

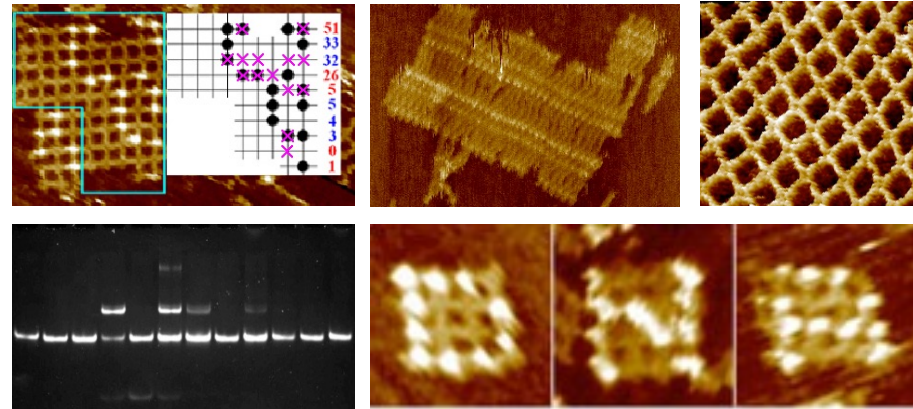
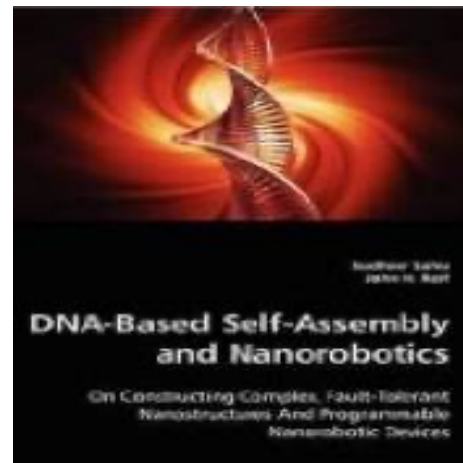
# DNA Tiles & Lattices



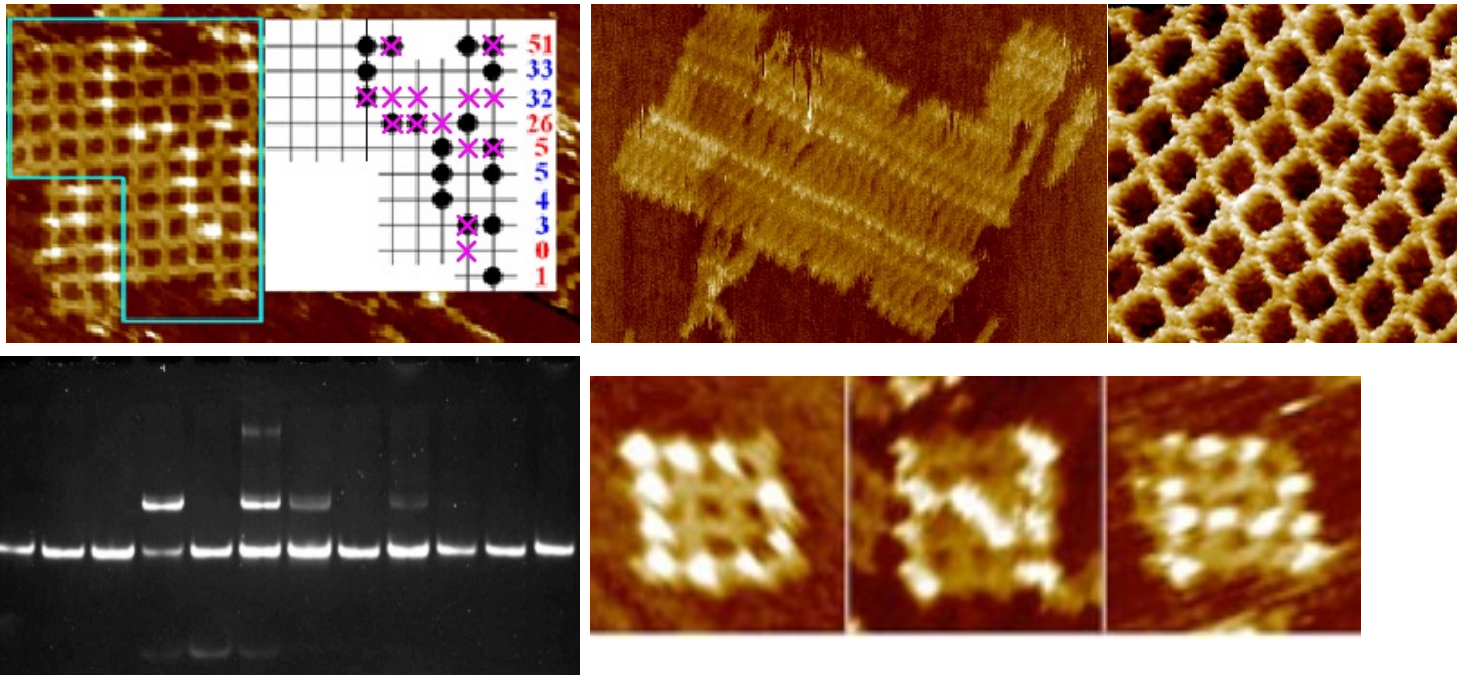
**John Reif**

**Dept CS**

**Duke University**



# DNA Tiles & Lattices



# Organization

- **Overview of DNA & DNA Self-Assembly**
- **DNA Tiles**
- **2D DNA Lattices**
- **Programmable Molecular Patterning via DNA Lattices**
- **Transformations of DNA Lattices**
- **3D DNA 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 Britannica on the head of a pin?

*“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 information is 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

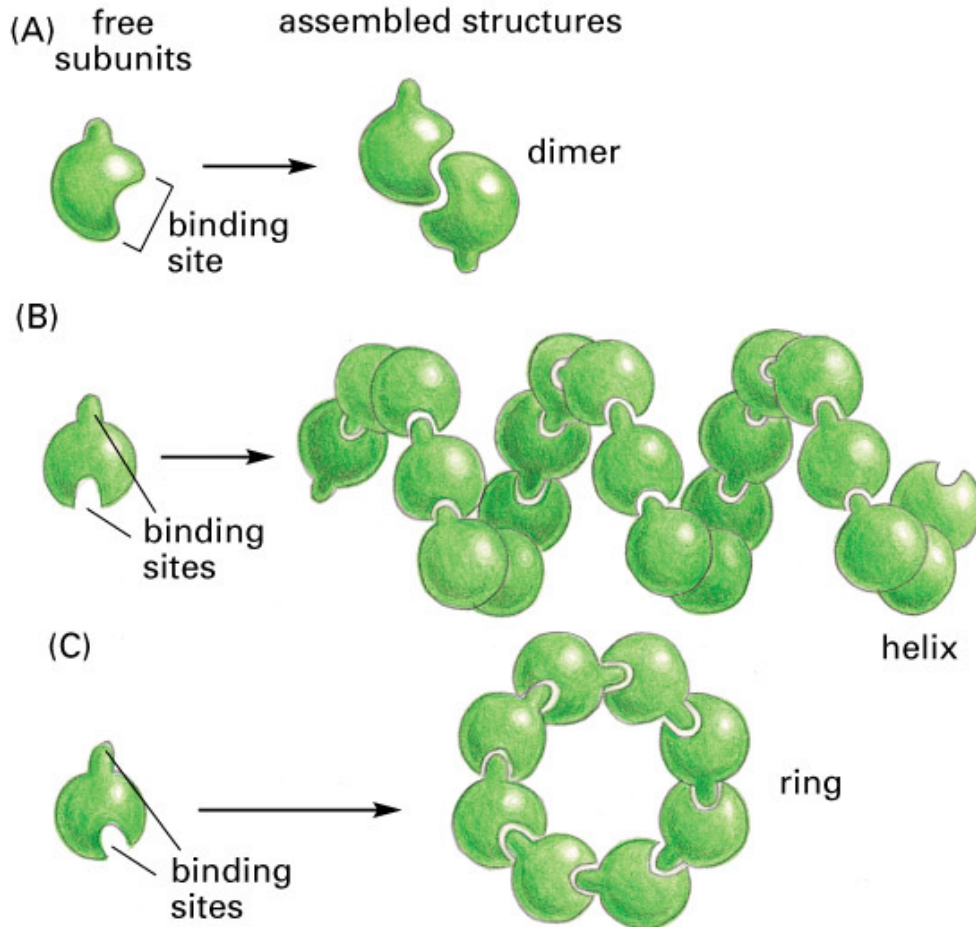
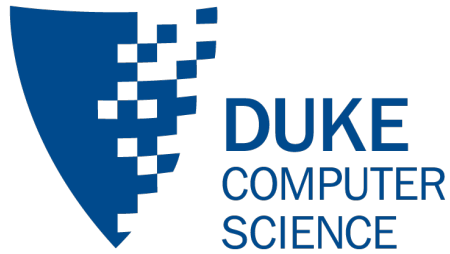


Figure 3-25. Molecular Biology of the Cell, 4th Edition.

From microscopic living cells to gigantic galaxies



# Why study self-assembly?

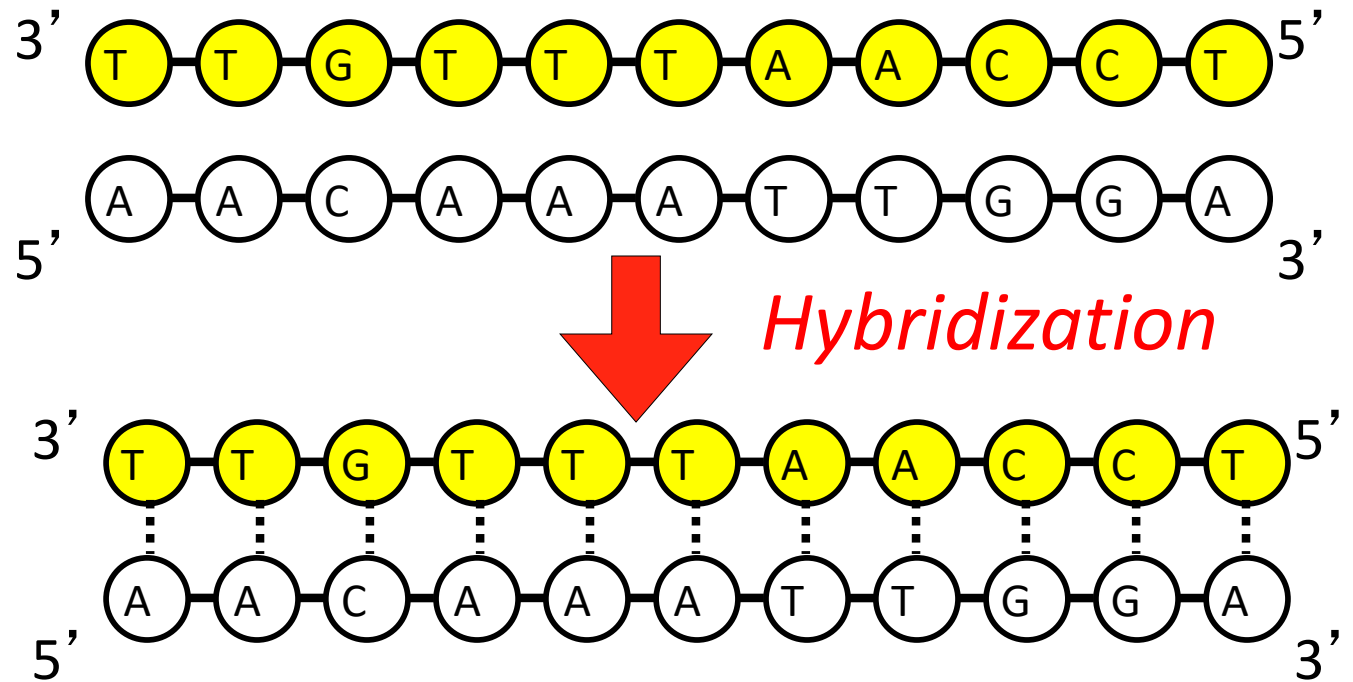
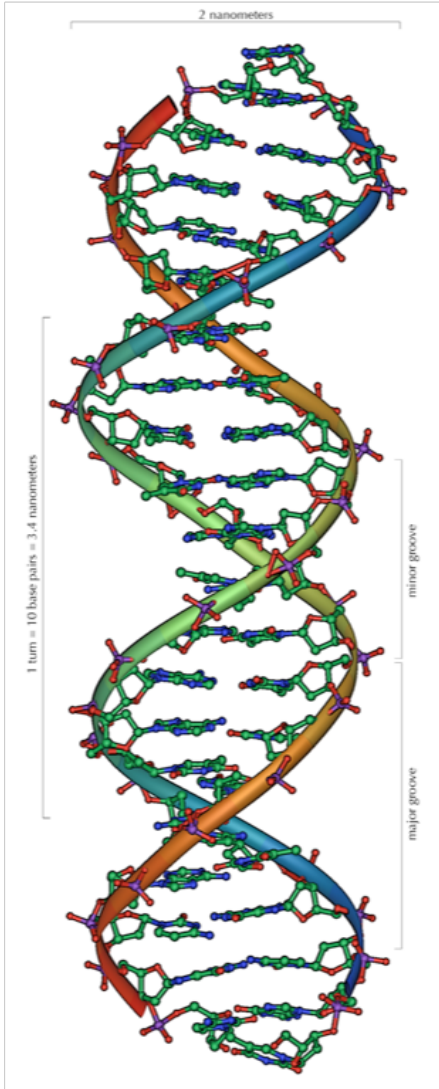
- Brings about order from disorder.
  - Interesting at a philosophical level
- Plays a fundamental role in biology; in formation of living cell.
  - Attempt to understand life must include a thorough study of self-assembly.
- One of the few known methods for the construction and manipulation of nanostructures.
- 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

# Why use DNA for Self-Assembly of Nanostructures?

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)



# Key to DNA Self-Assembly



# What is DNA Self-Assembly?

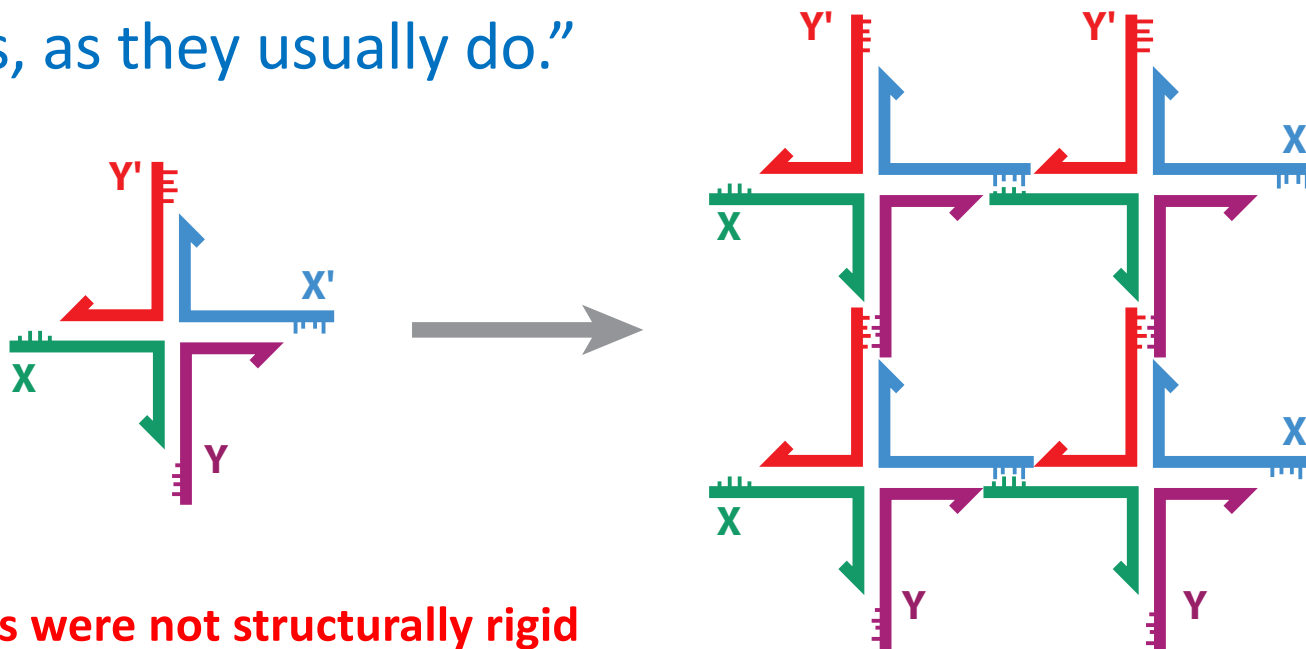
Programming DNA strands to organize themselves into nanoscale shapes, patterns, and devices through Watson-Crick base-pairing.

# First Work in DNA Nanotechnology

## Seeman 1982:

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

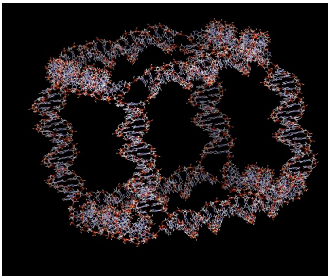
- “It is possible to generate sequences of oligomeric nucleic acids which will preferentially associate to form migrationally immobile junctions, rather than linear duplexes, as they usually do.”



**Note: These Tiles were not structurally rigid**

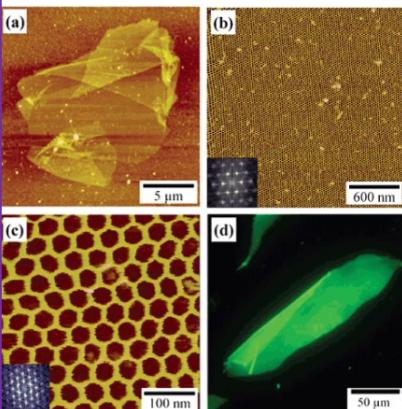
# Some results of DNA self-assembly

**NYU 1991**



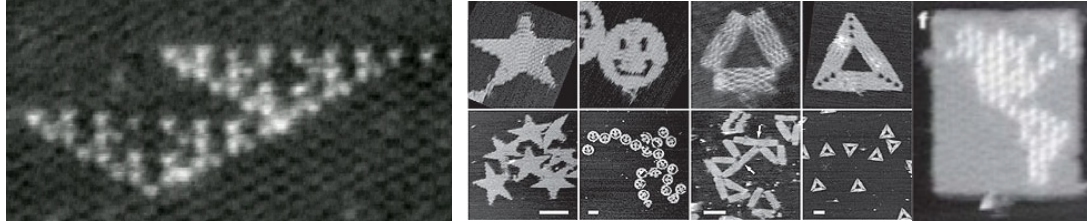
The Electrophoretic Properties Of A DNA Cube And Its Substructure Catenanes : Mao And Seeman

**Purdue 2005**



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

**2004** **Caltech** **2006**

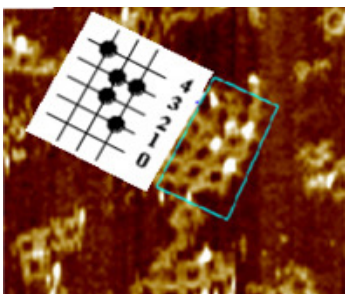


Algorithmic Self-assembly Of DNA Sierpinski Triangles: Rothmund, Papadakis, Winfree

Folding DNA To Create Nanoscale Shapes And Patterns: Rothmund

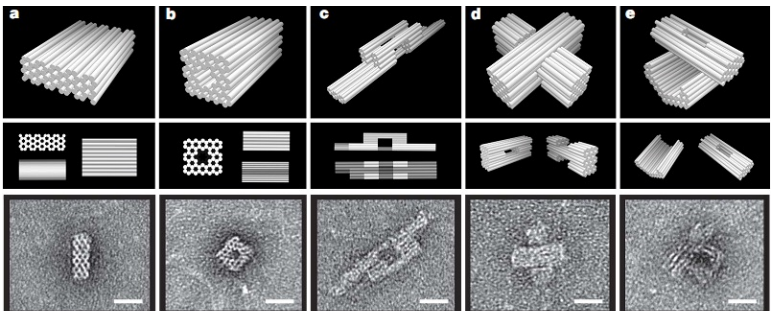
**Unpublished Data:** Majumder, Reif

**Duke**



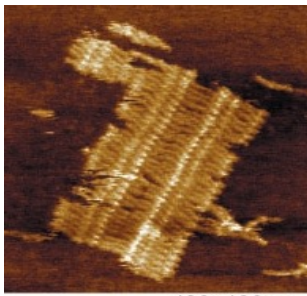
**2009**

**Harvard**



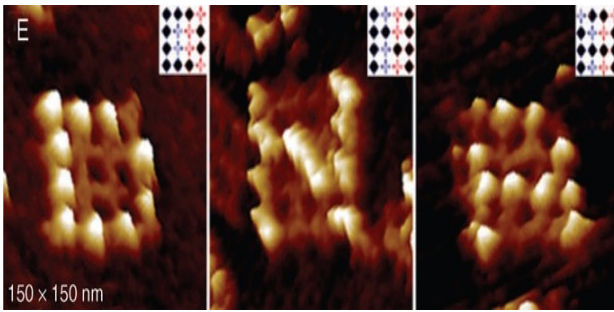
Self-assembly Of DNA Into Nanoscale Three-dimensional Shapes: Douglas, Dietz, Liedl, Hogberg, Graf, Shih

**2003**



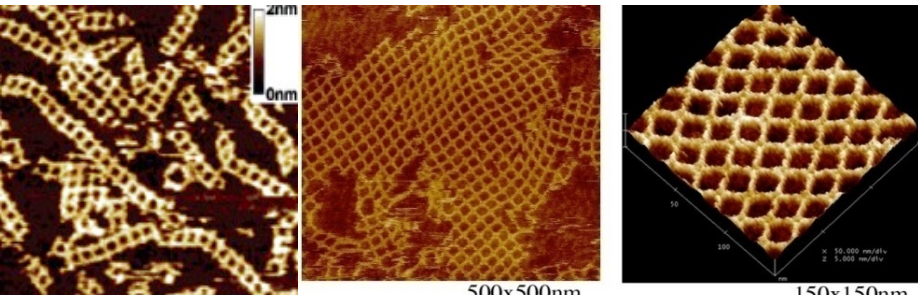
Directed Nucleation Assembly Of DNA Tile Complexes For Barcode-patterned Lattices: Yan, Labean, Feng, Reif

**2006**



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

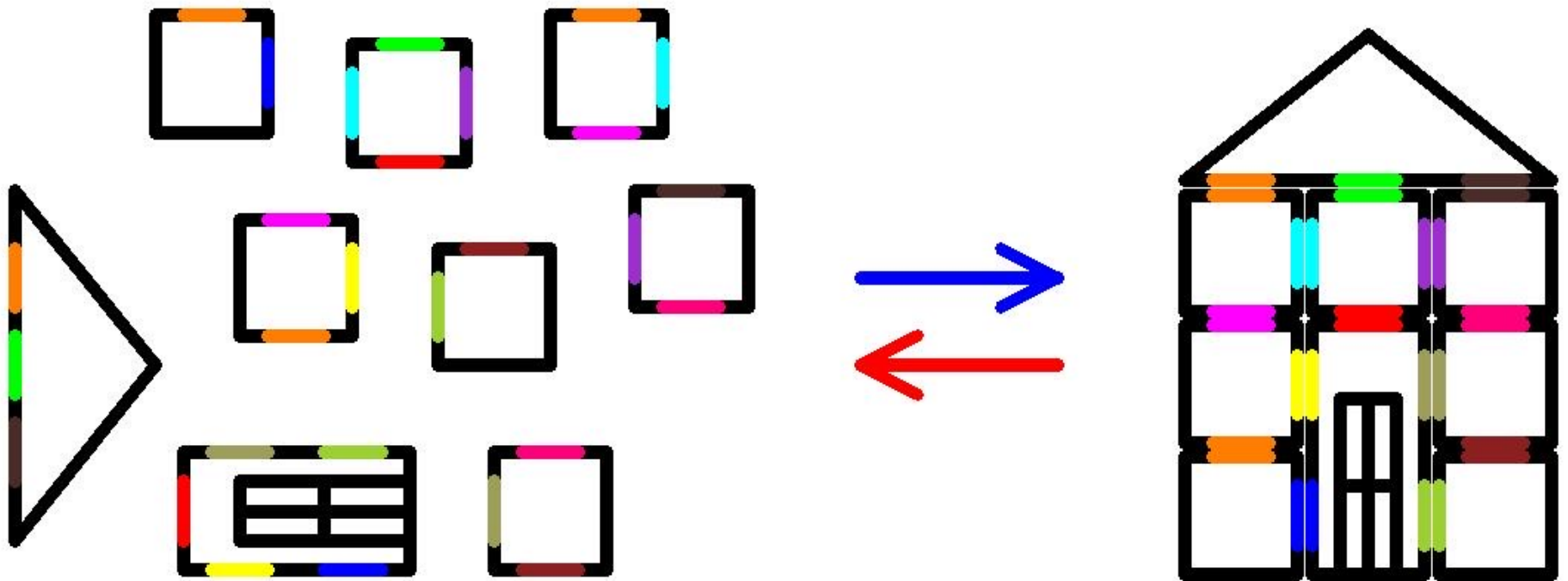
**2003**



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

# **Introduction to Tile Self- Assembly**

# Construction with “*Smart*” Building Blocks



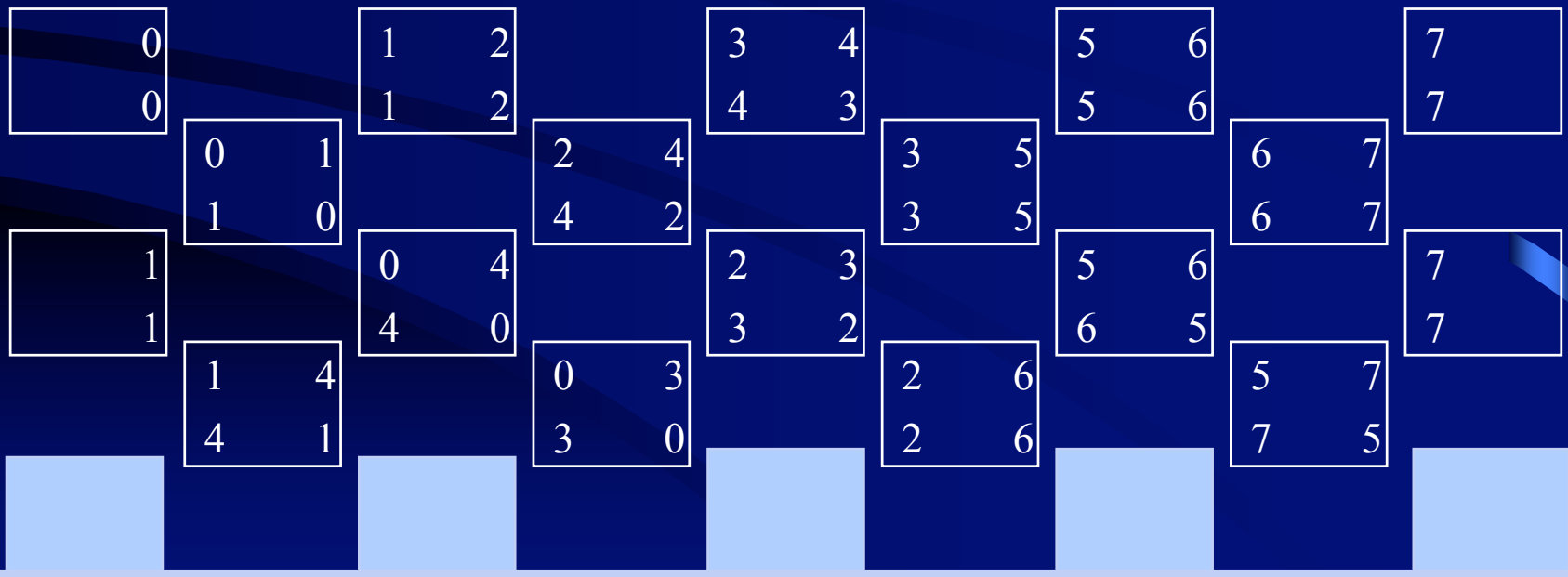
A tiling assembly using ‘Smart Bricks’ with affinity between colored pads.

# Computation with “Smart Bricks”

## Sorting

A	B
A	B

A	B
B	A



A tiling assembly using 'Smart Bricks' to Sort 8 Keys.

# Scales of Tiling Assemblies:

## – Meso-Scale Tiling Assemblies:

- have tiles of size a few millimeters up to a few centimeters.

## – Molecular-Scale Tiling Assemblies:

- have tiles of size up to a few hundred Angstroms.

# Tile Pad Binding Mechanisms

Used for the preferential matching of tile sides

- **Molecular Affinity (Seeman, NYU): Molecular-Scale**
  - hydrogen bonding of complementary DNA or RNA bases
- **Magnetic Attraction (Univ Wisconsin): Meso-Scale**
  - pads with magnetic orientations constructed by curing polymer/ferrite composites in the presence of strong magnet fields, or
- **pads with patterned strips of magnetic orientations [Reif].**
- **Shape Complementarity: [Whitesides, Harvard U]: Meso-Scale**
  - using the conformational shape affinity of the tile sides to hold them together.
- **Capillary Force [Whitesides, Harvard U], [Rothmund, 1999]: Meso-Scale**
  - using hydrophobic/hydrophilic (capillary) effects at surface boundaries that generate lateral forces.

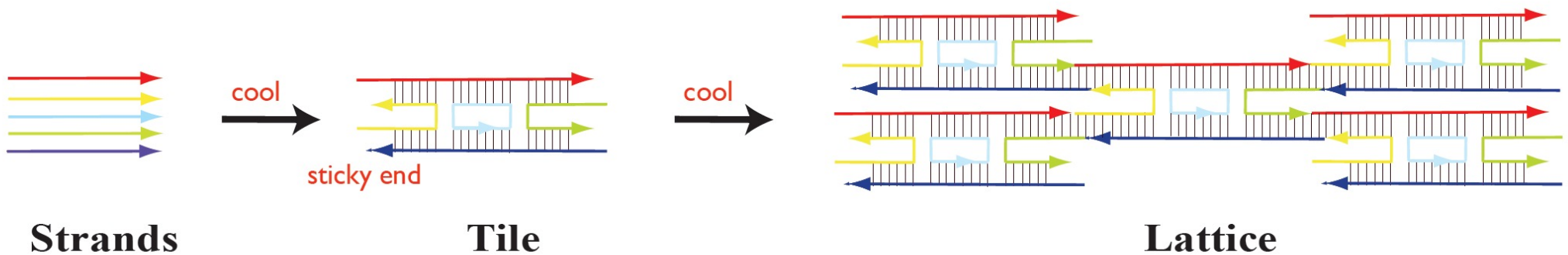


# Design & Experimental Demonstration of DNA Tiles and Lattices

# 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)

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

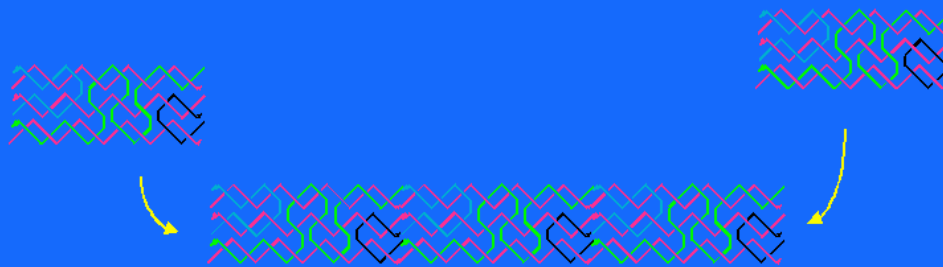


# Programming Self-assembly of DNA Tilings

## = Design of Pads of DNA Tiles.

- **Pads:** complementary base sequences determining neighbor relations of tiles in final assembly
- **Large-Scale Computational Tilings** formed during assembly:
  - encode valid mappings of input to output.
  - local tile association rules insure only valid computational lattices form regardless of temporal ordering of binding events.

### Global and Local Parallelism by Linear Assembly

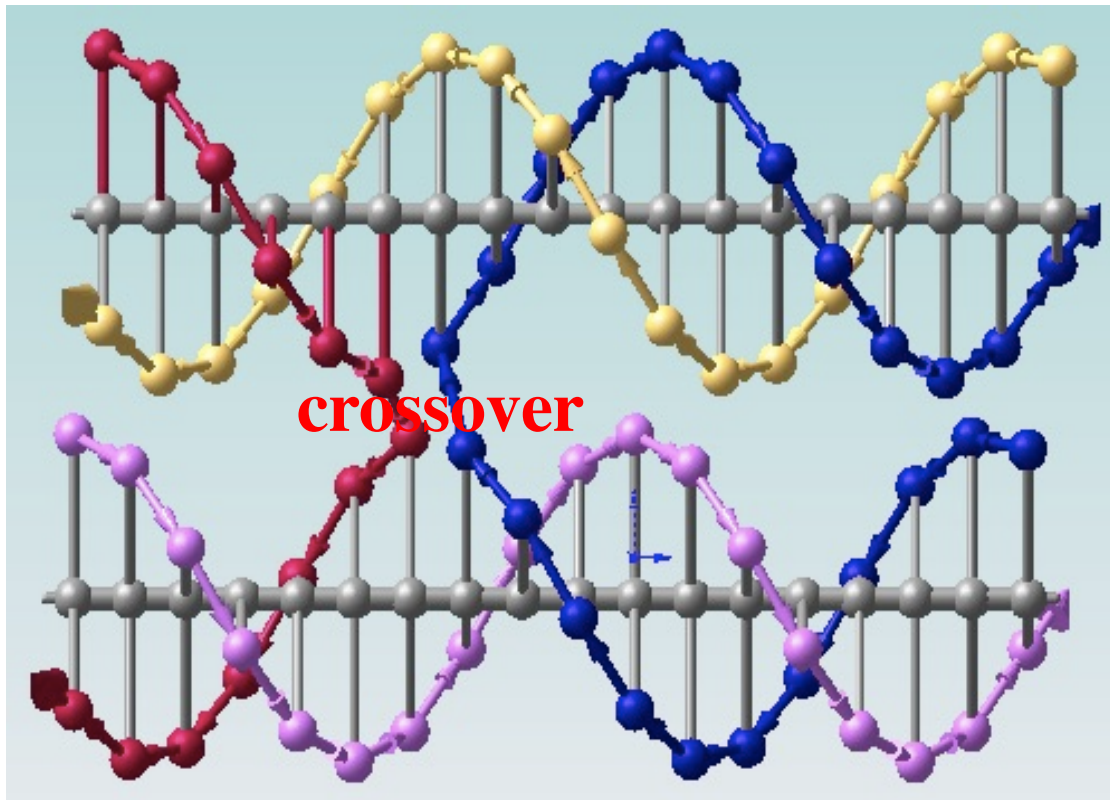


Simultaneous, parallel assembly of input and output strands.

- **Key Advantage of DNA Self-Assembly for DNA Computing:**
  - Use a sequence of only **4 laboratory procedures**:
    - mixing the input oligonucleotides to form the DNA tiles,
    - allowing the tiles to self-assemble into superstructures,
    - ligating strands that have been co-localized, and
    - performing a single separation to identify the correct output.

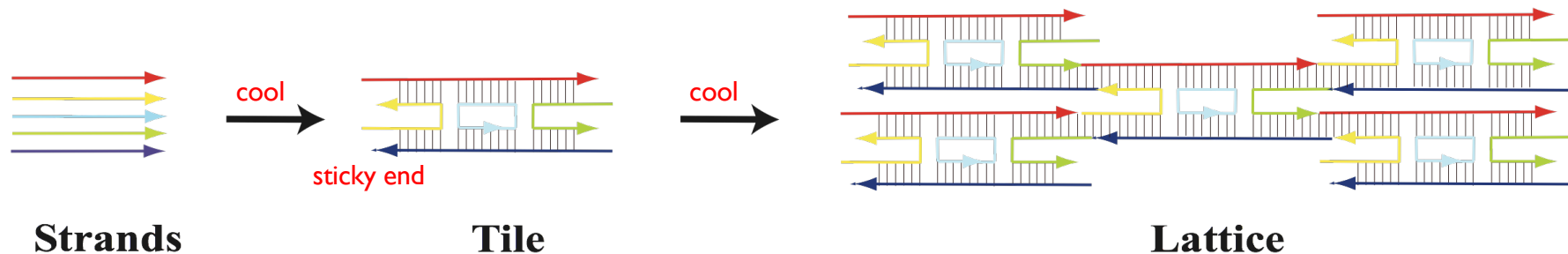
# DNA tiles

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



- **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.

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



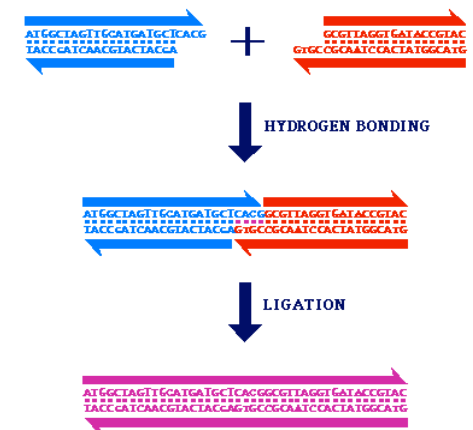
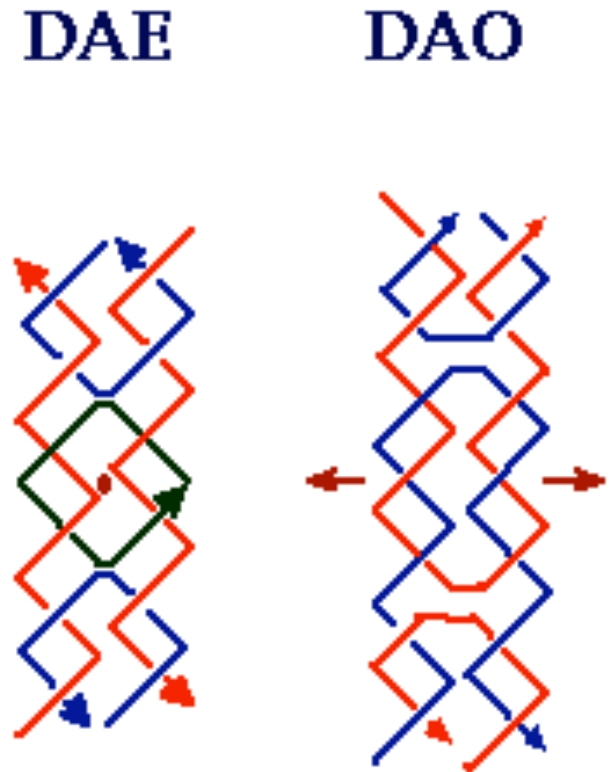
# DNA Tiles:

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

## Double-crossover (DX) Tiles

### [Winfree, Seeman]:

- consist of two double-helices fused by crossover
  - DAE contains an Even number of helical half-turns between crossover points.
  - DAO contains an Odd number.
- **Anti-parallel crossovers:**
    - cause a reversal in direction of strand propagation through the tile following exchange of strand to a new helix.
    - DAO and DAE are double-crossover DX tiles with two anti-parallel crossovers.
  - **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.

