Programming Nanoscale Structure Using DNA-Based Information

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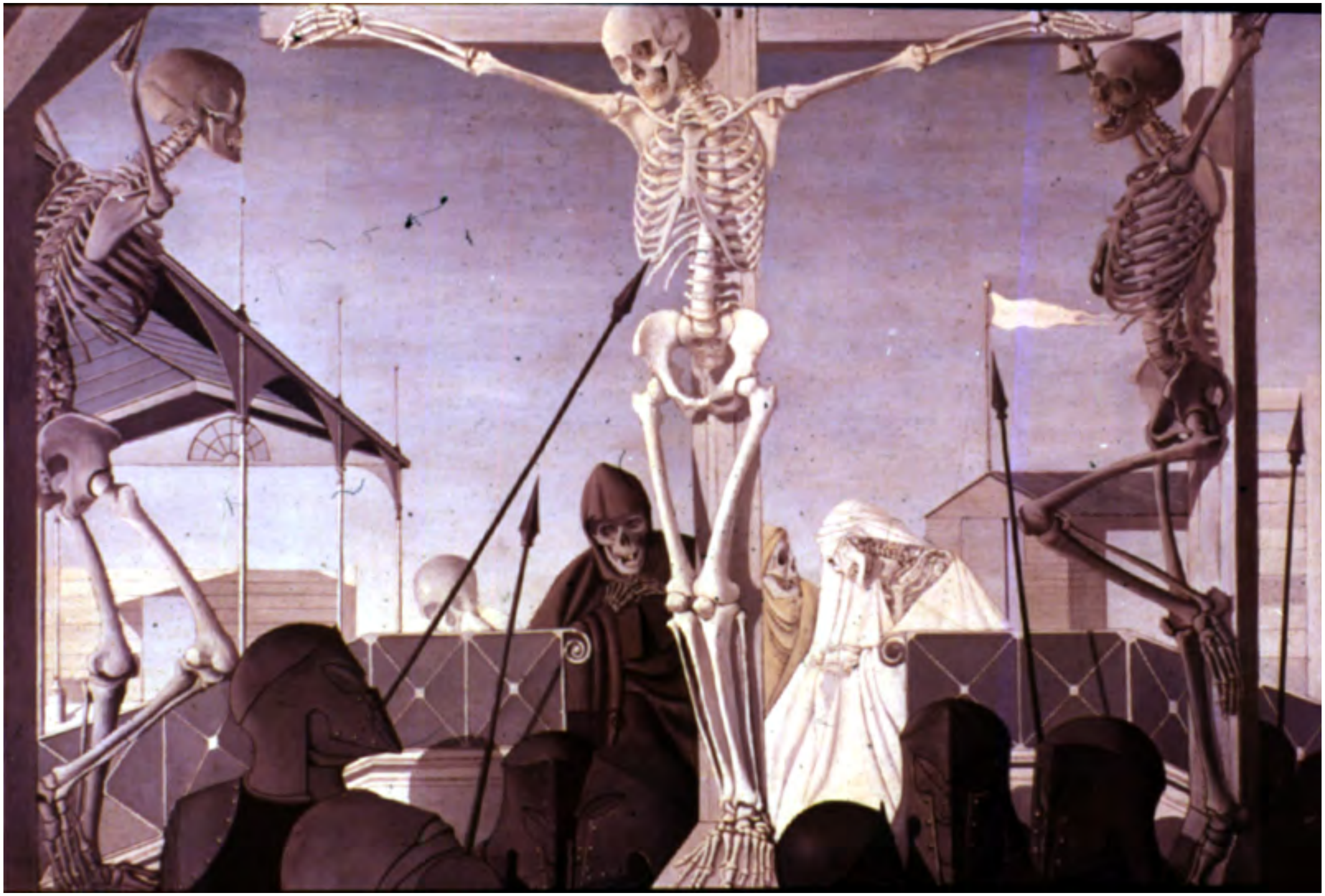
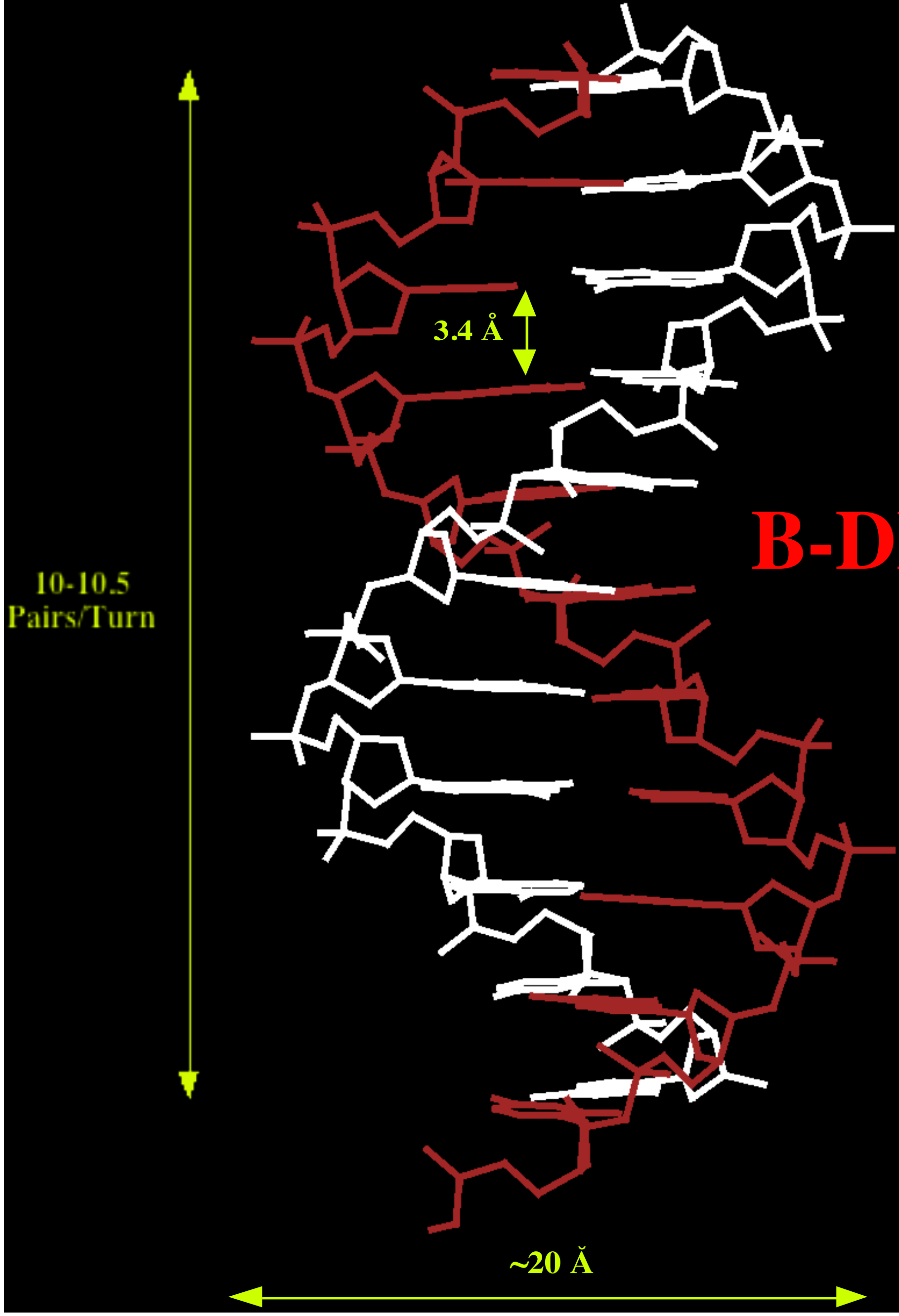
Visions of the Theory of Computing
Berkeley, CA
May 30, 2013



