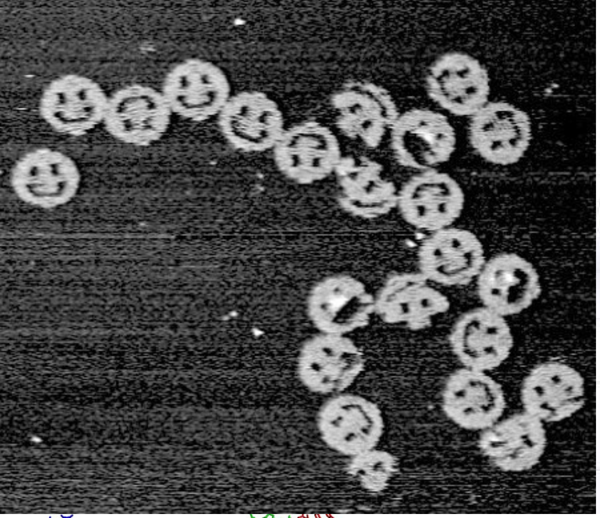
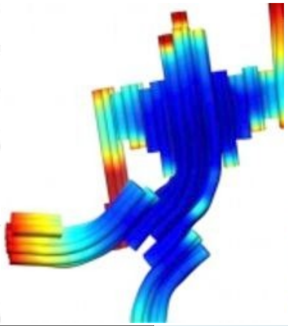
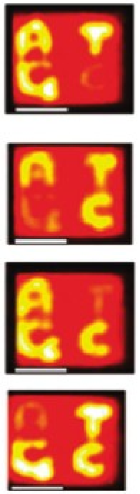
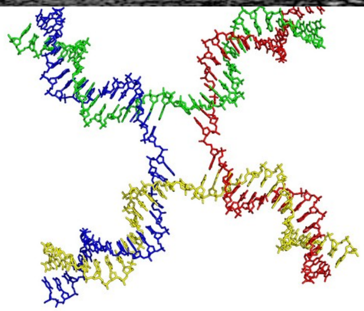
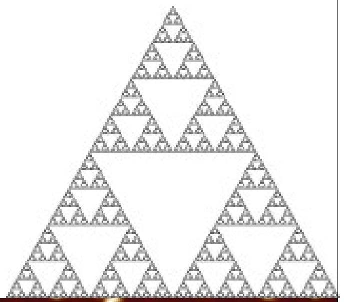


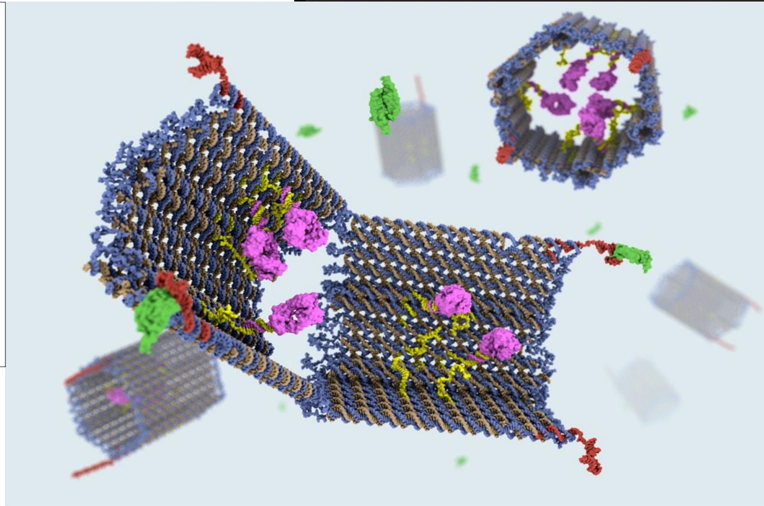
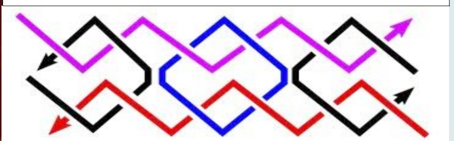
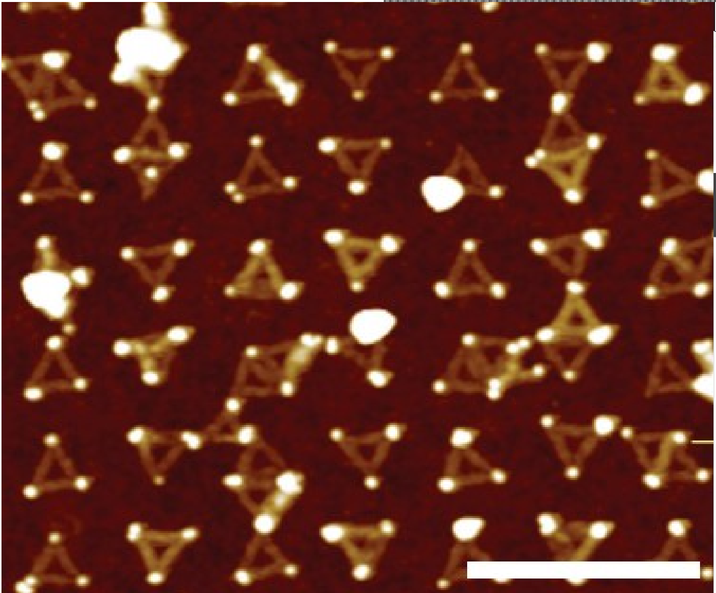
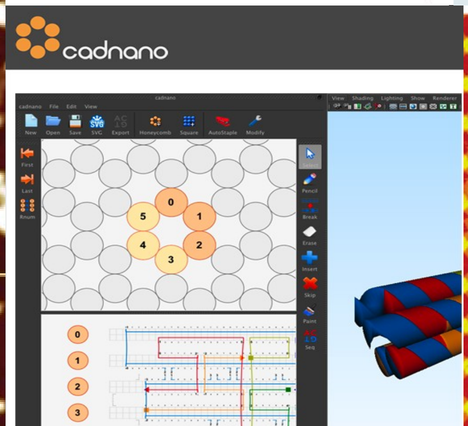