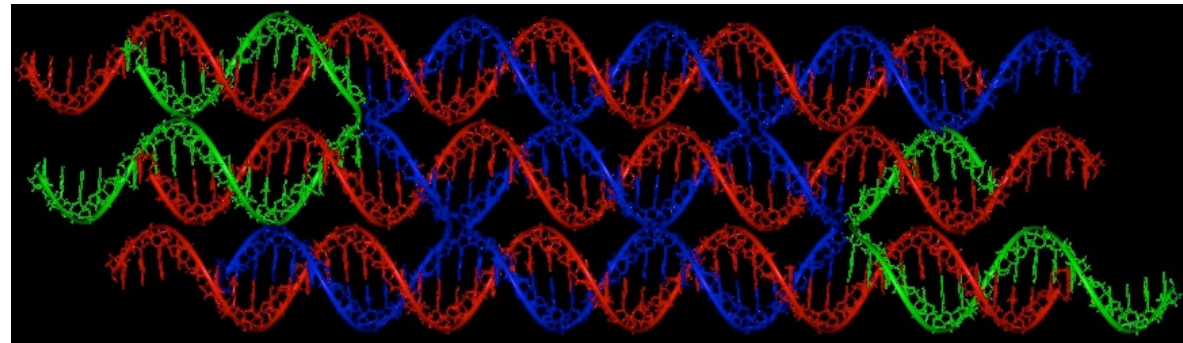
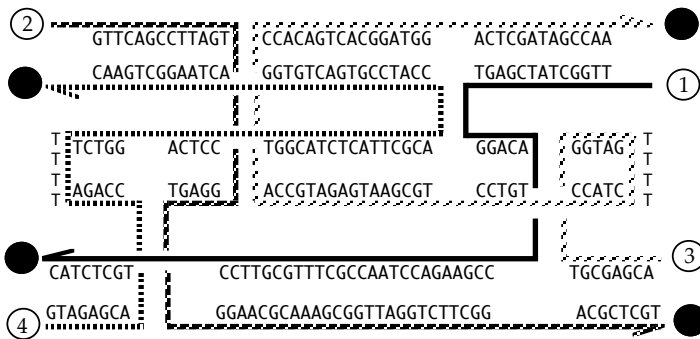
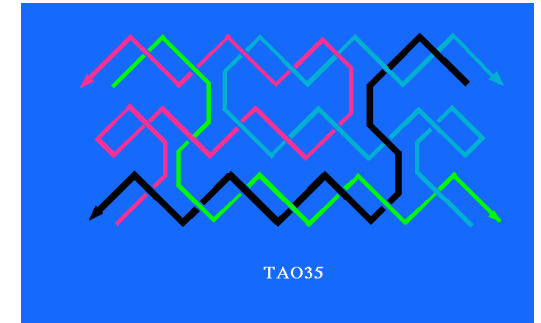
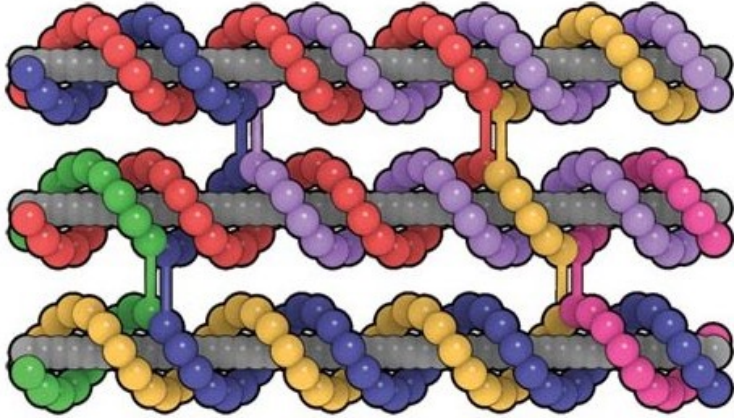


# Triple Crossover (TX) Tiles

- **Is extension of the DX tile**
- **TX has 3 DNA helices made of 4 strands**



# TX Tiles

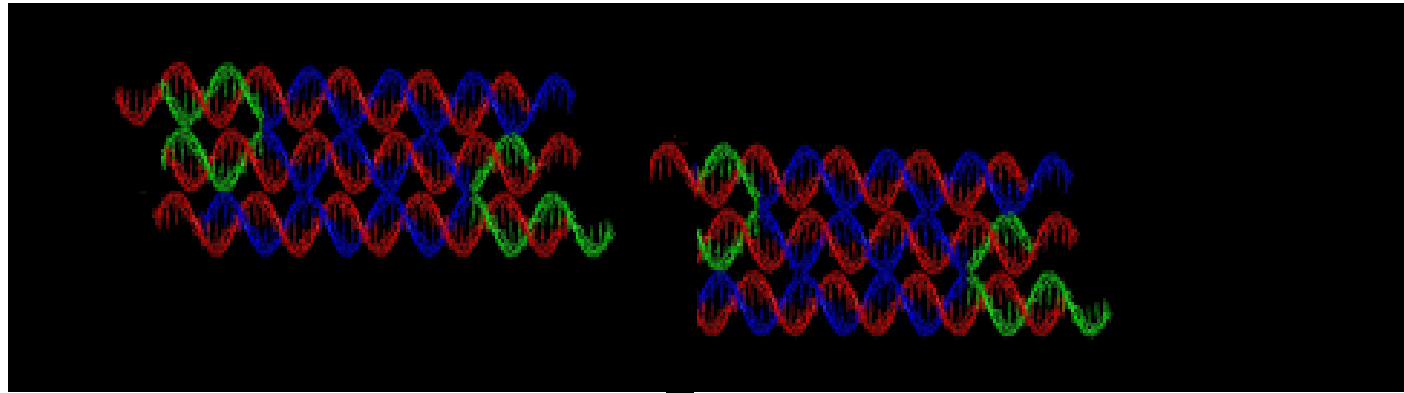


## Triple-crossover (TX) Tiles [LaBean, Reif et al, J. Am. Chem. Soc., 2000]:



- 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.

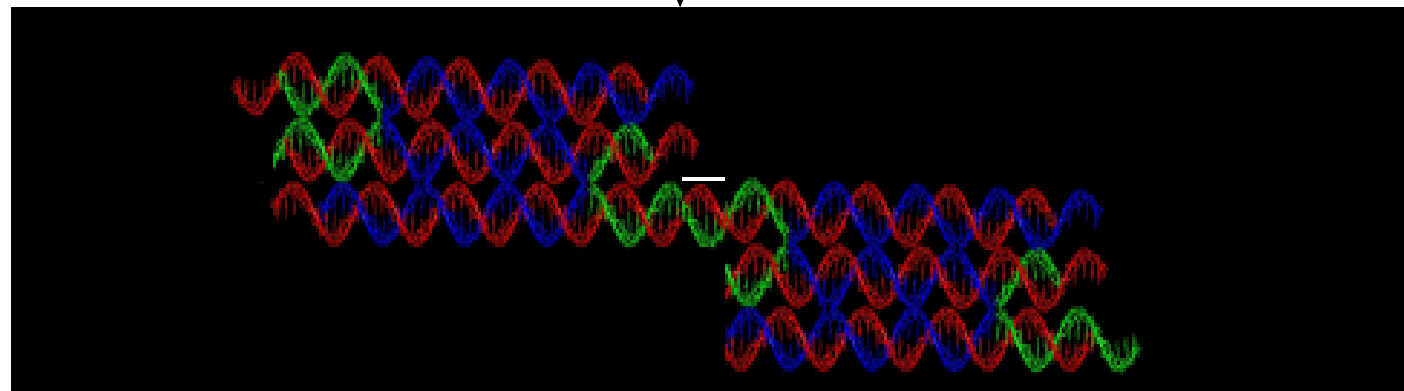
**Unique Sticky Ends on DNA tiles.** Input layers can be assembled via unique sticky-ends at each tile joint thereby requiring one tile type for each position in the input layer.



**Tiling self-assembly:**

proceeds by the selective annealing of tiles to compose together to

of the pads of distinct tiles, which allows form a controlled tiling lattice.





# **DNA Tile Design Software**

# DNA Tile Design Software

- **Why do we need DNA sequence optimization?**
- ***DNA-Design* Software by Winfree (Random Search Algorithm)**
- **Improved with Evolutionary algorithm**
- =
- **Graphical User Interface**

# Software Interface

The screenshot displays the 'DNA Design' software interface. At the top, a menu bar includes 'File', 'Edit', and 'Tile'. The main workspace shows four DNA strand configurations, each with 3' and 5' ends indicated by arrows. The strands are color-coded: red, green, magenta, and cyan. Each configuration consists of two strands with various 'N' and 'NN' labels representing nucleotides and their pairings. The bottom control panel contains several buttons: 'DEFINE CROSSOVERS', 'EDIT BASES', 'SET 5' END', 'SET 3' END' (highlighted in blue), 'TOGGLE PAIRING STATES', 'SET EQ CONSTRAINTS', and 'SHOW EQ CONSTRAINT'.

# Setting 5' end

The screenshot displays the DNA Design software interface. The window title is "DNA Design". The menu bar includes "File", "Edit", and "Tile". The main workspace shows four DNA strand configurations, each with 3' and 5' ends indicated by arrows. The strands are composed of nucleotides represented by "N" characters, with some nucleotides highlighted in different colors (red, blue, green, magenta, cyan, yellow) to represent different base types. The configurations are arranged vertically, showing different ways to set the 5' end of the DNA strands.

At the bottom of the interface is a control panel with the following buttons:

- DEFINE CROSSOVERS
- EDIT BASES
- SET 5' END** (highlighted in blue)
- SET 3' END
- TOGGLE PAIRING STATES
- SET EQ CONSTRAINTS
- SHOW EQ CONSTRAINT

# Setting 3' end

The screenshot displays the 'DNA Design' software interface with a menu bar (File, Edit, Tile) and a toolbar at the bottom. The main workspace shows four DNA sequence diagrams, each with a 3' end arrow on the left and a 5' end arrow on the right. The sequences are represented by 'N' characters, with some 'NN' pairs. The diagrams illustrate different 3' end settings:

- Diagram 1 (Blue):** Shows a sequence with blue 'NN' pairs and red 'N' characters. The 3' end is marked with a blue arrow.
- Diagram 2 (Green):** Shows a sequence with green 'NN' pairs and green 'N' characters. The 3' end is marked with a green arrow.
- Diagram 3 (Magenta):** Shows a sequence with magenta 'NN' pairs and magenta 'N' characters. The 3' end is marked with a magenta arrow.
- Diagram 4 (Yellow):** Shows a sequence with yellow 'NN' pairs and yellow 'N' characters. The 3' end is marked with a yellow arrow.

The toolbar at the bottom contains the following buttons:

- DEFINE CROSSOVERS
- EDIT BASES
- SET 5' END
- SET 3' END** (highlighted in blue)
- TOGGLE PAIRING STATES
- SET EQ CONSTRAINTS
- SHOW EQ CONSTRAINT

# Defining Junctions

The screenshot displays the DNA Design software interface. The main window shows a DNA sequence with four horizontal tracks. The top track is the reference sequence, with 3' and 5' ends indicated. The second track shows junctions defined by vertical lines of various colors (blue, green, red, black) connecting the reference sequence to the second track. The third track shows junctions defined by vertical lines of various colors (magenta, blue, red, black) connecting the reference sequence to the third track. The bottom track shows the reference sequence with small colored dots (blue, orange, cyan, yellow) indicating specific positions. The software has a menu bar with 'File', 'Edit', and 'Tile'. At the bottom, there is a toolbar with buttons: 'DEFINE CROSSOVERS' (highlighted in blue), 'EDIT BASES', 'SET 5' END', 'SET 3' END', 'TOGGLE PAIRING STATES', 'SET EQ CONSTRAINTS', and 'SHOW EQ CONSTRAINT'.

# Editing Bases

The screenshot displays a DNA Design software window with a menu bar (File, Edit, Tile) and a toolbar (DEFINE CROSSOVERS, EDIT BASES, SET 5' END, SET 3' END, TOGGLE PAIRING STATES, SET EQ CONSTRAINTS, SHOW EQ CONSTRAINT). The main workspace shows four horizontal tracks of DNA strands, each with 3' and 5' ends indicated. The top track features colored bases (blue, green, red) and some are labeled with letters (A, C, G). The second track has magenta bases. The third track has red and blue bases. The bottom track is mostly greyed out. The interface is used for editing DNA sequences and constraints.

# Setting WC constraints

The screenshot displays the DNA Design software interface with a menu bar (File, Edit, Tile) and a main workspace showing four DNA strands. The strands are oriented with 3' ends at the top and 5' ends at the bottom. The top strand is primarily black with some blue, green, and red segments. The second strand has magenta and blue segments. The third strand has red and blue segments. The bottom strand is mostly black with cyan segments. Vertical lines connect complementary bases between strands, with colors matching the bases they connect. Some bases are labeled with 'C', 'G', 'A', and 'GA'. The bottom control bar contains several buttons: DEFINE CROSSOVERS, EDIT BASES, SET 5' END, SET 3' END, TOGGLE PAIRING STATES (highlighted in blue), SET EQ CONSTRAINTS, and SHOW EQ CONSTRAINT.



# Adding the Tile to Tile Set

The screenshot displays the 'DNA Design' software interface. At the top, a menu bar includes 'File', 'Edit', and 'Tile'. The 'Tile' menu is open, showing options: 'Clear', 'Add to Tile Set', 'Optimize Tile Set', and 'Update Display'. The main workspace contains four DNA double-strand diagrams, each with 3' and 5' ends labeled. The top diagram uses red and blue 'N' characters. The second diagram uses green 'N' characters. The third diagram uses magenta 'N' characters. The fourth diagram uses cyan and yellow 'N' characters. At the bottom, a toolbar contains buttons for 'DEFINE CROSSOVERS', 'EDIT BASES', 'SET 5' END', 'SET 3' END', 'TOGGLE PAIRING STATES', 'SET EQ CONSTRAINTS' (highlighted in blue), and 'SHOW EQ CONSTRAINT'. On the right side, a vertical panel titled 'Current' contains a sub-panel labeled 'Tile 1'.

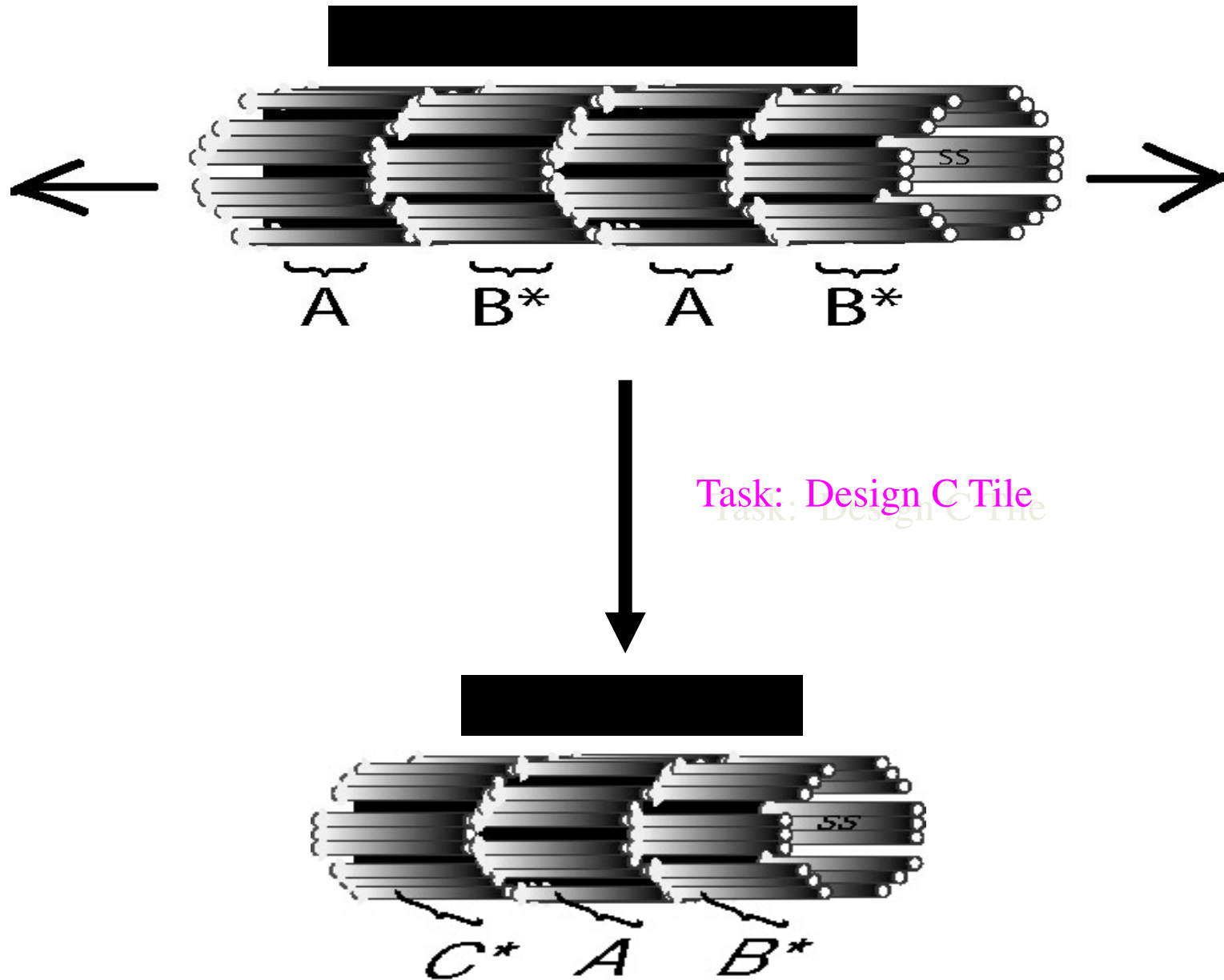
# Tile A (Optimized)

The screenshot displays the DNA Design software interface. The main window shows a DNA sequence with several crossovers highlighted in different colors: blue, green, purple, and red. The sequence is represented by two strands, with 3' and 5' ends indicated. The crossovers connect the strands at various positions, forming a complex structure. The software interface includes a menu bar (File, Edit, Tile) and a control panel at the bottom with buttons for: DEFINE CROSSOVERS, EDIT BASES (highlighted in blue), SET 5' END, SET 3' END, TOGGLE PAIRING STATES, SET EQ CONSTRAINTS, and SHOW EQ CONSTRAINT. On the right side, there is a panel with a 'Current' label and three buttons: Tile 1 (highlighted in blue), Tile 2, and Tile 3.

# Tile B ( Optimized)

The screenshot displays a software window titled "DNA Design" with a menu bar containing "File", "Edit", and "Tile". The main workspace shows a DNA sequence with four horizontal tracks. The top track is the 3' to 5' strand, and the bottom track is the 5' to 3' strand. The sequence is composed of nucleotides (A, C, G, T) and unknowns (N). Several regions are highlighted with colored lines: a blue line connects a 'G' in the top strand to a 'C' in the bottom strand; a green line connects a 'G' in the top strand to a 'C' in the bottom strand; a red line connects a 'G' in the top strand to a 'C' in the bottom strand; and a purple line connects a 'G' in the top strand to a 'C' in the bottom strand. The bottom track contains a large block of 'NN' characters. On the right side, a "Current" panel shows three buttons: "Tile 1", "Tile 2" (which is highlighted in blue), and "Tile 3". At the bottom of the window, a control panel contains several buttons: "DEFINE CROSSOVERS", "EDIT BASES" (highlighted in blue), "SET 5' END", "SET 3' END", "TOGGLE PAIRING STATES", "SET EQ CONSTRAINTS", and "SHOW EQ CONSTRAINT".

## Example: Designing C Tile for Nano-Barrel



# Tile C ( To be optimized)

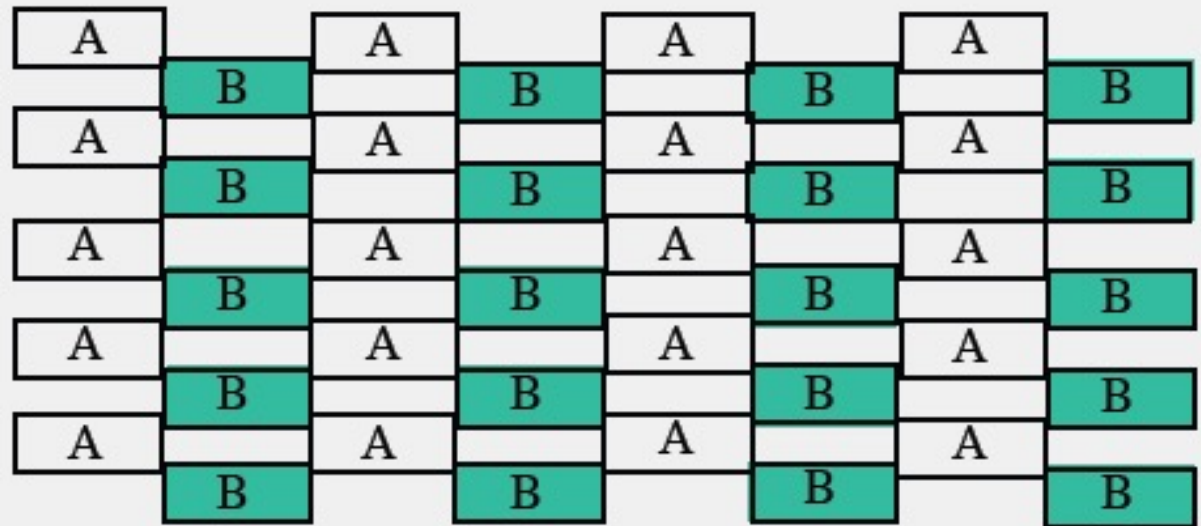
The screenshot displays a software window titled "DNA Design" with a menu bar containing "File", "Edit", and "Tile". The main workspace shows a DNA tile design with four horizontal strands. The top two strands are connected by a vertical stem, and the bottom two strands are also connected by a vertical stem. The bases are color-coded: blue, green, red, and purple. Some bases are labeled with specific nucleotides: "CT", "G", "C", "NT", "A", "C", "G", "GA", "T", "C", "G", "AG", and "C". The strands are labeled with 3' and 5' ends. On the right side, there is a control panel with a "Current" dropdown menu and three buttons labeled "Tile 1", "Tile 2", and "Tile 3". At the bottom, there is a toolbar with buttons for "DEFINE CROSSOVERS", "EDIT BASES", "SET 5' END", "SET 3' END", "TOGGLE PAIRING STATES", "SET EQ CONSTRAINTS", and "SHOW EQ CONSTRAINT".

# Tile C ( Optimized)

The screenshot displays a software window titled "DNA Design" with a menu bar containing "File", "Edit", and "Tile". The main workspace shows four DNA strands, each with a 3' and 5' end indicated by arrows. The strands are populated with nucleotide bases (A, T, C, G) and "NN" (non-nucleotide) placeholders. Colored lines connect complementary bases between adjacent strands, representing crossovers or pairings. The colors used are blue, green, red, and purple. The top strand has a blue line connecting 'A' to 'T', a green line connecting 'G' to 'C', and a red line connecting 'T' to 'A'. The second strand has a purple line connecting 'G' to 'C' and a red line connecting 'T' to 'A'. The third strand has a purple line connecting 'G' to 'C' and a red line connecting 'T' to 'A'. The bottom strand is mostly composed of "NN" placeholders.

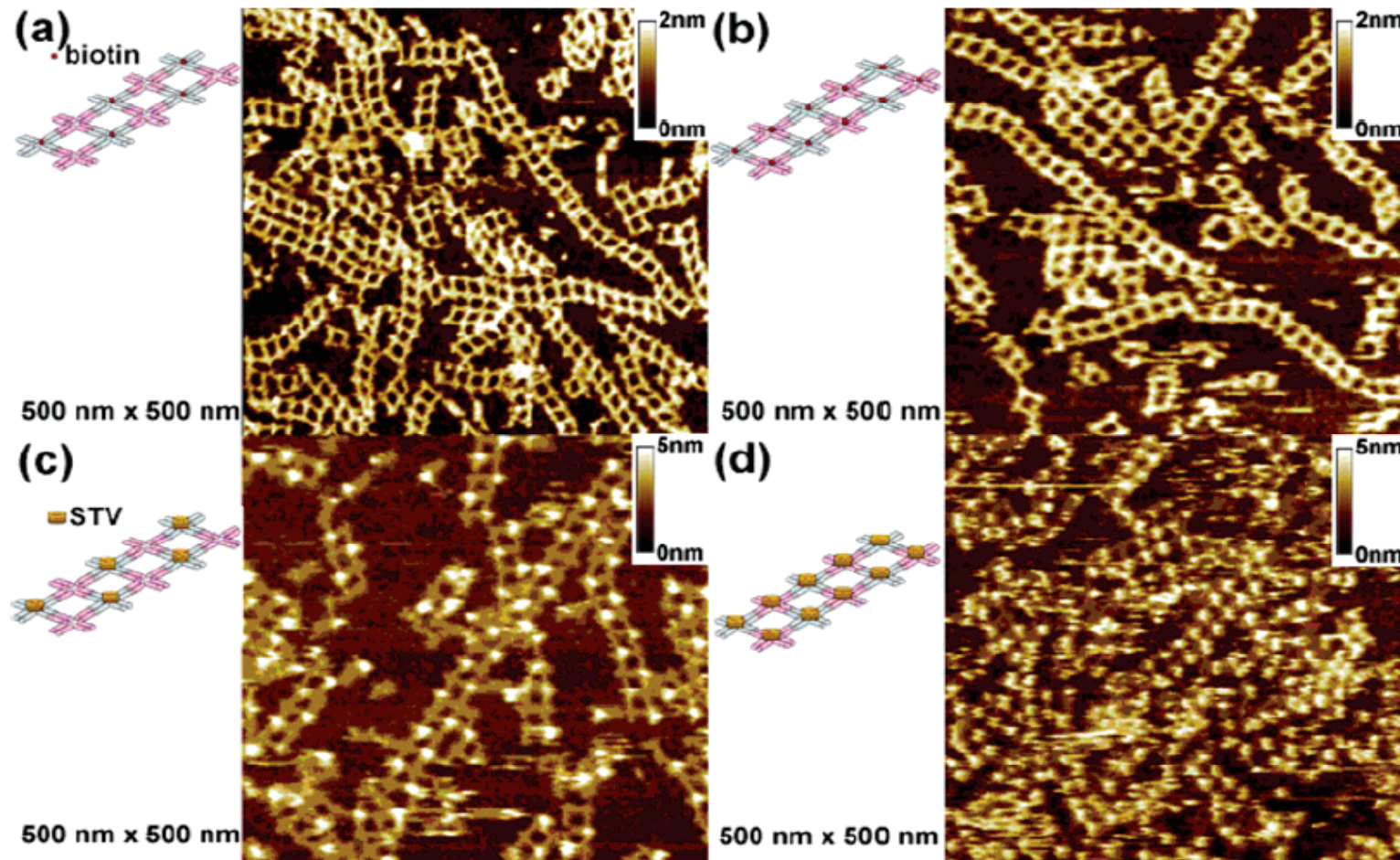
On the right side, a vertical control panel is visible, showing a list of tiles: "Tile 1", "Tile 2", and "Tile 3". "Tile 3" is highlighted in blue. Below this panel, a control bar contains several buttons: "DEFINE CROSSOVERS", "EDIT BASES", "SET 5' END" (highlighted in blue), "SET 3' END", "TOGGLE PAIRING STATES", "SET EQ CONSTRAINTS", and "SHOW EQ CONSTRAINT".

## Lattices using TX Tiles



# Linear DNA TX lattices with biotin covalently bound to DNA tiles

Can be used for patterning of heteromaterials using DNA-directed assembly.

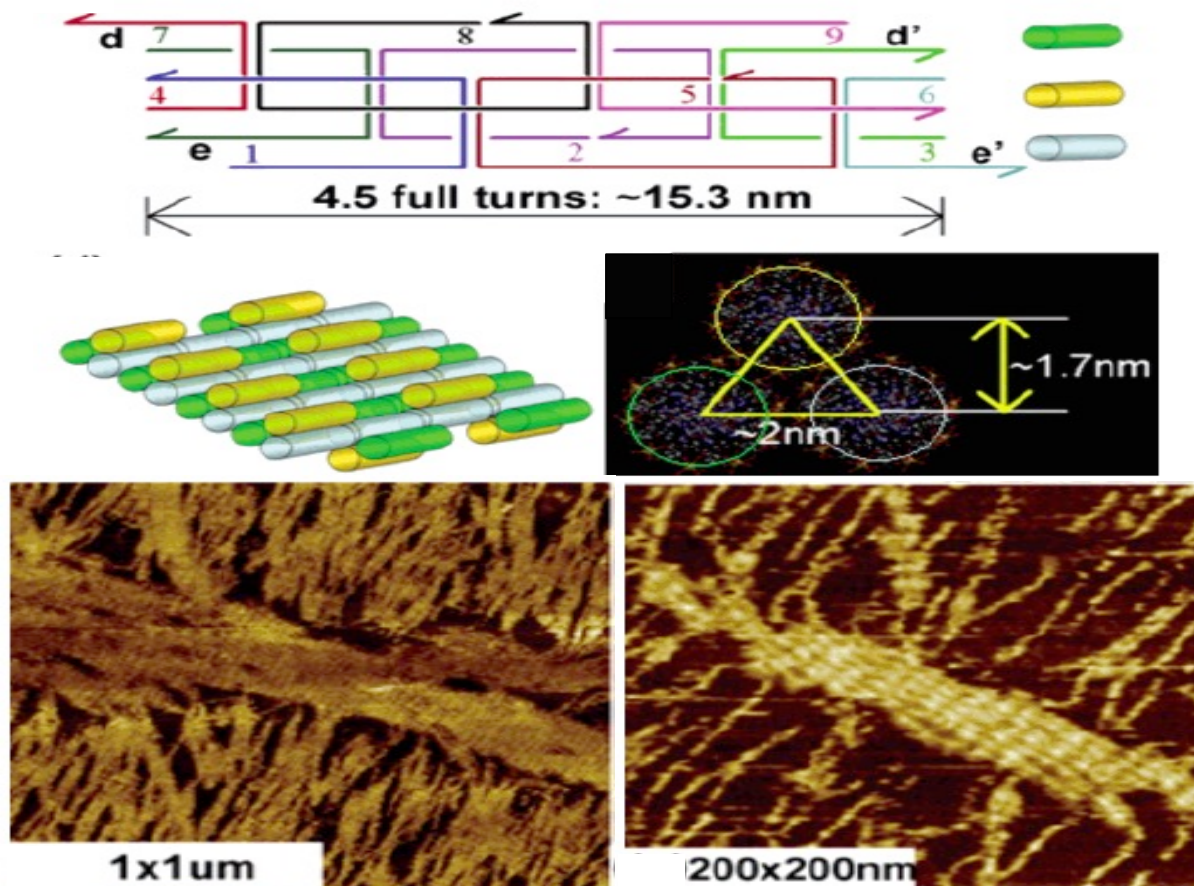


Sung Ha Park, Peng Yin, John Reif, Thomas LaBean, and Hao Yan, (2005)  
Programmable DNA Self-assemblies for Nanoscale Organization of Ligands and  
Proteins, *Nano Letters* 5(4) 729-733.



# Three-helix bundle DNA tile Lattice

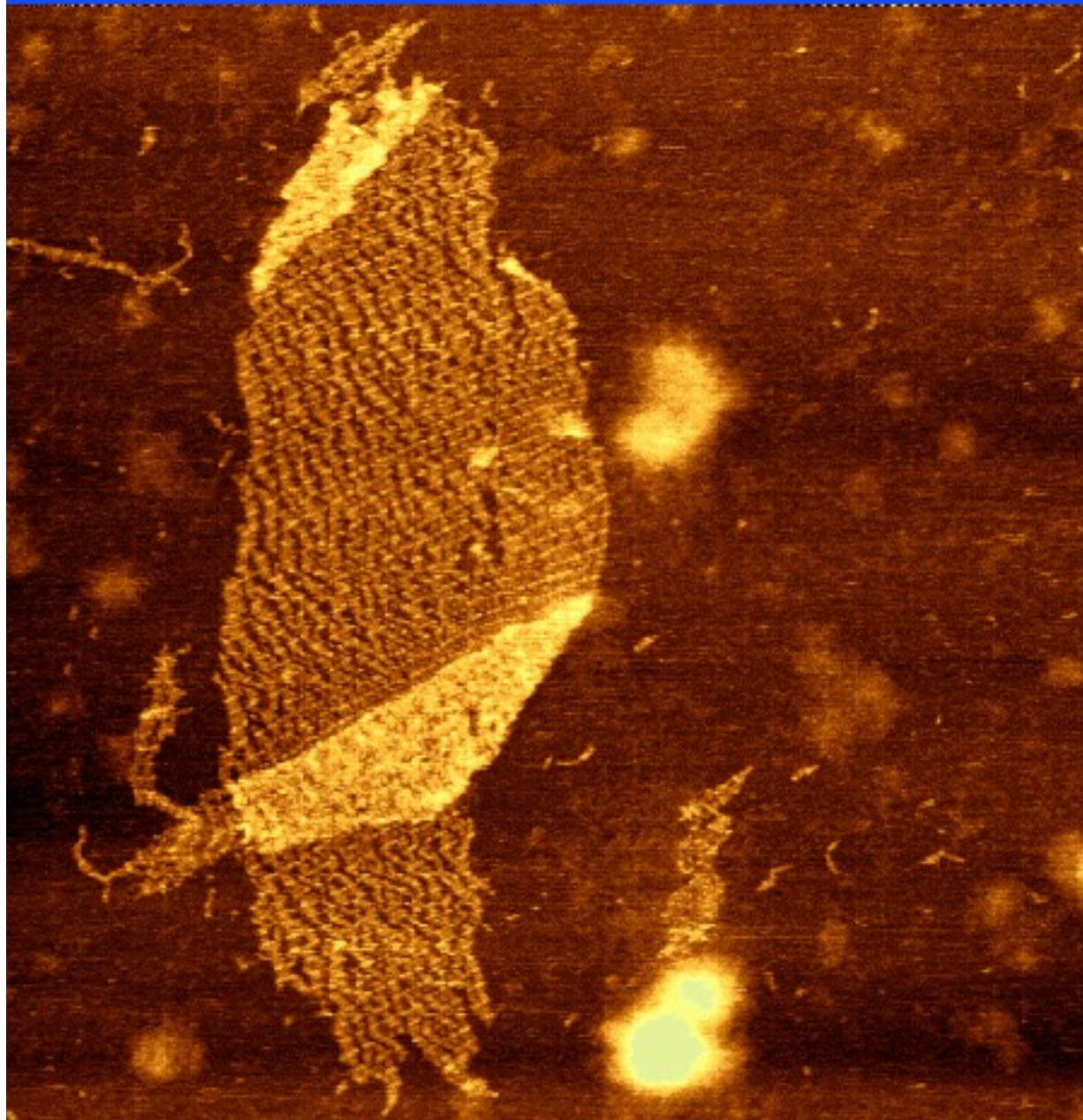
- Demonstrated for 1D and 2D self-assemblies
  - Provides potential for tiling in the third dimension.
  - The linear structures were used as templates for the electroless deposition of silver and formation of highly conductive silver nanowires with diameters of 20 – 30 nm.
- This tile type increases the toolbox of molecular building blocks with which to attack nano construction projects and patterning of heteromaterials using DNA-directed assembly.



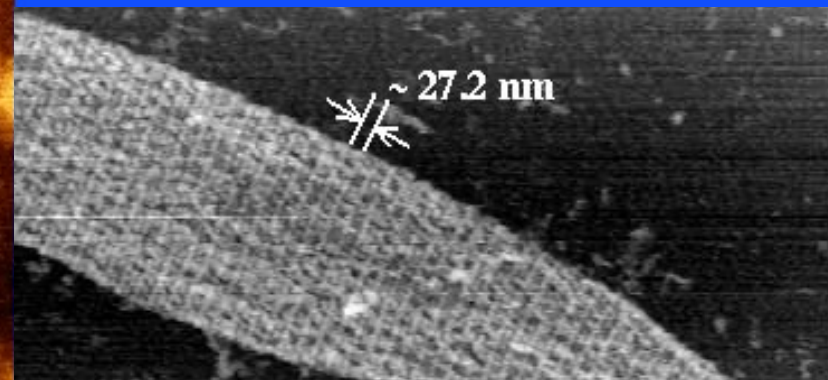
Sung Ha Park, Robert Barish, John Reif, Gleb Finkelstein, Hao Yan and Thomas LaBean, (2005) Three-Helix Bundle DNA Tiles Self-Assemble into 2D Lattice or 1D Templates for Silver Nanowires, *Nano Letters* 5(4) 693-696.

# Large Scale DNA Self-Assembled Tilings

TX Lattice, with Visualization by Atomic Force Microscope.



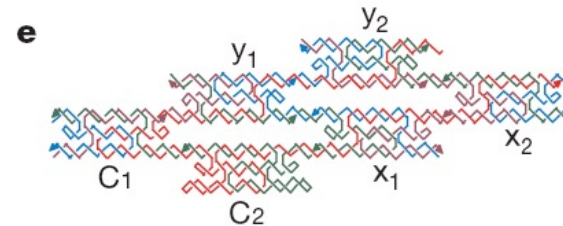
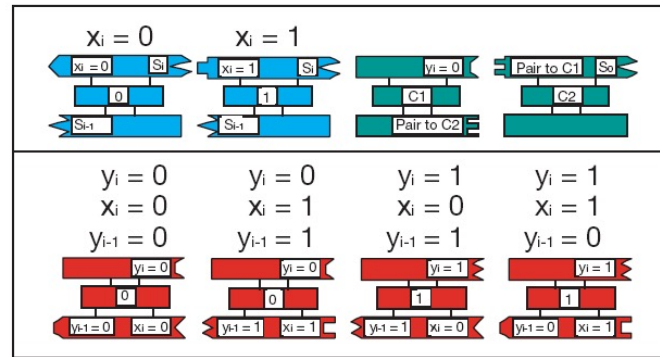
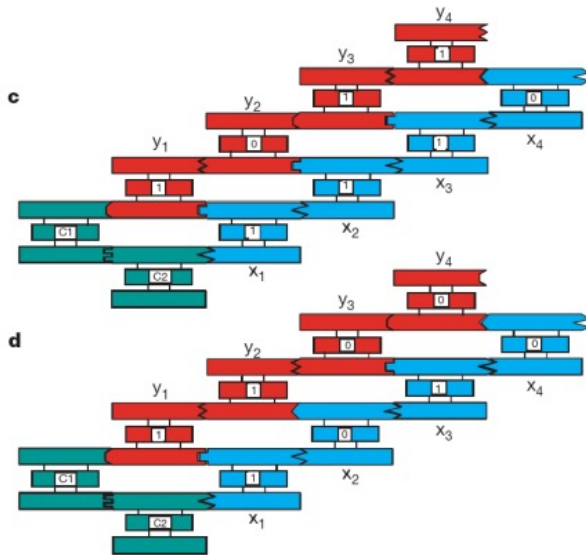
AB\* Lattice. An atomic force microscope image of DNA lattice formed by two TAO tiles one of which contains an extra loop directed out of the plane. These loops form the visible stripe features with the expected spacing of  $\sim 28$  nm.



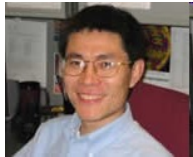
# Computational DNA Lattices

# Experimental Demonstrations of Molecular Computation via DNA Tiling

- First experimental demonstration of computation via molecular self-assembly: Computation of XOR using DNA triple-crossover molecules:
  - Mao, LaBean, Reif, Seeman, *Logical Computation Using Algorithmic Self-Assembly of DNA Triple-Crossover Molecules*



# First Experimental Demonstration Computation via Tiling Assembly: 1D DNA Tiling Computation:



- C Mao, T H LaBean, **J H Reif**, N C Seeman, Logical Computation using Algorithmic Self-assembly of DNA Triple-crossover Molecules, *Nature* (2000)



- Hao Yan, Liping Feng, Thomas H. LaBean, and **John Reif**, Parallel Molecular Computations of Pairwise Exclusive-Or (XOR) Using DNA "String Tile" Self-Assembly, *JACS* (2003).