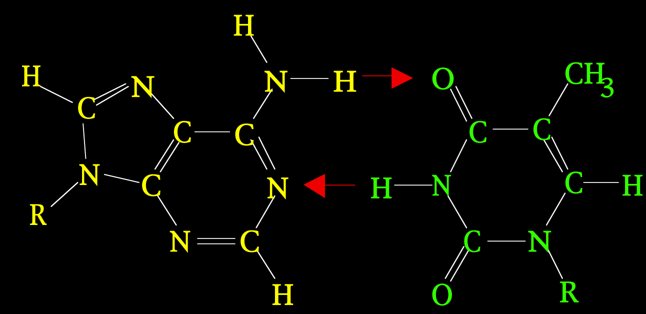
DNA Is a Nanoscale Object



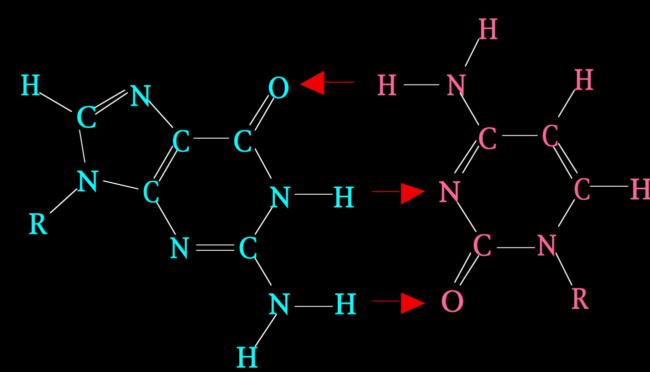
B-DNA

DNA BASE PAIRS

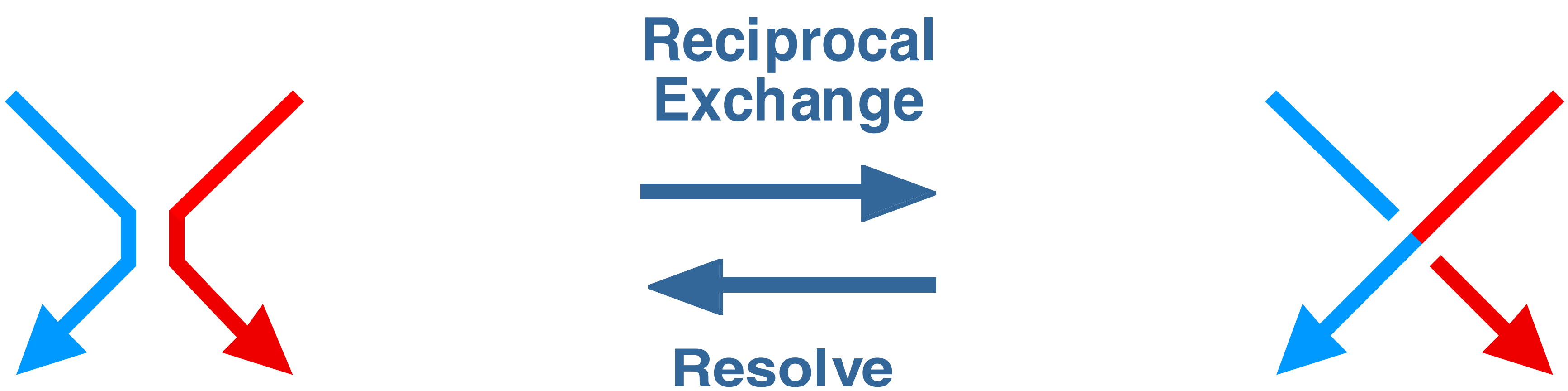
A T



G C

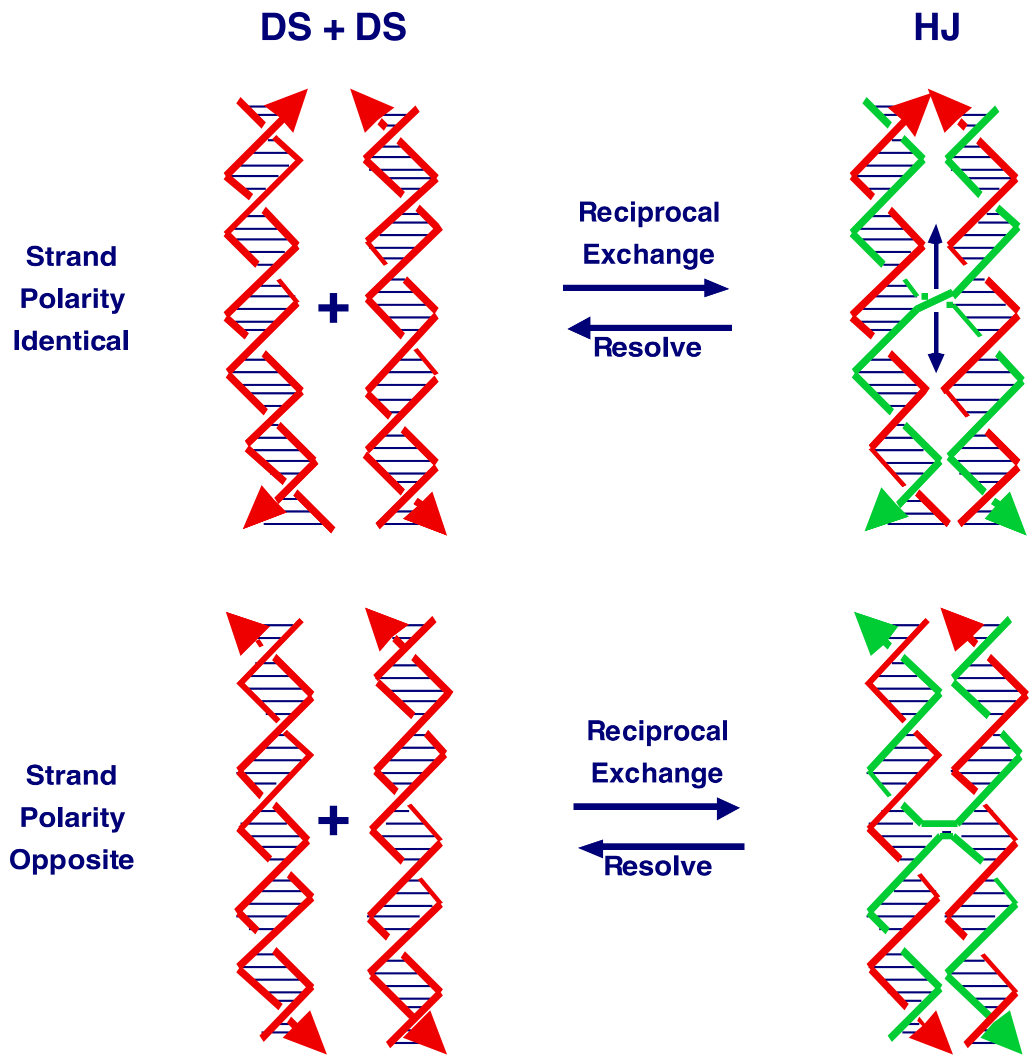


Reciprocal Exchange:
A Theoretical Biokleptic Tool To Generate New DNA Motifs



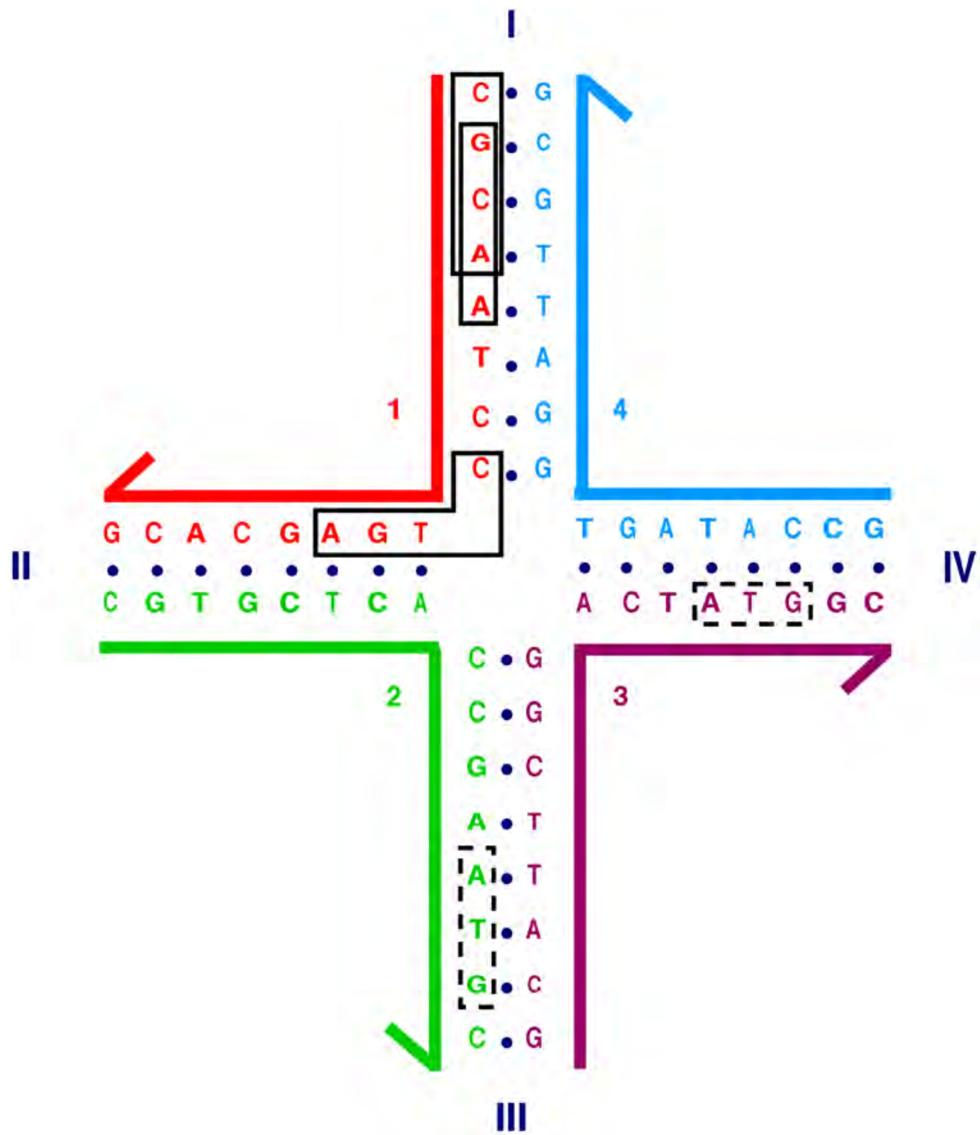
Seeman, N.C. (2001), *NanoLett*. **1**, 22-26.

Reciprocal Exchange in a Double Helical Context



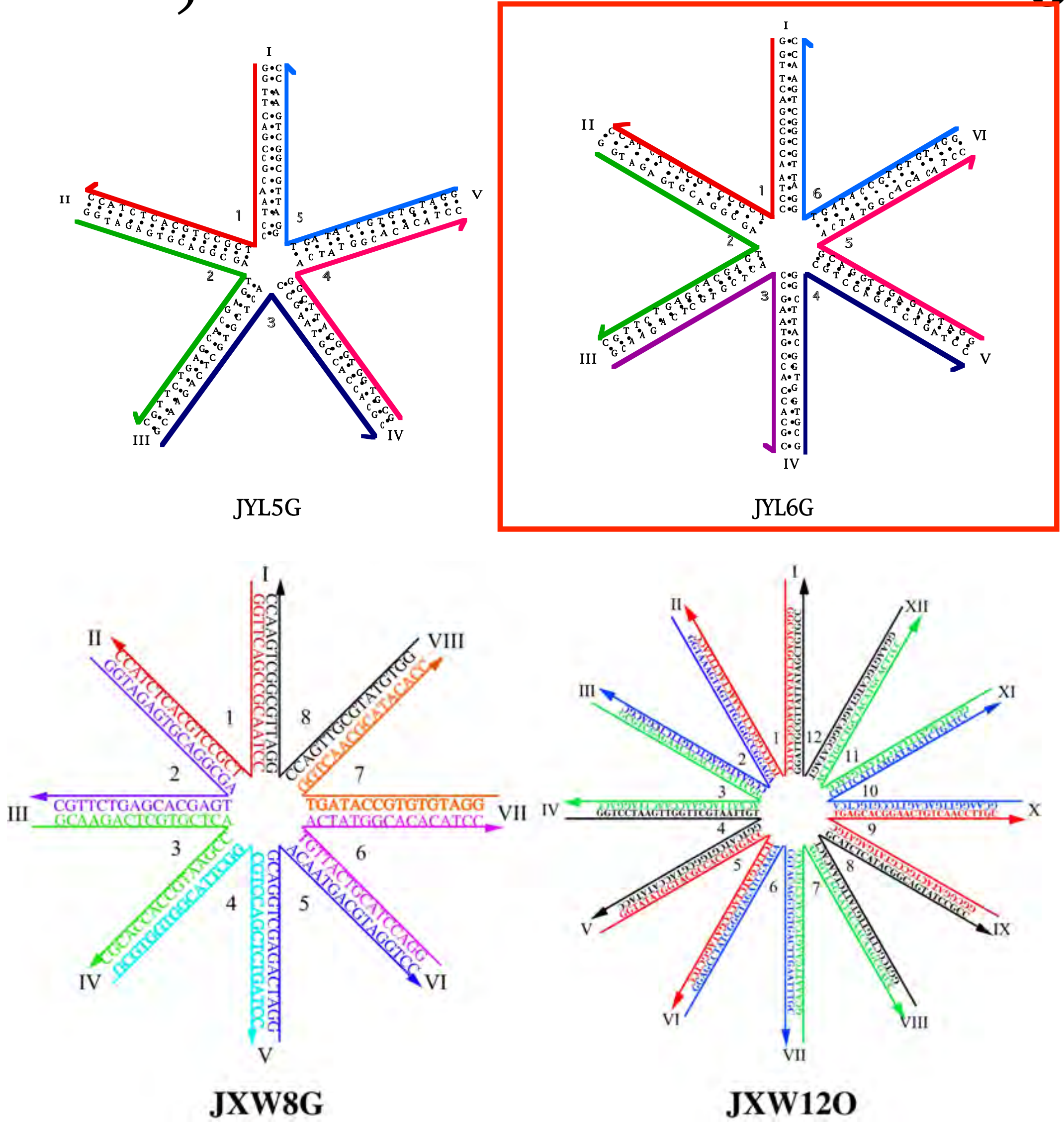
Seeman, N.C. (2001), *NanoLett*. **1**, 22-26.