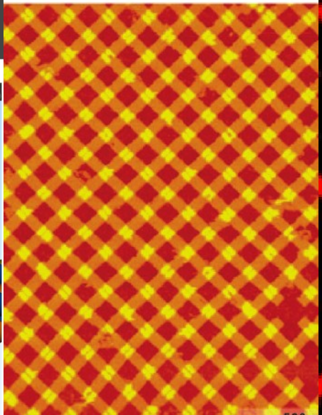
Simpson College

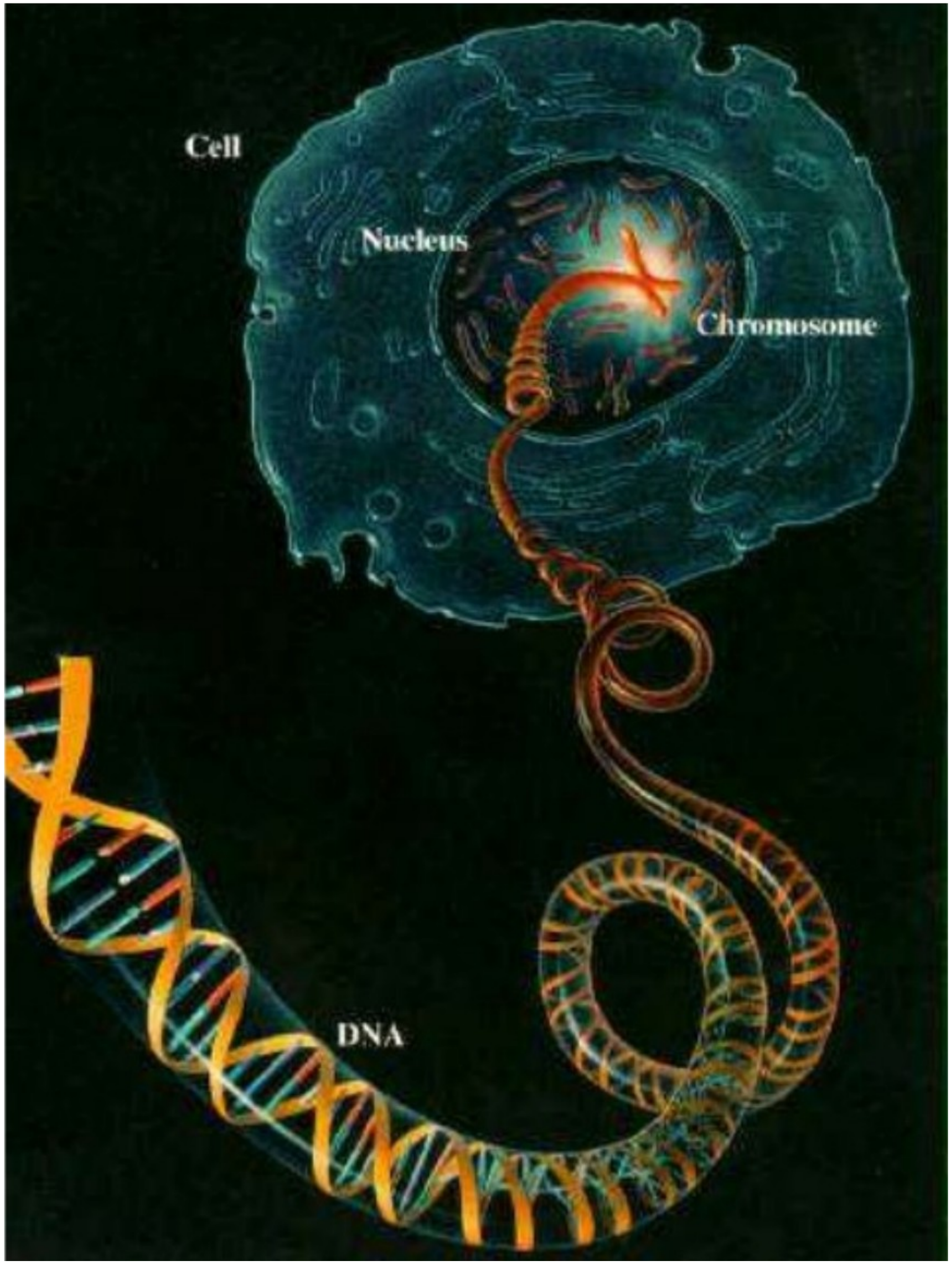
DNA Nano-
Technology

Brian & Divita

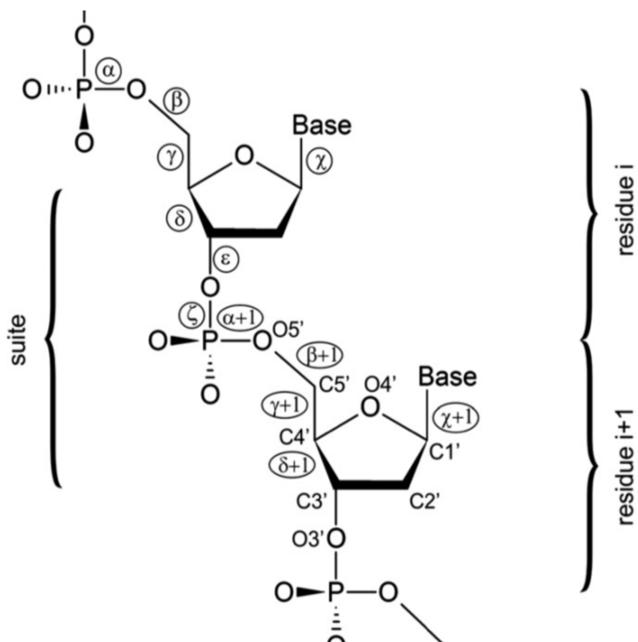
3/20/15 @ 3:30p

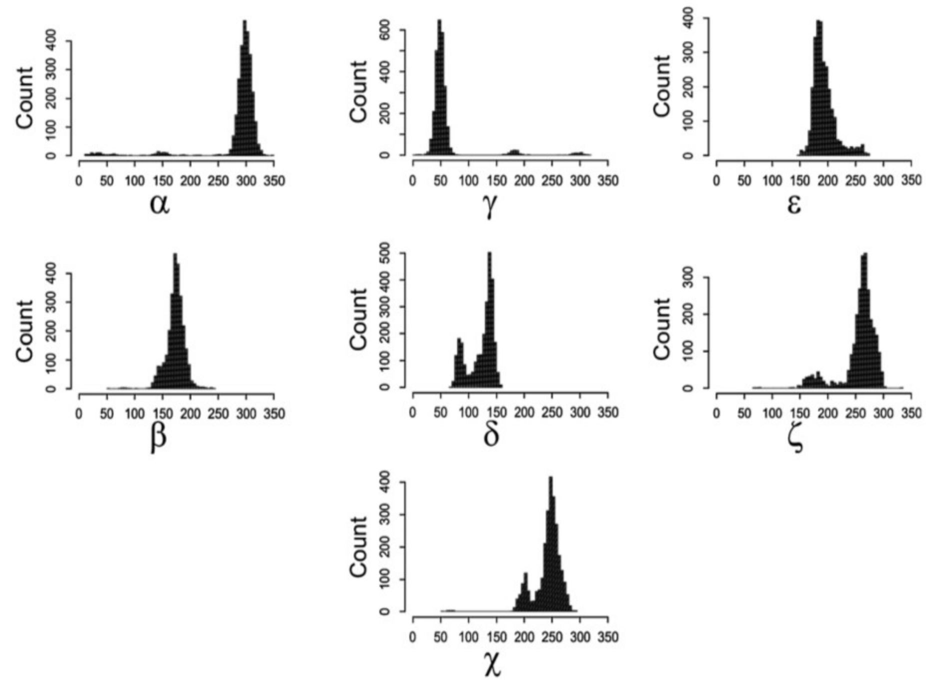









Cell
Nucleus
Chromosome
DNA

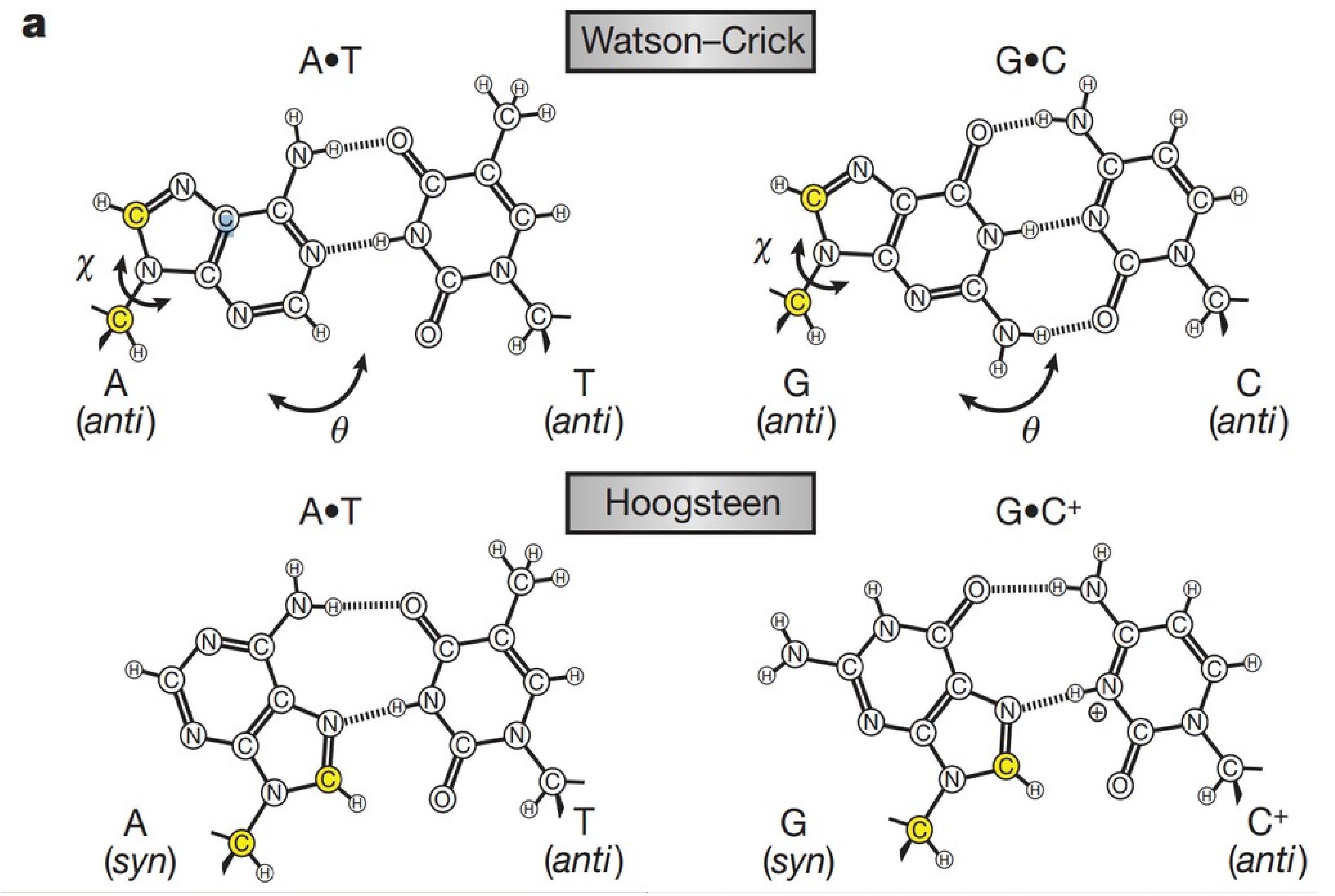
Properties of DNA: Torsion Angles





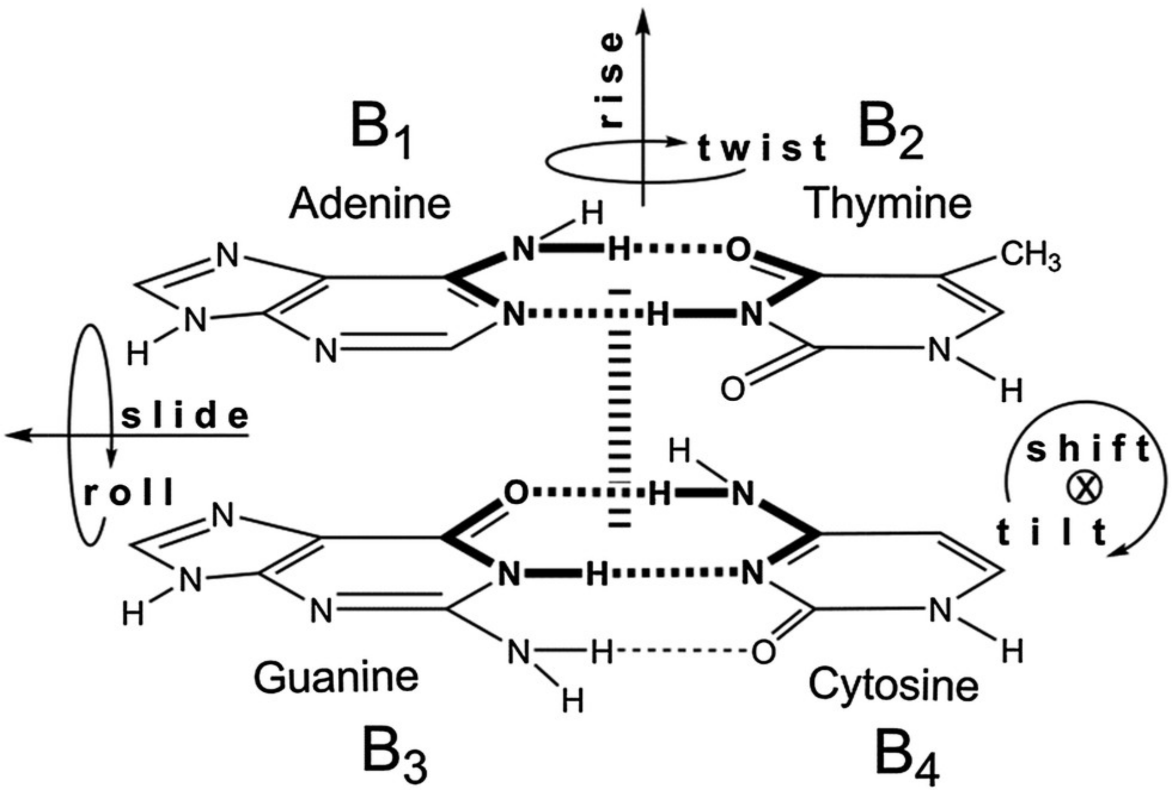
Šponer, Jiří, et al. "The DNA and RNA sugar–phosphate backbone emerges as the key player. An overview of quantum-chemical, structural biology and simulation studies." Physical Chemistry Chemical Physics 14.44 (2012): 15257-15277.

Properties of DNA:
WC Base Pairs



Honig, Barry, and Remo Rohs. "Biophysics: flipping watson and crick." Nature 470.7335 (2011): 472-473.

Properties of DNA: Stacking



Karabıyık, Hande, Resul Sevinçek, and Hasan Karabıyık. "π-Cooperativity effect on the base stacking interactions in DNA: is there a novel stabilization factor coupled with base pairing H-bonds?." Physical Chemistry Chemical Physics 16.29 (2014): 15527-15538.

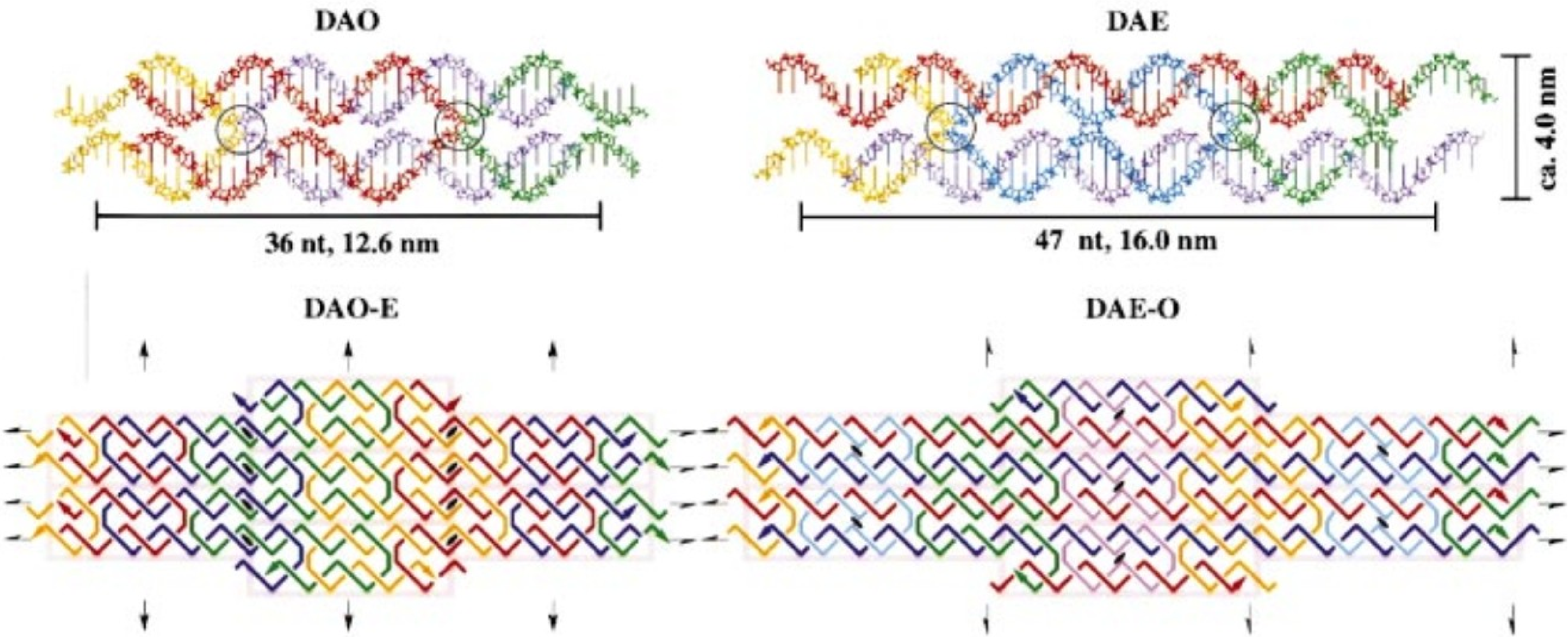
Three areas of DNA Nanotech:

- DNA Tiles and the Tile Assembly Model
- DNA Strand Displacement and Chemical Reaction Networks

- DNA Origami

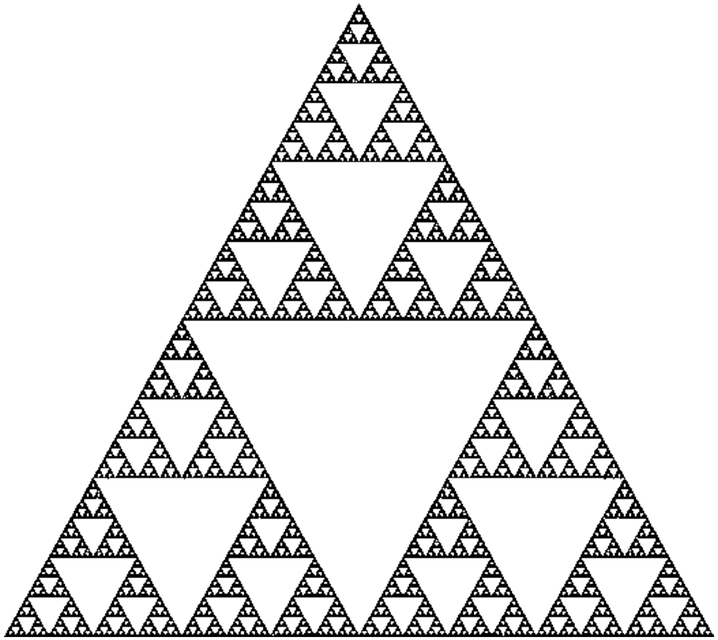
- There are others:
  - eg. DNA nano-walkers...

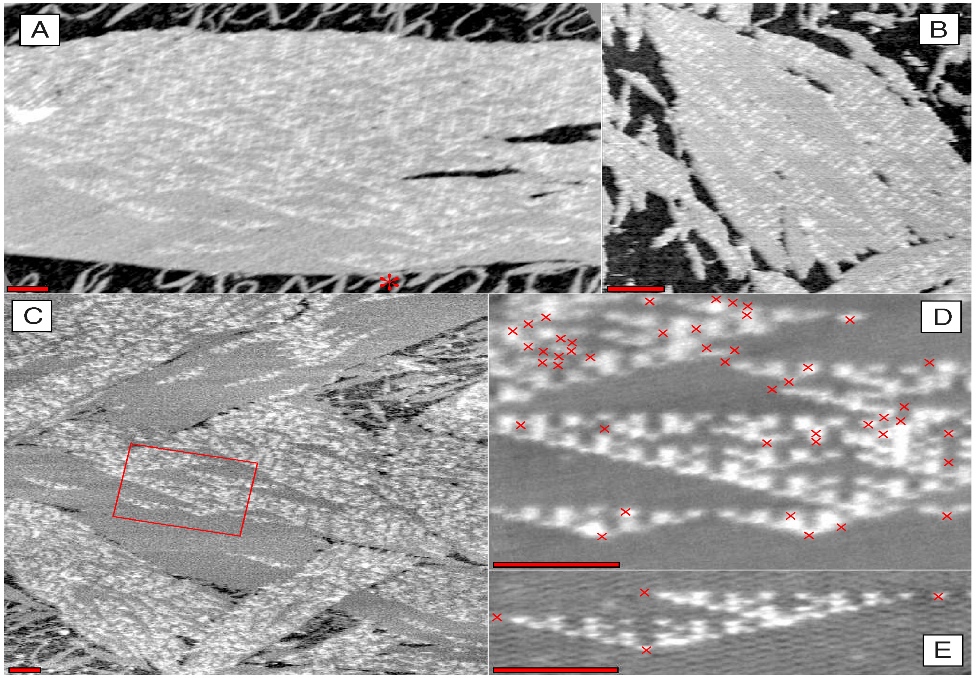
DNA Tiles



Winfree, Erik, et al. "Design and self-assembly of two-dimensional DNA crystals." Nature 394.6693 (1998): 539-544.

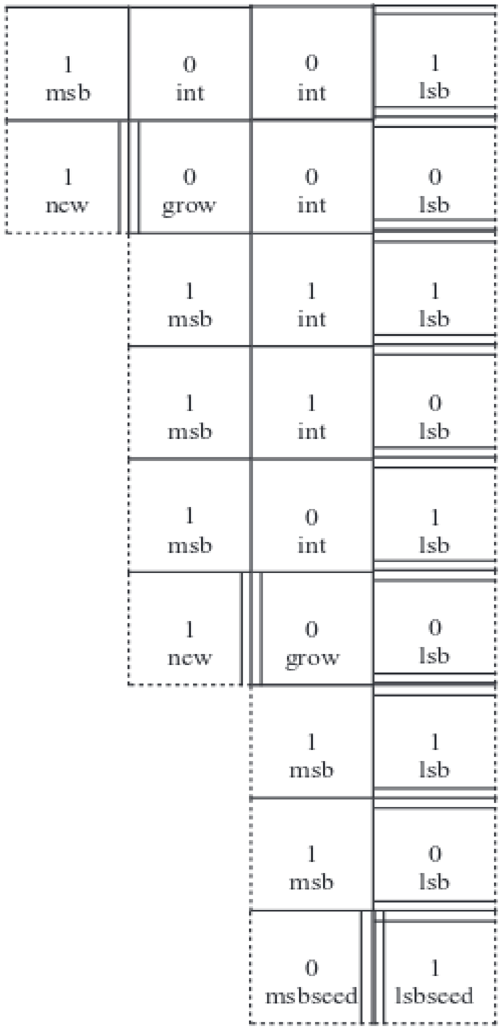
Sierpinski Triangle from Tiles

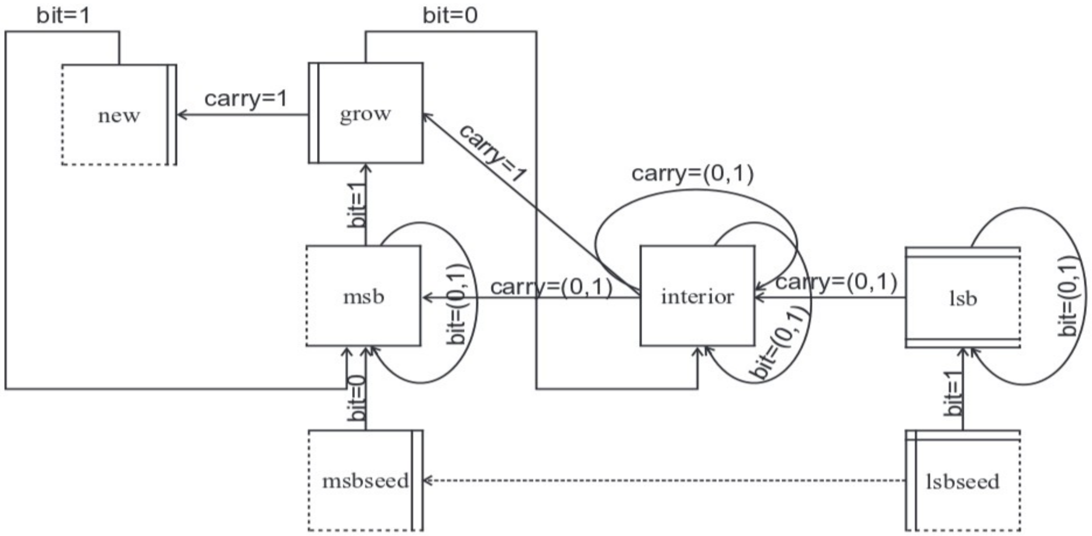


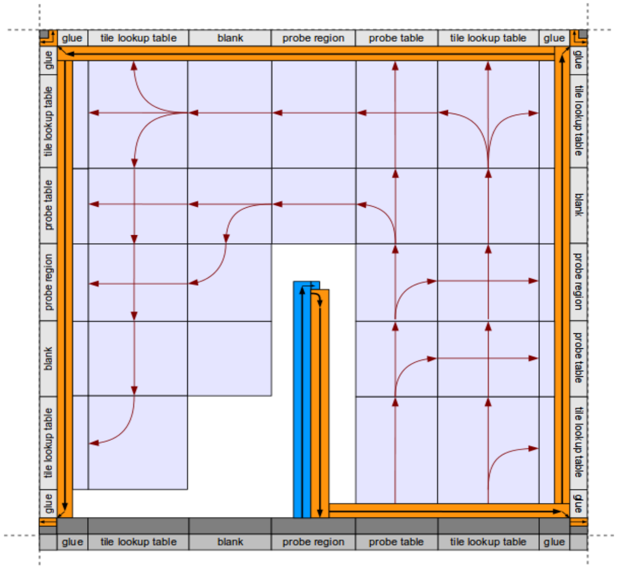


Rothemund, Paul WK, Nick Papadakis, and Erik Winfree. "Algorithmic self-assembly of DNA Sierpinski triangles." PLoS biology 2.12 (2004): e424.