- **String Tile Addition Pads:**

- The sticky end pads on right encode:
  - carry bits coming in and  $I_{A_i}$  and  $I_{B_i}$  encode the two input bits.
- Left-hand pads pass new carry value on to next step
- Reporter strands indicated by arrows;  $O_i$  encodes: output bit.

tile	$c_i$	$I_{A_i}$	$I_{B_i}$	$O_i$	$c_{i+1}$
1	0	0	0	0	0
2	0	0	1	1	0
3	0	1	0	1	0
4	0	1	1	0	1
5	1	0	0	1	0
6	1	0	1	0	1
7	1	1	0	0	1
8	1	1	1	1	1

0  
 1

$c_0$        $c_0$        $c_1$        $c_0$

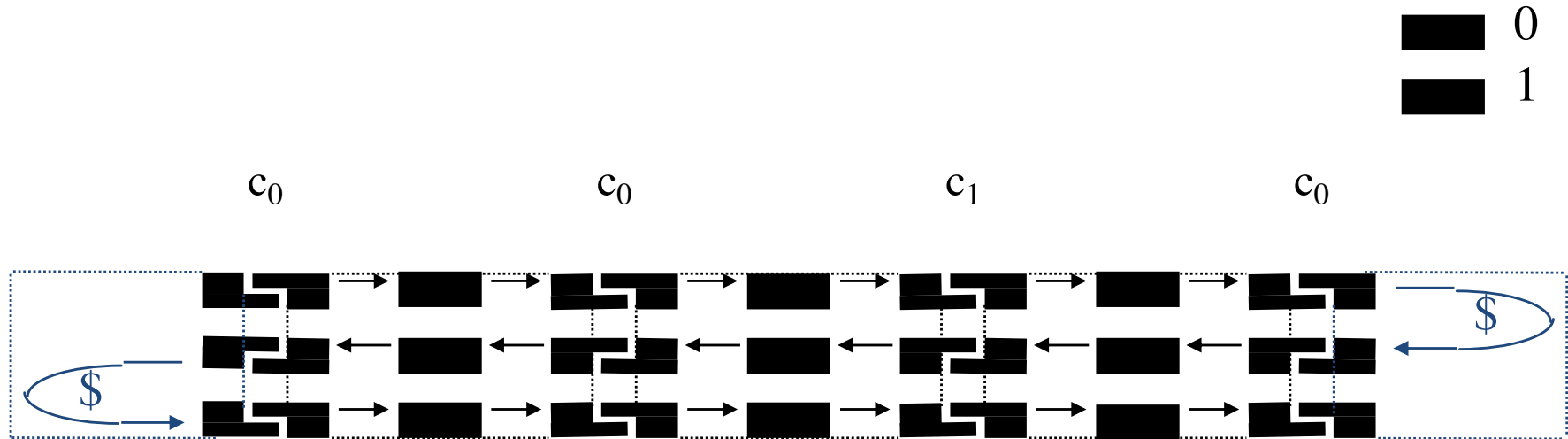
101  
 +001  
 110

1 0 1 \$ 0 1 1 \$ 0 0 1 =  $I_A$  \$  $O^R$  \$  $I_B$

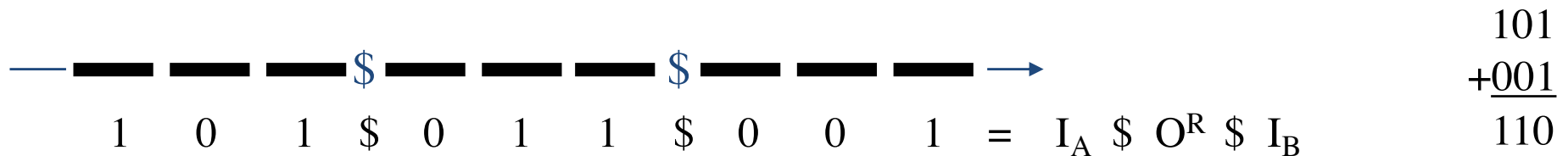
- **Pad Programming via Truth Table:**

- Column  $c_i$  gives values for the 3 right-hand pads ( $c1_i, \sim c2_i, c3_i$ )
- Column  $c_{i+1}$  gives value for the 3 left-hand pads ( $\sim c1_{i+1}, c2_{i+1}, \sim c3_{i+1}$ ).

# “String Tile” Addition:

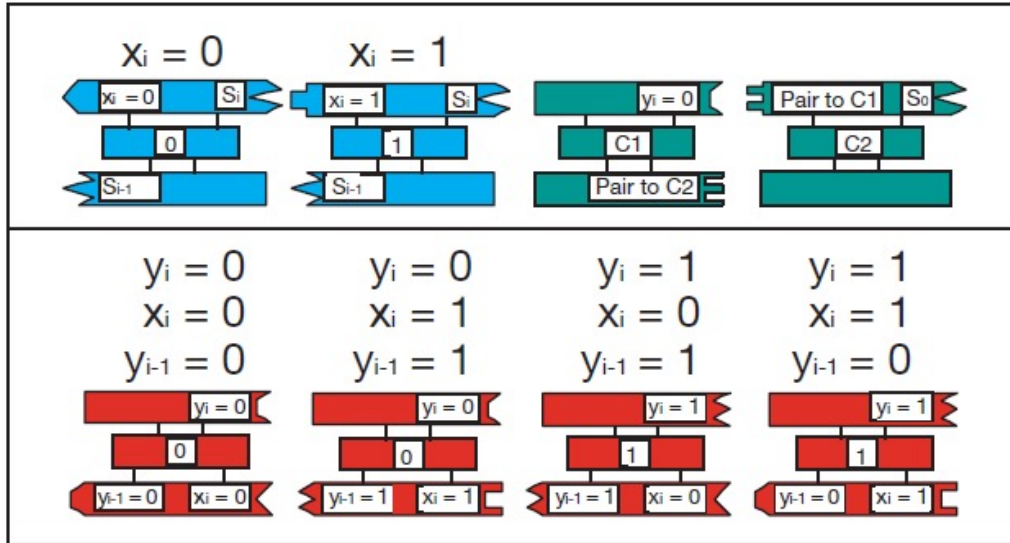


- Anneal strands to form assembly.
- Ligate reporter strand segments.
- Purify reporter strand and read values by PCR.

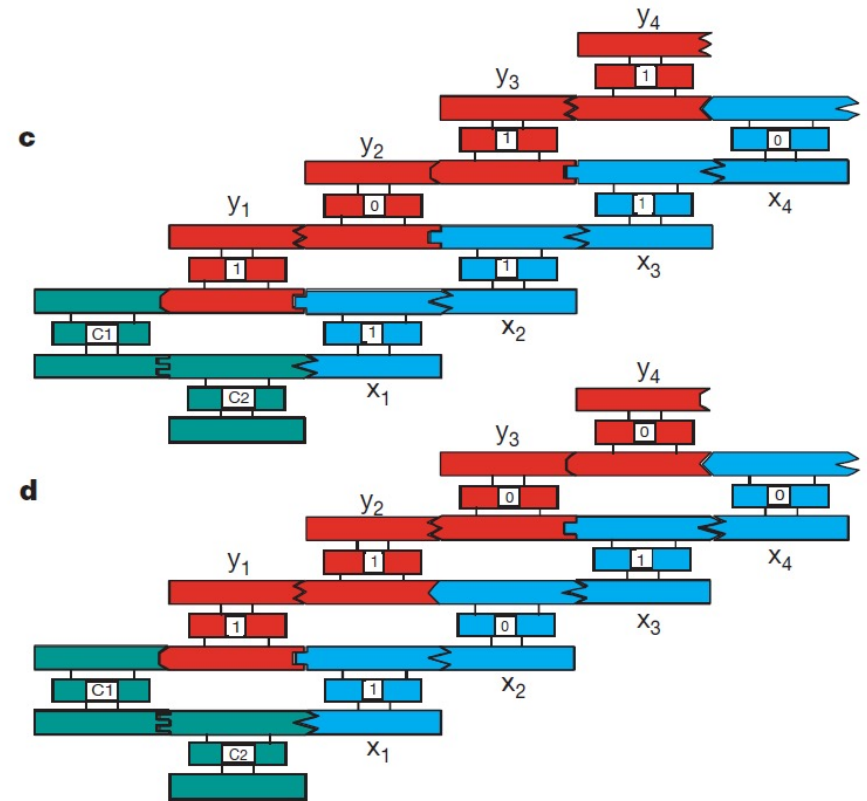


Hao Yan, Liping Feng, Thomas H. LaBean, and John Reif, Parallel Molecular Computations of Pairwise Exclusive-Or (XOR) Using DNA "String Tile" Self-Assembly, JACS (2003).

# The First Demonstration of Molecular Scale Computing using DNA Self-Assembly (TX tiles)



**TX Tiles for computing XOR**

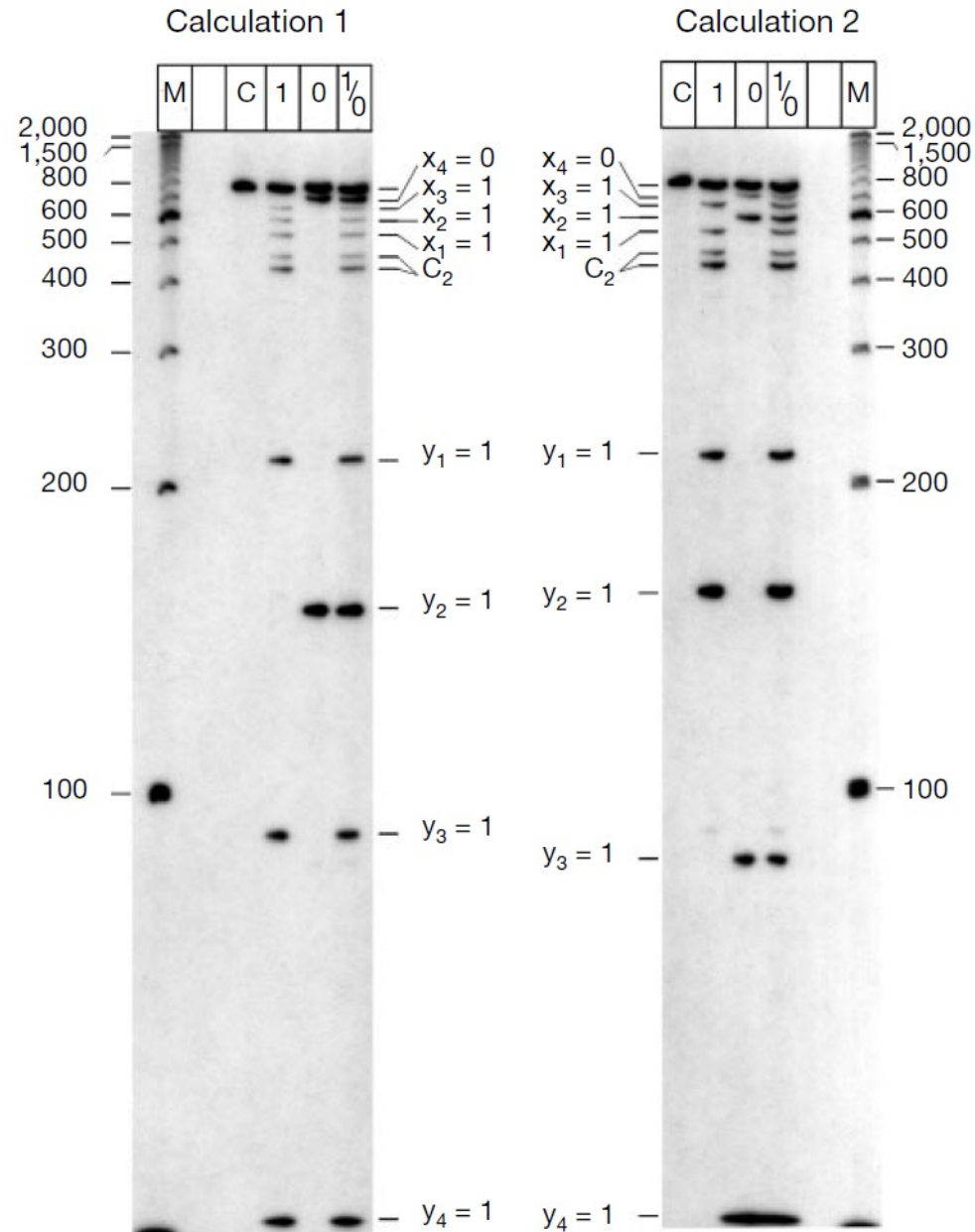


**TX Lattices computing XOR**

**C. Mao, T.H. LaBean, John H. Reif, N. C. Seeman, Logical Computation Using Algorithmic Self-Assembly of DNA Triple-Crossover Molecules, Nature, vol. 407, Sept. 28 2000, pp. 493-495**



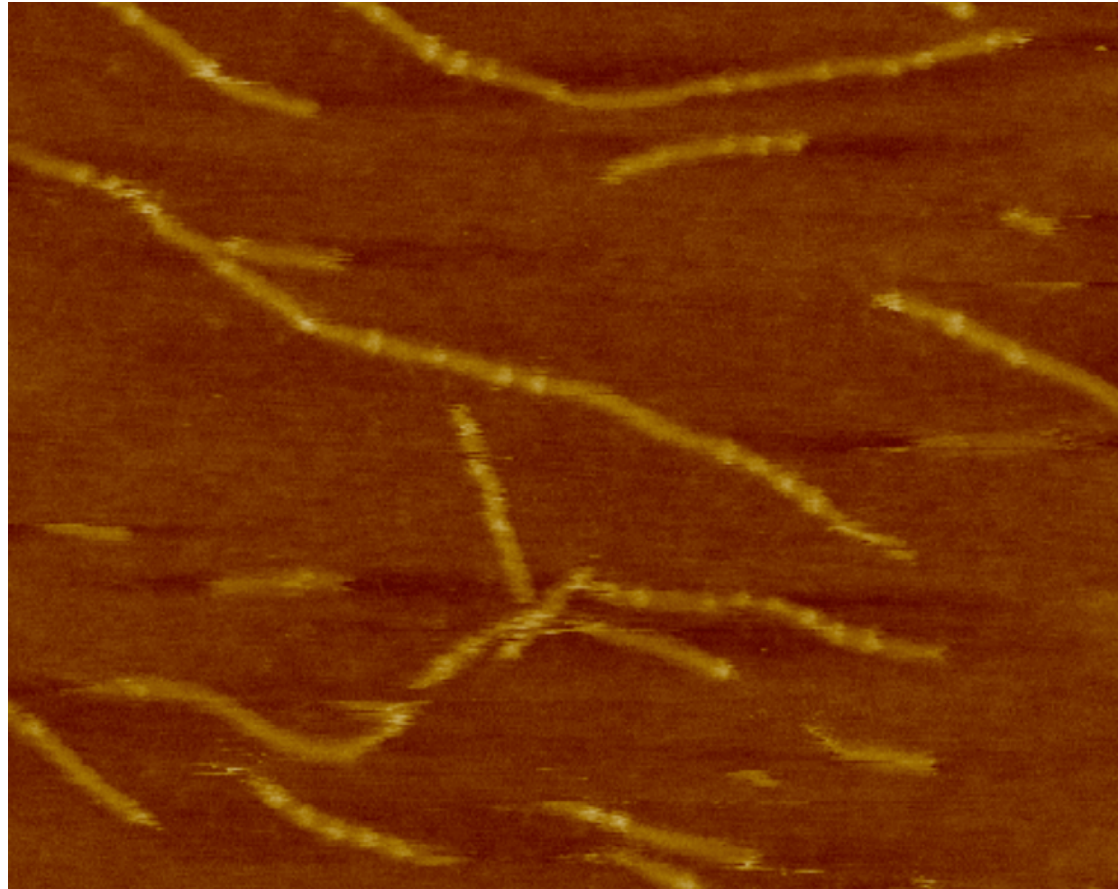
# Gel Electrophoresis Demonstration of Computing using TX tiles



## TAE Assemblies for XOR Computation



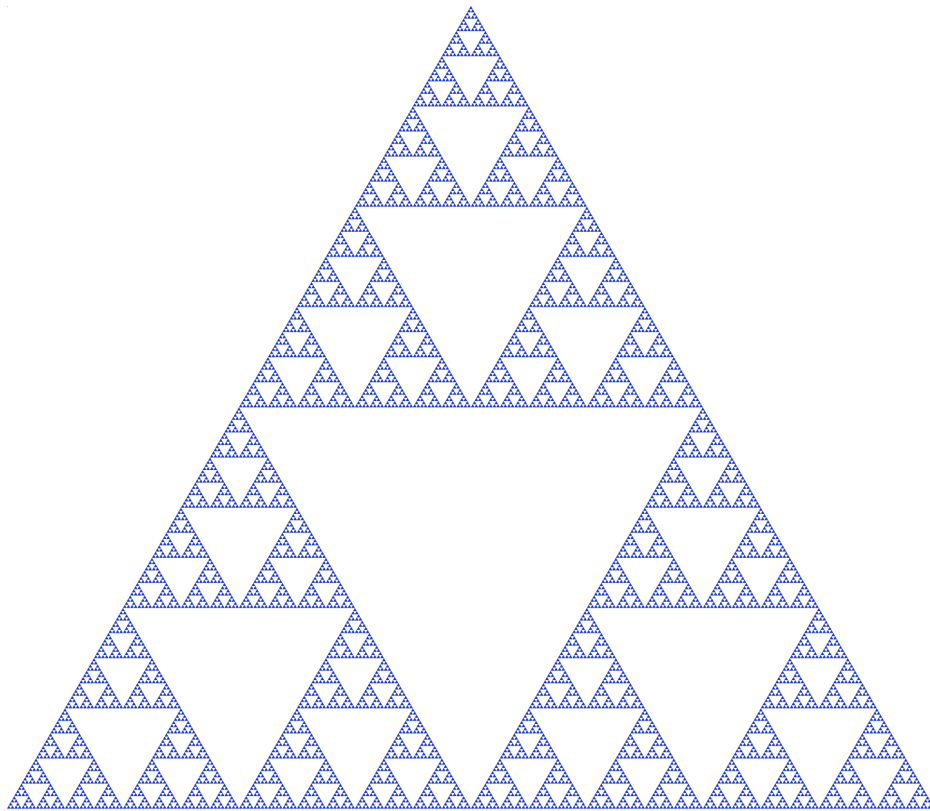
## XOR via TAE Computational Complex with Visual Readout



*Hao Yan, Liping Feng, Thomas H. LaBean, and John Reif, Parallel Molecular Computations of Pairwise Exclusive-Or (XOR) Using DNA "String Tile" Self-Assembly, JACS (2003).*

# 2D DNA Tiling Computation of a Sierpinski Triangle

**Sierpinski Triangle** is the Pascal Triangle taken mod 2

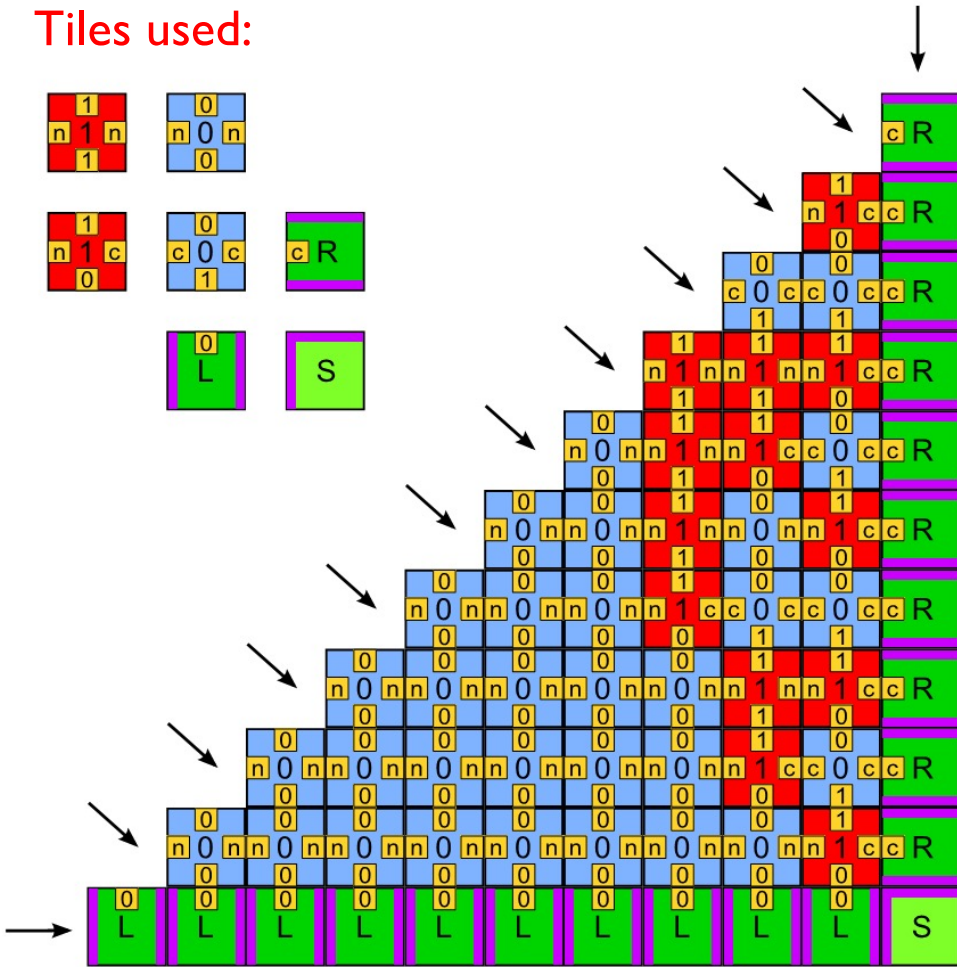
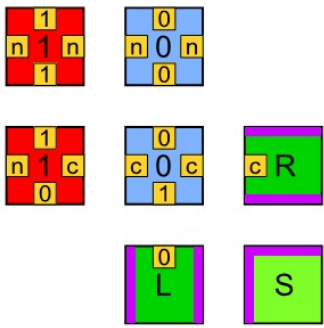


Paul W K Rothemund & Erik Winfree  
California Institute of Technology

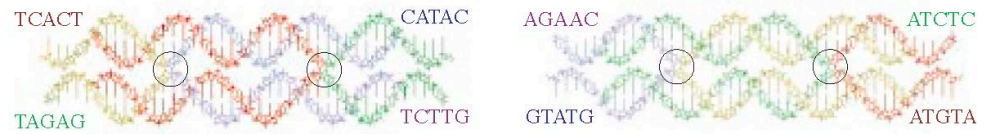
- ***Paul W.K. Rothemund, Nick Papadakis, Erik Winfree, Algorithmic Self-Assembly of DNA Sierpinski Triangles. PLoS Biology (2004)***

# Experimental demonstration of Sierpinski Triangle computation via 2D DNA self-assembly:

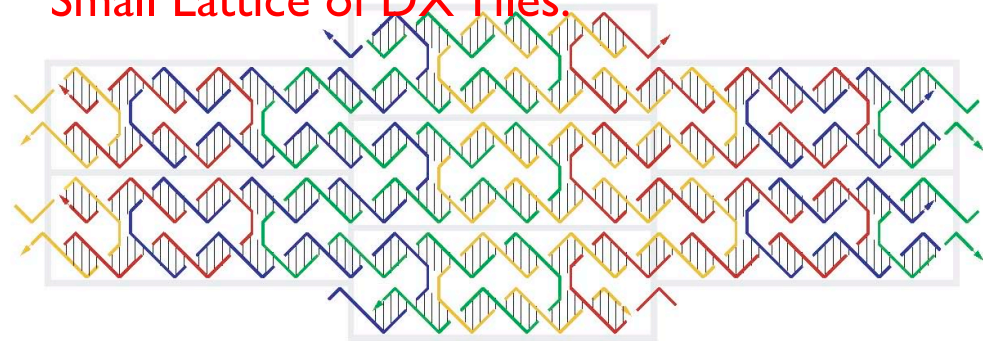
Tiles used:



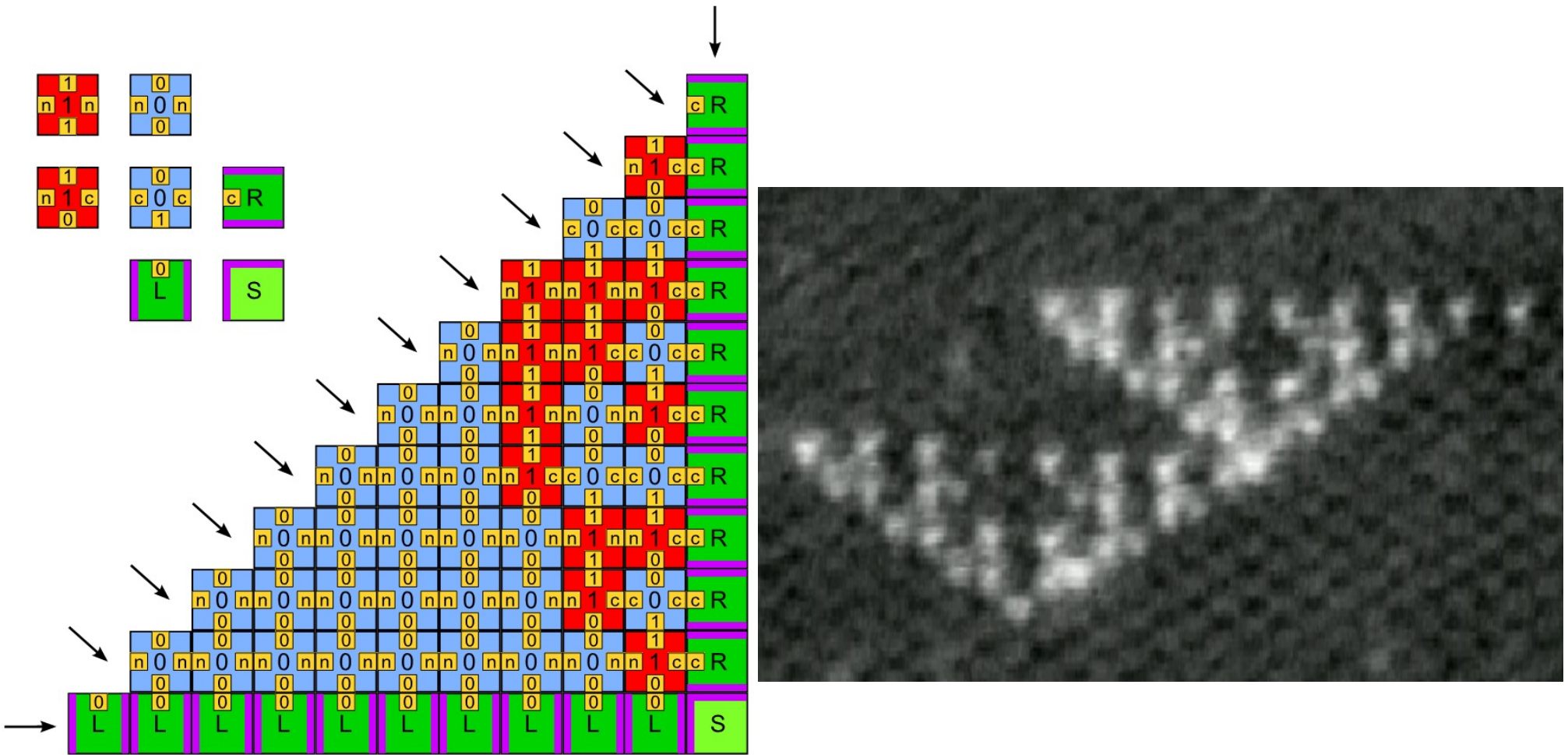
Used DX Tiles for Computation:



Small Lattice of DX Tiles:

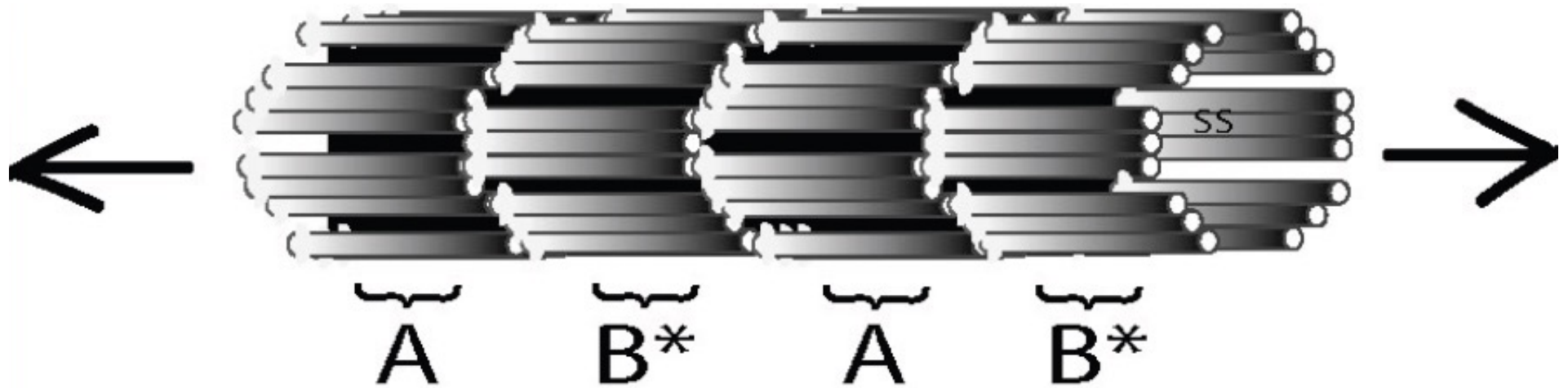


# Experimental demonstration of Sierpinski Triangle computation via 2D DNA self-assembly:



# DNA Tubes & Ribbons

# TX tubes



# Example: Designing C Tile for Nano-Barrel

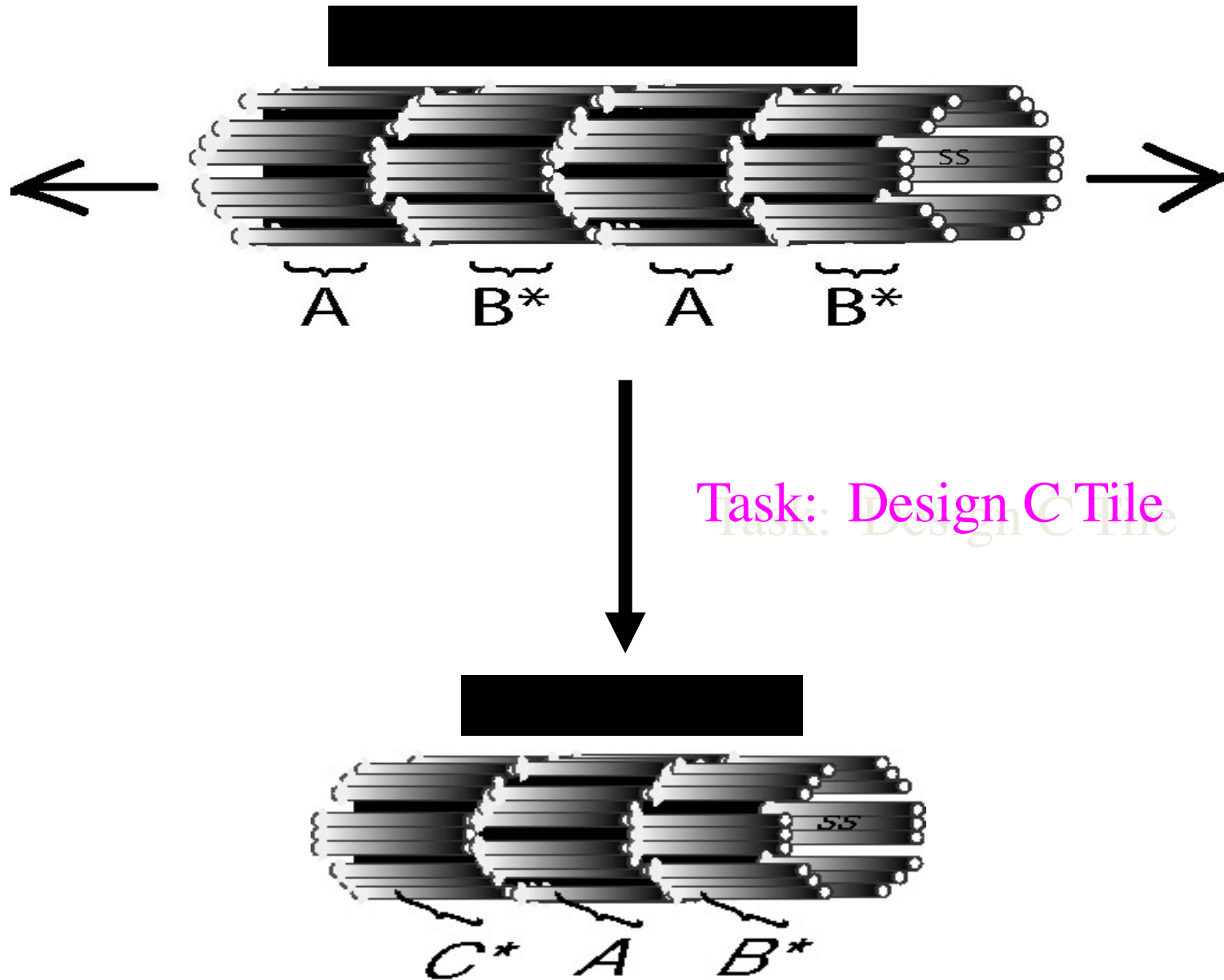
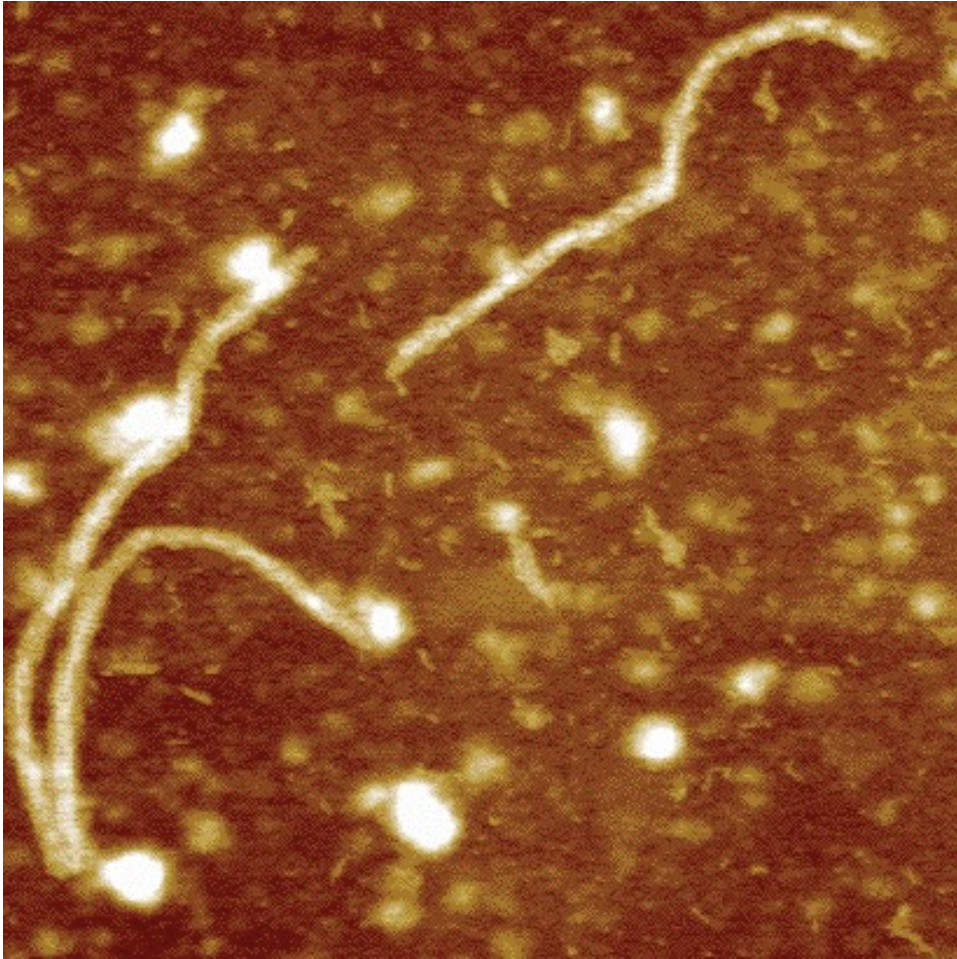


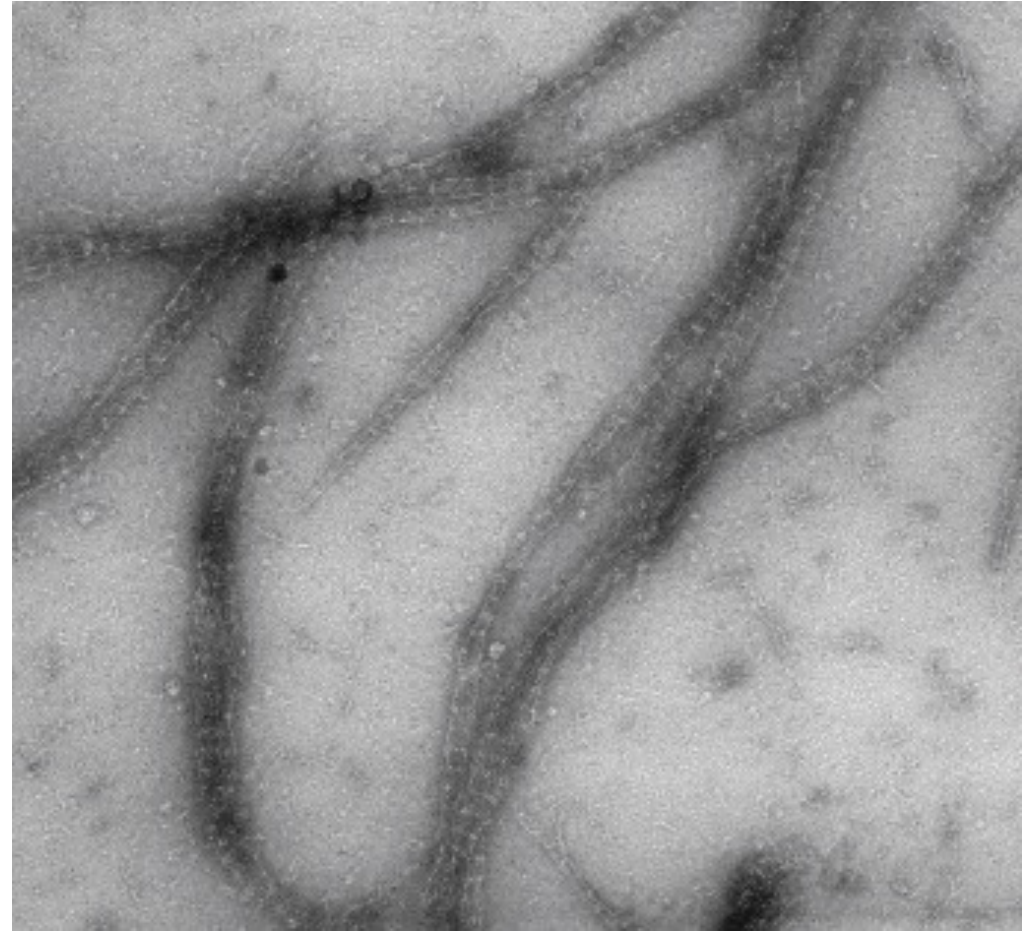
Figure Credit: Thomas. Labean



# TX tubes



AFM Imaging



TEM Imaging

Science

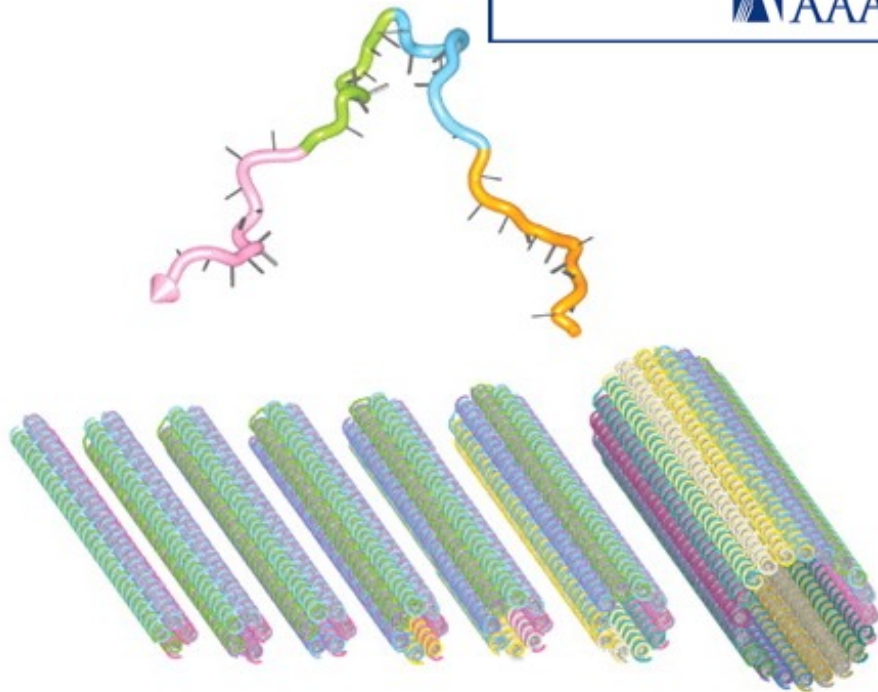
AAAS

# Programming DNA Tube Circumferences

Peng Yin, Reif, et al

*Science* **321**, 824 (2008);