Design of Immobile Branched Junctions: Minimize Sequence Symmetry



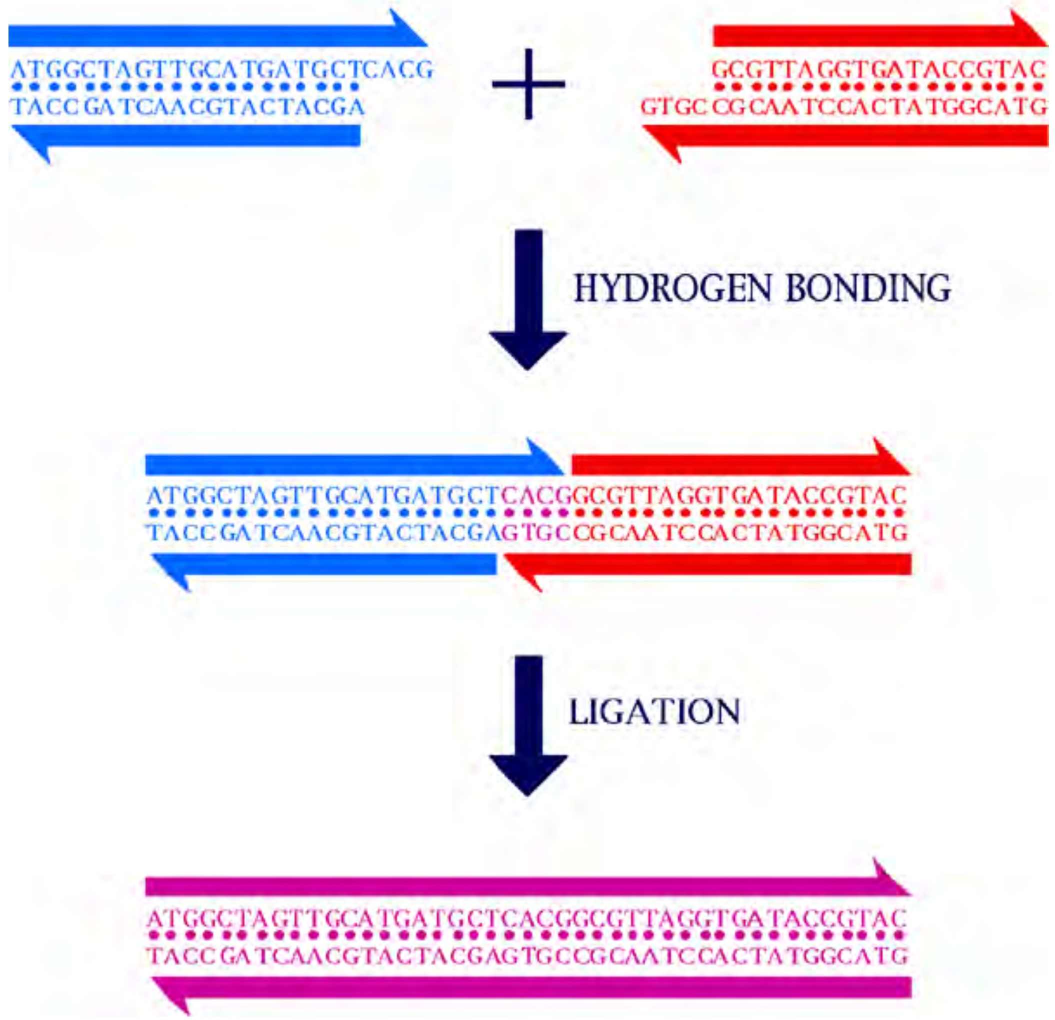
Seeman, N.C. (1982), *J. Theor.Biol*. **99**, 237-247.

5-Arm, 6-Arm, 8-Arm and 12-Arm Junctions

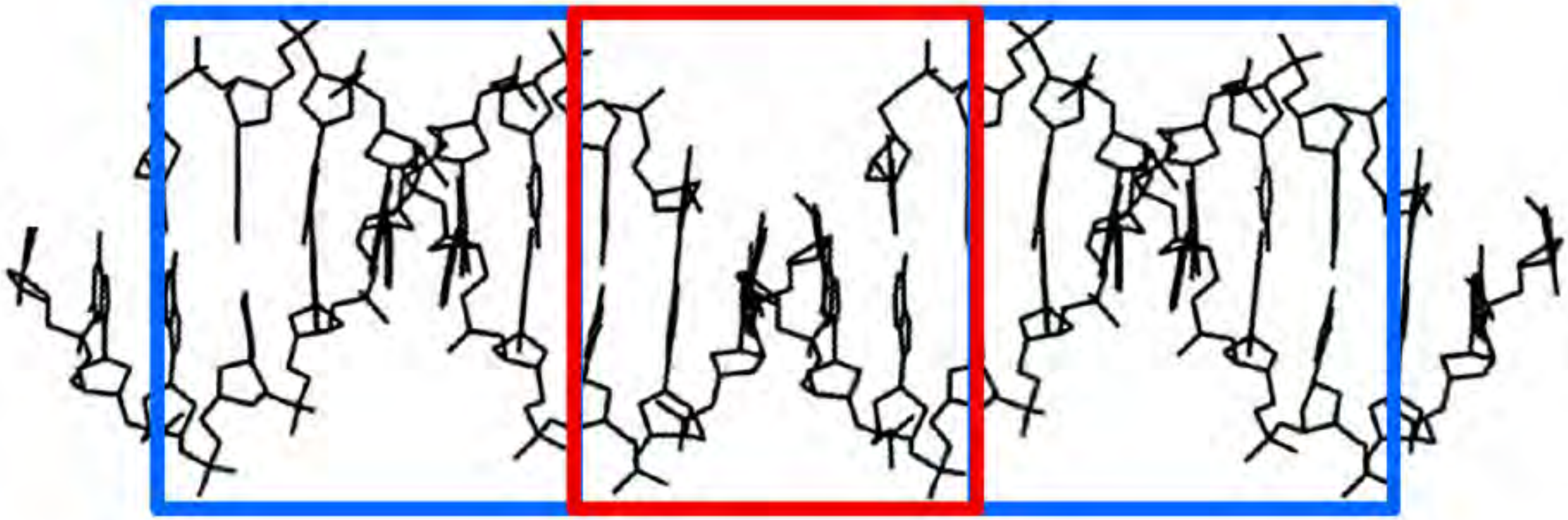


Wang, Y., Mueller, J.E., Kemper, B. & Seeman, N.C. (1991), *Biochemistry* **30**, 5667-5674.
Wang, X. & Seeman, N.C. (2007), *J. Am. Chem. Soc.* **129**, 8169-8176.

Sticky-Ended Cohesion: Easily Programmed Affinity

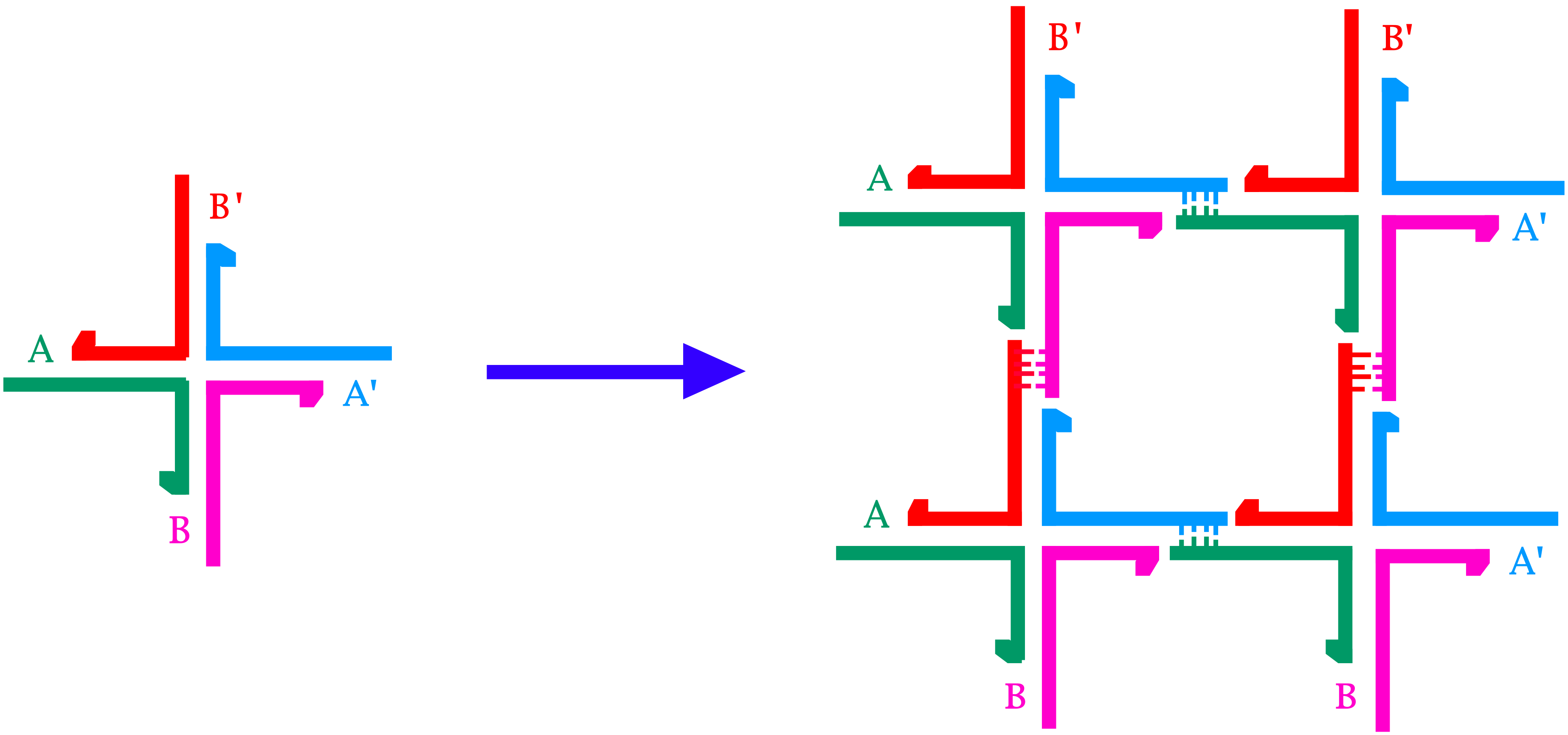


Sticky-Ended Cohesion: Structure



Qiu, H., Dewan, J.C. & Seeman, N.C. (1997) *J. Mol. Biol.* **267**, 881-898.

The Central Concept of Structural DNA Nanotechnology: Combine Branched DNA with Sticky Ends to Make Objects, Lattices and Devices



Seeman, N.C. (1982), *J. Theor.Biol*. **99**, 237-247.

