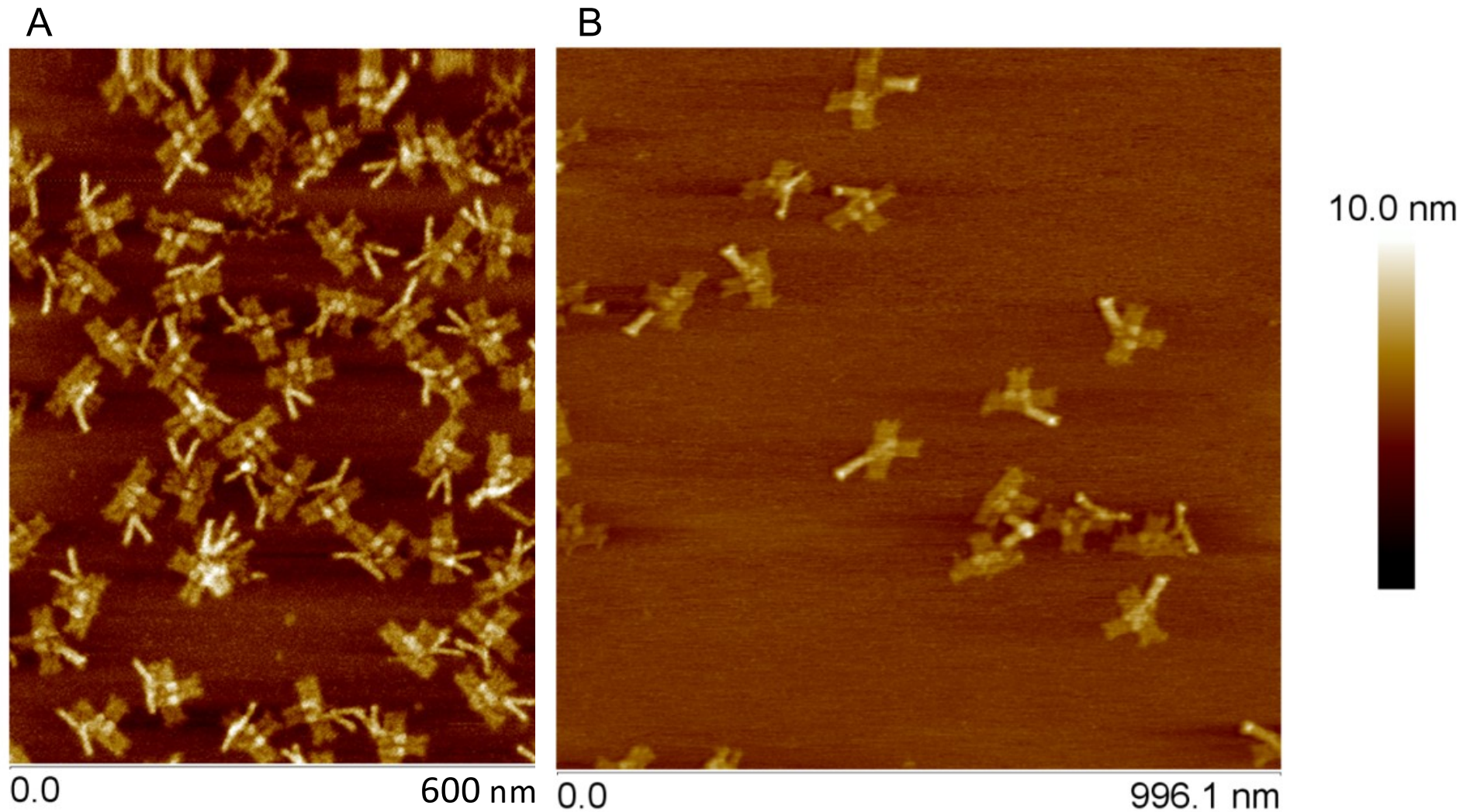


MD simulation of pinceraction



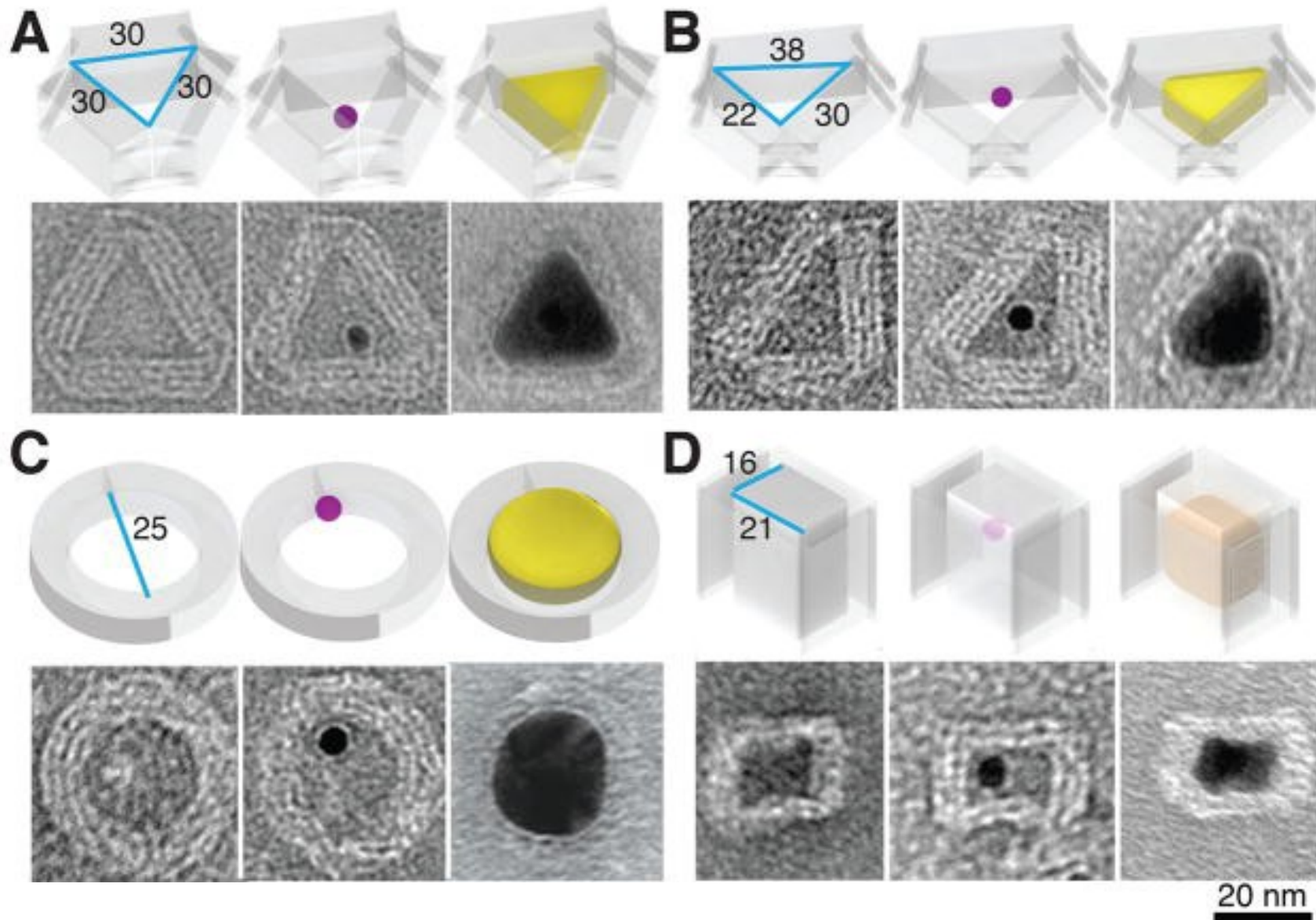
AFM images of CO-3970 sensor before and after introduction of target species (steptavidin). Closed state in Figure B indicates successful capture.