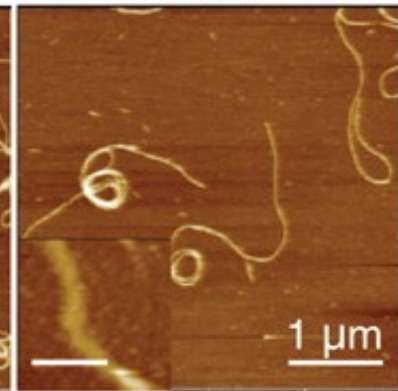
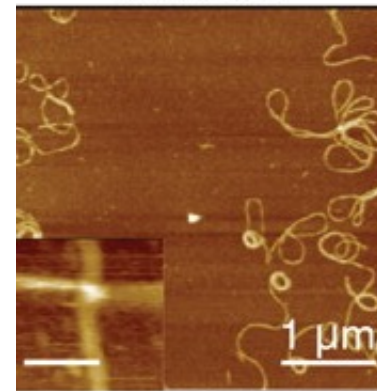
DOI: 10.1126/science.1157312



4-helix tube



5-helix tube



6-helix tube



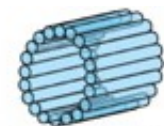
7-helix tube



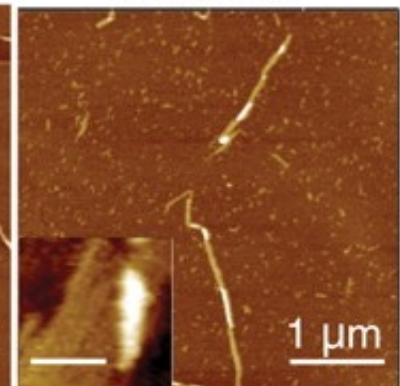
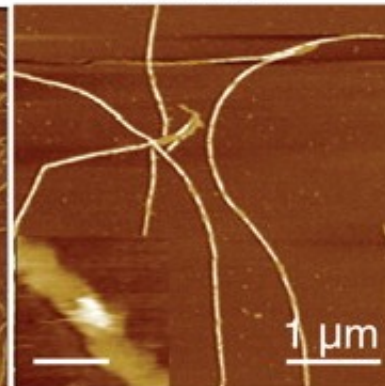
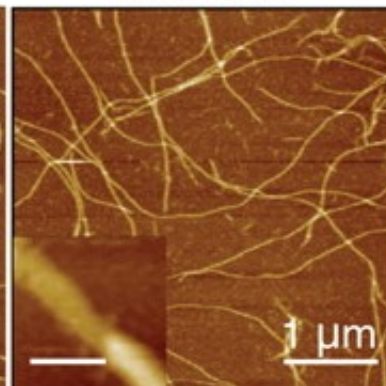
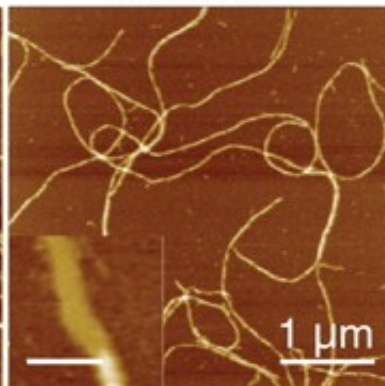
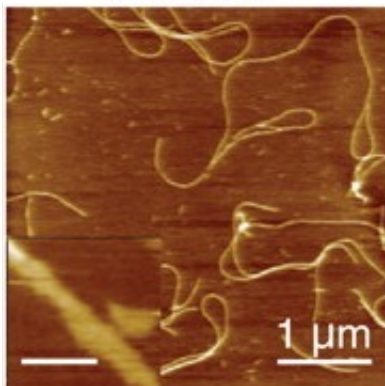
8-helix tube



10-helix tube



20-helix tube

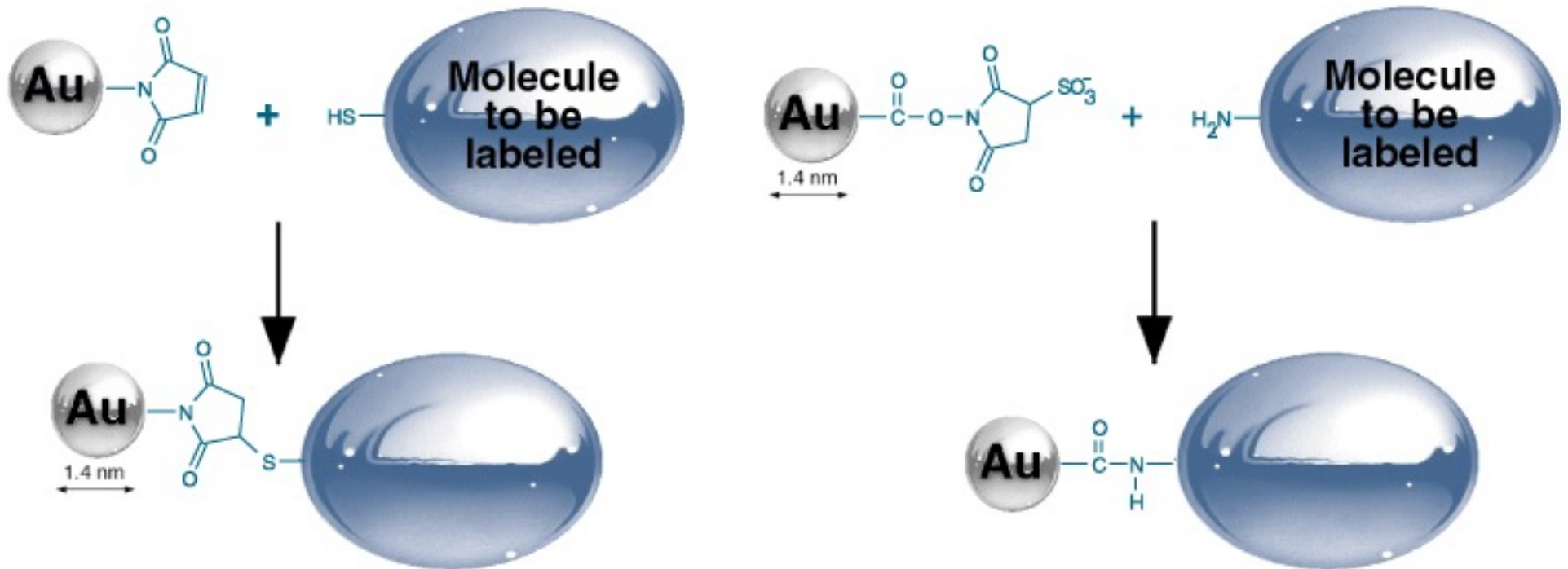


# An Application of DNA lattices:

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

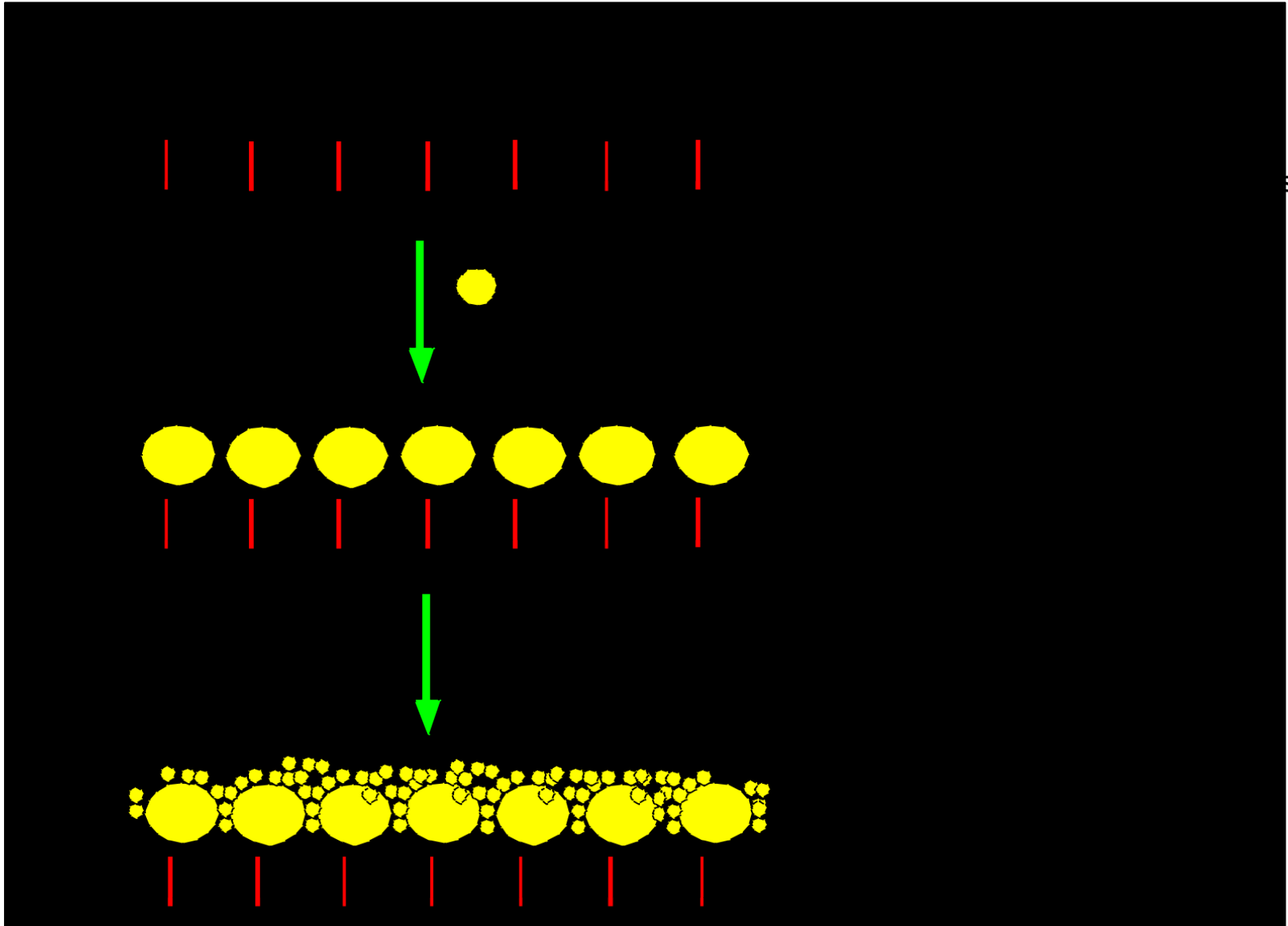
# Attachment Chemistries to DNA

- nanogold + thiol (SH)
- nanogold + amino (NH<sub>2</sub>)
- Other (biotin/avidin, Au/S, etc.)



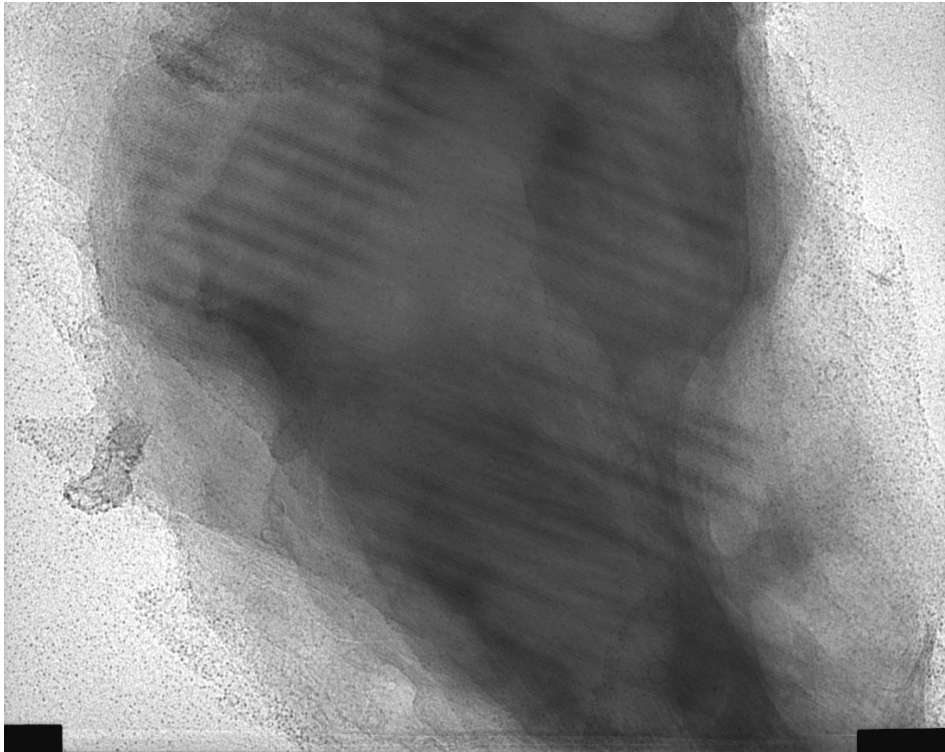
## Forming Gold Wires on DNA Tiling Lattices:

- DNA strands attached to gold beads hybridize at selected tiles of DNA array.
- Gold wires forms by fusion of free gold beads to beads attached to DNA array.
- Molecular electronics components can self-assemble between the gold beads.

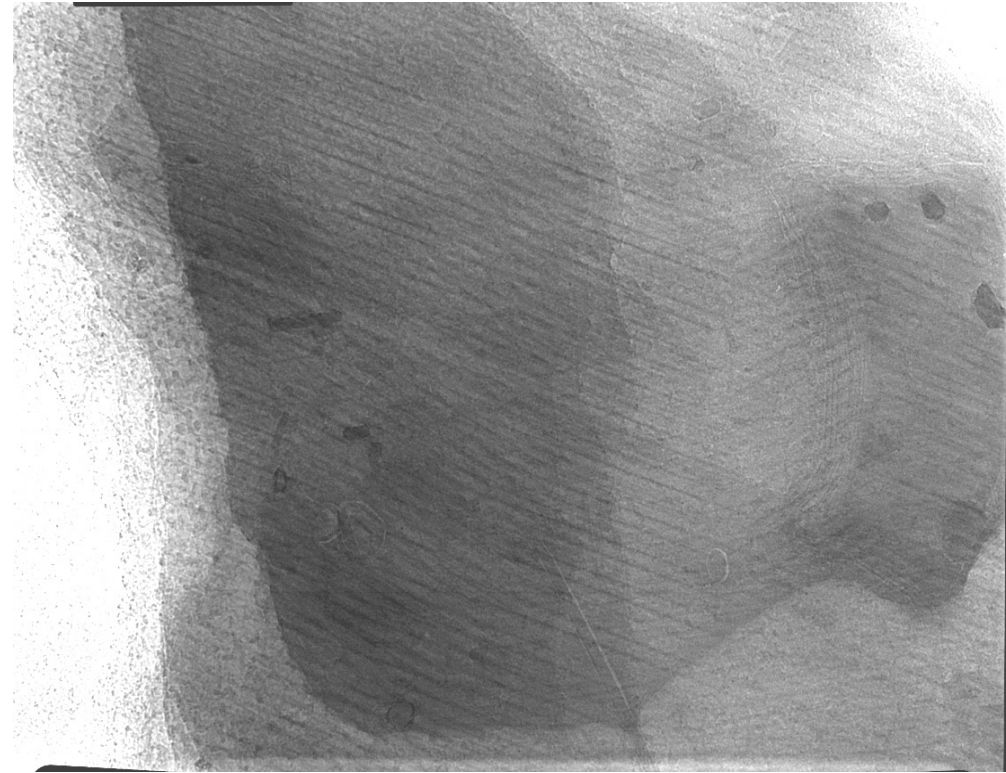


# Nanogold Patterning of a DNA Lattice

## TEM images of TAO lattices



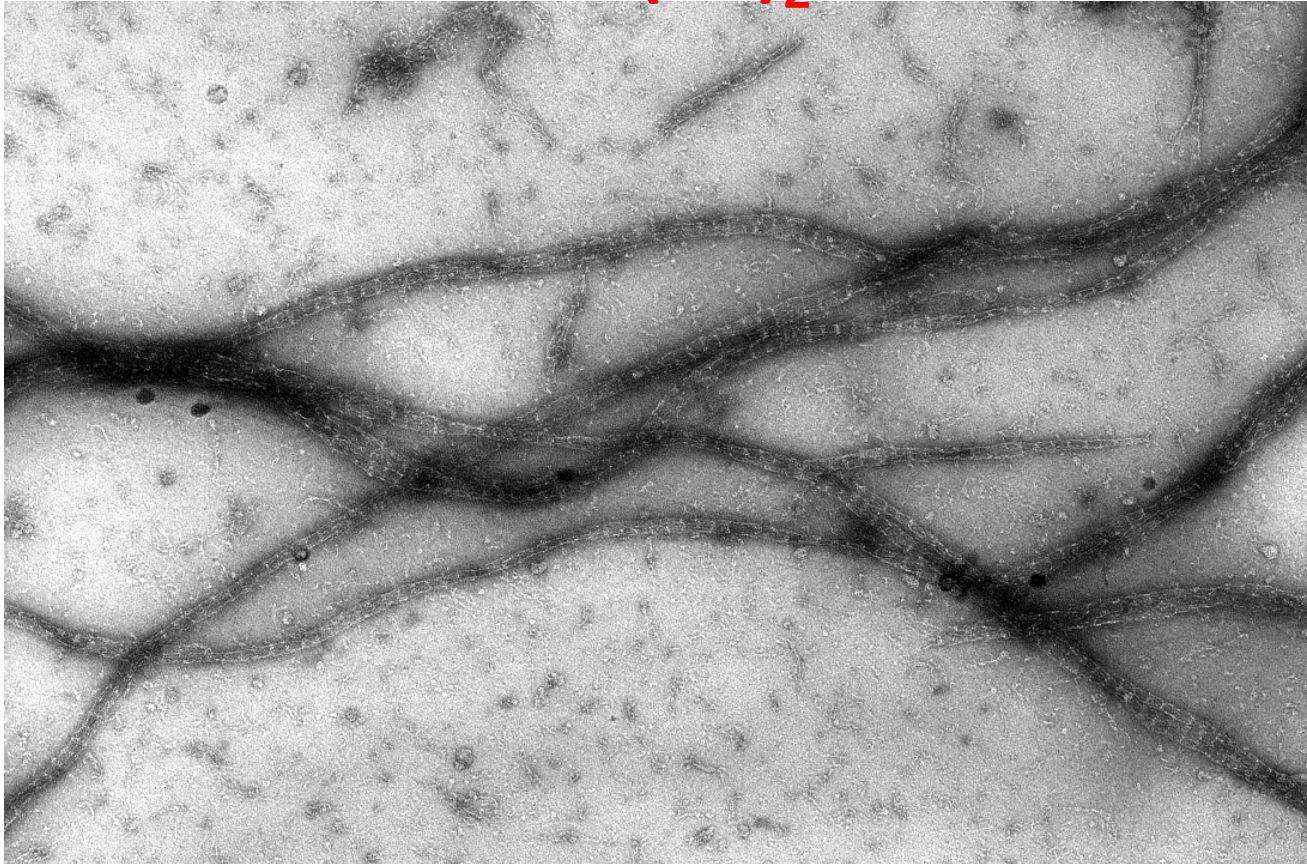
**AB\* TAO Lattice**



**ABCD\* DX Lattice**

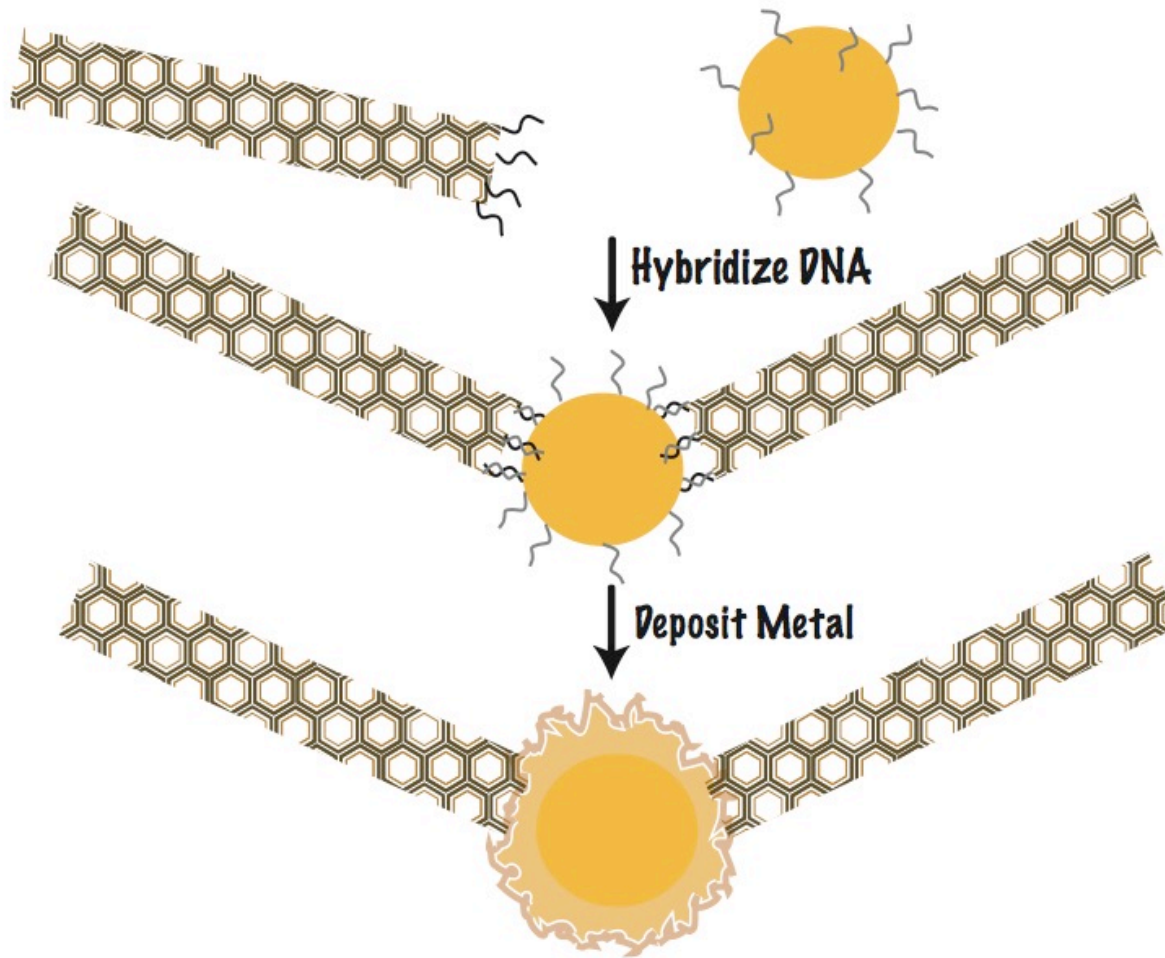
- **Moiré` interference patterns** indicates patterned gold nanoparticles are present in multiple layers.
- **Electron Diffraction Patterns** indicates nanogold is bound in lattice pattern

## DNA Fibers from $AB^*(SH)_2$ Tile Lattice



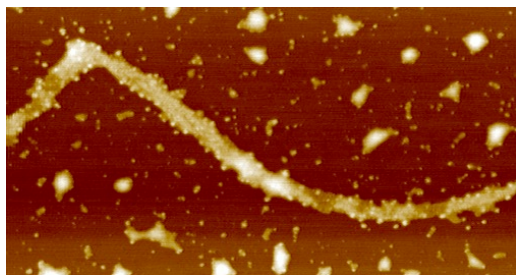
- **Self-Assembled DNA Lattices forming fibers of between 5 and 10 microns in length with uniform width (~25 nm) from TAO tiles.**
- **The fibers result from annealing reactions containing two tile types, A and B\*, in which the B\* tiles carry a dsDNA stem orthogonal to the tile plane and terminating with a thiol (SH) group on the end of both protruding strands.**
- **It appears that the thiols associate with other thiols on neighboring tiles and cause a characteristic curling of the lattice resulting in formation of tubes instead of sheets.**
- **An additional dsDNA stem protruding from the “underside” of B\* tiles produces the stripes visible on the outside of the tubes.**

# Using DNA for Targeted Conductive Nanowire Connections



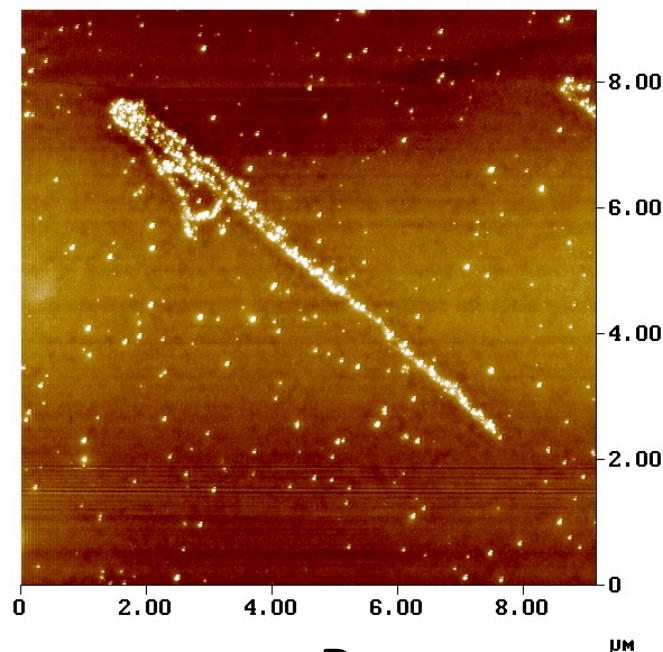


# Targeted Metallization of AB\* Fibers: AFM images of progressive metallization of AB\*(SH)<sub>2</sub>(NH<sub>2</sub>) Fibers.



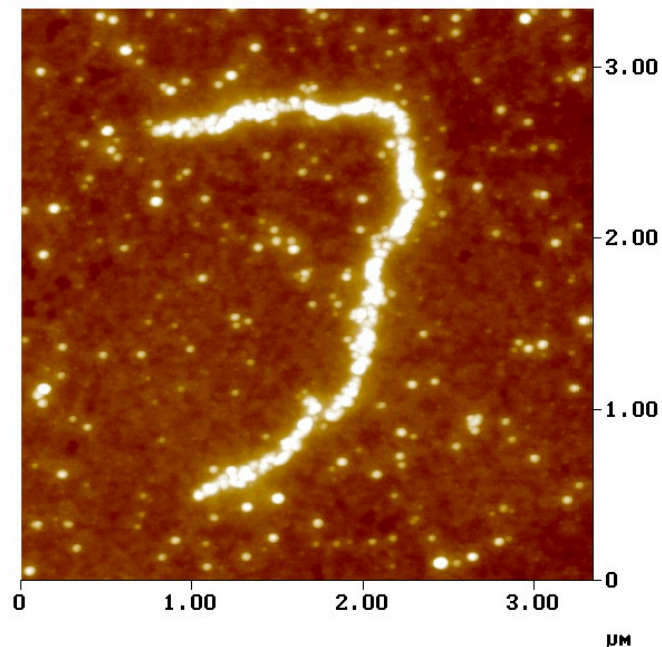
A

**Monofunctional  
nanogold (1.4 nm)  
bound to NH<sub>2</sub> groups  
on surface of fibers.**



B

**Silver Enhanced  
staining deposited  
silver on the bound  
gold (2 minutes).**



C

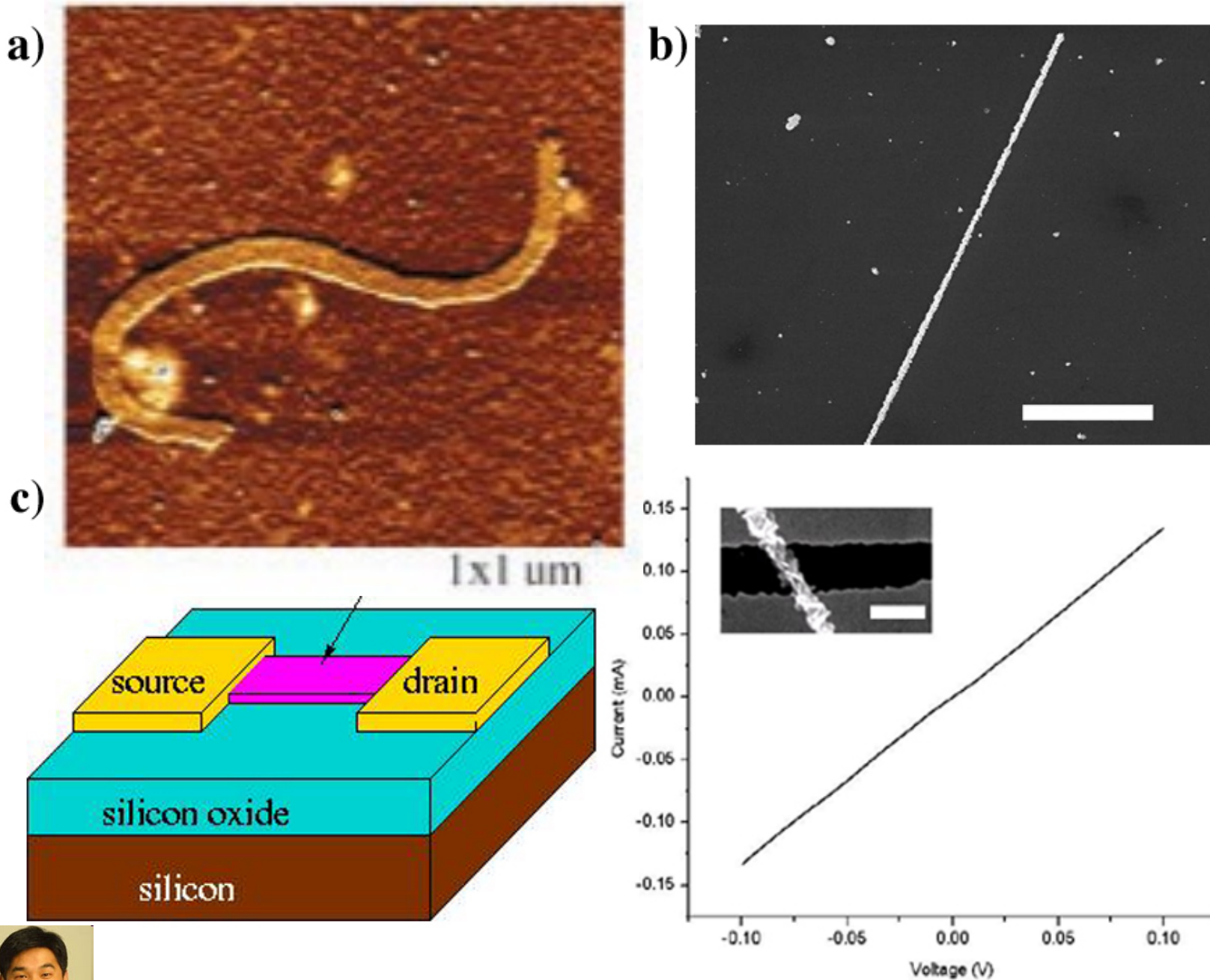
**Silver Enhance staining  
(5 minutes). Note  
nearly continuous metal  
wire.**

# Procedure of Electrical Measurement of DNA-Based Metallized Nanotubes

Process of experimental Setup for measuring conductivity of DNA-based devices

- Compact electronic circuit may be possible using nanometer-scale DNA nanotubes
- Position controllable using carefully designed DNA bases

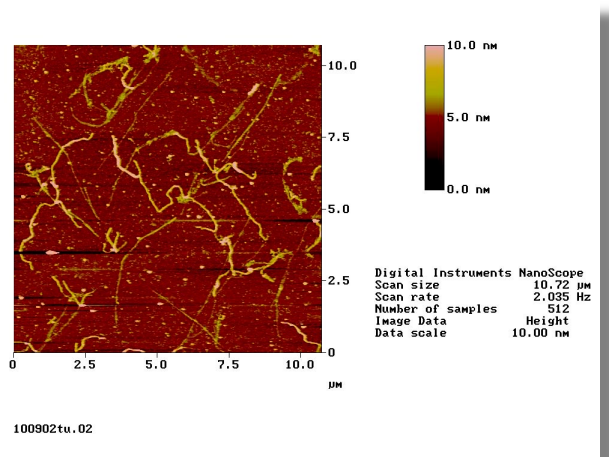
# Silver (Au) Metallization of 4x4 DNA Lattice ribbon and Conductivity Measurement



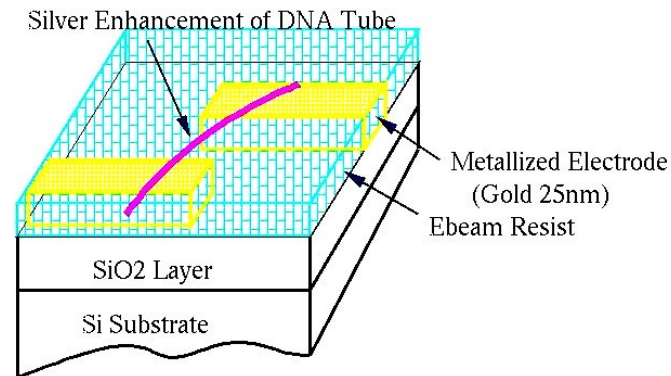
Hao Yan, Sung Ha Park, Liping Feng, **John Reif**, and Thomas H. LaBean, *Science* (2003)

# Two Processes of Conductivity Measurement for Metallized DNA Nanotubes

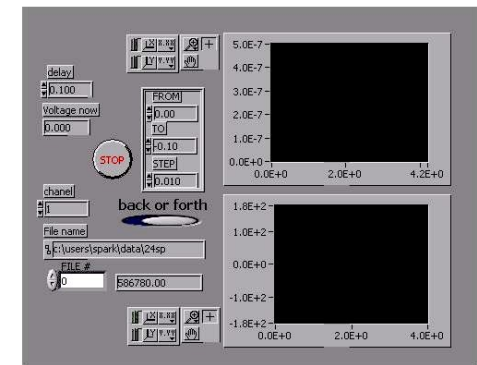
*Random Deposition Nanotubes with Electron Beam Lithography  
process*



(a)

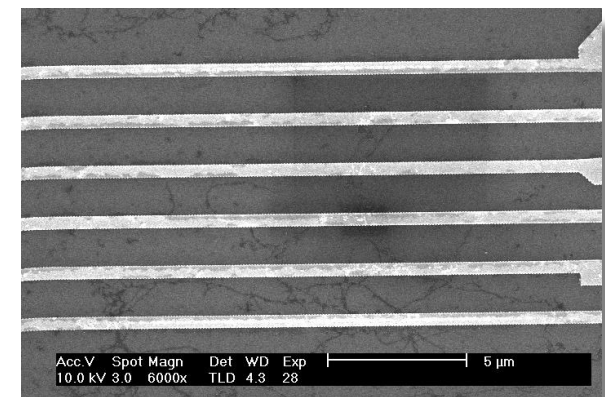


(b)

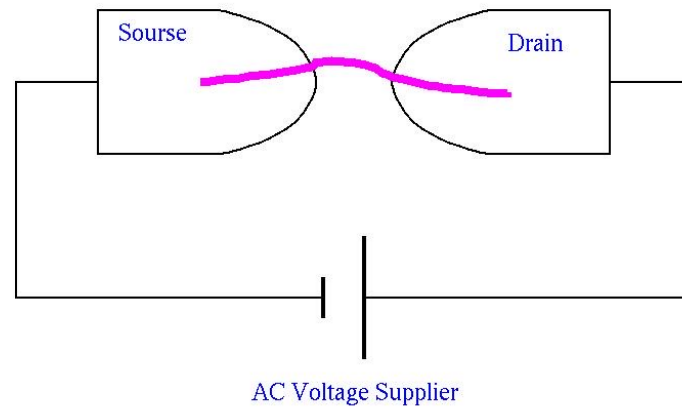


(c)

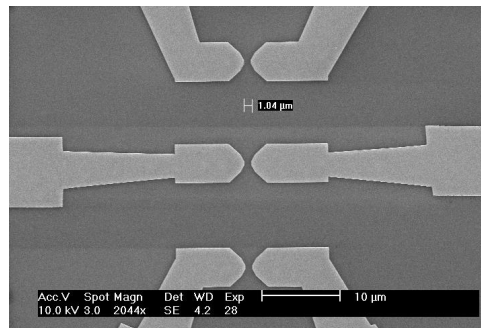
- (a) Preparation Metallized DNA Tubes on Silicon Substrate
- (b) Electron Beam Patterning
- (c) Electric Measurement using LabView Interface



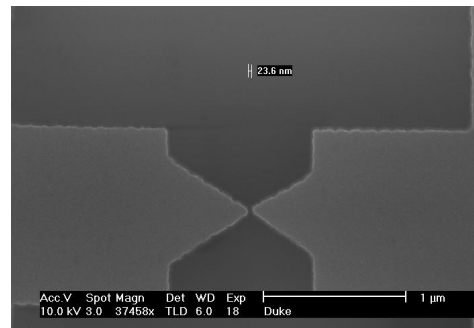
# Trapping DNA Nanotubes using AC Voltage