OBJECTIVES AND APPLICATIONS FOR OUR LABORATORY

ARCHITECTURAL CONTROL AND SCAFFOLDING

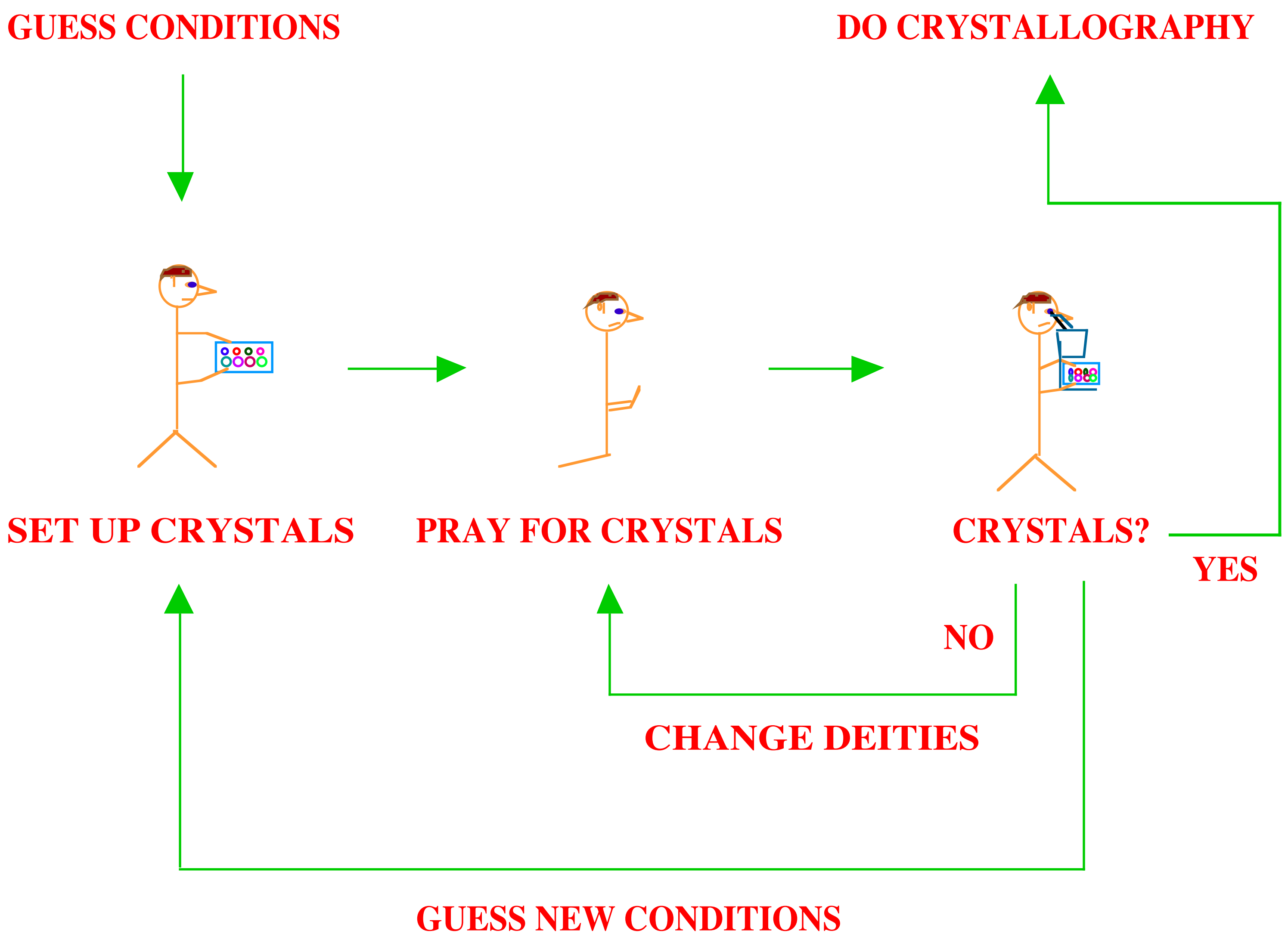
[1] MACROMOLECULAR CRYSTALLIZATION (PERIODIC IN 2D AND 3D).
[2] NANOELECTRONICS ORGANIZATION (PERIODIC IN 2D AND 3D).
[3] DNA-BASED COMPUTATION (APERIODIC IN 2D OR 3D).
[4] CONTROL OF POLYMER AND MATERIALS COMPOSITION & TOPOLOGY.

NANOMECHANICAL DEVICES

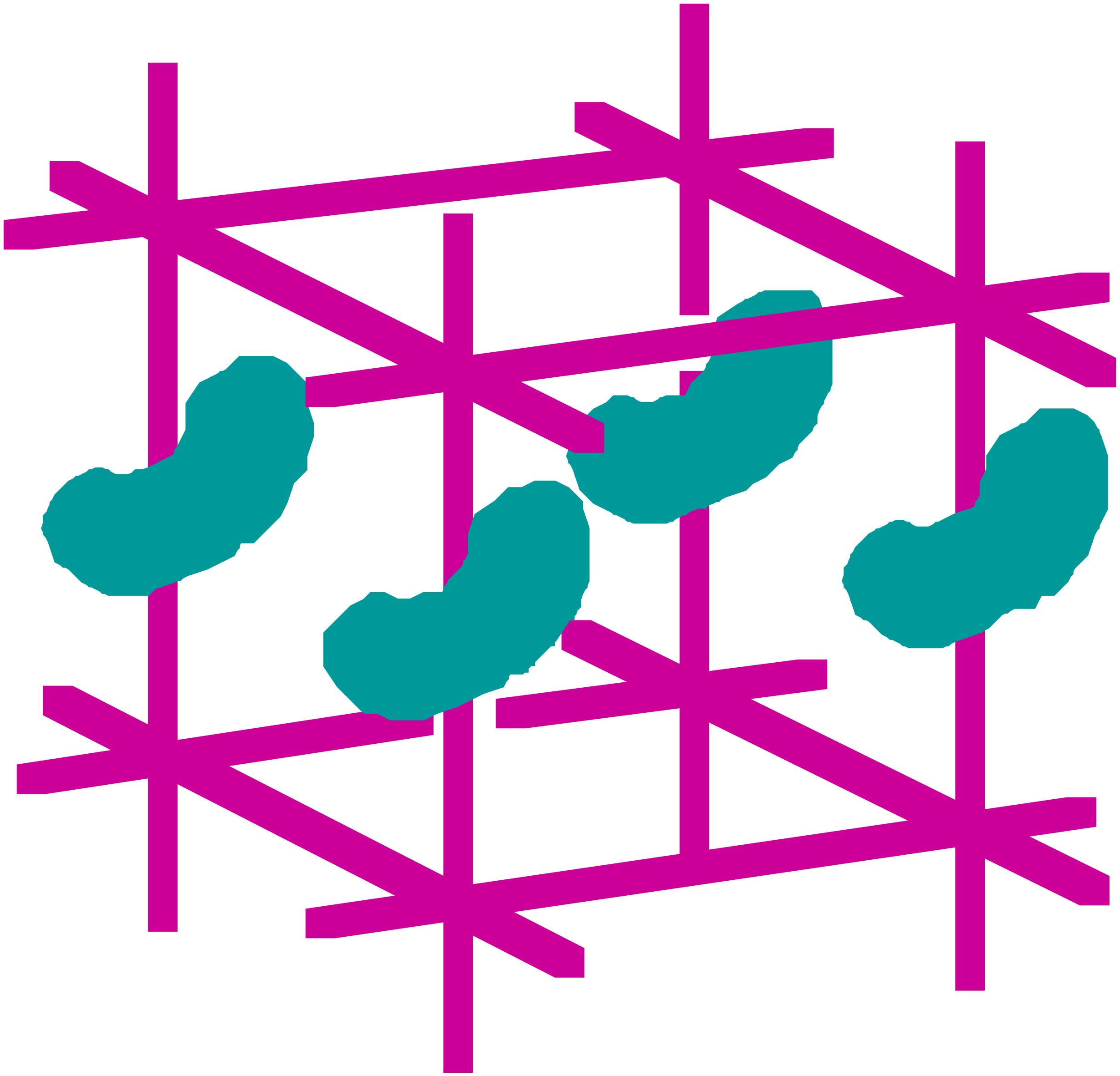
[1] NANOROBOTICS.
[2] NANOFABRICATION.

SELF-REPLICABLE SYSTEMS

CURRENT CRYSTALLIZATION PROTOCOL

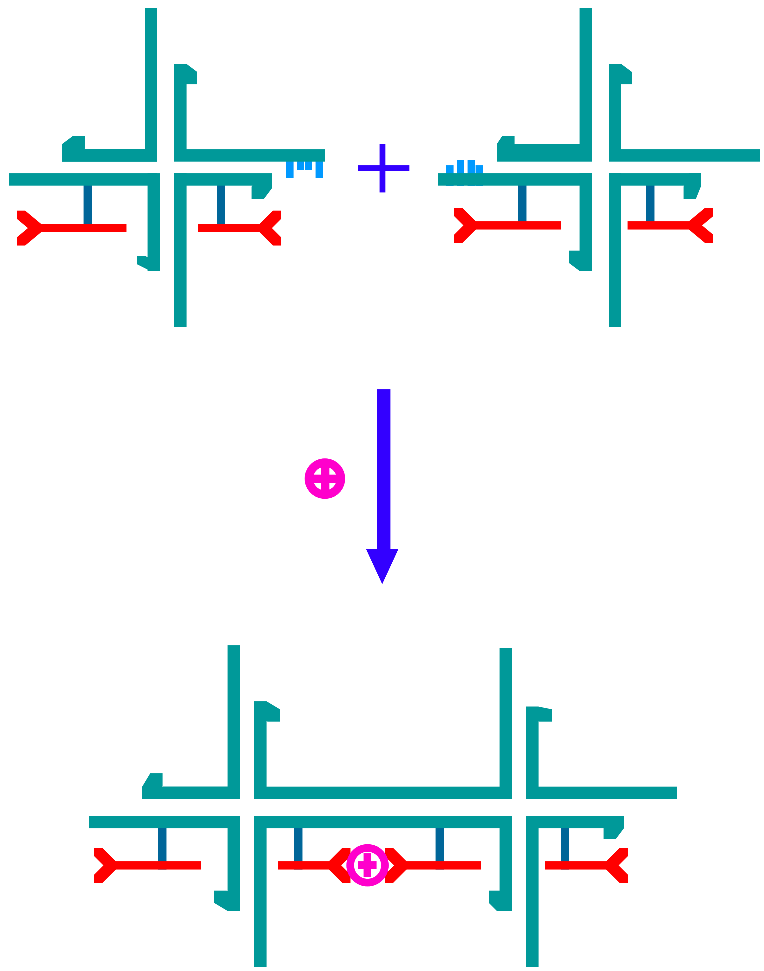


A New Suggestion for Producing Macromolecular Crystals



Seeman, N.C. (1982), *J. Theor.Biol.* **99**, 237-247.

A Method for Organizing Nano-Electronic Components



Robinson, B.H. & Seeman, N.C. (1987), *Protein Eng*. **1**, 295-300..

Why DNA?

Nucleic Acid Sequences Can Be Programmed and Synthesized, Leading to Information-Based Structural, Dynamic and Catalytic Chemistry

Predictable Intermolecular Interactions:
Both Affinity and Structure.

Can Design Shape by Selecting Sequence:
Robust Branched Motifs Programmable by Sequence.

Convenient Automated Chemistry:
Both Vanilla DNA and Useful Derivatives.

Convenient Modifying Enzymes:
Ligases, Exonucleases, Restriction Enzymes, Topoisomerases.

Locally A Stiff Polymer:
Persistence Length ~500 Å; Stiff Branched Motifs Have Been Developed.

Robust Molecule:
Can Heat Individual Strands without Doing Damage.

Amenable to Molecular Biology and Biotechnology Techniques:
Gels, Autoradiography, PCR.

