DNA as a Molecular Engineering Platform for Defense Applications

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HDIAC

1 Dec 2020

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PARABON®
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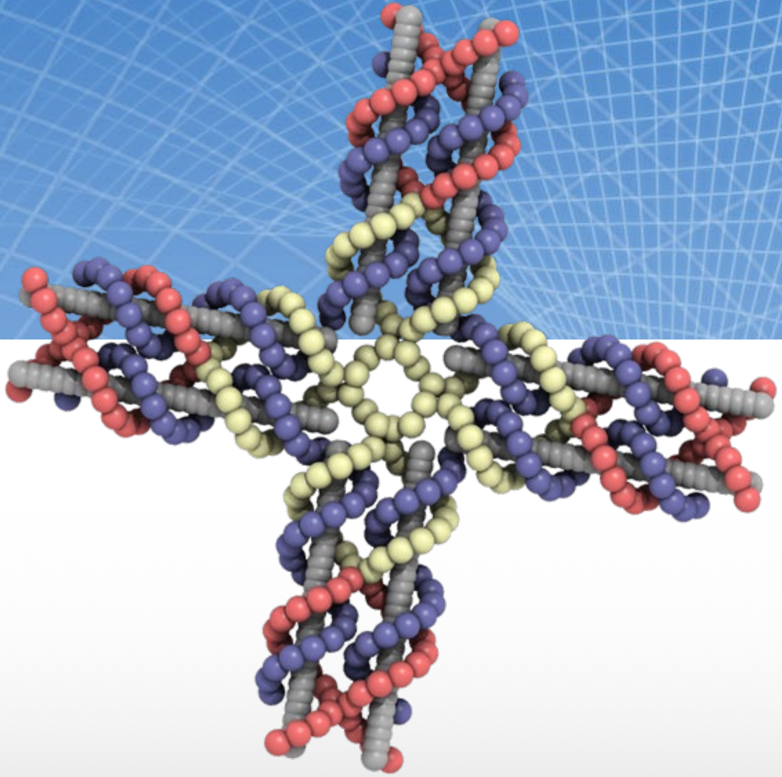
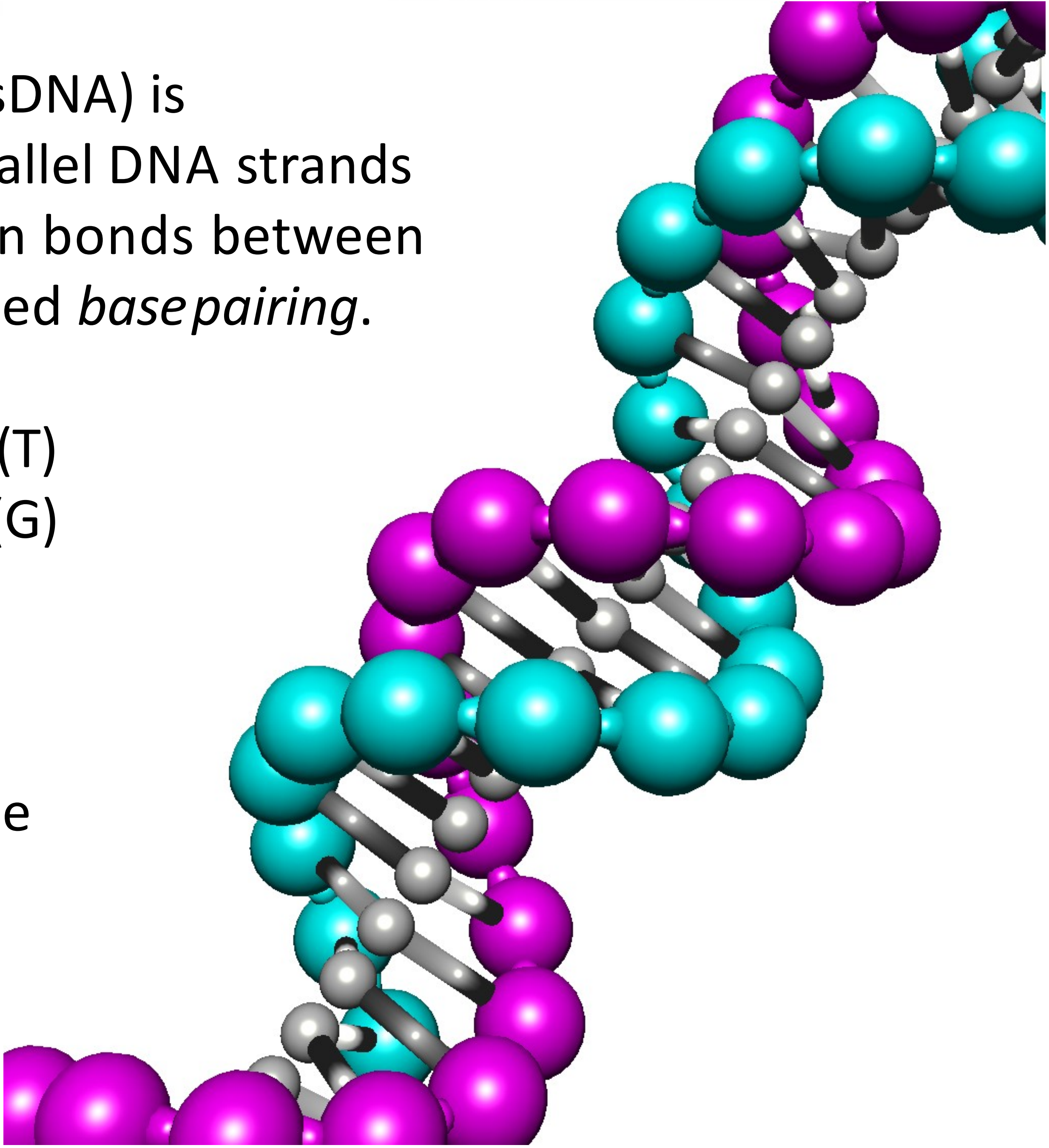


DNA Basics



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) <-> thymine (T)
cytosine (C) <-> guanine (G)

Single bead per nucleotide representation

DNA Basics

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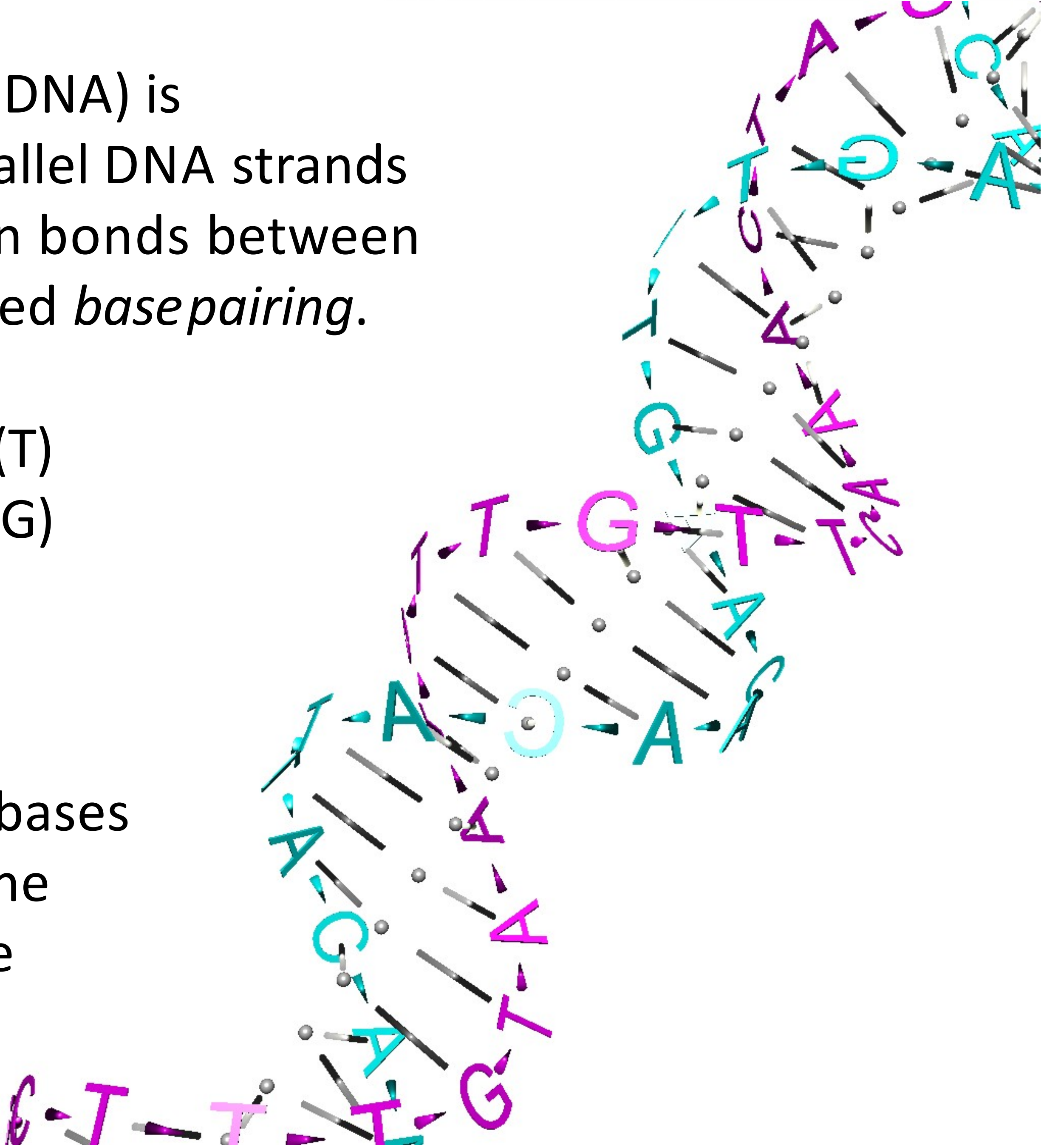
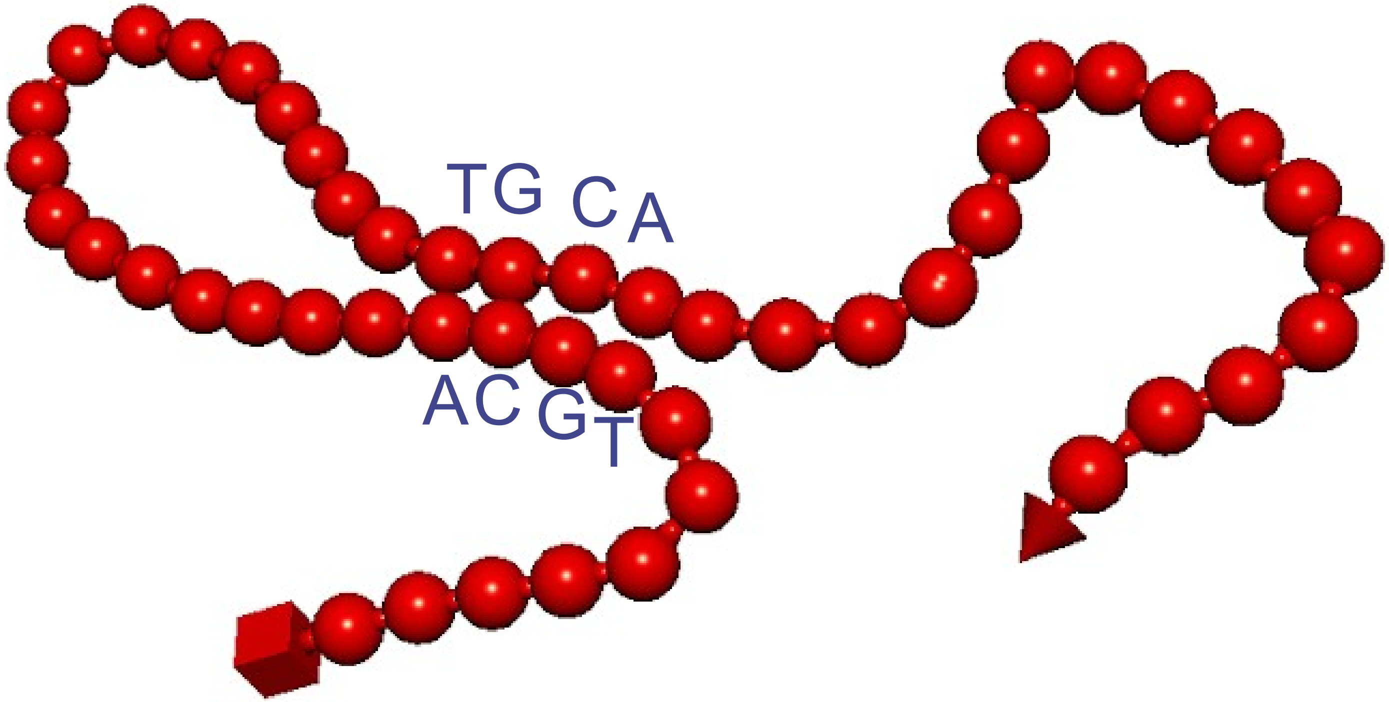