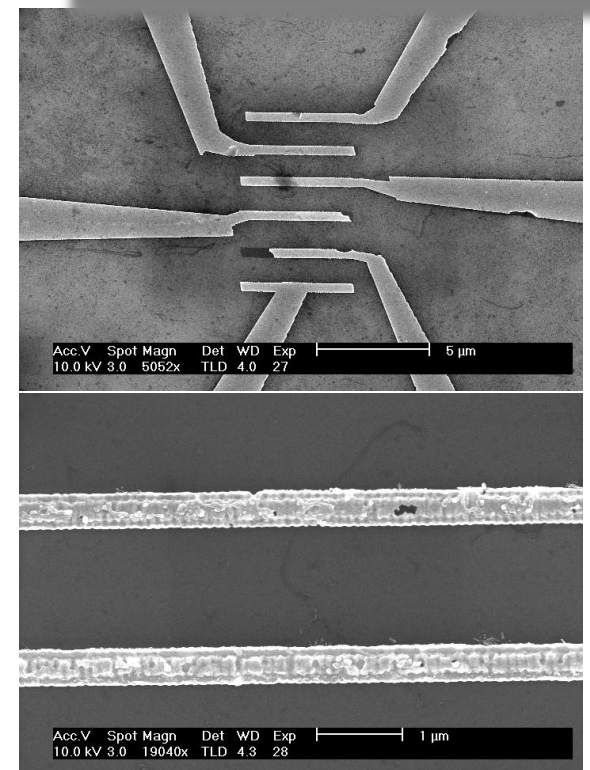
**(a) Preparation of Metal Electrodes**



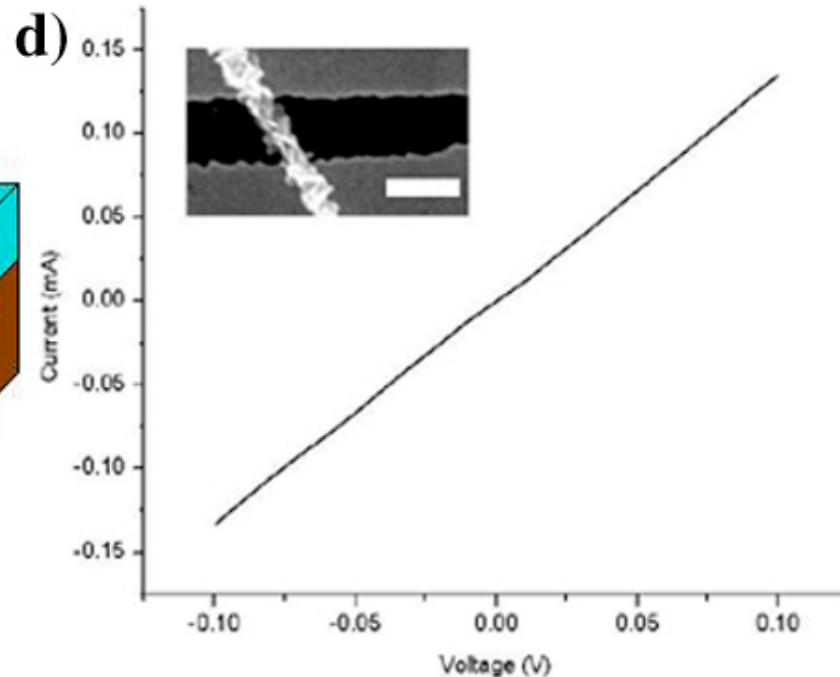
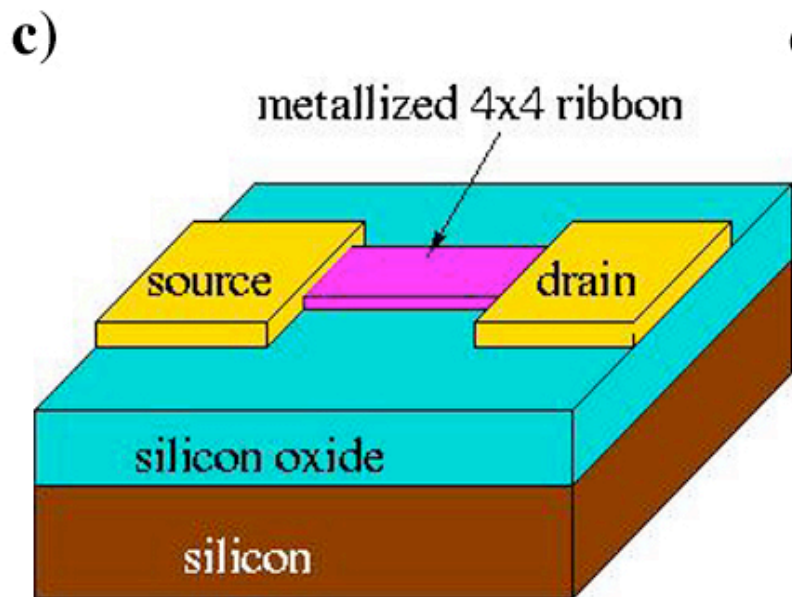
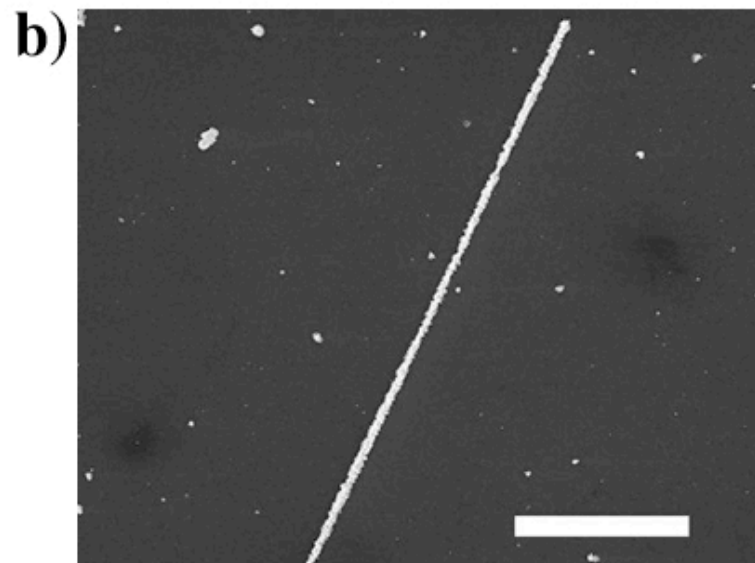
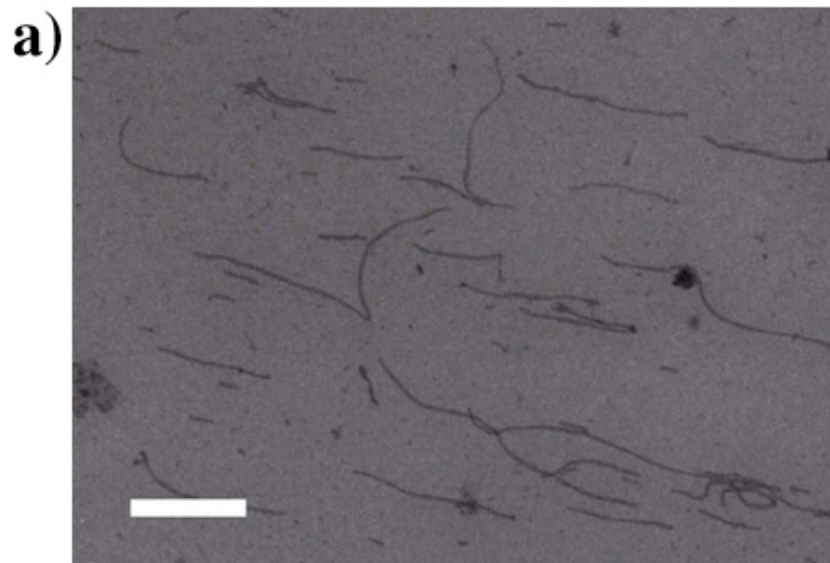
**(b) Trapping Tubes ; Apply AC Voltages (e.g., 1V, 50kHz, 30sec)**



**(c) After Trapped Tubes**



# 2-Step procedure Au Metallization of 4x4 ribbon and Conductivity Measurement



# Patterned DNA Lattices

# Directed Nucleation Assembly:

A method for assembly of complex patterns

- Use artificially synthesized DNA strands that specify the pattern and around which 2D DNA tiles assemble into the specified pattern.
- The permanent features of the 2D pattern are generated uniquely for each case.

# Directed Nucleation Self Assembly Steps:

- an input DNA strand is synthesized that encodes the required pattern
- then specified tiles assemble around blocks of this input DNA strand, forming the required 1D or 2D pattern of tiles.

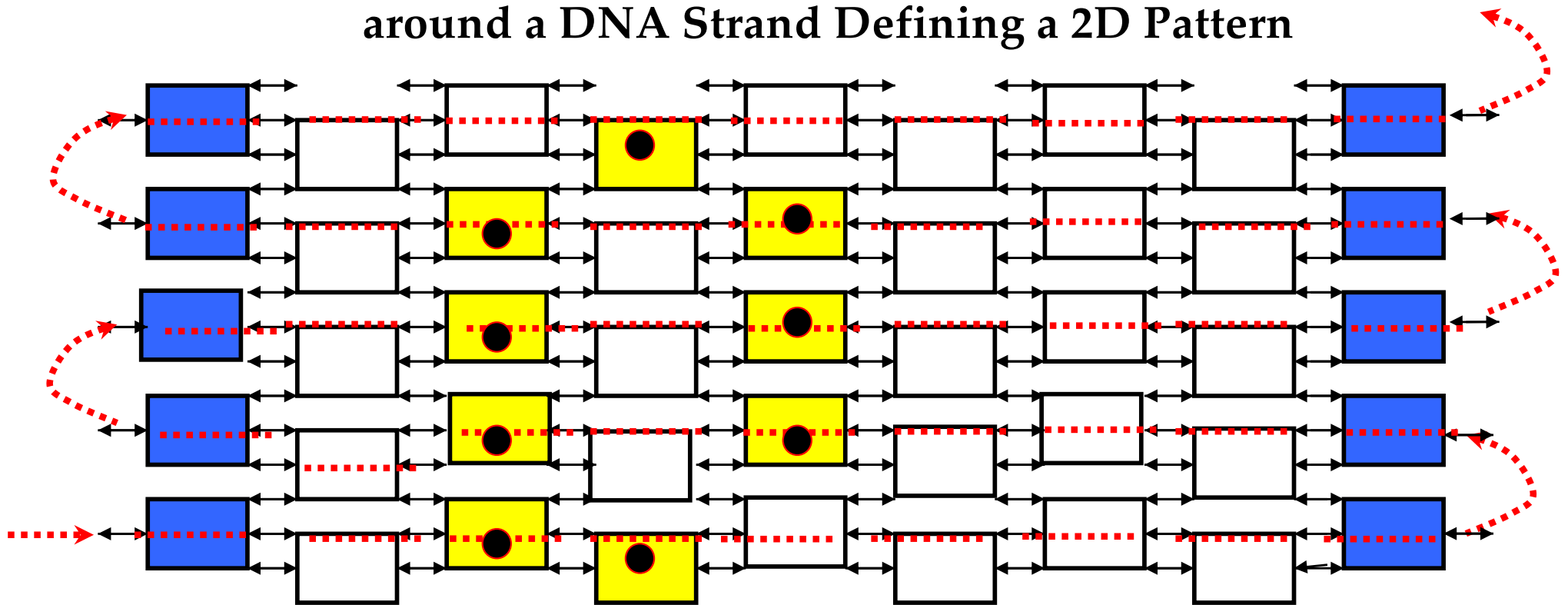


# 2D DNA Self-Assembled Tiling

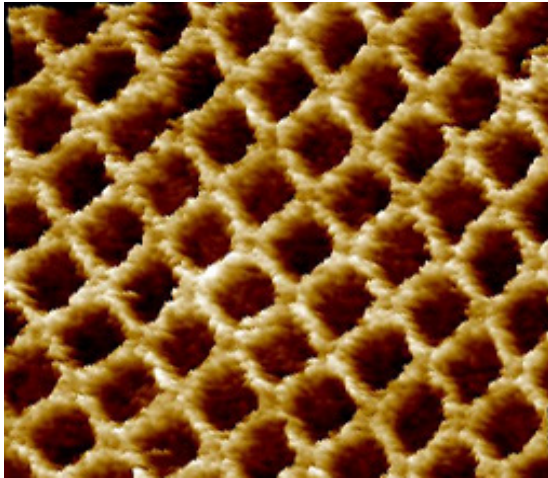
## The Process of Assembling a 2D Pattern by Directed Nucleation:

### Self Assembly of Tiles

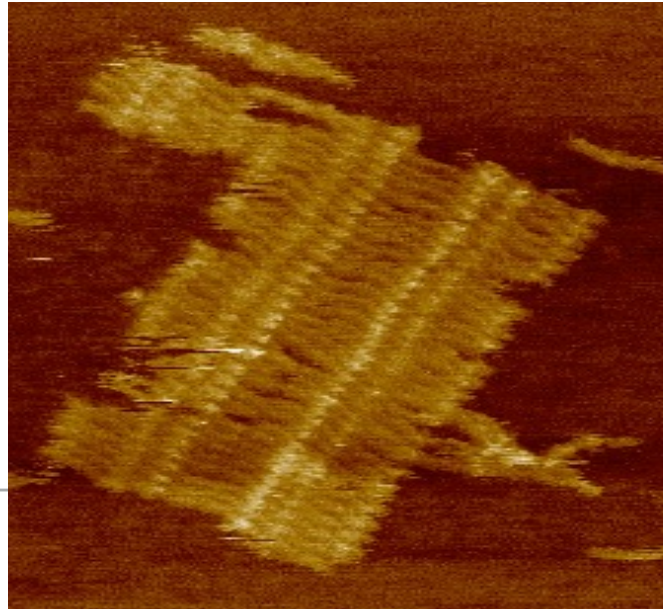
around a DNA Strand Defining a 2D Pattern



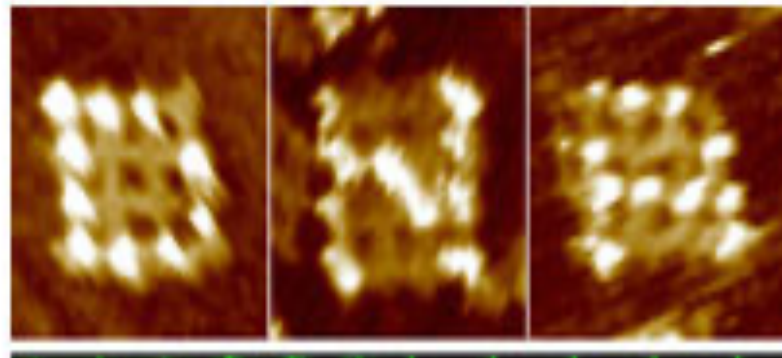
# Programmable Patterned DNA Nanostructures



**NOT Patterned**

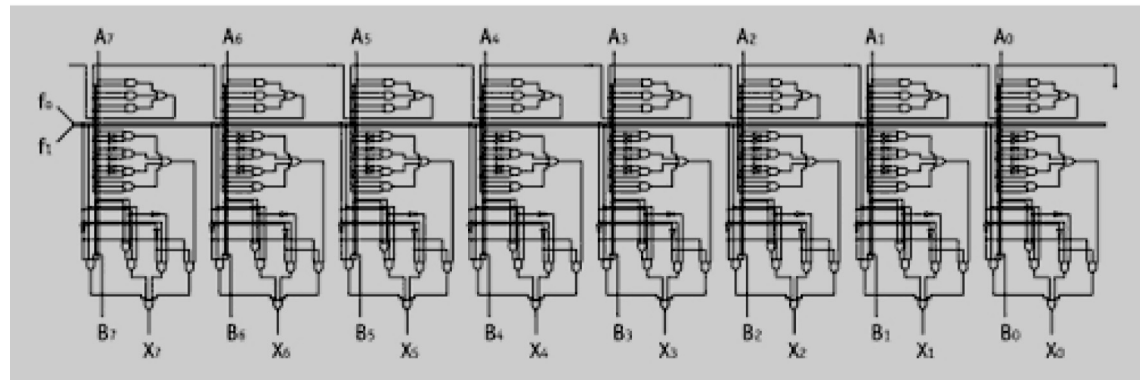
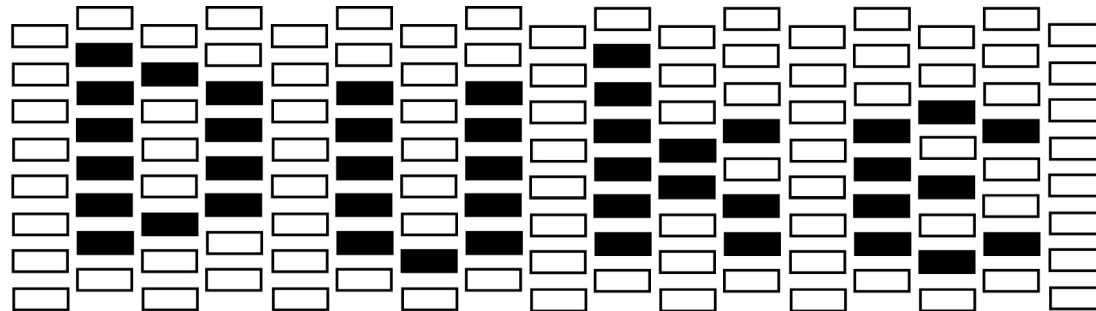


**Patterned**



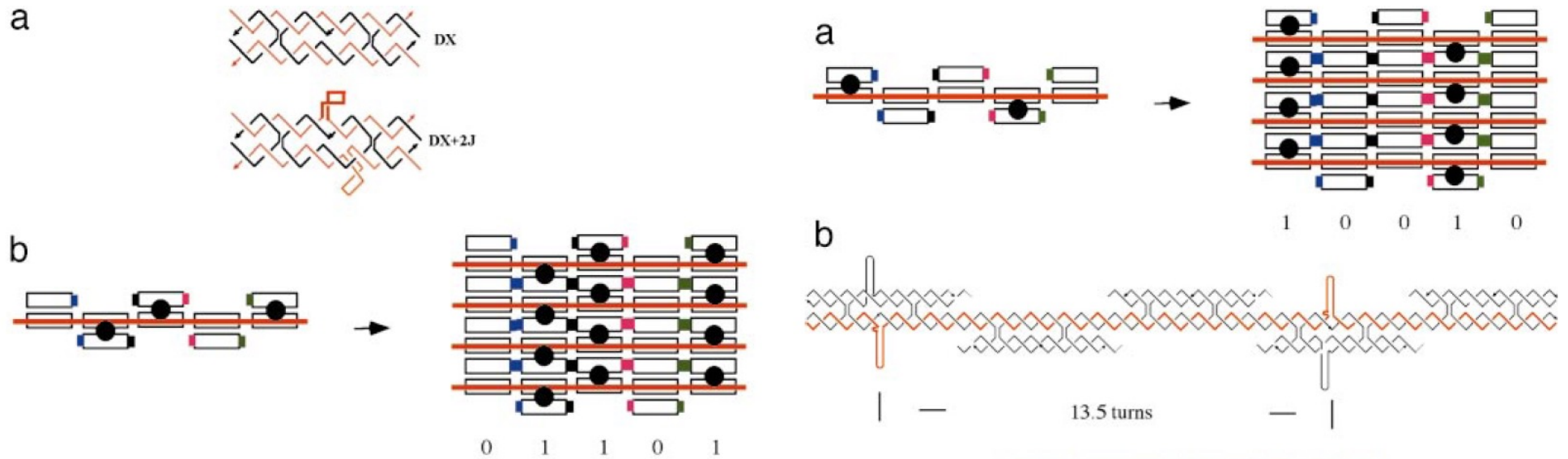
# Patterned DNA lattices:

- 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).*

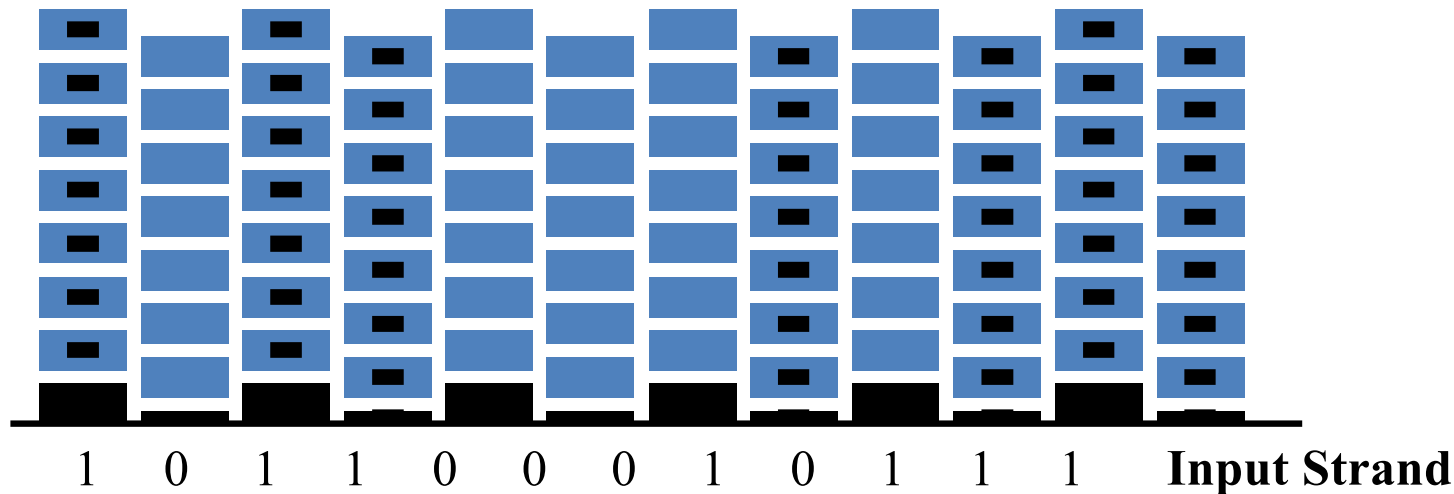
- Multiple tiles of an input layer can be assembled around a single, long DNA strand we refer to as a **scaffold strand** (shown as black lines in the figures).



Hao Yan



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



### ▪Extends 2D arrays into simple aperiodic patterning:

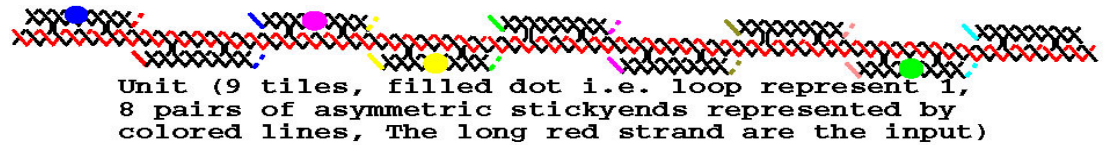
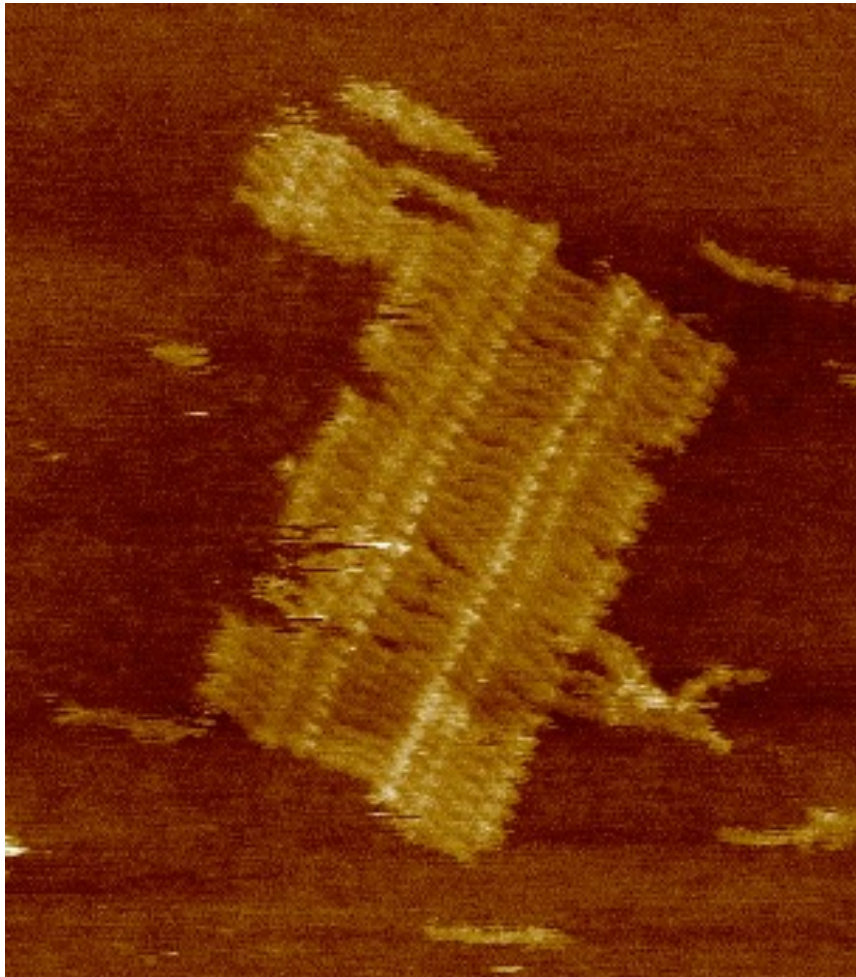
- The pattern of 1s and 0s is propagated up the growing tile array.
- The 1-tiles are decorated with a DNA stem-loop pointing out of the tile plane (black rectangle) and 0-tiles are not.
- Columns of loop-tiles and loopless-tiles can be distinguished by AFM as demonstrated with periodic AB\* lattice.

# Barcode Lattice for Rendering 1 D Patterns:

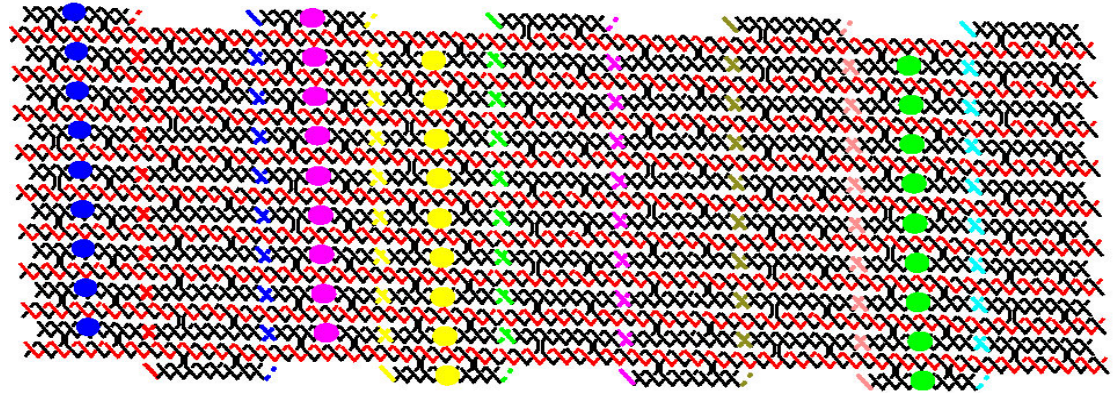
*H Yan, T LaBean, L Feng, J. Reif, PNAS (2003).*



Hao Yan

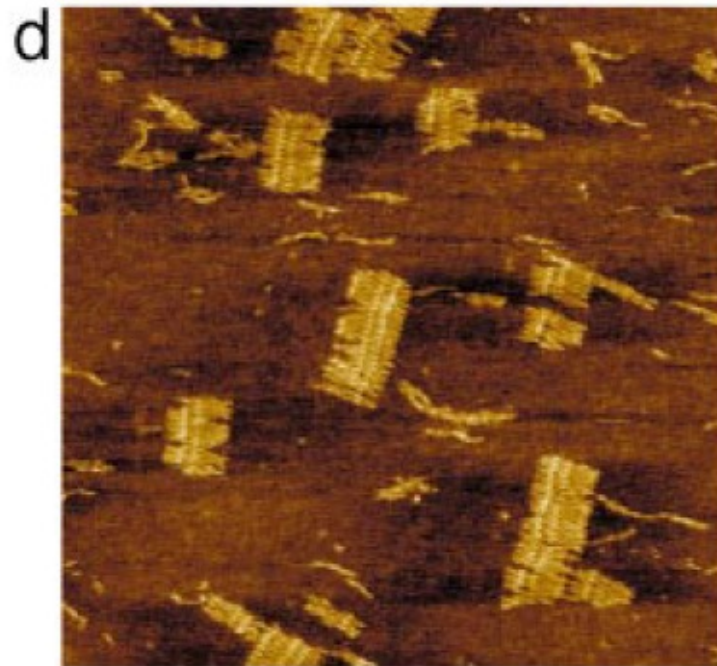
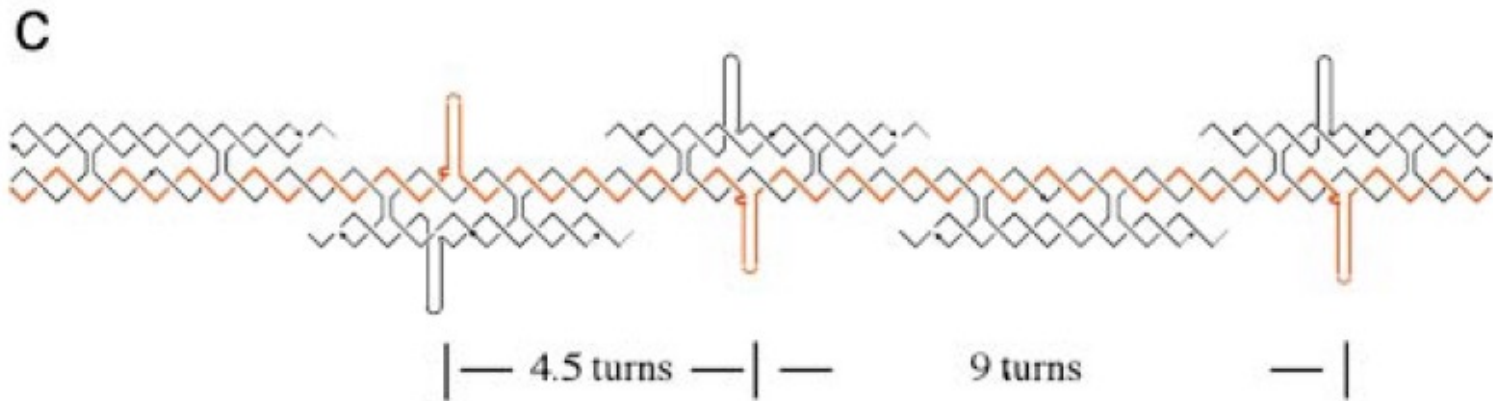


Unit (9 tiles, filled dot i.e. loop represent 1, 8 pairs of asymmetric stickyends represented by colored lines, The long red strand are the input)