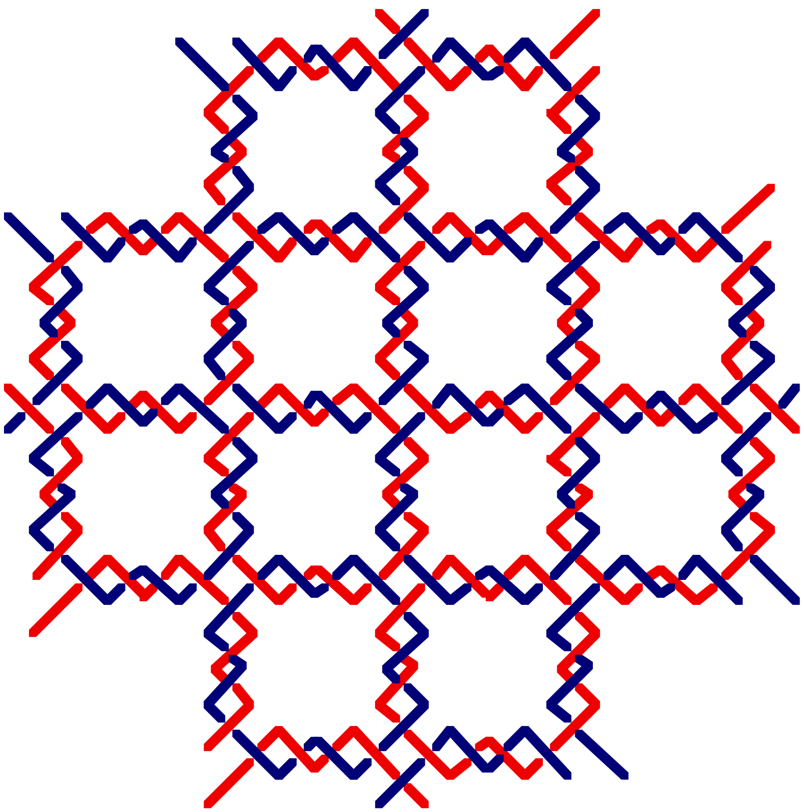
Externally Readable Code when Paired:
Different Points in a Lattice Can be Addressed.

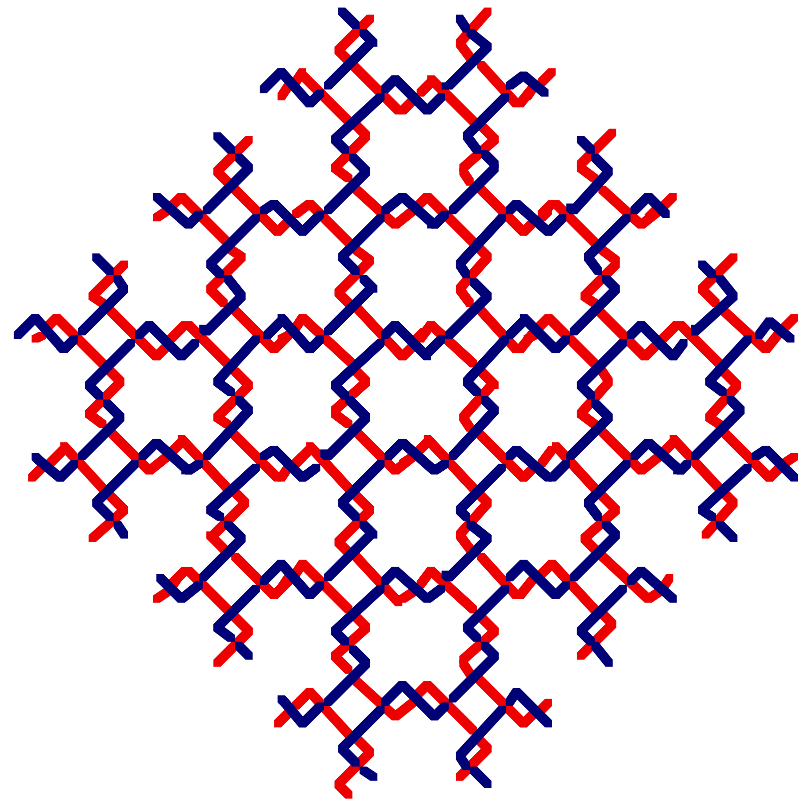
High Functional Group Density:
Every 3.4 Å Nucleotide Separation.

Prototype for Many Derivatives:
The Gene Therapy Enterprise Has Generated Hundreds of Analogs

Self-Replicable and Therefore Selectable:
May be Able to Make and Improve Constructs Inexpensively.

DNA Topology Affects DNA Nanoconstructions





What Is the Intellectual Goal of Structural DNA Nanotechnology?

Controlling the Structure of Matter in 3D to the Highest Extent (Resolution) Possible, so as to Understand the Connection between the Molecular and Macroscopic Scales.

“What I cannot create, I do not understand.”
--Richard P. Feynman
(Inverse not necessarily true.)

STRUCTURAL AND TOPOLOGICAL ASSEMBLIES

Polyhedral Catenanes

Cube: Junghuei Chen

Truncated Octahedron: Yuwen Zhang

Cube

Chen, J. & Seeman. N.C. (1991), *Nature* **350**, 631-633.

Truncated Octahedron

Zhang, Y. & Seeman, N.C. (1994), *J. Am. Chem. Soc*. **116**, 1661-1669.

STRUCTURAL ASSEMBLIES

Construction of Crystalline Arrays

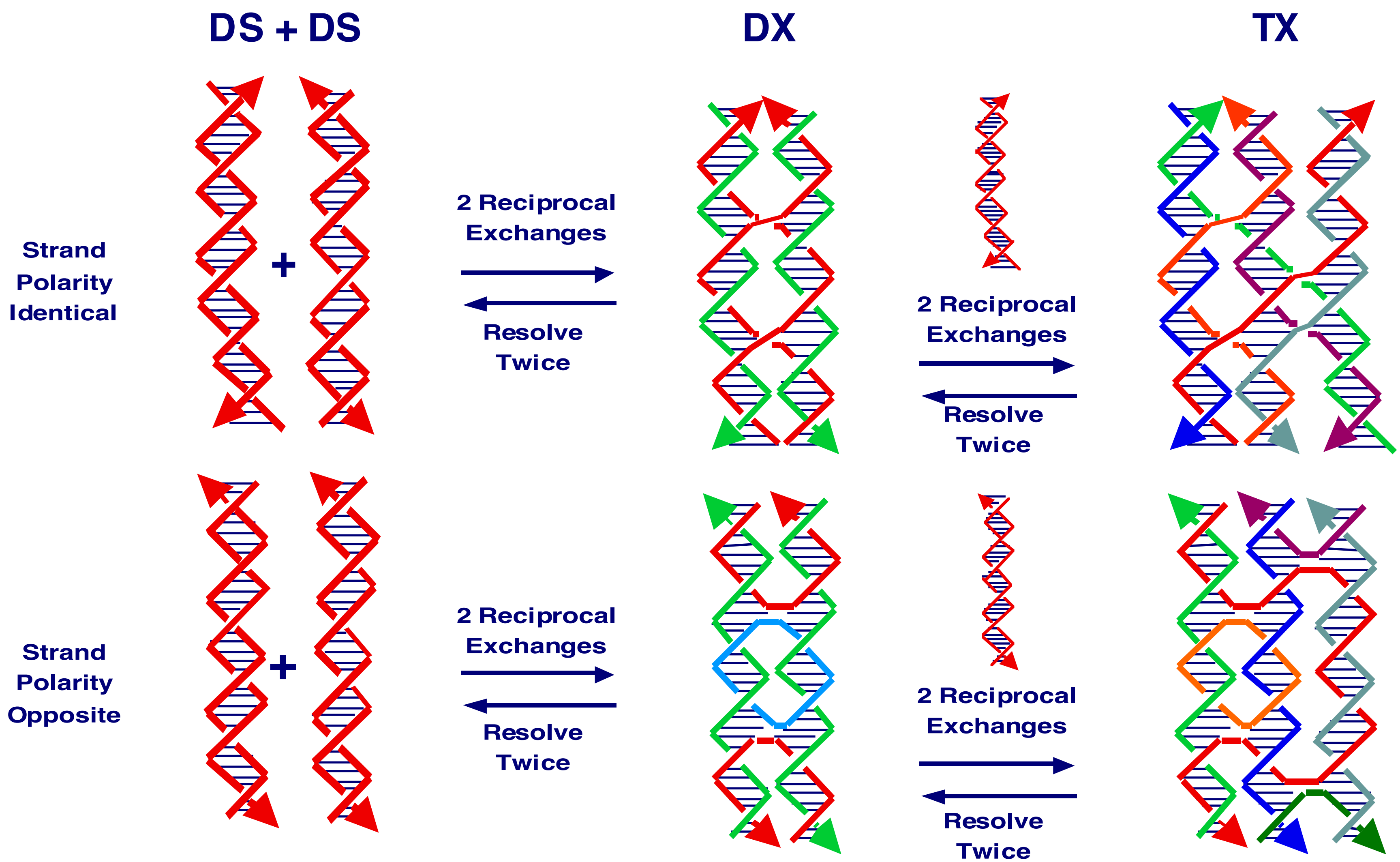
REQUIREMENTS FOR LATTICE DESIGN COMPONENTS

