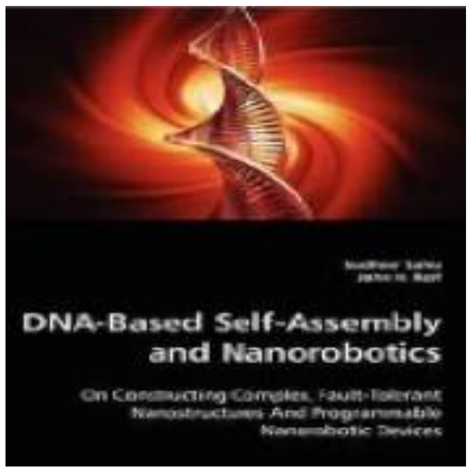
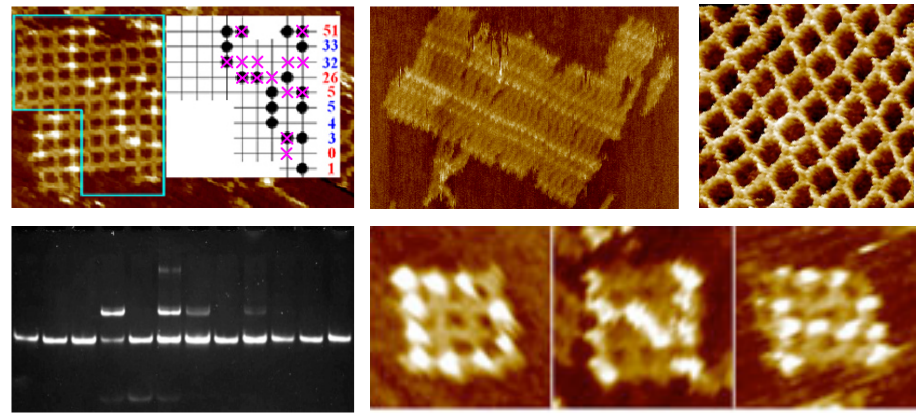
Self-Assembled DNA Nanostructures

John Reif

Dept CS

Duke University

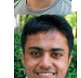




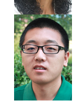
Reif's DNA Self-Assembly Group

Current Graduate Students

Hieu Bui 

Sudhanshu Garg 

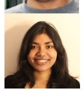
Reem Mokhtar 

Tianqi Song 

Prior Recent Graduate Students

Nikhil Gopalkrishnan 

Harish Chandran 

Urmi Majumder 

Peng Yin 

Harish Chandran 

Organization of talk

- **Overview of DNA & DNA Self-Assembly**

- **Novel self-assembly DNA nanostructures: DNA Tiles and DNA Lattices**

- **Programmable Molecular Patterning via DNA Lattices**

- **2D & 3D DNA Origami**

- **3D lattices via double decker tiles**

Introduction to DNA Self-Assembly

Feynman's Ill-Conceived Top-Down Approach to Nanotechnology

Feynman ("Plenty of room at the bottom", 1959):

•Can the doctor be swallowed? (Albert Hibbs)

•Can we build tiny factories that can arrange atoms the way we want?

•Can we write the 24 volumes of the Encyclopedia Brittanica on the head of a pin?

=> Suggested a Top-Down Approach to Nanotechnology

"This fact - that enormous amounts of information can be carried in an exceedingly small space - is, of course, well known to the biologists, and resolves the mystery which existed before we understood all this clearly, of how it could be that, in the tiniest cell, all of the information for the organization of a complex creature such as ourselves can be stored. All this information---whether we have brown eyes, or whether we think at all, or that in the embryo the jawbone should first develop with a little hole in the side so that later a nerve can grow through it - all this informationis contained in a very tiny fraction of the cell in the form of long-chain DNA molecules in which approximately 50 atoms are used for one bit of information about the cell."

Self-assembly in nature

Spontaneous organization of components into stable superstructures due to local interactions

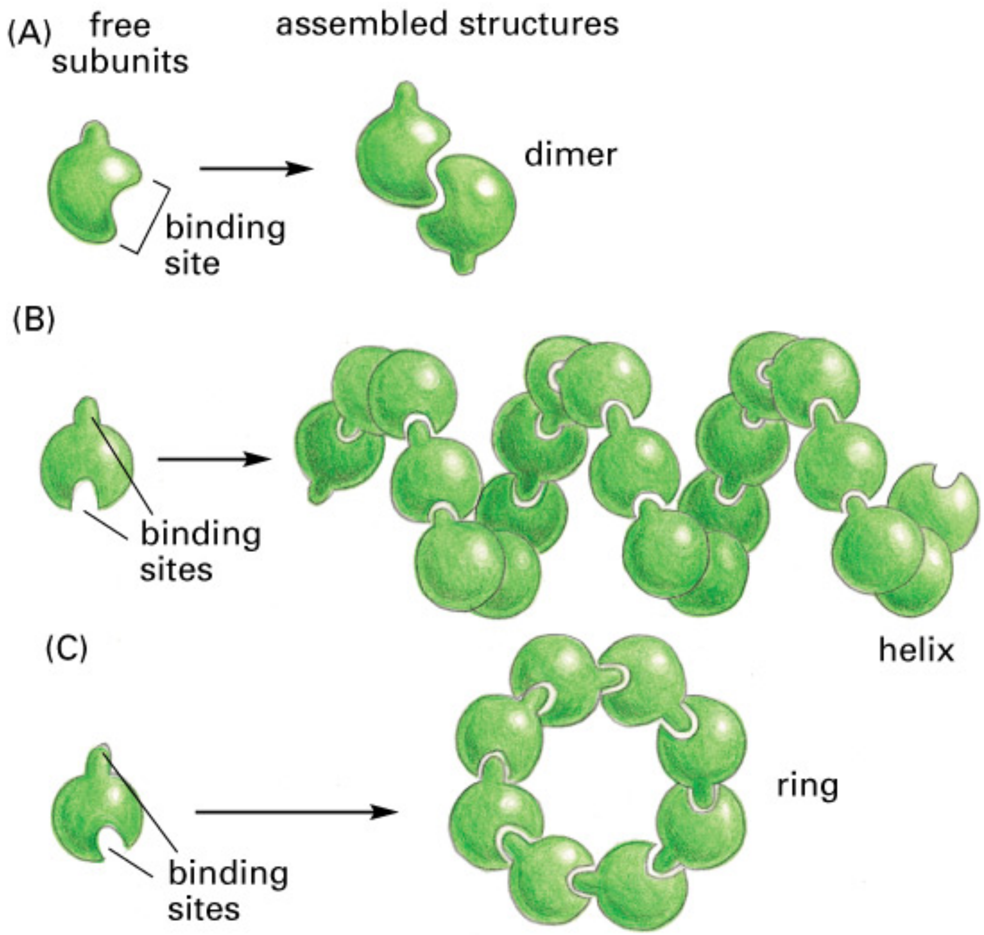


Figure 3–25. Molecular Biology of the Cell, 4th Edition.

From microscopic living cells to gigantic galaxies

Why study self-assembly?

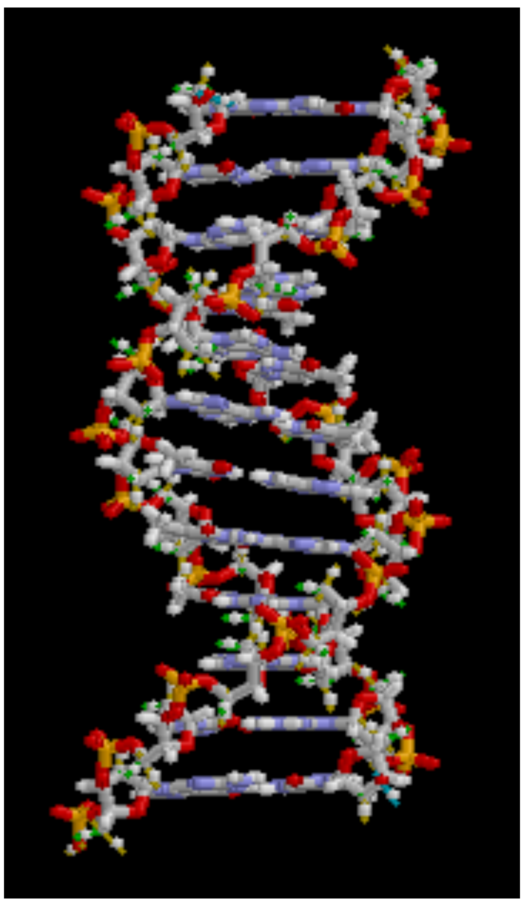
- Plays a fundamental role in biology, especially in formation of living cell
    - Attempt to understand life must include a through study of SA

- One of the few known methods for the construction and manipulation of nanostructures

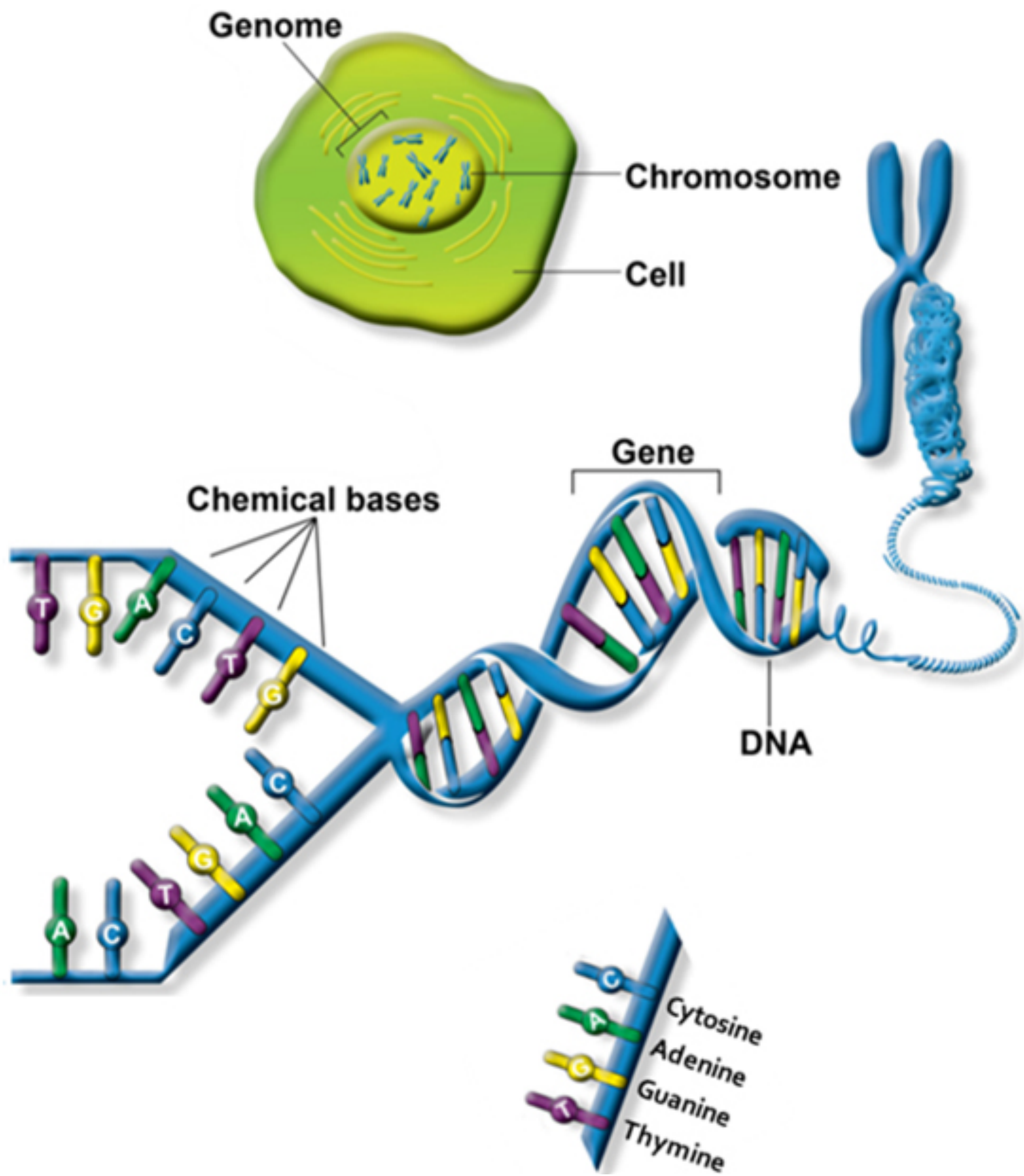
- Any Turing-computable function can be computed via self-assembly of Wang tiles
    - New paradigm of computing
    - Lower bounds proved in theoretical self-assembled systems can be translated (by appropriate reductions) to Turing systems

- Brings about order from disorder
    - Interesting at a philosophical level

Double Stranded DNA



Source: Wikipedia.com

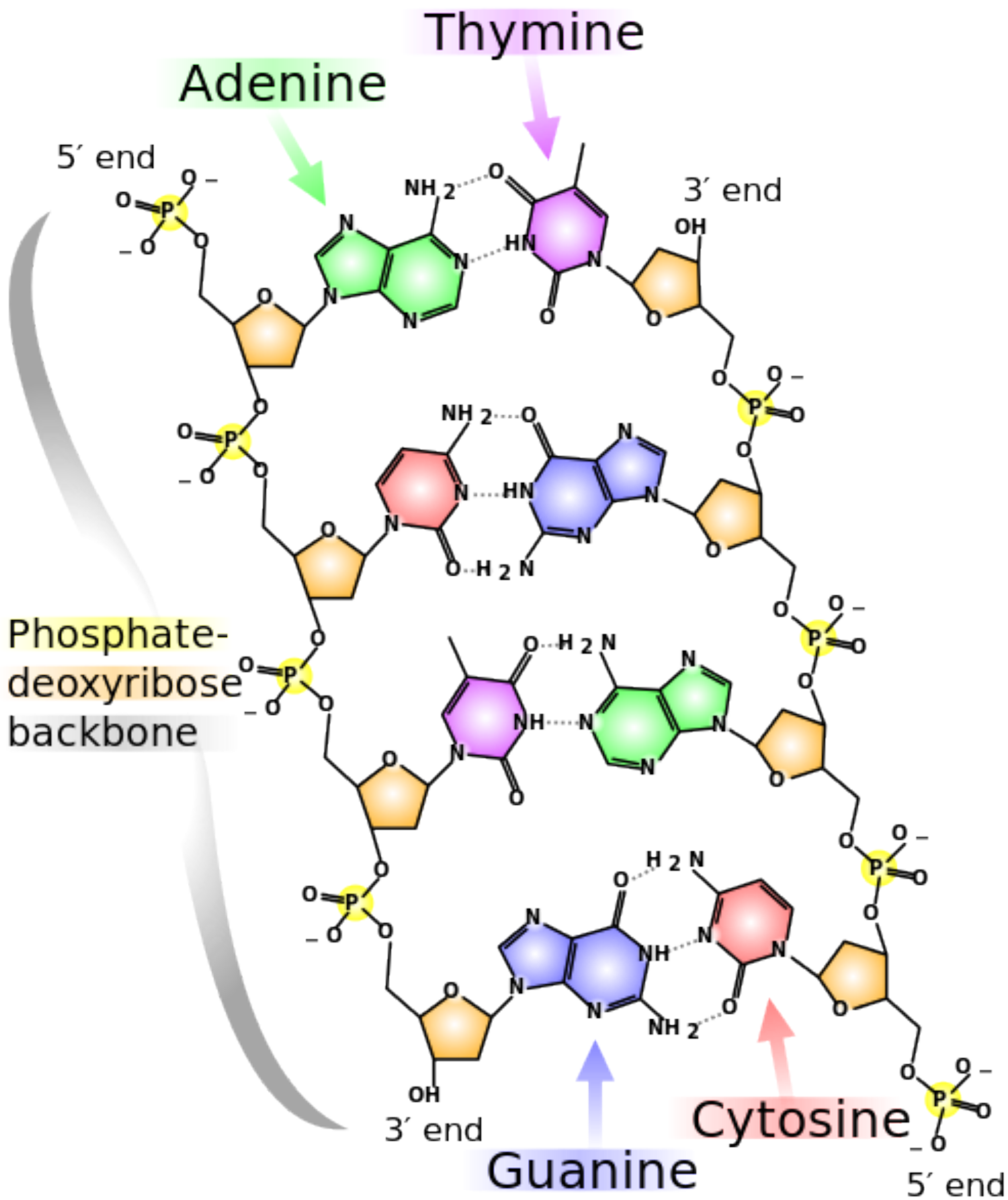


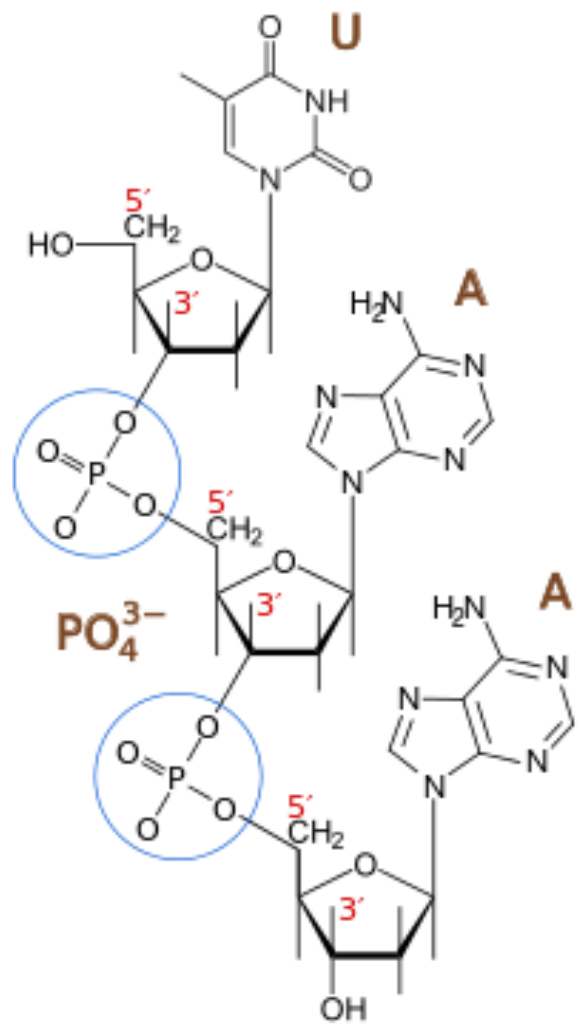
Source: http://www.coriell.org/assets/images/personalized-medicine/dna-genes-snps-enlarged.jpg

Overview

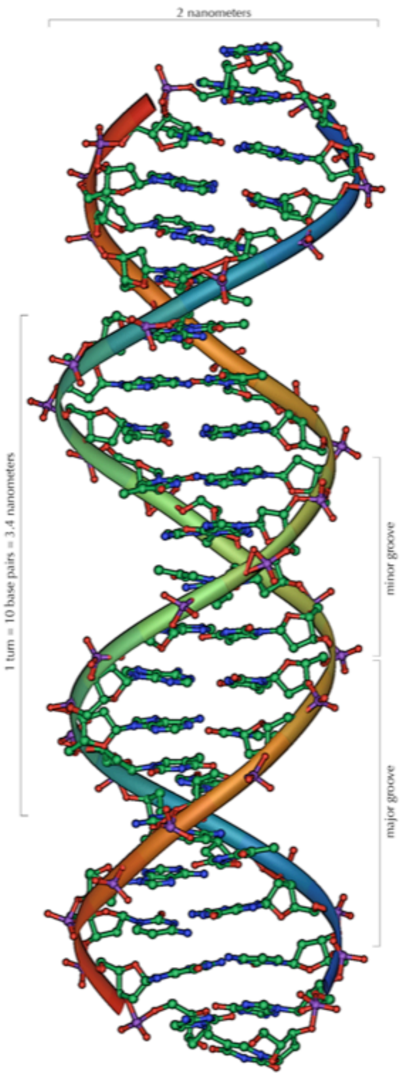
- Why DNA?
  1. Natural nanoscale material
  2. Ability to carry information can be exploited in self-assembly process
  3. Well established base-pairing model in which the stability of a base-pair depends on their identity (A-T, C-G)

Overview

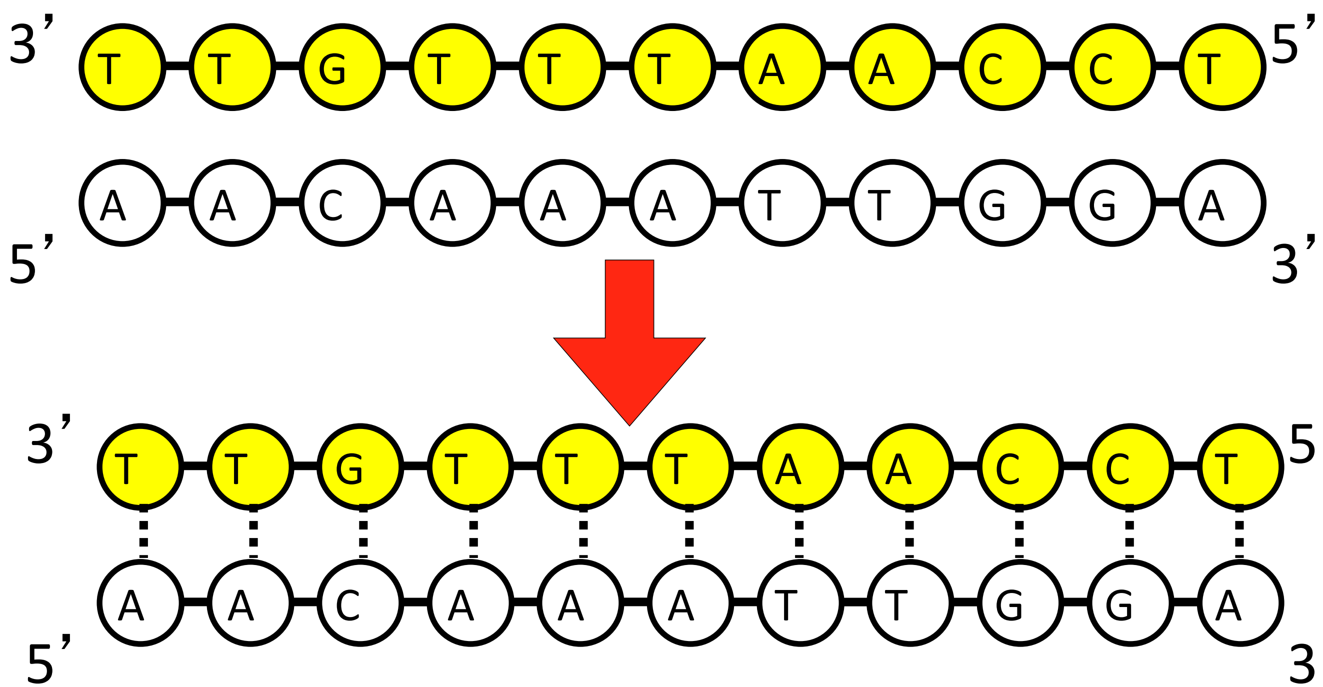

Thymine
Adenine
5′ end
3′ end
Phosphate-
deoxyribose
backbone
3′ end
5′ end
Guanine
Cytosine


U
A
A
PO_4^{3-}
5′
3′
HO
OH

Key to DNA Self-Assembly



Hybridization



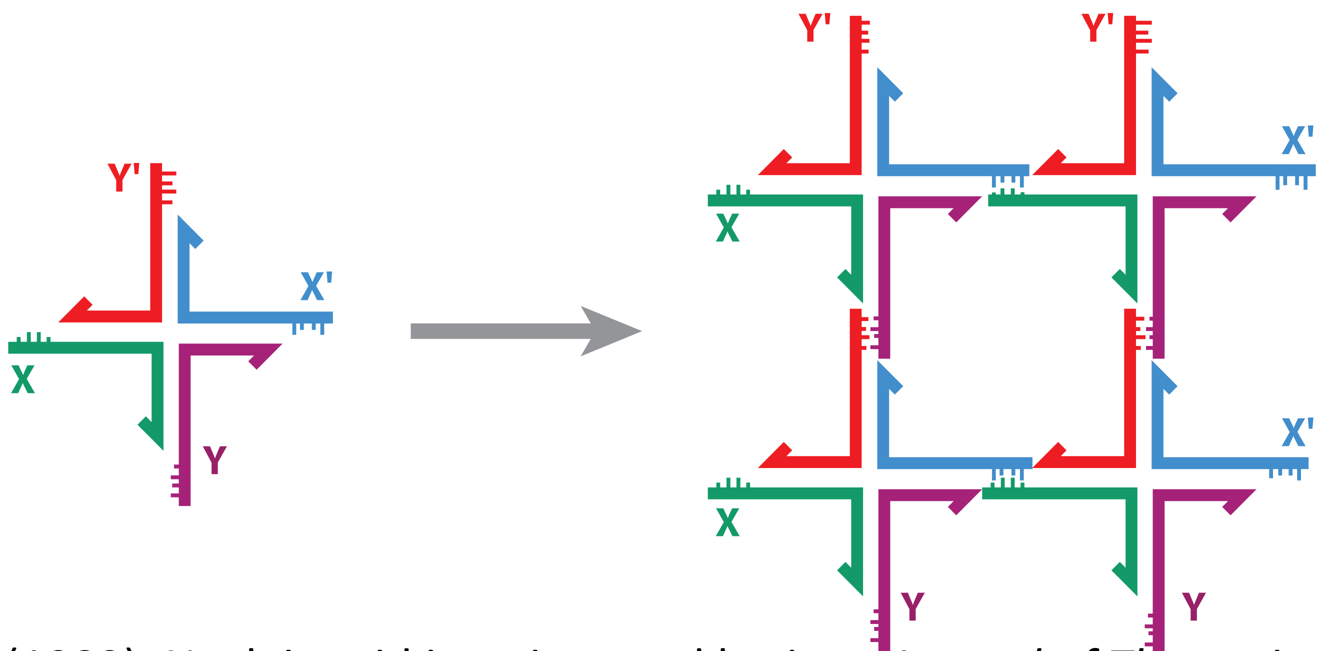
What is DNA Self-Assembly?

Programming DNA strands to organize themselves into nanoscale shapes, patterns, and devices through Watson-Crick base-pairing.

DNA Nanotechnology

Seeman 1982:

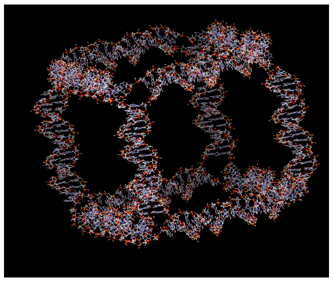
• "It is possible to generate sequences of oligomeric nucleic acids which will preferentially associate to form migrationally immobile junctions, rather than linear duplexes, as they usually do."