LAMP & DNA Tile Theory (TAM)



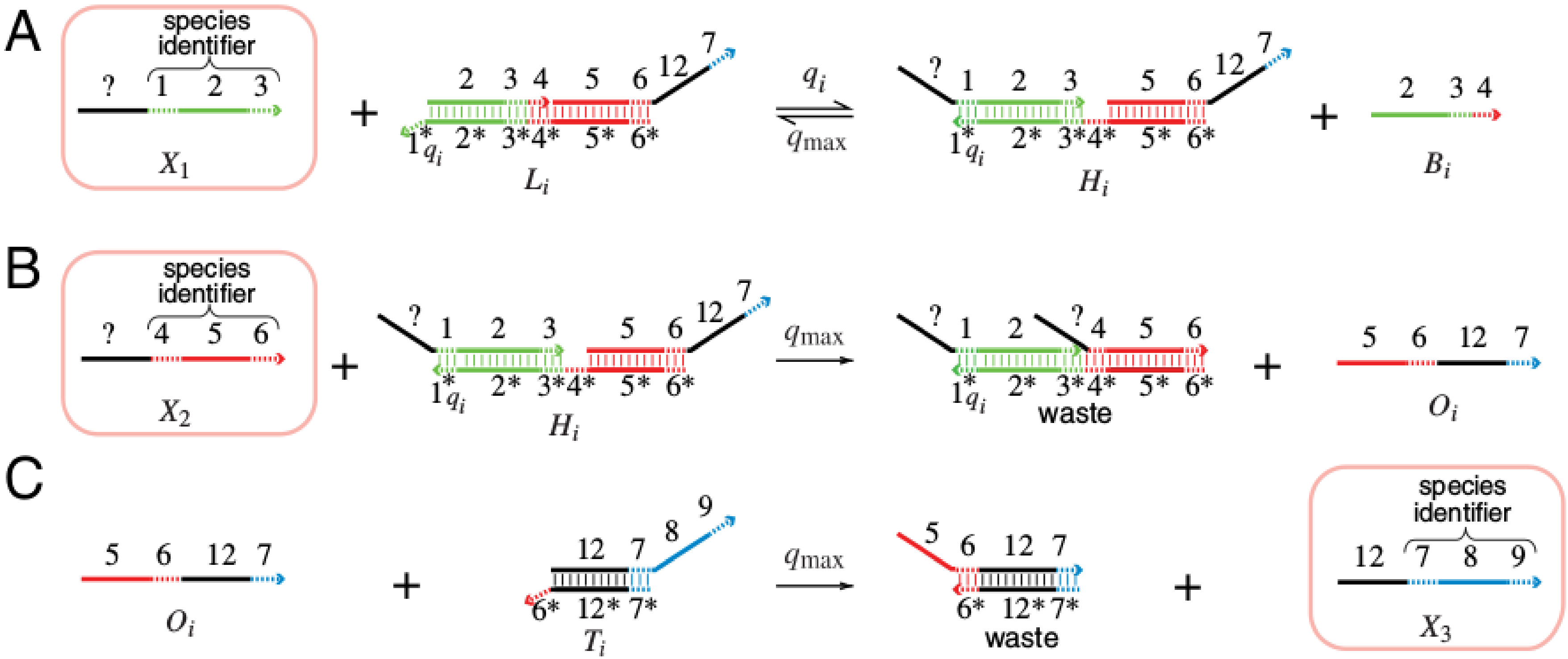




Doty, David, and Matthew J. Patitz. "A domain-specific language for programming in the tile assembly model." DNA Computing and Molecular Programming. Springer Berlin Heidelberg, 2009. 25-34.

Doty, David, et al. "The tile assembly model is intrinsically universal." Foundations of Computer Science (FOCS), 2012 IEEE 53rd Annual Symposium on. IEEE, 2012.

DNA Strand Displacement



Soloveichik, David, Georg Seelig, and Erik Winfree. "DNA as a universal substrate for chemical kinetics." Proceedings of the National Academy of Sciences 107.12 (2010): 5393-5398.

LAMP: Creating Computational Devices

Automated Requirements Analysis for a Molecular Watchdog Timer

Samuel J. Ellis, Eric R. Henderson, Titus H. Klinge, James I. Lathrop, Jack H. Lutz, Robyn R. Lutz, Divita Mathur, and Andrew S. Miner

Iowa State University
Ames, IA 50011, U.S.A.
{sjellis, telomere, tklinge, jil, lutz, rlutz, divita, asminer}@iastate.edu

Ellis, Samuel J., et al. "Automated requirements analysis for a molecular watchdog timer." Proceedings of the 29th ACM/IEEE international conference on Automated software engineering. ACM, 2014.

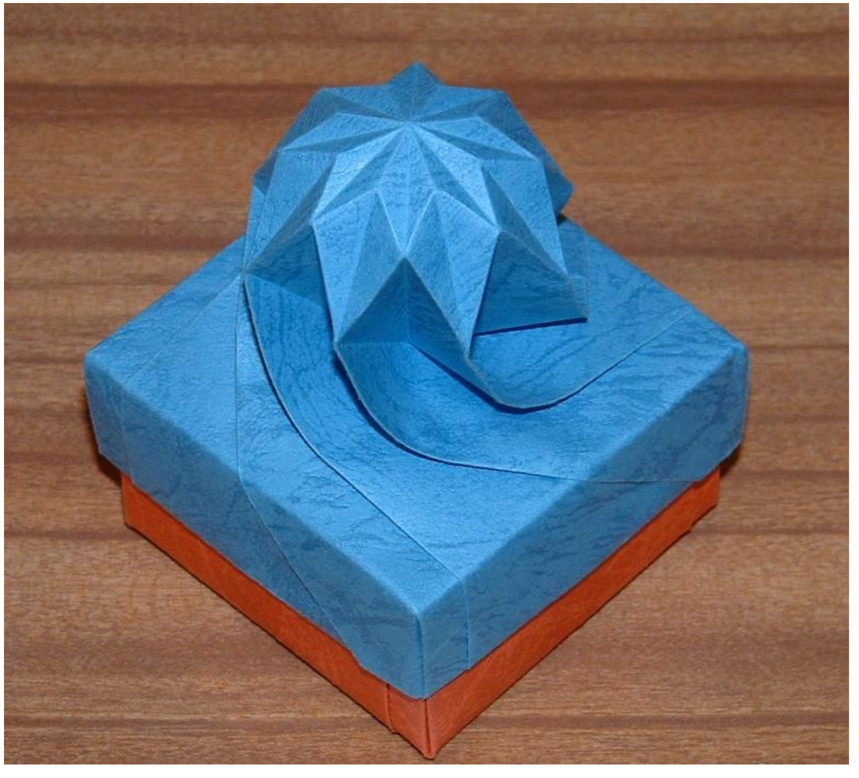
DNA, a tool in the world of Nanotechnology

Origami – folding, sculpting.

http://www.wired.com/dangerroom/2011/03/army-enlists-dna-origami-to-spot-outbreaks/

Traditional Origami

- Fold “2D” pieces of paper to form three dimensional shapes.
- Folds are kept in place by creases in the paper.

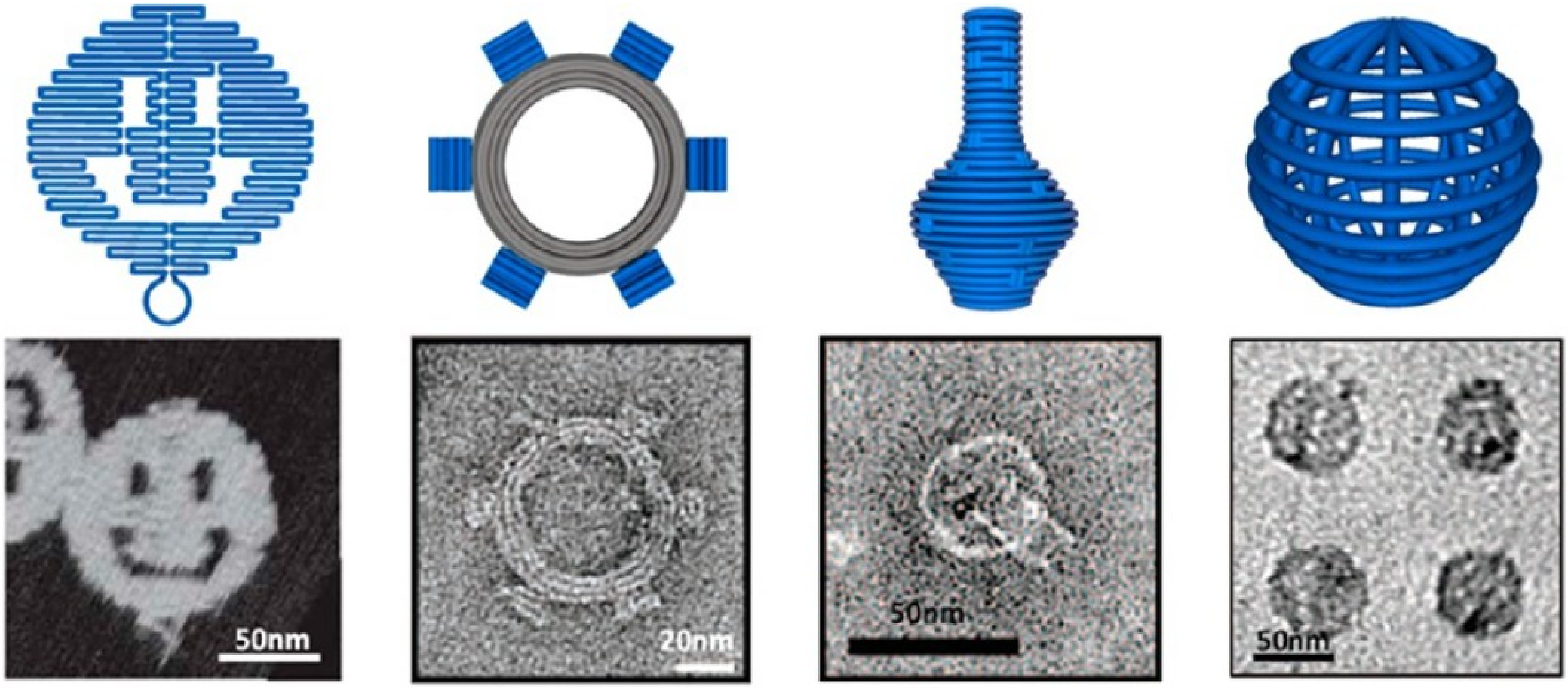


Artist: Chris Palmer

Artist: Joel Cooper

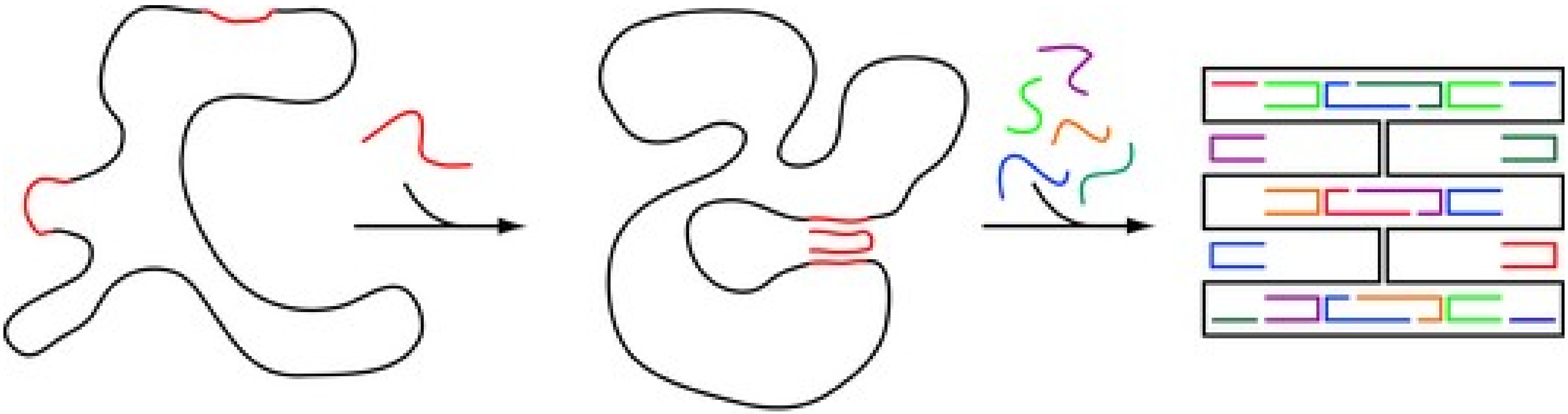
DNA Origami

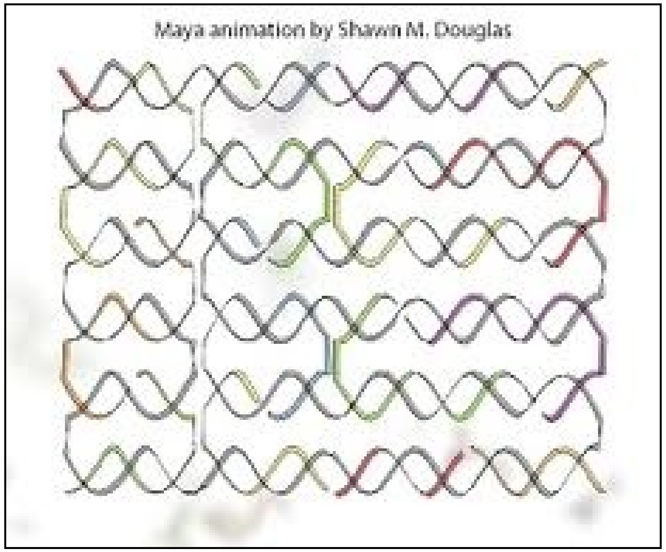
- Fold a long “1D” strand of DNA to form two and three dimensional shapes.
- Folds are kept in place by small *staple* strands.



Zhang, Fei, et al. "Structural DNA Nanotechnology: State of the Art and Future Perspective." Journal of the American Chemical Society 136.32 (2014): 11198-11211.