Segments of consecutive bases that base pair are called the *reverse complement* of one another.

DNA Basics

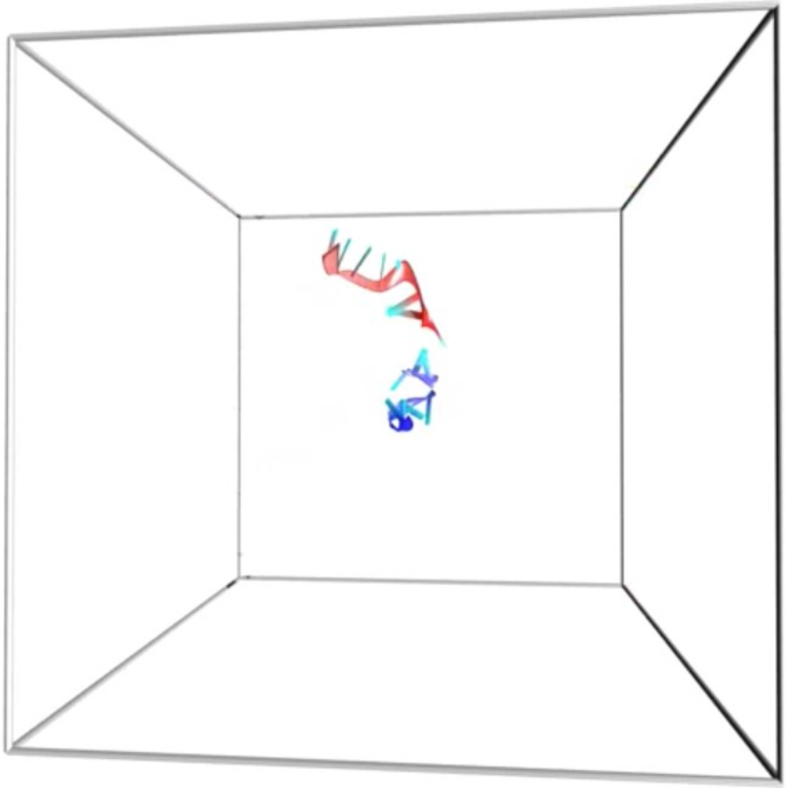
Single-stranded DNA (ssDNA) is not helical and can complement with itself along stretches that are complementary.



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

Duplex Hybridization (Video 1)