Artificial Antibodies



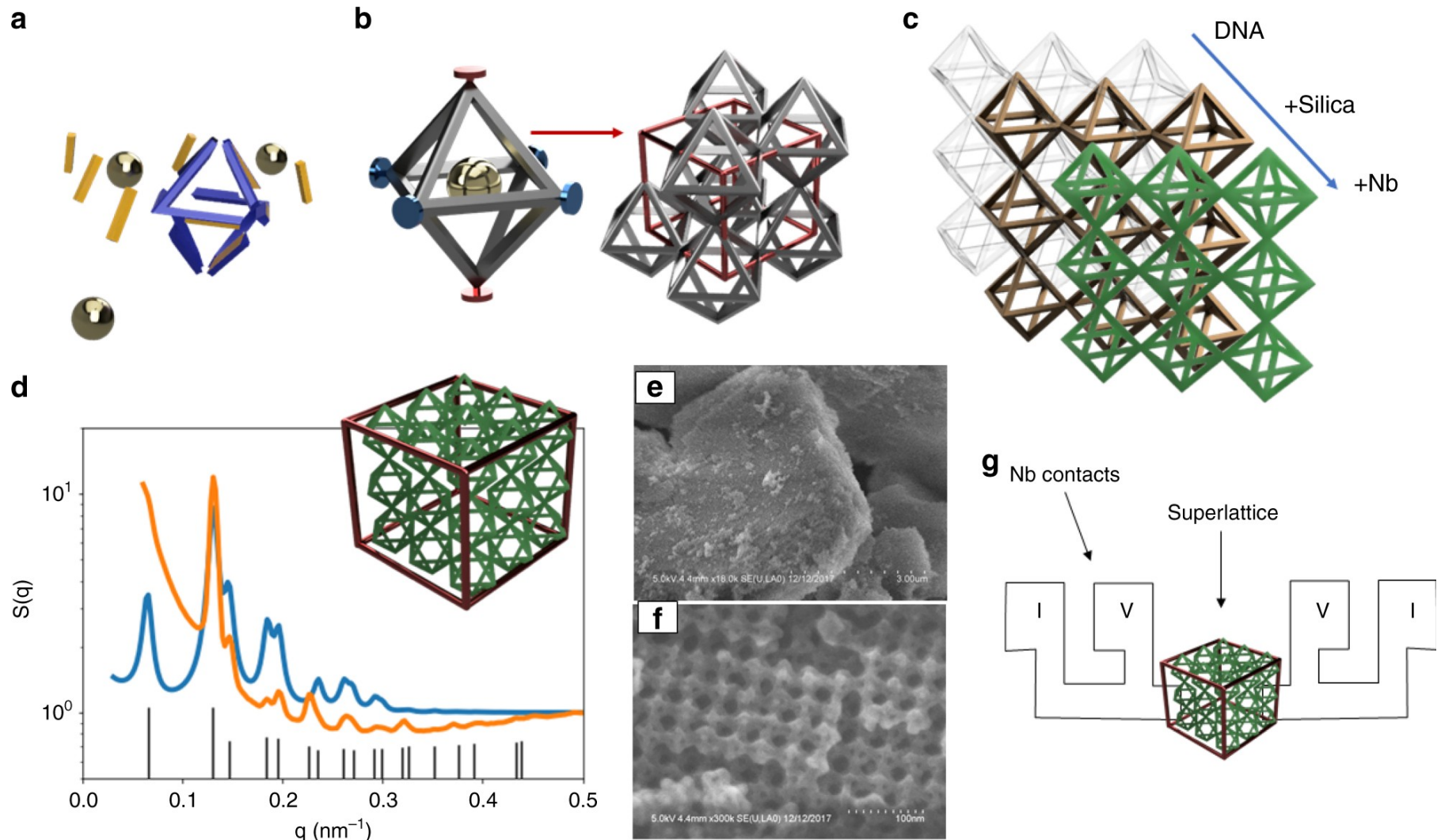
AFM images of CO-3970 sensor before and after introduction of target species (steptavidin). Closed state in Figure B indicates successful capture.