Seeman, N. C. (1982). Nucleic acid junctions and lattices. *Journal of Theoretical Biology*, *99*(2), 237–247. doi:10.1016/0022-5193(82)90002-9

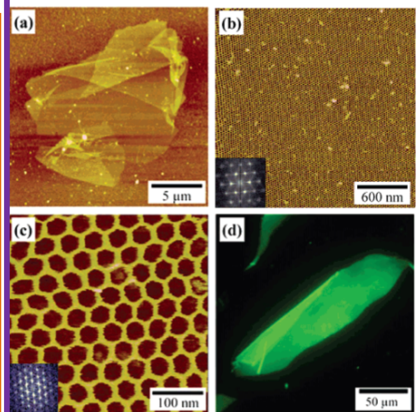
Some results of DNA self-assembly

NYU 1991



The Electrophoretic Properties Of A DNA Cube And Its Substructure Catenanes : Mao And Seeman

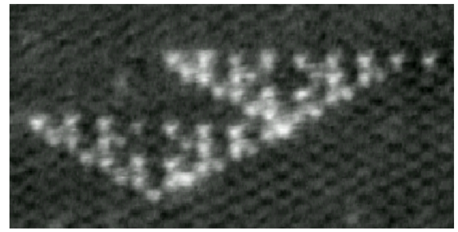
Purdue 2005



Self-assembly Of Hexagonal DNA Two-dimensional (2D) Arrays: He, Chen, Liu, Ribbe, And Mao

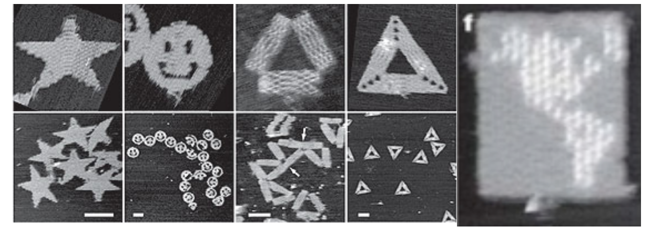
Caltech

2004



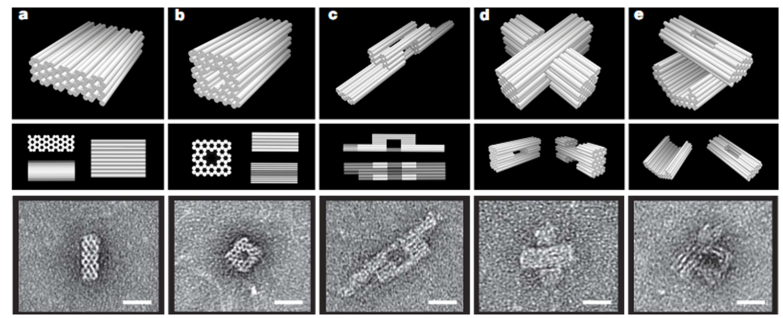
Algorithmic Self-assembly Of DNA Sierpinski Triangles: Rothemund, Papadakis, Winfree

2006



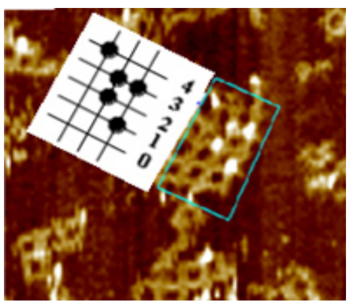
Folding DNA To Create Nanoscale Shapes And Patterns: Rothemund

Harvard 2009



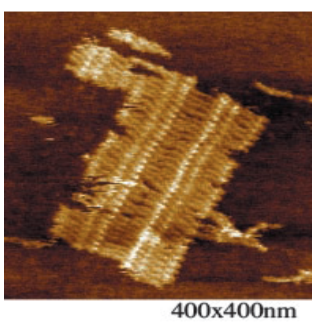
Self-assembly Of DNA Into Nanoscale Three-dimensional Shapes: Douglas, Dietz, Liedl, Hogberg, Graf, Shih

Duke



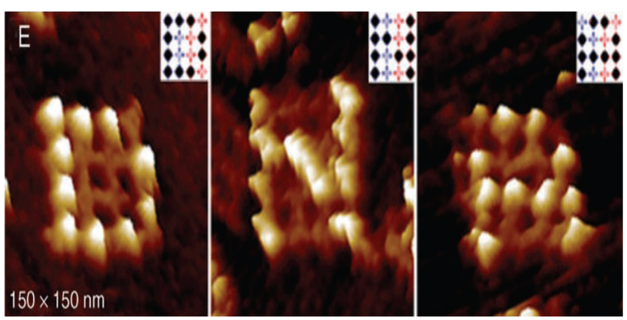
Unpublished Data: Majumder, Reif

2003



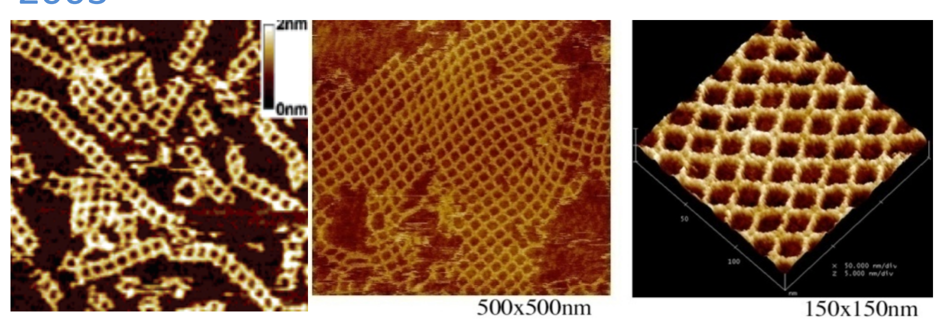
Directed Nucleation Assembly Of DNA Tile Complexes For Barcode-patterned Lattices: Yan, Labean, Feng, Reif

2006



Finite-size, Fully-addressable DNA Tile Lattices Formed By Hierarchical Assembly Procedures : Park, Pistol, Ahn, Reif, Lebeck, Dwyer, Labean

2003

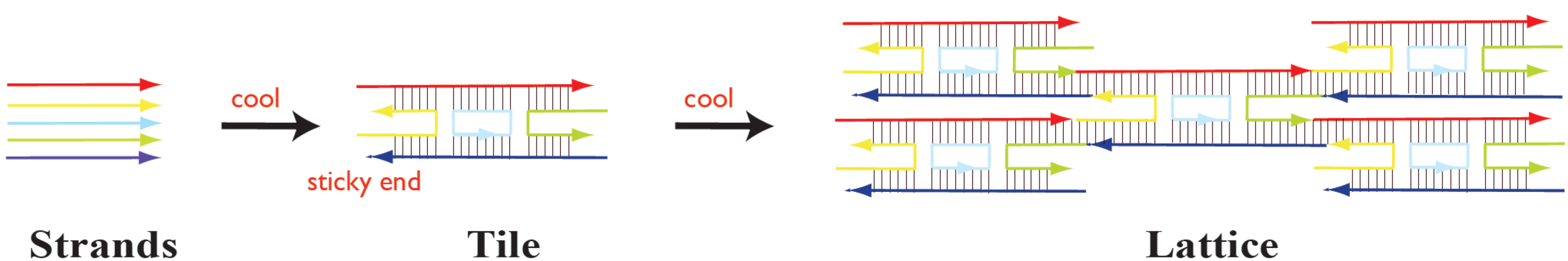


4x4 DNA Tile And Lattices: Characterization, Self-assembly And Metallization Of A Novel DNA Nanostructure Motif : Yan, Park, Finkelstein, Reif And Labean

Design & Experimental Demonstration of DNA Tiles and Lattices

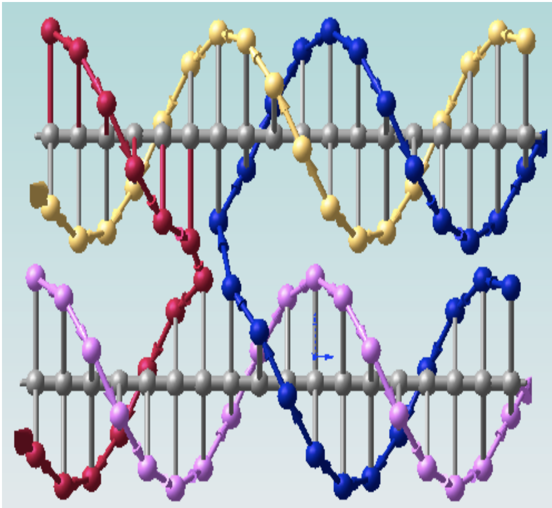
Example: Self-assembly of DNA lattices

- Driven by Watson-Crick base pairing : A T & C G
- Leads to energy minimization of the final structure
  - Base pairing and base stacking
- Programmability:
  - AGTGC sticks to GCACT (reverse complement)



DNA tiles

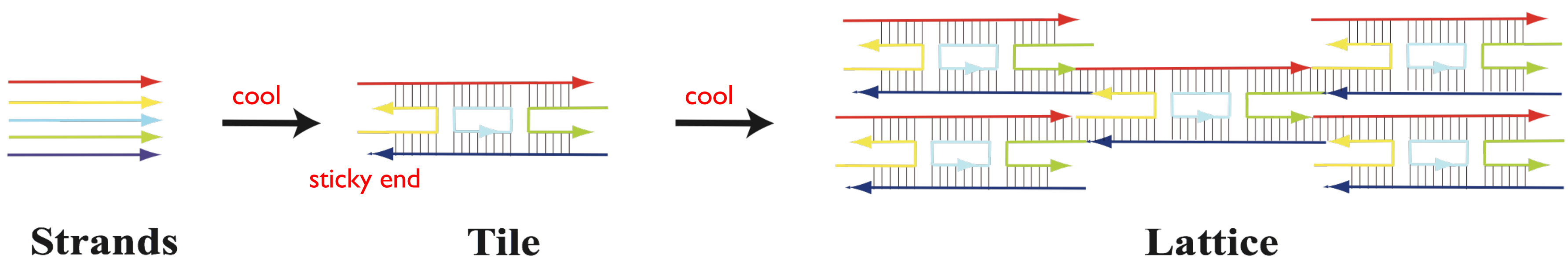
DNA molecules self-assembled from artificially synthesized single stranded DNA.



Branched Junction

- Anti-parallel crossovers:
  - cause a reversal in direction of strand propagation through the tile following exchange of strand to a new helix.
- Pads:
  - Tiles have sticky ends that preferentially match the sticky ends of certain other DNA tiles.
  - The sticky ends facilitate the further assembly into tiling lattices.
  - Total of 4 Pads of single stranded DNA at ends.

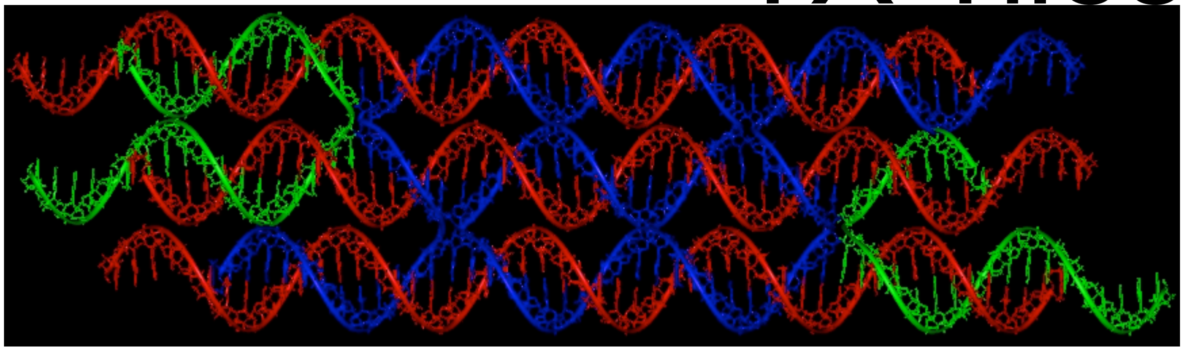
Self-Assembly from DNA strands, to Tiles, to Lattices

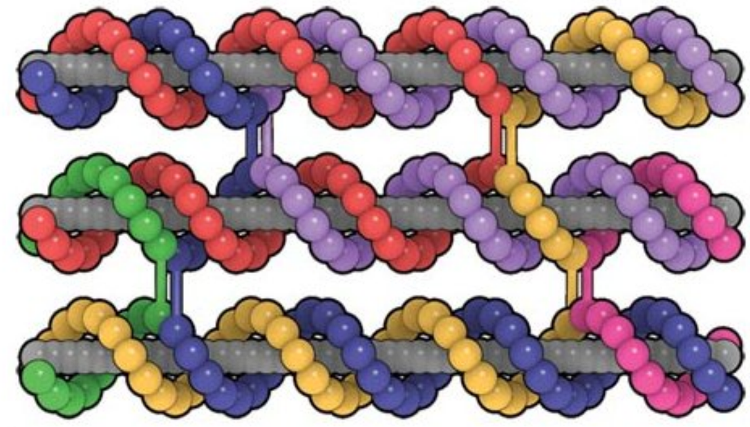


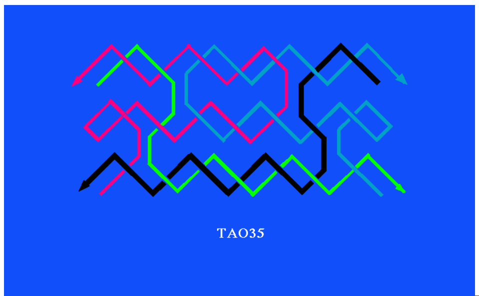
TX tiles

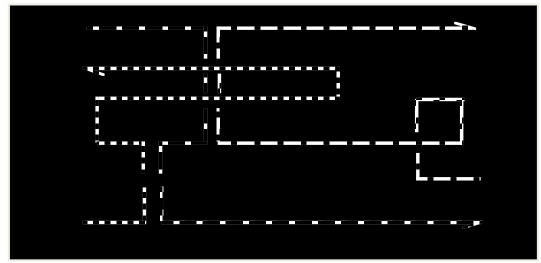
- TX tile – extension of the DX tile
- Three helices made of 4 strands

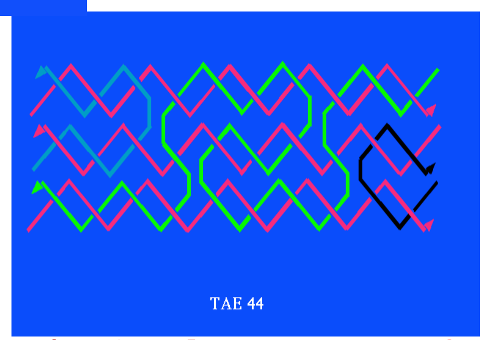
TX Tiles





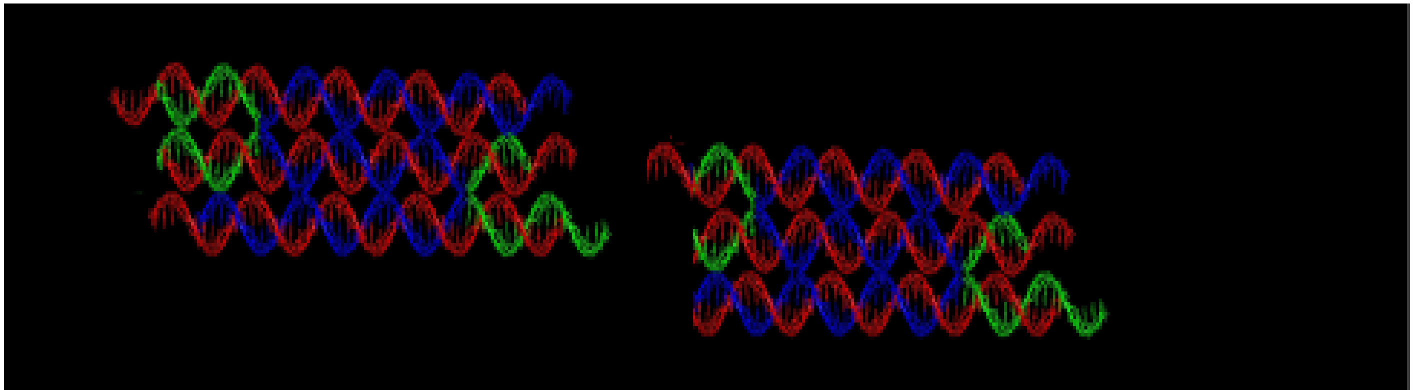






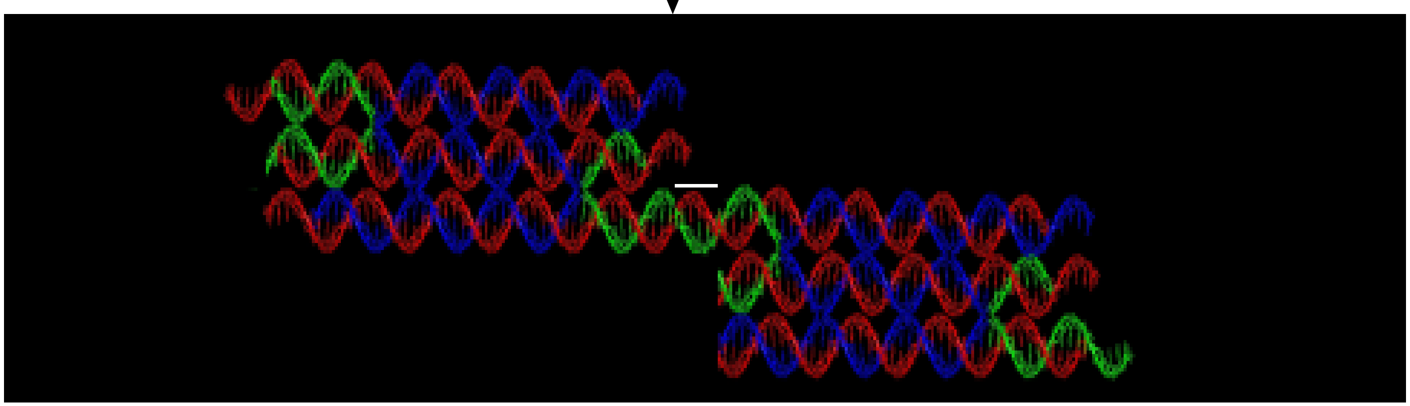
- Triple-crossover (TX) Tiles [LaBean, Reif et al, J. Am. Chem. Soc., 2000]:
  - consist of three double-helices fused by crossover strands.
  - TAE contains an Even number of helical half-turns between crossover points.
  - TAO contains an Odd number.
- Total of 6 Pads of single stranded DNA at ends.

Unique Sticky Ends on DNA tiles. Input layers can be assembled via unique sticky-ends at each tile joint thereby requiring one tile type for each position in the input layer.

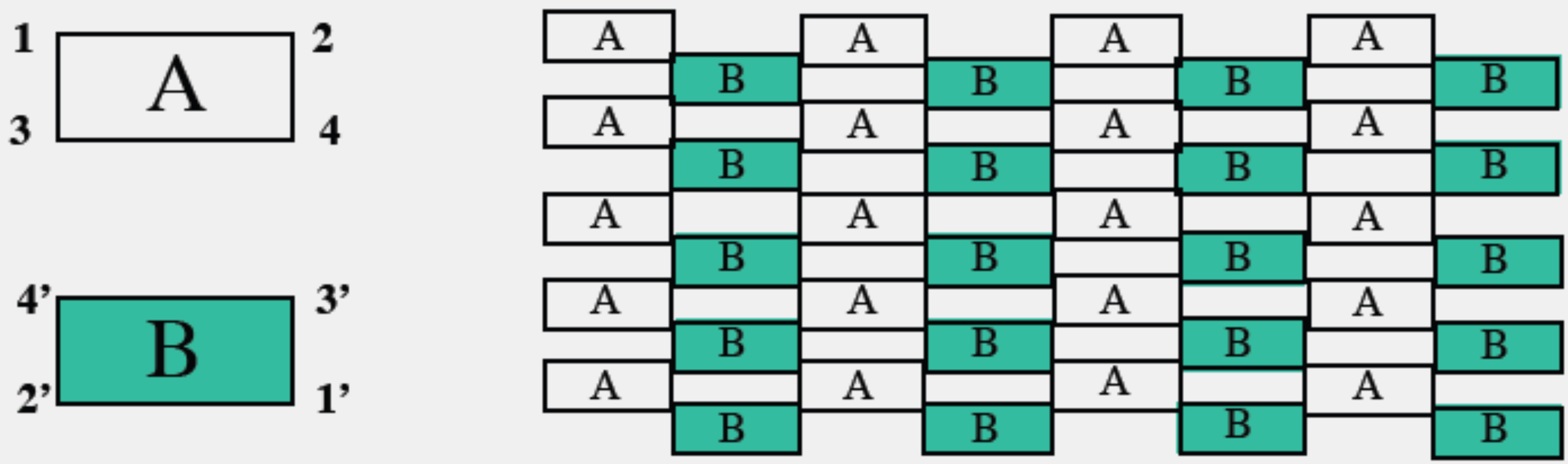


Tiling self-assembly:

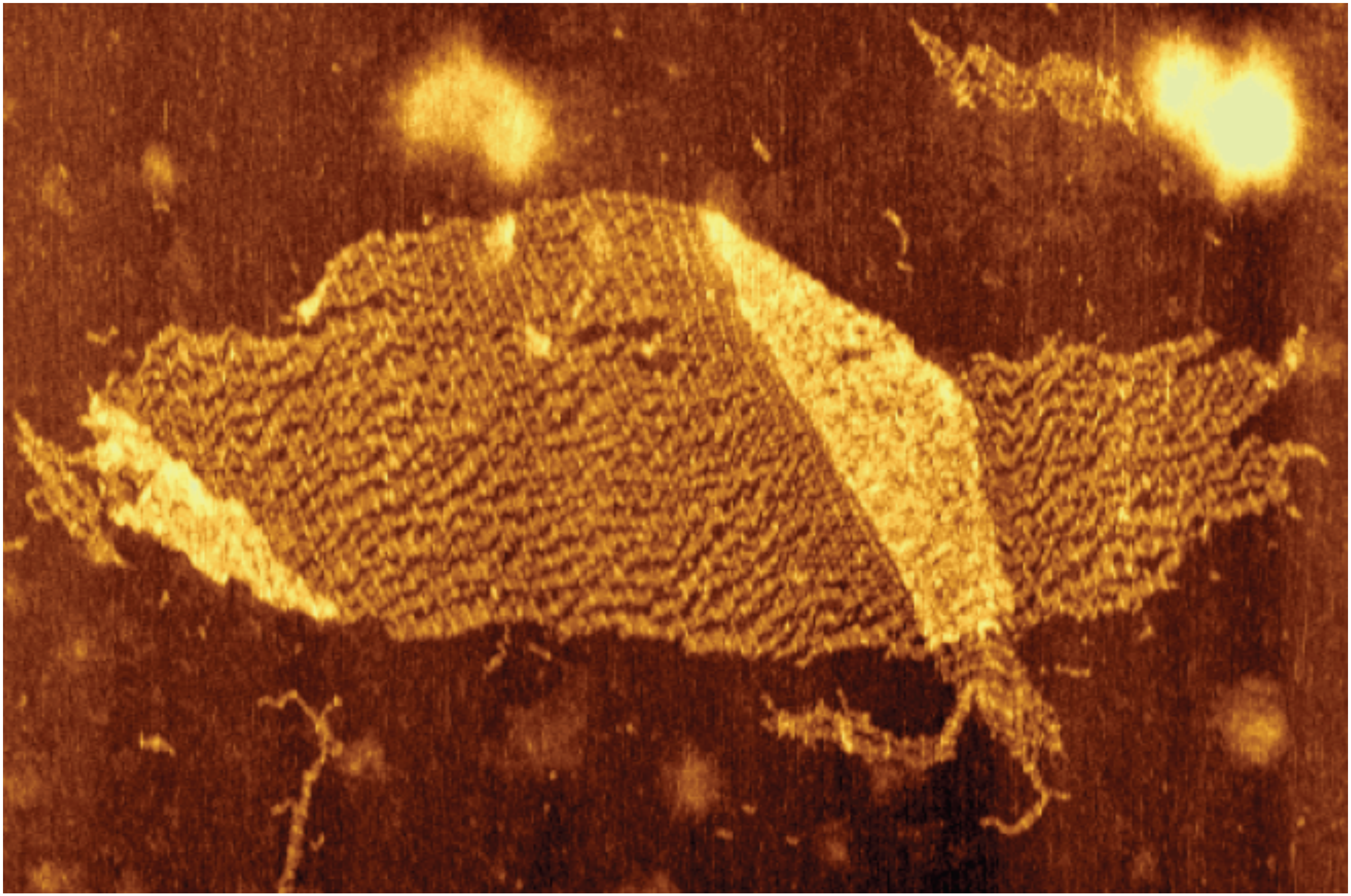
proceeds by the selective annealing of the pads of distinct tiles, which allows tiles to compose together to form a controlled tiling lattice.



TX lattices

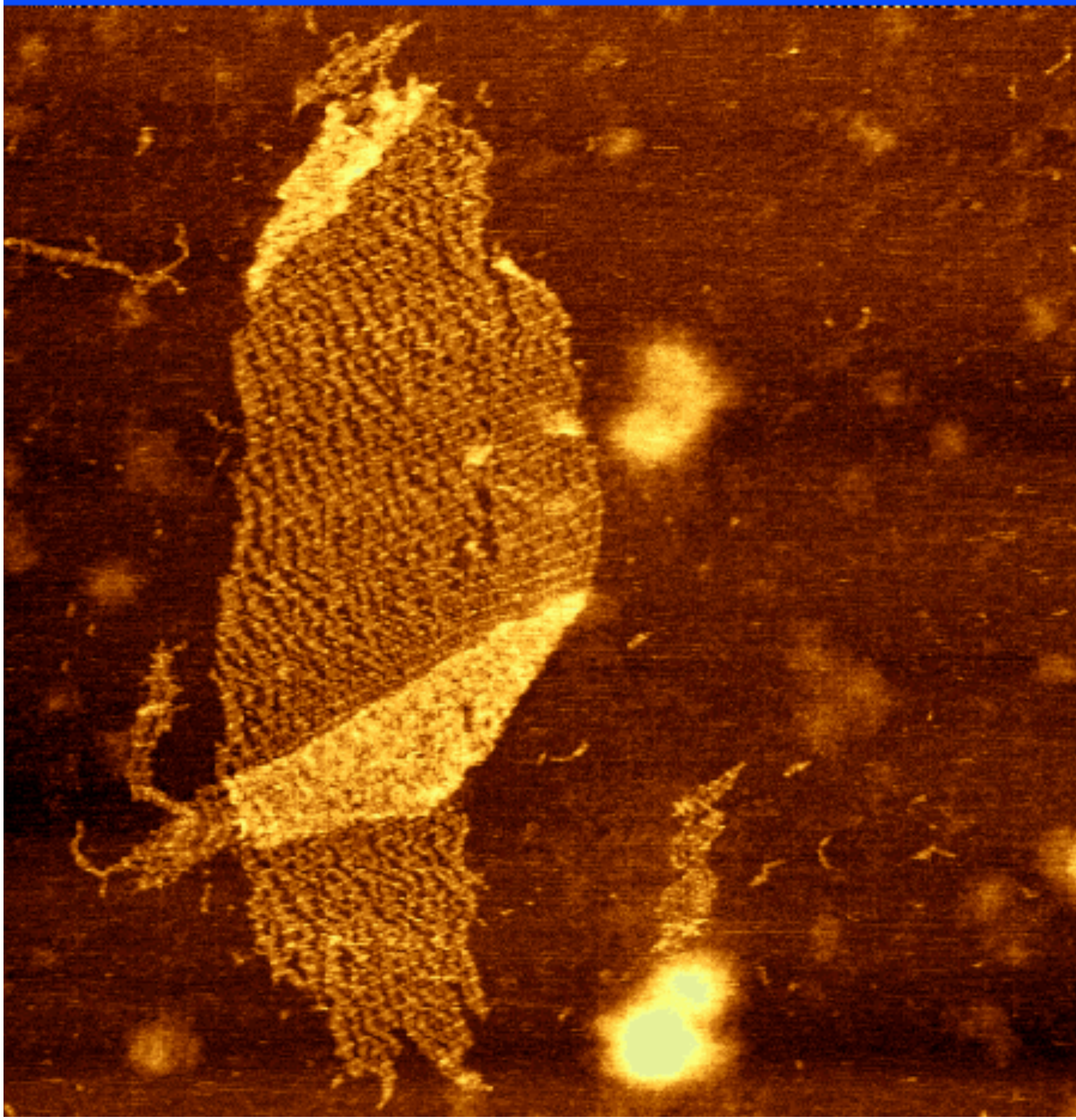


TX lattices

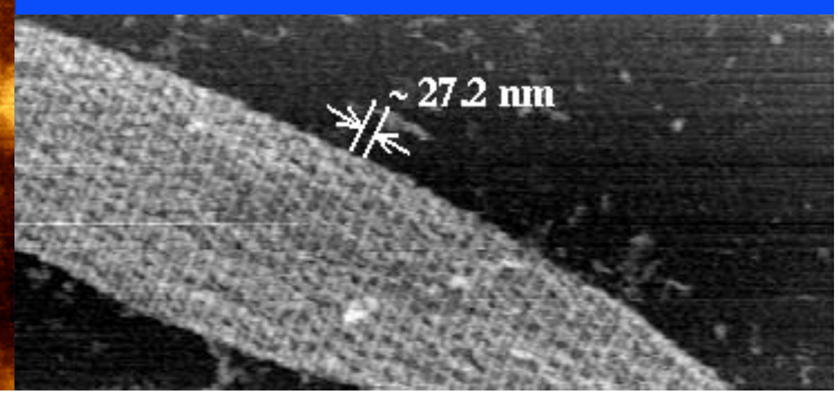


Large Scale DNA Self-Assembled Tilings

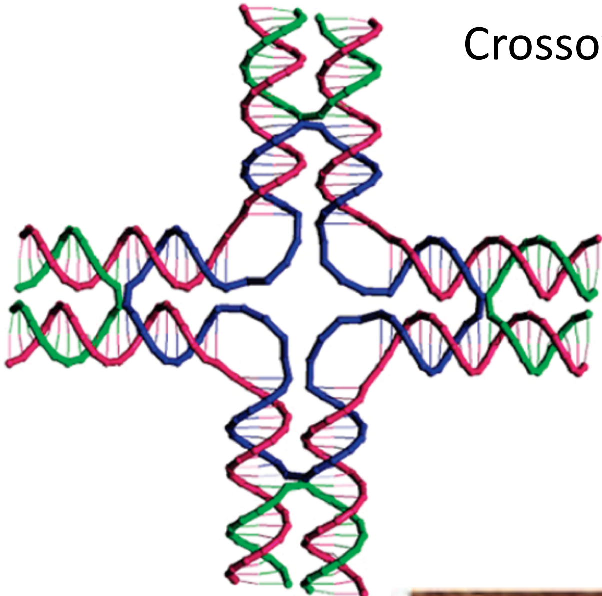
Visualization by Atomic Force Microscope.

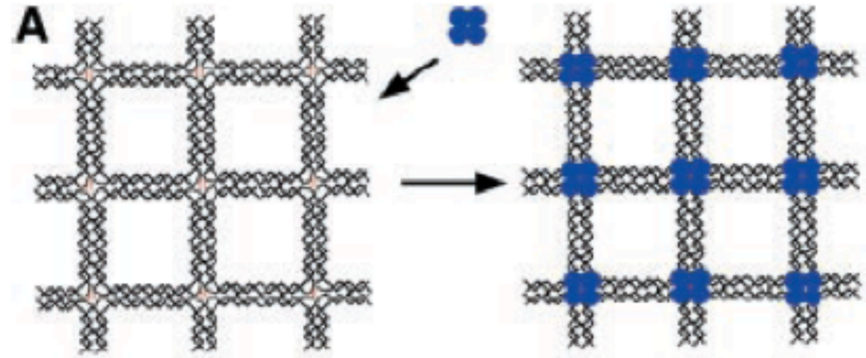


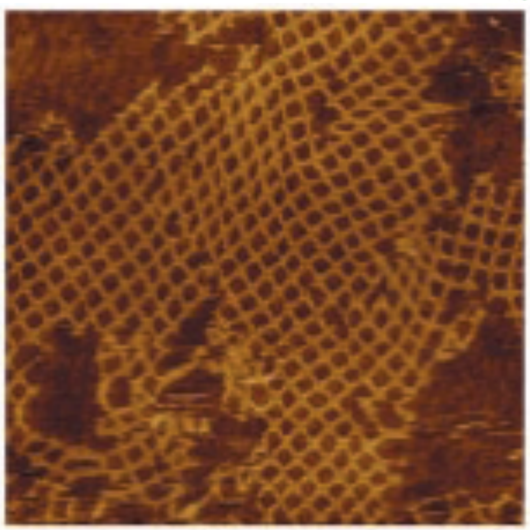
AB* Lattice. An atomic force microscope image of DNA lattice formed by two TAO tiles one of which contains an extra loop directed out of the plane. These loops form the visible stripe features with the expected spacing of ~28 nm.