oxDNA Simulation

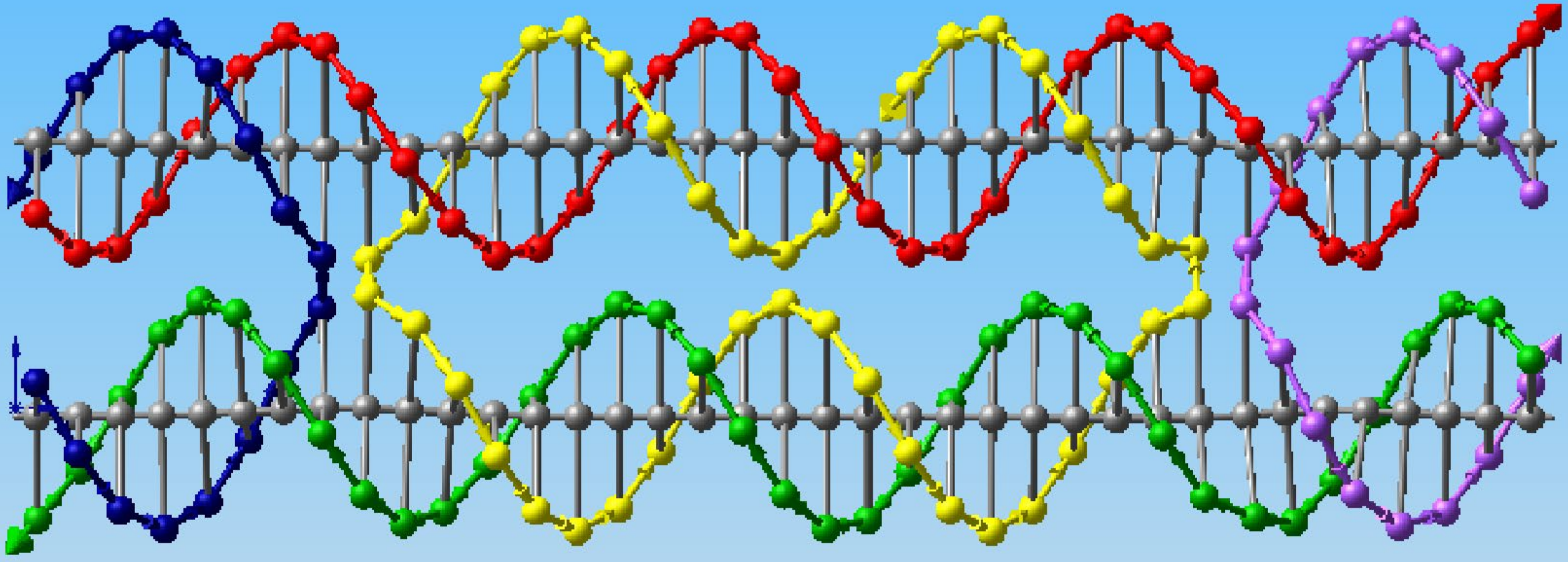


P. Šulc, F. Romano, T. E. Ouldridge, L. Rovigatti, J. P. K. Doye, A. A. Louis, J. Chem. Phys. 137, 135101 (2012)

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

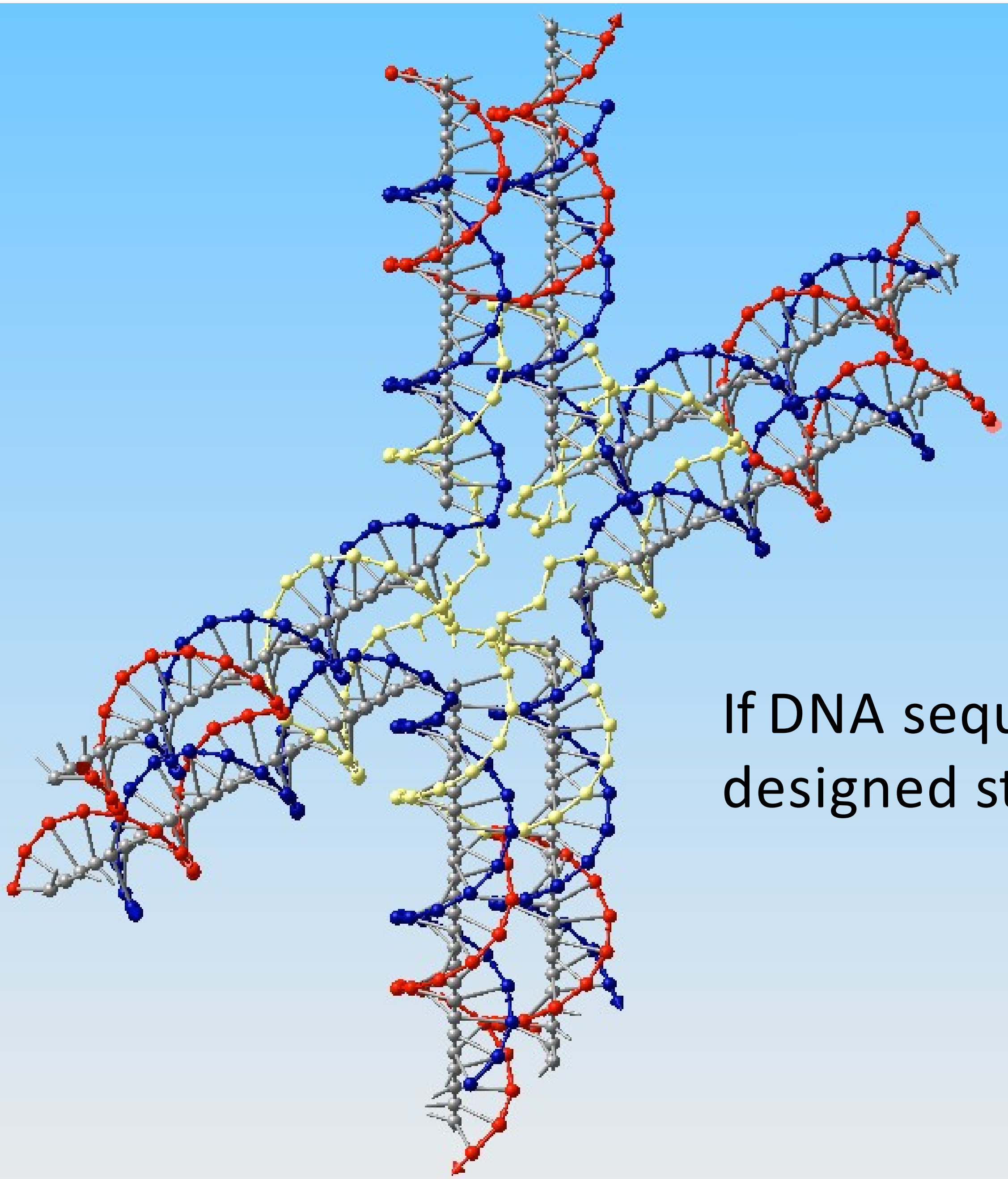
Structural DNA

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



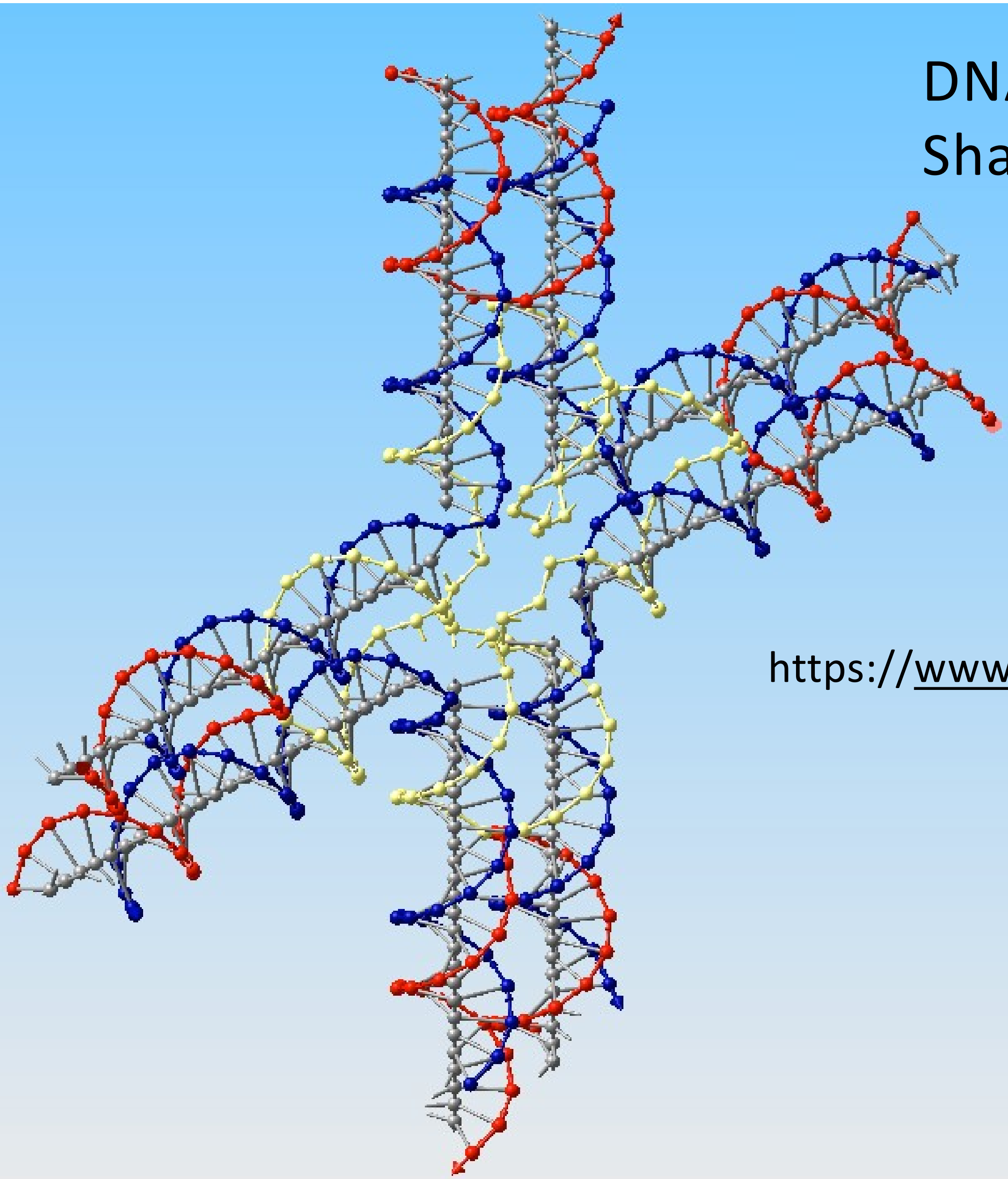
Notice how the blue, yellow and lavender strands participate in both the upper and lower helices.

Structural DNA



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

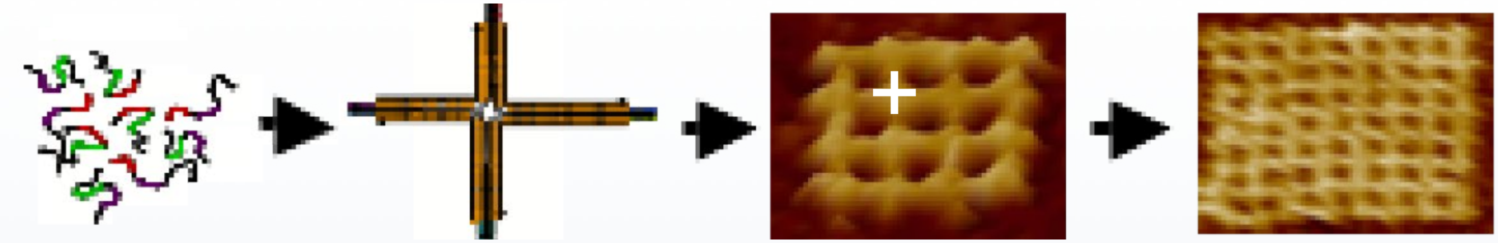
Origami Hybridization (Video 2)



DNA origami folding animation
Shawn Douglas

https://www.youtube.com/watch?v=p4C_aFlyhfI

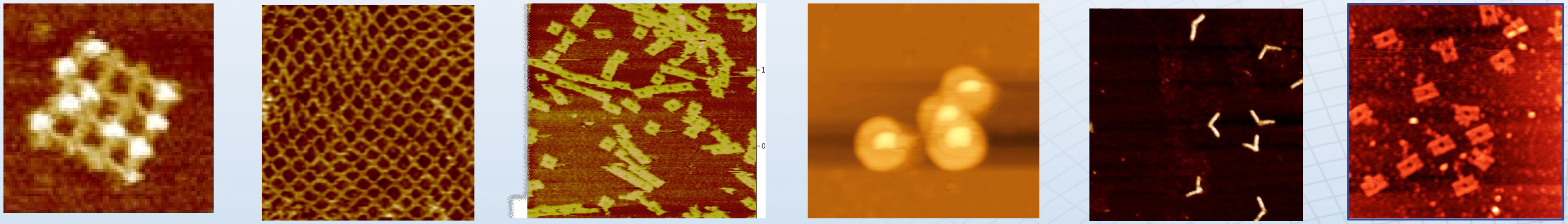
Example DNA Nanostructures



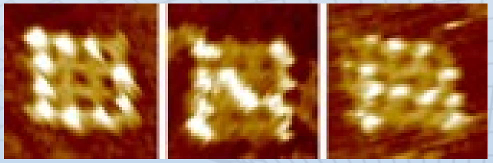
9 DNA strands 1 DNA "+" motif 4x4 grid 8x8 grid

Grid-shaped
nano-carriers
assembled with
DNA "+" motifs

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.



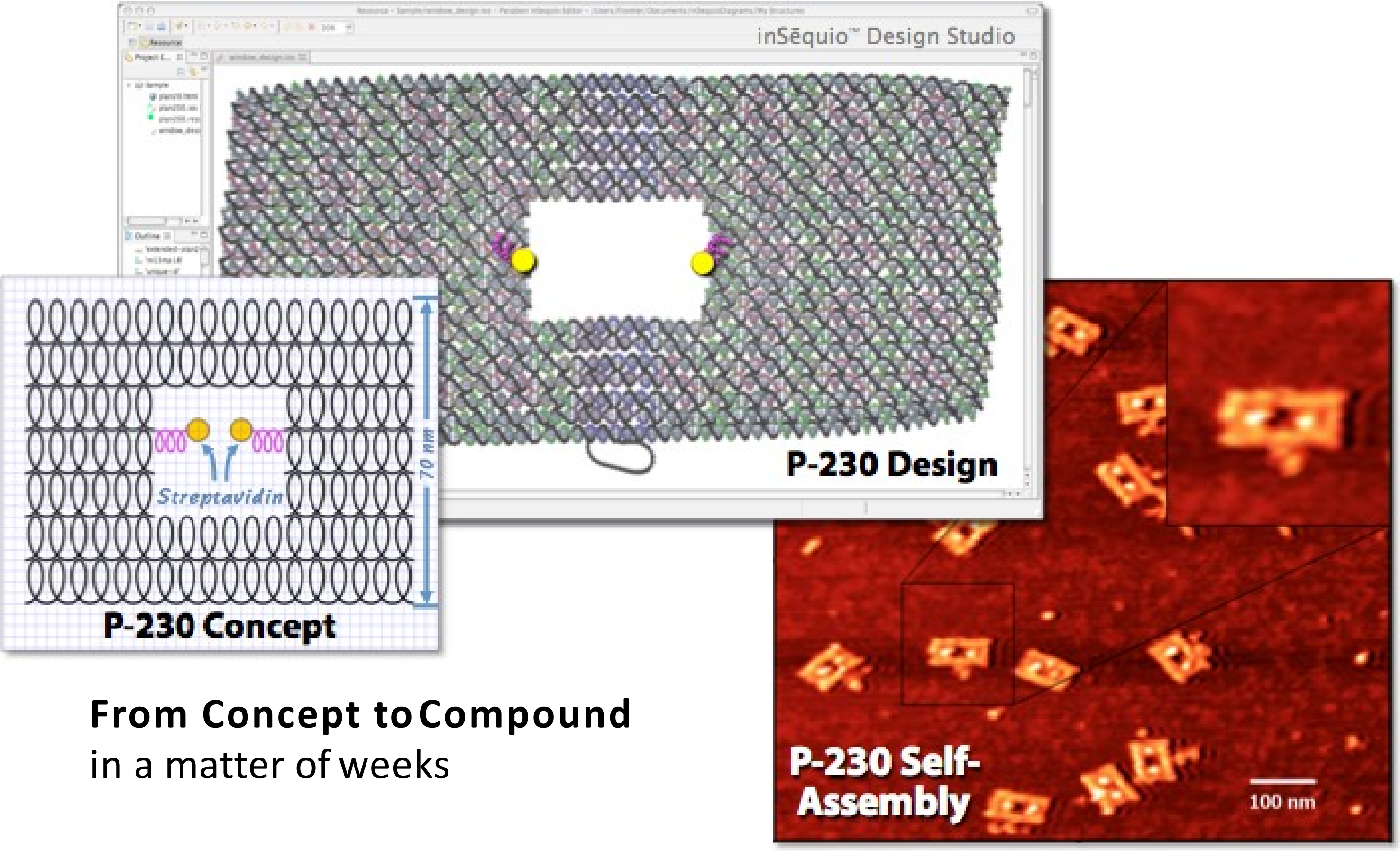
AFM images showing just a few of the types of nanostructures that can be produced with Essemblix.