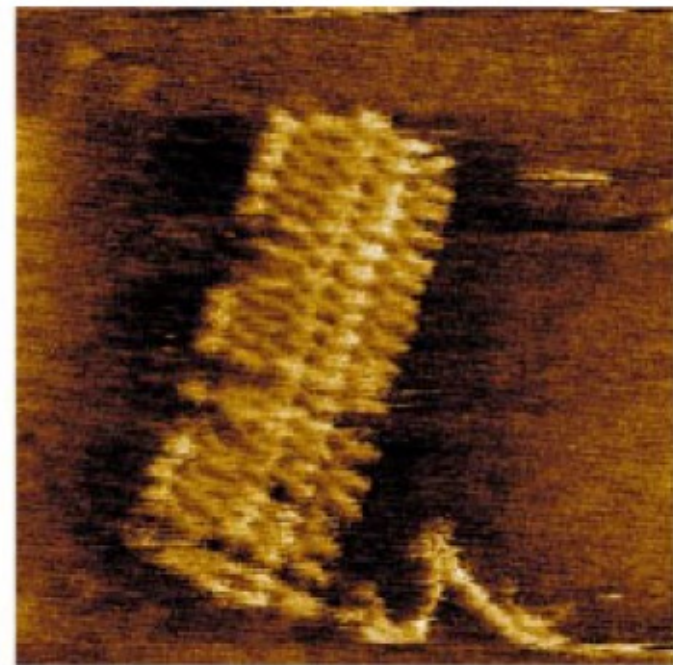


**Barcode lattice displays banding patterns dictated by the same sequence of bit values programmed on each layer.**

# Barcoded lattices



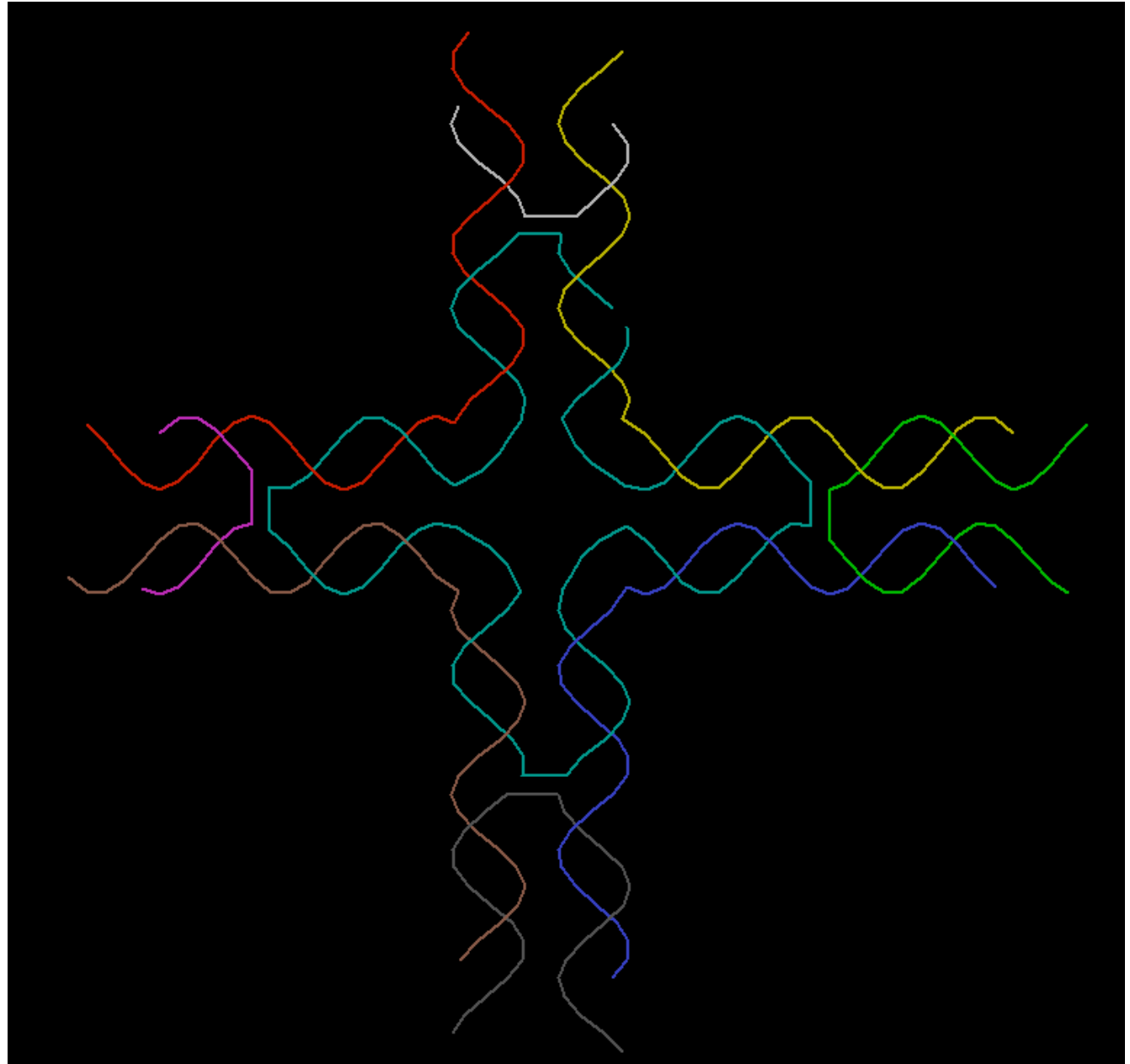
800x800nm



250x250nm

# Cross Tiles and their DNA Lattices

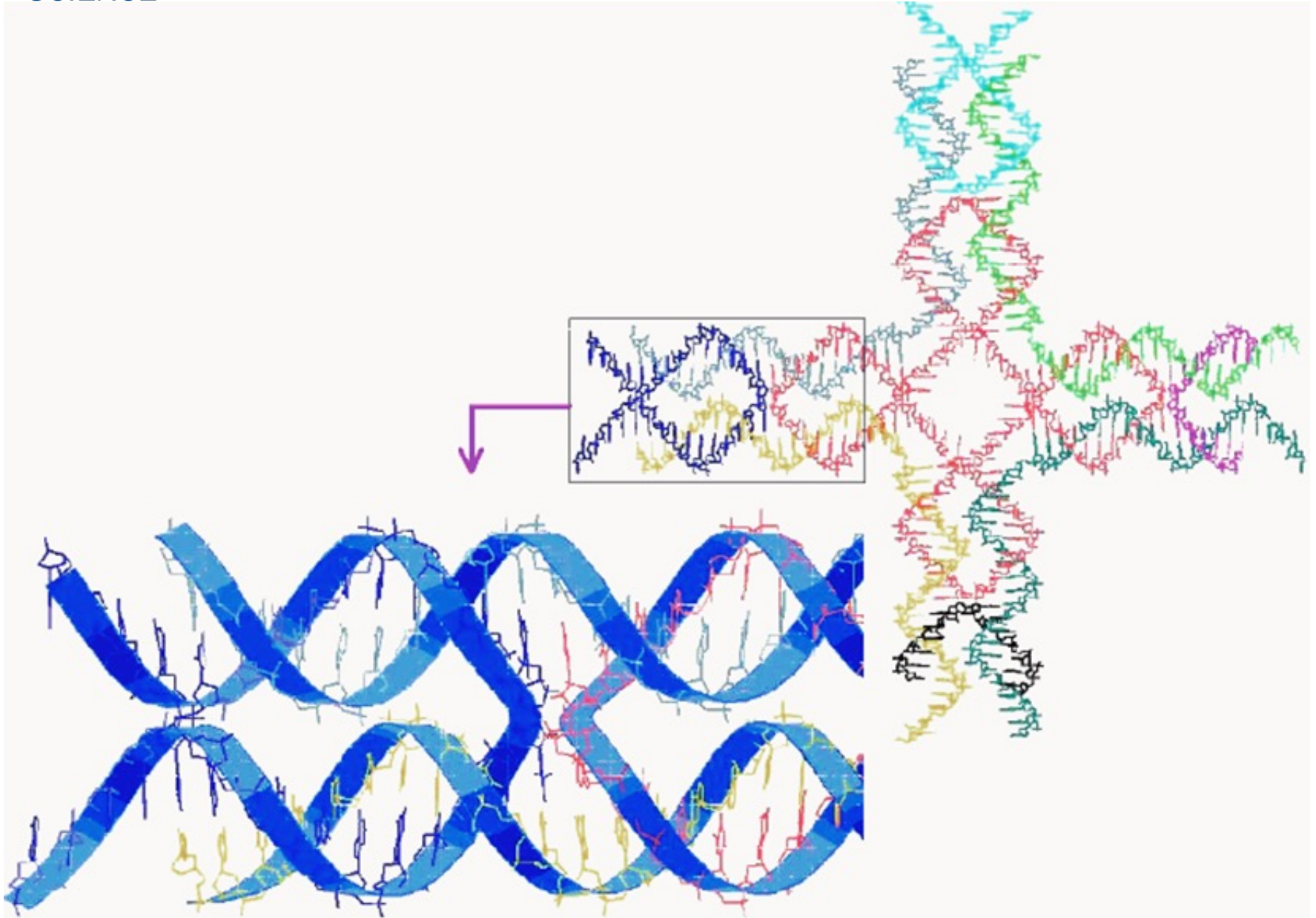
**DNA Cross  
Tile**

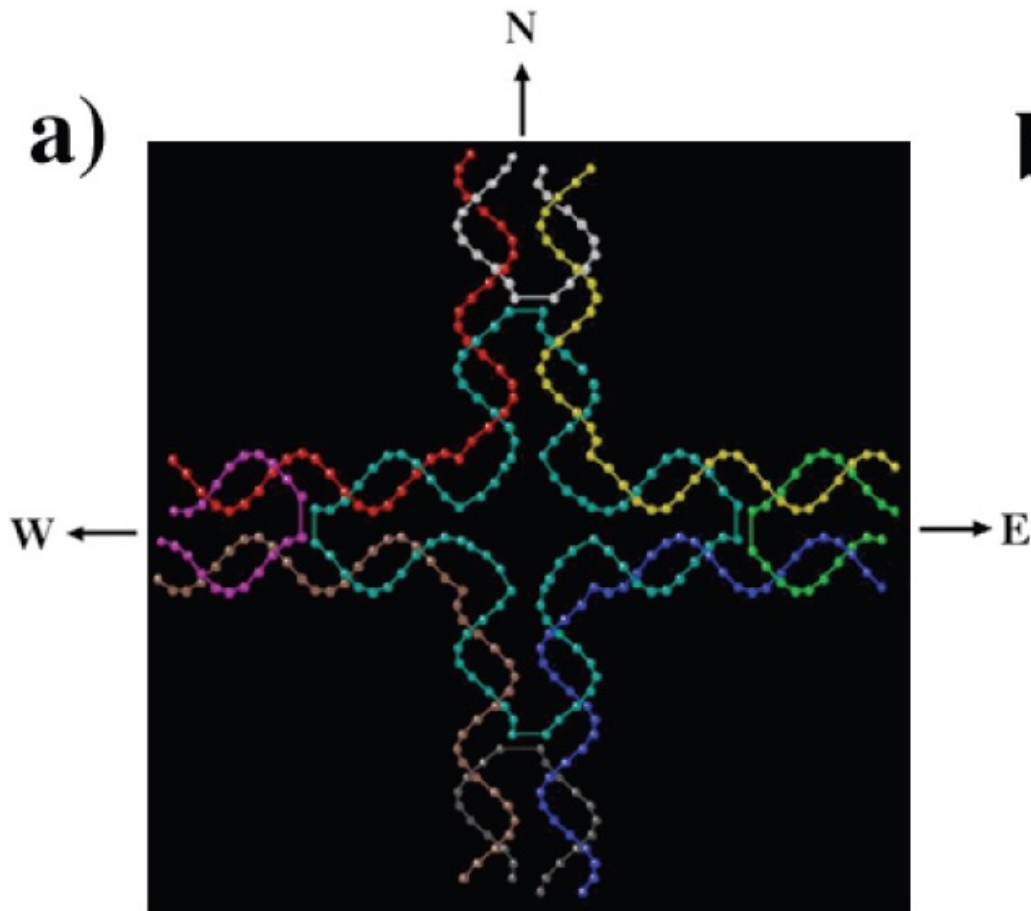




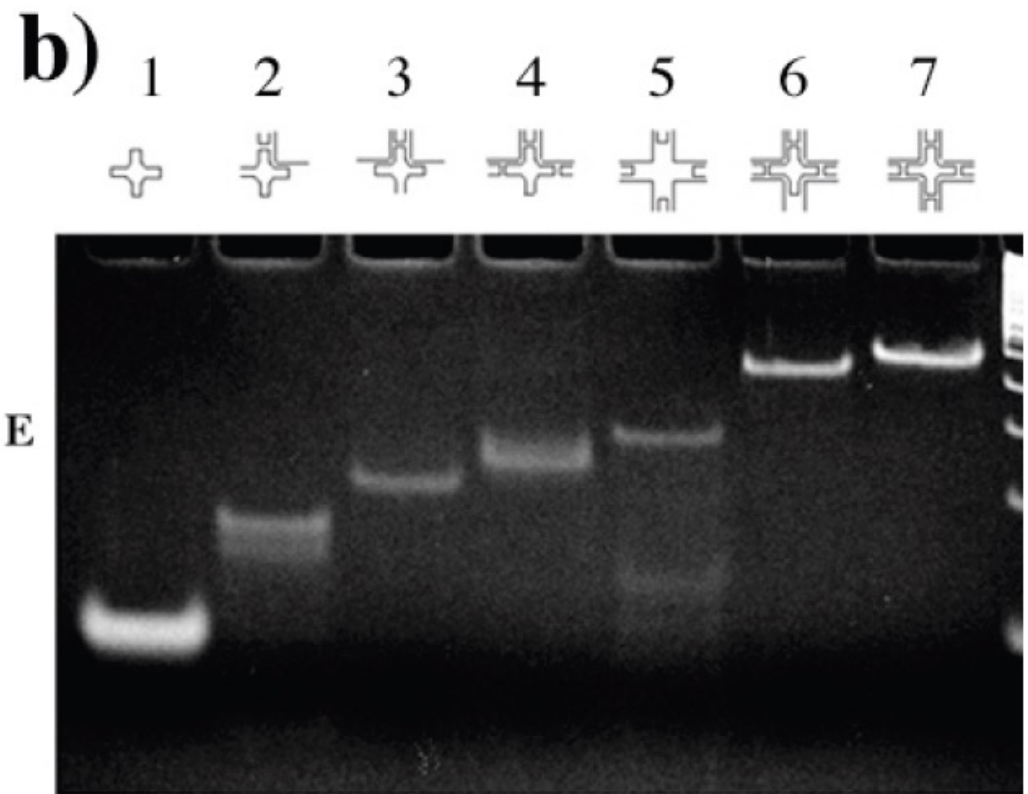


# DNA Cross Tile



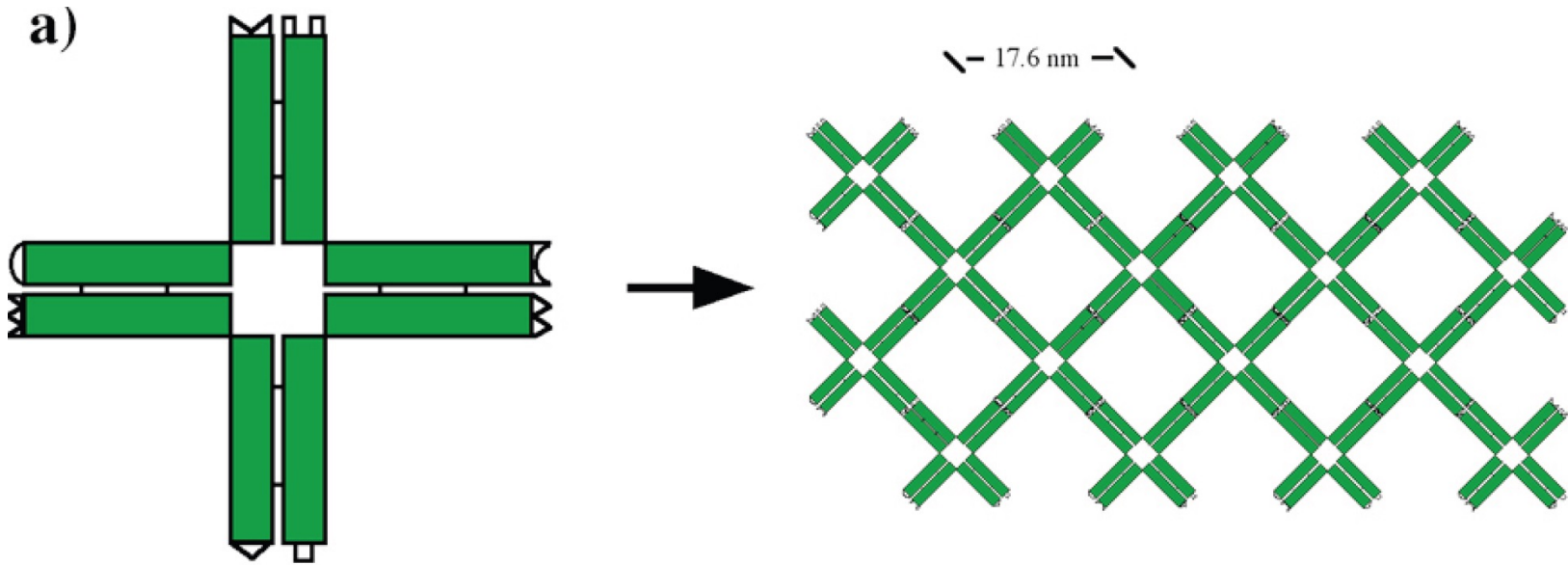


**DNA Cross Tile**

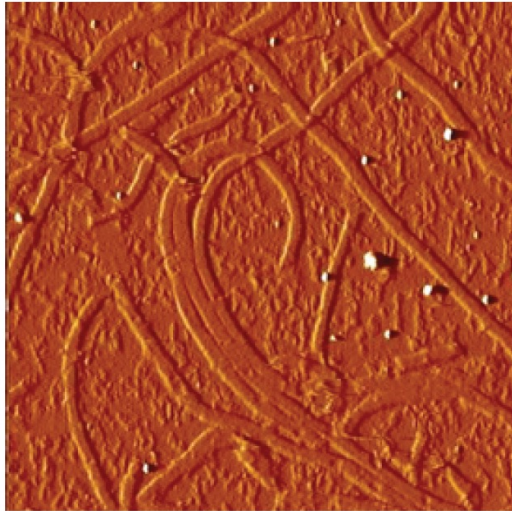


**Gel Electrophoresis  
Data**

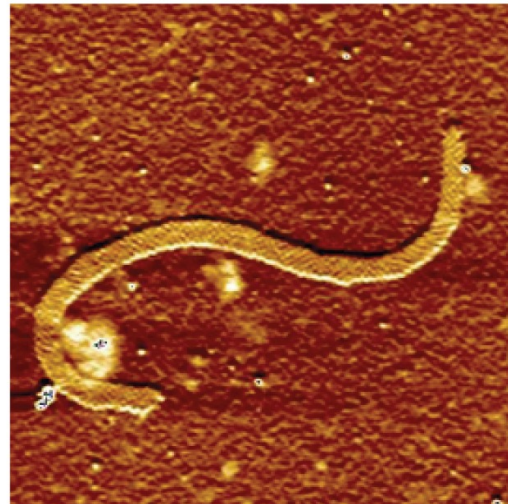
# Uncorrugated cross tile tubes



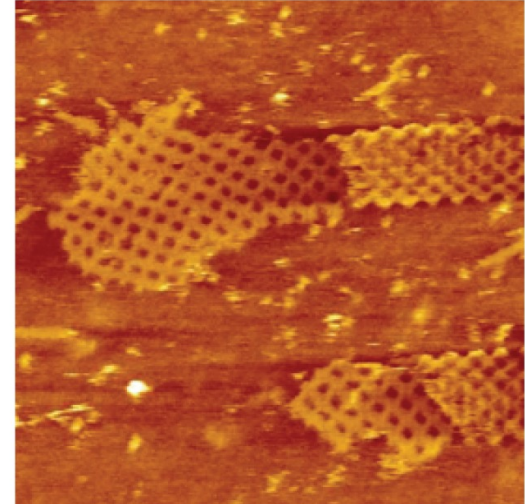
b)



3x3  $\mu\text{m}$

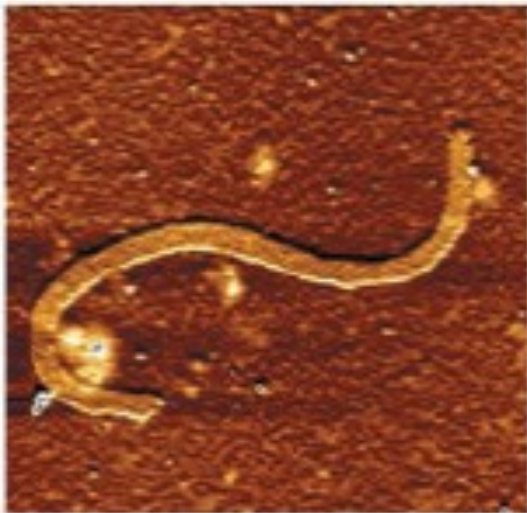
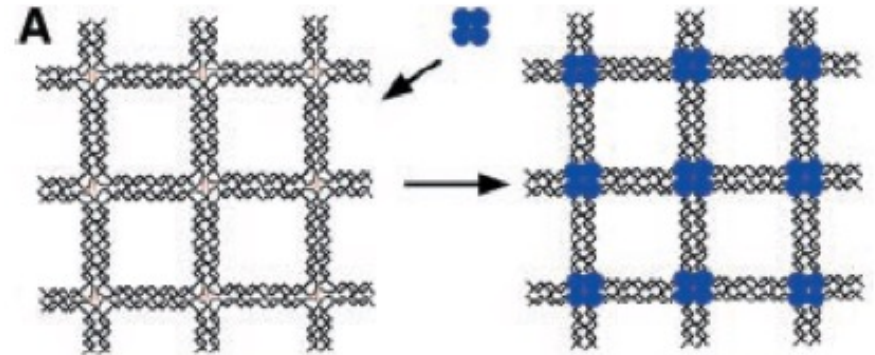
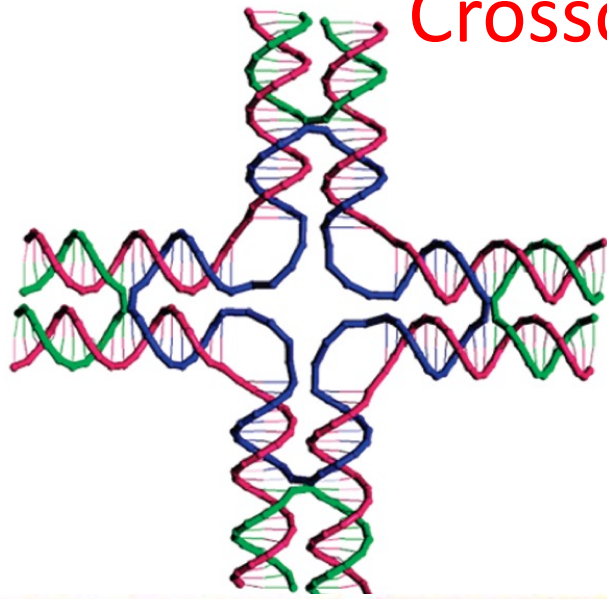


1x1  $\mu\text{m}$

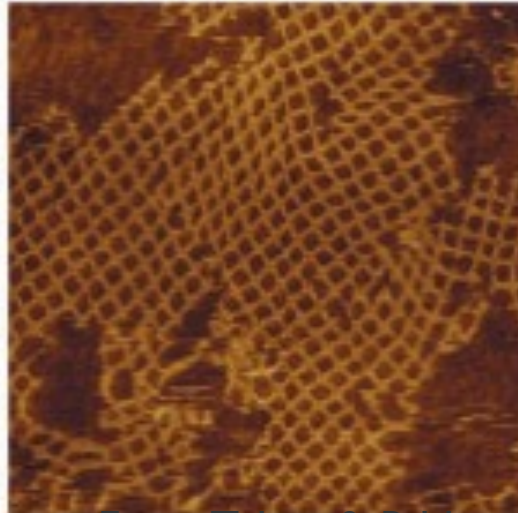


500x500 nm

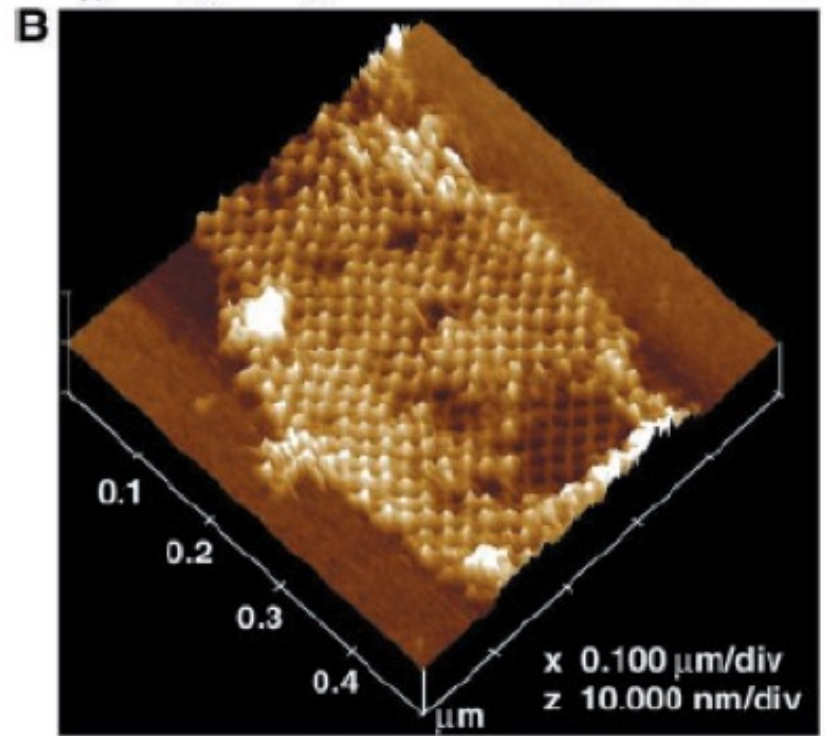
# Crossover DNA Tiles and their Lattices



**Naturally  
form Tube Lattices**



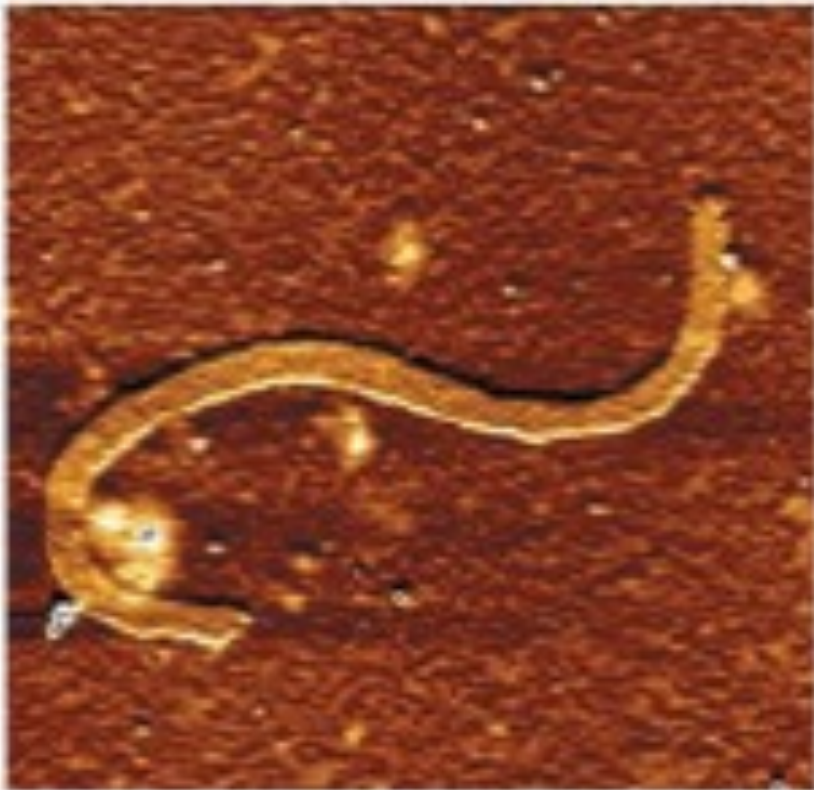
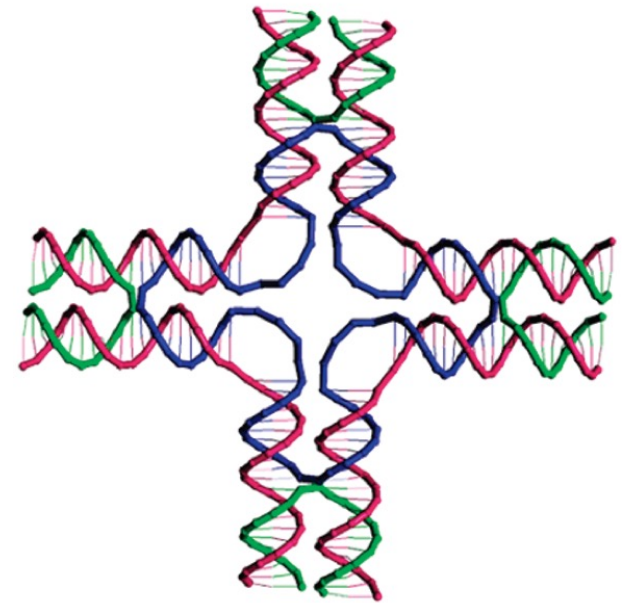
Form Tubes & Ribbons  
**Used Corrugation to  
form 2D Grid Lattices**



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

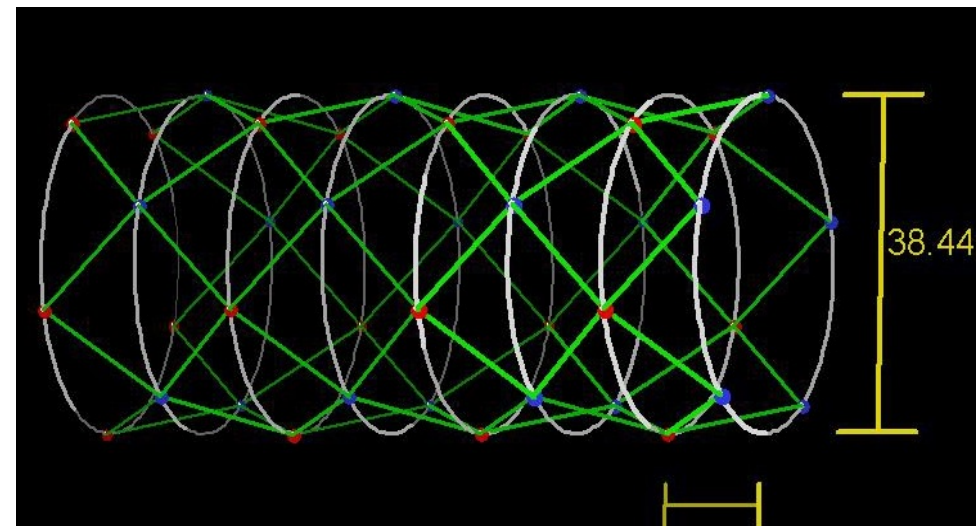
# Crossover DNA Tiles and their Lattices

**Crossover DNA Tiles have some out-of-plate curvature, so naturally form Tube Lattices**

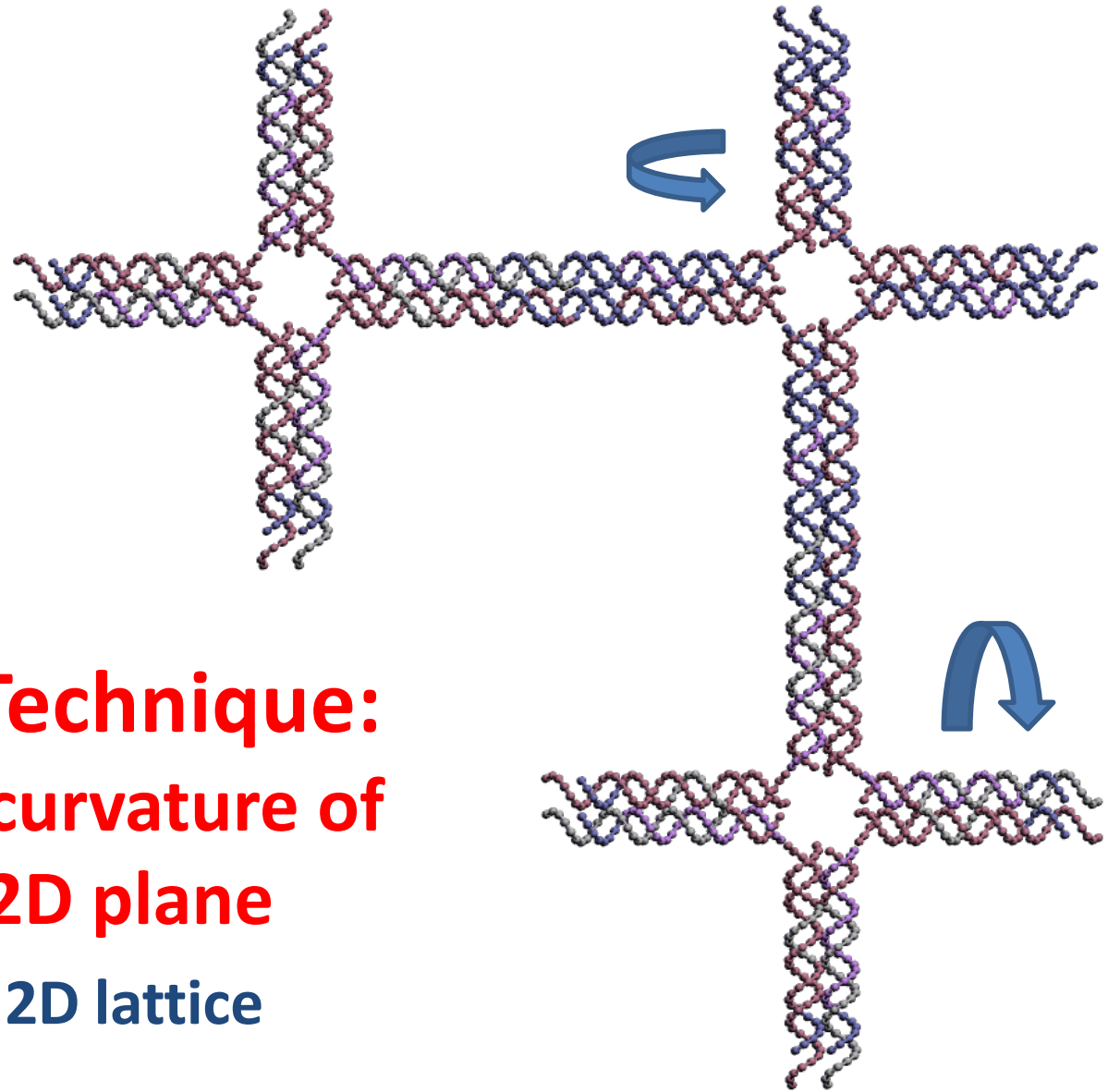


1x1 um

**Tubes Self-Assembled from Uncorrugated Crossover tile:**

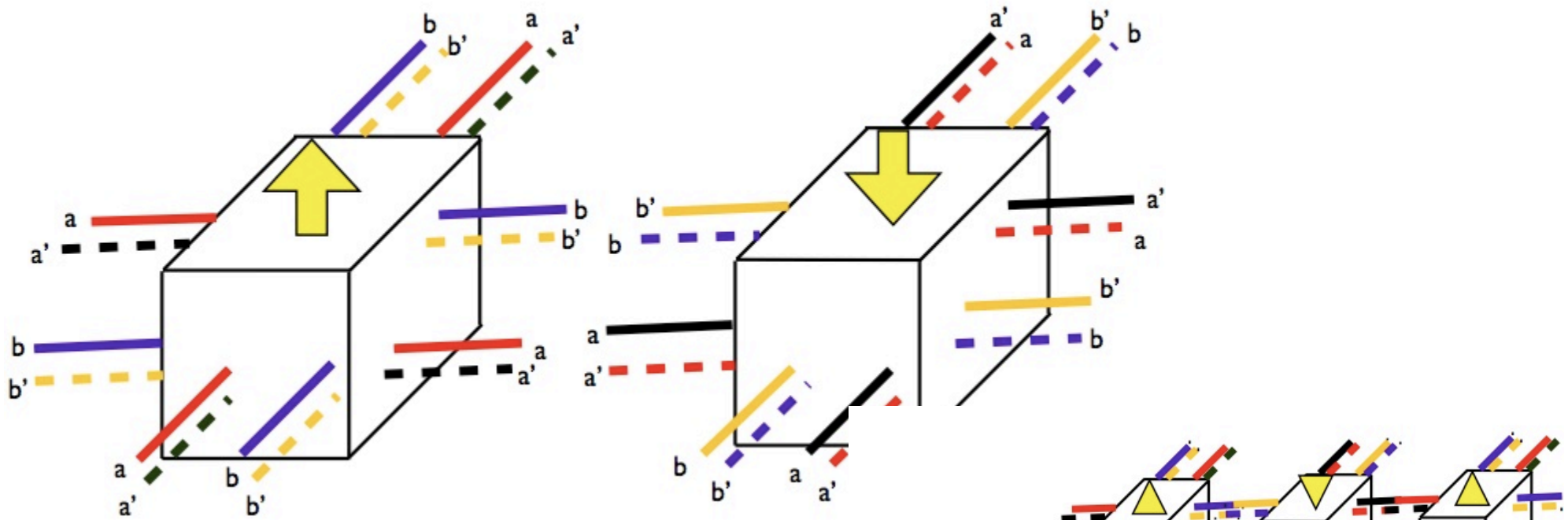


12.08nm

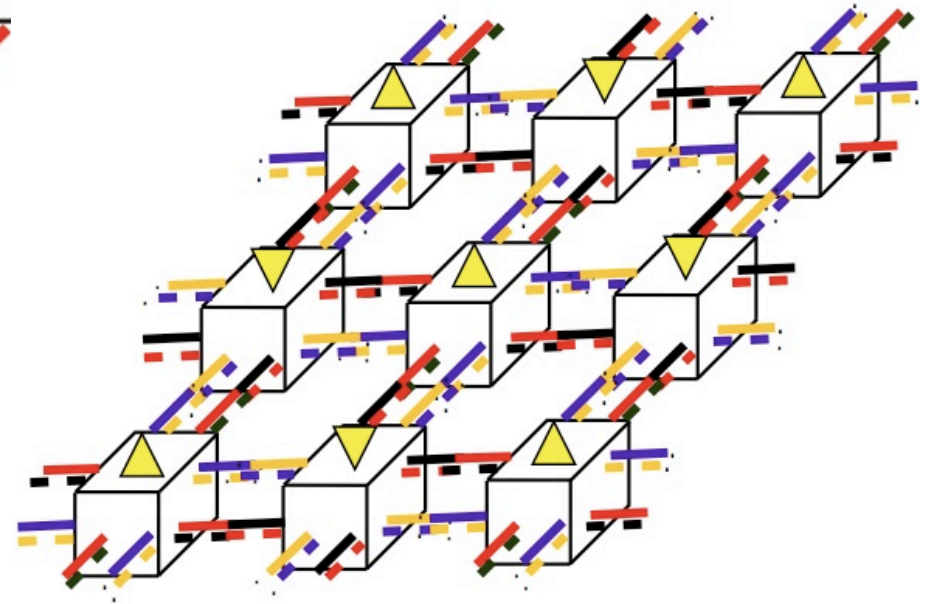


**Corrugation Technique:**  
**Used to cancel curvature of**  
**Tiles out of 2D plane**  
**=> Results in a flat 2D lattice**

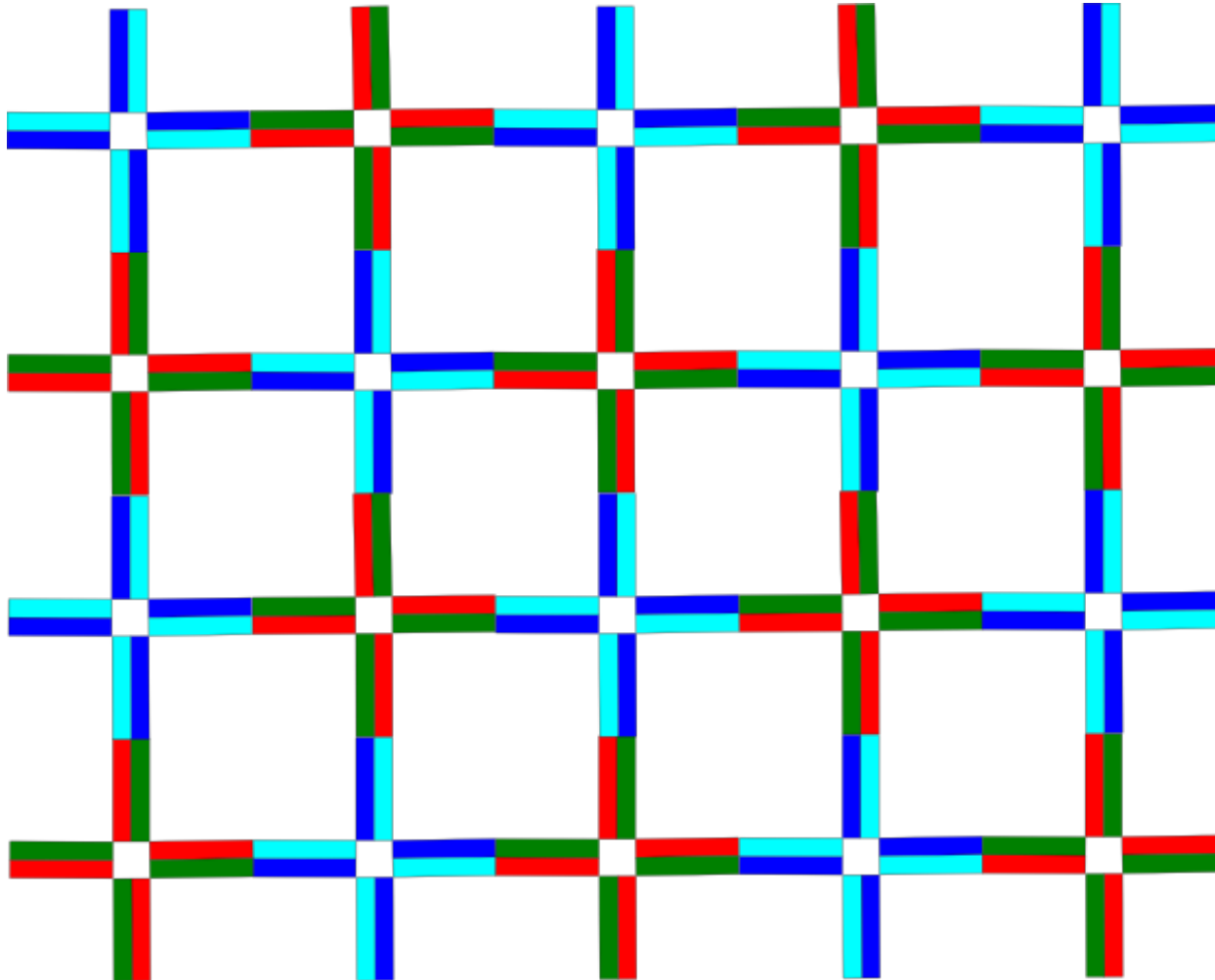
# 2D Corrugation to Cancel Lattice Curvature



## 2D Pad Programming of Crossover Tiles



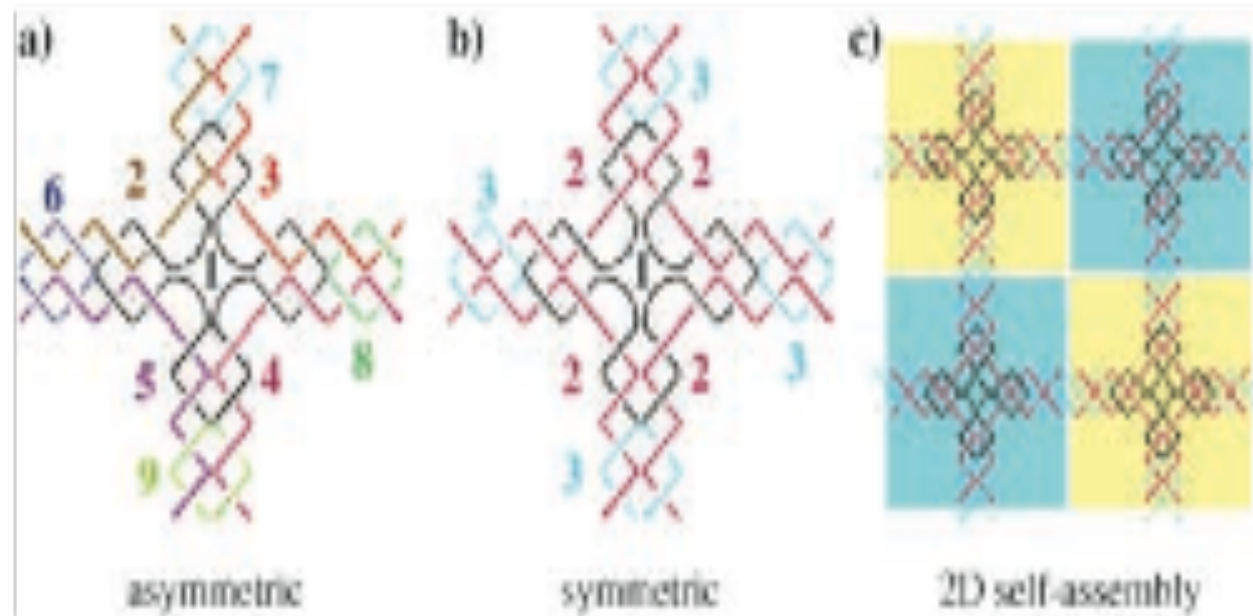
# 2D lattice design



Corrugation

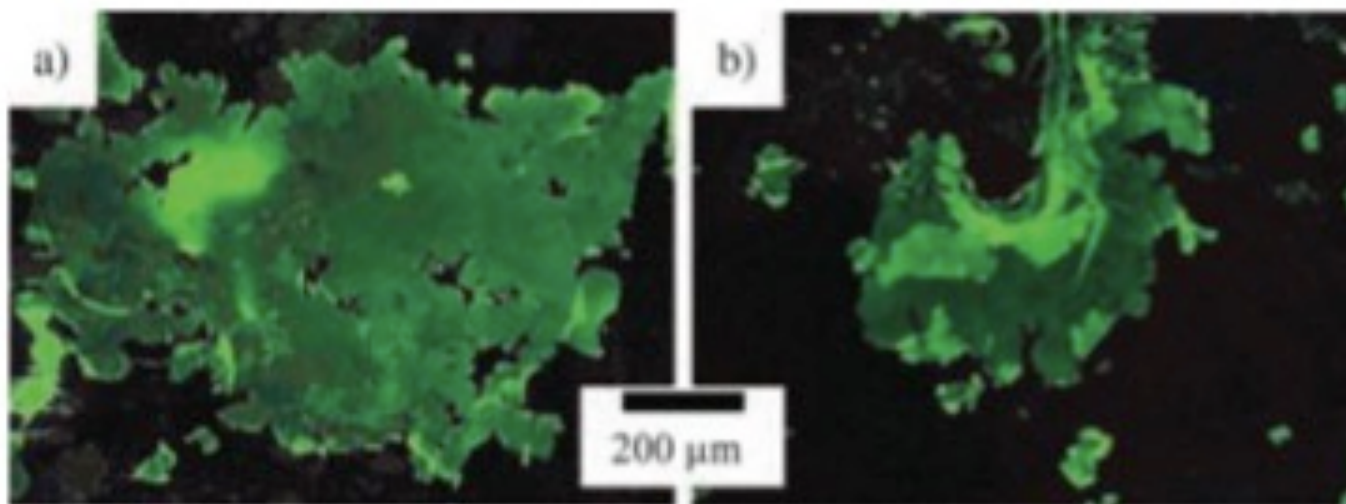


# Cross tiles: Nano-Grid Assembly in 2D



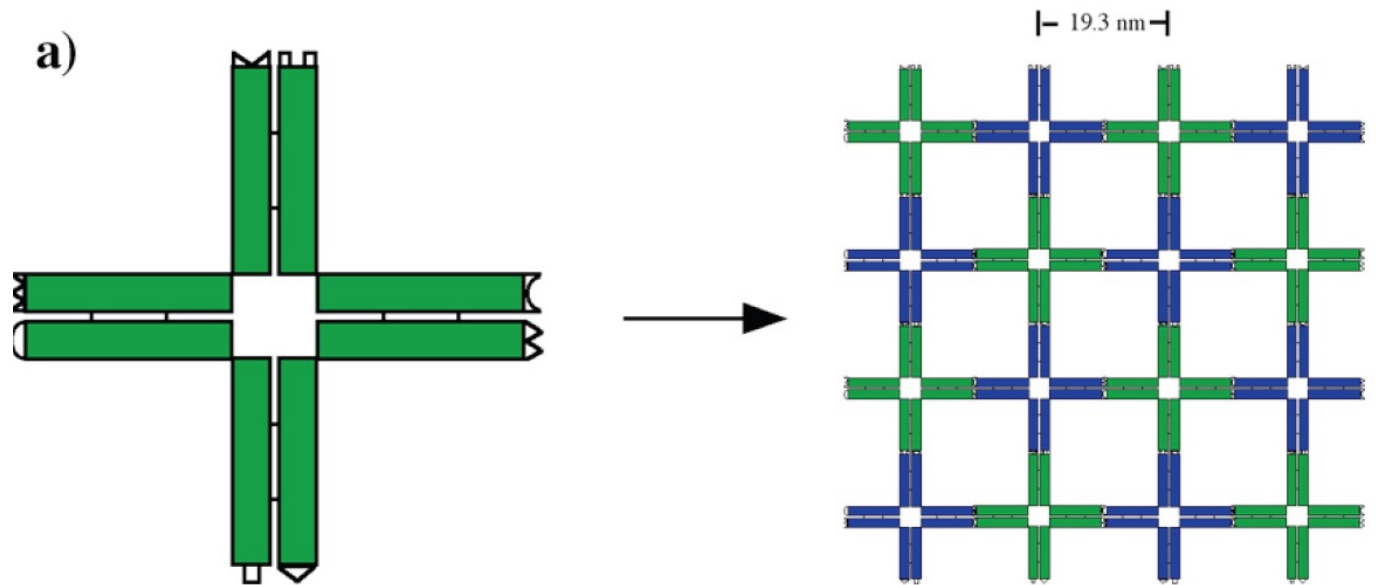
Figures adopted from He et al, 2005

## Symmetric Cross Tiles

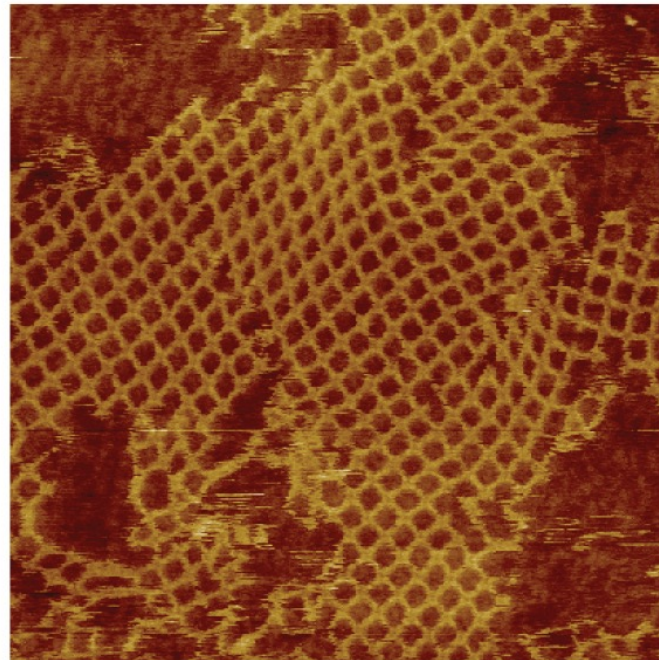


Corrugation allows creation of enormous lattices

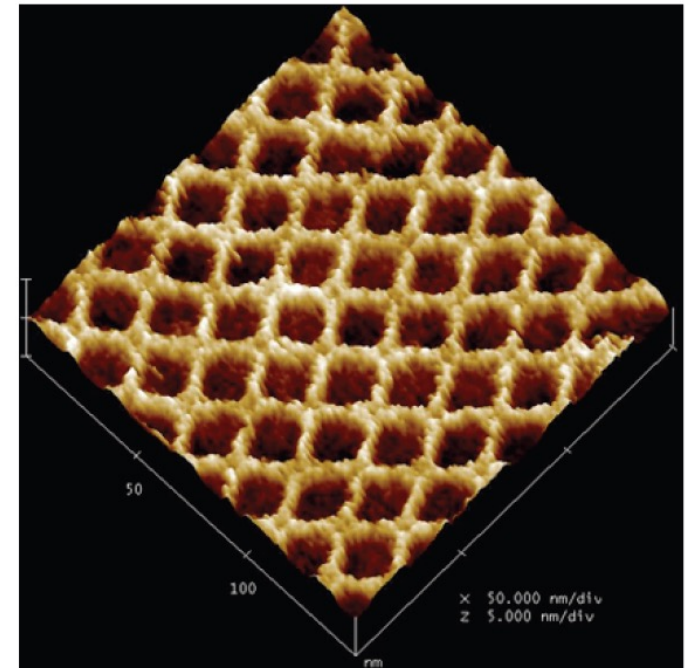
# Corrugated cross tile lattices



b)