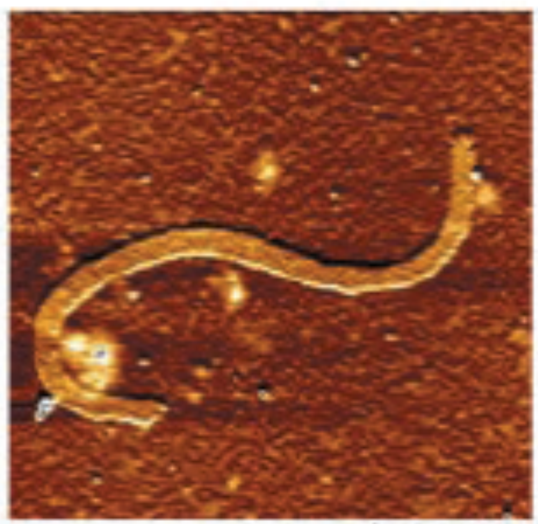
Crossover DNA Tiles and their Lattices



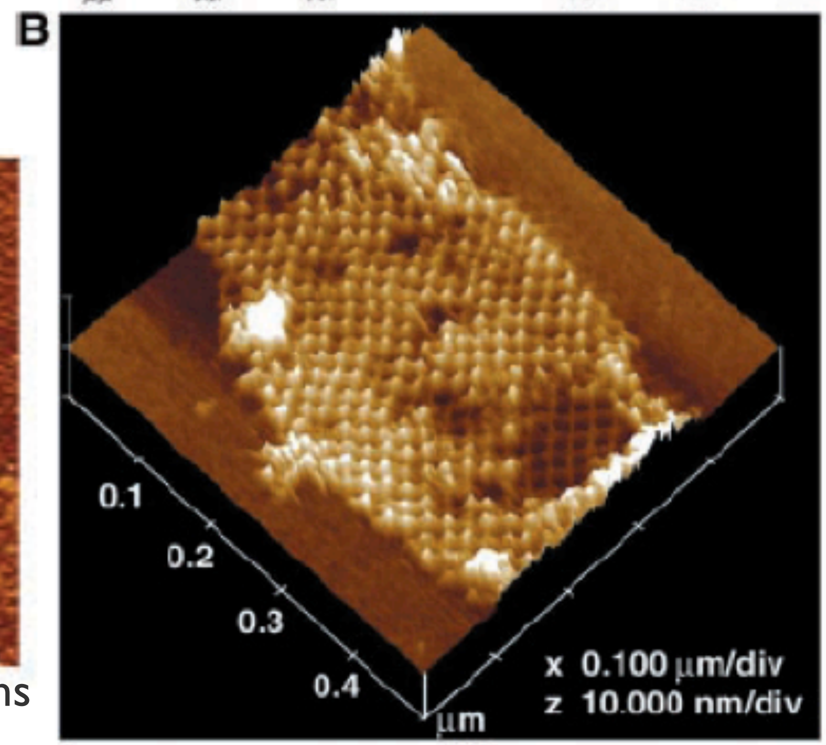




500x500 nm



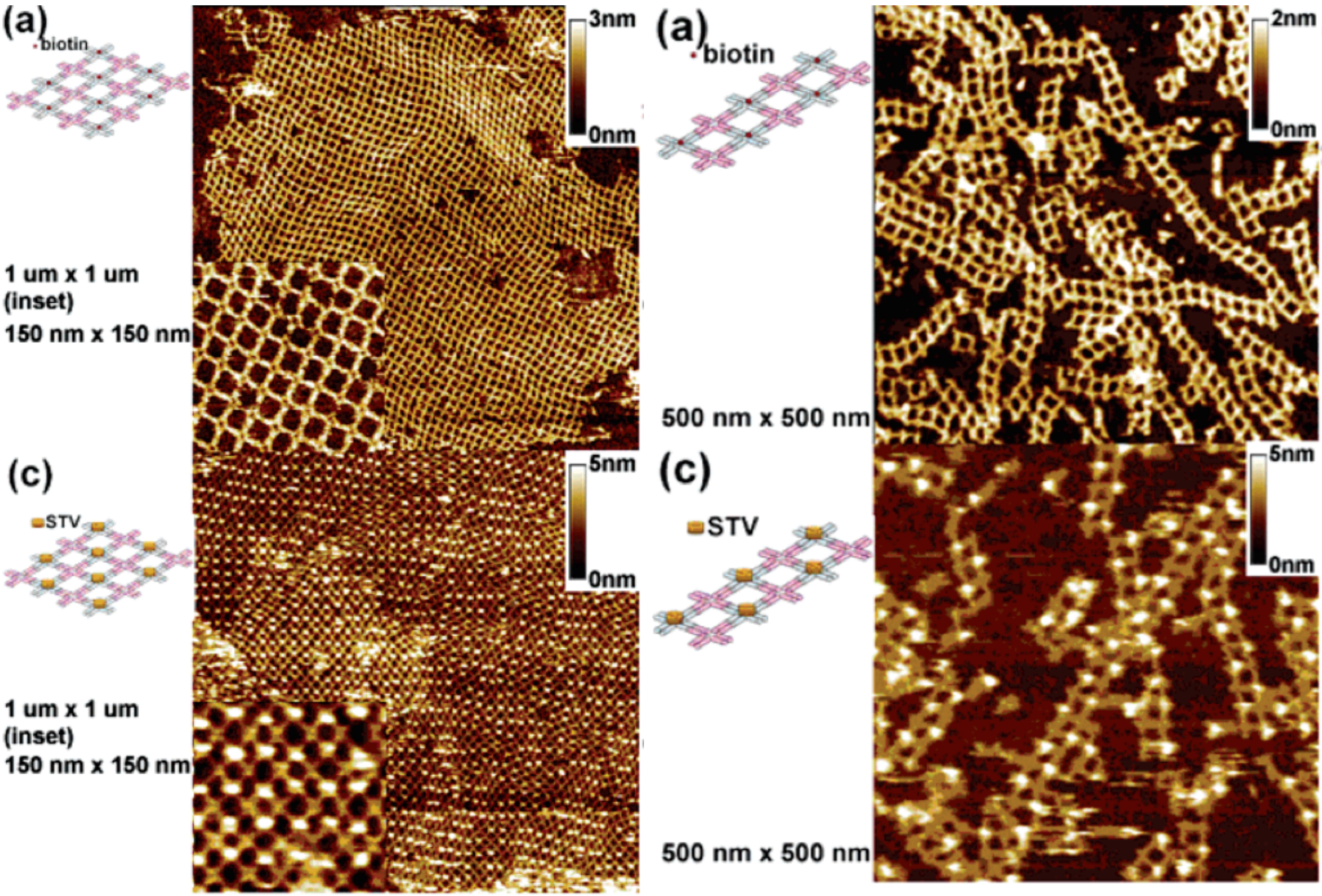
Also form Tubes & Ribbons



500x500nm

Used Corrugation to form 2D Grid Lattices

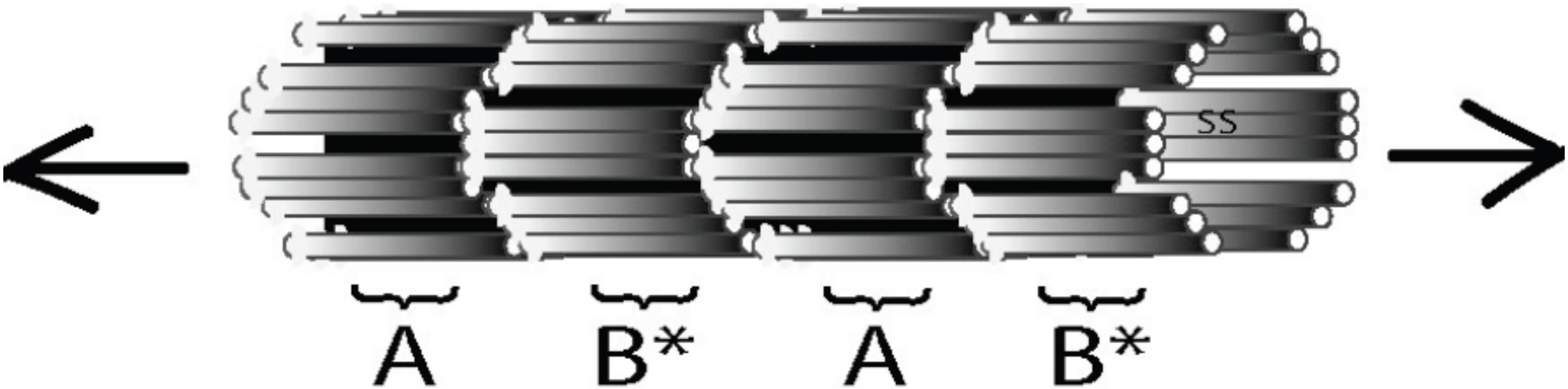
Hao Yan, Sung Ha Park, Liping Feng, John Reif, and Thomas H. LaBean, Science (2003)



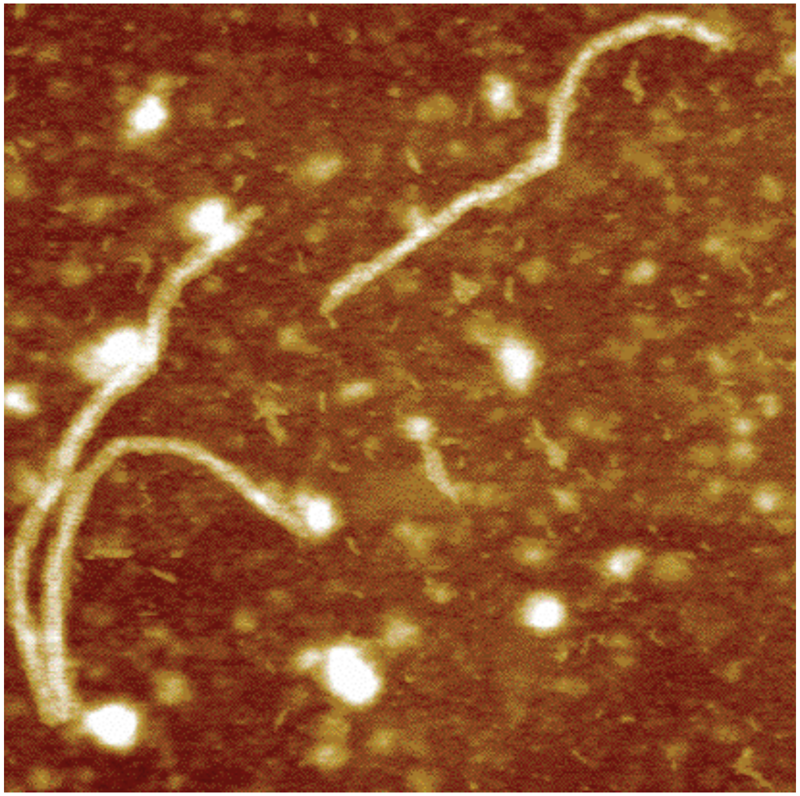
Nano Letters **5**, 729-733 (2005)

DNA Tubes & Ribbons

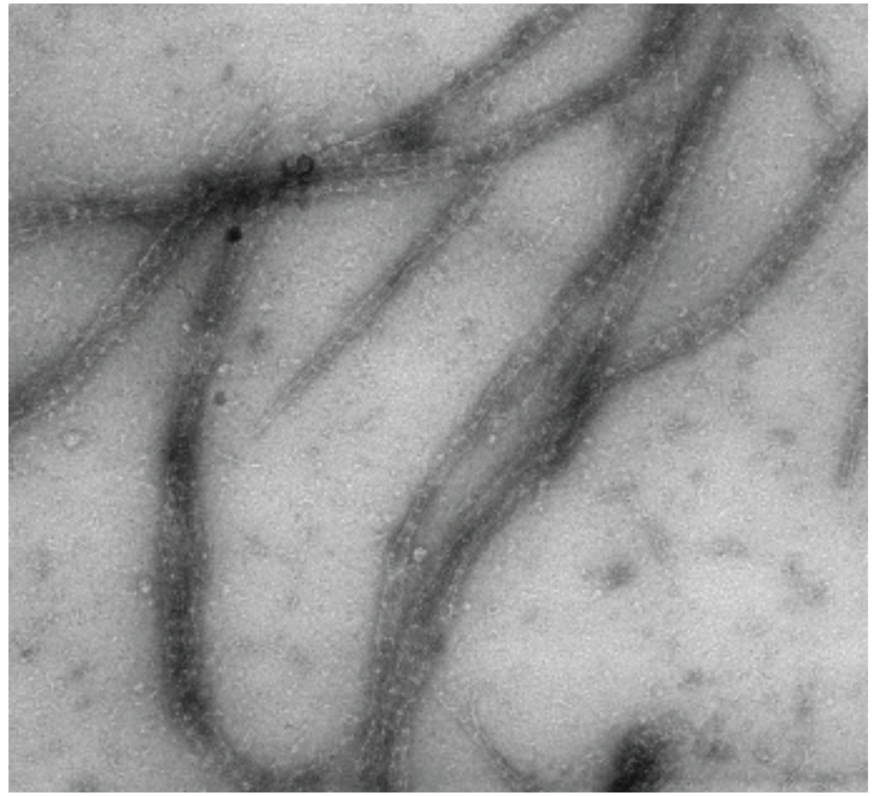
TX tubes



TX tubes

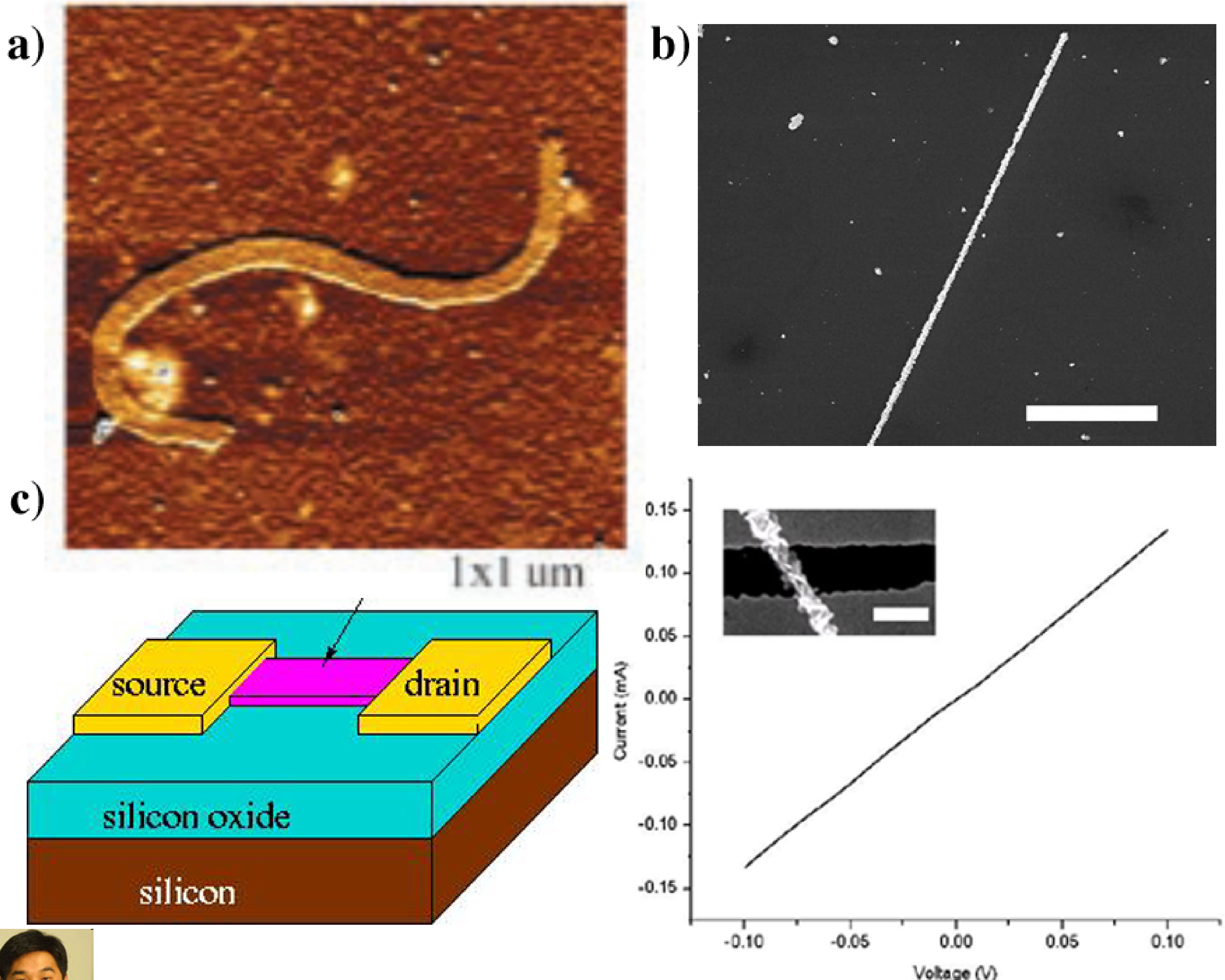


AFM



TEM

Au Metallization of 4x4 ribbon and Conductivity Measurement



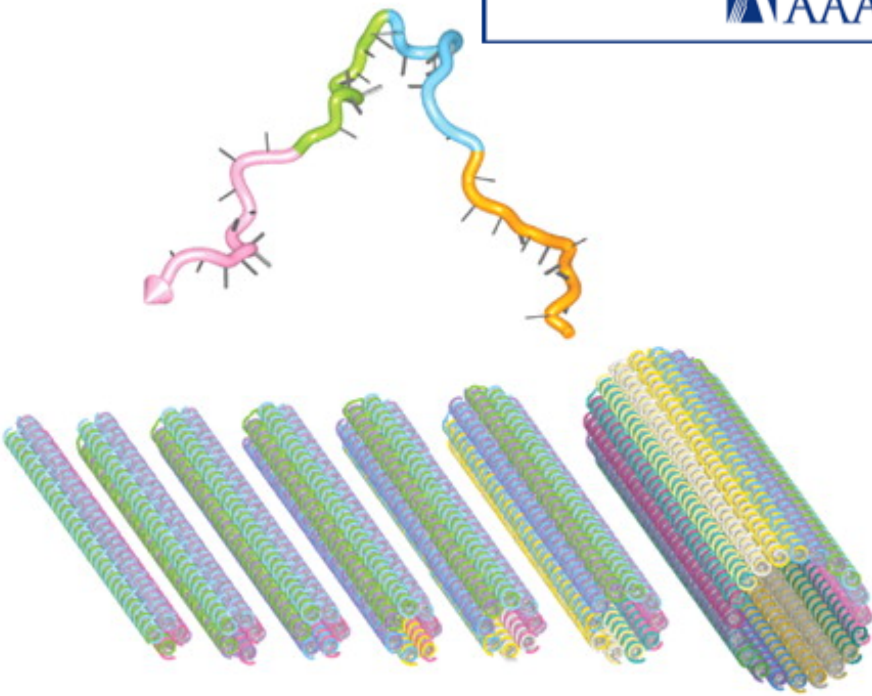
Hao Yan, Sung Ha Park, Liping Feng, John Reif, and Thomas H. LaBean, Science (2003)

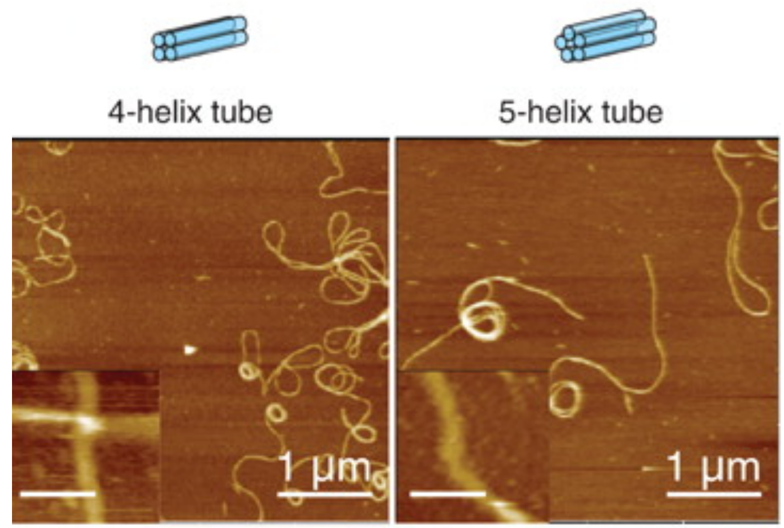
Science AAAS

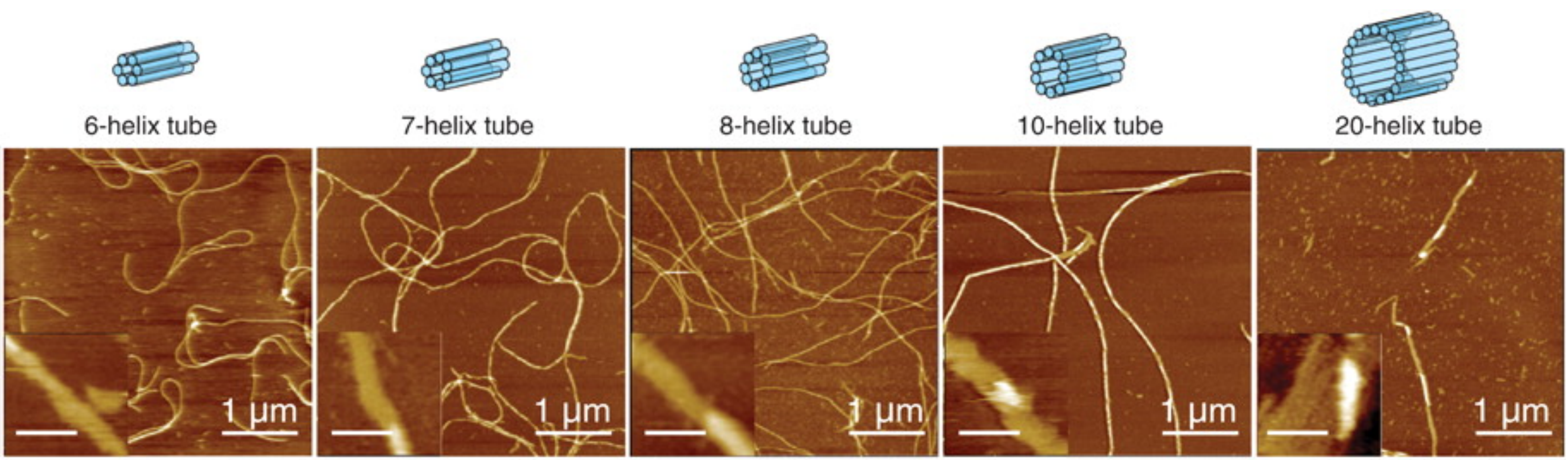
Programming DNA Tube Circumferences

Peng Yin, Reif, et al

Science **321**, 824 (2008);
DOI: 10.1126/science.1157312

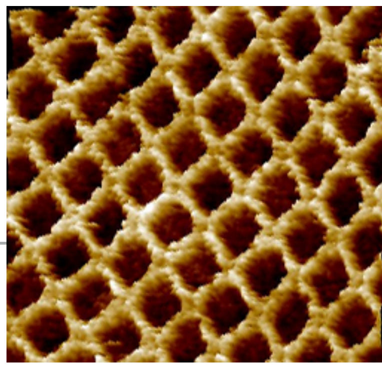


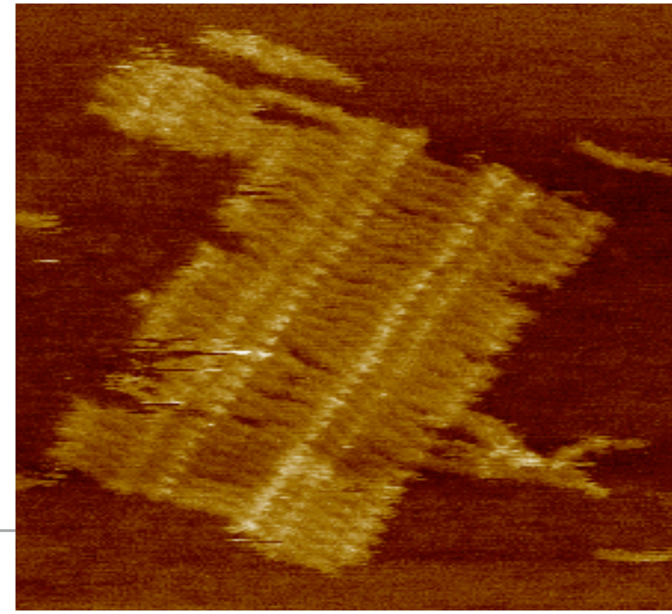




Patterned DNA Lattices

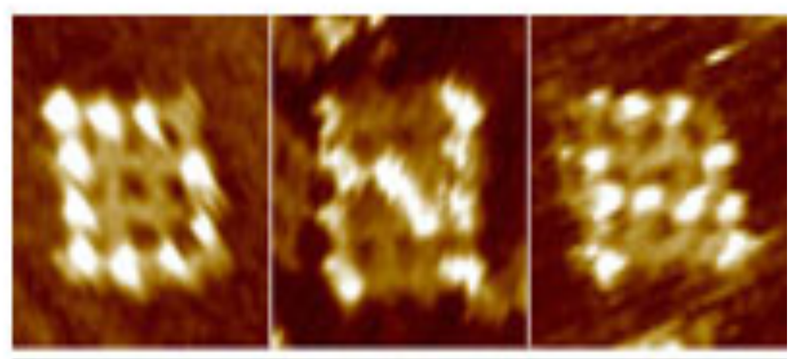
Programmable Patterned DNA Nanostructures





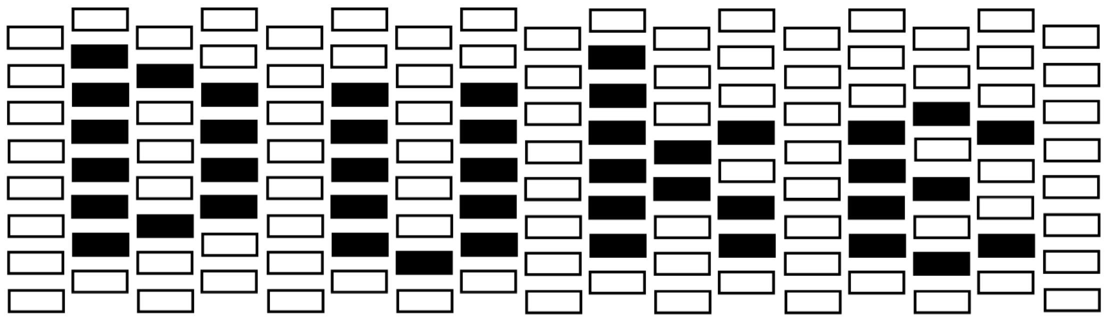
NOT Patterned

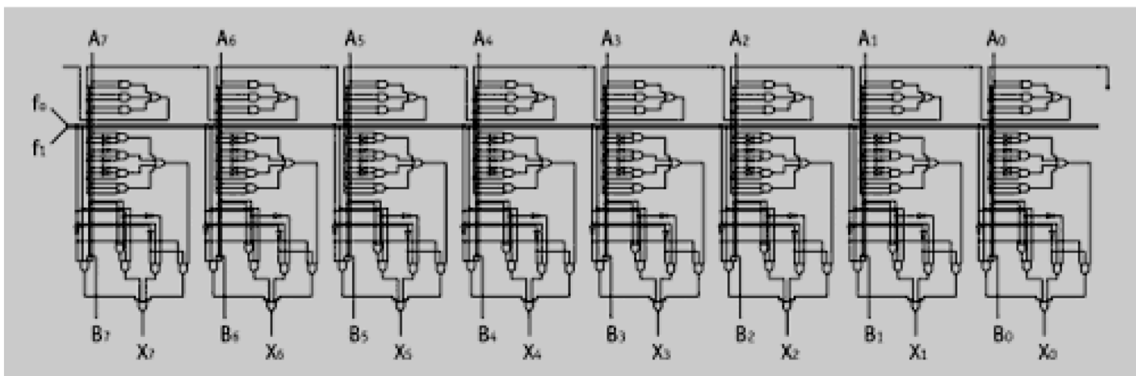
Patterned



Patterned DNA lattices:

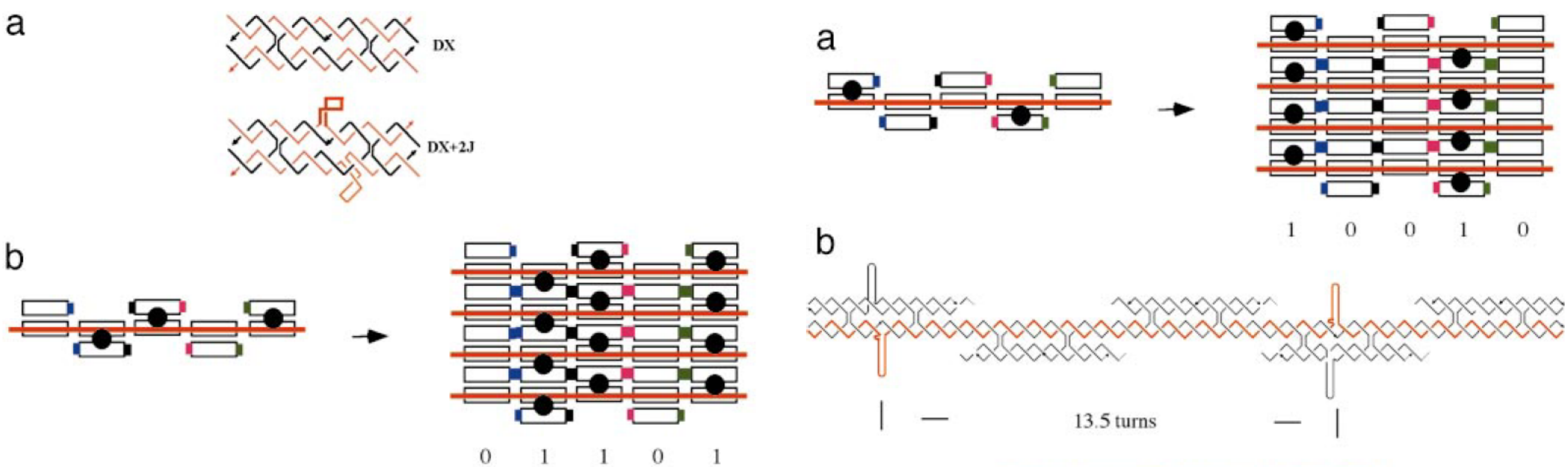
- Allows for Attachment of Nanoparticles at Specific Sites on Lattice





- Application:Molecular Electronics:
  - Layout of molecular electronic circuit components on DNA tiling arrays.