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

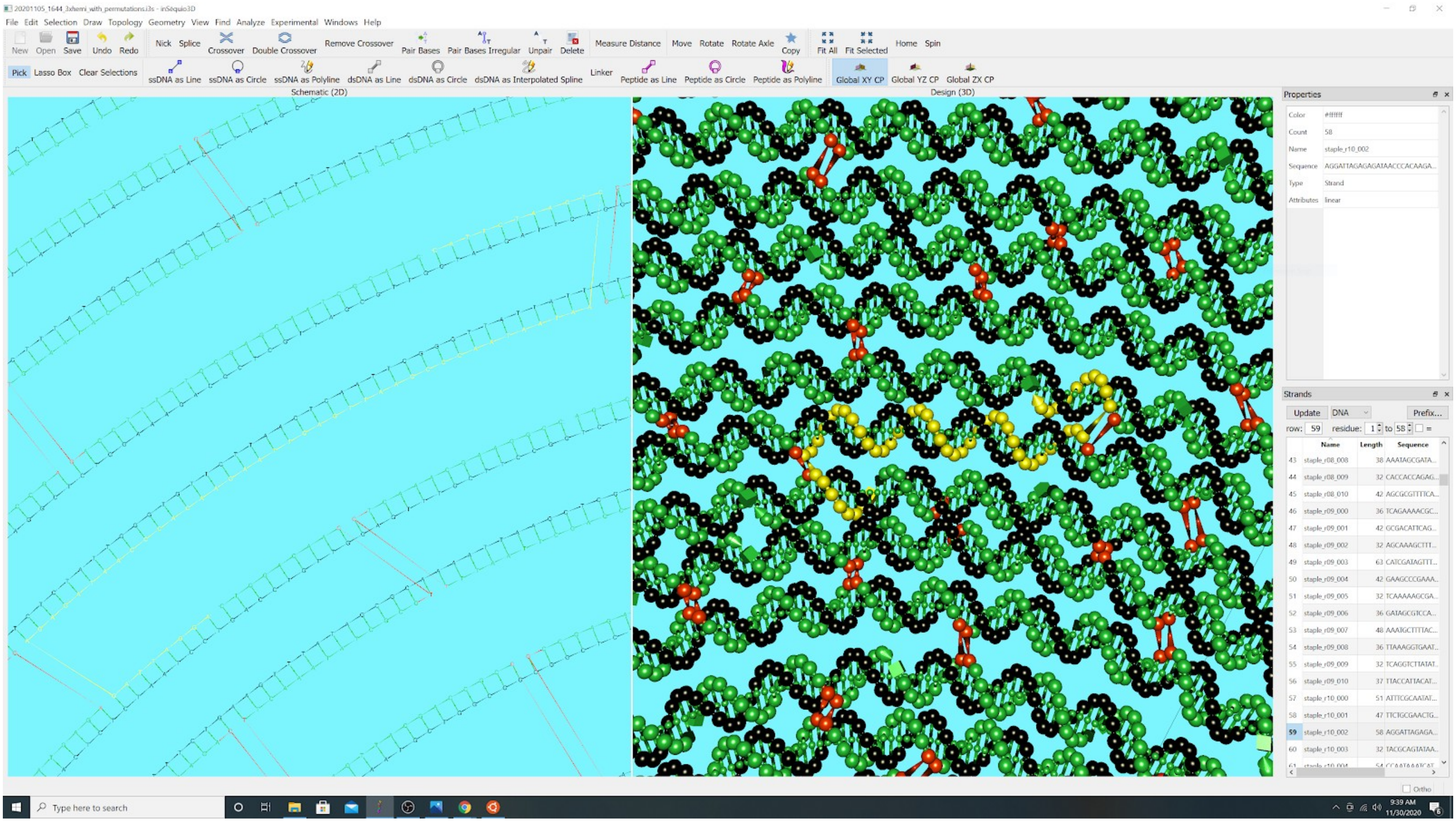
inSēquio Design Studio

Parabon's **inSēquio™ 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)



Properties

Color	#ffffff
Count	58
Name	staple_r10_002
Sequence	AGGATTAGAGAGATAACCCACAAGA...
Type	Strand
Attributes	linear

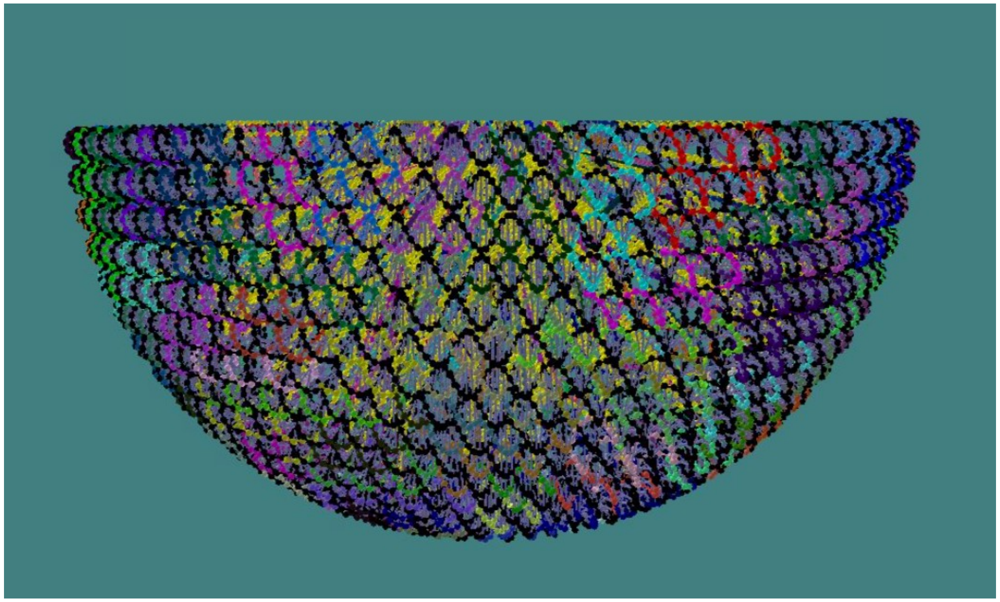
Strands

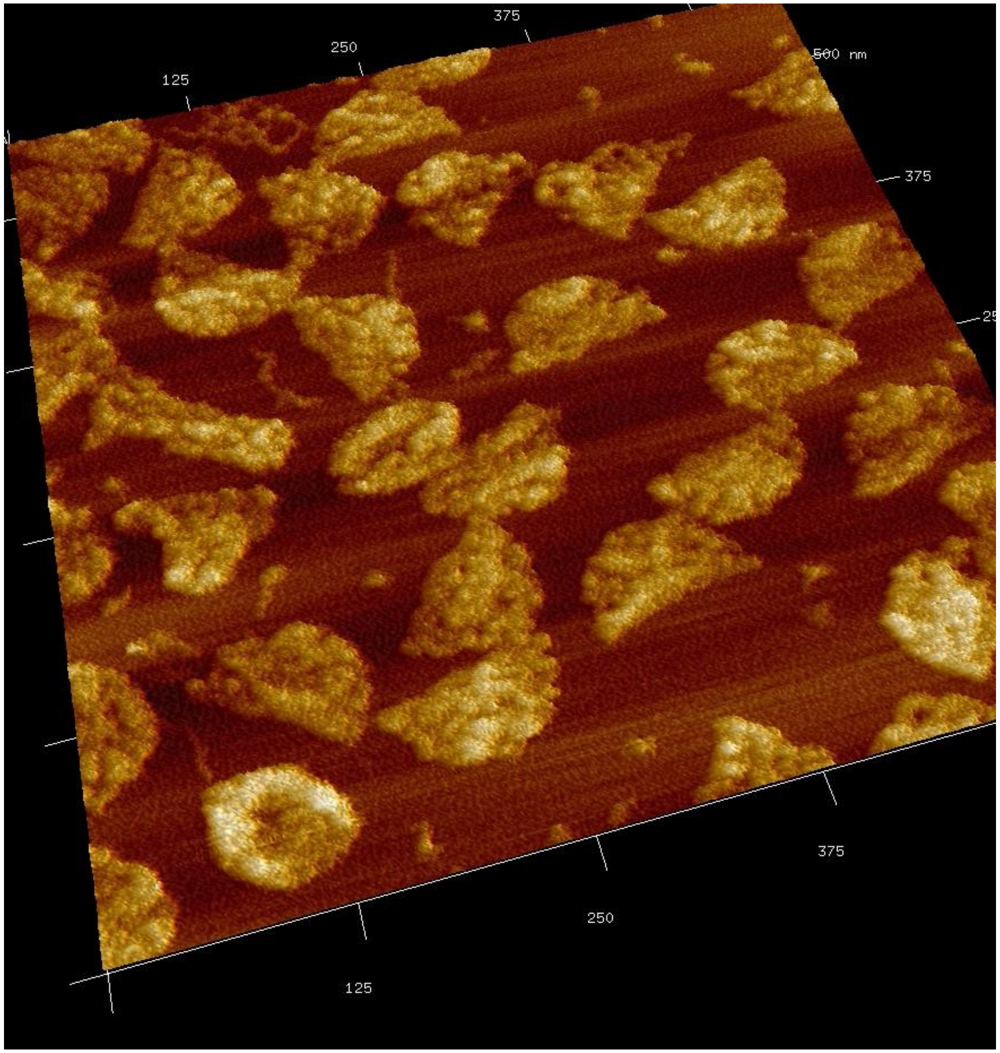
Update DNA Prefix...