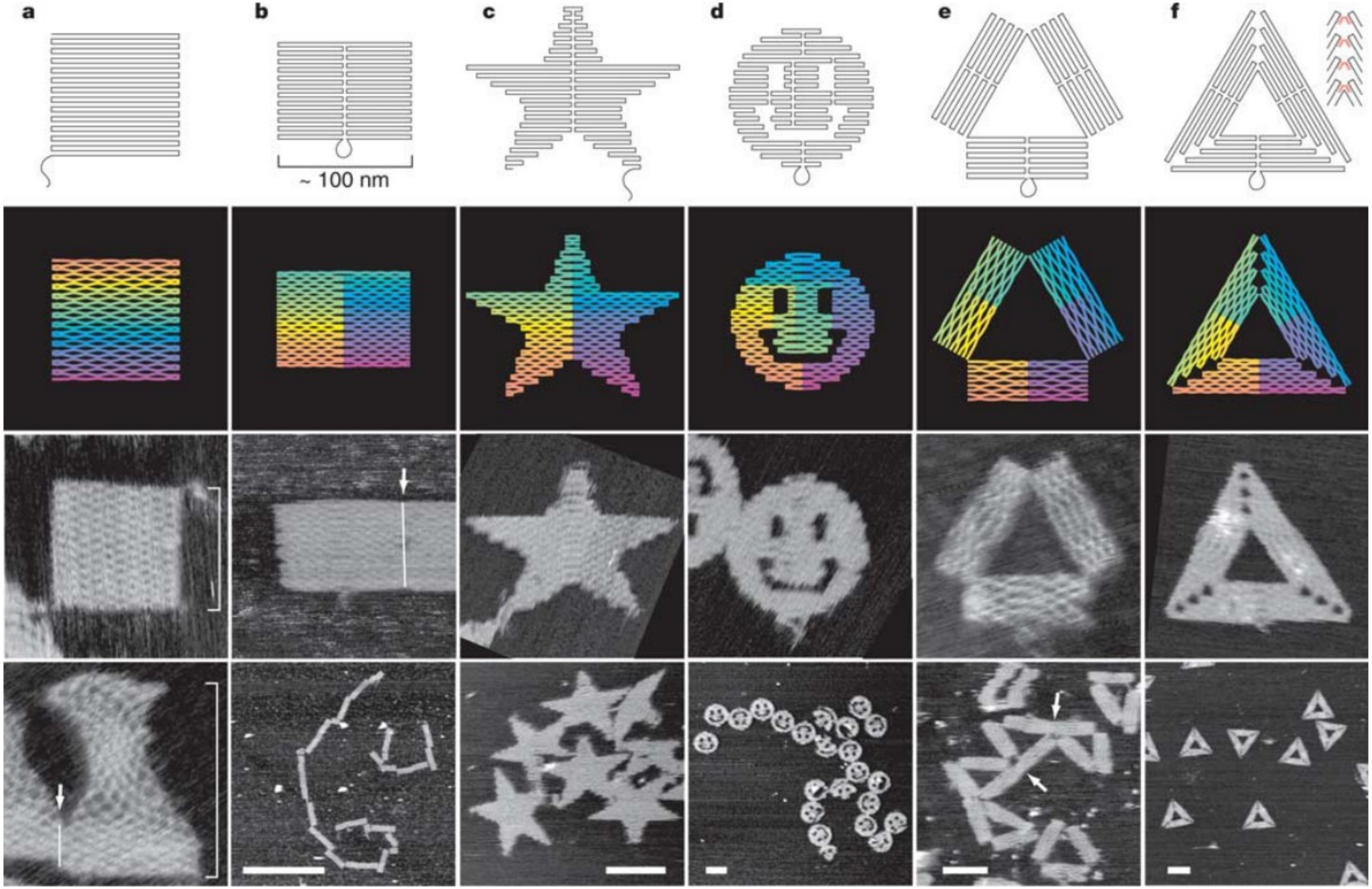
How it Works





http://209.20.81.220/intro.html

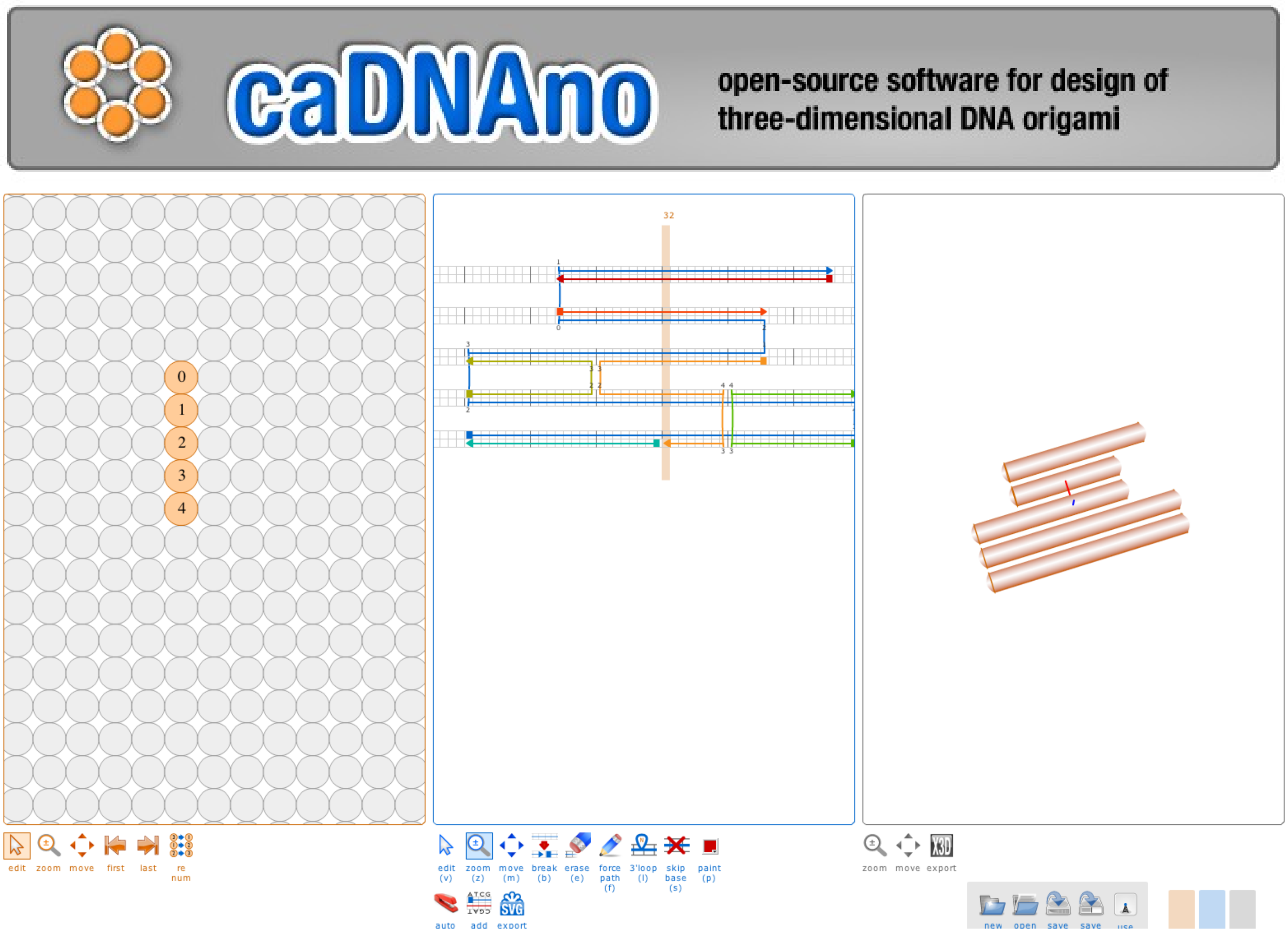
2D Structures…



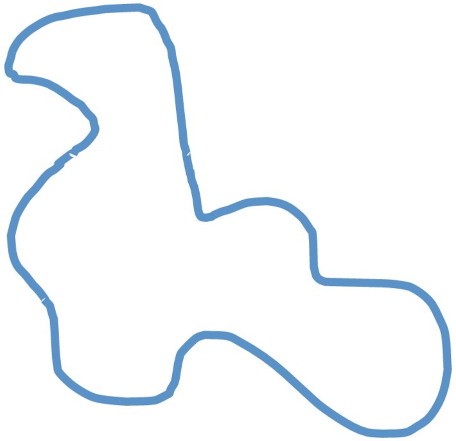
DOI: 10.1038/nature04586

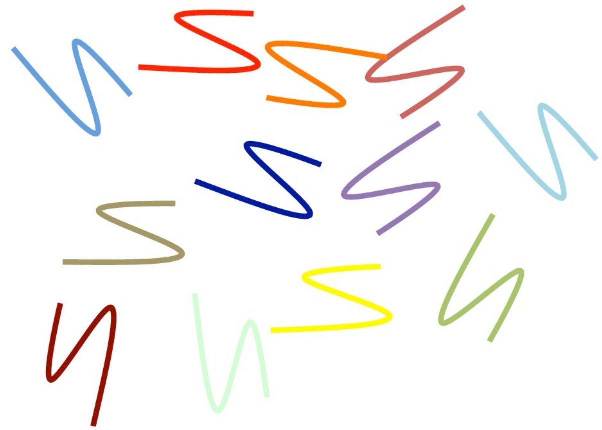
…or ANYTHING Your Imagination Can Make!

How to Build Your DNA Origami



How to build your DNA Origami

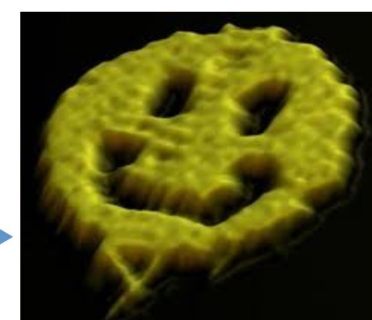




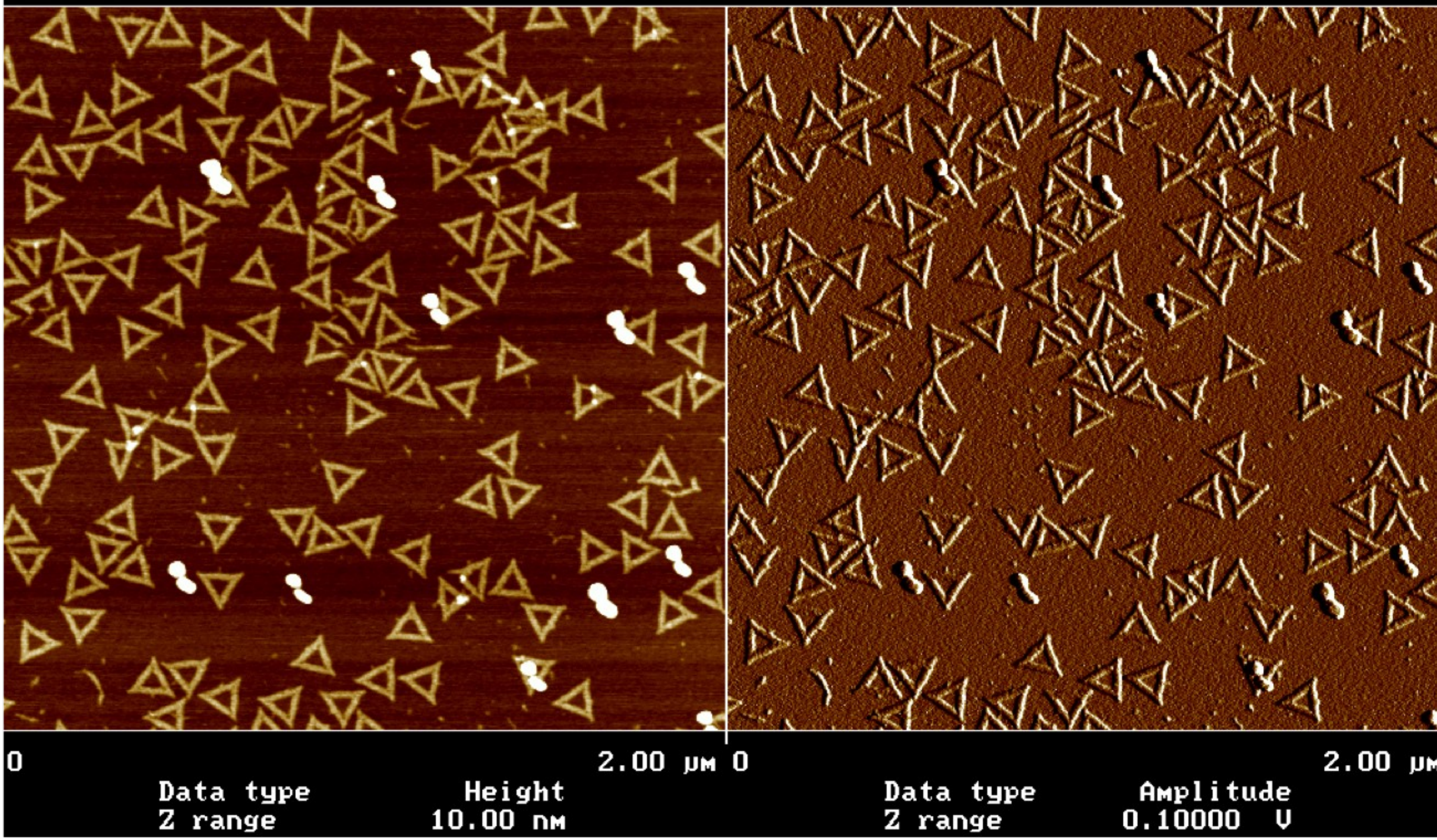
Scaffold: m13mp18 ssDNA, 7249nt

Staples: 20-60nt long oligos

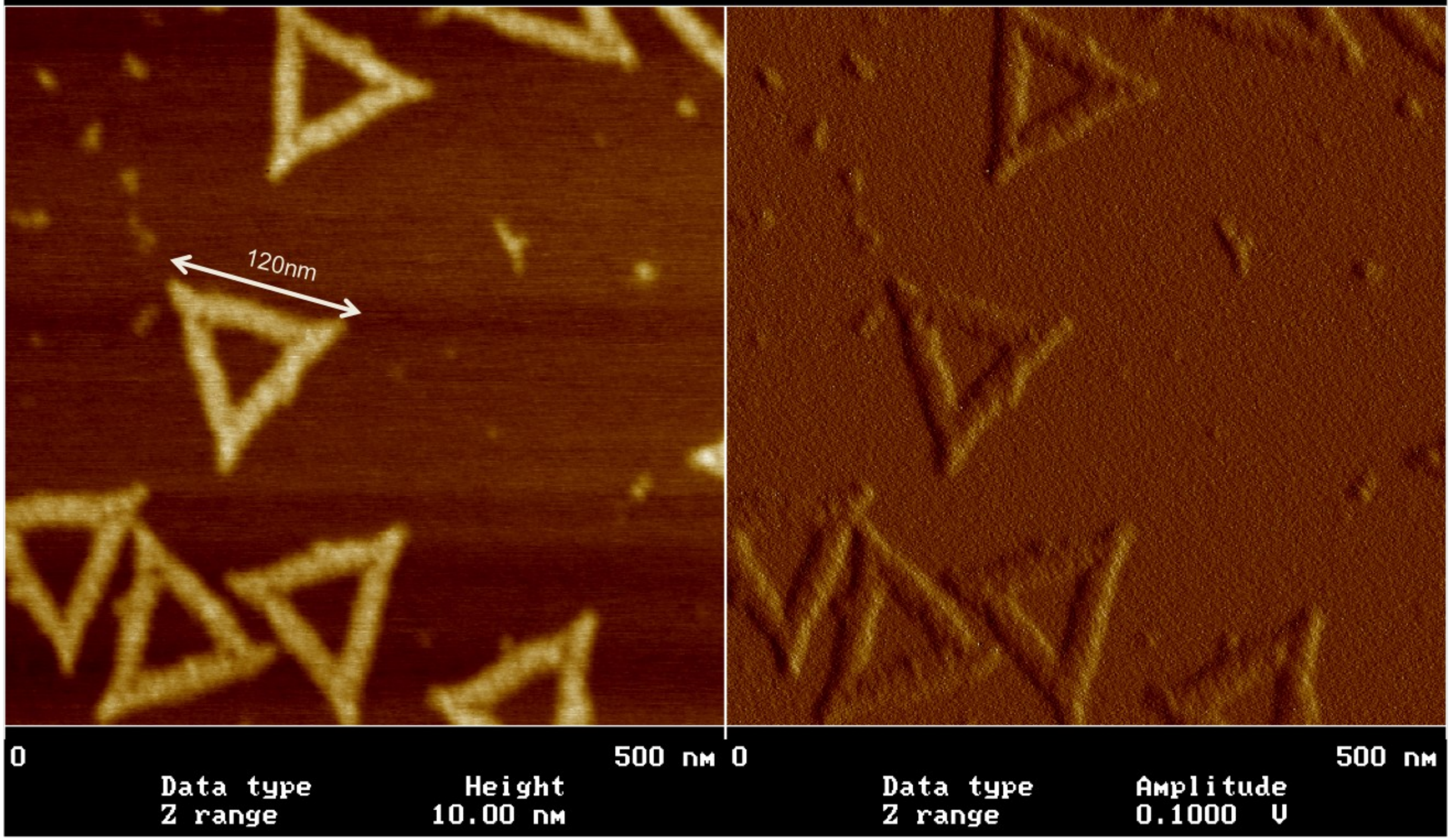
Heat it. Cool it.



From the Henderson Lab (0112MBB)

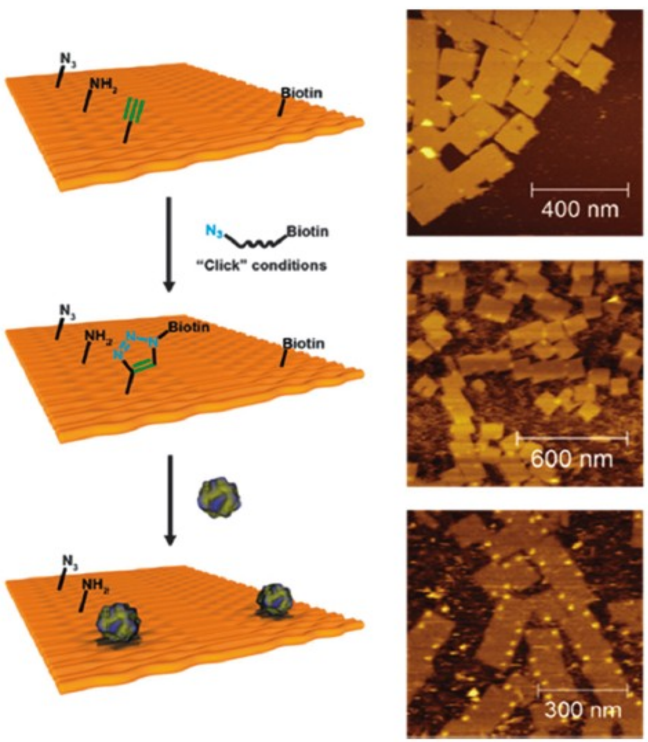


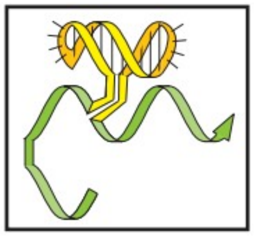
You are welcome anytime!