Barcoded lattices



Hao Yan, Thomas H. LaBean, Liping Feng, and John H. Reif, **Directed Nucleation Assembly of Barcode Patterned DNA Lattices**, Proceedings of the National Academy of Science(PNAS), Volume 100, No. 14, pp. 8103-8108, July 8, (2003)

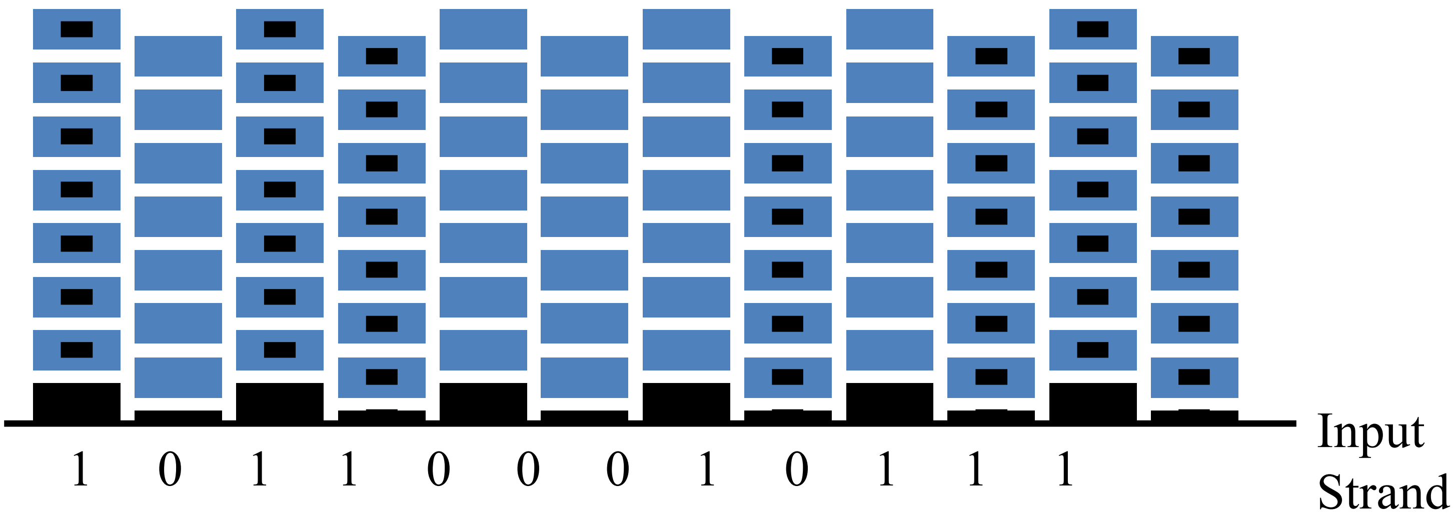
Molecular Pattern Formation using Scaffold Strands for Directed Nucleation:

H Yan, T LaBean, L Feng, J. Reif, PNAS (2003).

Hao Yan

- Multiple tiles of an input layer can be assembled around a single, long DNA strand we refer to as a scaffold strand (shown as black lines in the figures).

Barcode lattice displays banding patterns dictated by the sequence of bit values programmed on the input layer



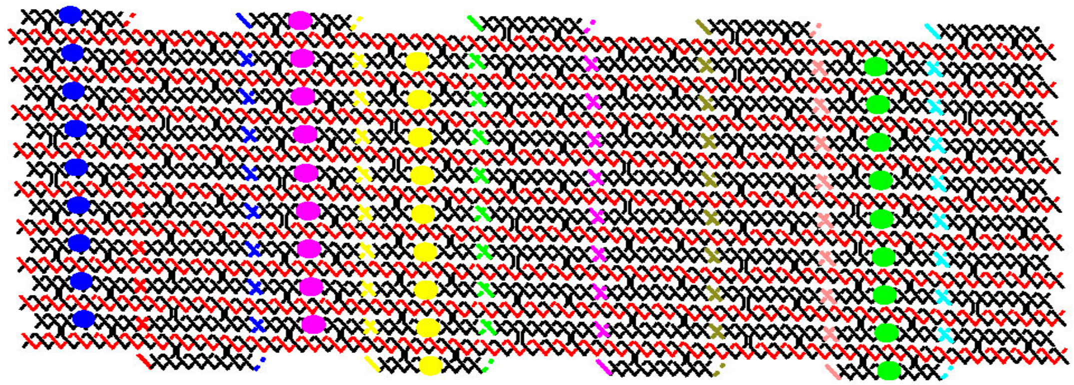
- Extends 2D arrays into simple aperiodic patterning:
  - The pattern of 1s and 0s is propagated up the growing tile array.
  - The 1-tiles are decorated with a DNA stem-loop pointing out of the tile plane (black rectangle) and 0-tiles are not.
  - Columns of loop-tiles and loopless-tiles can be distinguished by AFM as demonstrated with periodic AB* lattice.

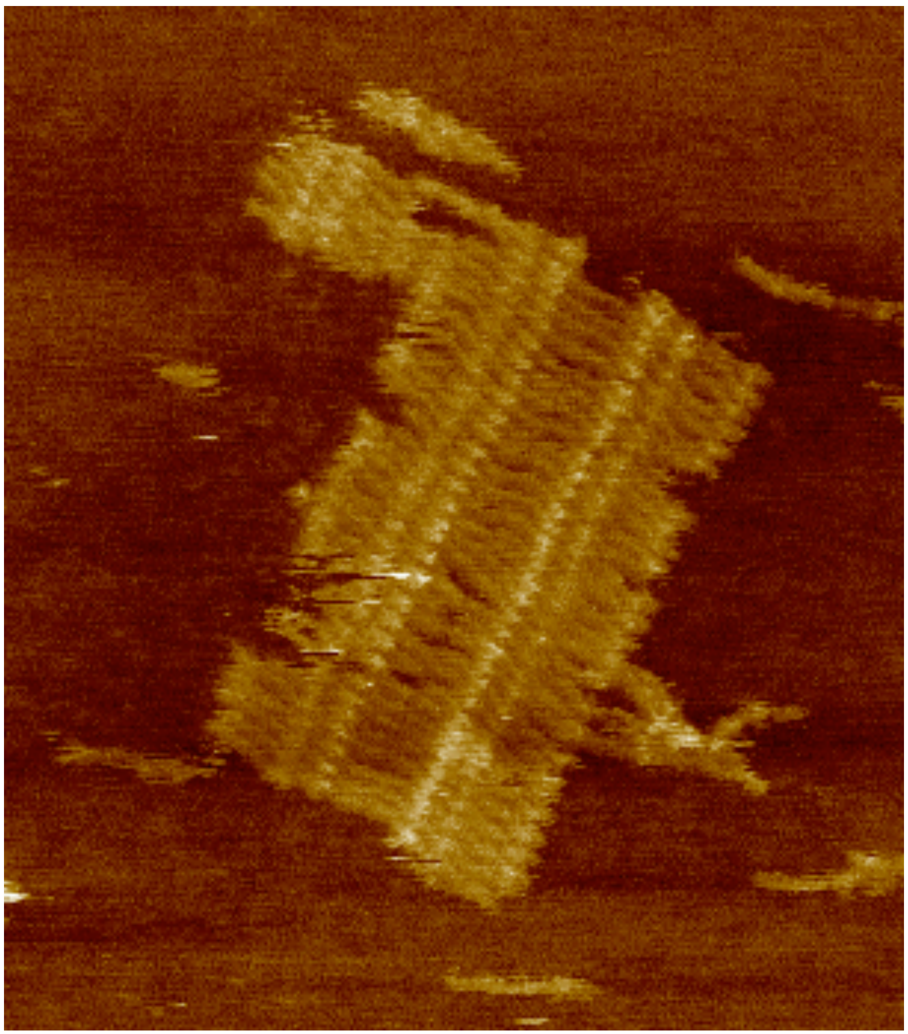
Barcode Lattice for Rendering 1 D Patterns:

H Yan, T LaBean, L Feng, J. Reif, PNAS (2003).

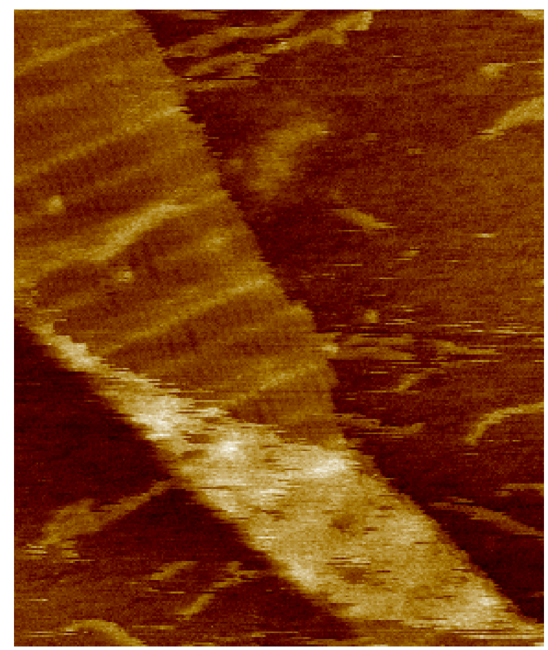
Hao Yan

Unit (9 tiles, filled dot i.e. loop represent 1,
8 pairs of asymmetric stickyends represented by
colored lines, The long red strand are the input)

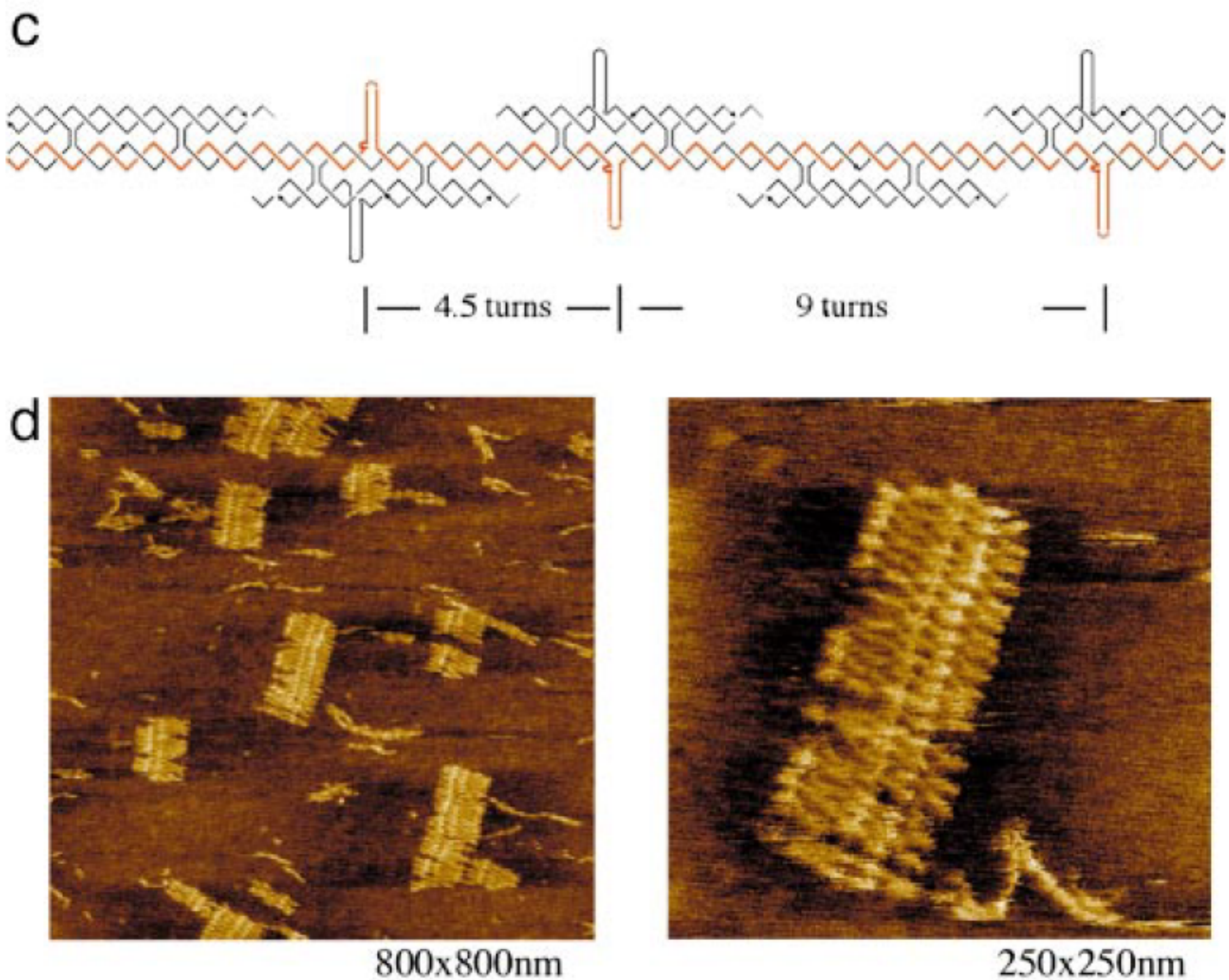




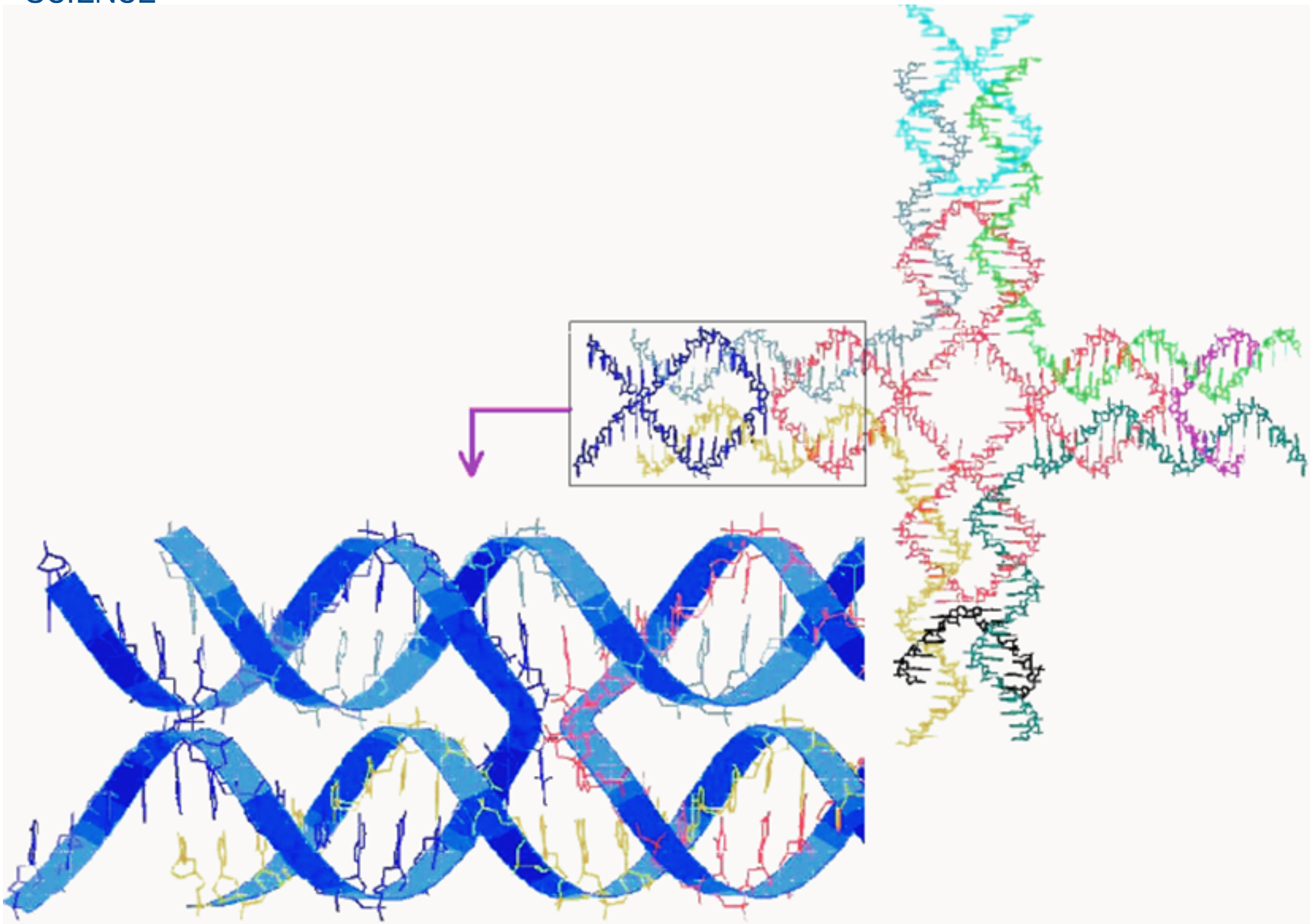
Barcode lattice displays banding patterns dictated by the same sequence of bit values programmed on each layer.



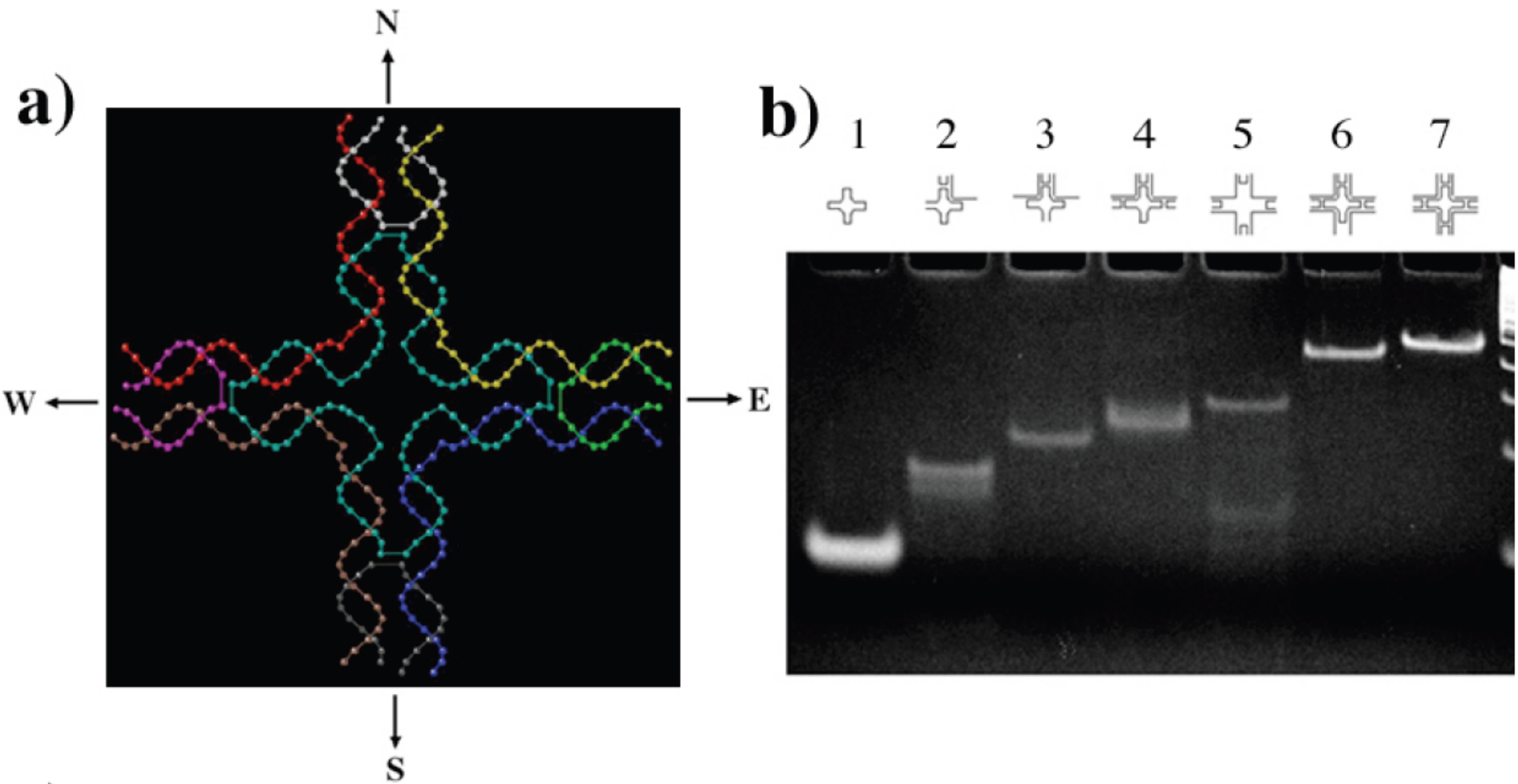
Barcoded lattices



Cross tile

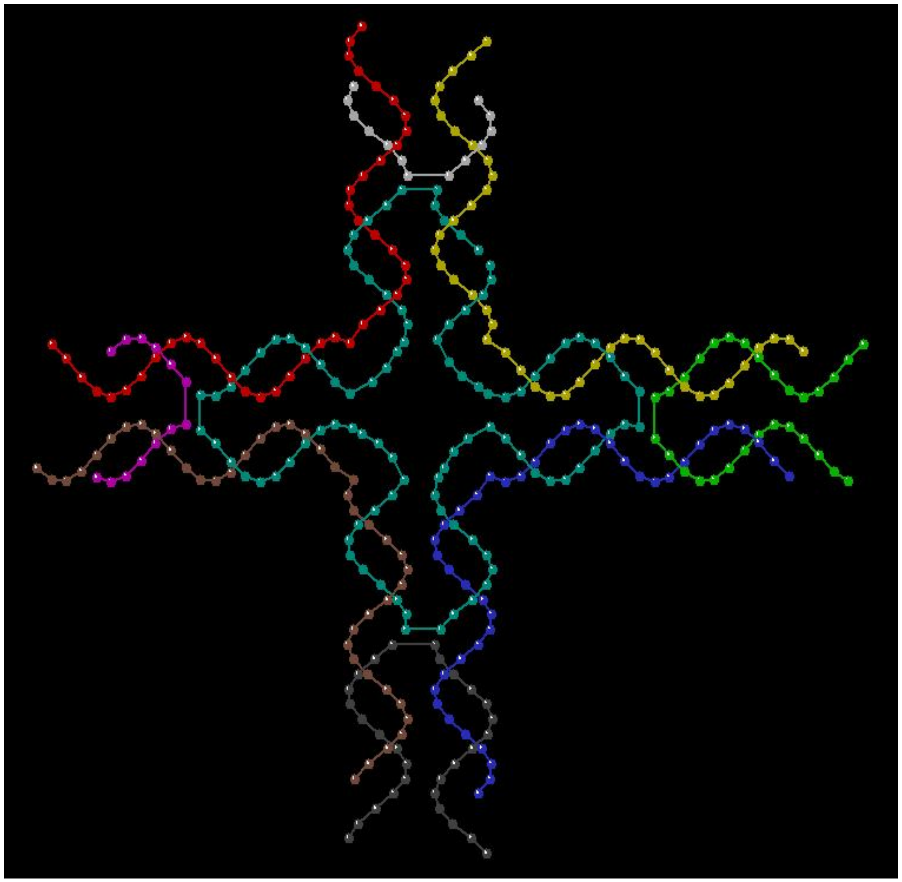


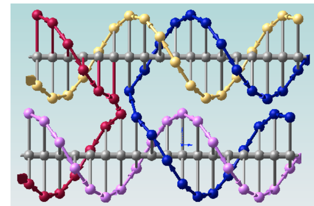
Cross tile



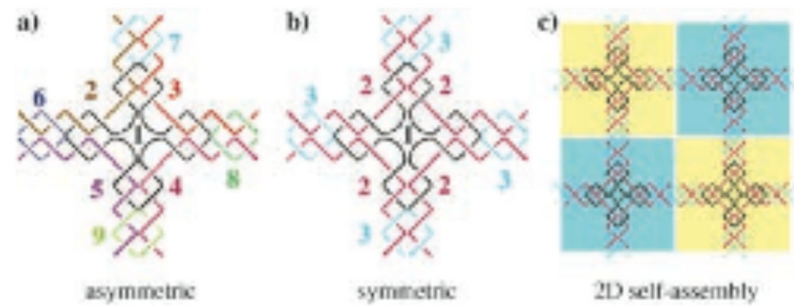
Cross tiles: Grid Assembly in 2D

Cross Tile



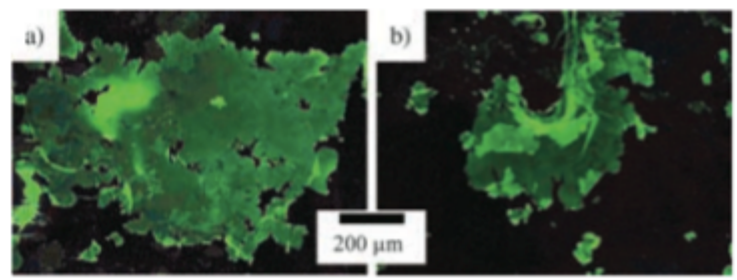


Branched Junction



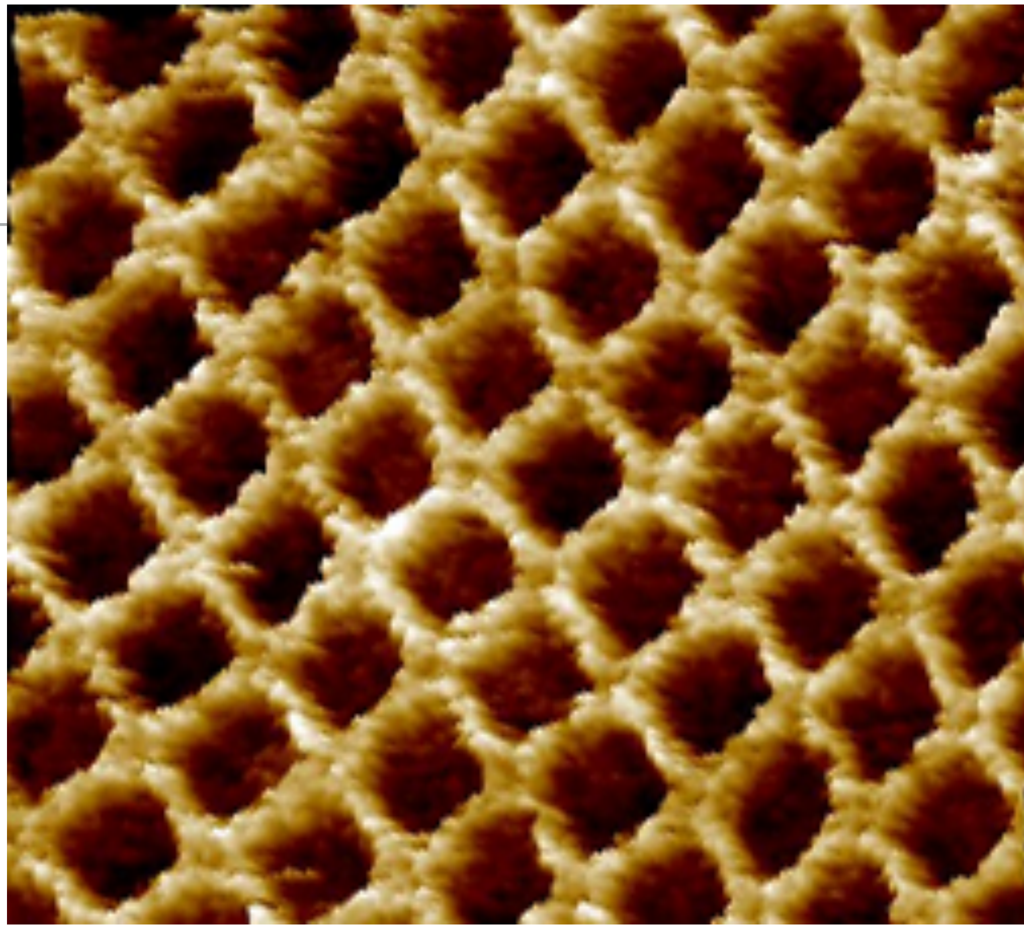
Figures adopted from He et al, 2005

Symmetric Tile

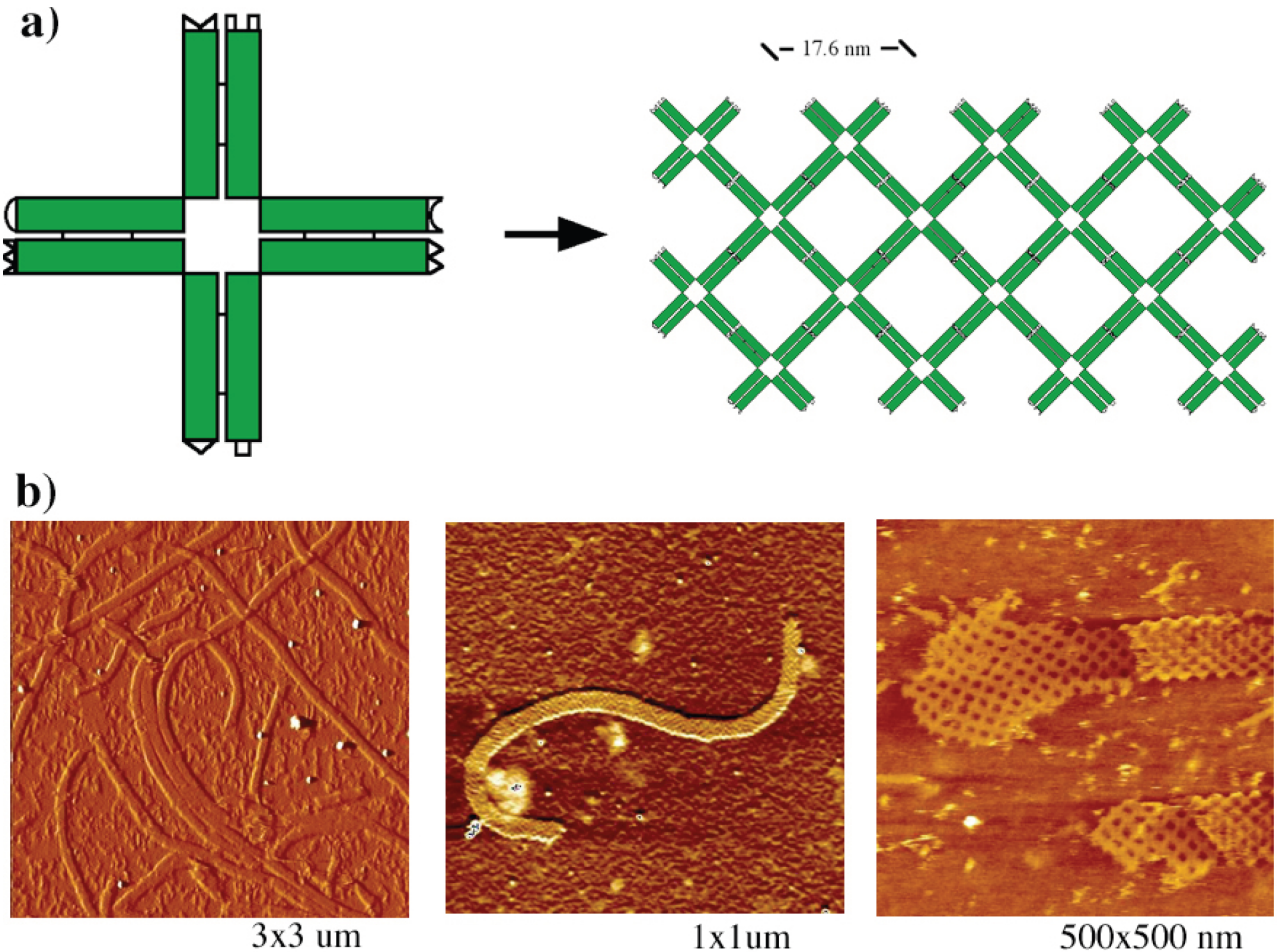


Corrugation creates enormous lattices

Cross Tile Lattices: Highly uniform molecular scale lattices far below VLSI scales