row: 59 residue: 1 to 58 ☐ =

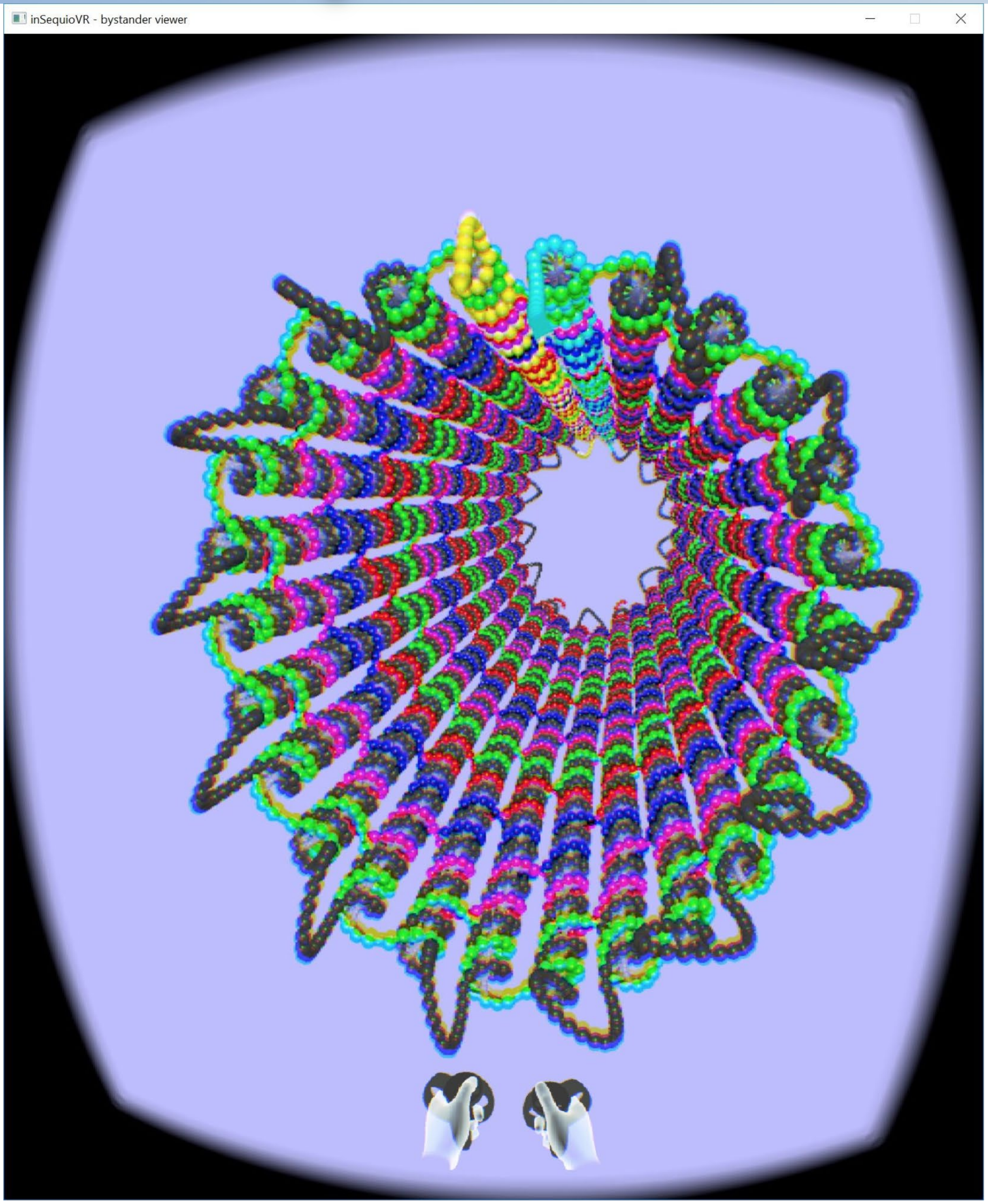
	Name	Length	Sequence
43	staple_r08_008	38	AAATAGCGATA...
44	staple_r08_009	32	CACCACCAGAG...
45	staple_r08_010	42	AGCGCGTTTTCA...
46	staple_r09_000	36	TCAGAAAACGC...
47	staple_r09_001	42	GCGACATTCAG...
48	staple_r09_002	32	AGCAAAGCTTT...
49	staple_r09_003	63	CATCGATAGTTT...
50	staple_r09_004	42	GAAGCCCGAAA...
51	staple_r09_005	32	TCAAAAAGCGA...
52	staple_r09_006	36	GATAGCGTCCA...
53	staple_r09_007	48	AAATGCTTTTAC...
54	staple_r09_008	36	TTAAAGGTGAAT...
55	staple_r09_009	32	TCAGGTCTTATAT...
56	staple_r09_010	37	TTACCATTACAT...
57	staple_r10_000	51	ATTTCGCAATAT...
58	staple_r10_001	47	TTCTGCGAACTG...
59	staple_r10_002	58	AGGATTAGAGA...
60	staple_r10_003	32	TACGCAGTATAA...