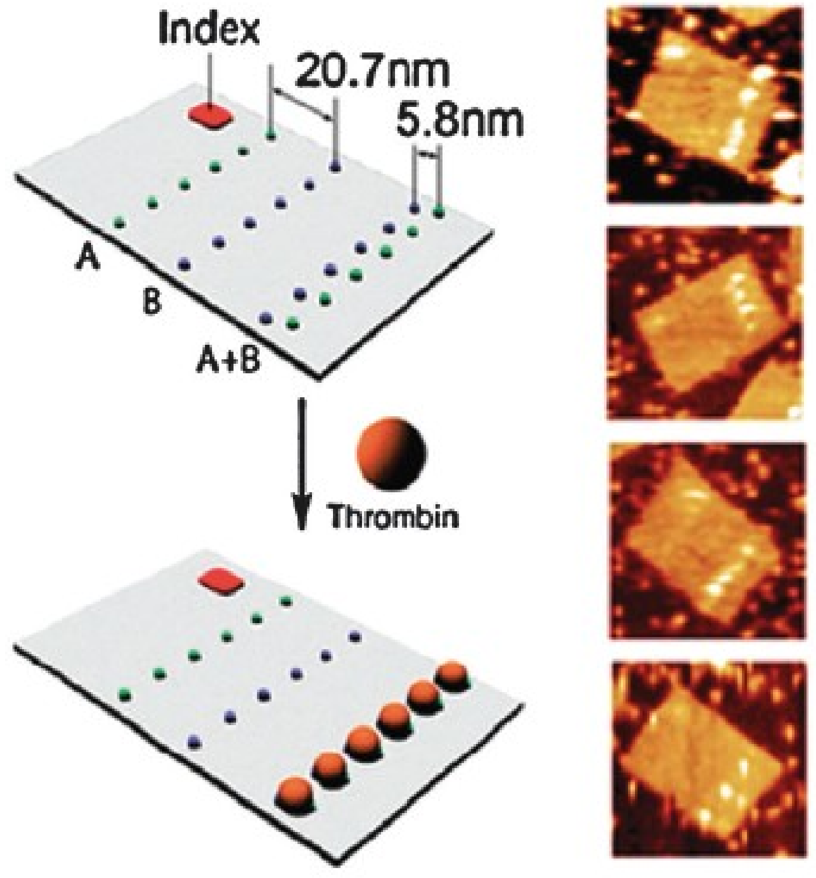


Functionalization: Molecular ‘bread board’

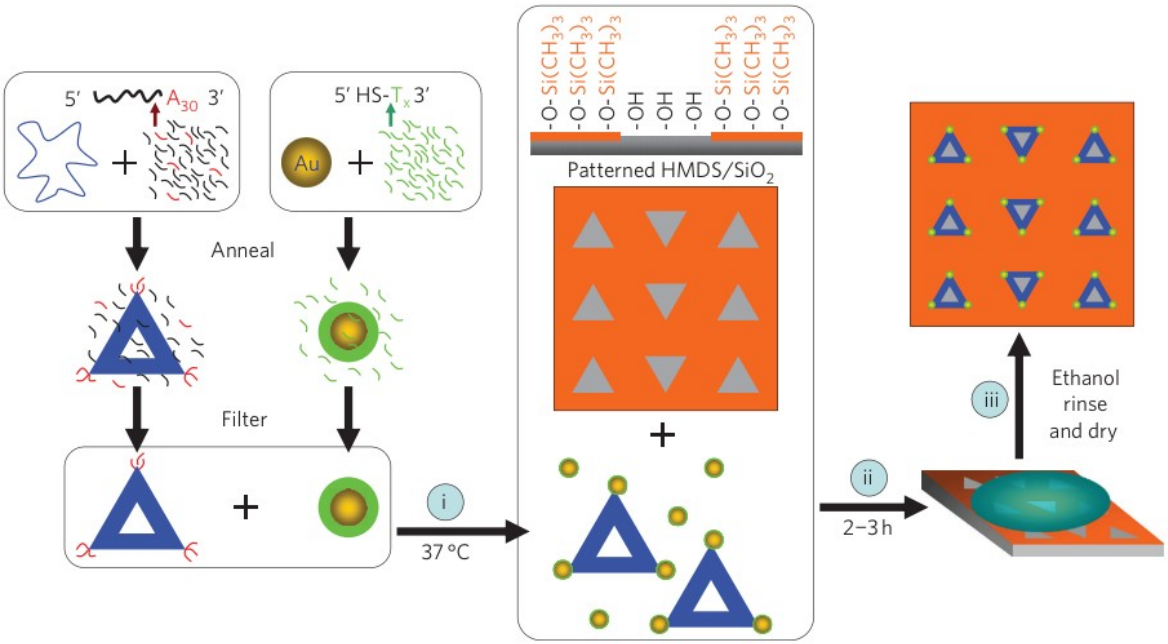
Addressibility: Modify staples with other molecules and add to the pool of staples. Heat it. Cool it. Image it. Study **single-molecule** chemical reactions.

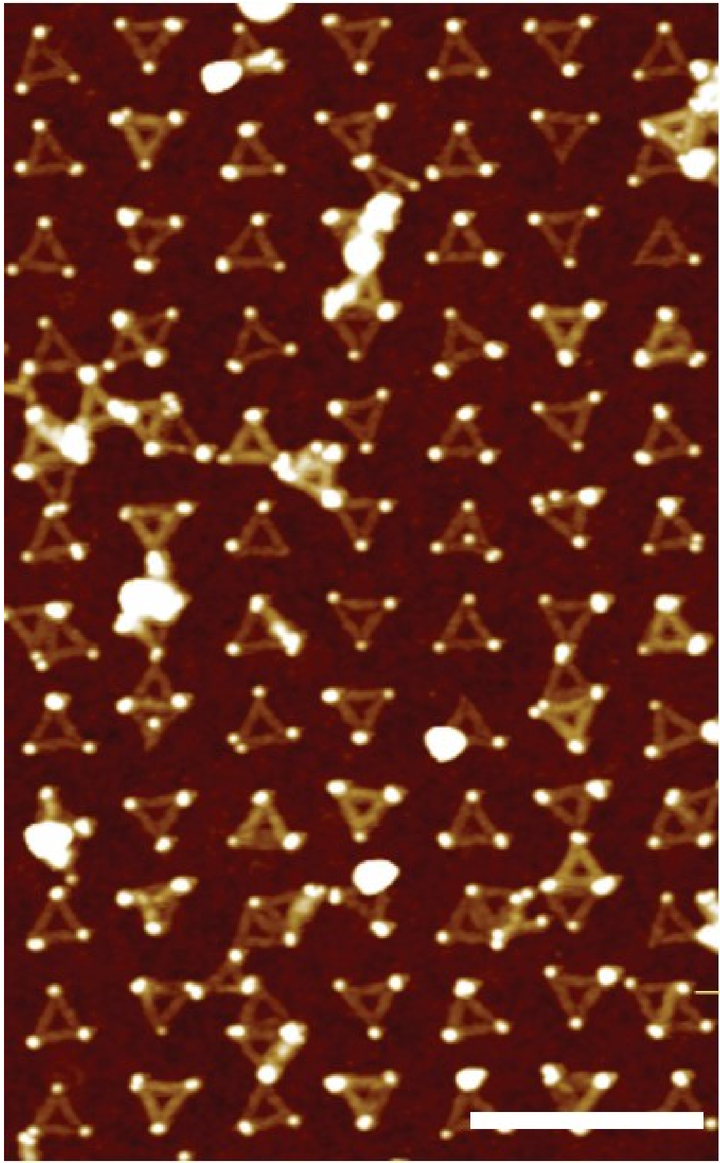






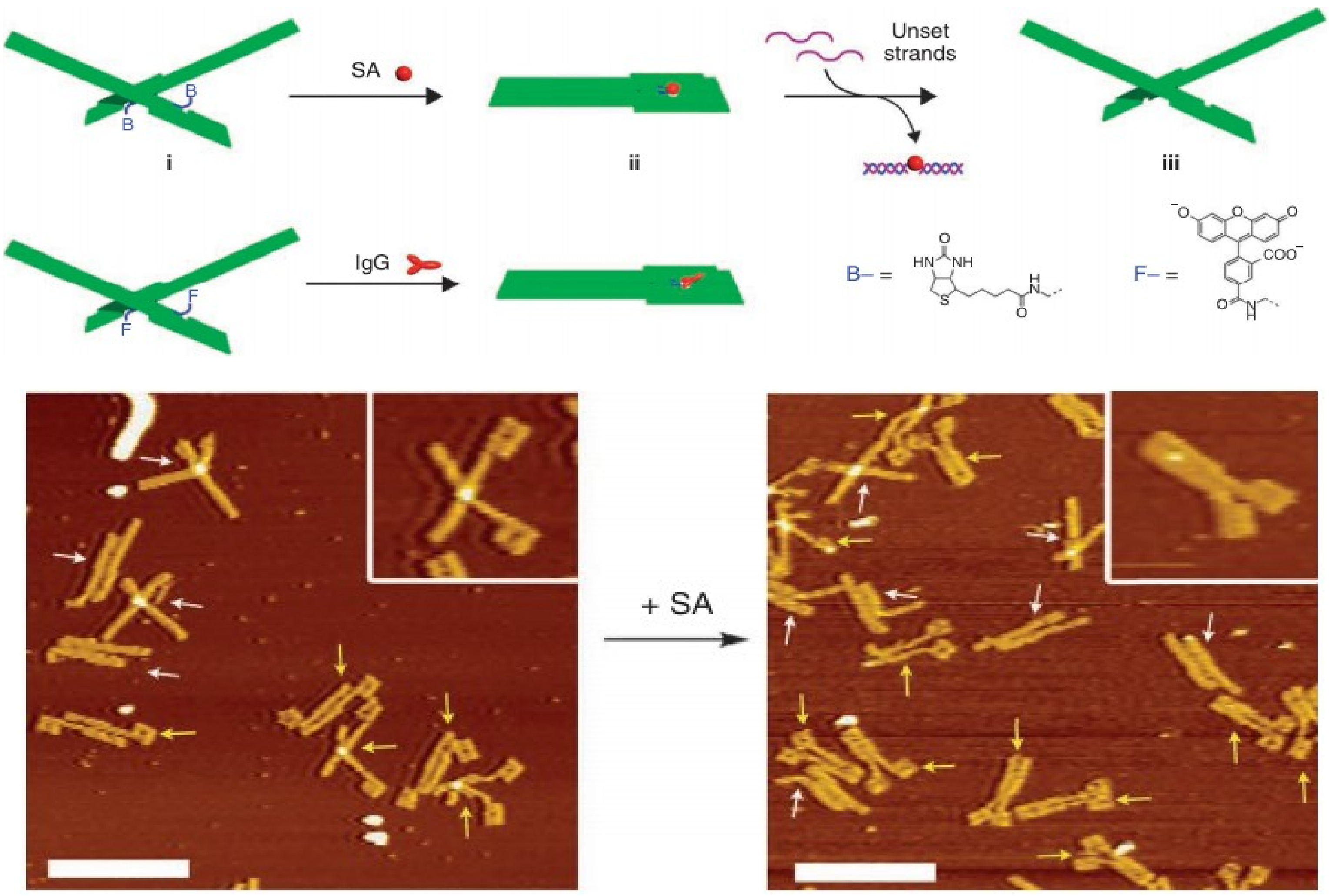
Control Over Nano- Patterning



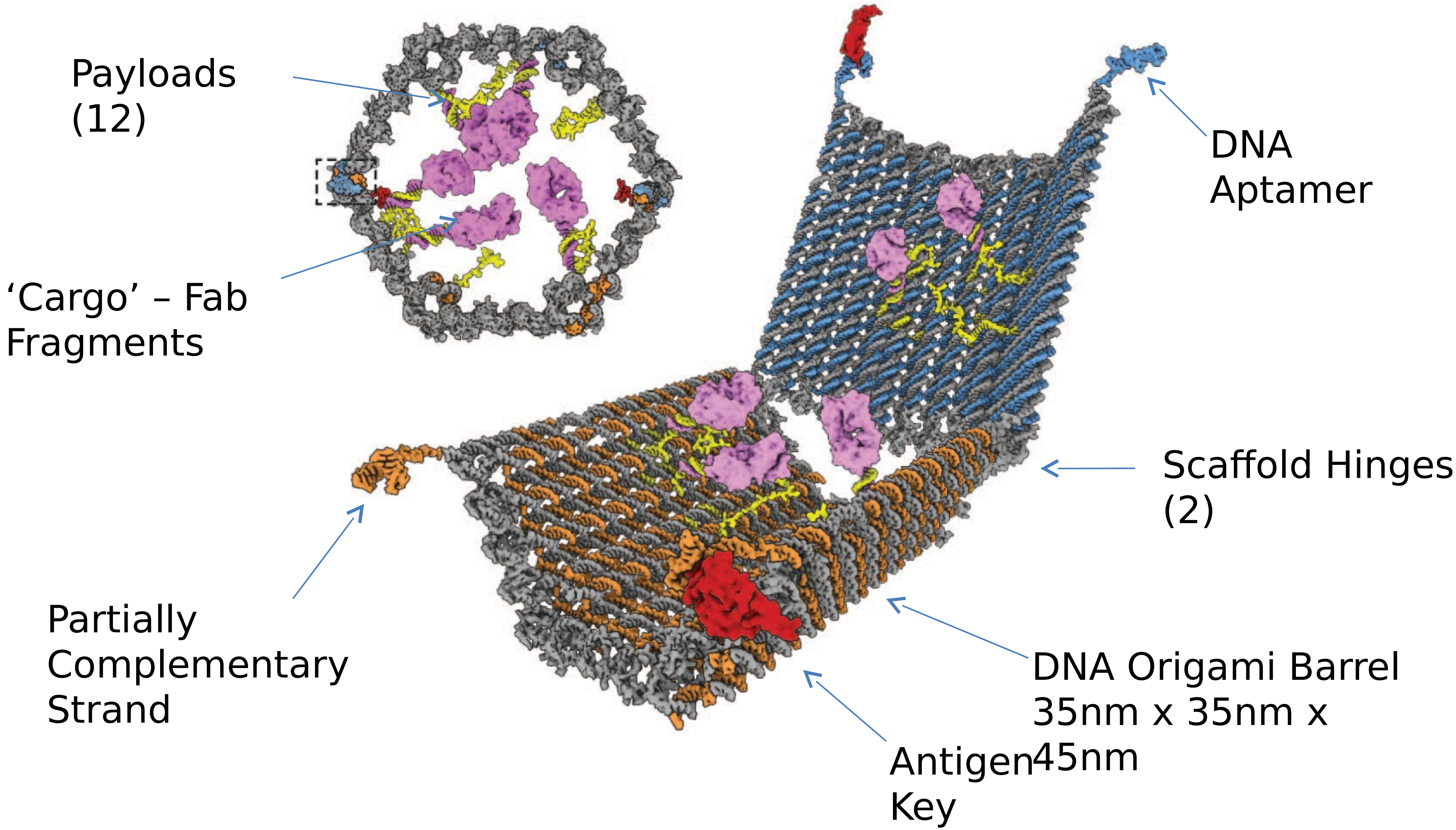


Use of DNA Origami to arrange ‘sub-10-nm’ components over macroscopic areas by combining top-down lithography and bottom-up self assembly. DNA Origami imparts more control over position and orientation during deposition.

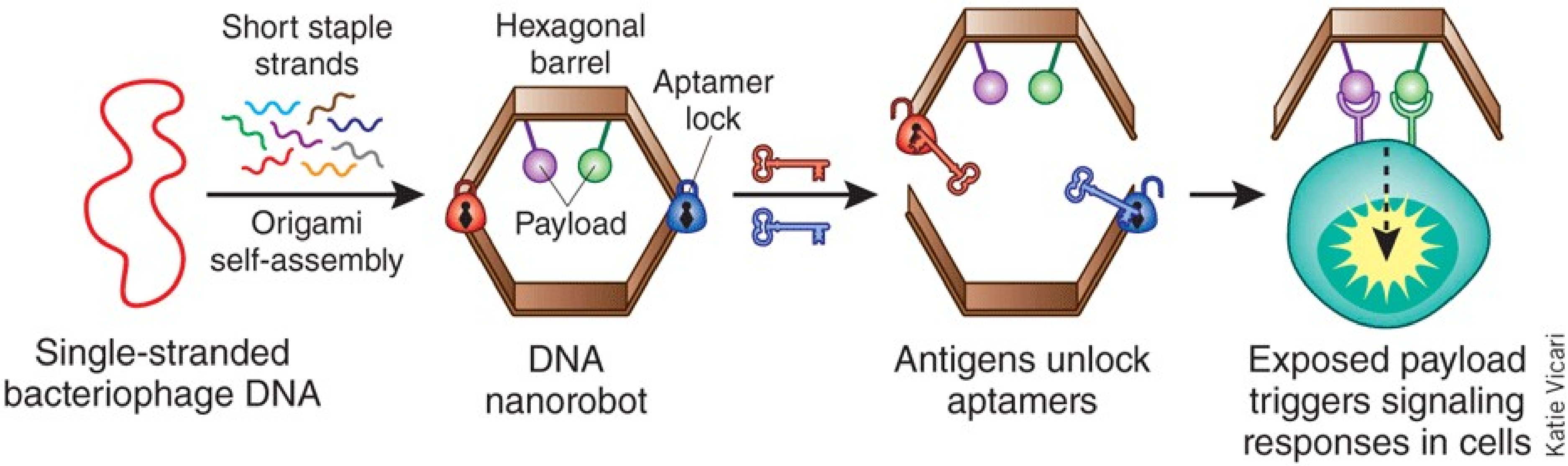
Dynamic Systems- Molecular ‘Pliers’



‘Nanorobot’, for Delivery of Molecular Payloads

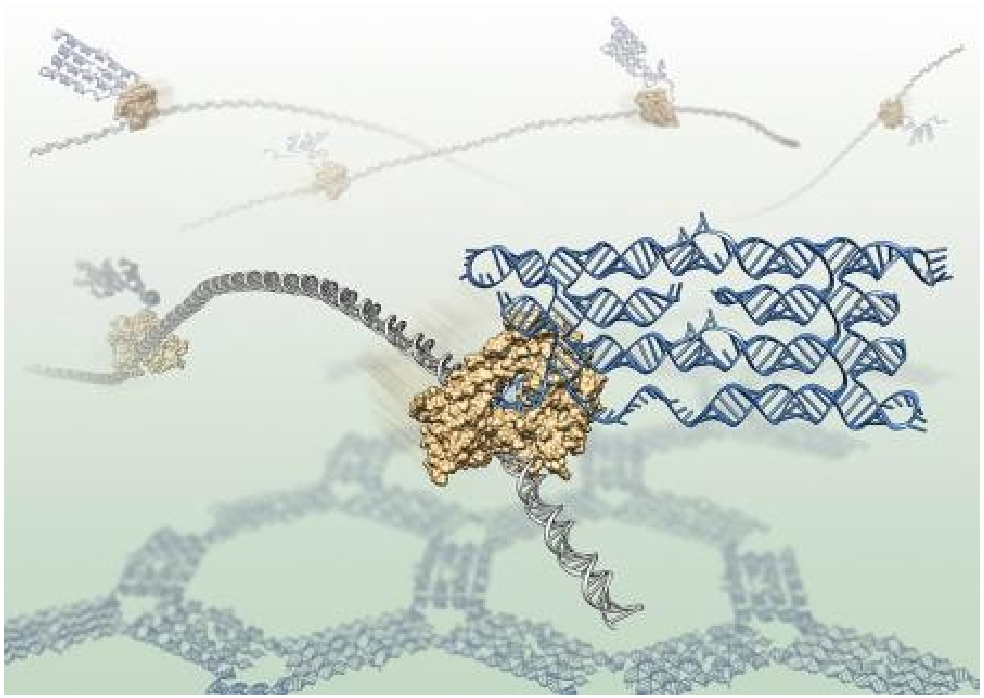


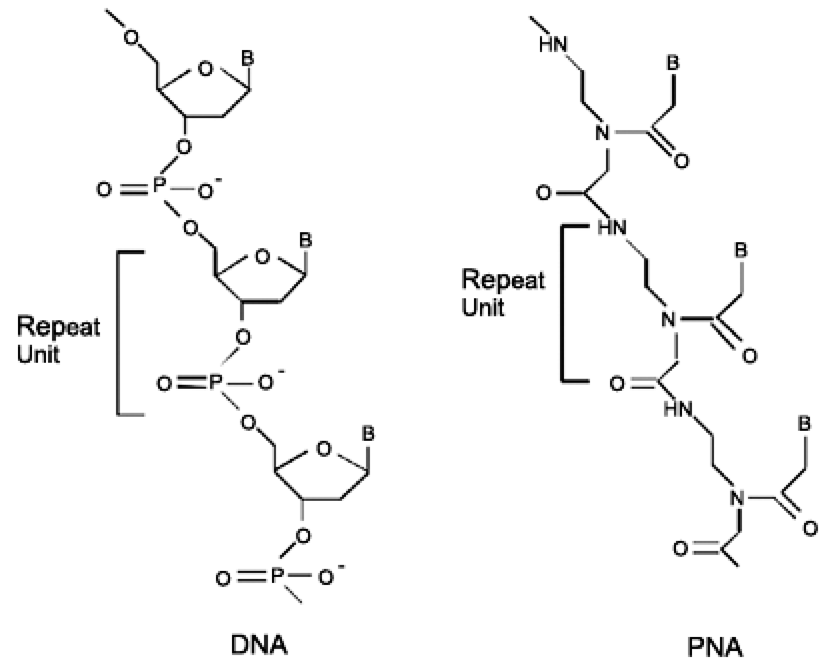
Delivers Right at the Cell, Unlocked by Cell Surface Receptors



Fu, Jinglin, and Hao Yan. "Controlled drug release by a nanorobot." Nature biotechnology 30.5 (2012): 407-408.