500x500nm

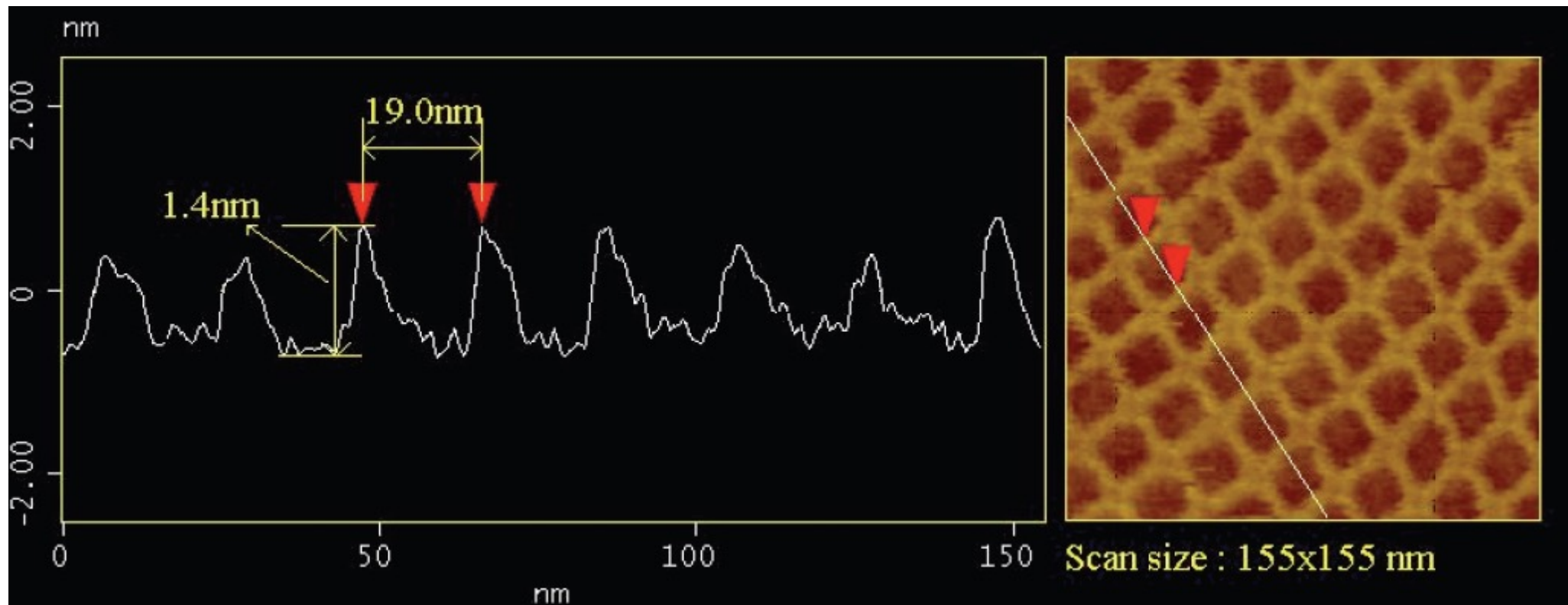


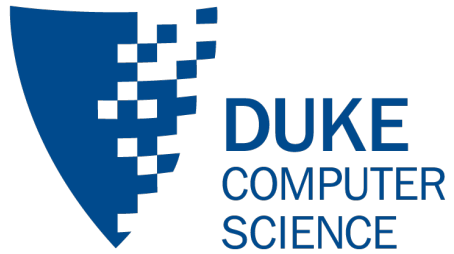
150x150nm

**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 lattices: Highly uniform molecular scale lattices far below VLSI scales

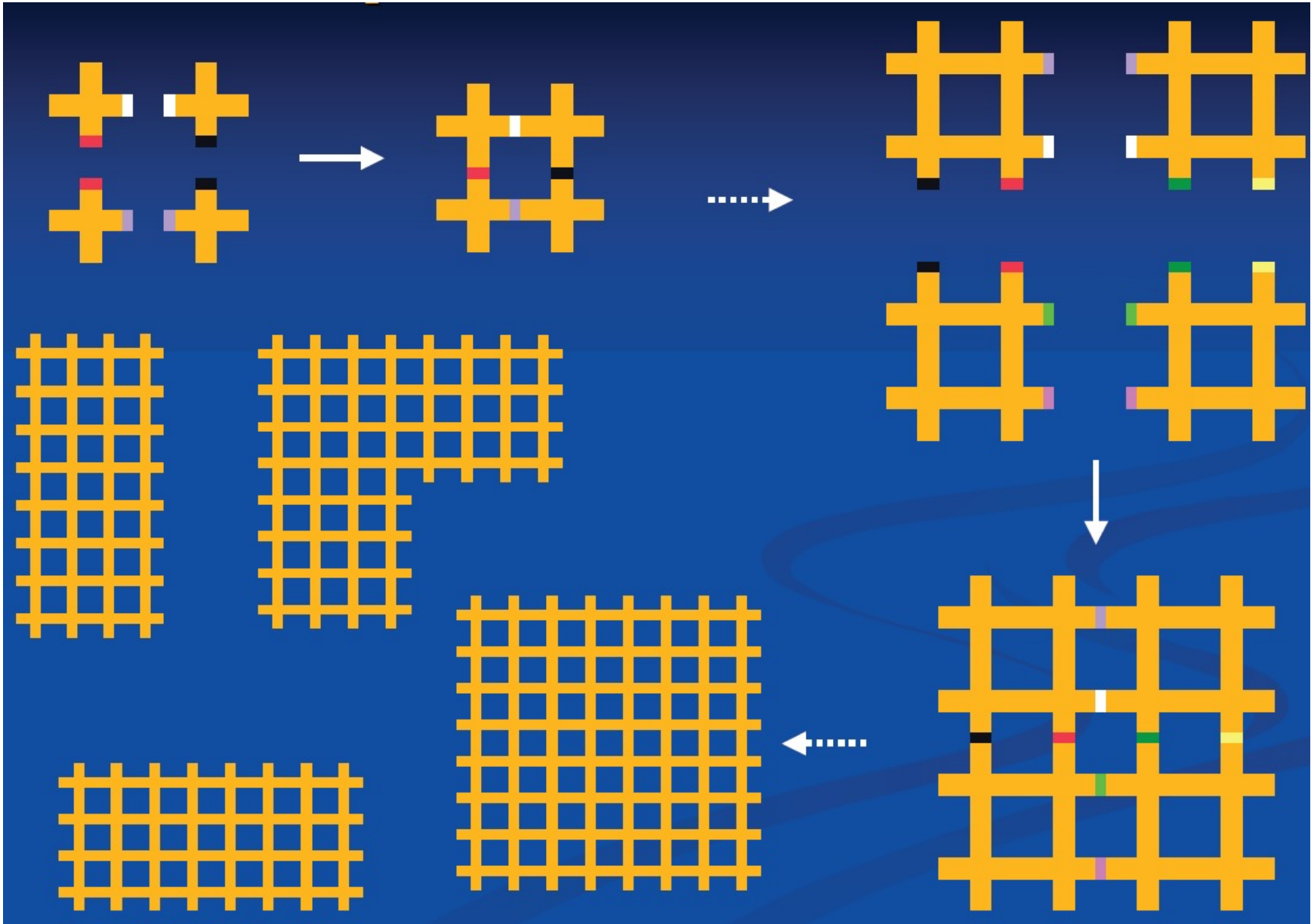




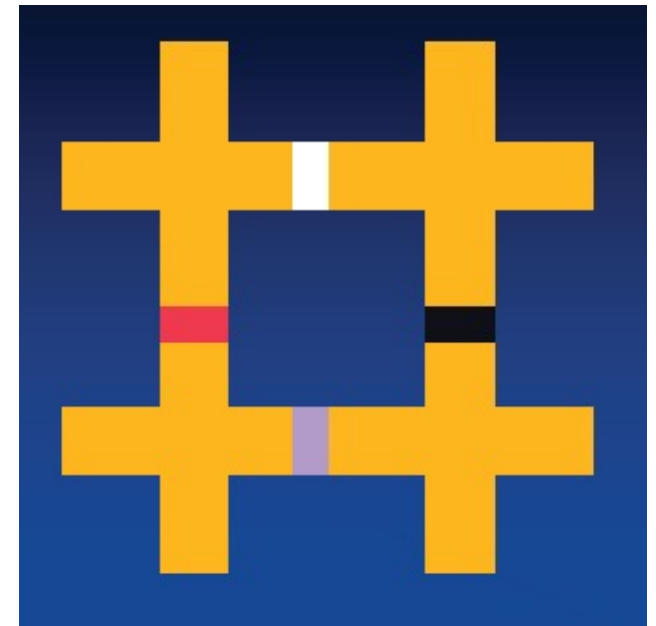
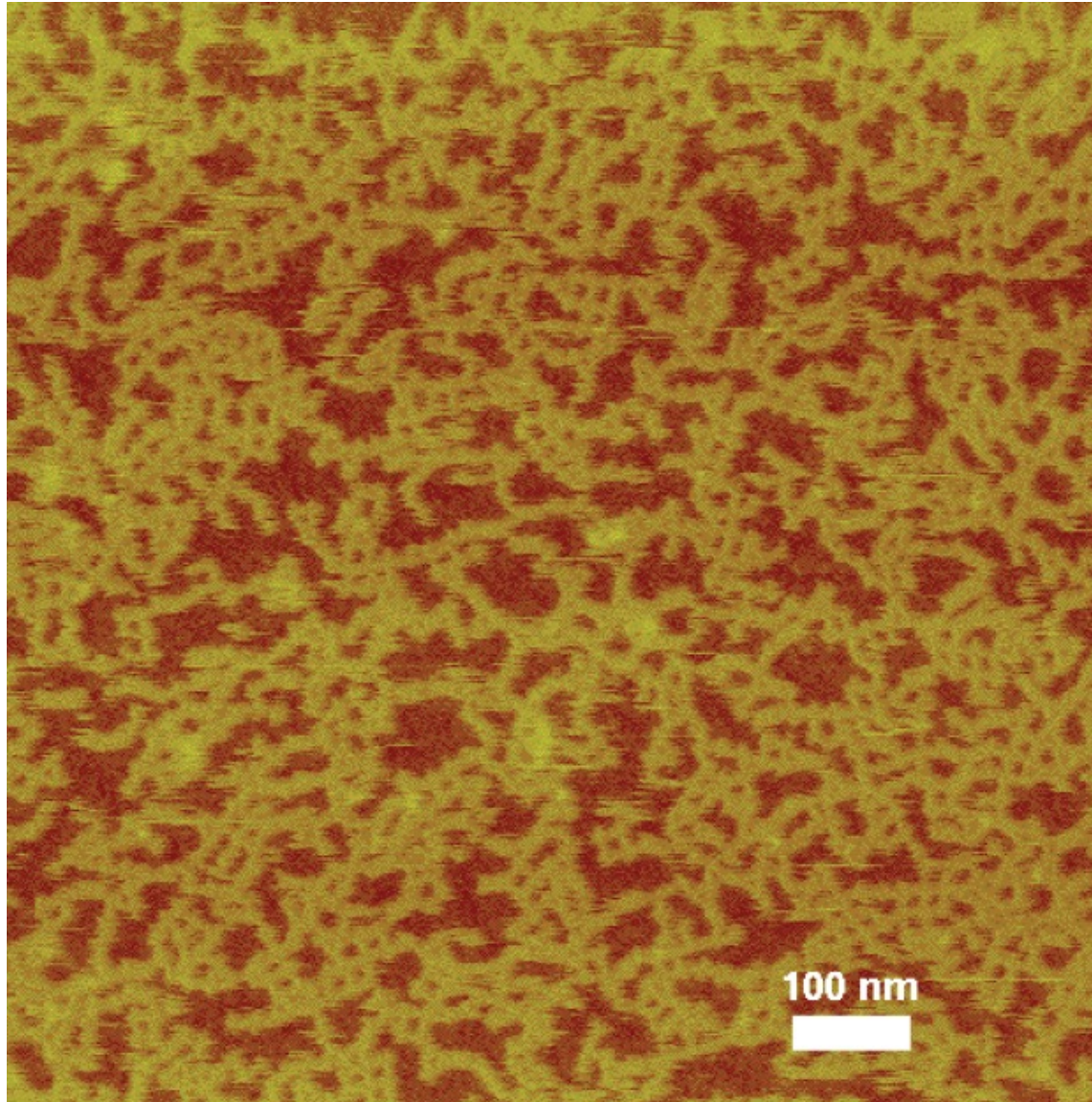
# Hierarchical Tile Assemblies

*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.*

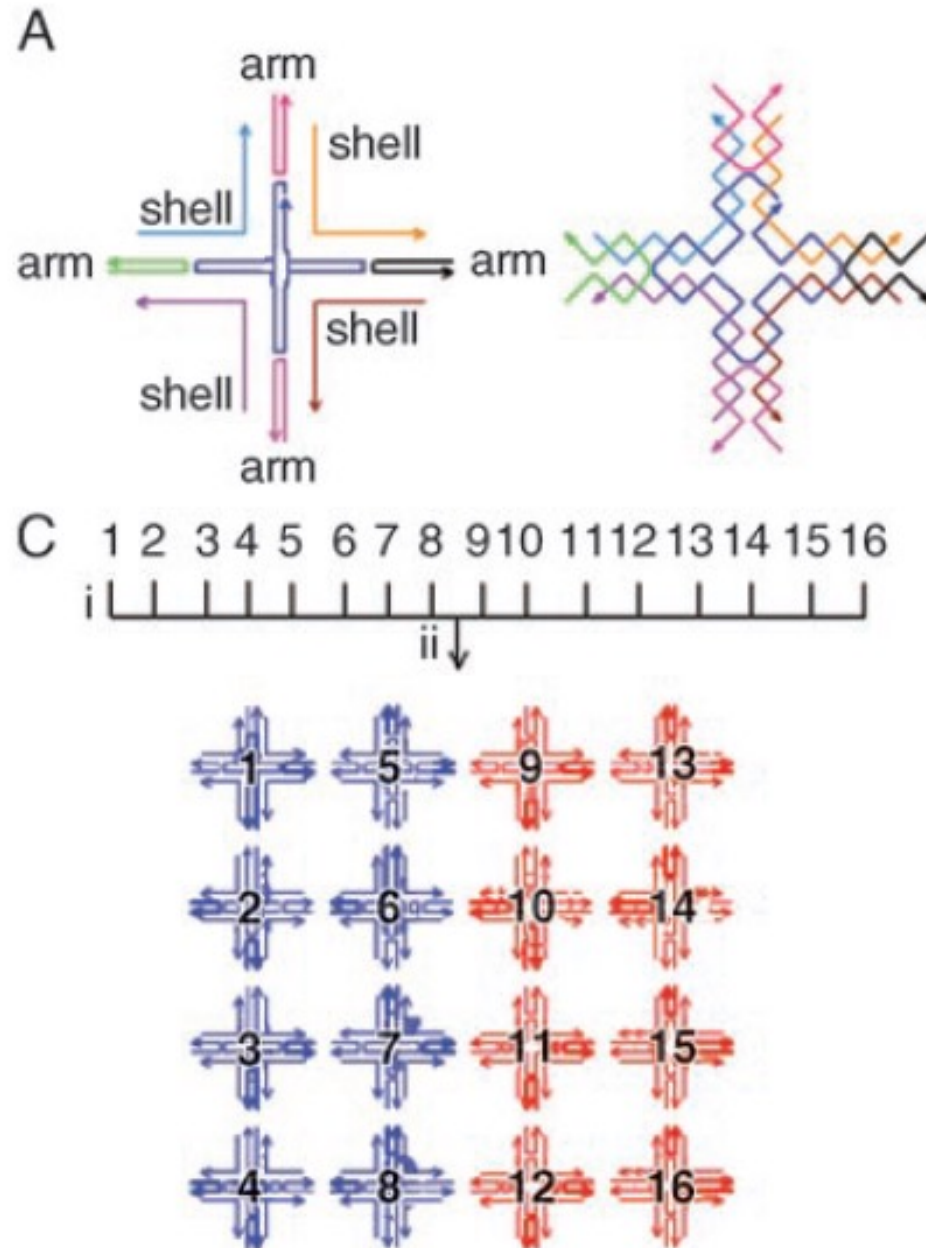
# Hierarchical Lattices of cross tiles



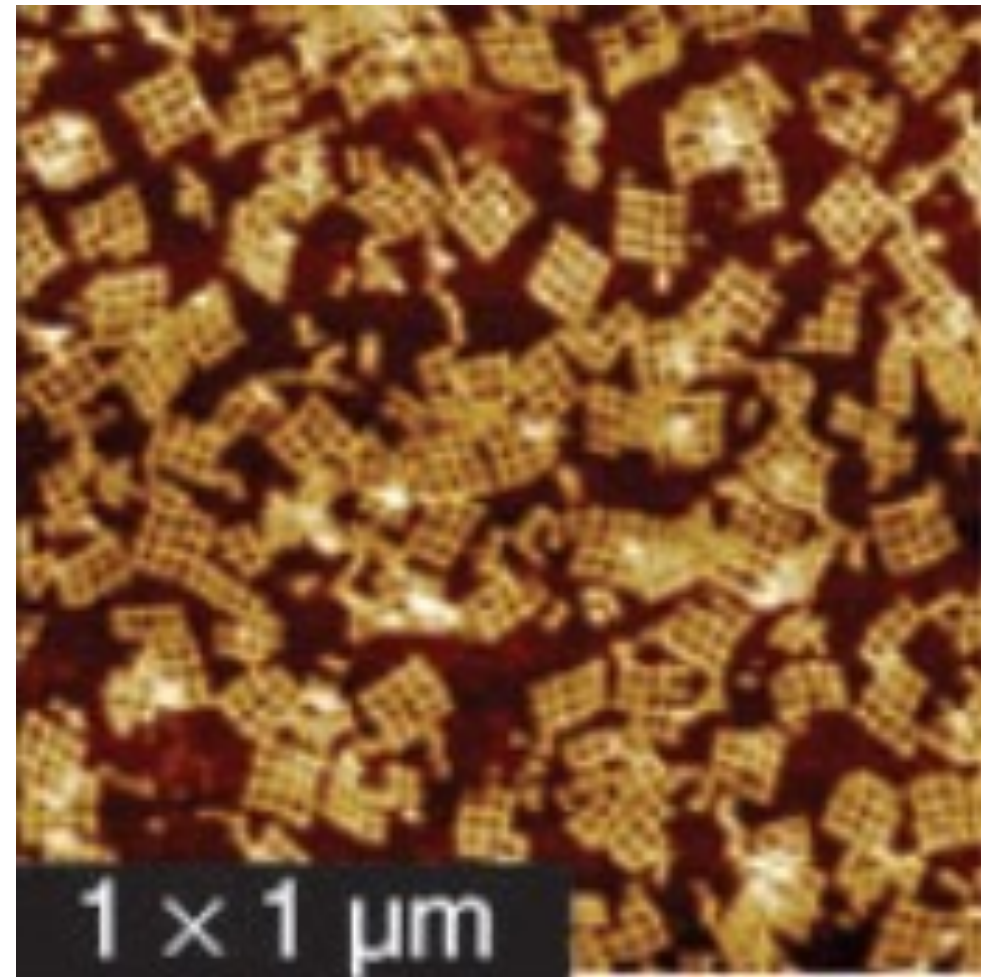
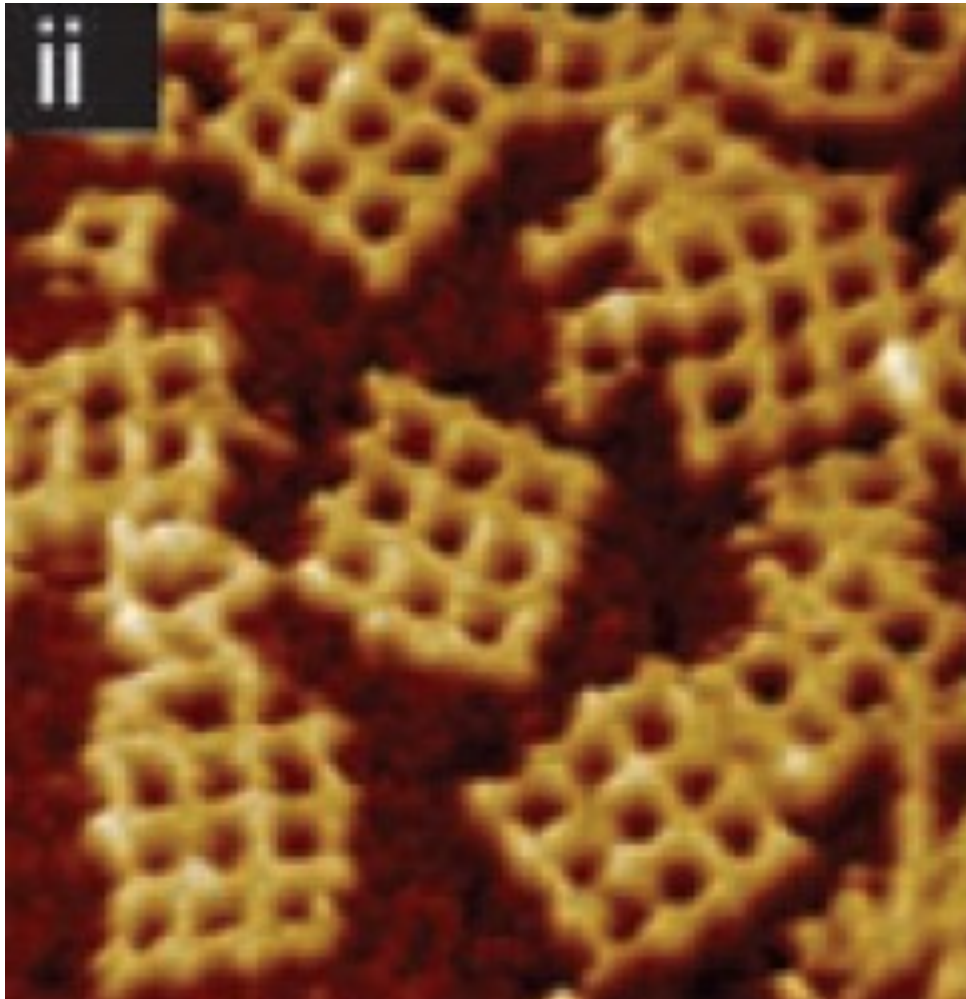
# Hierarchical Assembly of cross tiles



# Addressable cross tiles used for Hierarchical Assembly



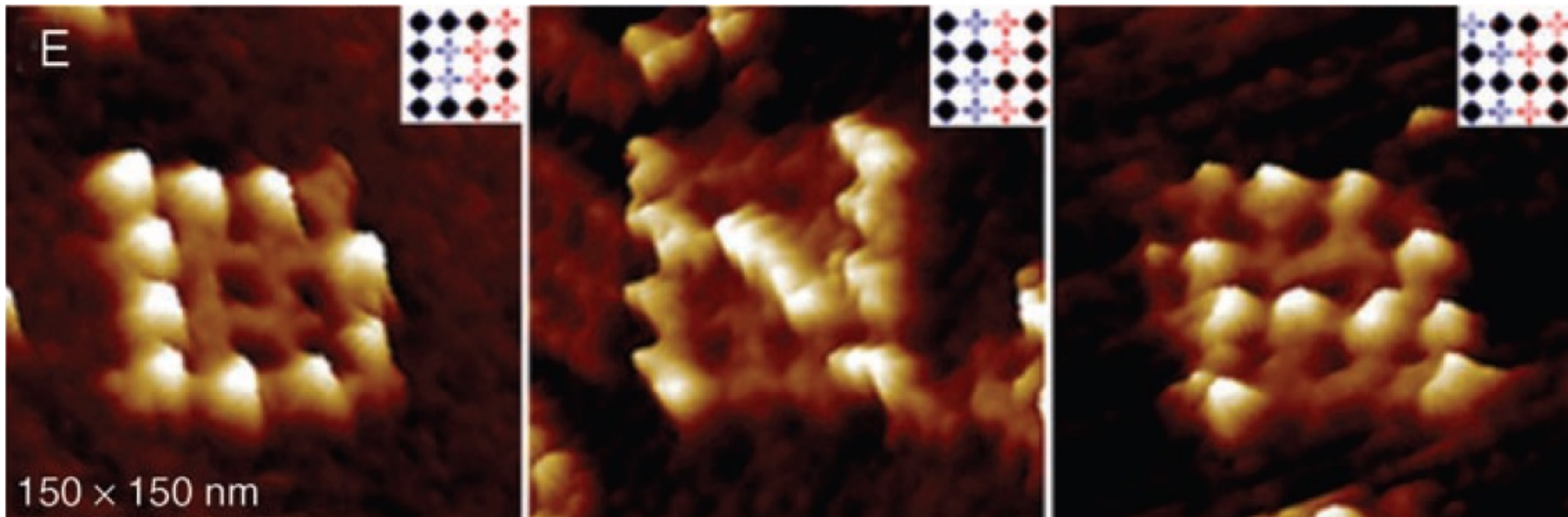
# Addressable cross tiles used for Hierarchical Assembly



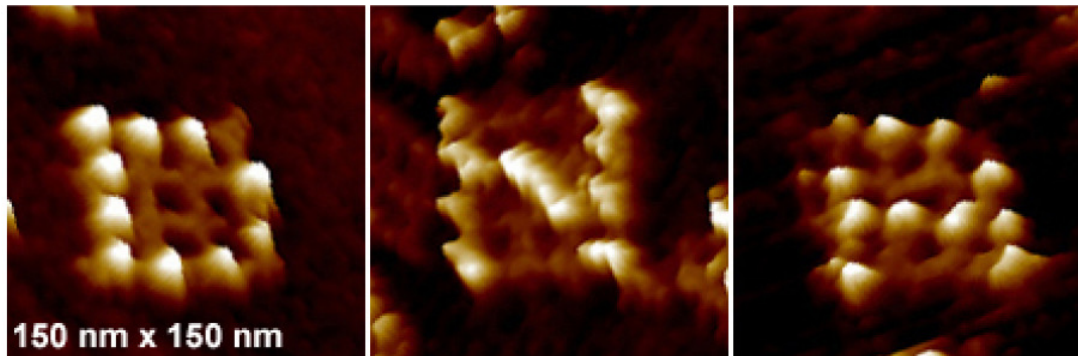
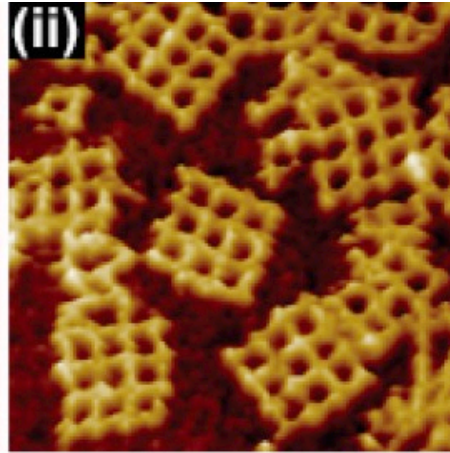
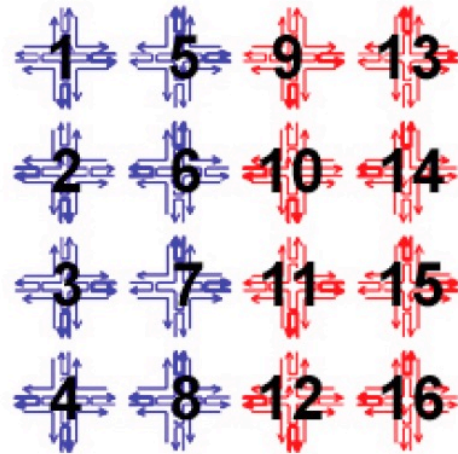
***Sung Ha Park, Constantin Pistol, Sang Jung Ahn, John H. Reif, Alvin R. Lebeck, Chris Dwyer, and Thomas H. LaBean, Finite-Size, Fully Addressable DNA Tile Lattices Formed by Hierarchical Assembly Procedures, Angewandte Chemie [International Edition], Volume 45, Issue 5, pp. 735-739***



# Molecular Scale Patterning using Hierarchical Assembly of cross tiles

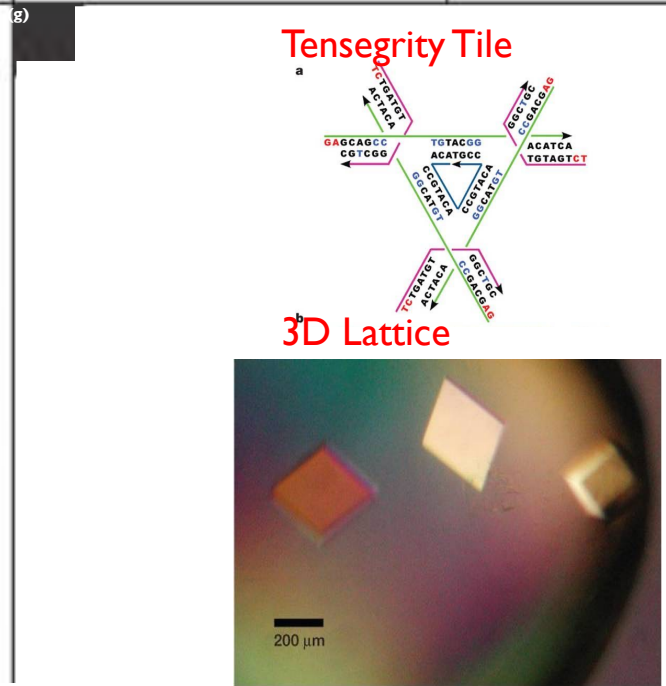
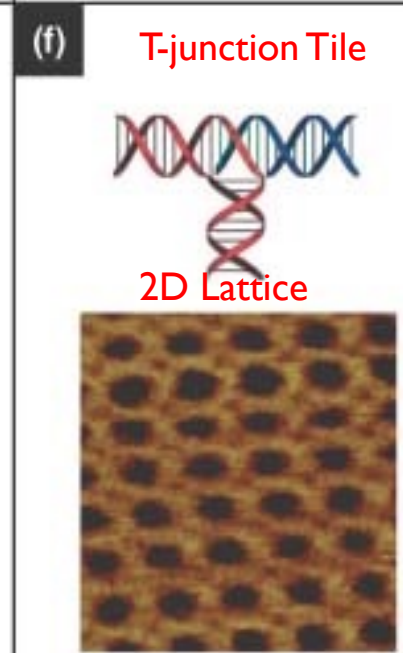
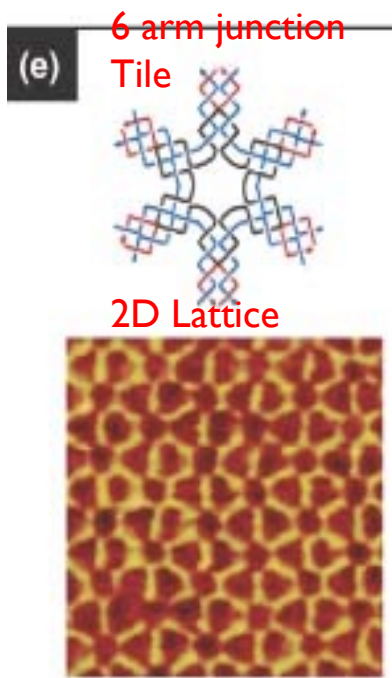
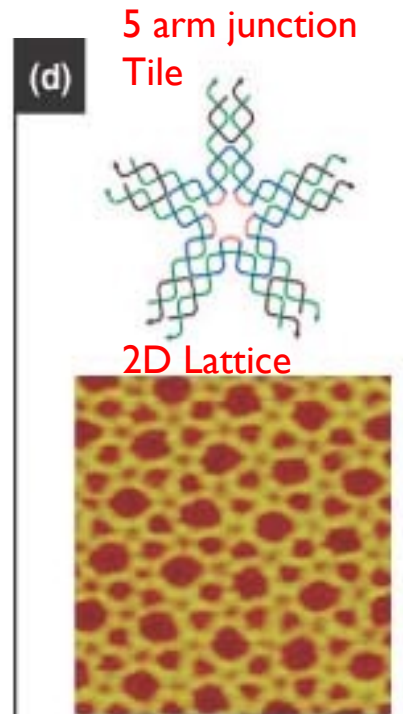
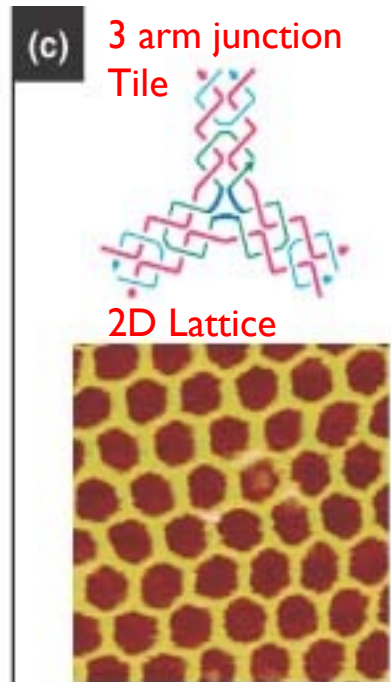
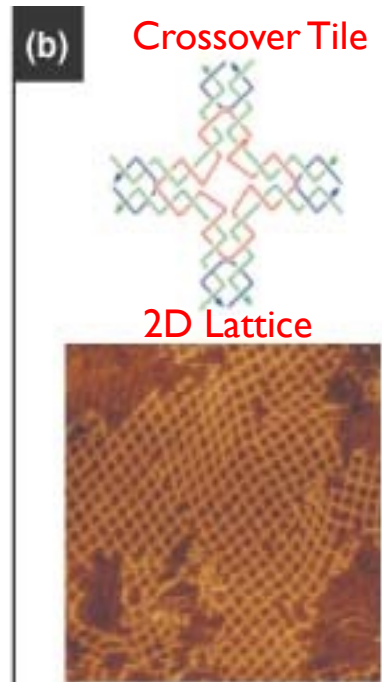
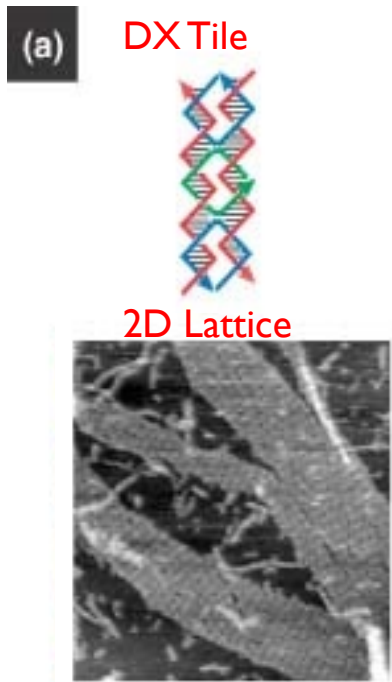


# Hierarchical Assembly of DNA Lattices with 2 D Pattern “DNA”



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.