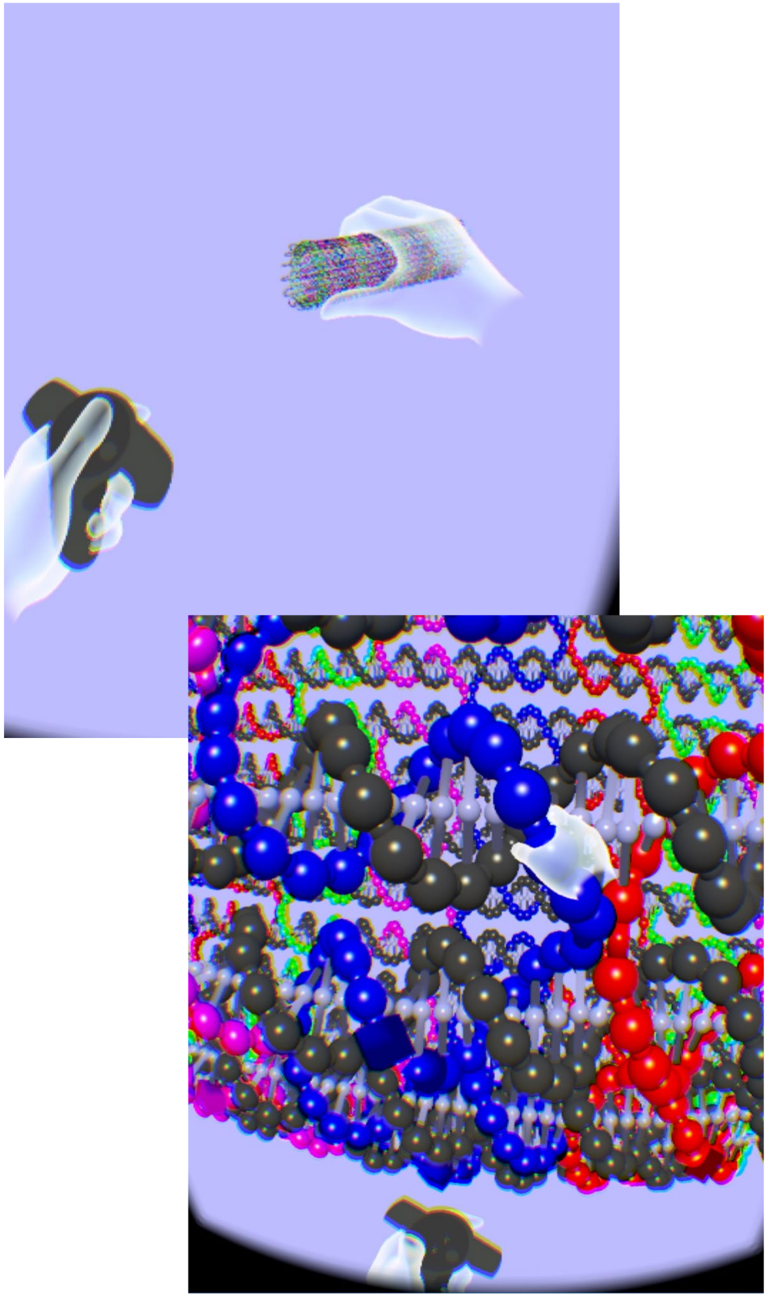
inSēquioVR



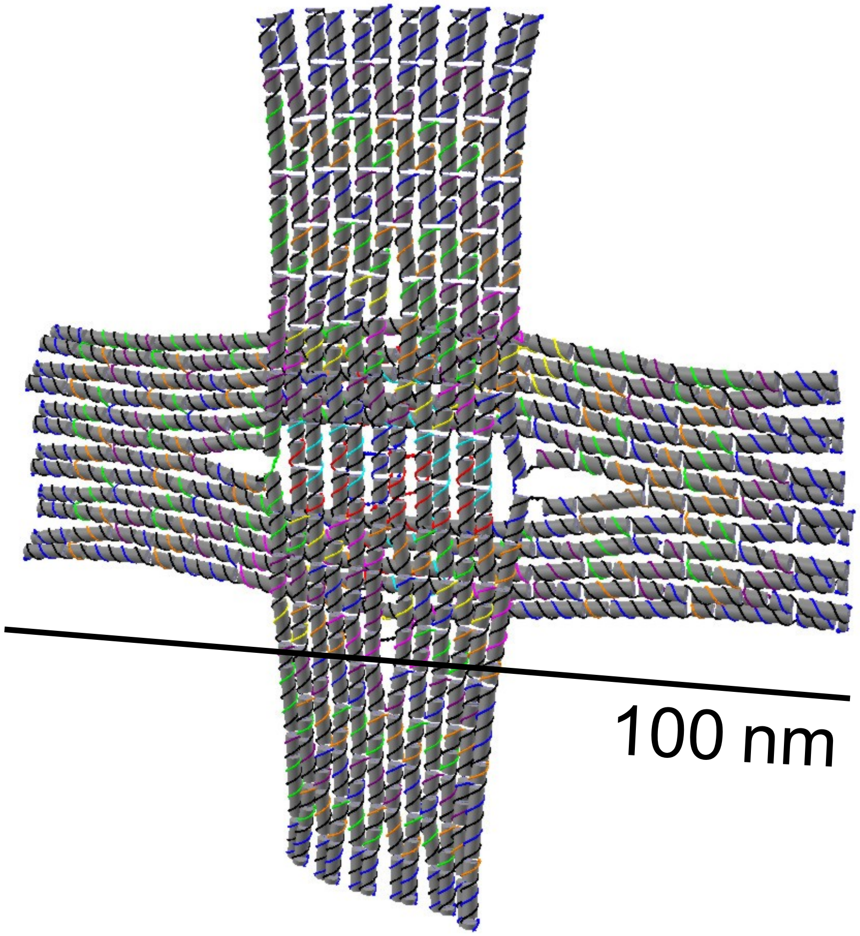


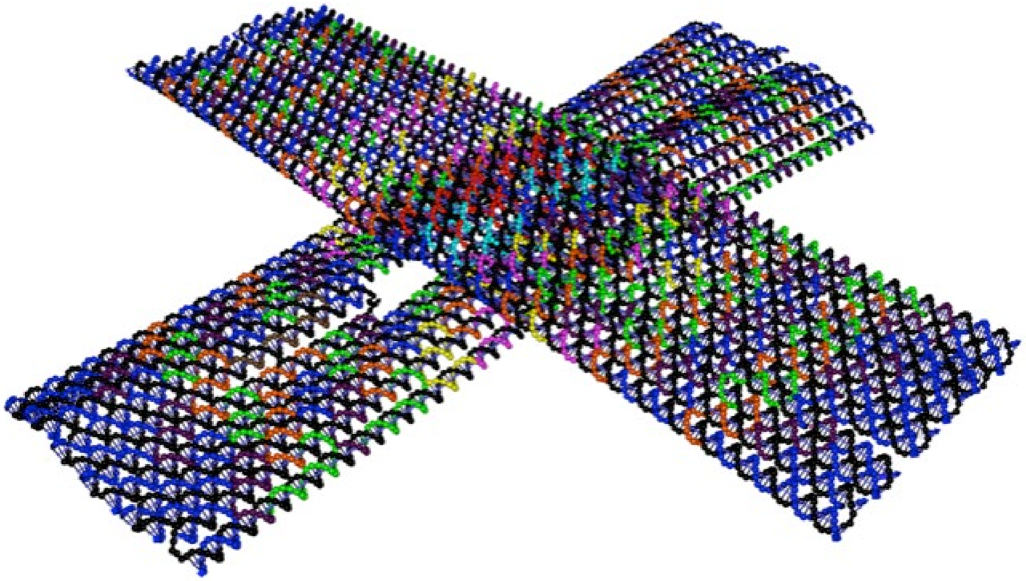
inSēquioVR





Cross-Tile Origami

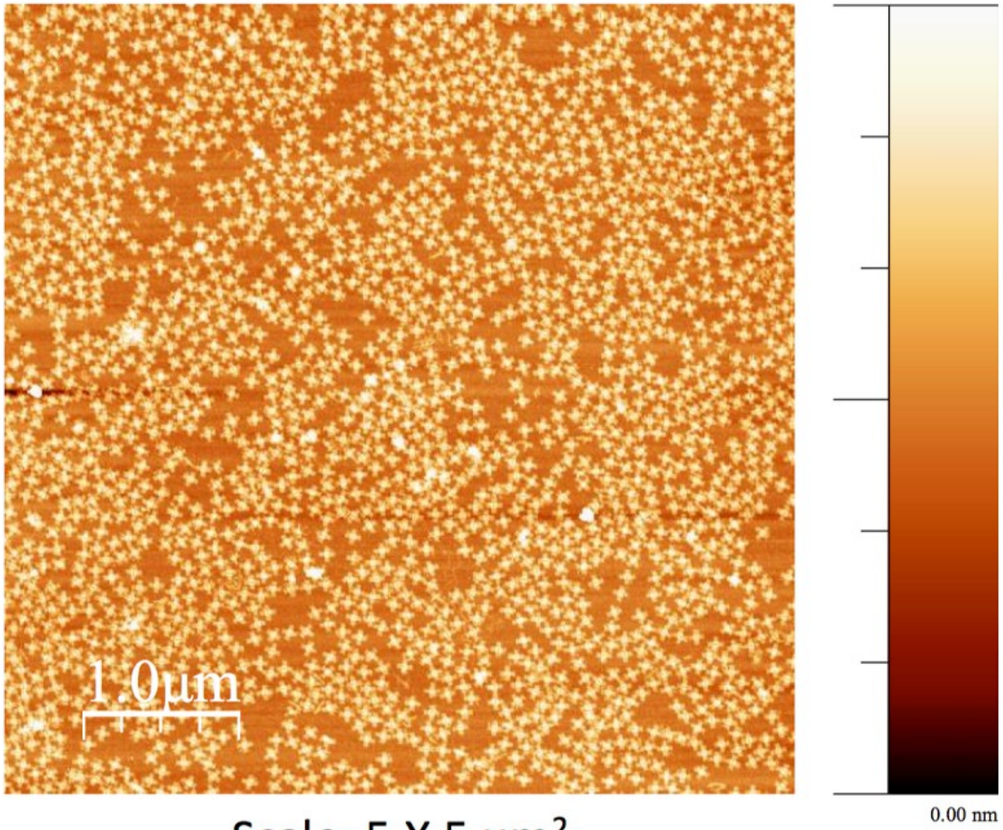




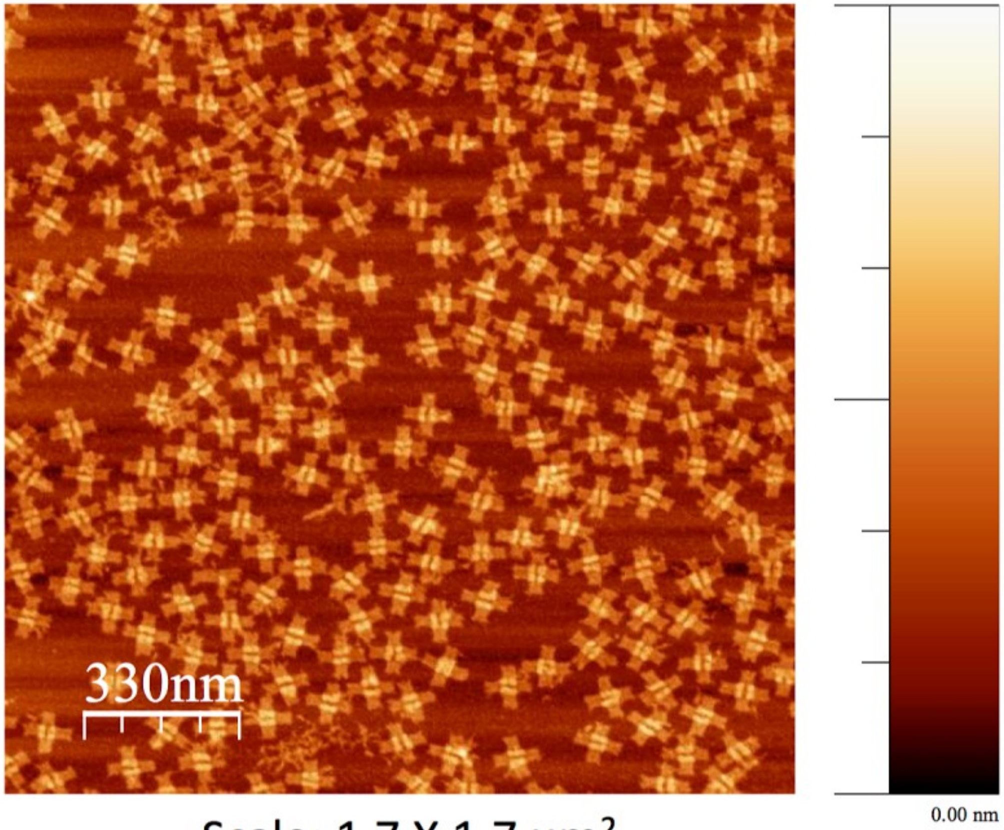
Circumscribing a Human Hair

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



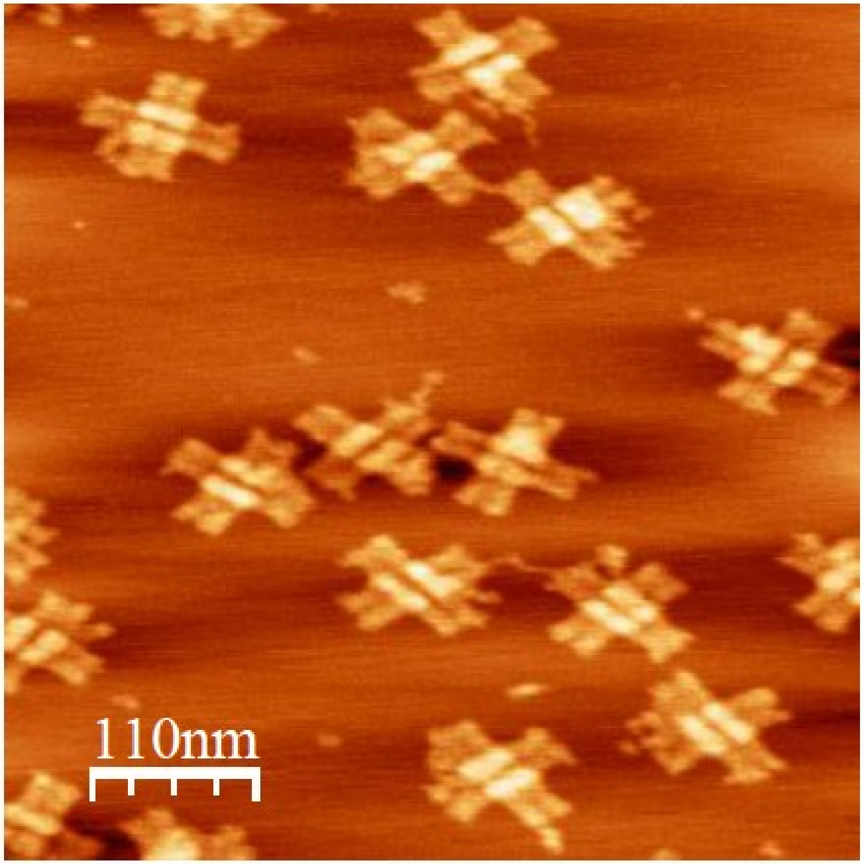
Scale: 5 X 5 µm²