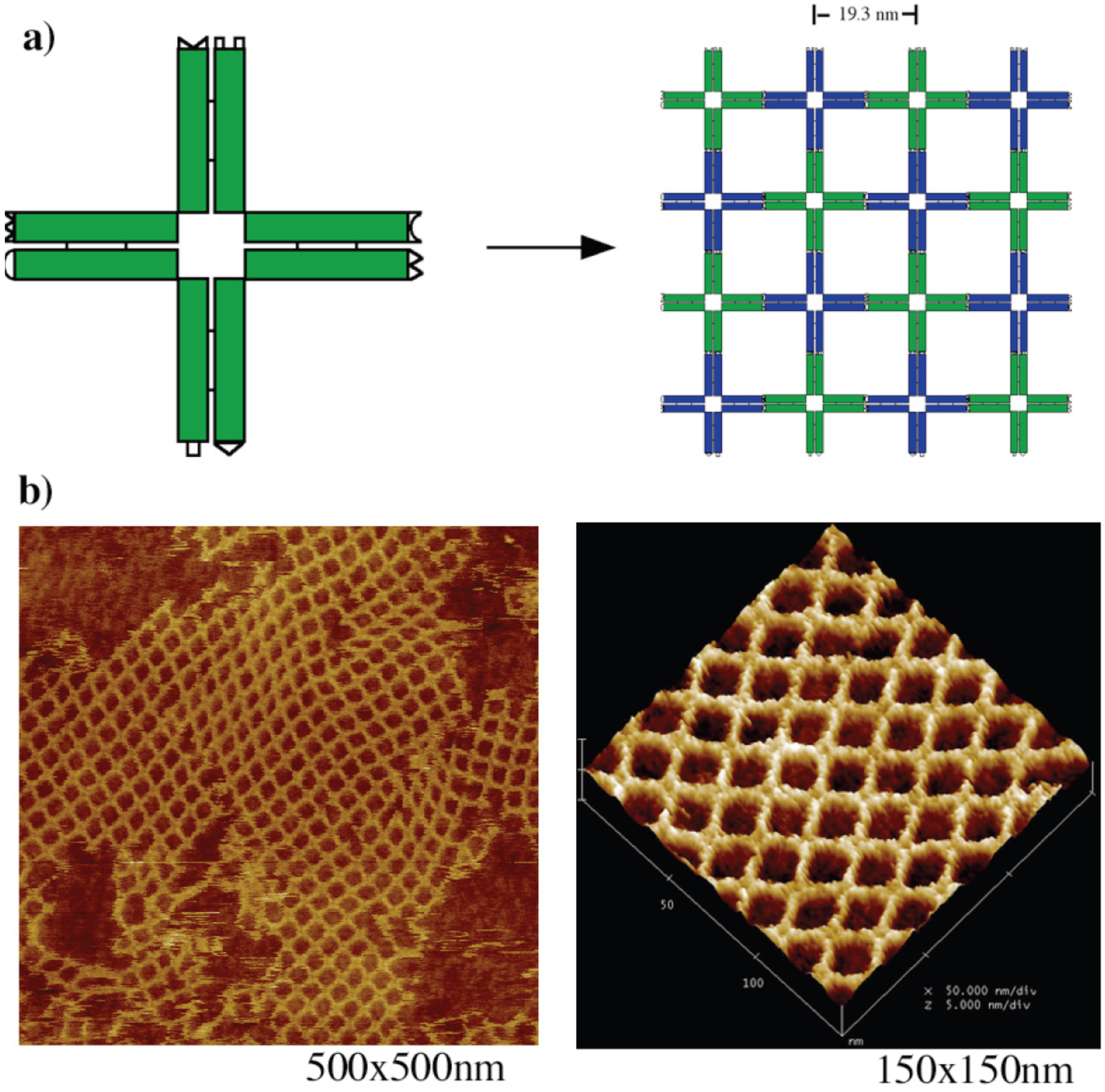


Uncorrugated cross tile tubes

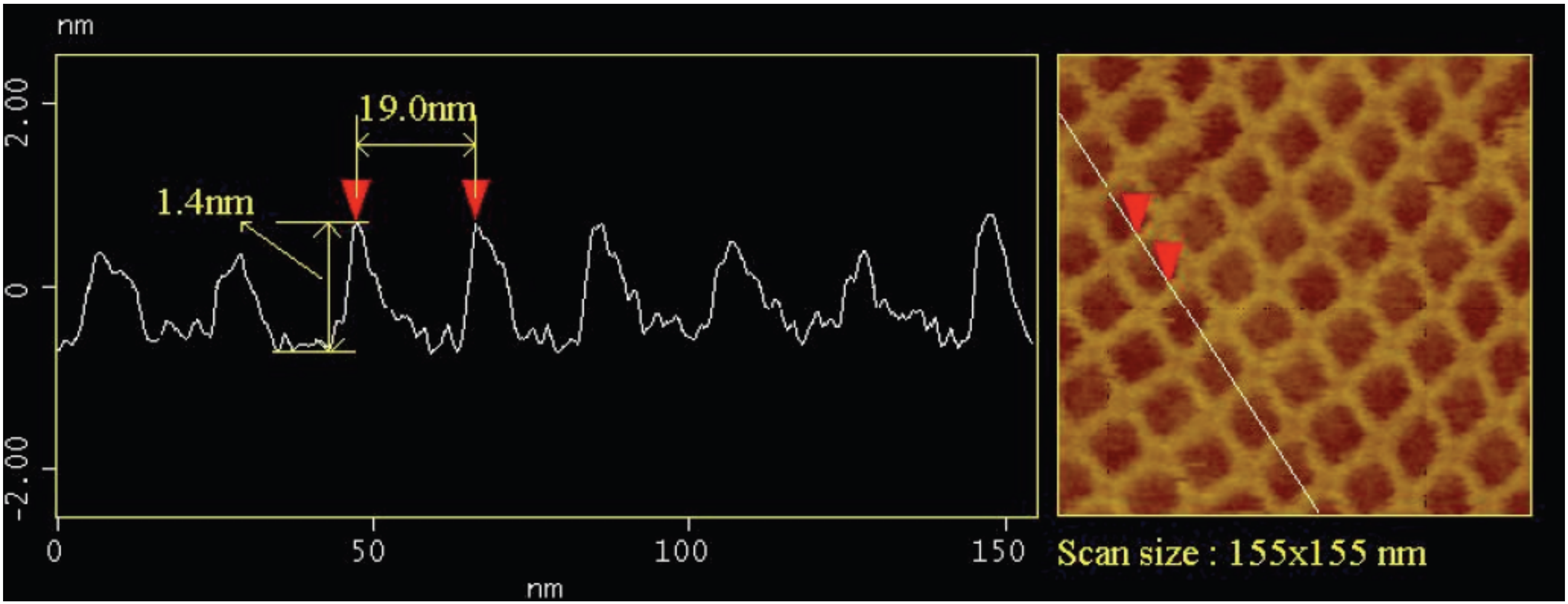


Corrugated cross tile lattice

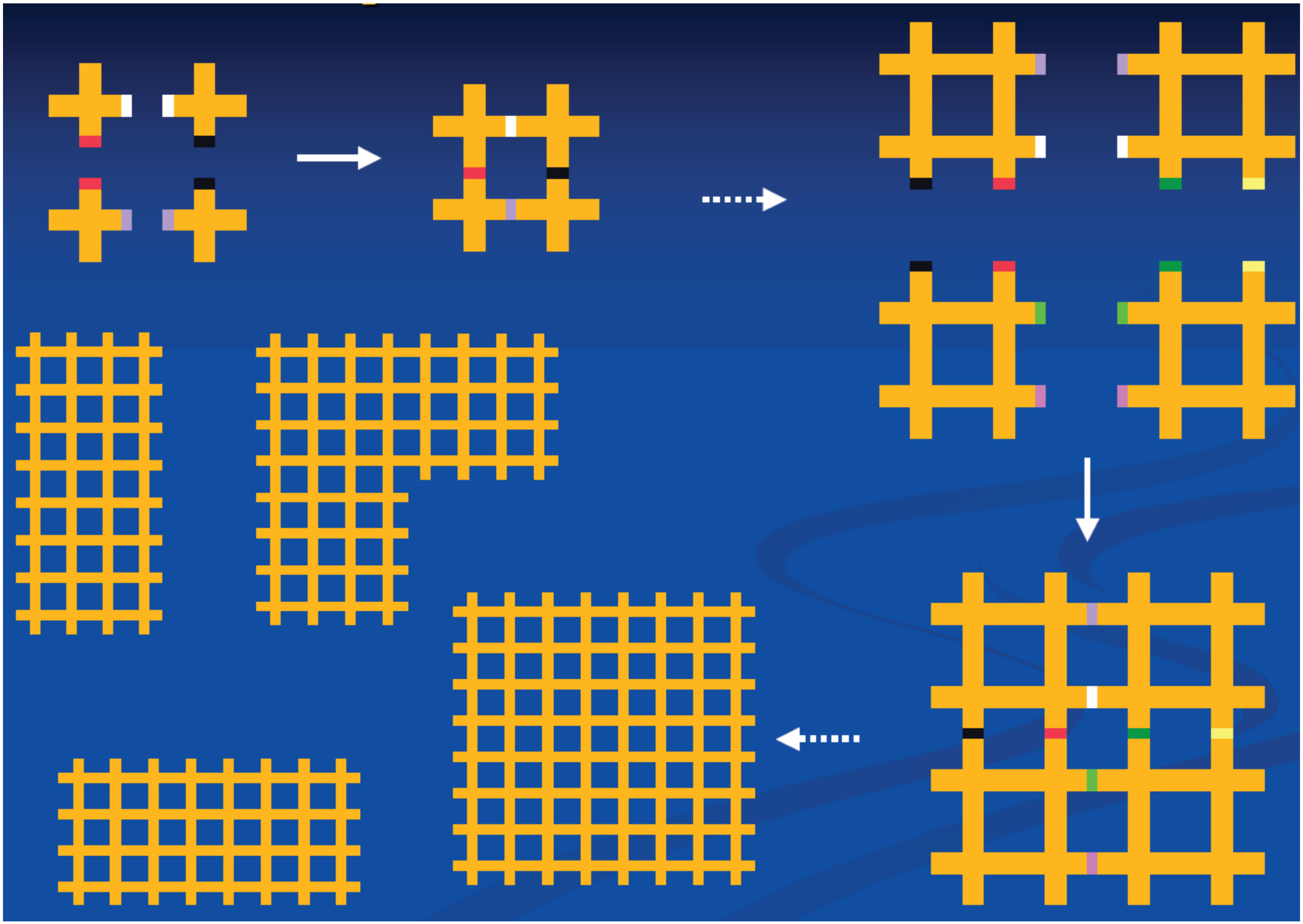
Hao Yan, Sung Ha Park, Gleb Finkelstein, John H. Reif, and Thomas H. LaBean, **DNA-Templated Self-Assembly of Protein Arrays and Highly Conductive Nanowires**, Science, Vol. 301, pp. 1882-1884, Sep 26 2003.



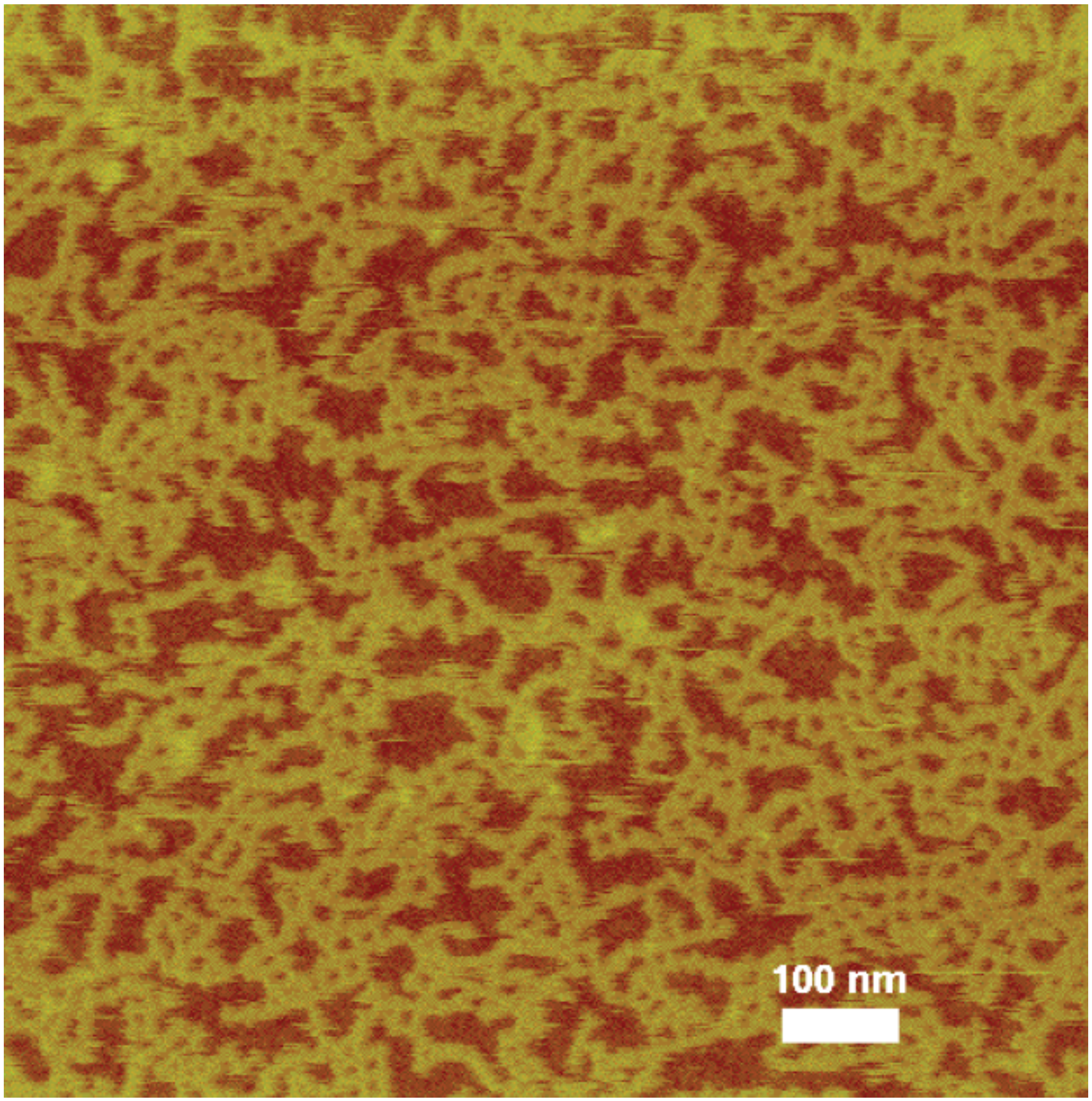
Corrugated cross tile

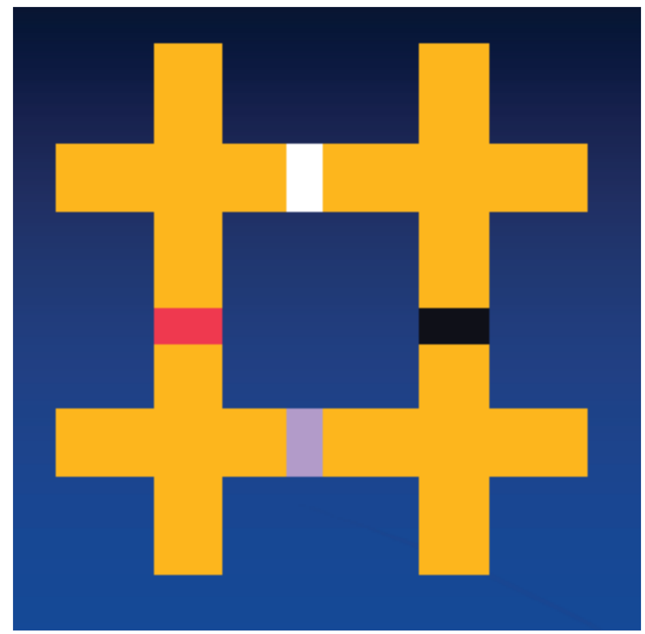


Hierarchical cross tile

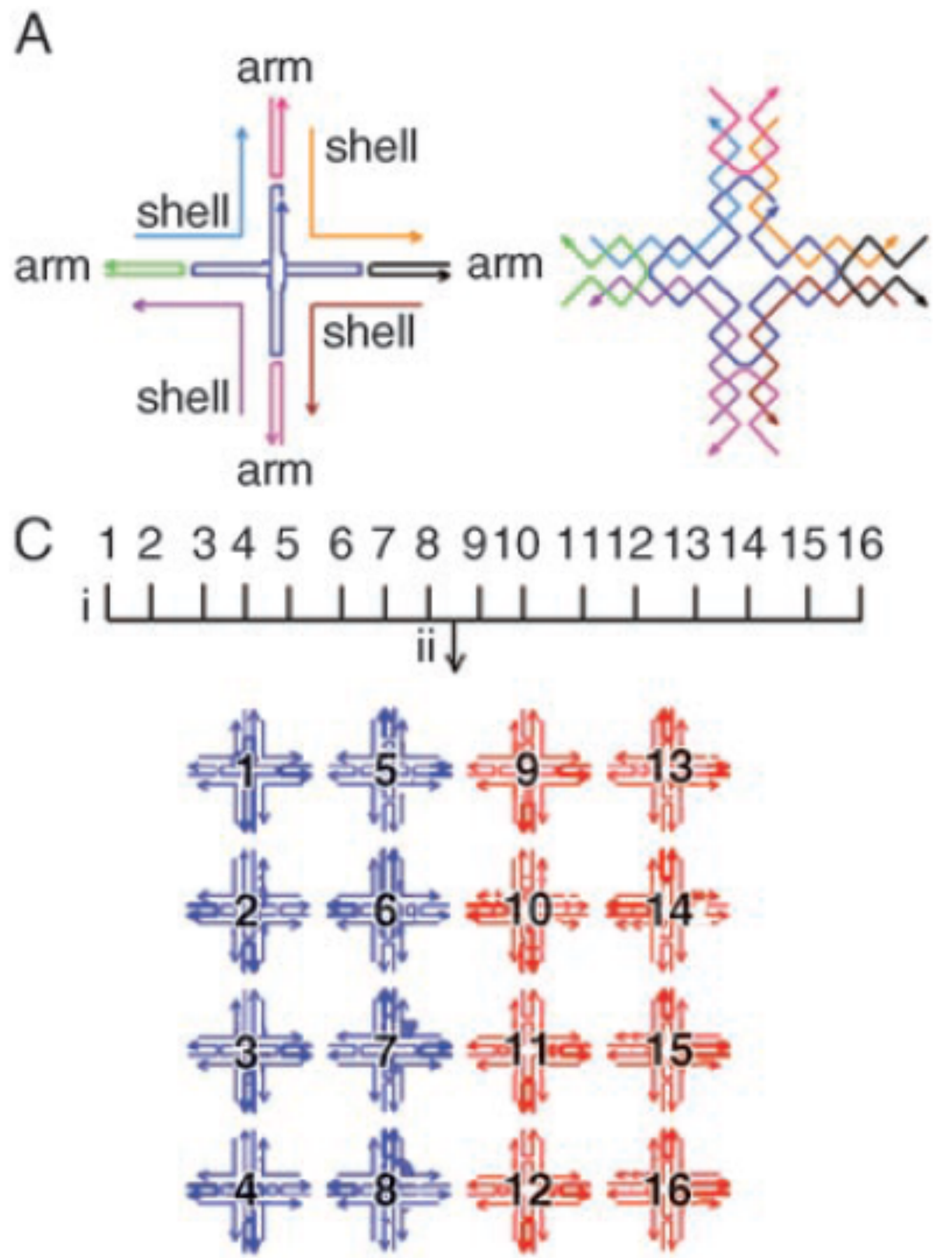


Hierarchical Assembly of cross tiles

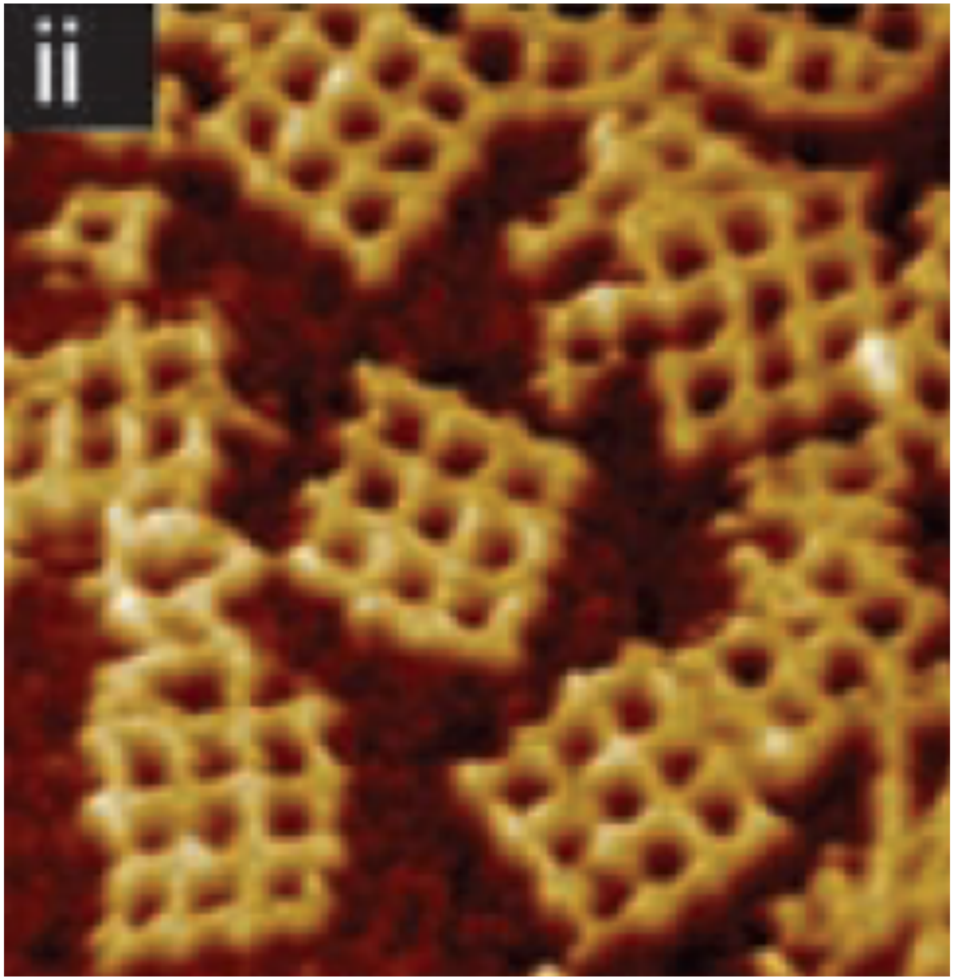


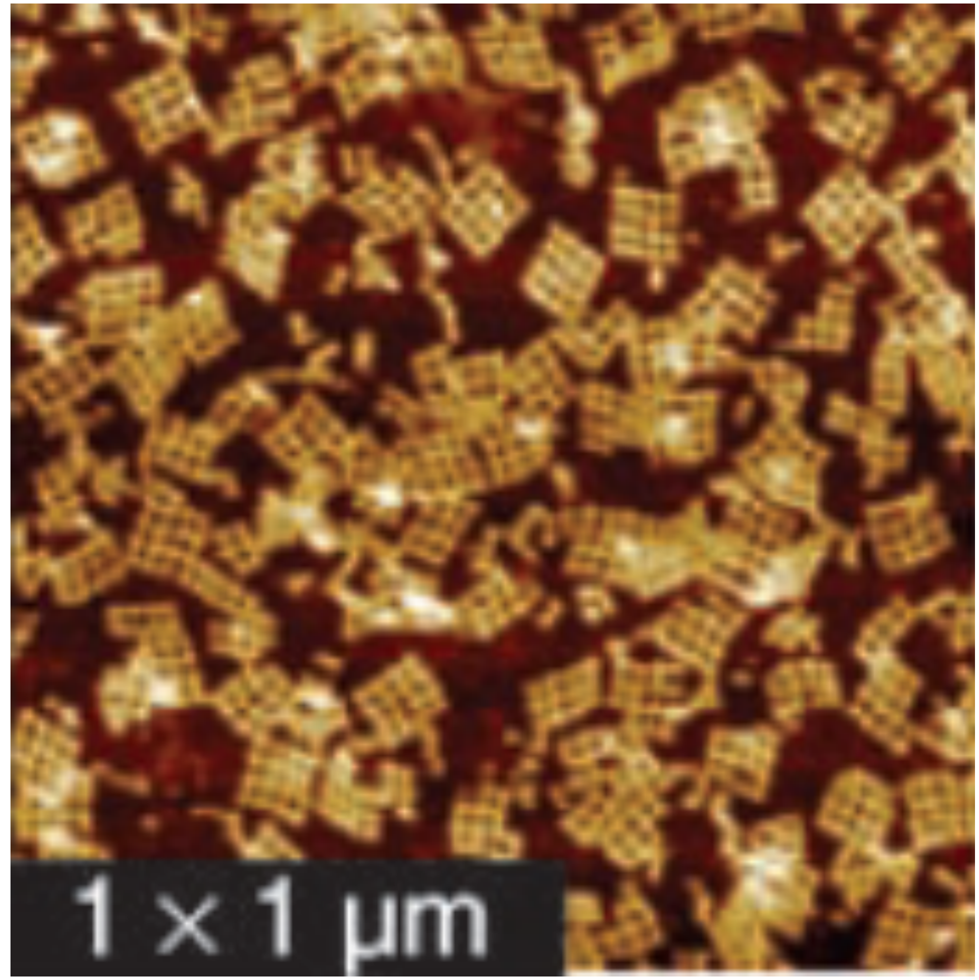


Addressable cross tile



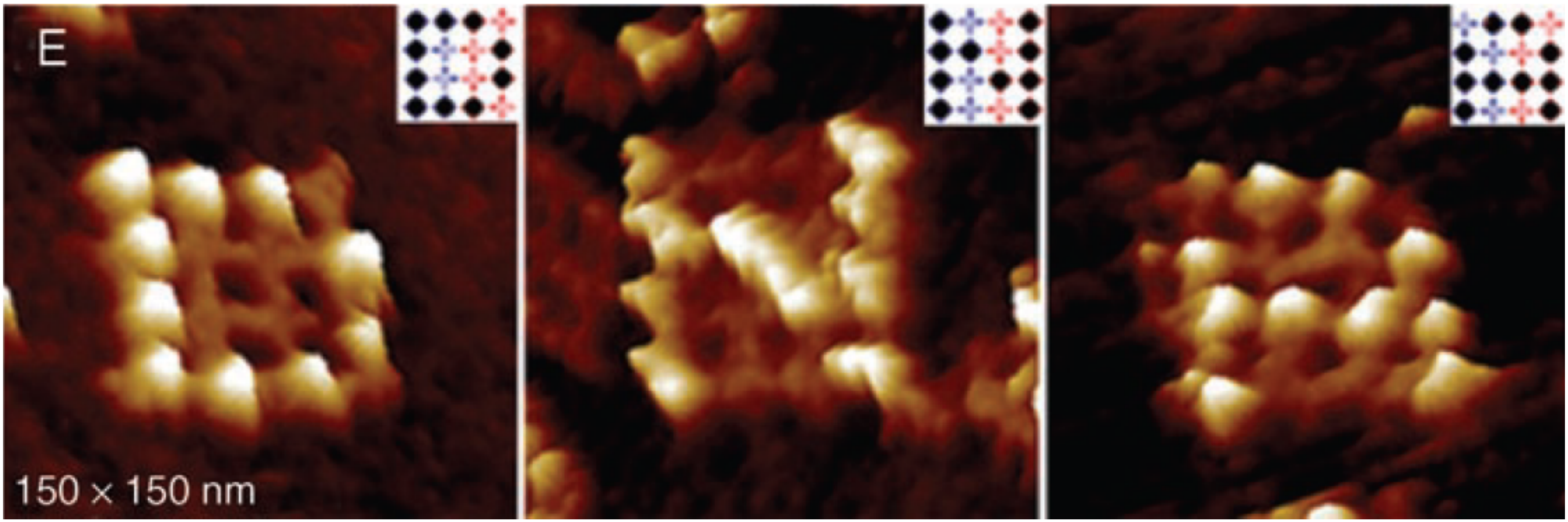
Addressable cross tile



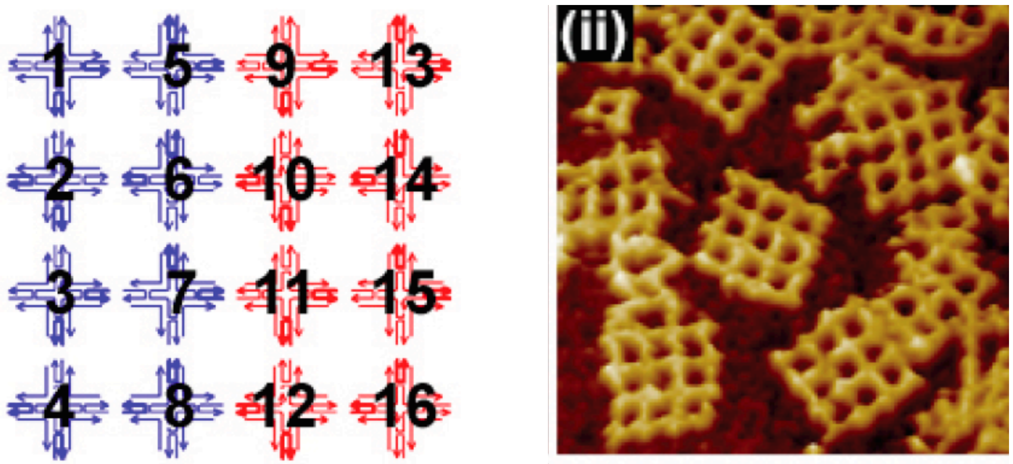


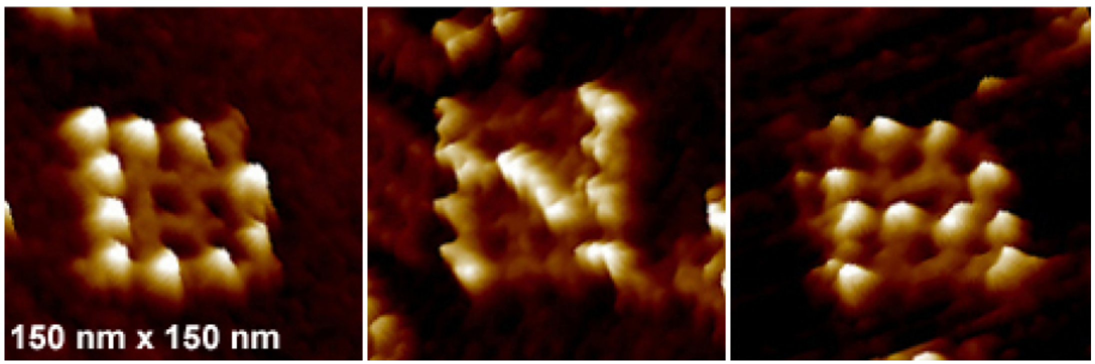
Sung Ha Park, Constantin Pistol, Sang Jung Ahn, John H. Reif, Alvin R. Lebeck, Chris Dwyer, and Thomas H. LaBean, **Finite-Size, Fully Addressable DNA Tile Lattices Formed by Hierarchical Assembly Procedures**, Angewandte Chemie [International Edition], Volume 45, Issue 5, pp. 735-739