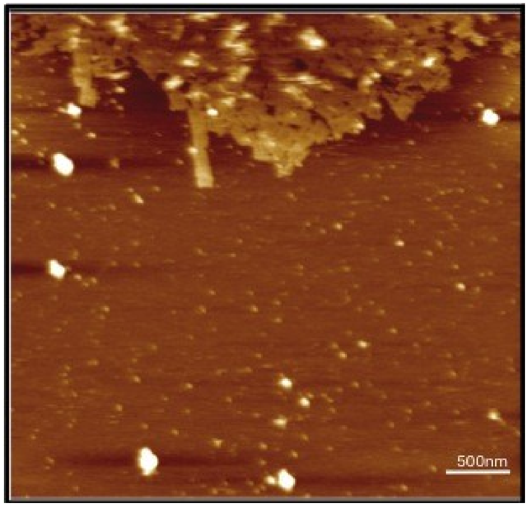
RNA Origami

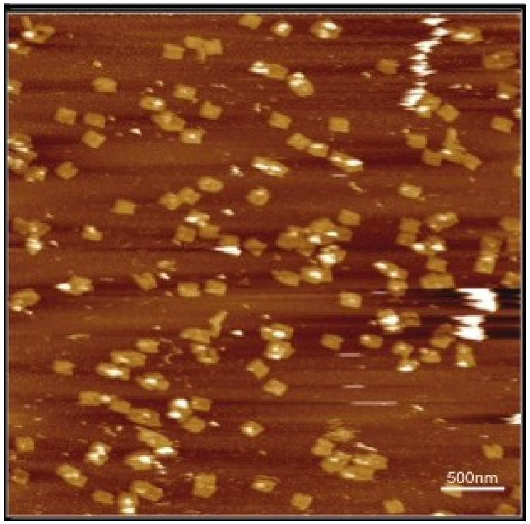


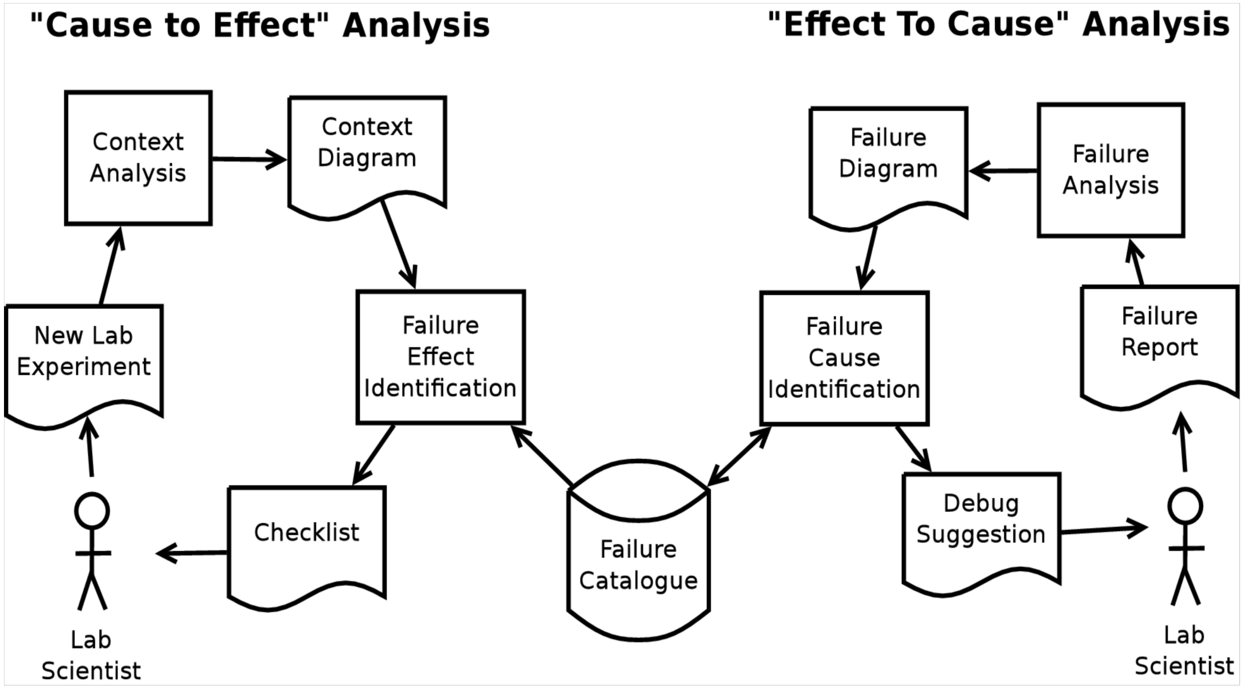


Geary, Cody, Paul WK Rothemund, and Ebbe S. Andersen. "A single-stranded architecture for cotranscriptional folding of RNA nanostructures." Science 345.6198 (2014): 799-804.
Nielsen, Peter E., et al. "Peptide nucleic acids." U.S. Patent No. 5,539,082. 23 Jul. 1996.

LAMP: DNA Origami Failures

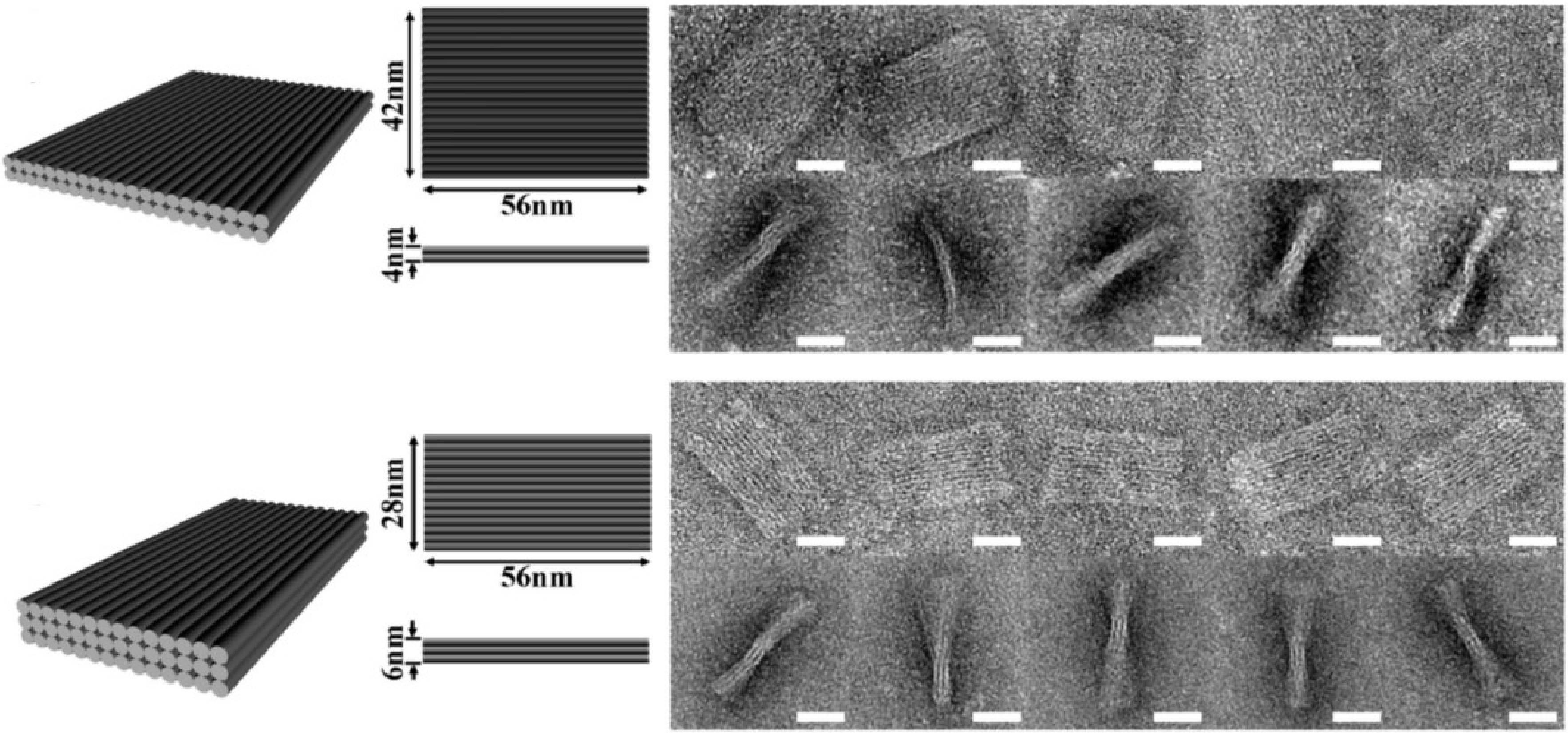






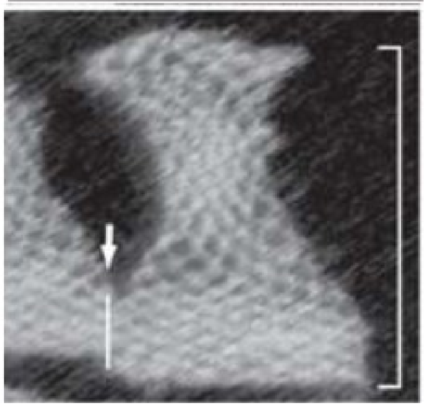
Thein Than Tun, Robyn Lutz, Brian Nakayama, Yijun Yu, Divita Mathur and Bashar Nuseibeh. “The role of environmental assumptions in failures of DNA nanosystems,” COUFLESS 2015, Florence, Italy. ACM, 2015.

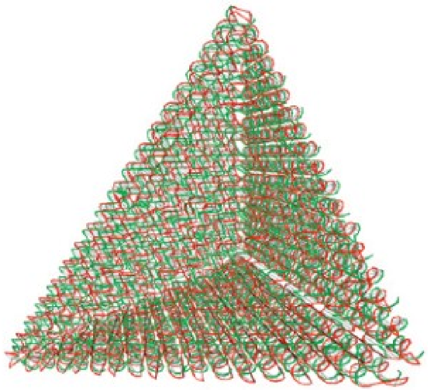
Global Twisting

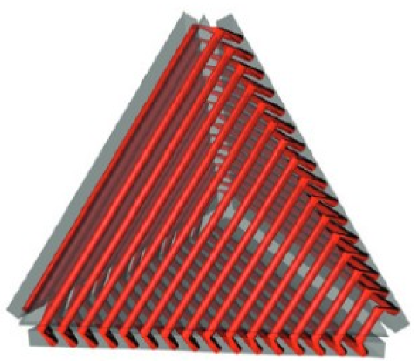


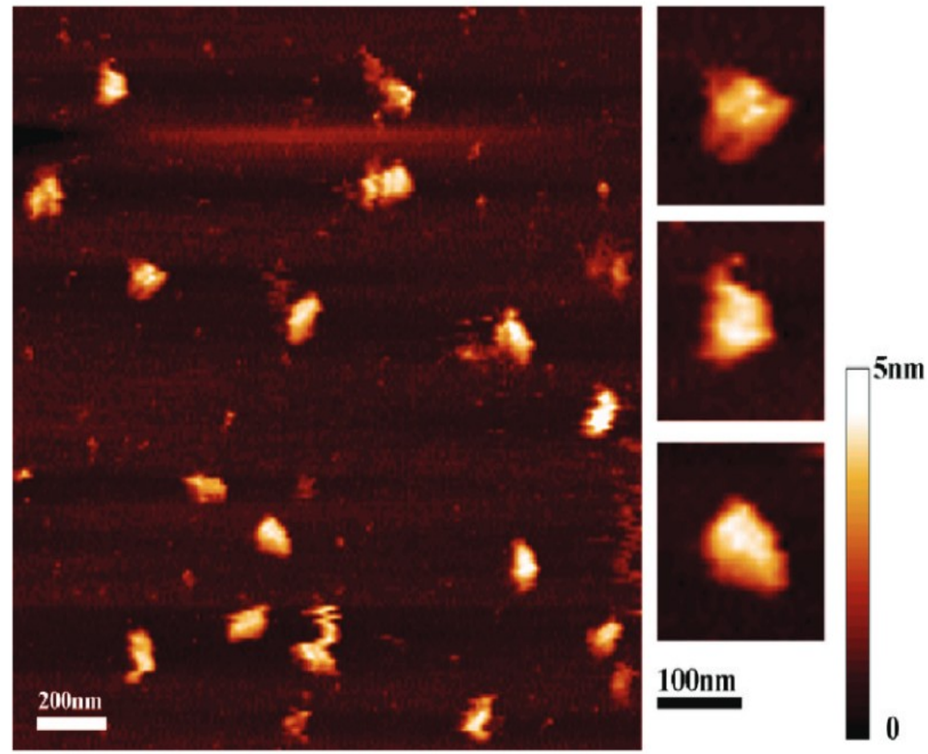
Ke, Yonggang, et al. "Multilayer DNA origami packed on a square lattice." Journal of the American Chemical Society 131.43 (2009): 15903-15908.

AFM Interference



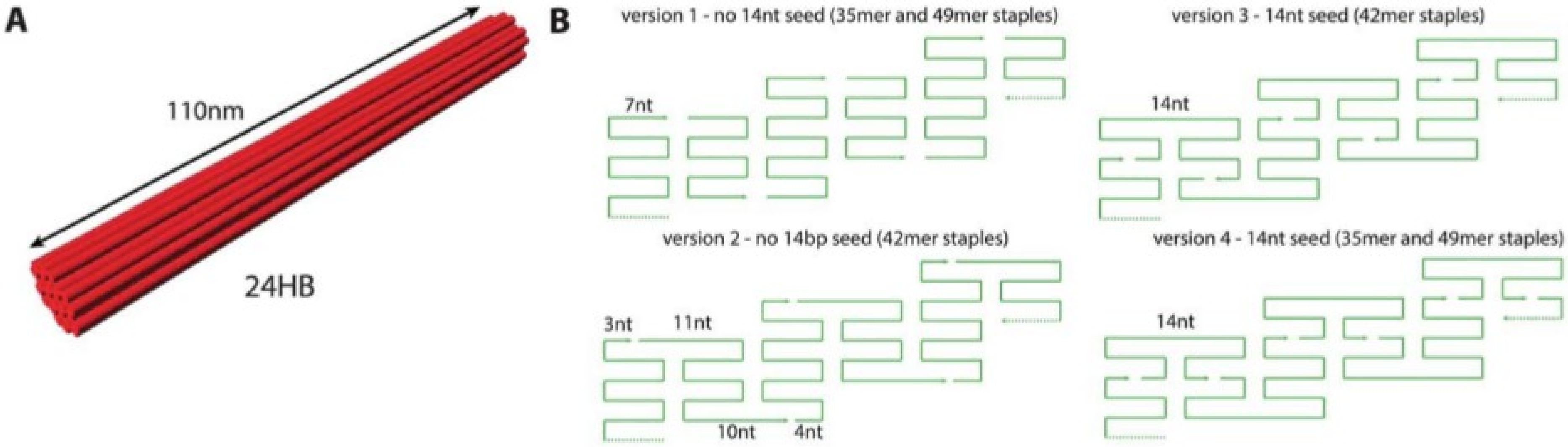






Rothemund, Paul WK. "Folding DNA to create nanoscale shapes and patterns." Nature 440.7082 (2006): 297-302.
Ke, Yonggang, et al. "Scaffolded DNA origami of a DNA tetrahedron molecular container." Nano letters 9.6 (2009): 2445-2447.