Nanoscale Molding



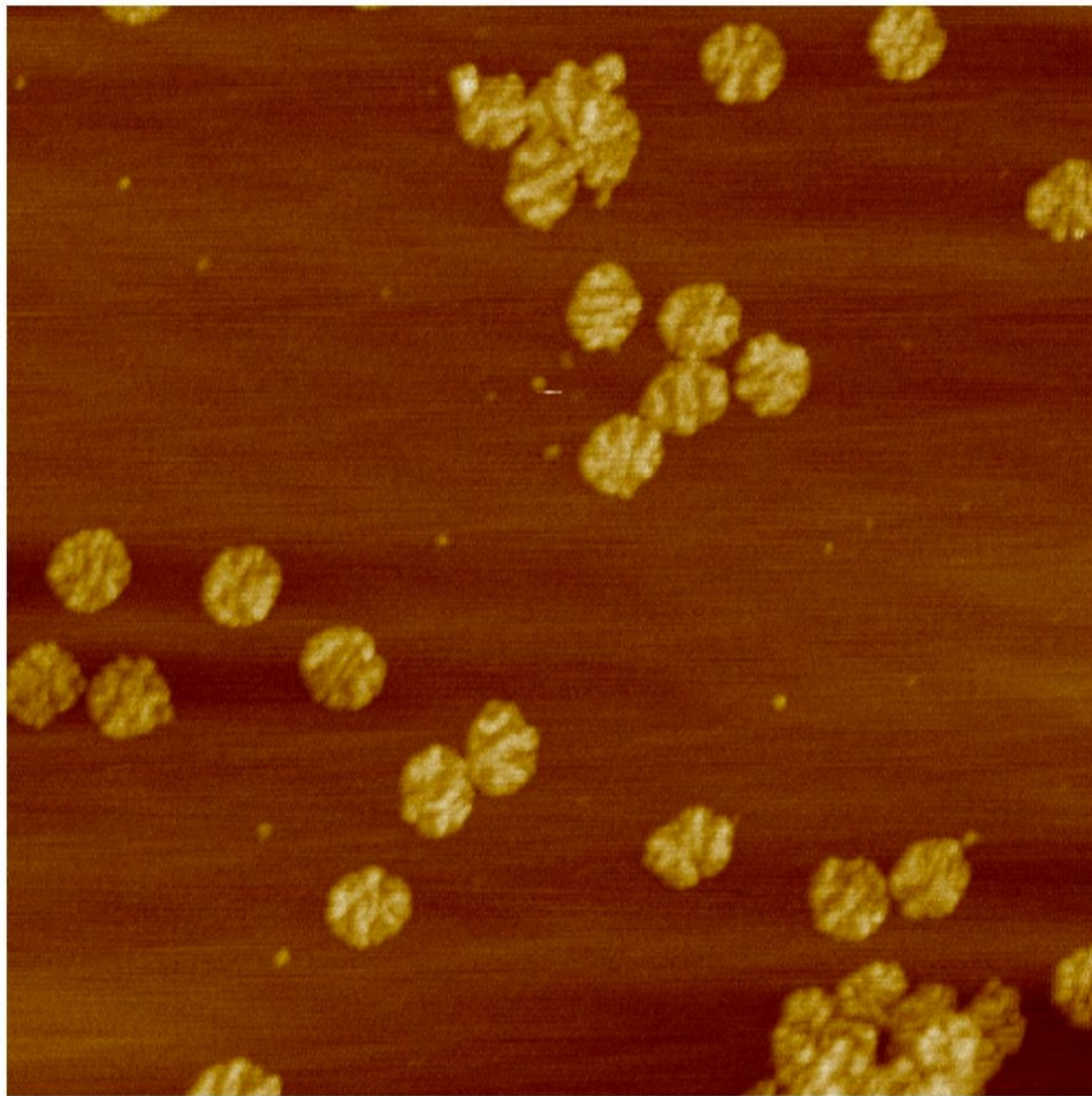
Sun, Wei, et al. "Casting inorganic structures with DNA molds." *Science* 346.6210 (2014).

Superconducting 3D Structures



Shani, Lior, et al. "DNA-assembled superconducting 3D nanoscale architectures." *Nature communications* 11.1 (2020): 1-7.

DNA Nanocarriers



0.0

Height

1.7 μm

Parabon has several federally funded projects to explore use of DNA nanocarriers.

Two NIAID projects to develop vaccines against HIV.

One anticipated NCI project to develop a novel treatment for prostate cancer.

One DoD-funded project to develop cognitive boosting agents.

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