Molecular Scale Patterning using Hierarchical Assembly of cross tiles



Hierarchical Assembly of DNA Lattices with 2 D Pattern "DNA"





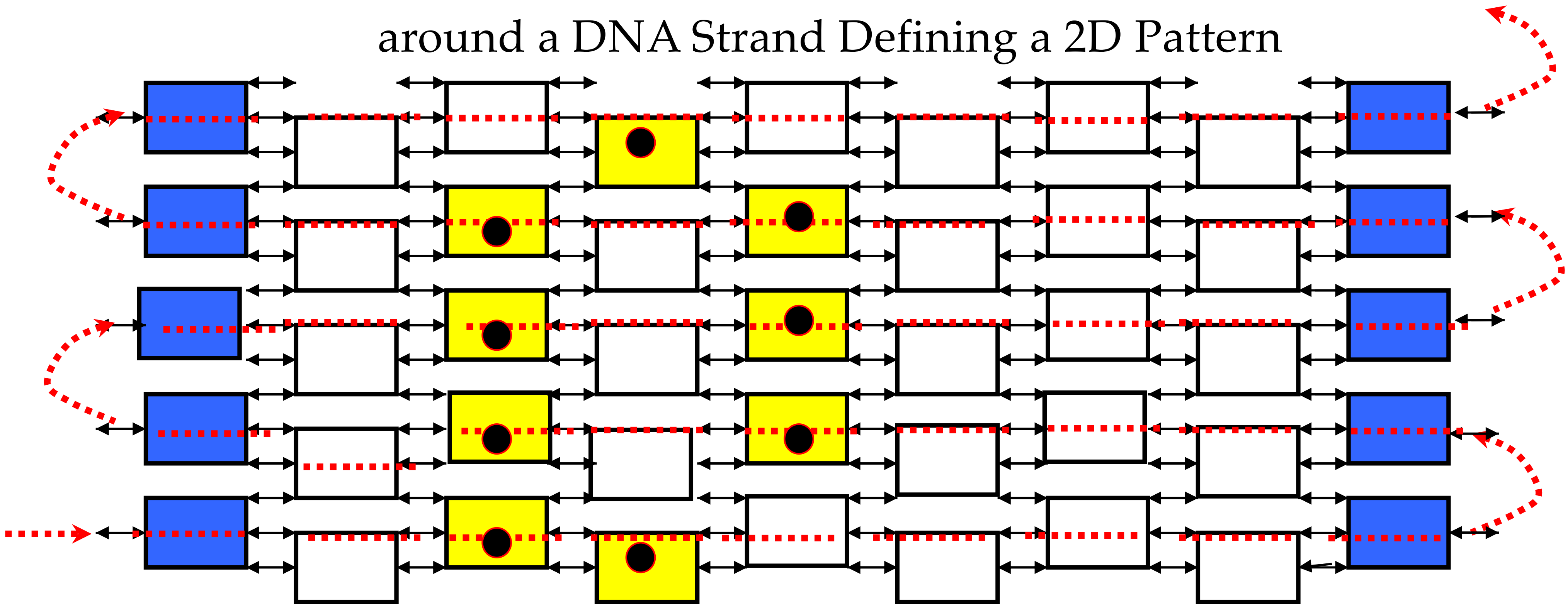
Sung Ha Park, Constantin Pistol, Sang Jung Ahn, John H. Reif, Alvin R. Lebeck, Chris Dwyer, and Thomas H. LaBean, Finite-Size, Fully Addressable DNA Tile Lattices Formed by Hierarchical Assembly Procedures, Angewandte Chemie [International Edition], 2006.

Assembling a 2 D Pattern by

Directed Nucleation :

Self Assembly of Tiles

around a DNA Strand Defining a 2D Pattern

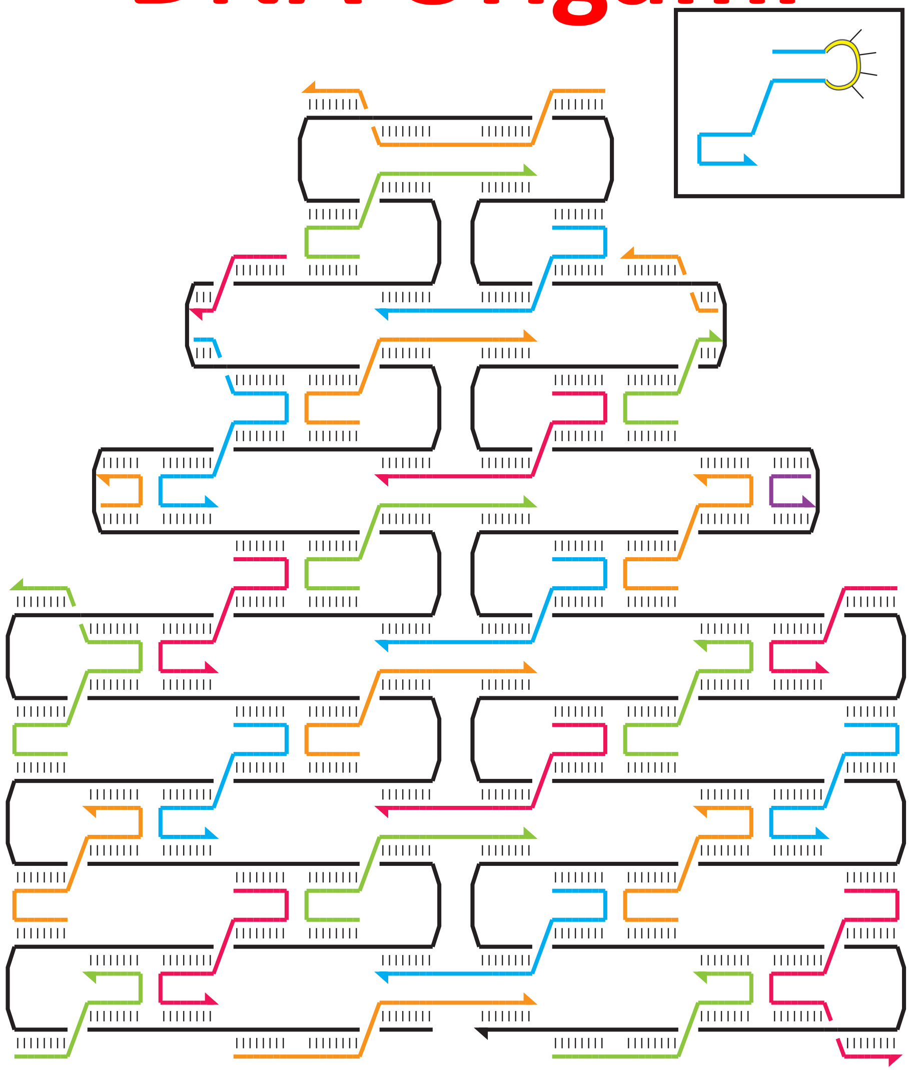


Design Idea by LaBean & Reif, early 2000s

DNA Origami

Paul W K Rothemund's
DNA Origami

e



2006 - **Folding DNA to create nanoscale shapes and patterns**

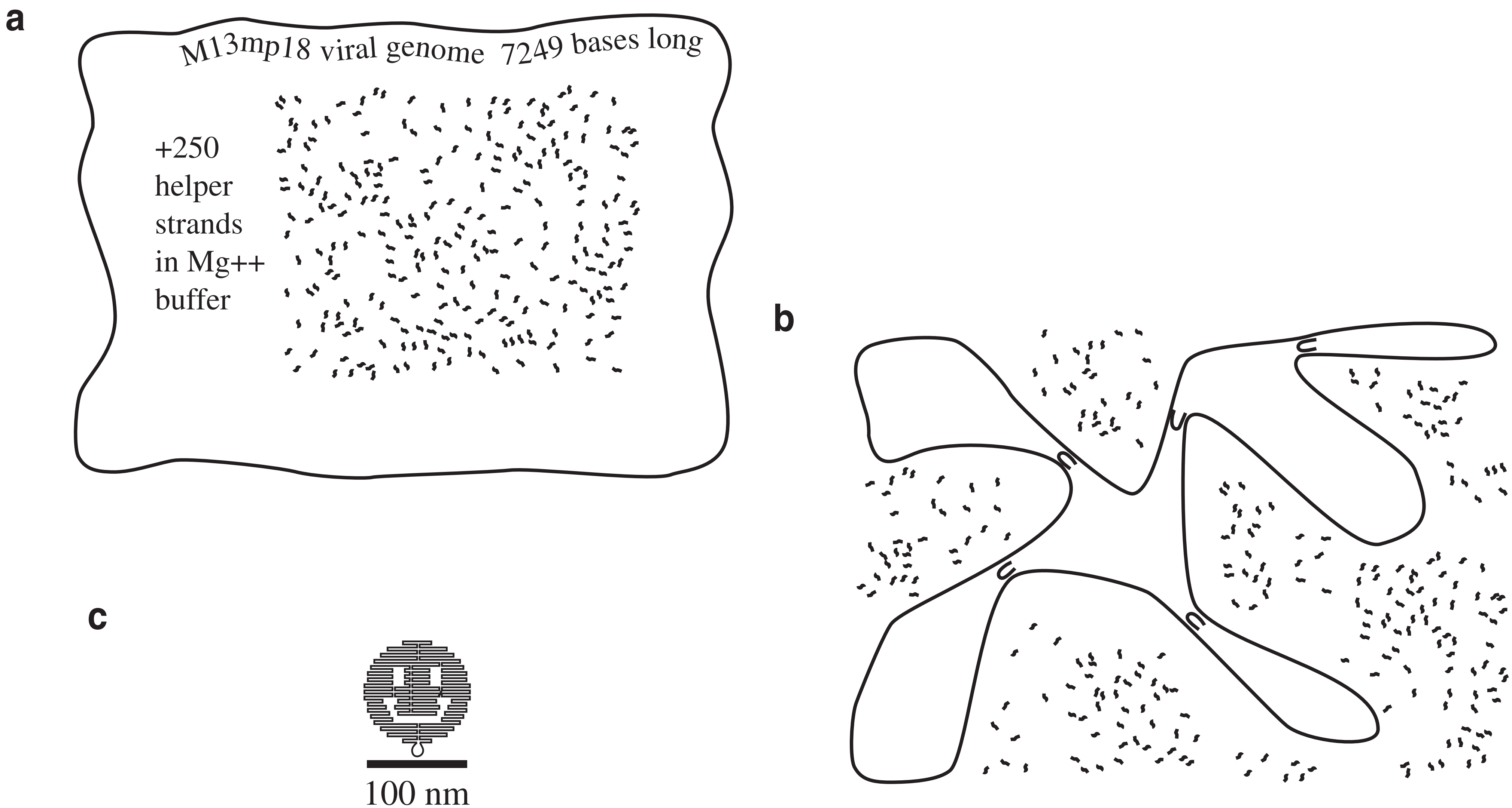
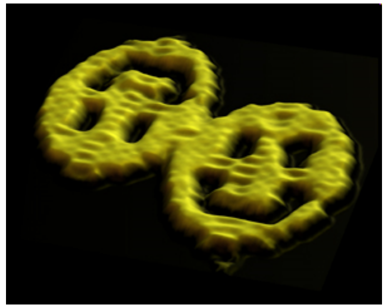


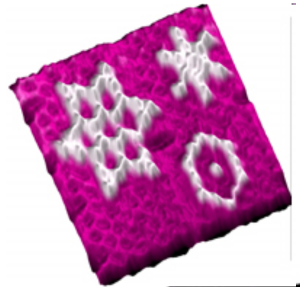
Fig. 6. A cartoon depicts folding of DNA origami as temperature changes from 90 C to 20 C.

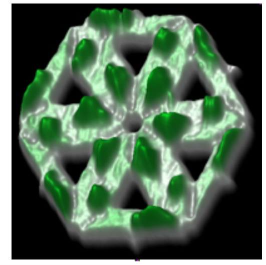
2005 – Design of DNA Origami

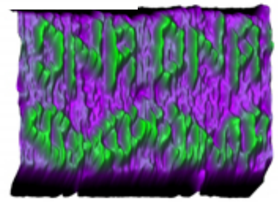
DNA Origami

Nature, 2006



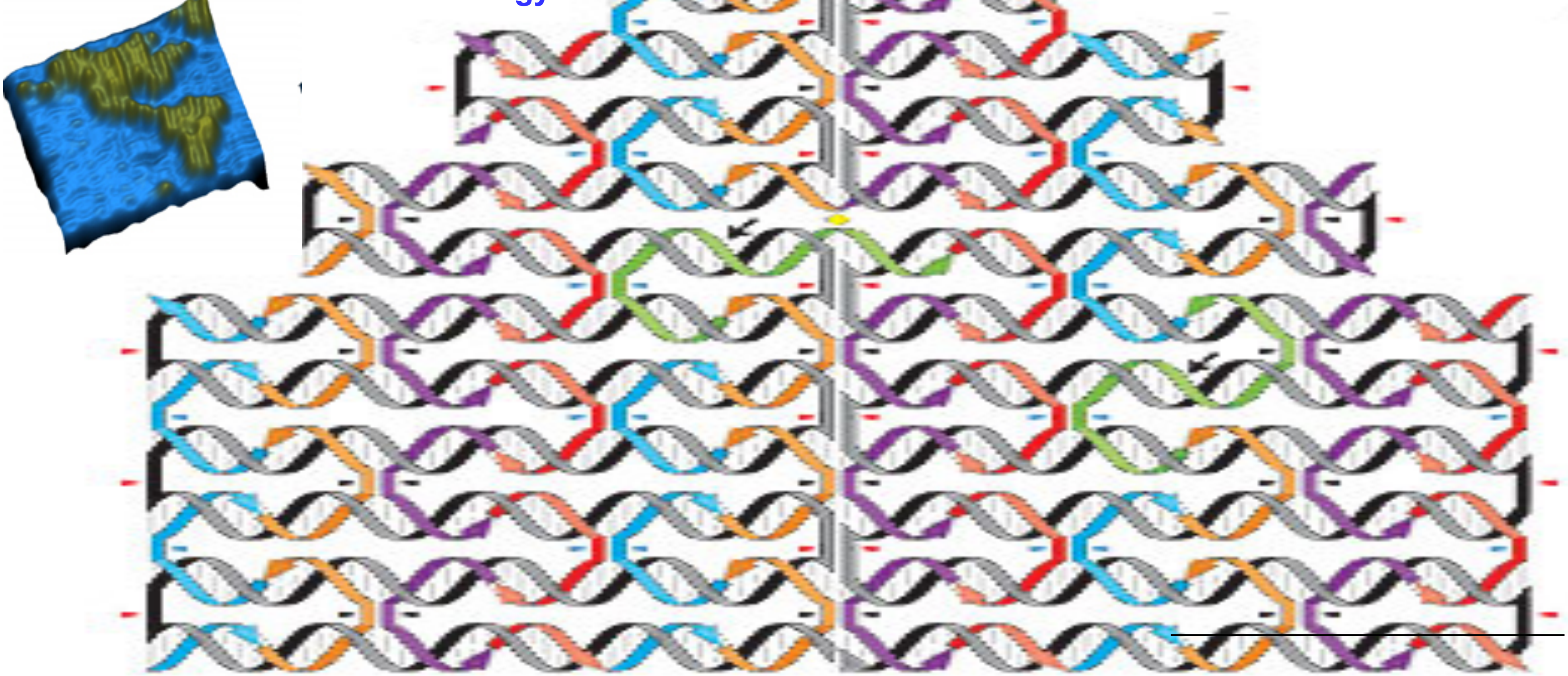






Paul W K Rothemund

California Institute of Technology



PWK Rothemund, *Nature* **440**, 297 (2006)

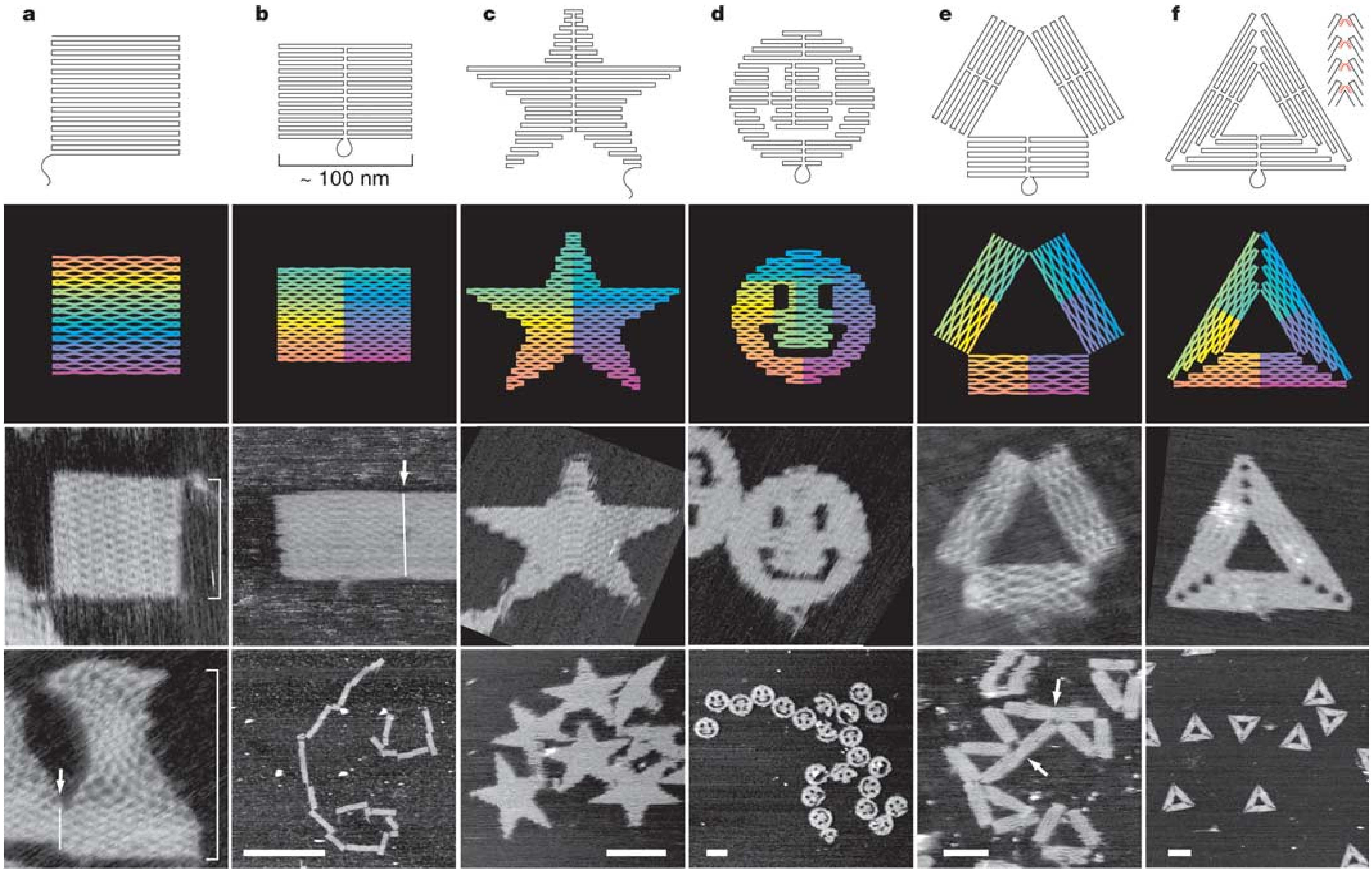
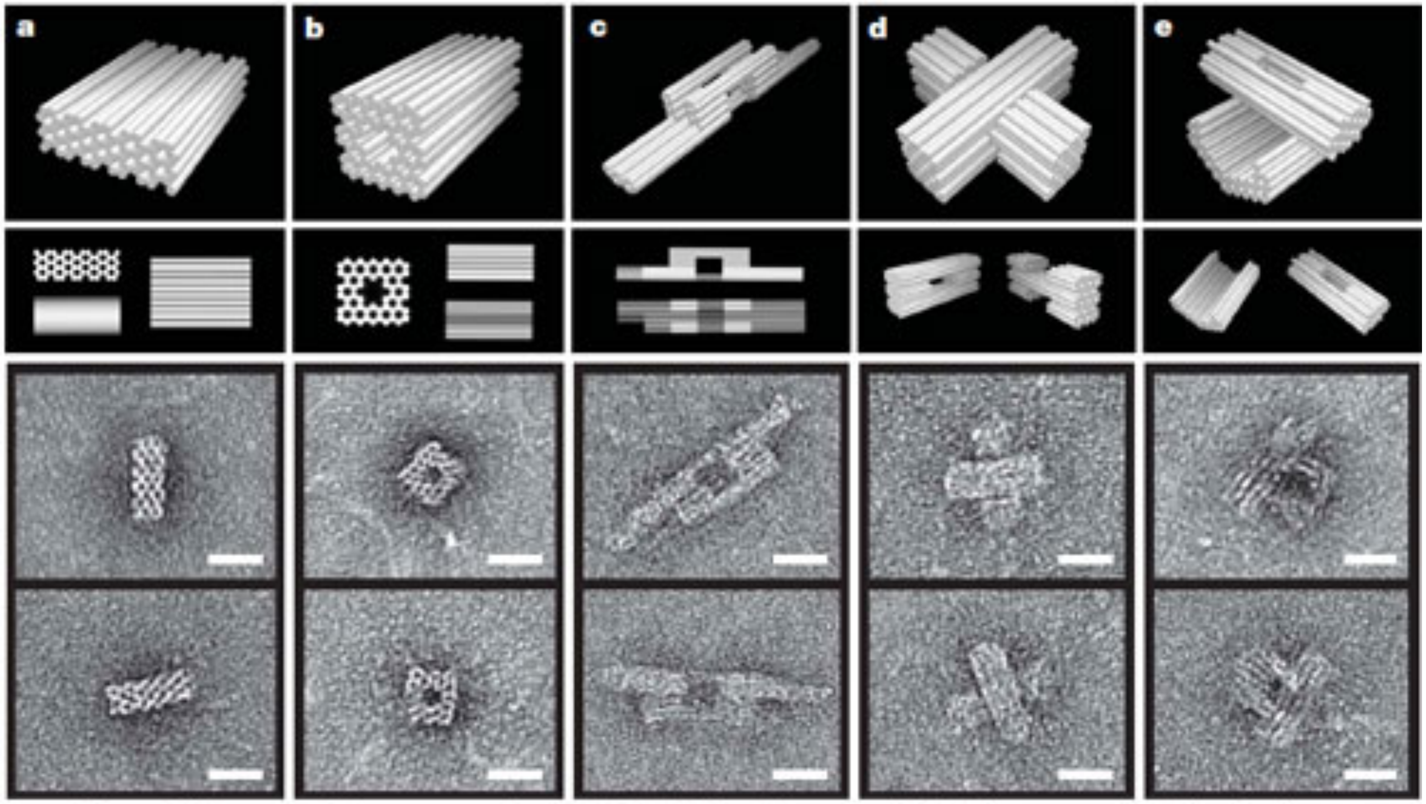


Figure 2 | DNA origami shapes. Top row, folding paths. **a**, square; **b**, rectangle; **c**, star; **d**, disk with three holes; **e**, triangle with rectangular domains; **f**, sharp triangle with trapezoidal domains and bridges between them (red lines in inset). Dangling curves and loops represent unfolded sequence. Second row from top, diagrams showing the bend of helices at crossovers (where helices touch) and away from crossovers (where helices bend apart). Colour indicates the base-pair index along the folding path; red is the 1st base, purple the 7,000th. Bottom two rows, AFM images. White lines and arrows indicate blunt-end stacking. White brackets in **a** mark the height of an unstretched square and that of a square stretched vertically (by a factor >1.5) into an hourglass. White features in **f** are hairpins; the triangle is labelled as in Fig. 3k but lies face down. All images and panels without scale bars are the same size, 165 nm × 165 nm. Scale bars for lower AFM images: **b**, 1 μm; **c**–**f**, 100 nm.