PREDICTABLE INTERACTIONS

PREDICTABLE LOCAL PRODUCT STRUCTURES

STRUCTURAL INTEGRITY

Derivation of DX and TX Molecules

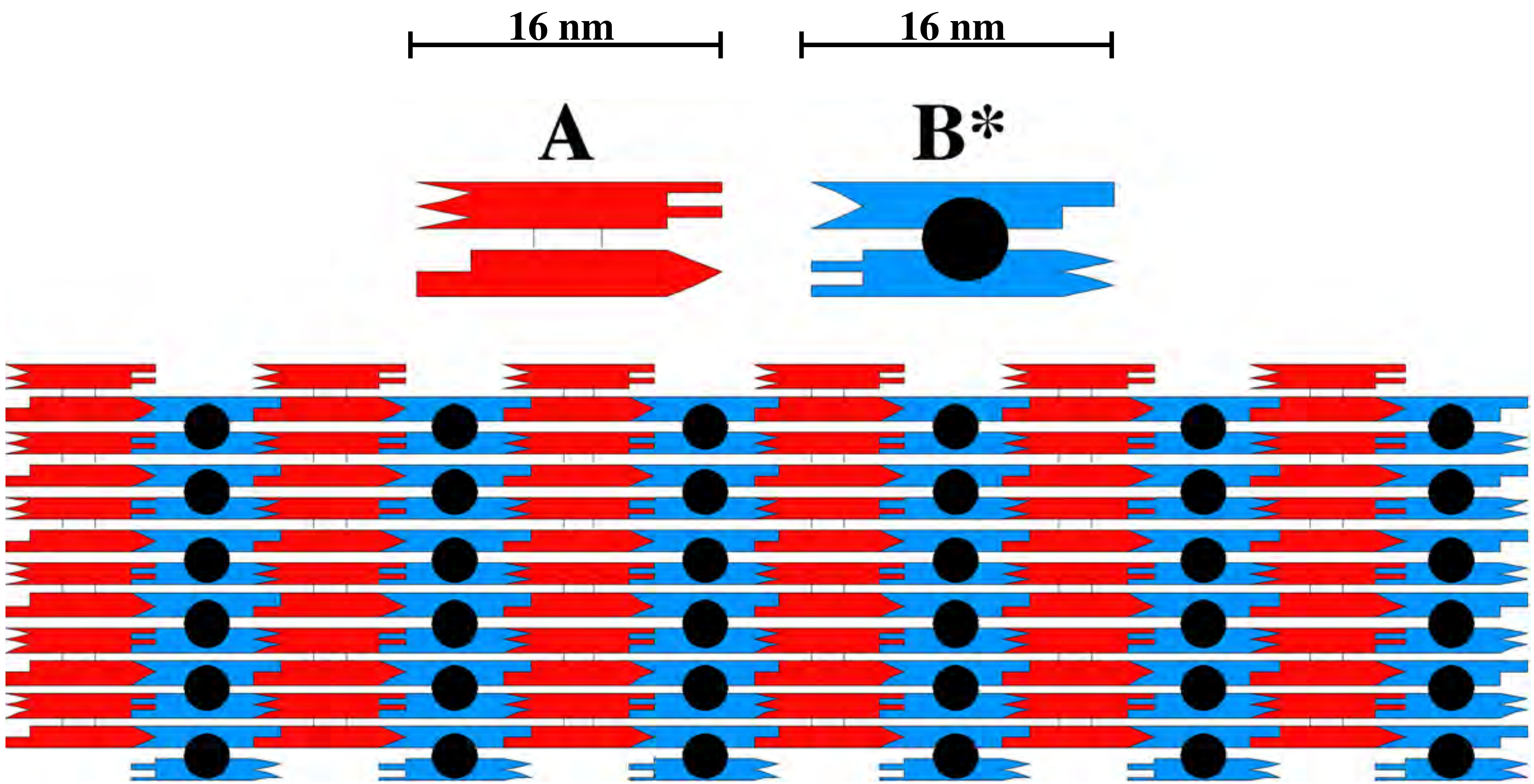


Seeman, N.C. (2001) *NanoLetters* **1**, 22-26.