Unoptimized Staple Strands



Ke, Yonggang, et al. "Two design strategies for enhancement of multilayer–DNA-origami folding: underwinding for specific intercalator rescue and staple-break positioning." Chemical Science 3.8 (2012): 2587-2597.

Origami Failure Catalog

11 Retrieved codings: "atomic force microscopy" from 7 files

AFM Distortion of Origami [244:333]Back

Atomic Force Microscopy returns either an altered structure, or it damages the structure.

AFM Distortion of Origami [344:1069]Back

Found when examining a DNA Origami dolphin. The tail of the dolphin was distorted when applying extra force on the AFM tip: "this tail distortion can clearly be assigned as an influence of the force exerted by the AFM tip" [1]. Furthermore, the direction of scanning affected the dolphin's tail [1]. In several 3d origami shapes with hollow cores [2][3][4], the AFM tip caused the shapes to either be shorter than expected [3] or caused the shapes to completely collapse [2][4]. Rothemund found that 26-helix squares were being stretched by the tip of the AFM creating hourglass shapes [5]. Furthermore, in labeled staple experiments (where the staple formed a hairpin), the AFM may have also damaged the labeled staples [5].

AFM Distortion of Origami [1078:1421]Back

: Atomic Force Microscopy works by scanning a 3 dimensional surface with a needle in order to create a height-map corresponding to the surface. (Note, this does not mean it only works for 3d origami. 2d origami also has a height). The force applied by the needle touching an origami can distort or destroy the intended structure of the origami.

AFM Distortion of Origami [1435:1804]Back

Increasing the resolution for an AFM, which also increases the force may create noticeable distortions [1]. Differences in design and AFM output, especially differences in height or in one direction, implies an unwanted interaction with the tip. Sequential imaging can show deformations that occur over time, which may suggest unwanted interactions with the needle [5].

AFM Distortion of Origami

<Analyzing Results Work><single-layer/hollow 3D origami><AFM (cantilever)><AFM (tip)><higher resolution><Component Failure>AFM Distortion of Origami:

Assumed Properties: AFM (tip, cantilever), Single-Layer 3D Origami (Hollow 3D Origami), Higher Resolution (higher force on tip)

Affected System Goals: Analysis, Feedback

Failure Type: Component

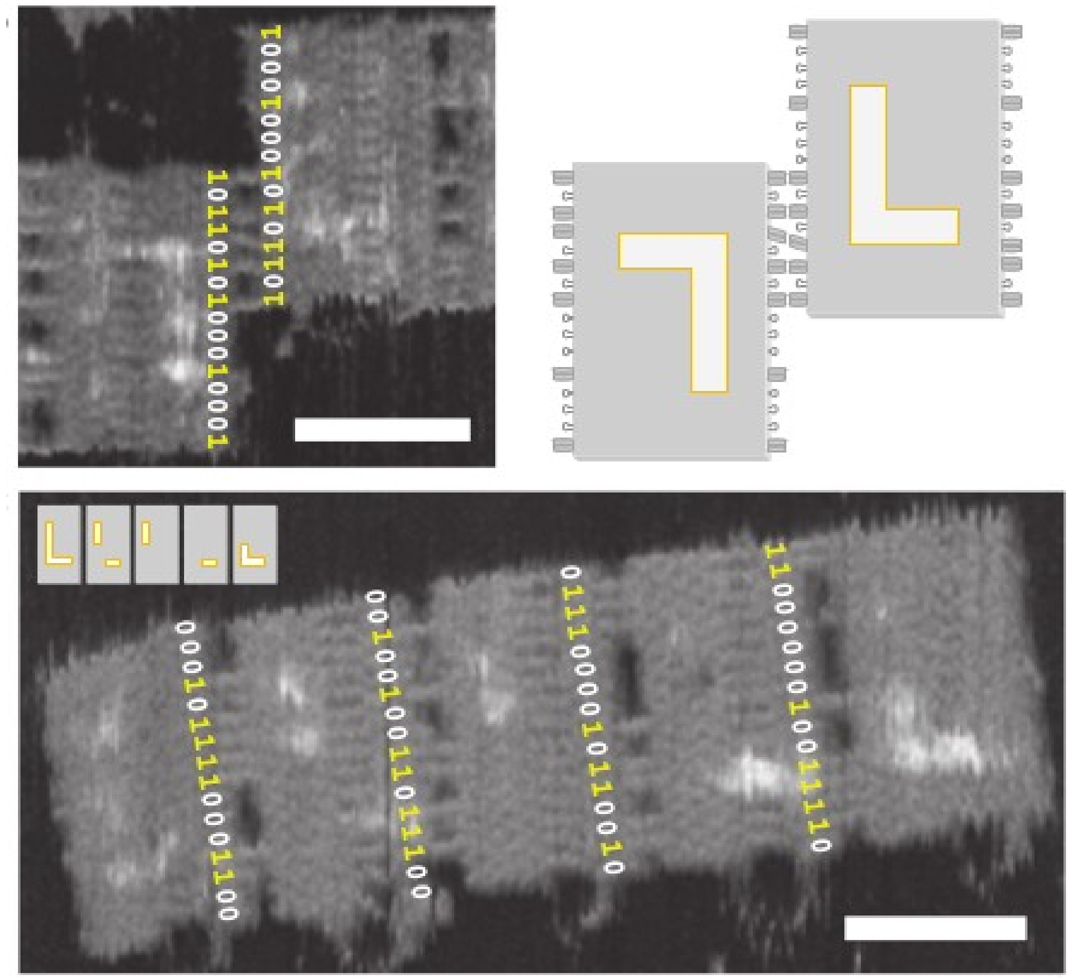
Description: <atomic force microscopy>Atomic Force Microscopy returns either an altered structure, or it damages the structure.

Origin: <atomic force microscopy>Found when examining a DNA Origami dolphin. The tail of the dolphin was distorted when applying extra force on the AFM tip: "this tail distortion can clearly be assigned as an influence of the force exerted by the AFM tip" [1]. Furthermore, the direction of scanning affected the dolphin's tail [1]. In several 3d origami shapes with hollow cores [2][3][4], the AFM tip caused the shapes to either be shorter than expected [3] or caused the shapes to completely collapse [2][4]. Rothemund found that 26-helix squares were being stretched by the tip of the AFM creating hourglass shapes [5]. <staple>Furthermore, in labeled staple experiments (where the staple formed a hairpin), the AFM may have also damaged the labeled staples [5].

Cause:<atomic force microscopy> Atomic Force Microscopy works by scanning a 3 dimensional surface with a needle in order to create a height-map corresponding to the surface. (Note, this does not mean it only works for 3d origami. 2d origami also has a height). The force applied by the needle touching an origami can distort or destroy the intended structure of the origami.

Thein Than Tun, Robyn Lutz, Brian Nakayama, Yijun Yu, Divita Mathur and Bashar Nuseibeh. “The role of environmental assumptions in failures of DNA nanosystems,” COUFLESS 2015, Florence, Italy. ACM, 2015. Accepted.

Leveraging Past Failures



Woo, Sungwook, and Paul WK Rothemund. "Programmable molecular recognition based on the geometry of DNA nanostructures." Nature chemistry 3.8 (2011): 620-627.

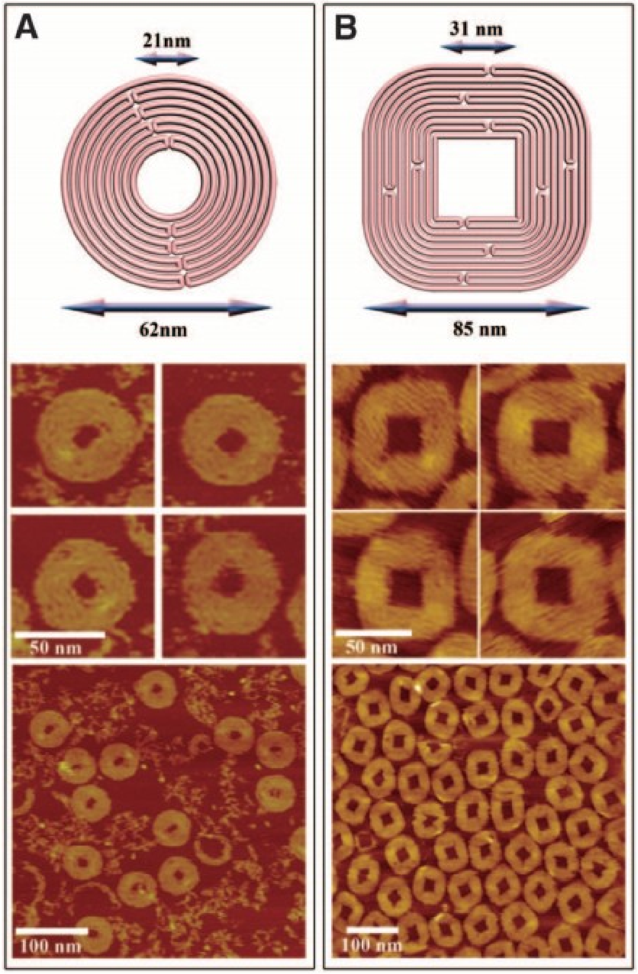
LAMP: Laboratory for Molecular Programming

UNDERGRADUATE STUDENTS

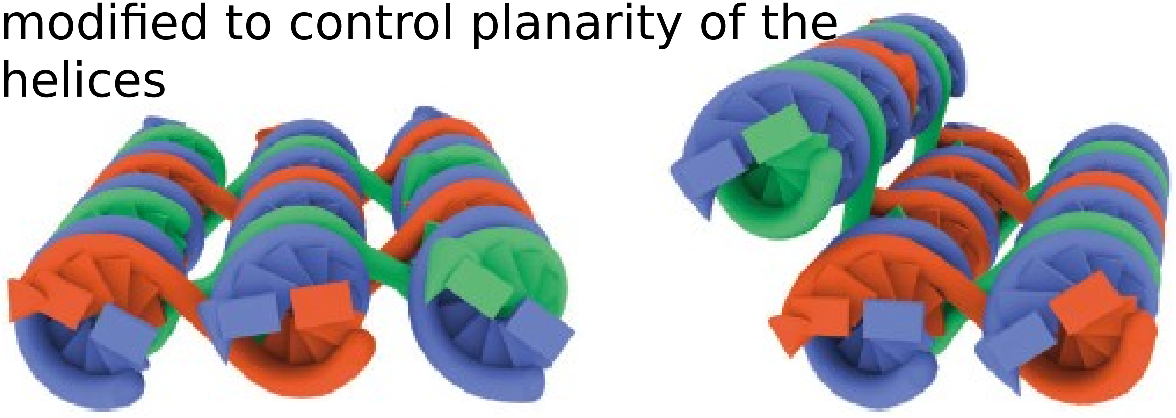
Davis Batten Computer Engineering	Adam Hammes Computer Science	Chase Koehler Computer Science
Charles Labuzzetta Mathematics	Jackson Maddox Computer Science	Gabrielle Ortman Computer Science
Blake Skaja Software Engineering	Nyle Sutton Computer Science Mathematics	Natalie Whitis Biophysics

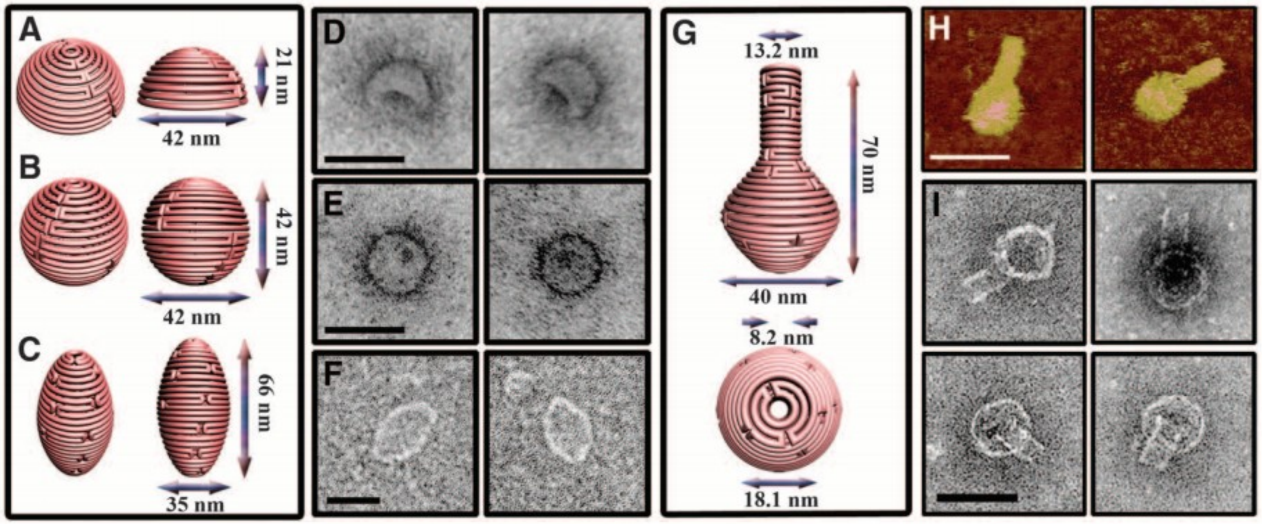
Thank You!

3D DNA Origami

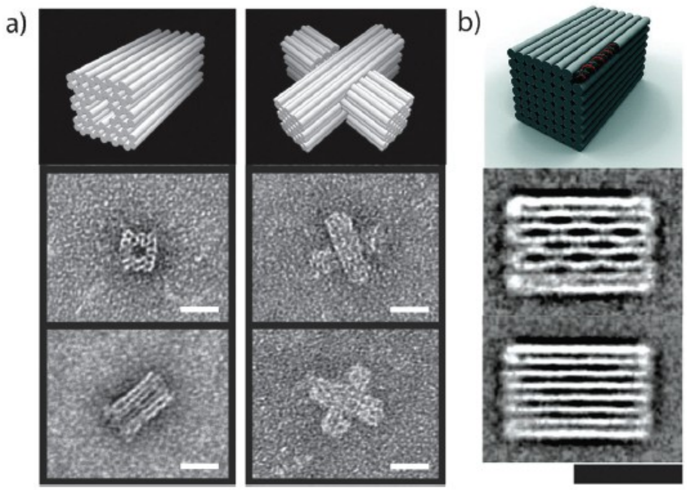


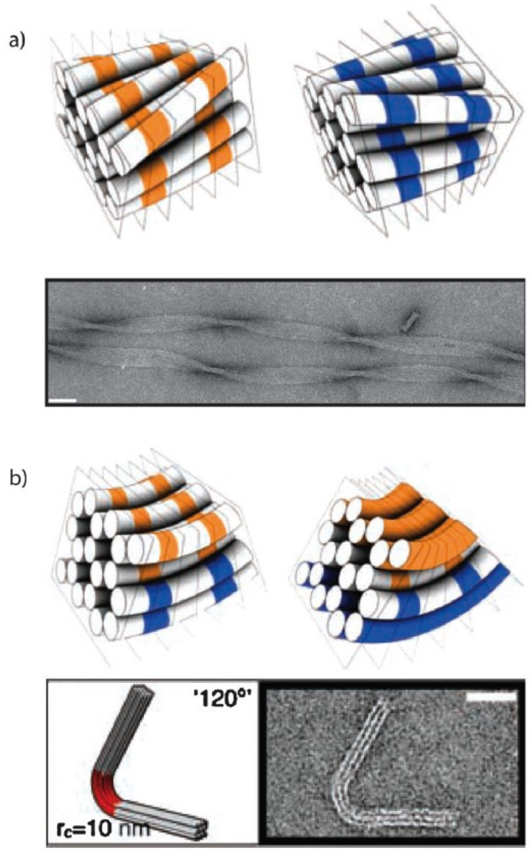
Crossover Arrangement can be modified to control planarity of the helices