3D DNA Origami



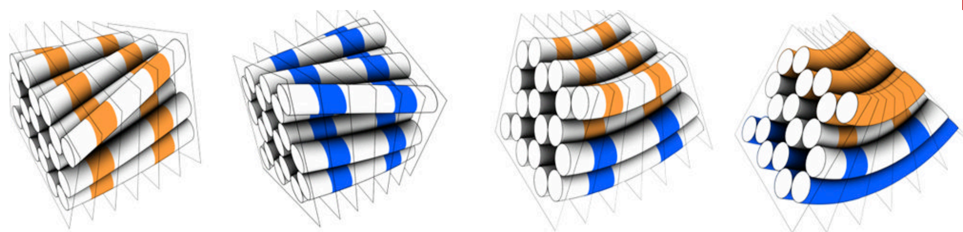
Monolith Square nut Railed bridge Slotted cross Stacked cross

Shawn M. Douglas, Hendrik Dietz, Tim Liedl, Björn Högberg, Franziska Graf & William M. Shih, Self-assembly of DNA into nanoscale three-dimensional shapes, Nature 459, 414-418(21 May 2009)

doi:10.1038/nature08016

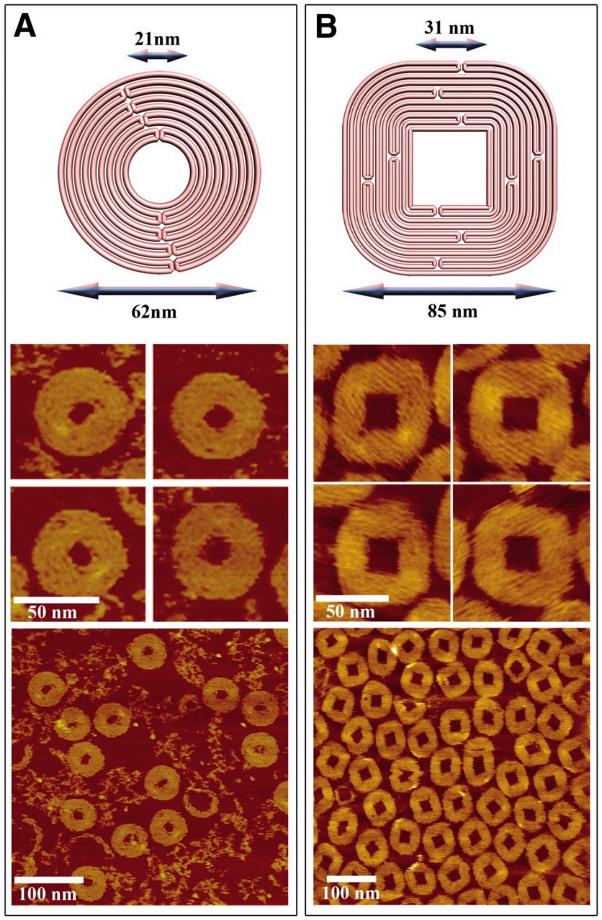
3D Shaped DNA Origami

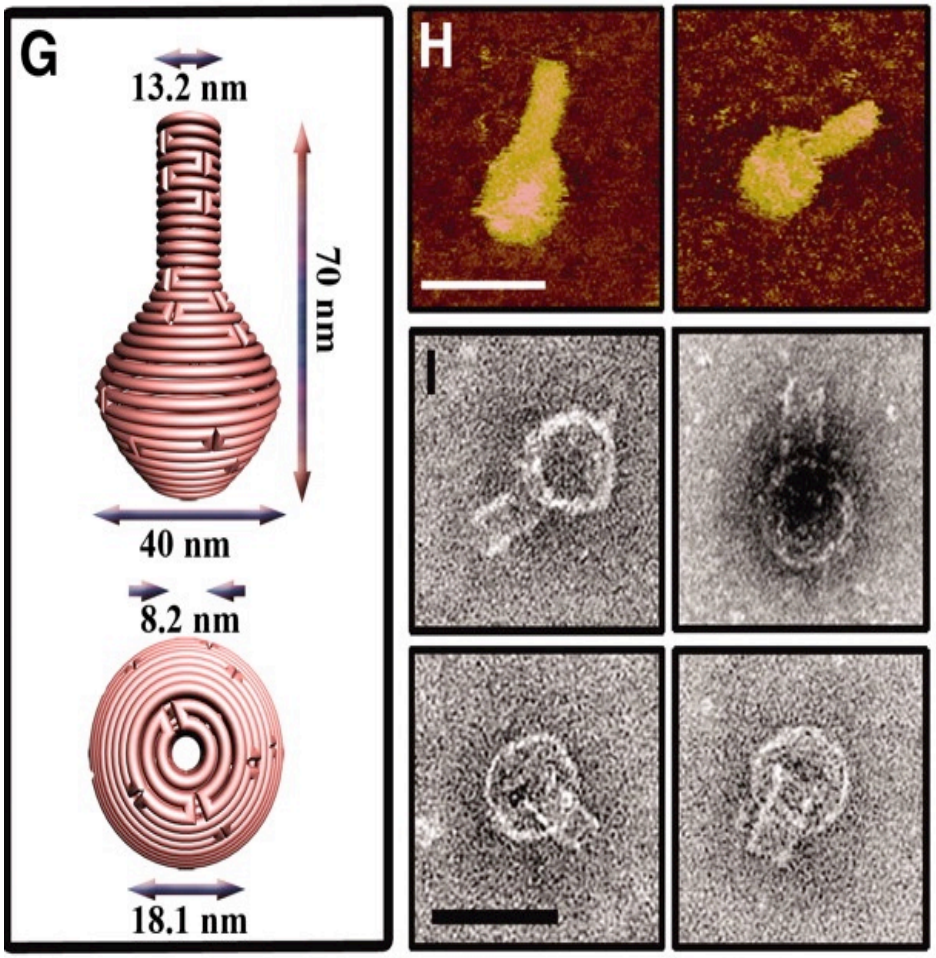
2009
Harvard



Folding DNA into Twisted and Curved Nanoscale Shapes.

3D Shaped DNA Origami





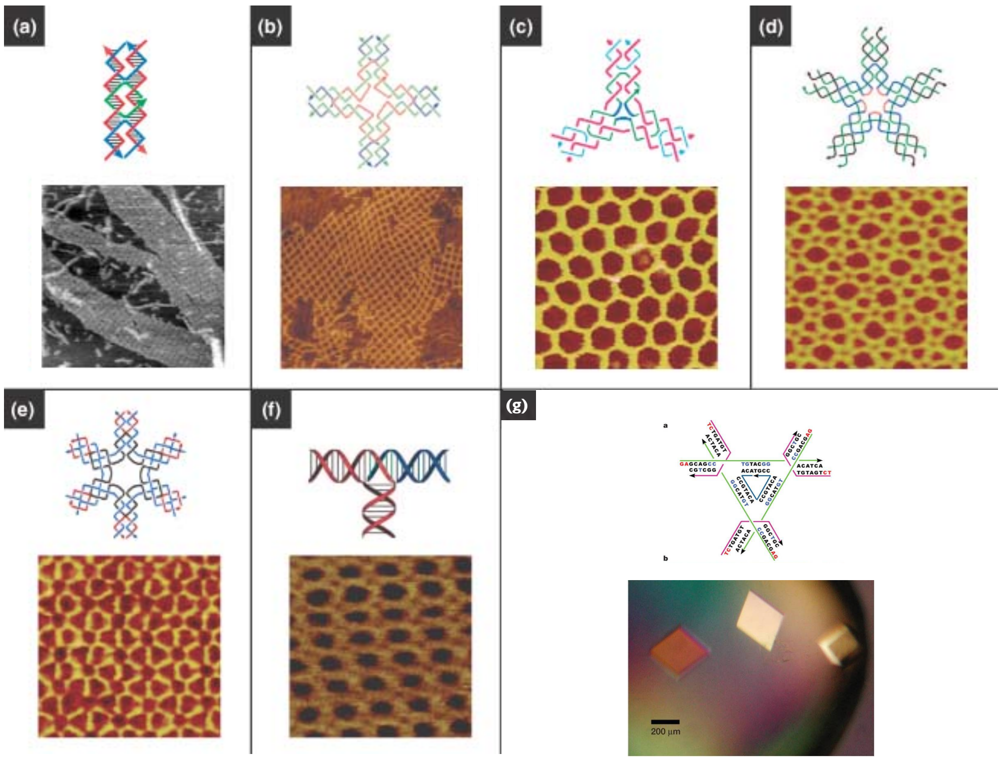
Han, Dongran et al. (2011). DNA origami with complex curvatures in three-dimensional space. *Science*, *332*(6027), 342–346. http://doi.org/10.1126/science.1202998

Double Decker Tiles & 3D DNA Lattices

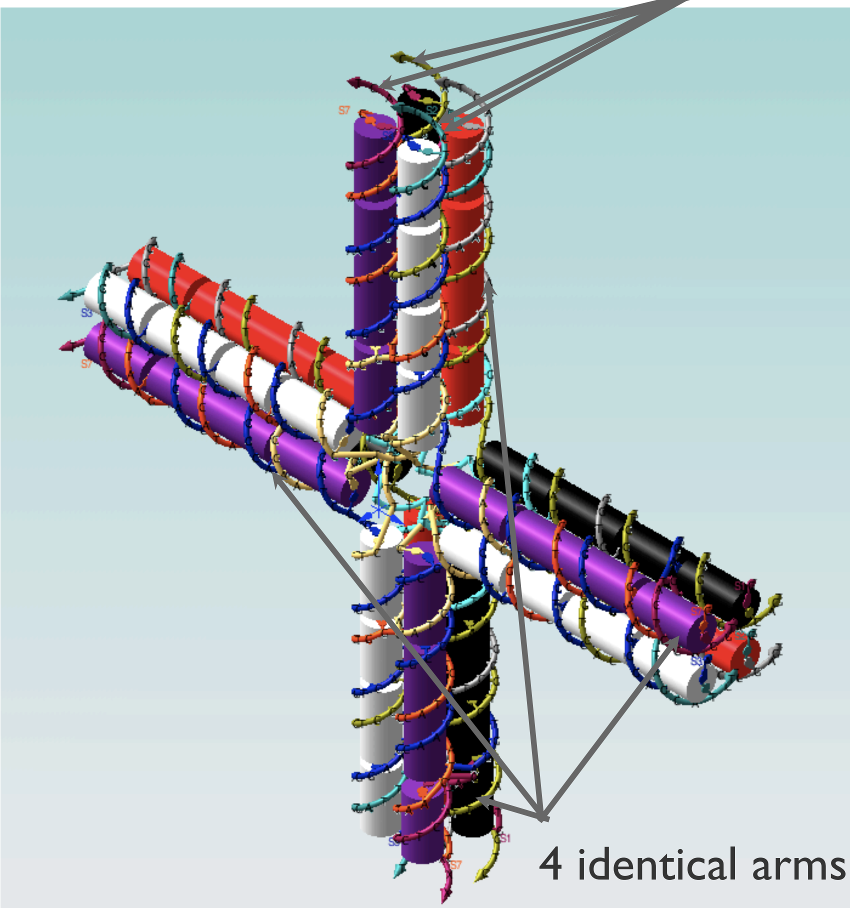
Urmi Majumdar, Abhijit Rangnekar, Kurt V. Gothelf, John H Reif and Thomas H LaBean, Design and Construction of Double-Decker Tile as a Route to Three-Dimensional Periodic Assembly of DNA, Journal American Chemical Society (JACS), Vol. 133, no. 11, pp. 3843—3845 (Feb. 2011)

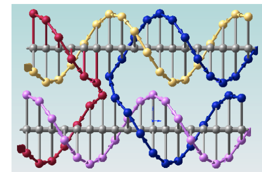
3D lattices via double decker cross tiles

- 2D lattices out of DNA tile
  - (a) DX tiles
  - (b) Four arm junction
  - (c) Three arm junction
  - (d) Five arm junction
  - (e) Six arm junction
  - (f) T-junction
- 3D lattices
  - (g)Tensegrity lattice
- Application of 3D lattices:
  - Imaging proteins
  - Organizing molecular electronic components
  - Organizing functional inorganic materials
  - Tile based computing