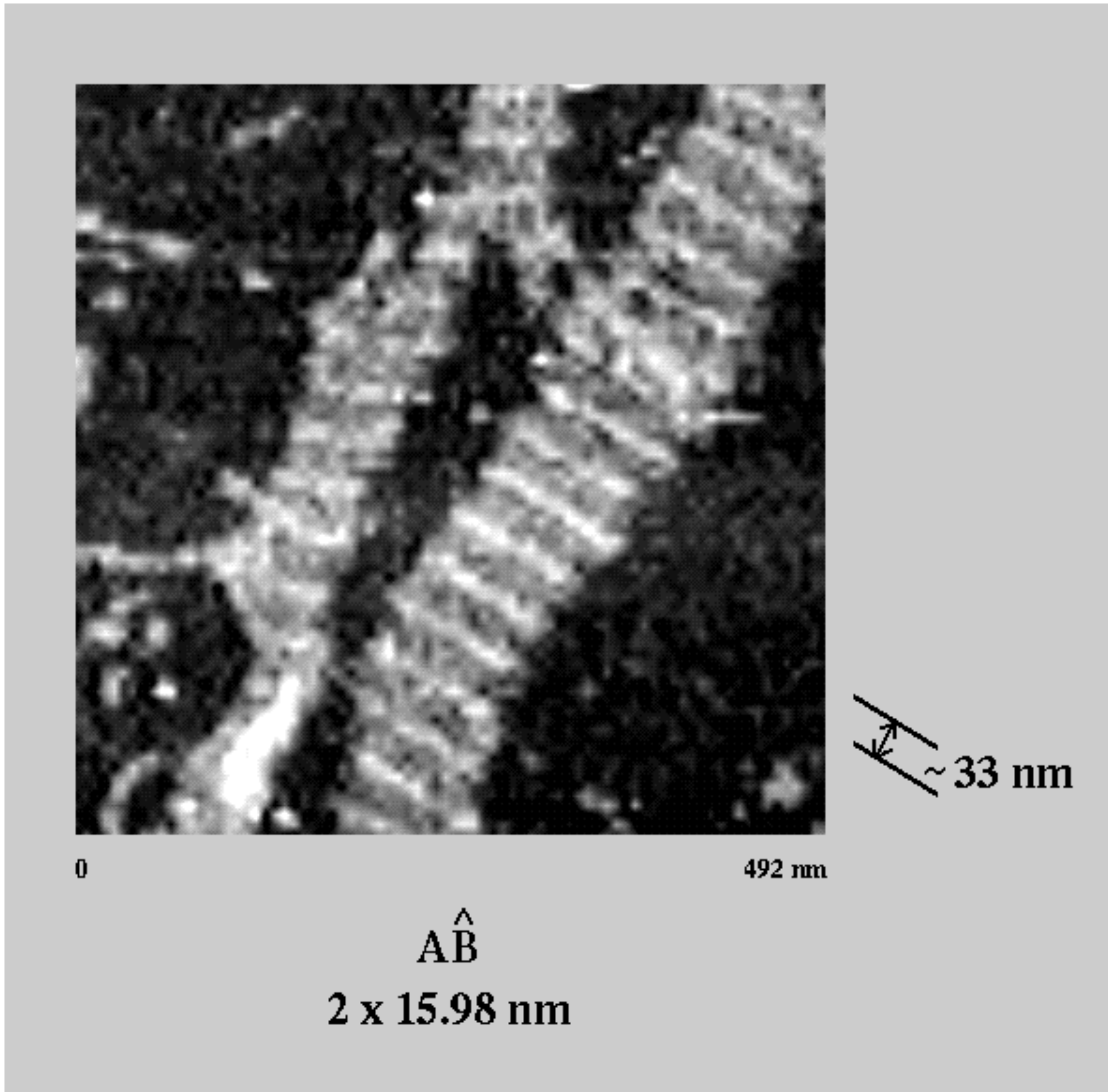
2D DX Arrays

Erik Winfree (Caltech)
Furong Liu
Lisa Wenzler

Schematic of a Lattice Containing 1 DX Tile and 1 DX+J Tile

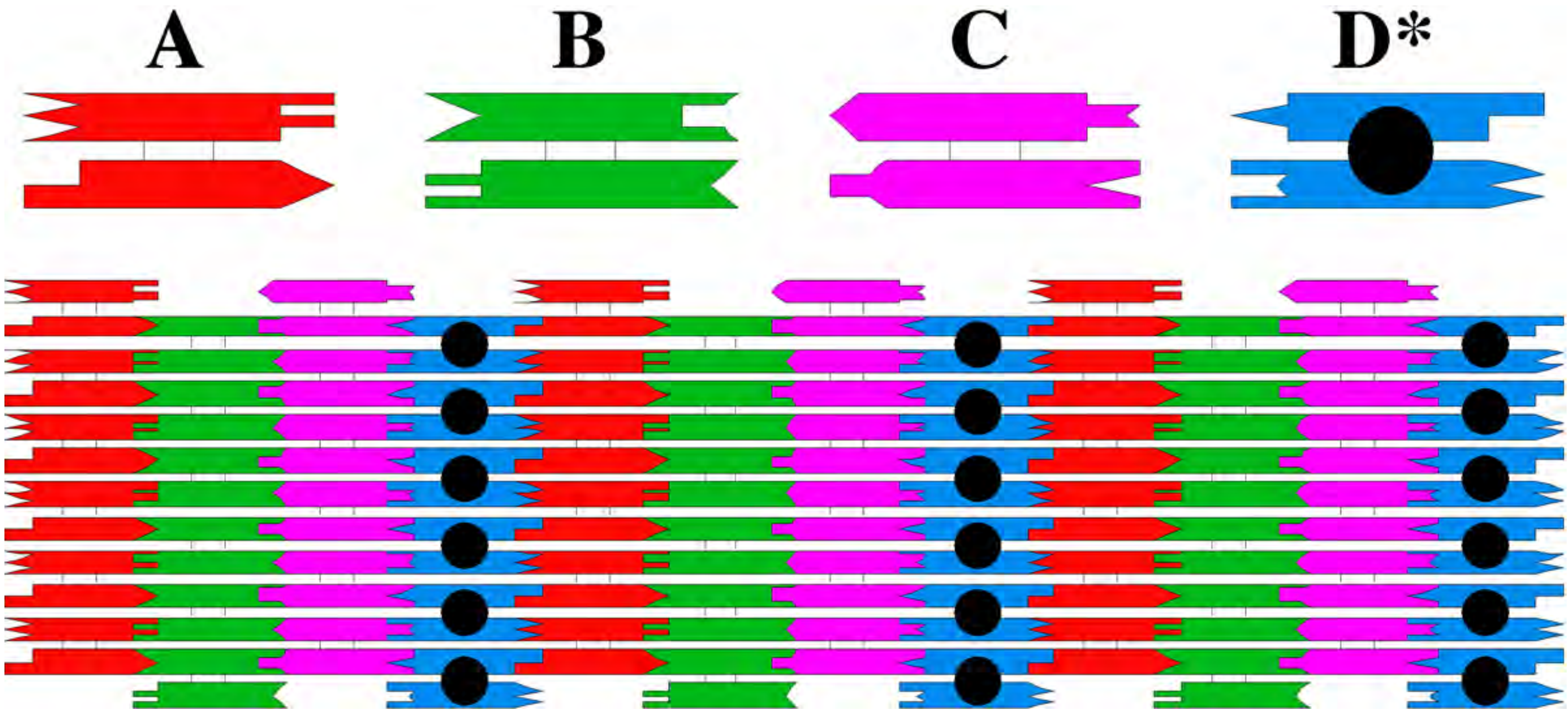


AFM of a Lattice Containing 1 DX Tile and 1 DX+J Tile

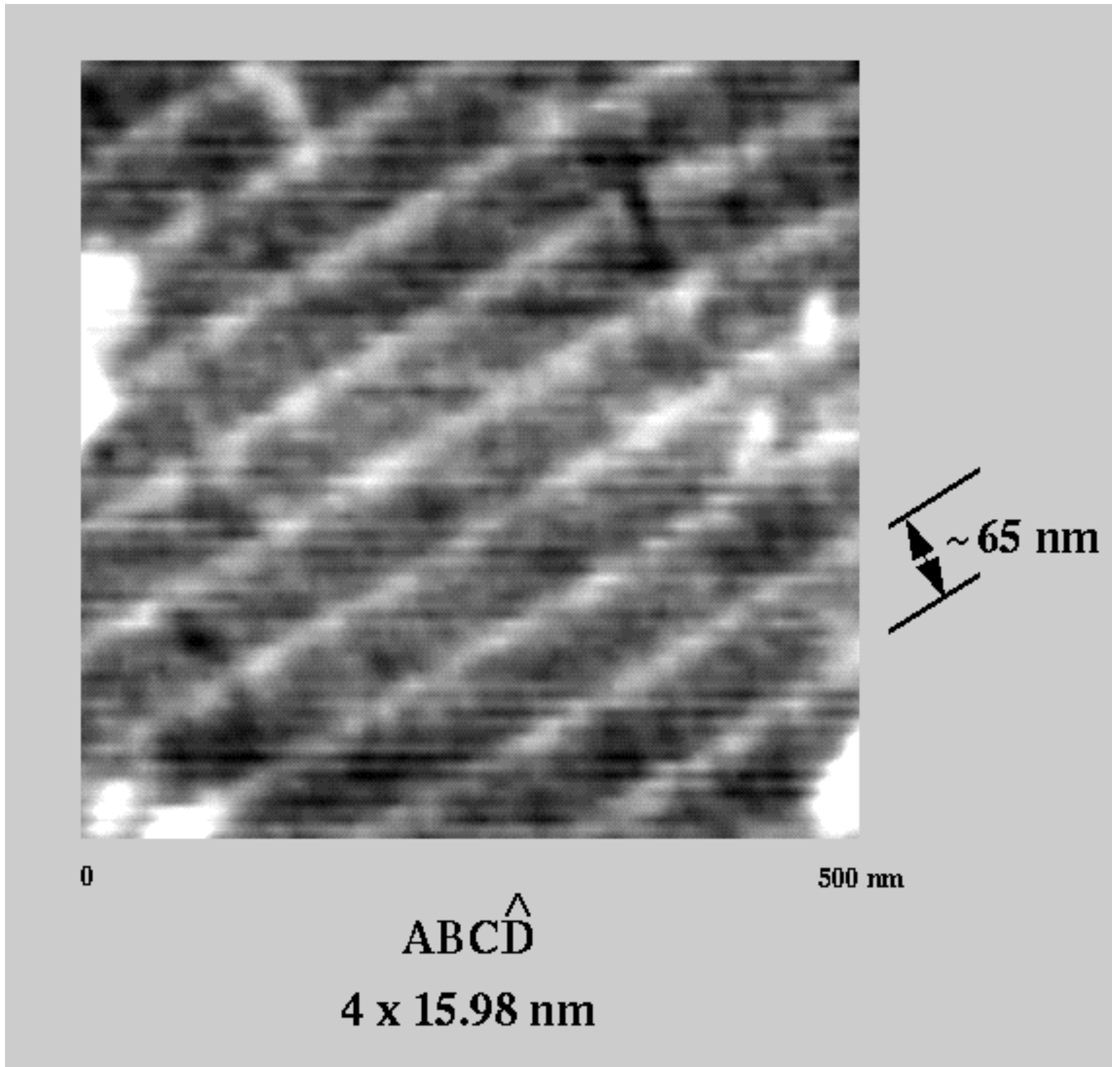


Winfree, E., Liu, F., Wenzler, L.A. & Seeman, N.C. (1998), *Nature* **394**, 539-544.

Schematic of a Lattice Containing 3 DX Tiles and 1 DX+J Tile



AFM of a Lattice Containing 3 DX Tiles and 1 DX+J Tile



Winfree, E., Liu, F., Wenzler, L.A. & Seeman, N.C. (1998), *Nature* **394**, 539-544.

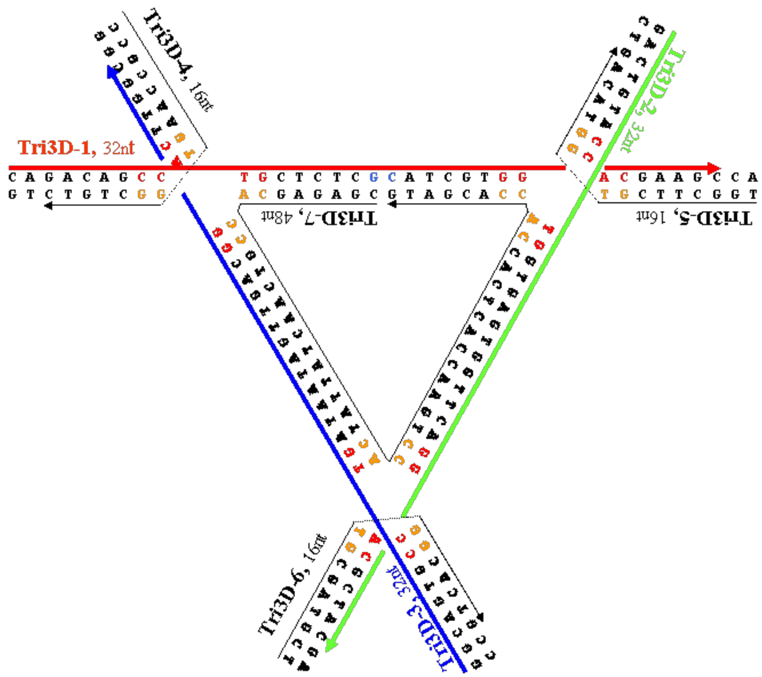
Three-Dimensional Self-Assembled Arrays: DESIGNED CRYSTALS!

Jianping Zheng, Jens J. Birktoft, Yi Chen (Purdue),
Tong Wang, Ruojie Sha, Pam Constantinou,
Steve Ginell (Argonne), Chengde Mao (Purdue)

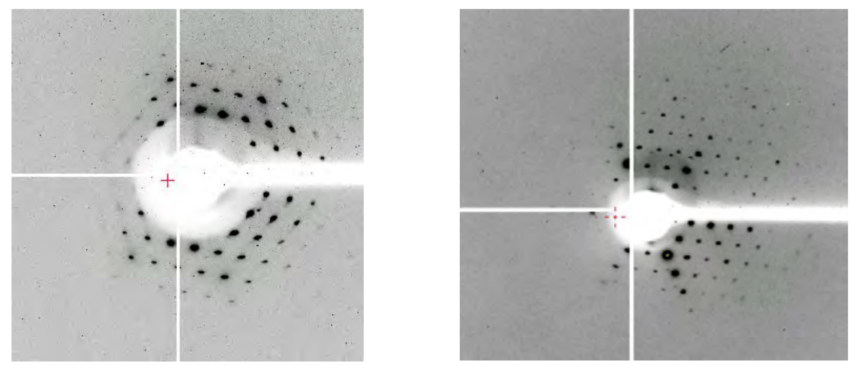
Diffraction Data Collected at
Brookhaven National Laboratory (NSLS) and
Argonne National Laboratory (APS)

A 3D DNA Tensegrity Triangle

[D.Liu, M. Wang, Z. Deng, R. Walulu & C.Mao, *J. Am. Chem. Soc.* **126**, 2324-2325 (2004)]



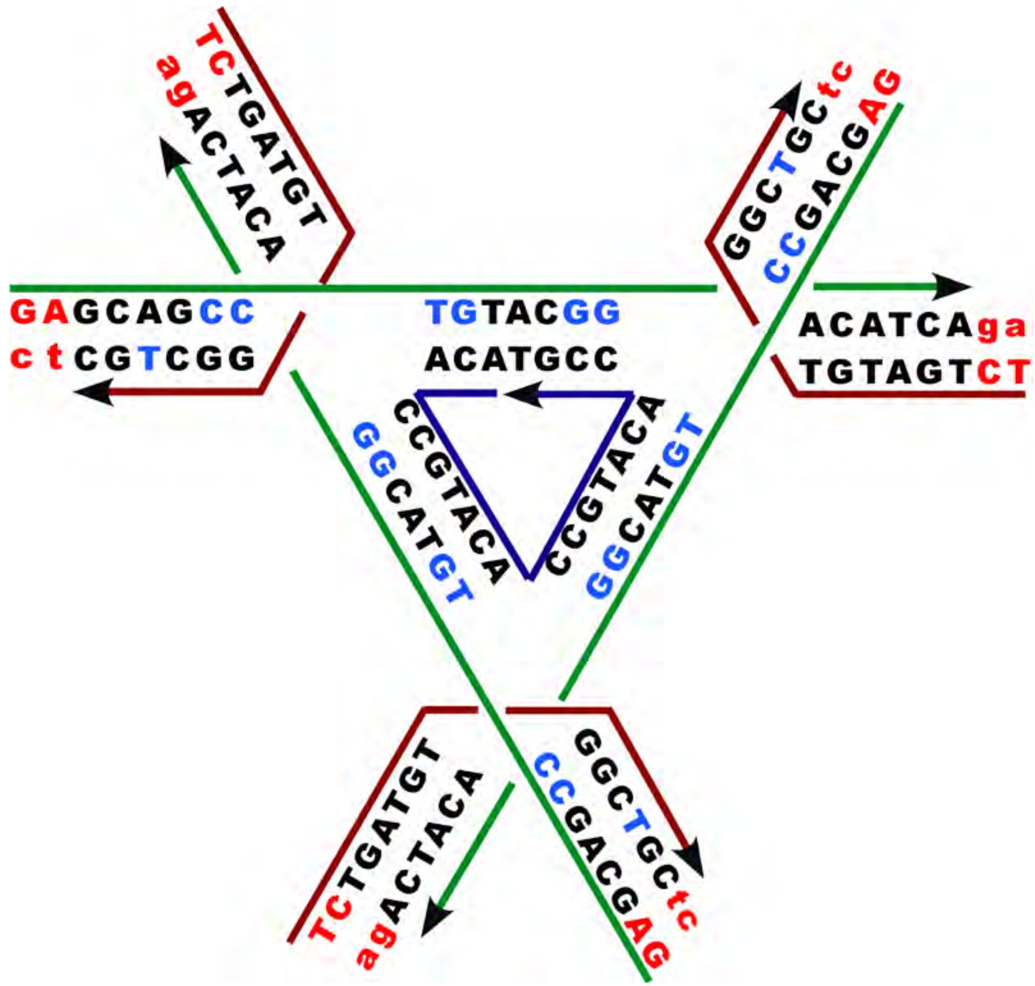
X-Ray Diffraction:
Predicted Spacings and Rhombohedral Symmetry
Resolution: ~10Å



Designed 142 A Edges

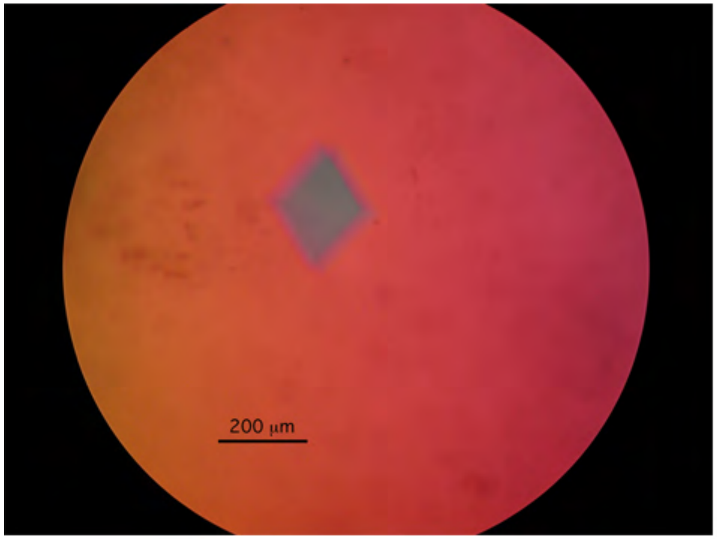
The Tensegrity Triangle Motif

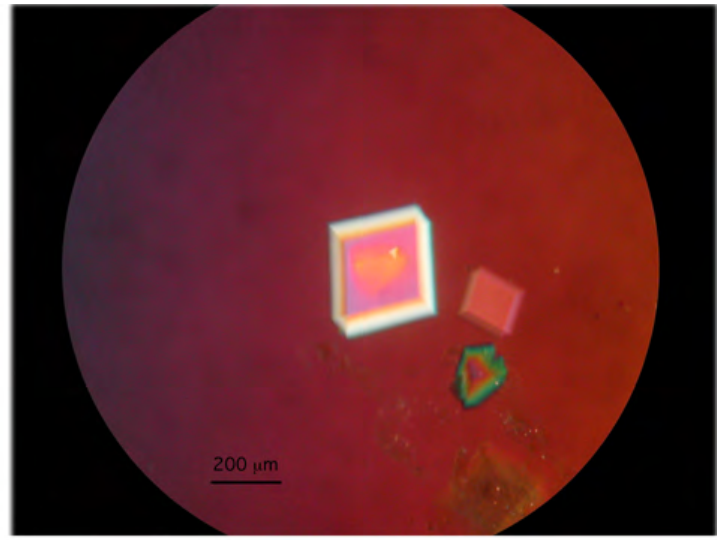
A Small Threefold Pseudosymmetric DNA Tensegrity Triangle