# Diverse DNA Tiles and Resulting DNA Lattices



# Double Decker Tiles and 3D DNA Lattices



Urmi Majumder, Duke

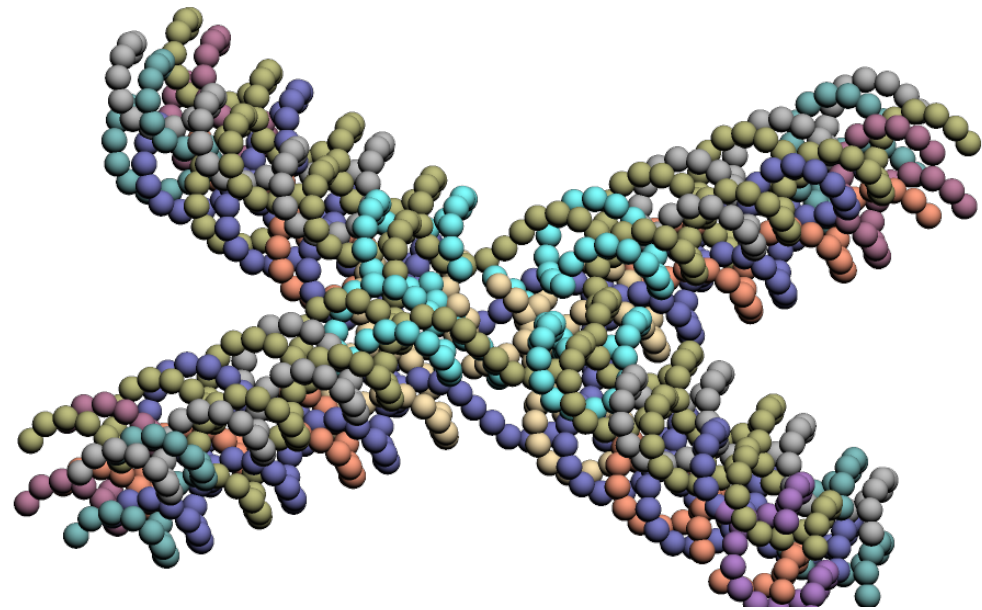
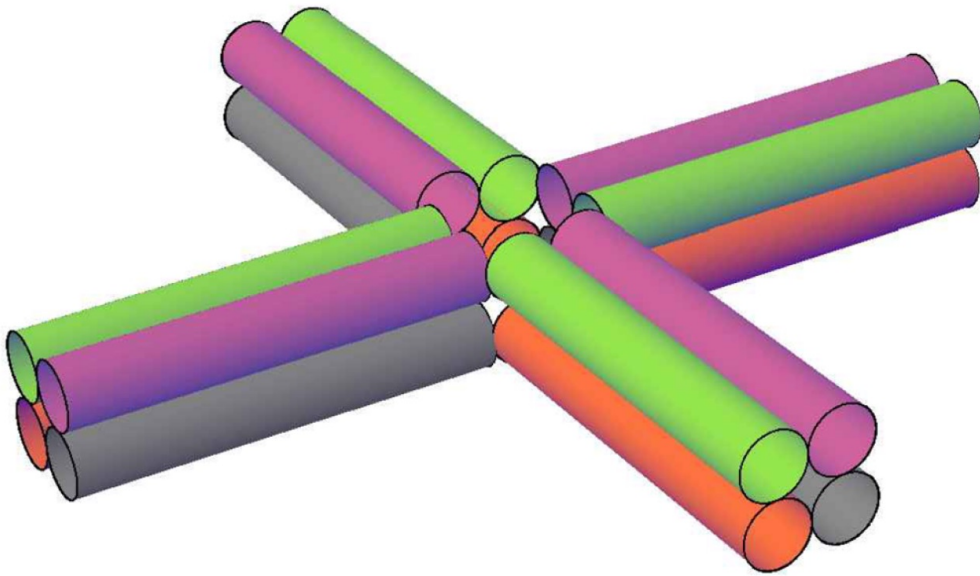
*Urmi Majumdar, Abhijit Rangnekar, Kurt V. Gothelf, John H Reif and Thomas H LaBean, Design and Construction of Double-Decker Tile as a Route to Three-Dimensional Periodic Assembly of DNA, Journal American Chemical Society (JACS), Vol. 133, no. 11, pp. 3843—3845 (Feb. 2011)*

# Application of 3D lattices:

- Imaging proteins
- Organizing molecular electronic components
- Organizing functional inorganic materials
- Tile based computing

# Double decker tiles:

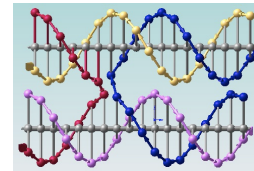
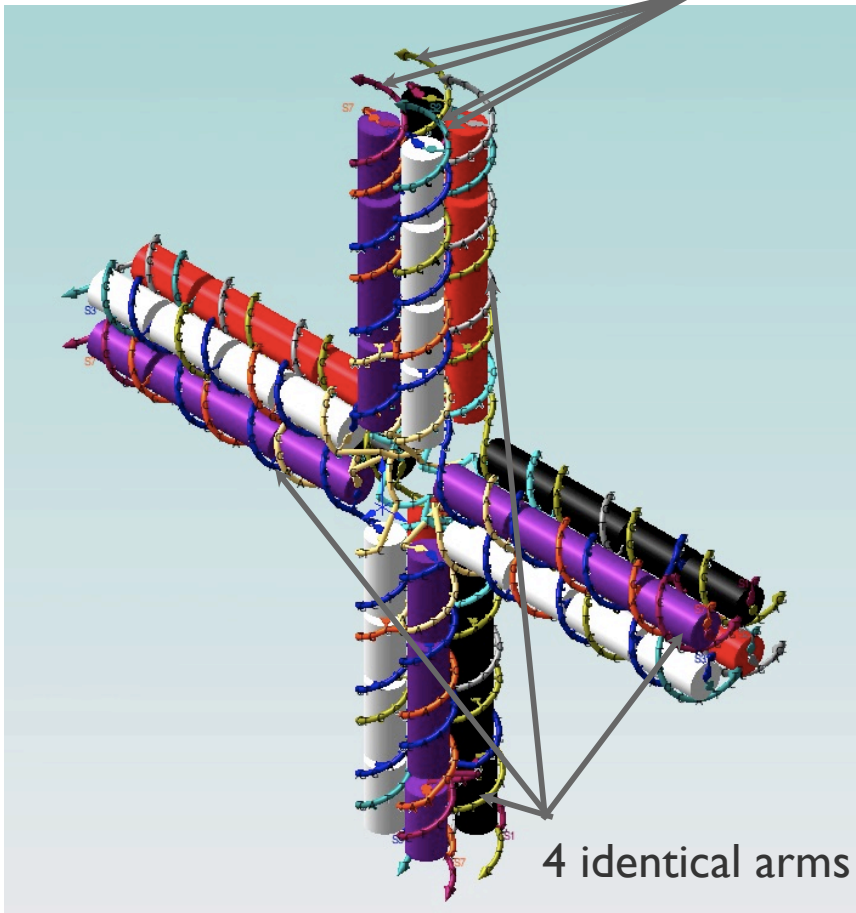
Used for 3D DNA Lattices



Four fold sequence symmetry

# Double-decker tiles: Route to Assembly in 3D

sticky ends



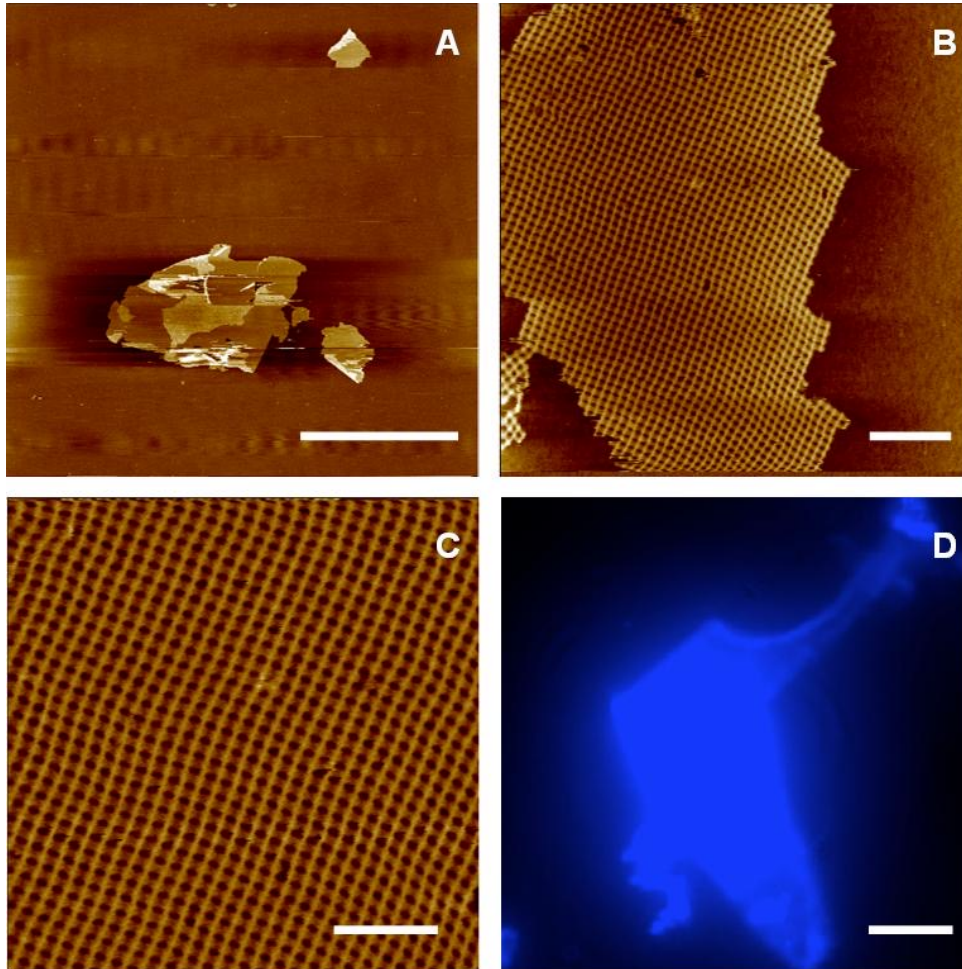
Branched Junction

2 cross tiles held together  
by branched junctions



Urmi Majumder, Duke

## Highly regular 2D lattices via double decker cross tiles



Atomic force microscopy images of the double-decker 2D lattice with corrugation.

The lattices are tens of micrometers in size.

The scale bars are:

(A) 10  $\mu\text{m}$ ,

(B) 300 nm

(C) 200 nm.

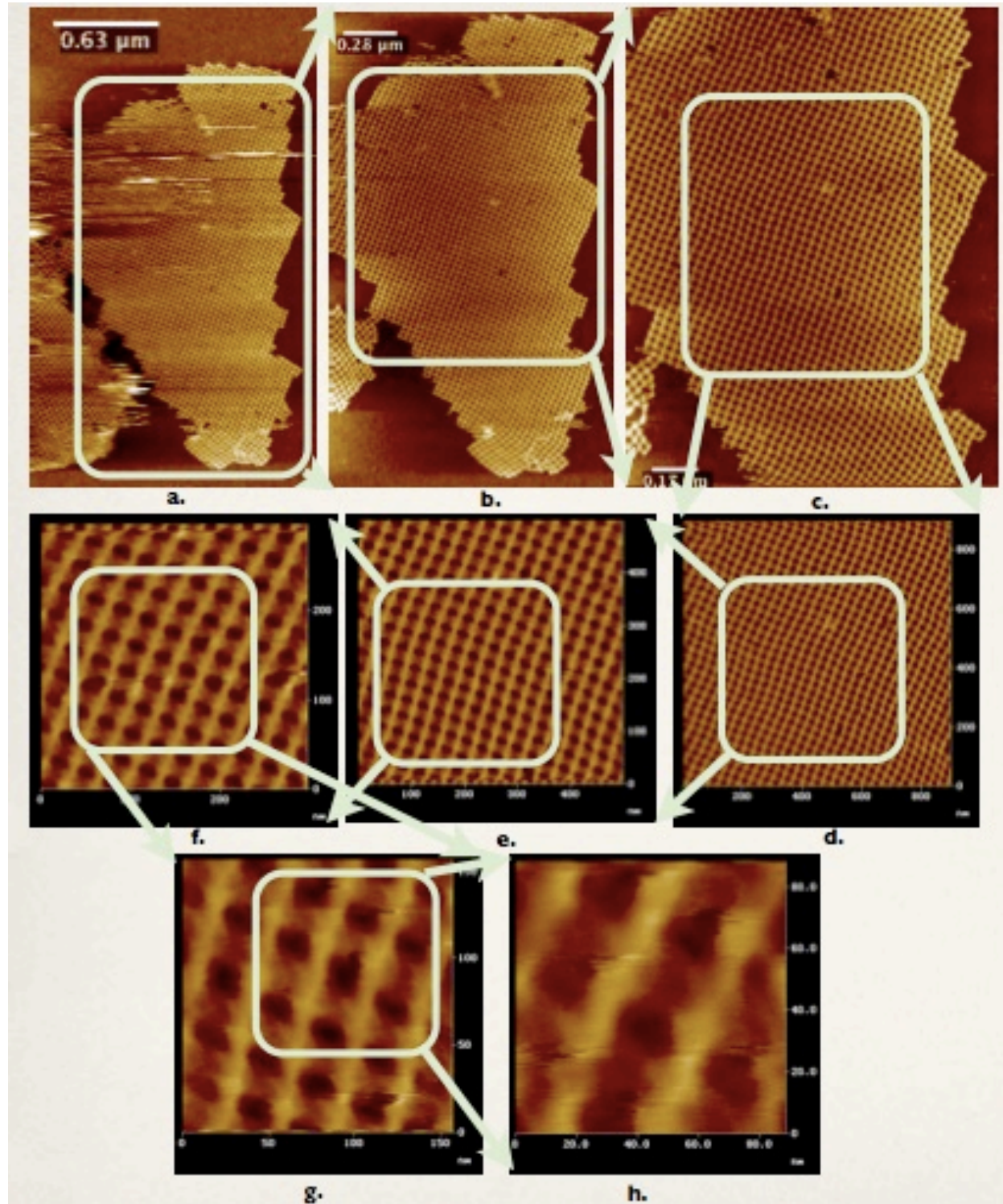
(D) Fluorescence microscopy image of the same sample. (The scale bar is 20  $\mu\text{m}$ ).

**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**



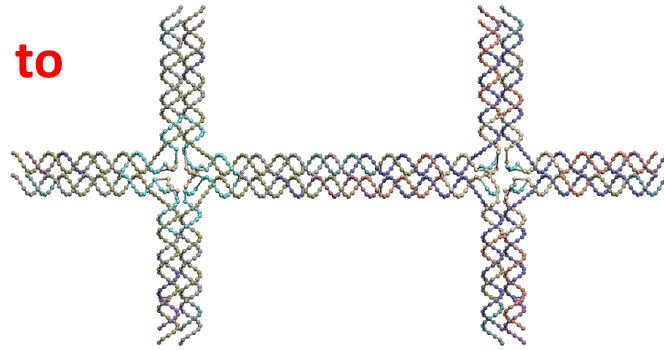
# 2D Lattices using Double-decker tiles

**Extremely Large,  
Regular 2D Grids  
with Predominant Unidirectional  
Banding**

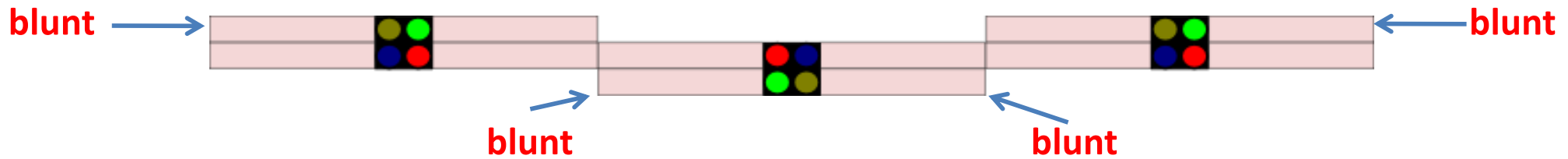
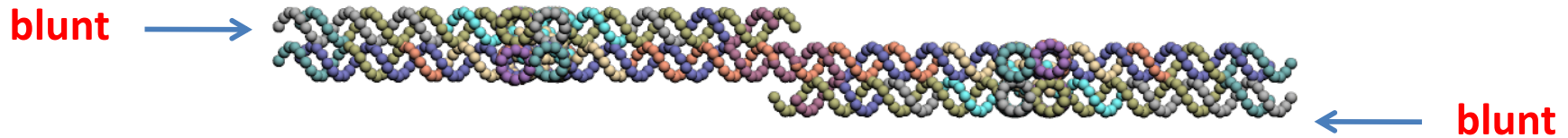


# 2D Staggered Lattices using Double-decker tiles

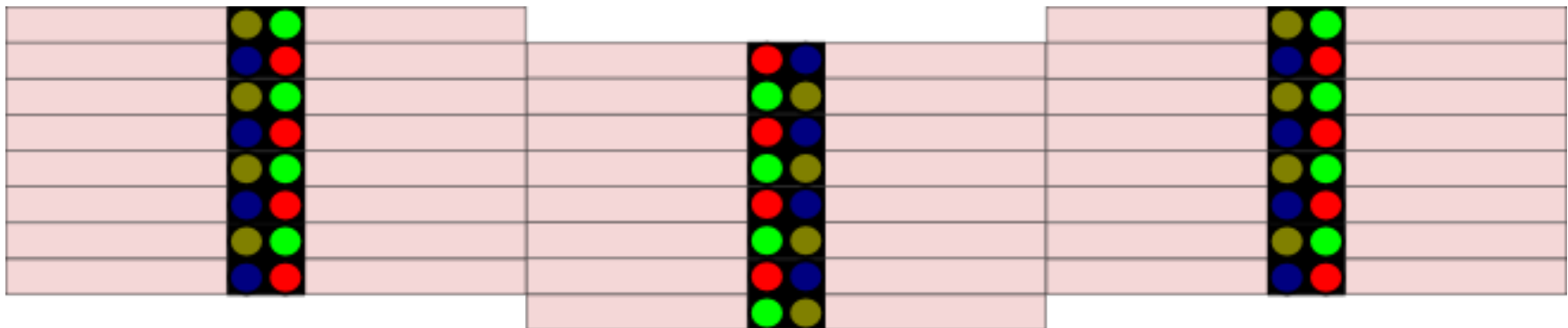
Use Corrugation to  
make flat in 2D:



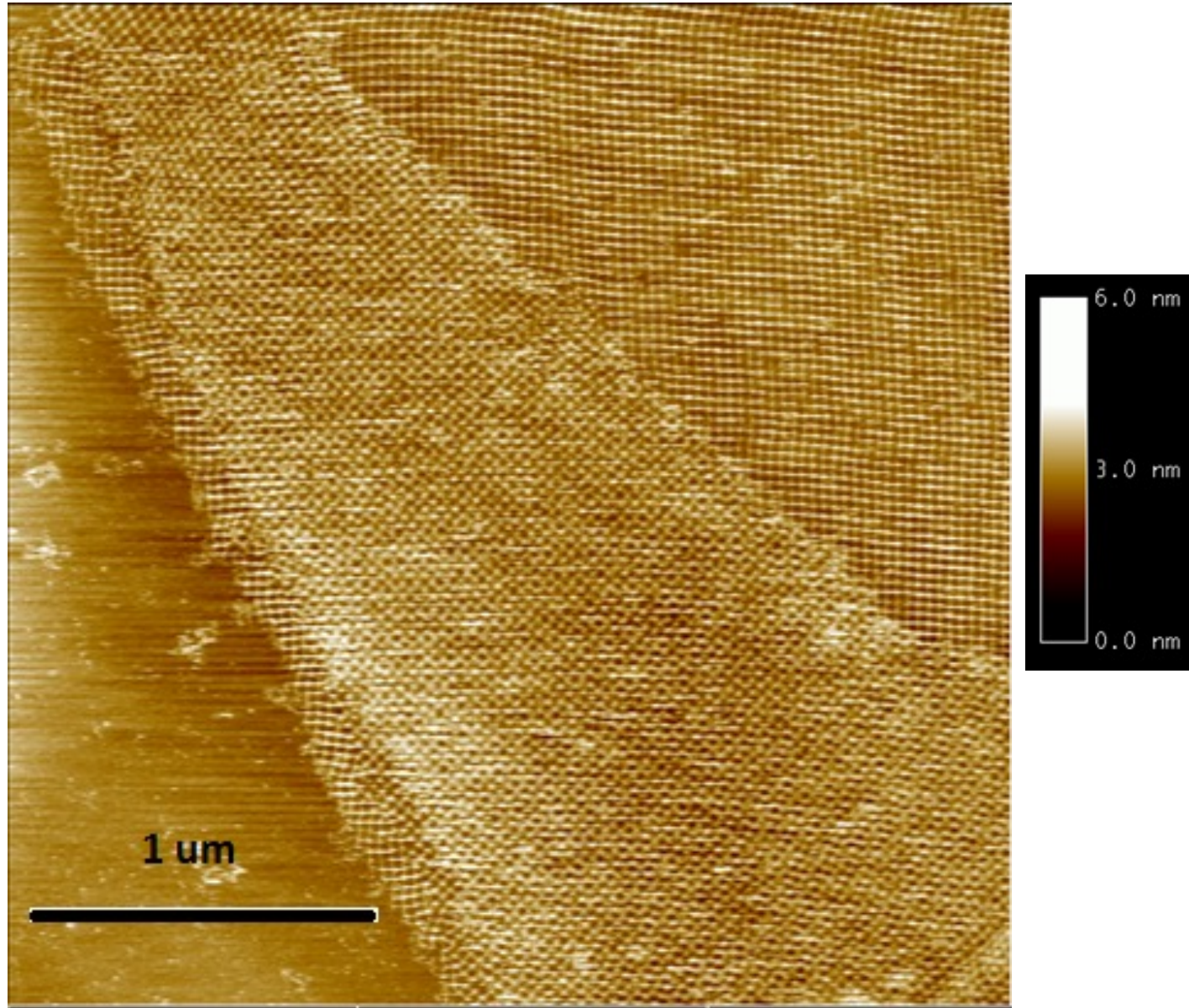
Staggered Attachments:



3D Lattice using Staggered Attachments:

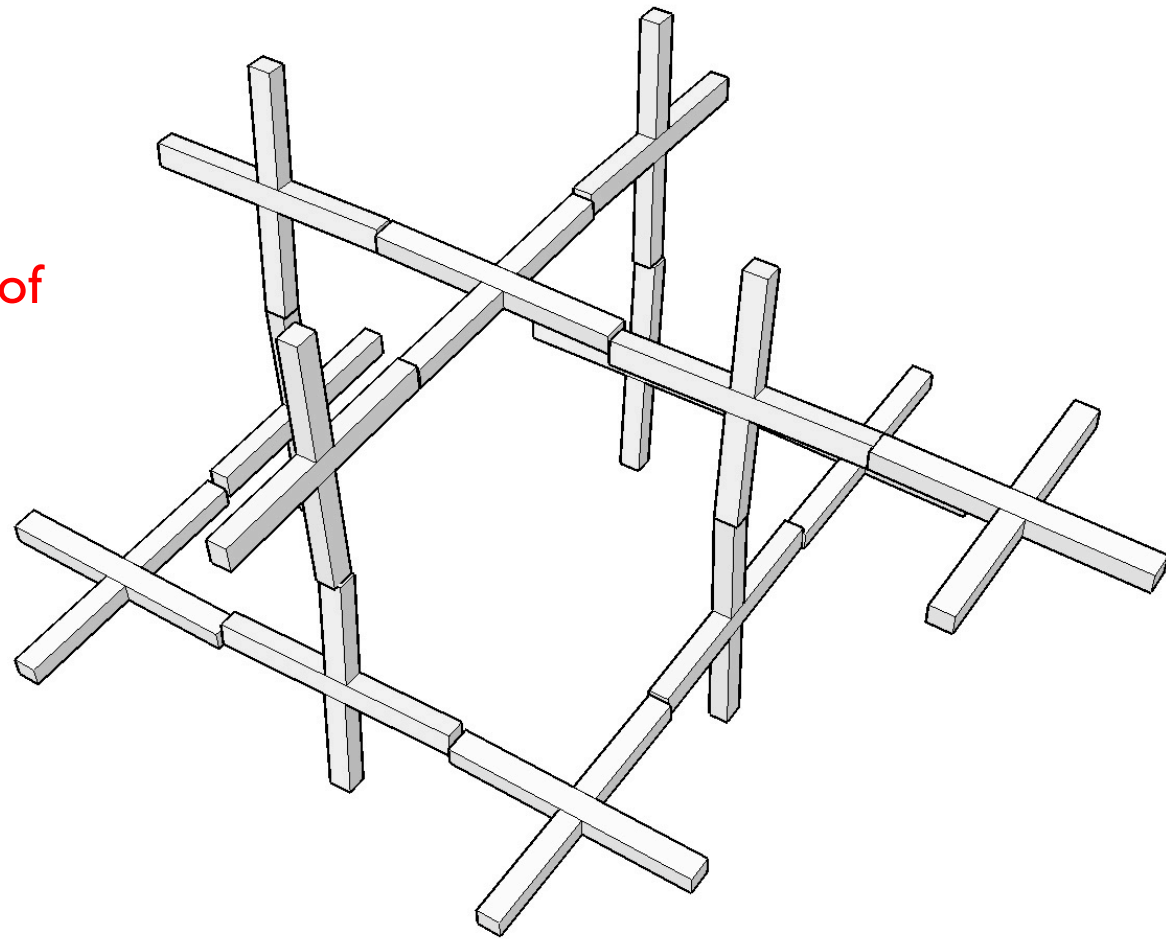


# 2D staggered lattices AFM



# Double-decker tiles: forming 3D Lattices

3D Arrangement of  
Double-Decker  
Tiles



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

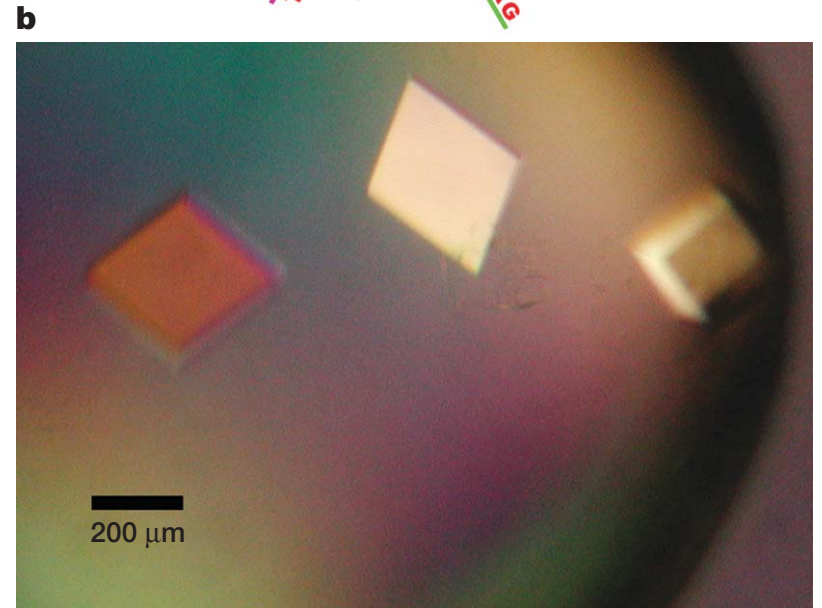
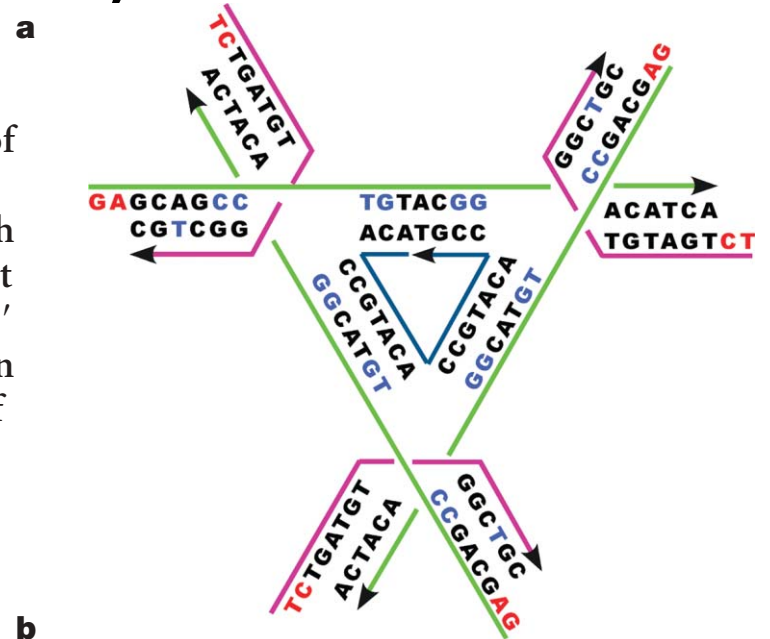


Urmi Majumder, Duke

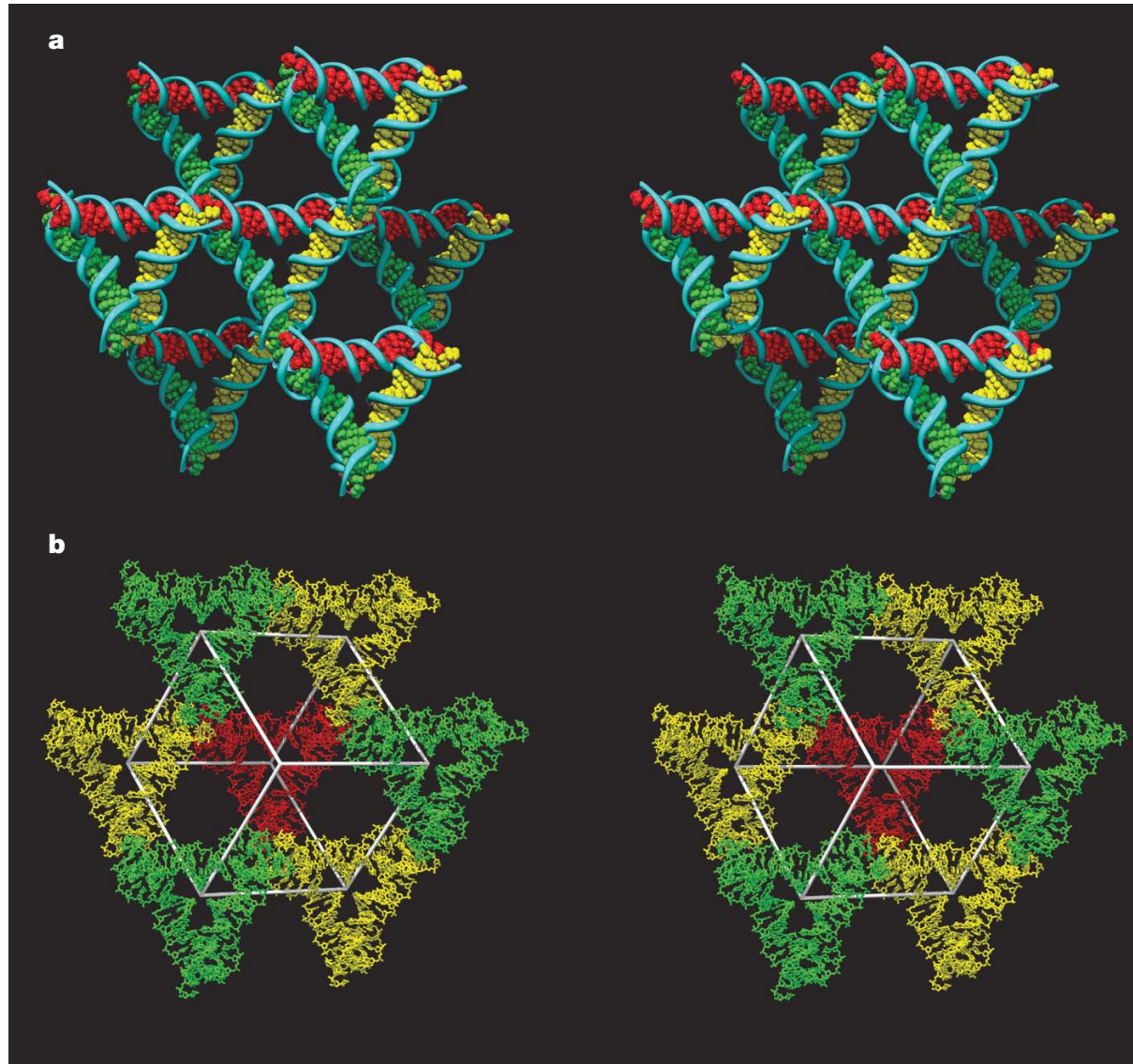
# Tensegrity Tiles & 3D lattices

(Seeman, Nature, 2009)

**Figure 1 | Schematic design, sequence, and crystal pictures.** **a**, Schematic of the tensegrity triangle. The three unique strands are shown in magenta (strands restricted to a single junction), green (strands that extend over each edge of the tensegrity triangle) and dark blue (one unique nicked strand at the centre passing through all three junctions). Arrowheads indicate the 3' ends of strands. Nucleotides with A-DNA-like characteristics are written in bright blue. Cohesive ends are shown in red letters. **b**, An optical image of crystals of the tensegrity triangle. The rhombohedral shape of the crystals and the scale are visible.



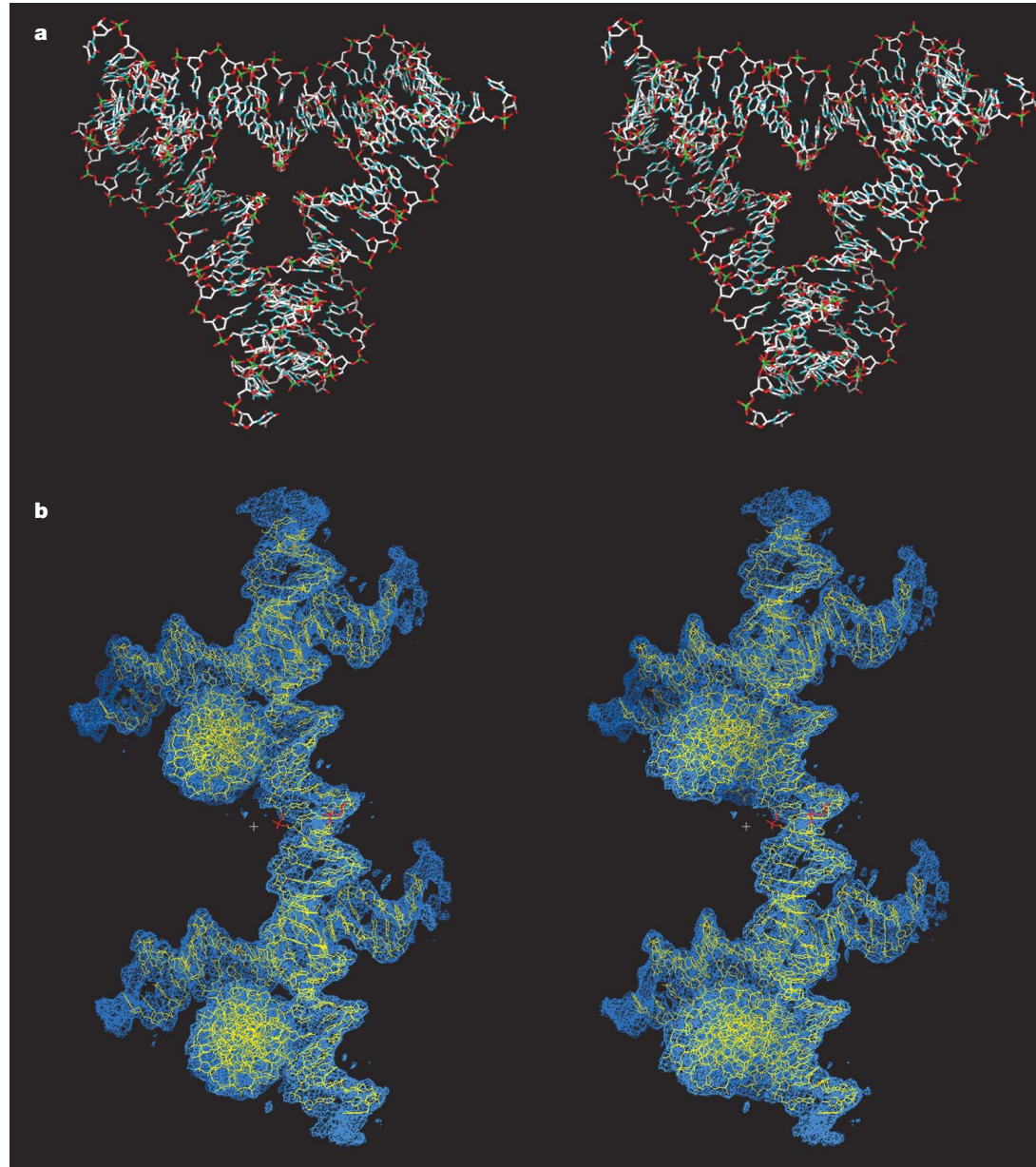
# Seeman's Tensegrity tiles & 3D lattices



**Figure 3 | Lattice formed by tensegrity triangles.** **a**, Surroundings of a triangle. This stereoscopic image distinguishes three independent directions by base-pair colour. The central triangle is flanked by six other triangles. **b**, Rhombohedral cavity formed by tensegrity triangles. This stereoscopic image shows seven of the eight triangles that comprise the rhombohedron's

corners. The cavity outline is drawn in white. The rear red triangle connects through one edge each to the three yellow triangles in a plane closer to the viewer. The yellow triangles are connected through two edges each to two different green triangles that are even nearer to the viewer.

# Seeman's Tensegrity tiles & 3D lattices



**Figure 2 | Views of the tensegrity triangle.** **a**, Stereoscopic view of the triangle down its three-fold axis. It is in the same orientation as the schematic in Fig. 1a. The helix on the top edge starts above the mean plane of the molecule at the left and proceeds to the rear as it moves to the right.

**b**, Stereoscopic view of two triangles in electron density. This image is perpendicular to an edge of the rhombohedron, showing the connection of two triangles by sticky ends. Sticky ends are magenta for emphasis. Some density features belonging to neighbouring molecules are not depicted.

# X-Ray Resolution of Seeman's Tensegrity tiles & 3D lattices

**Table 1 | Crystalline tensegrity triangle lattices**

Crystal number	Edge length (nucleotide pairs)	Space group	Inter-junction pairs	Rhombohedral cell dimensions	Resolution (Å)	Cross-section (nm <sup>2</sup> )	Cavity size (nm <sup>3</sup> )
1	21	<i>R3</i>	7	$a = 69.2 \text{ Å}, \alpha = 101.4^\circ$	4.0	23	103
2	21	<i>P1</i>	7	$a = 68.0 \text{ Å}, \alpha = 102.6^\circ$	5.0	23	101
3	31	<i>R3</i>	17	$a = 102.0 \text{ Å}, \alpha = 112.7^\circ$	6.1	62	366
4	31	<i>P1</i>	17	$a = 100.9 \text{ Å}, \alpha = 111.6^\circ$	6.3	61	373
5	32	<i>R3</i>	18	$a = 103.6 \text{ Å}, \alpha = 113.6^\circ$	6.5	64	367
6	32	<i>P1</i>	18	$a = 103.3 \text{ Å}, \alpha = 112.2^\circ$	6.5	64	395
7	42	<i>R3</i>	17	$a = 134.9 \text{ Å}, \alpha = 110.9^\circ$	11.0	123	1,104
8	42	<i>P1</i>	17	$a = 133.7 \text{ Å}, \alpha = 111.3^\circ$	14.0	120	1,048
9	42	<i>R3</i>	28	$a = 134.9 \text{ Å}, \alpha = 117.3^\circ$	10.0	117	643

The cross-sectional area and cavity size are derived from the lattice parameters. Cross-sections and cavity sizes are estimated by subtracting two radii of the double helix ( $\sim 10 \text{ Å}$ ) from the unit cell dimensions. The space group indicates whether deliberate three-fold rotational averaging has been performed; it has for those in *R3*, not for those in *P1*. Edge lengths and inter-junction distances (within triangles) are given in nucleotide pairs. Crystal 1 is the work reported here. The structures of crystals 3 and 7 have been determined by molecular replacement; others are in progress.