Double-decker tiles: Route to Assembly in 3D



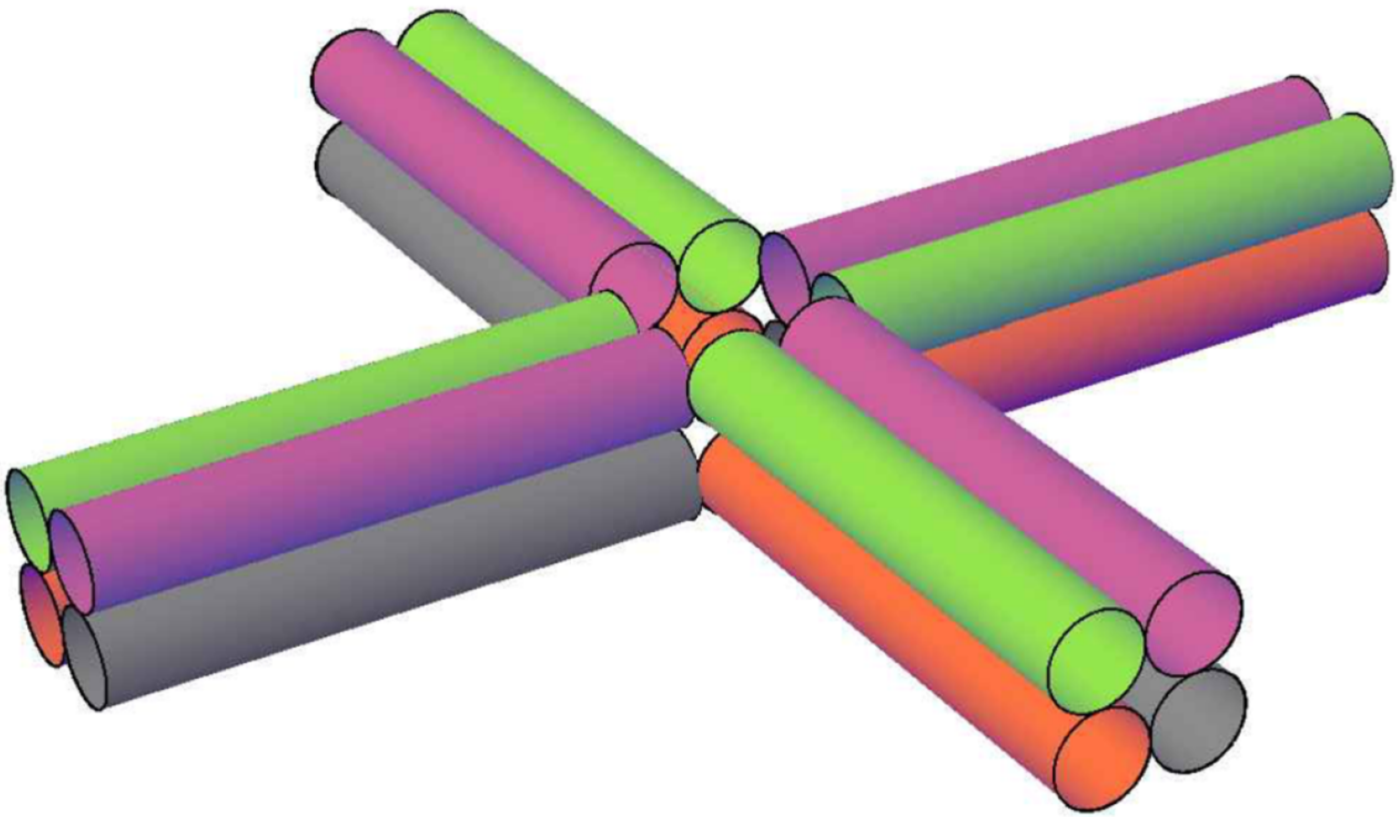


Branched Junction

2 cross tiles held together by branched junctions

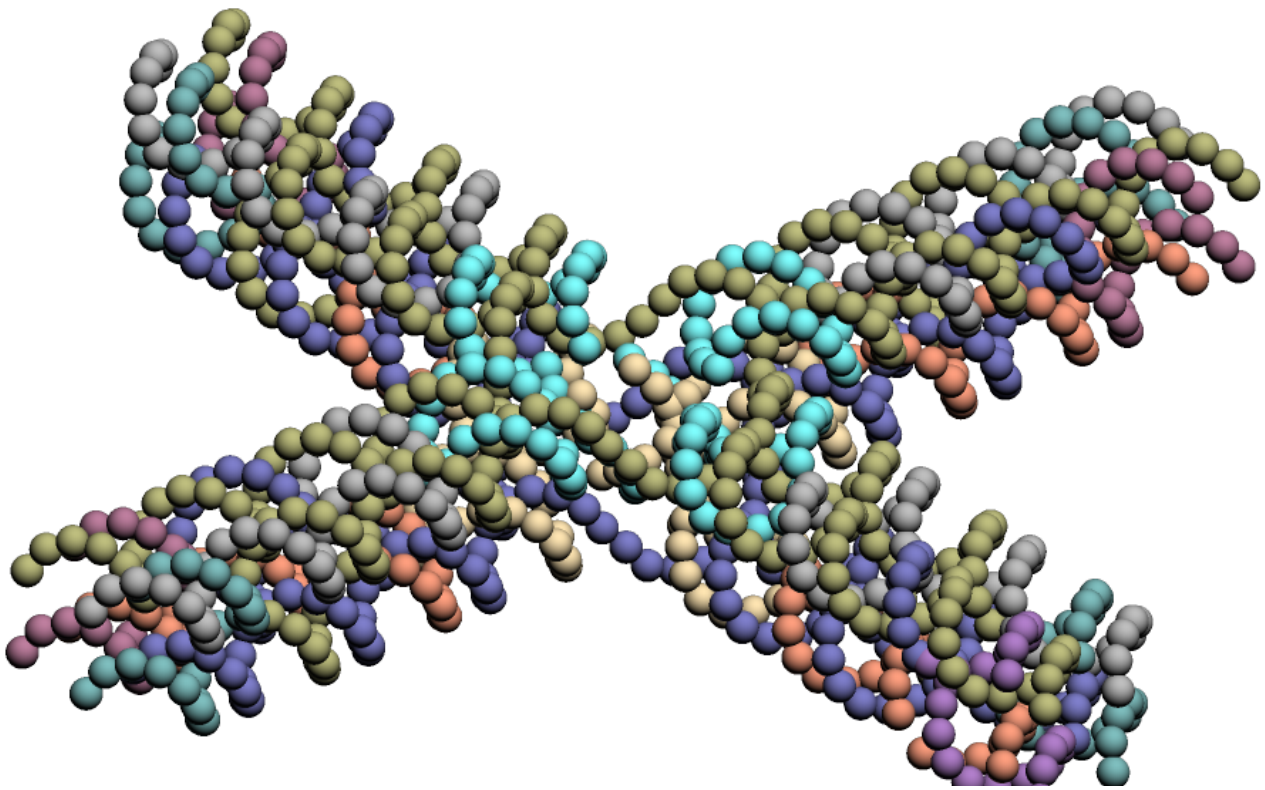
Urmi Majumder, Duke

Double decker tiles



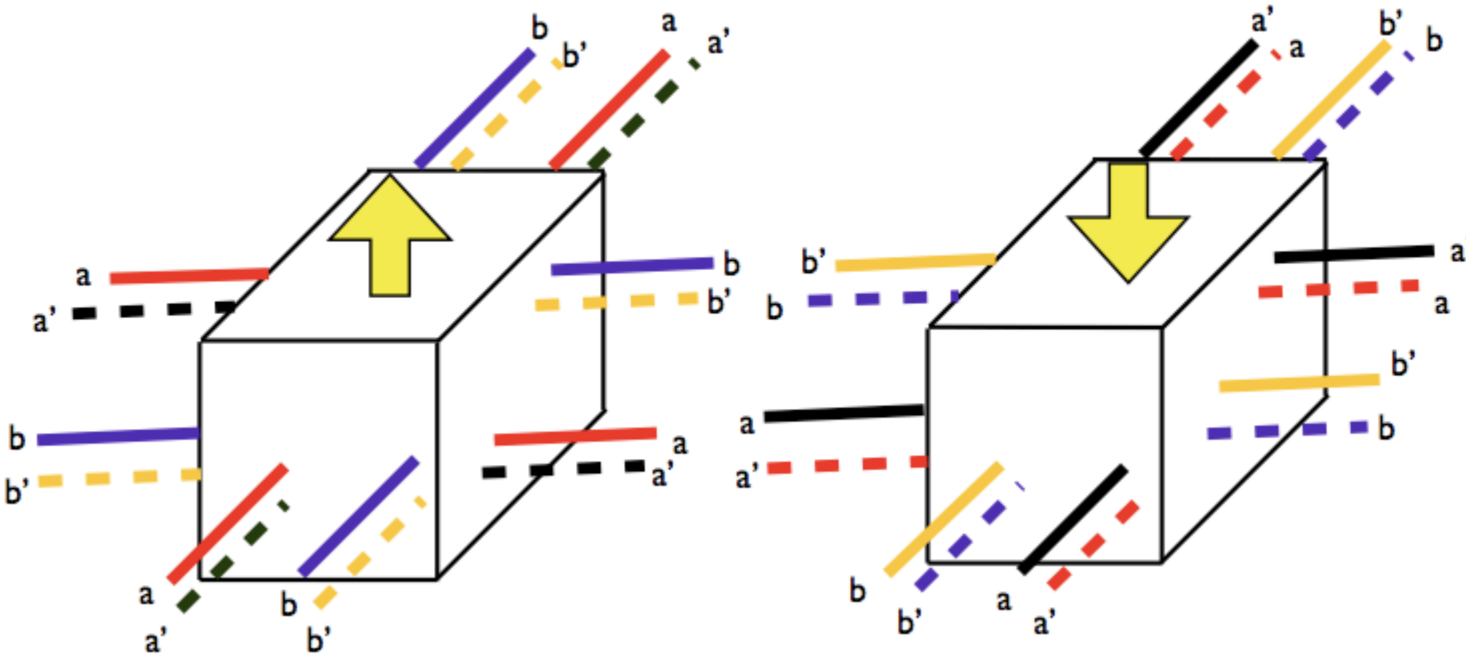
Four fold sequence symmetry

Double decker tiles



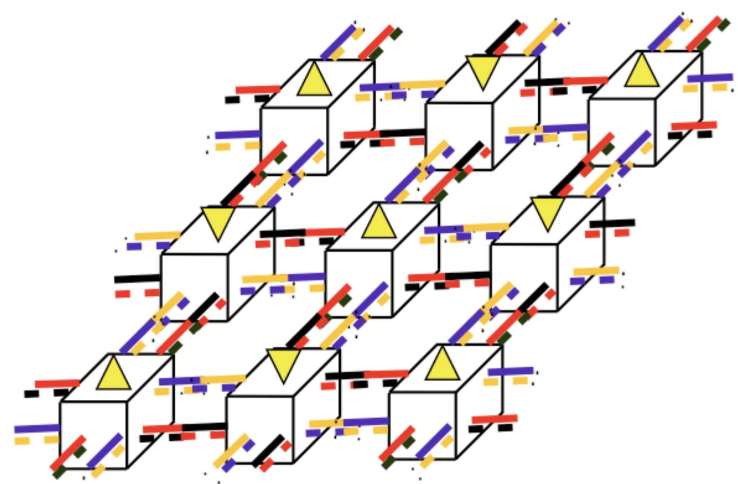
Four fold sequence symmetry

Double-decker tiles: Route to Assembly in 3D



2D Pad Programming of Double-Decker Tiles

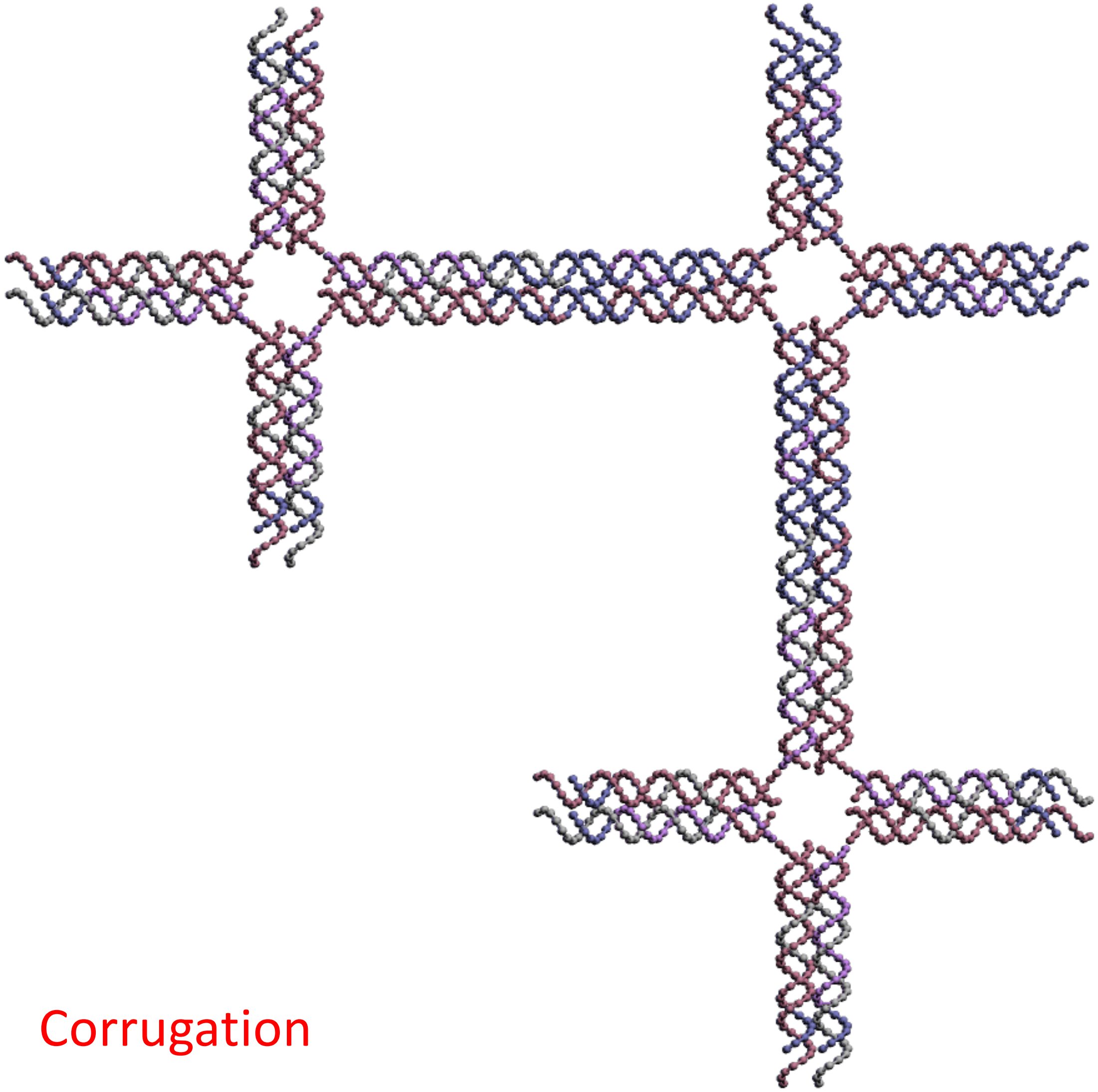
2D Corrugation



Corrugation cancels curvature of lattice
=> creates enormous lattices

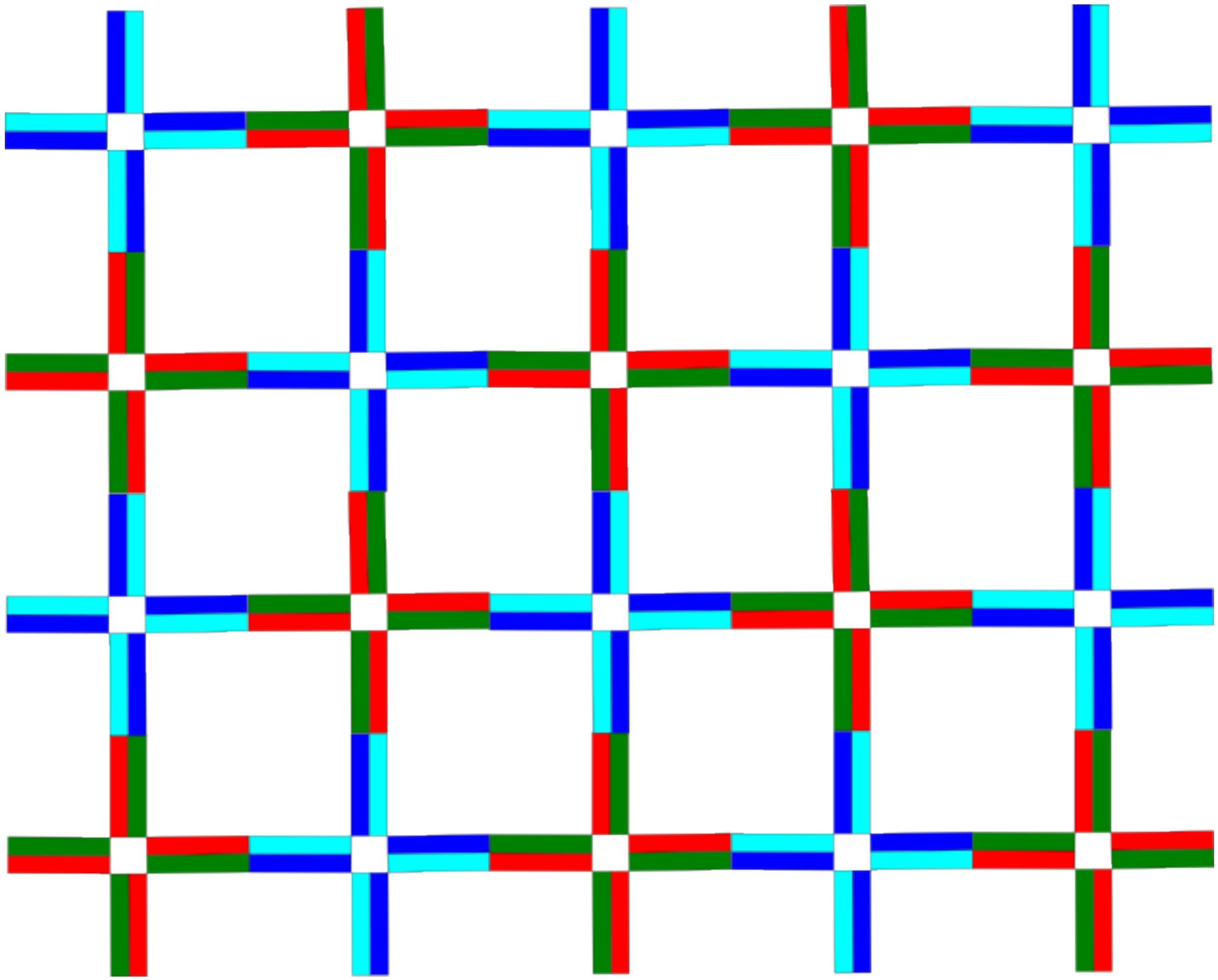
Urmi Majumder, Duke

2D lattice design



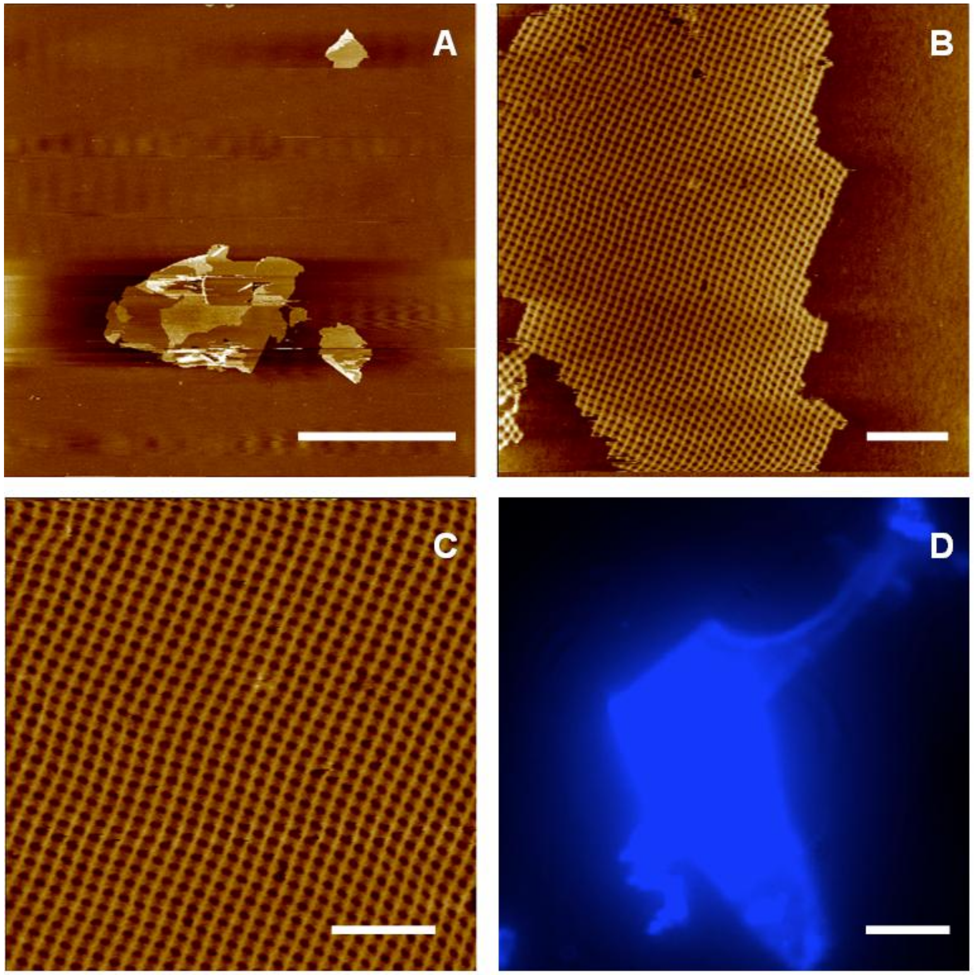
Corrugation

2D lattice design



Corrugation

Highly regular 2D lattices via double decker cross tiles

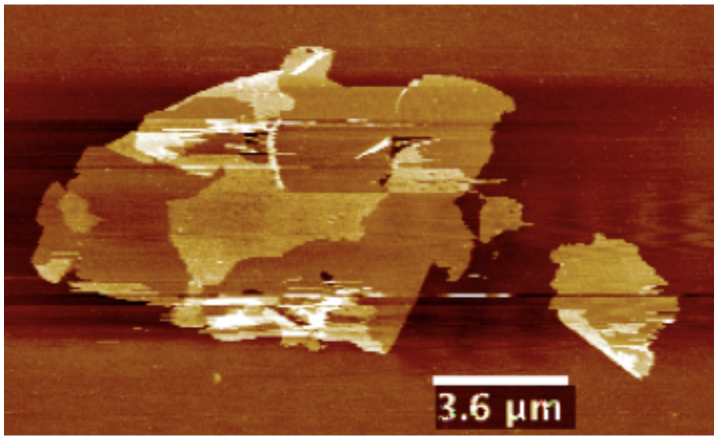


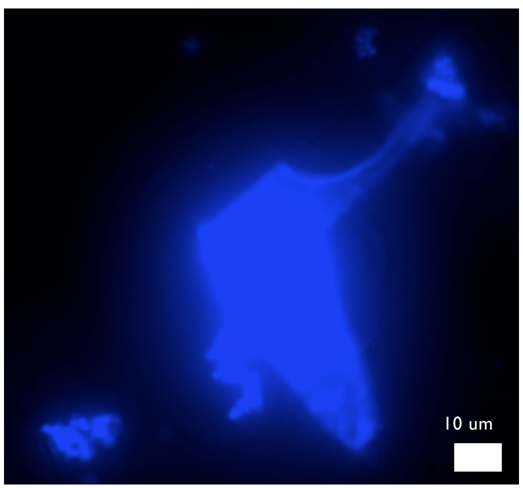
Atomic force microscopy images of the double-decker 2D lattice with corrugation. The scale bars are (A) 10 µm, (B) 300 nm (C) 200 nm. (D) Fluorescence microscopy image of the same sample. The scale bar is 20 µm. The lattices are tens of micrometers in size.

Urmi Majumder, Abhijit Rangnekar, Kurt V. Gothelf, John H. Reif and Thomas H. LaBean, **Design and Construction of Double-Decker Tile as a Route to Three-Dimensional Periodic Assembly of DNA**. J. Am. Chem. Soc., 2011, 133 (11), pp 3843–3845

Double-decker tiles: Route to Assembly in 3D

2D Lattices





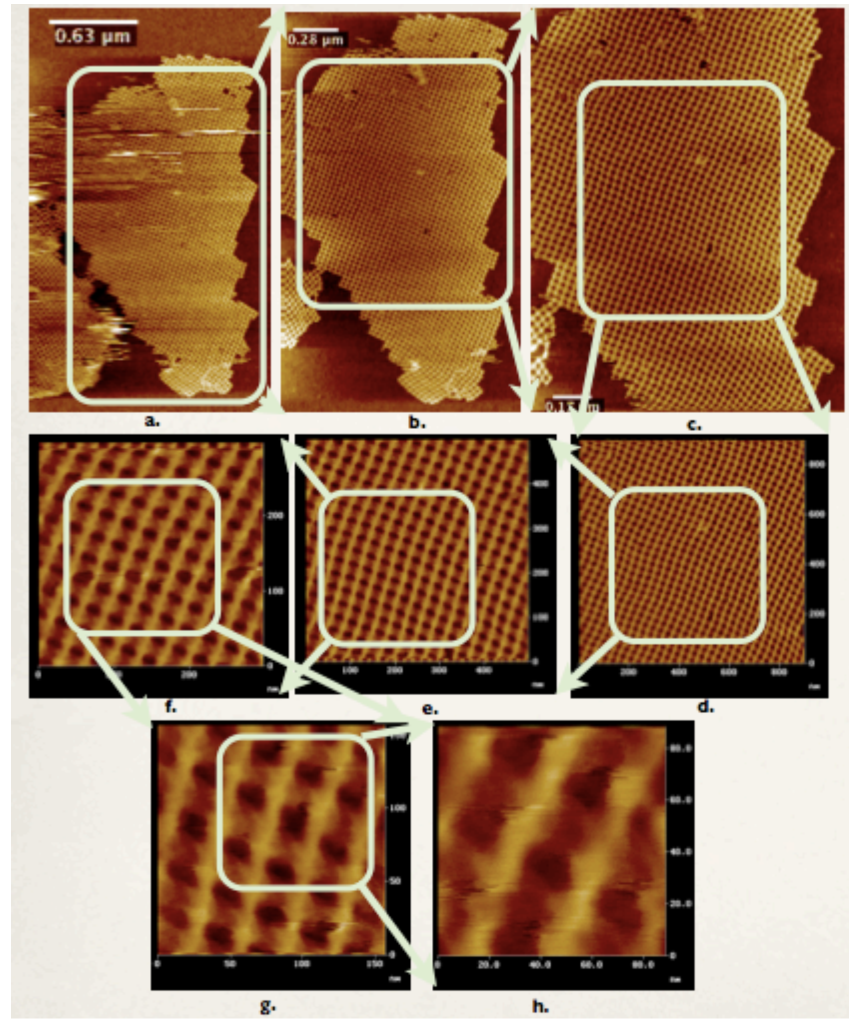
Urmi Majumder, Duke

2D Programmed Double-Decker Tiles

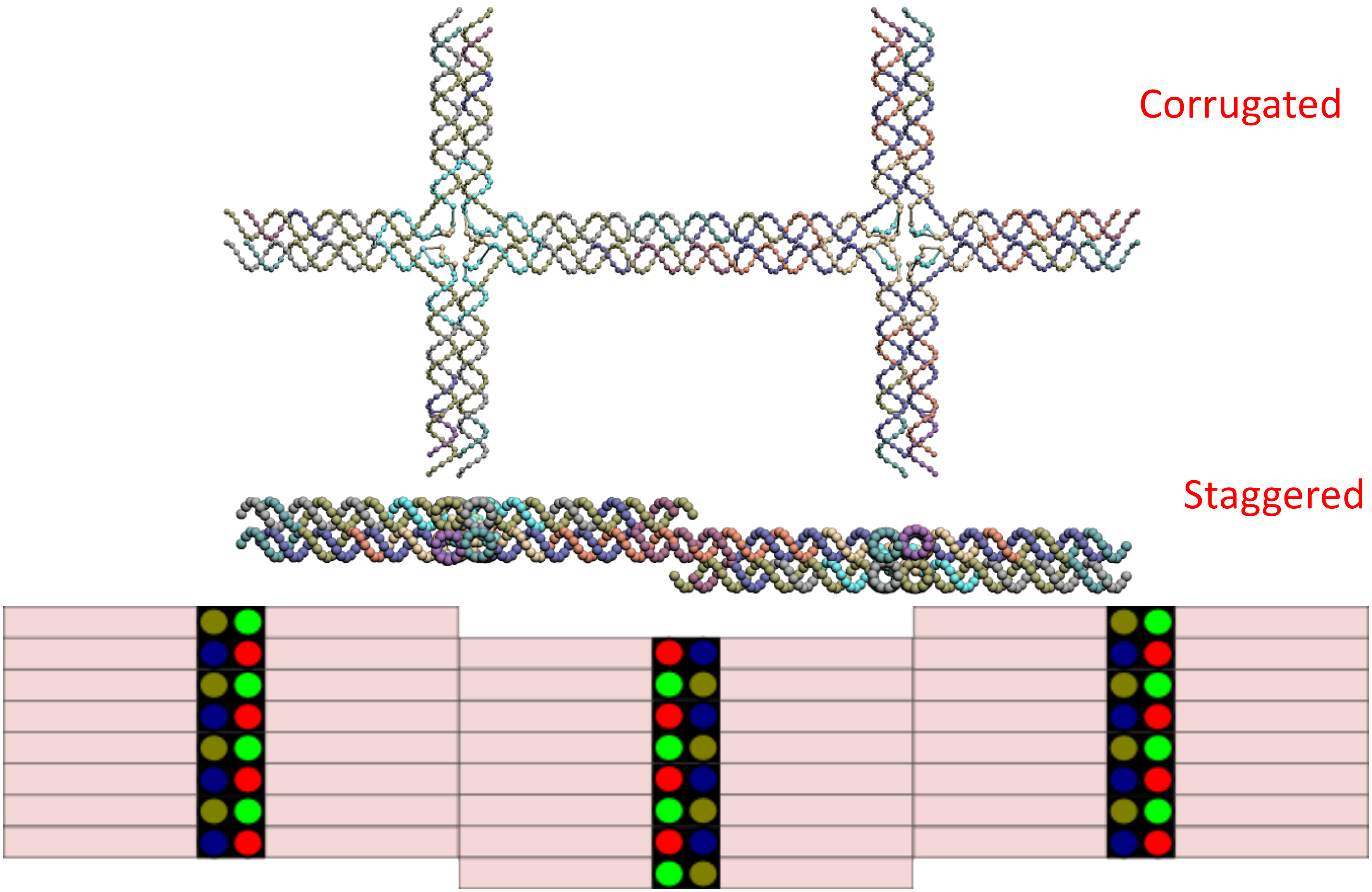
Yeilds:

Extremely Large, Regular 2D Grids

with Predominant Unidirectional Banding

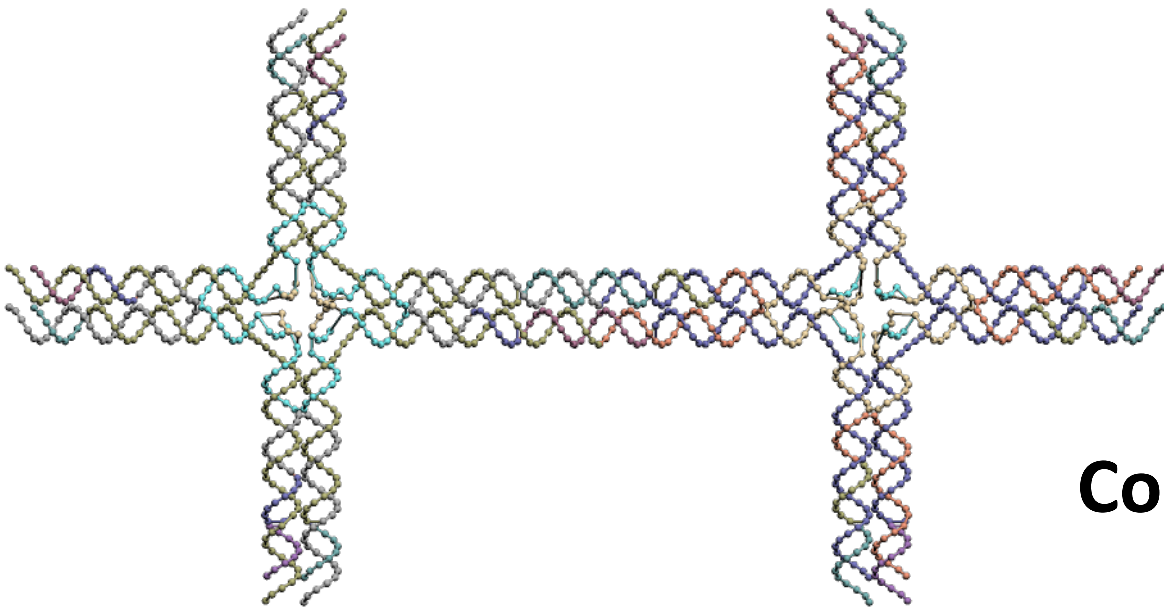


3D staggered lattices

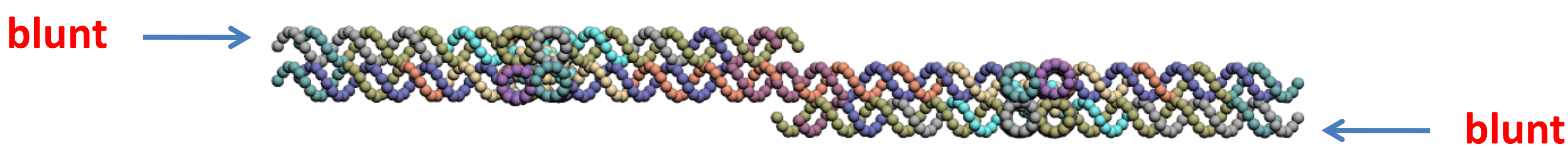


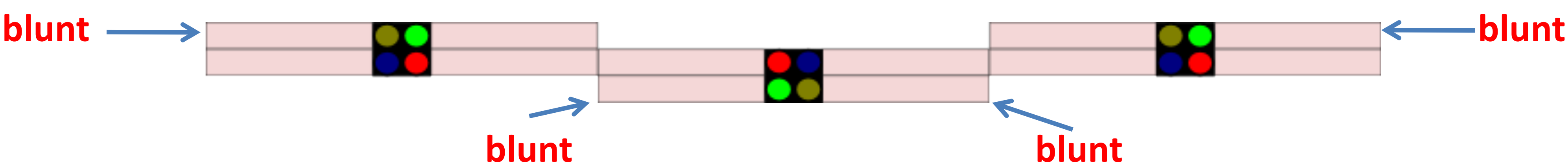
DUKE
COMPUTER
SCIENCE

2D staggered lattices



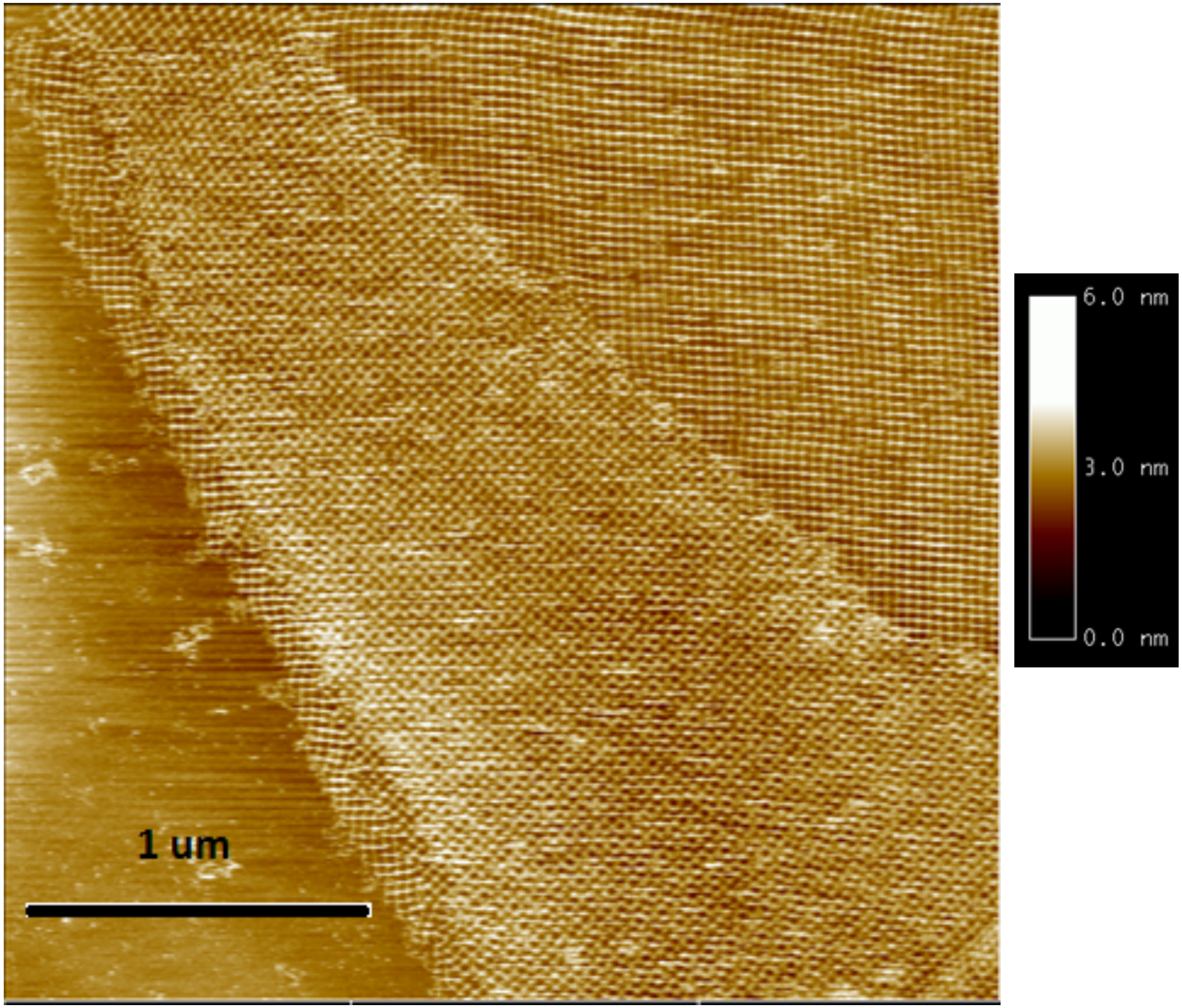
Corrugated



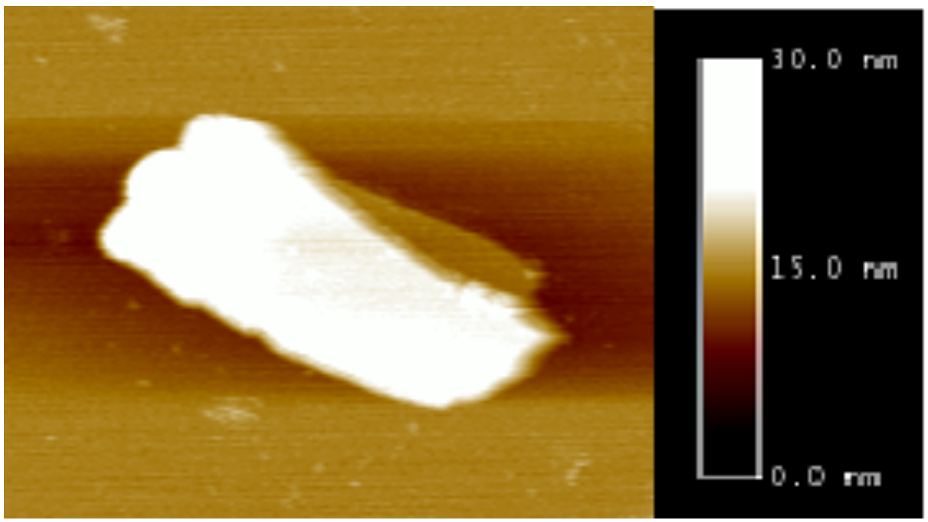


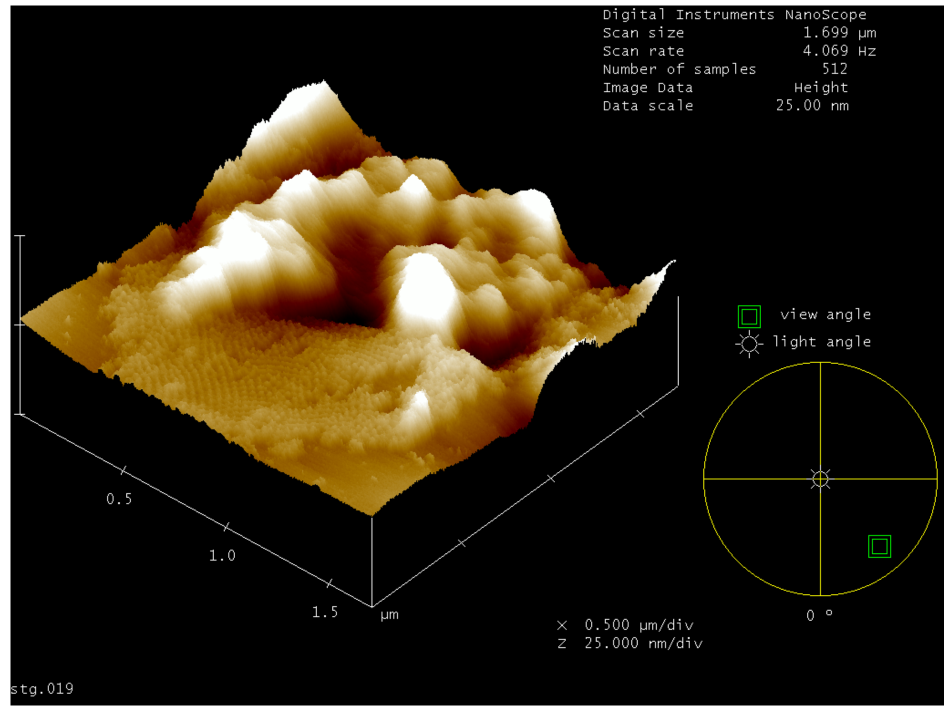
DUKE COMPUTER SCIENCE

2D staggered lattices AFM

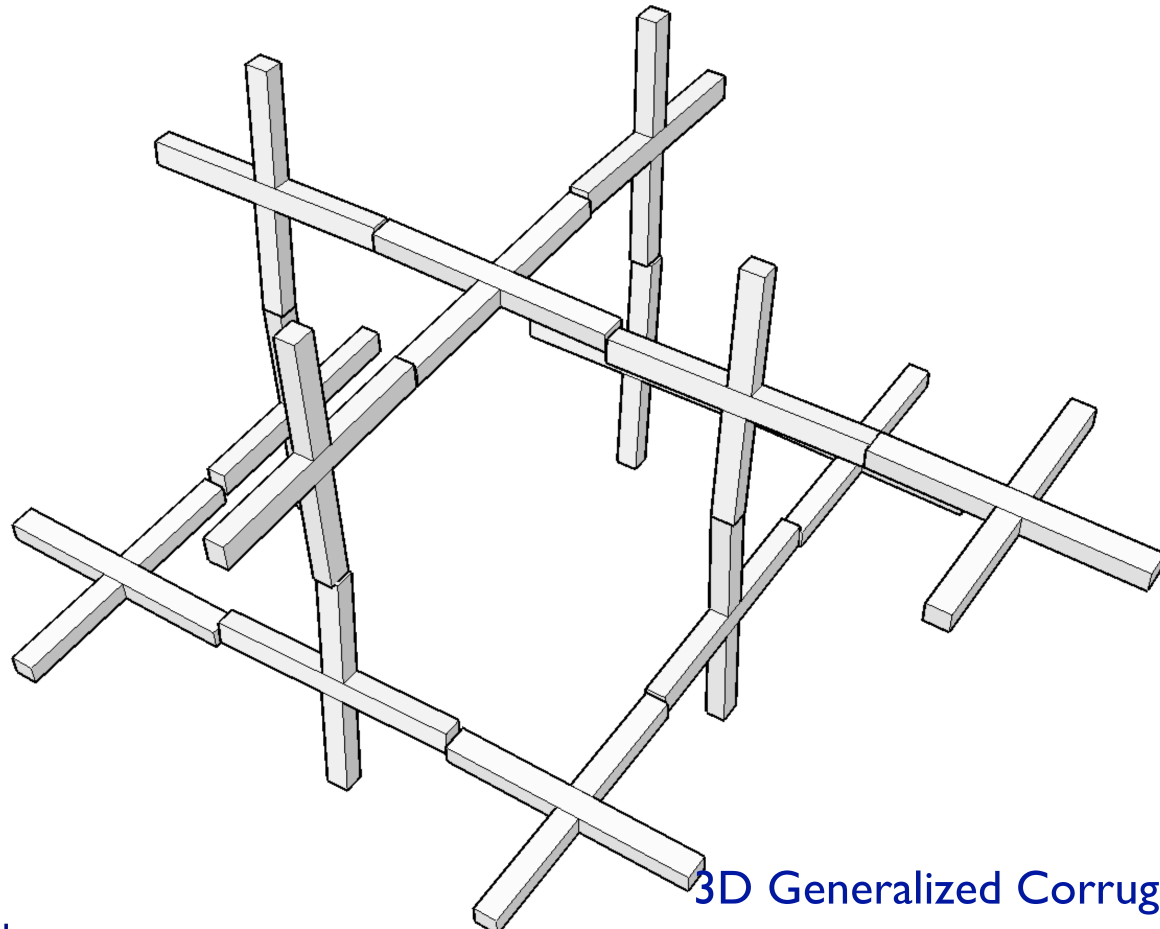


3D staggered lattices





Double-decker tiles: Route to Assembly in 3D



3D Programming of
Double-Decker
Tiles

3D Generalized Corrugation cancels curvature of lattice in all 3 dimensions !

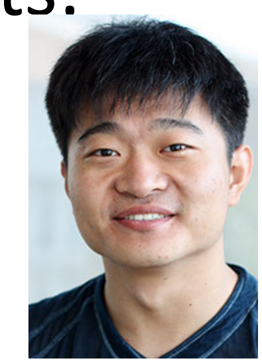
Urmi Majumder, Duke

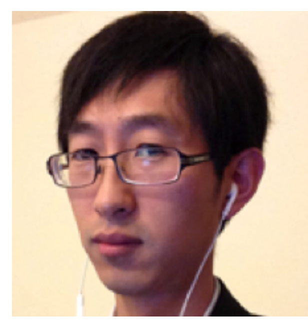
Reif Lab

- John Reif
  www.cs.duke.edu/~reif/

- PhD Candidates:
  - Sudhanshu Garg (~sgarg)
  - Hieu Bui (~hbui)
  - Reem Mokhtar (~reem)
  - Tianqi Song (~stq)

- 2nd Year Graduate Students:
  - Tong Niu
  - Guangjian (Jeff)





What we do

- John: interested in all things
- Hieu: building a DNA-origami-based circuit
- Sudhanshu: exponentially auto-catalytic system
- Tianqi: analog computer using DNA
- Reem:
  - Designing a self-reconfigurable DNA origami nanorobot
  - Building a software that can simulate DNA hybridization reactions using Graph Grammars, along with methods from scientific computing (and machine learning)

Reif Papers on the Web

Reif Papers on DNA nanoscience on the Web:

- http://www.cs.duke.edu/~reif/vita/papers.html

- **Survey on DNA Computation:**

Hieu Bui, Harish Chandran, Sudhanshu Garg, Nikhil Gopalkrishnan, Reem Mokhtar, Tianqi Song and John H Reif, DNA Computing, Chapter in Section 3: Architecture and Organization, Volume I: Computer Science and Software Engineering (Edited by Teofilo F. Gonzalez), The Computer Science Handbook, Third Edition (Editor-In-Chief Allen B. Tucker), Taylor & Francis Group, (2014).

Other Reif Papers on the Web:

- http://www.cs.duke.edu/~reif/vita/papers.html

Talk Locations on Reif's Website

- www.cs.duke.edu/~reif/paper/DNA-NanoscienceTalks

DNA Computing: Theory, Experiments & Software:

http://www.cs.duke.edu/~reif/paper/DNA-NanoscienceTalks/DNA-Computing/DNA-Computing.pdf

Self-Assembled DNA Nanostructures:

www.cs.duke.edu/~reif/paper/DNA-NanoscienceTalks/DNA-Nanostructures/DNA-Nanostructures.pdf

DNA-Based Programmable Autonomous Molecular Robotic Devices:

www.cs.duke.edu/~reif/paper/DNA-NanoscienceTalks/DNA-ProgAutoMolRobotics/DNA-ProgAutoMolRobotics.pdf