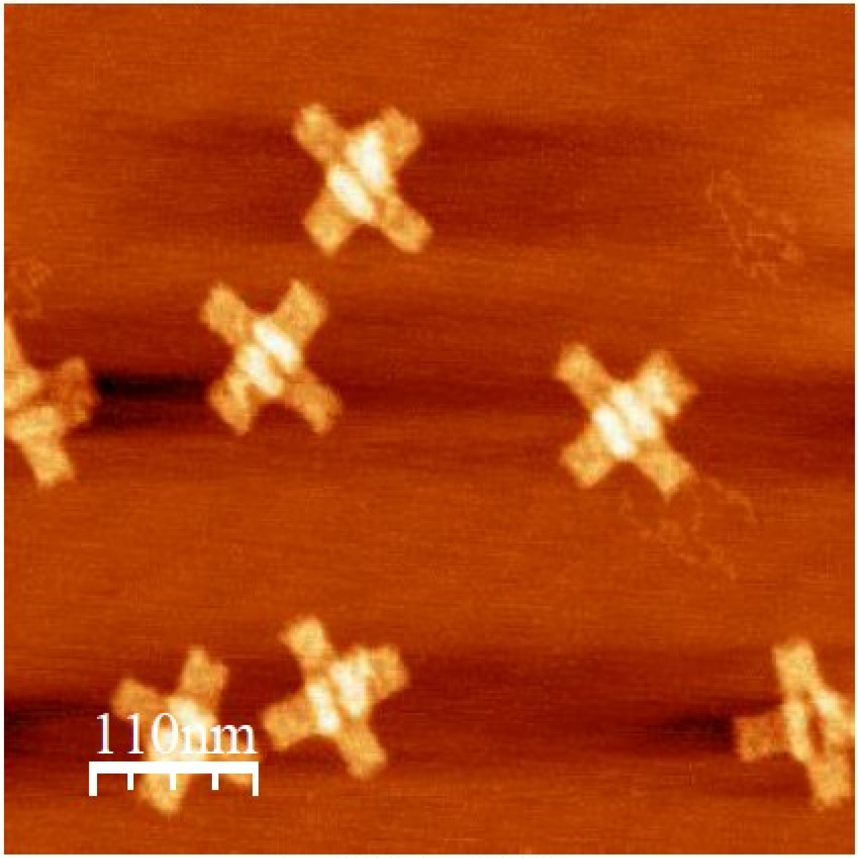
Scale: 1.7 X 1.7 µm²

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

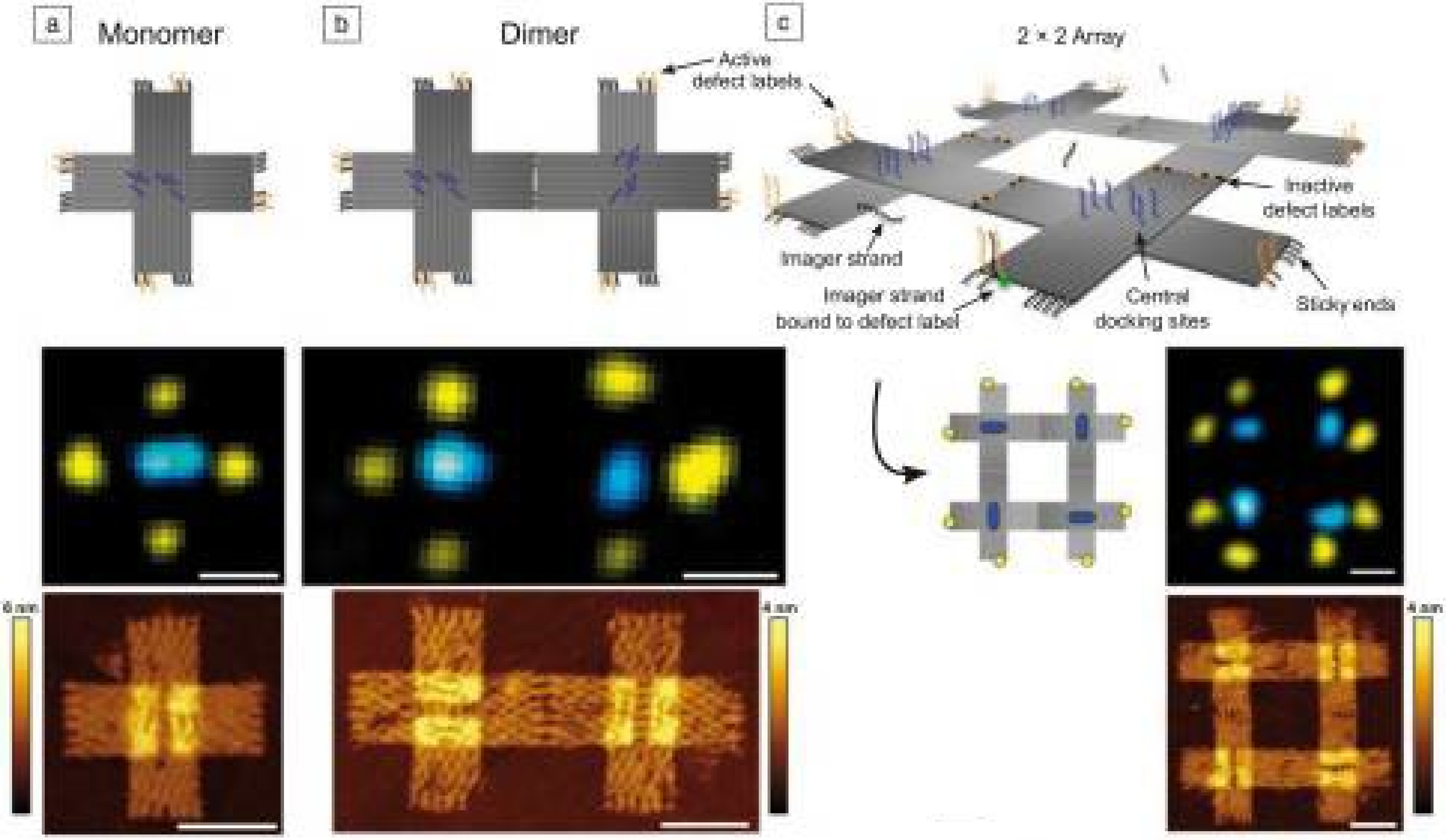


560 nm x 560 nm



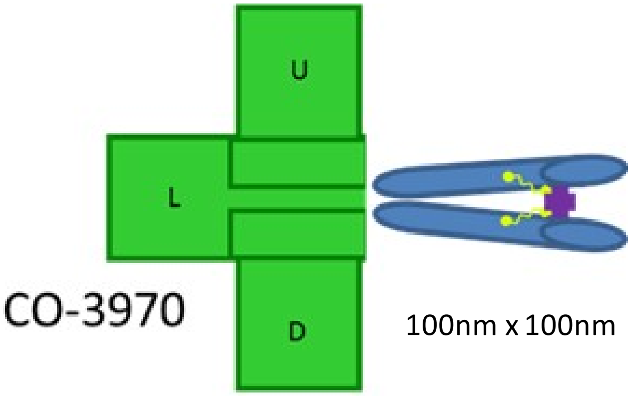
550 nm x 550 nm

Super-resolution Microscopy



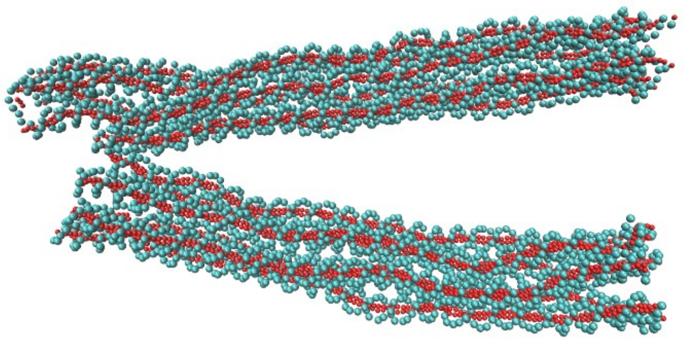
Graugnard, Elton, et al. "Nanometrology and super-resolution imaging with DNA." *MRS bulletin* 42.12 (2017): 951.