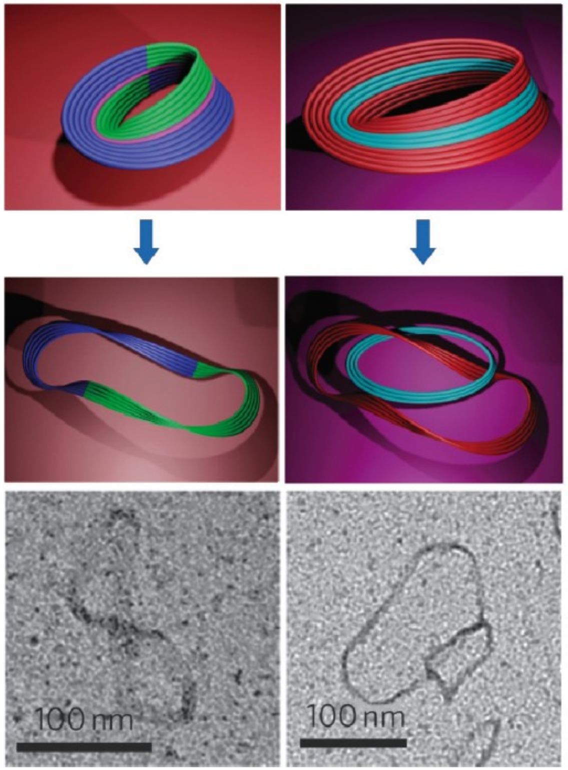




And more GWIZ structures



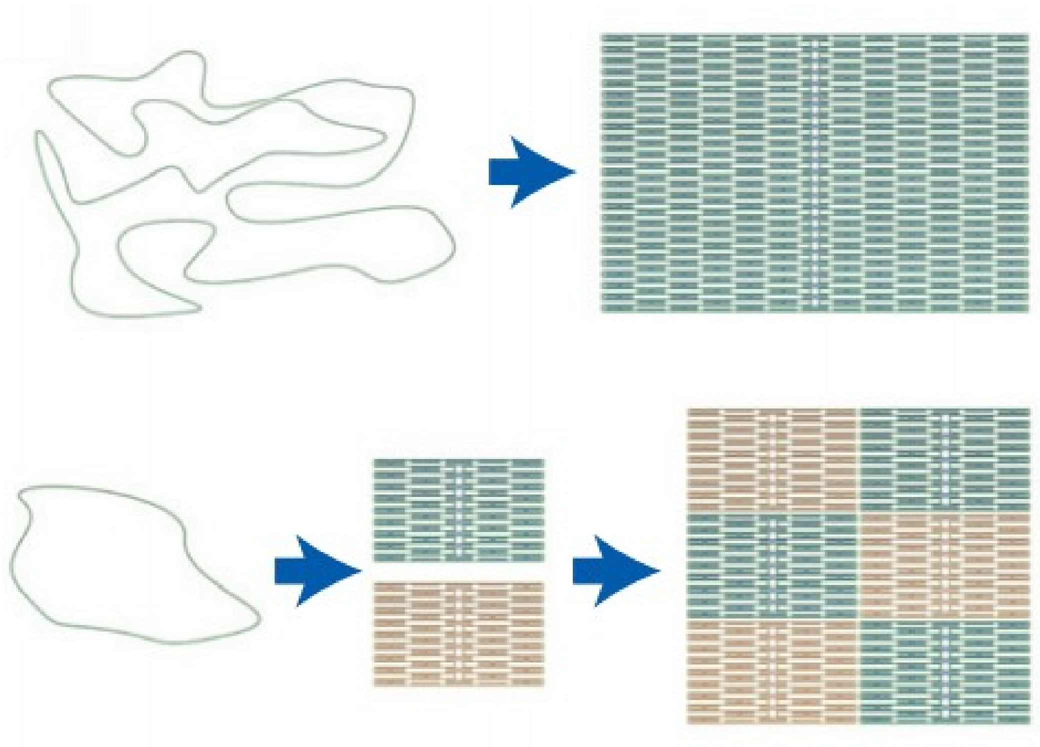




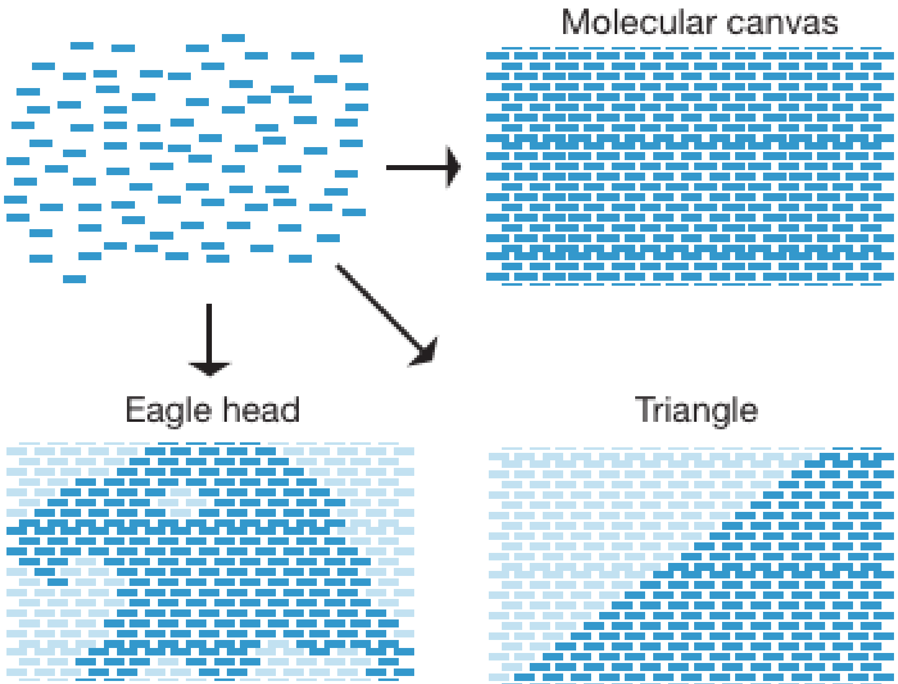
Mobius Strip, *DOI: 10.1038/nnano2010.193*

However, the biggest challenge – the scaffold

- Size – 7249nt
- Nature – m13mp18, a biological source
- Complexity – a handful of scaffolds available



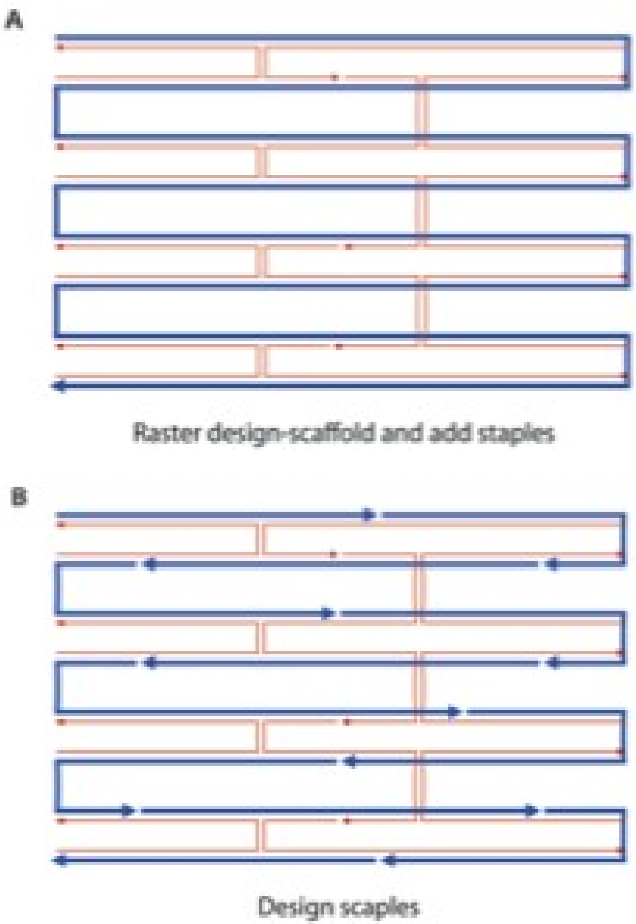
Recent approaches to address DNA Origami limitations

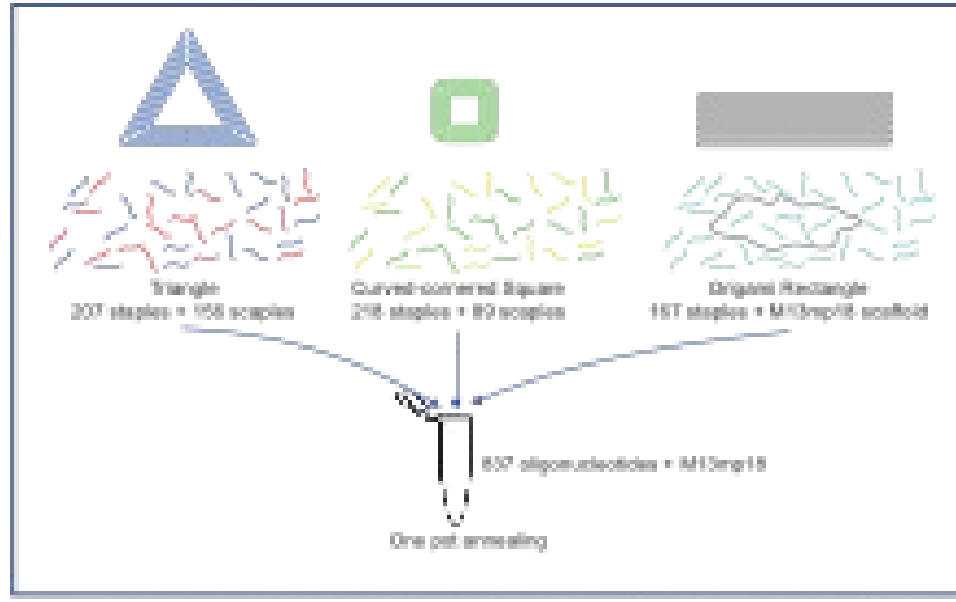


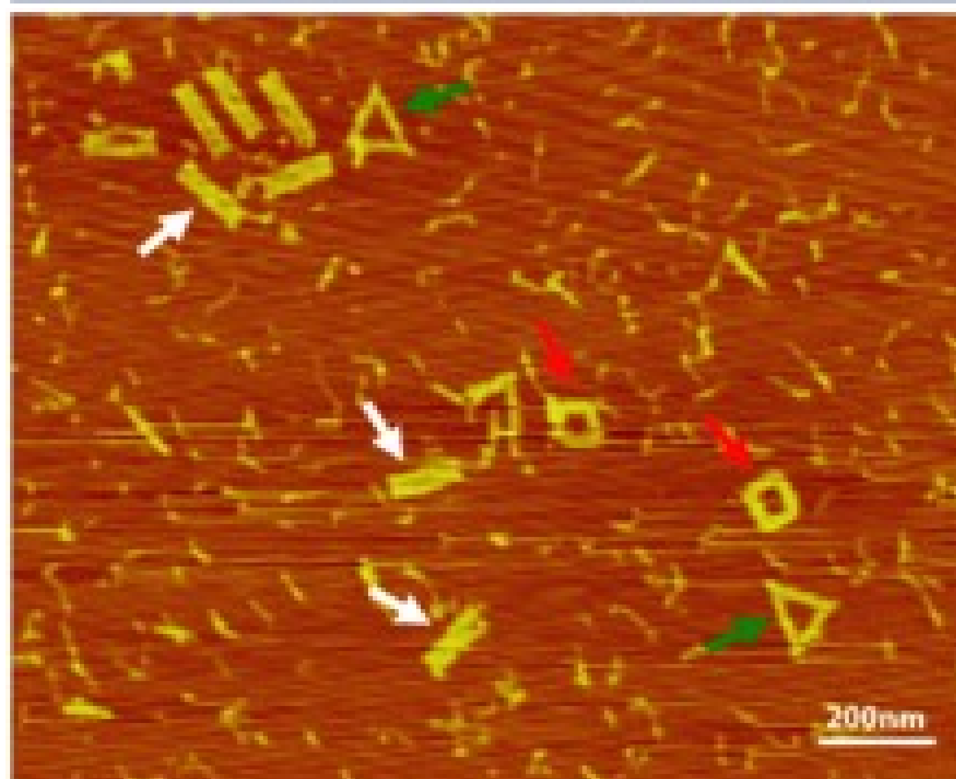
DOI: 10.1038/nature11075

1. Scaffold-less DNA nanostructures, going back to our roots?
2. A tradeoff – yield vs diversity

The ‘KISS’ solution to this issue

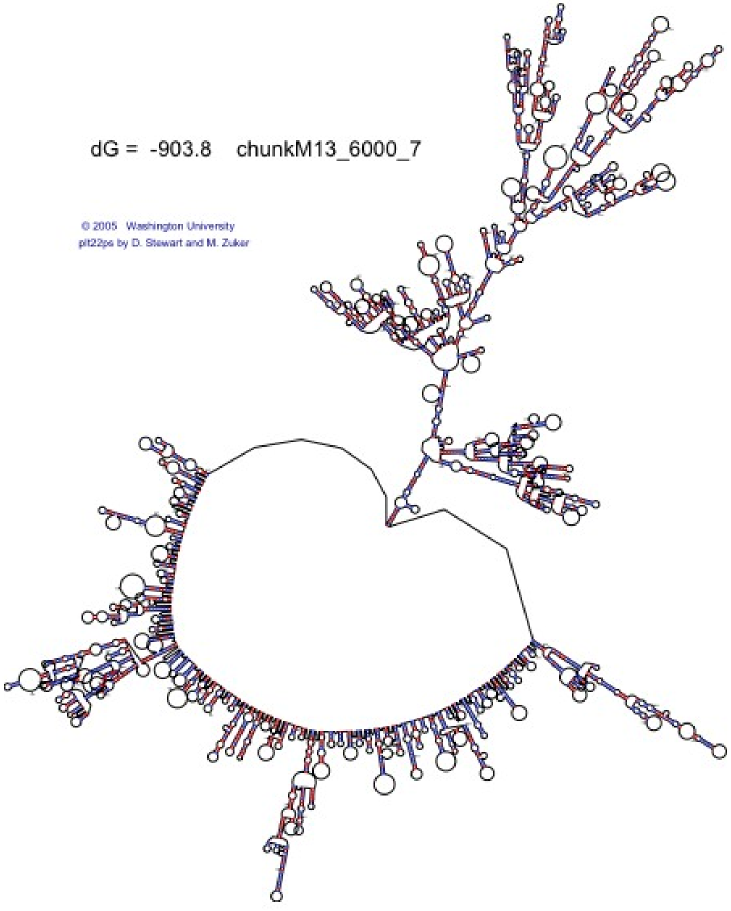




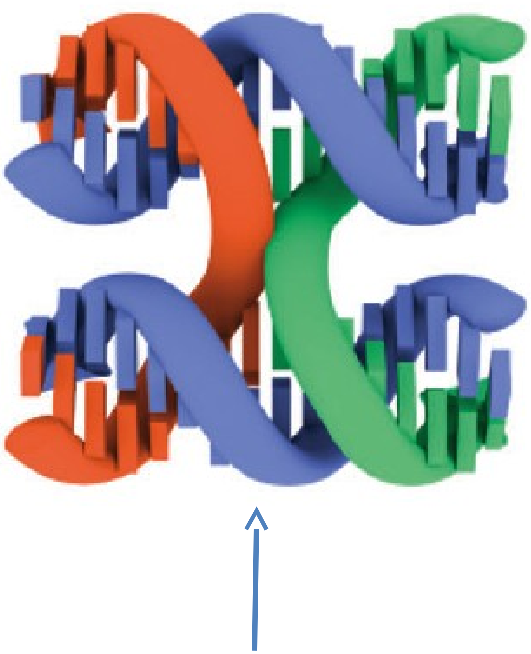


Submitted to ACS Synthetic Biology

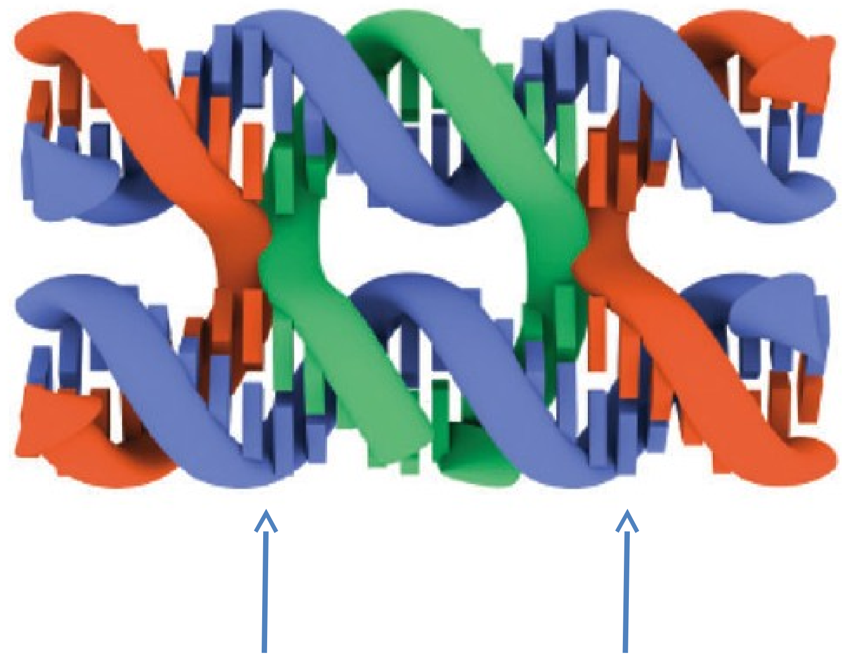
Twisted m13mp18



Use Anti-parallel Crossovers to Bring Helix Bundles Together



Crossov
er



Multiple crossovers
strategically placed

DOI: 10.1039/c1cs15057j

Fold ‘Scaffold’ using ‘Staples’

Scaffold: m13mp18 (7249nt), Staples: 20-60nt oligos, Buffer: TAE+Mg^{2+}