Artificial Antibodies

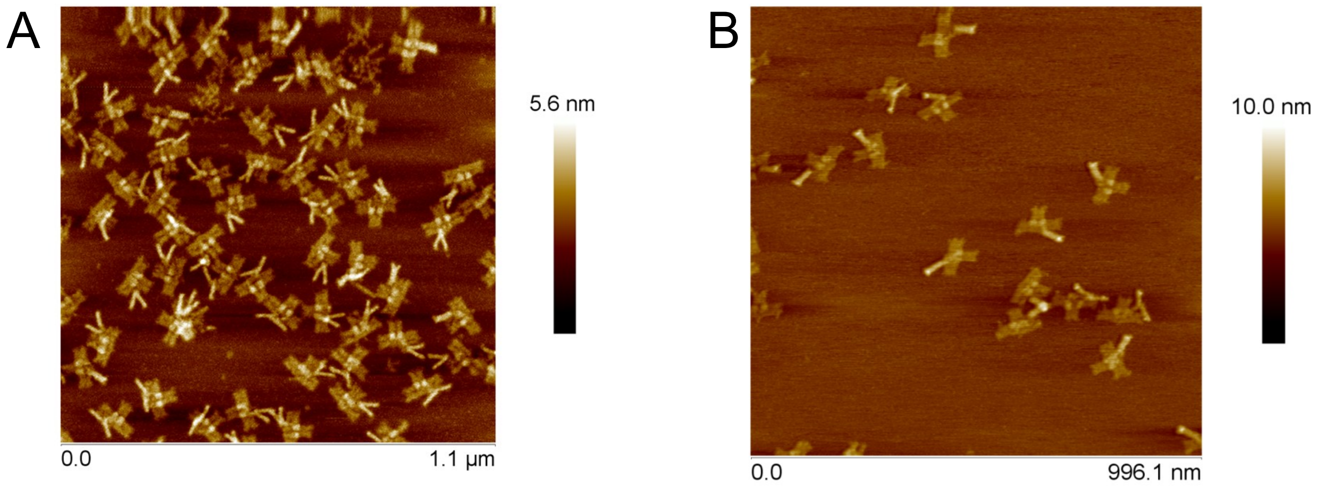


Single molecule nanosensor

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

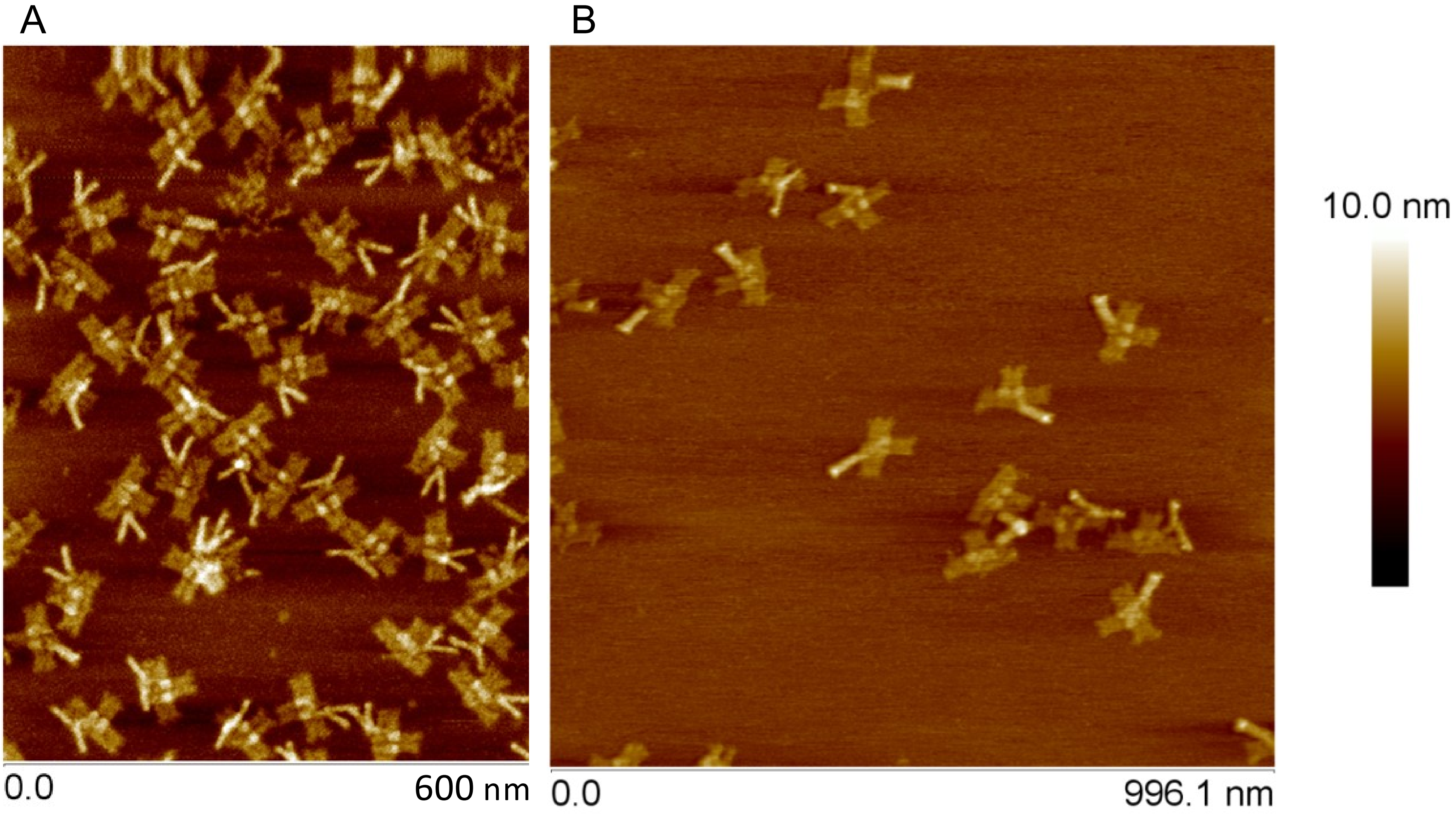


MD simulation of pinceraction



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

Artificial Antibodies



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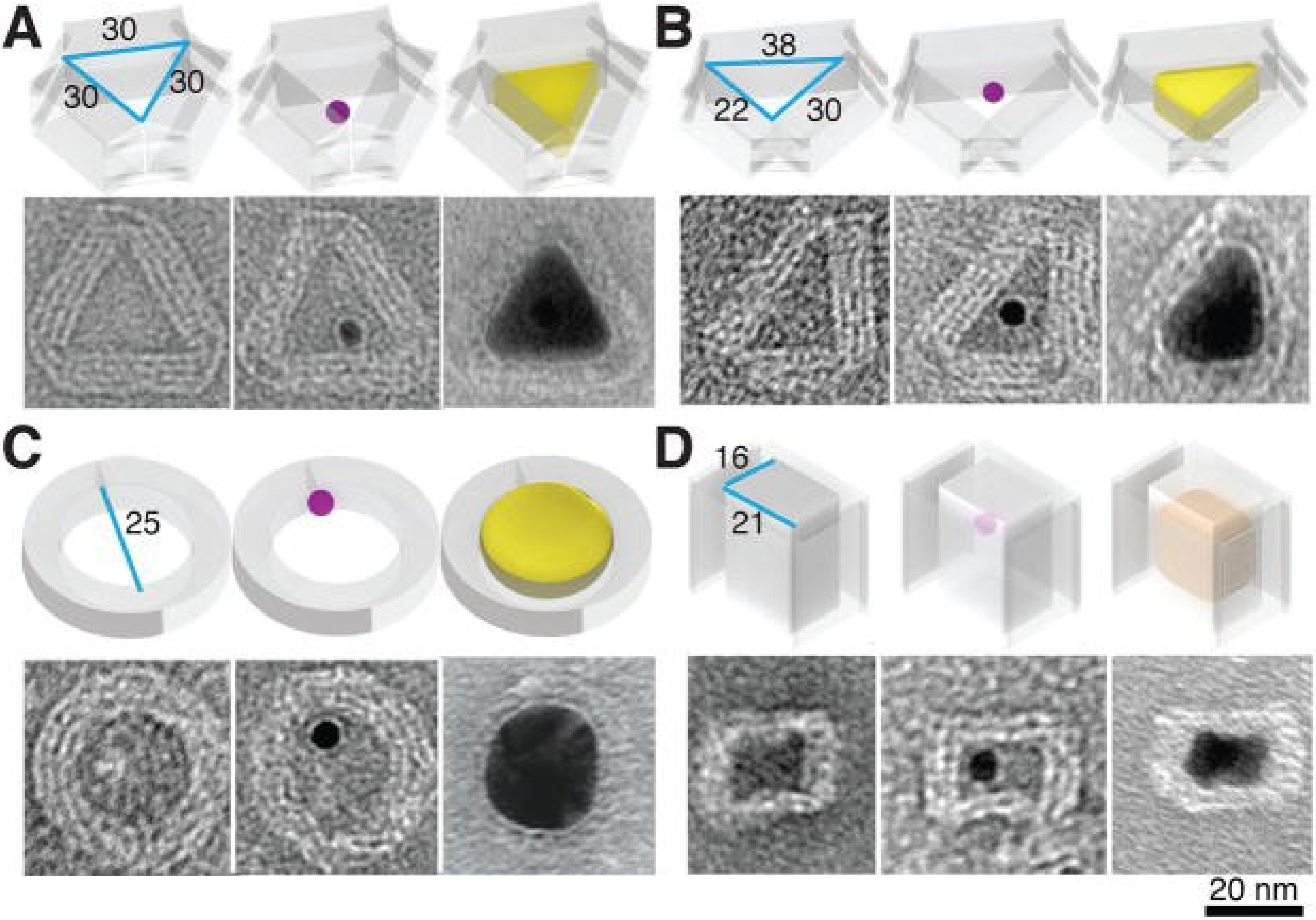
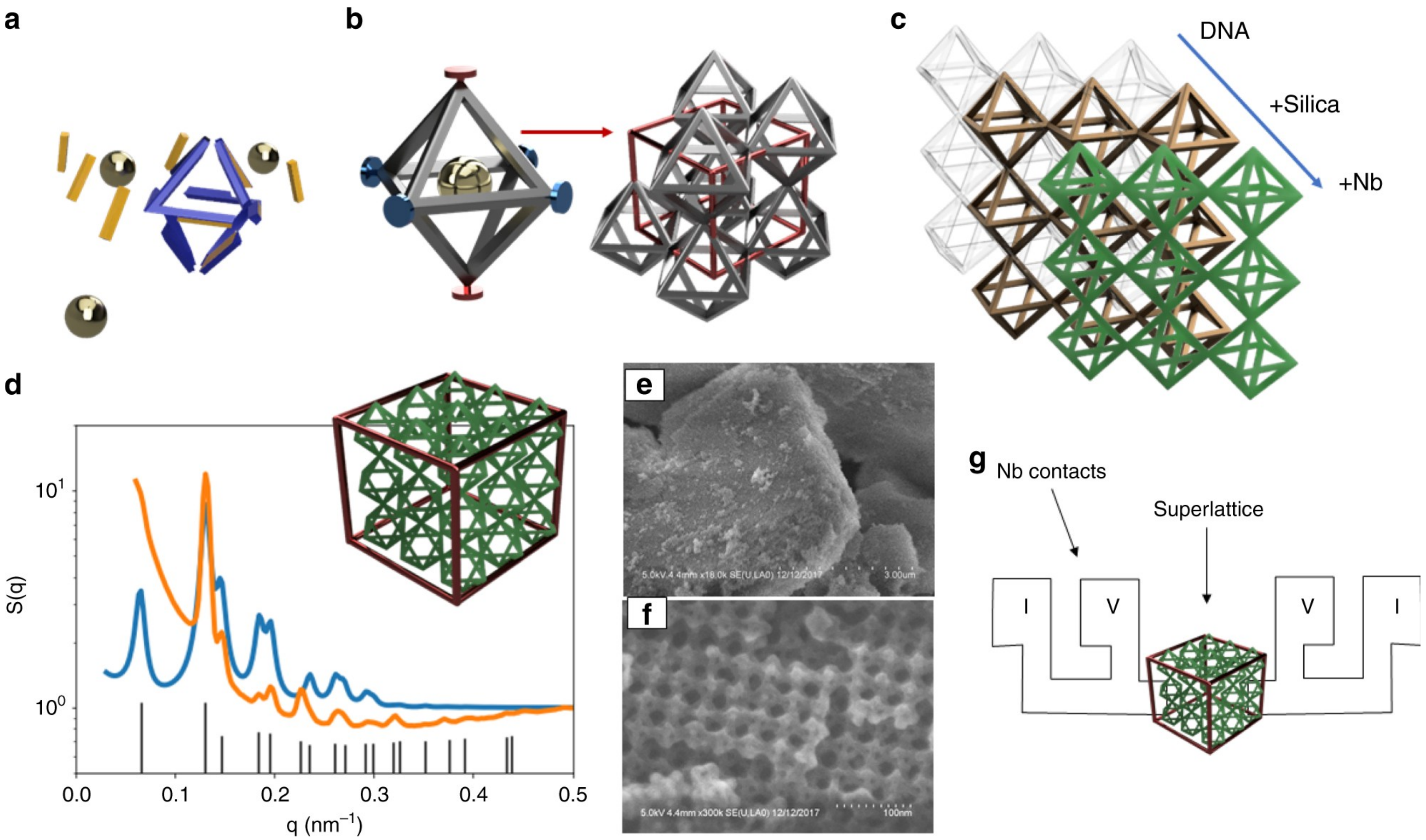
Nanoscale Molding



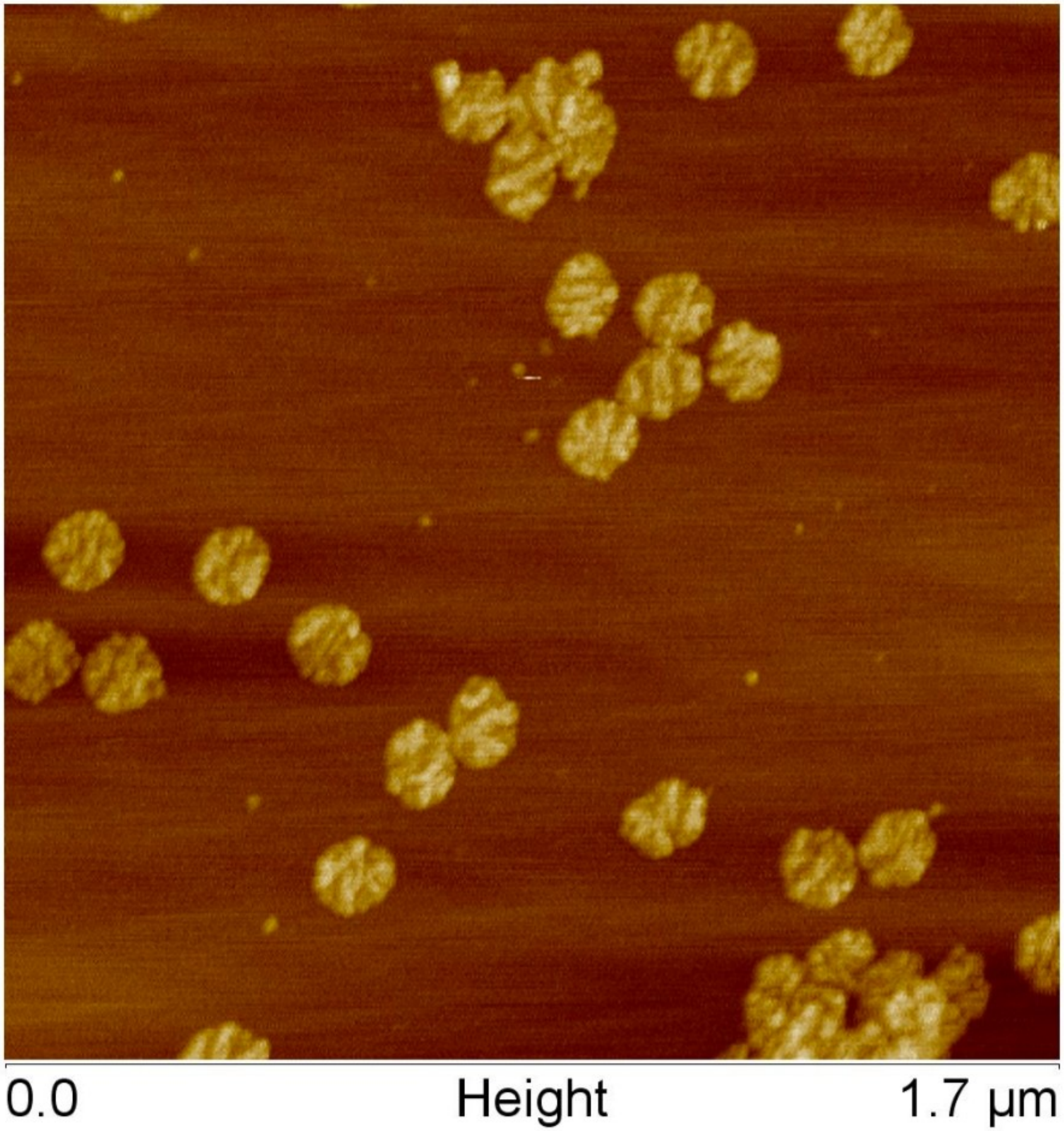
Sun, Wei, et al. "Casting inorganic structures with DNA molds." Science 346.6210 (2014).

Superconducting 3D Structures



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

DNA Nanocarriers



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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