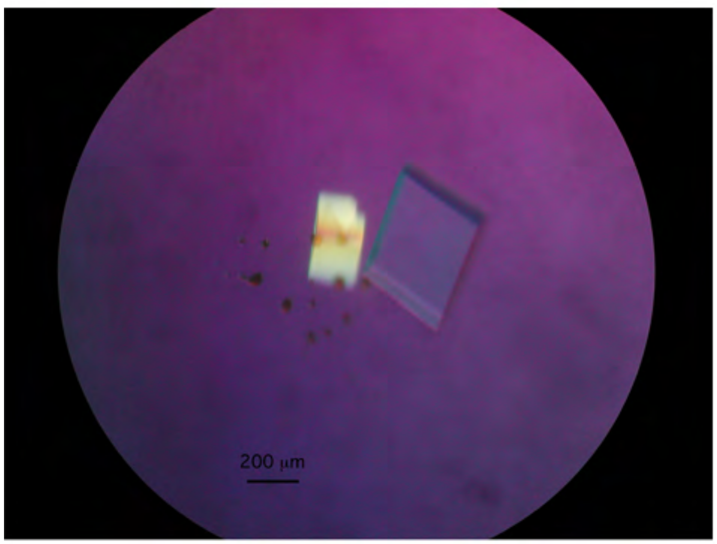


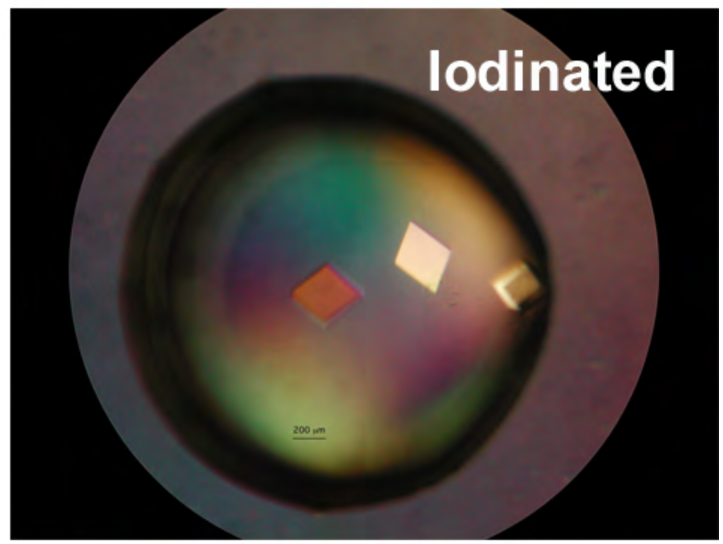
J. Zheng, J.J. Birktoft, Y. Chen, T. Wang, R. Sha,
P.E. Constantinou, S.L. Ginell, C. Mao & N.C. Seeman, *Nature* 461, 74-77 (2009).

Crystal Images



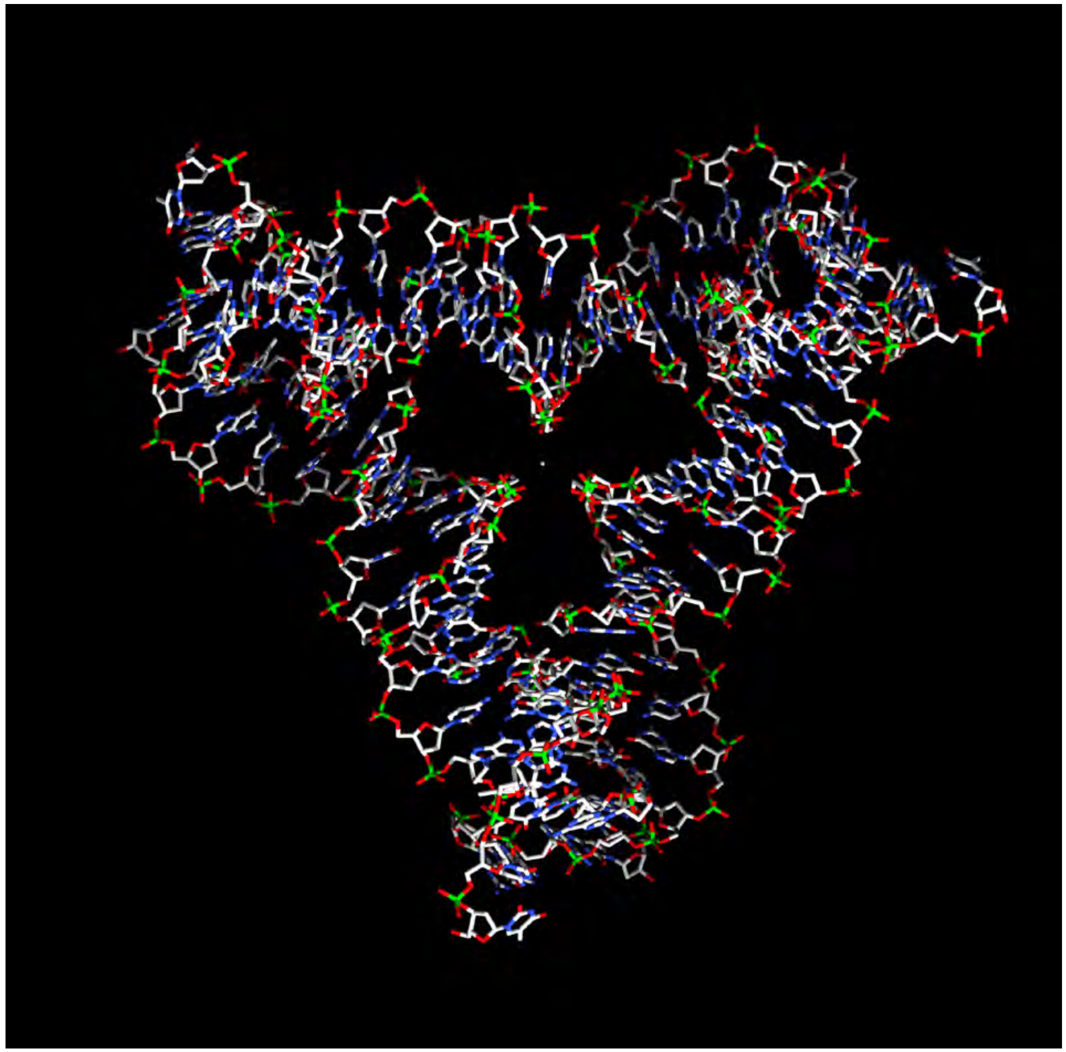






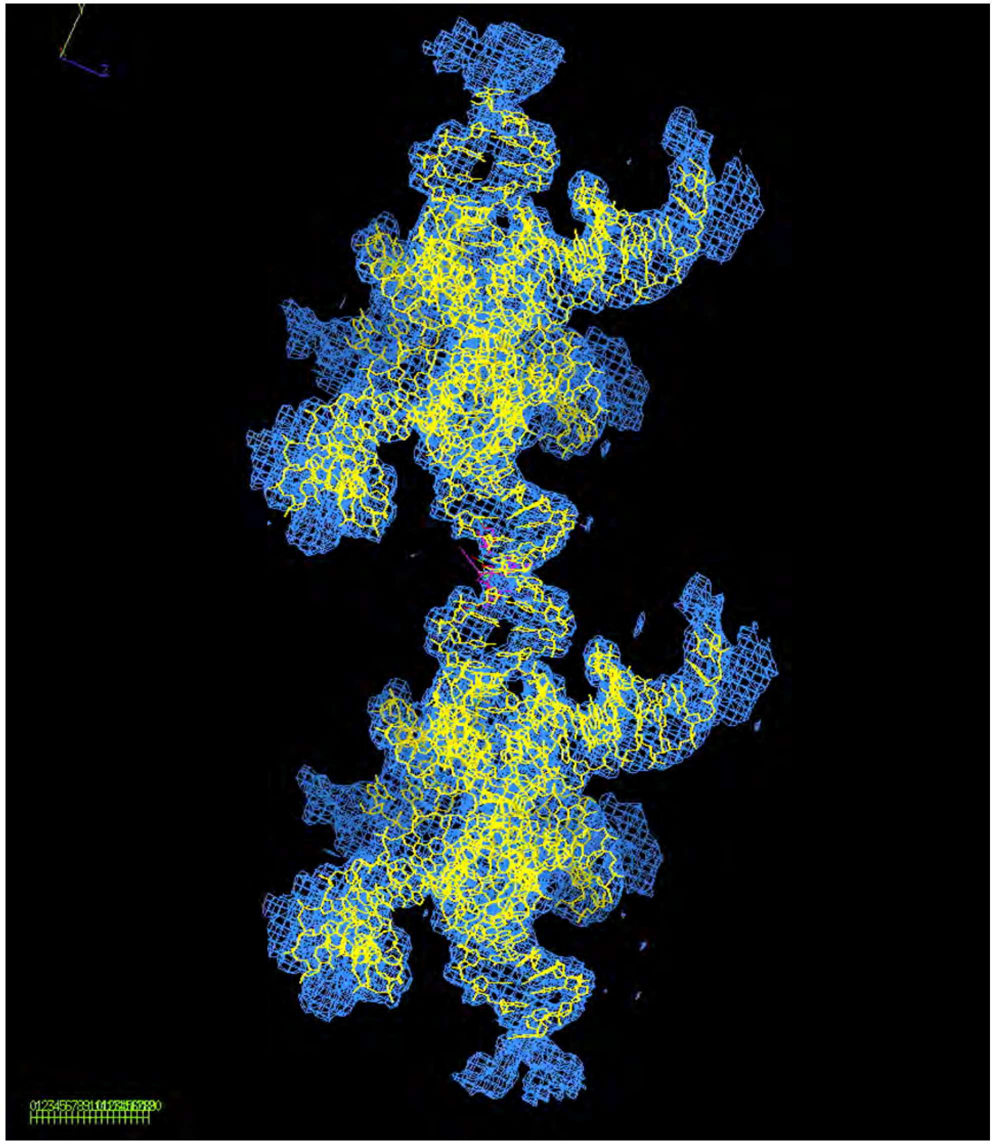
J. Zheng, J.J. Birktoft, Y. Chen, T. Wang, R. Sha,
P.E. Constantinou, S.L. Ginell, C. Mao & N.C. Seeman, *Nature* 461, 74-77 (2009).

Crystal Structure of the 2-Turn DNA Tensegrity Triangle



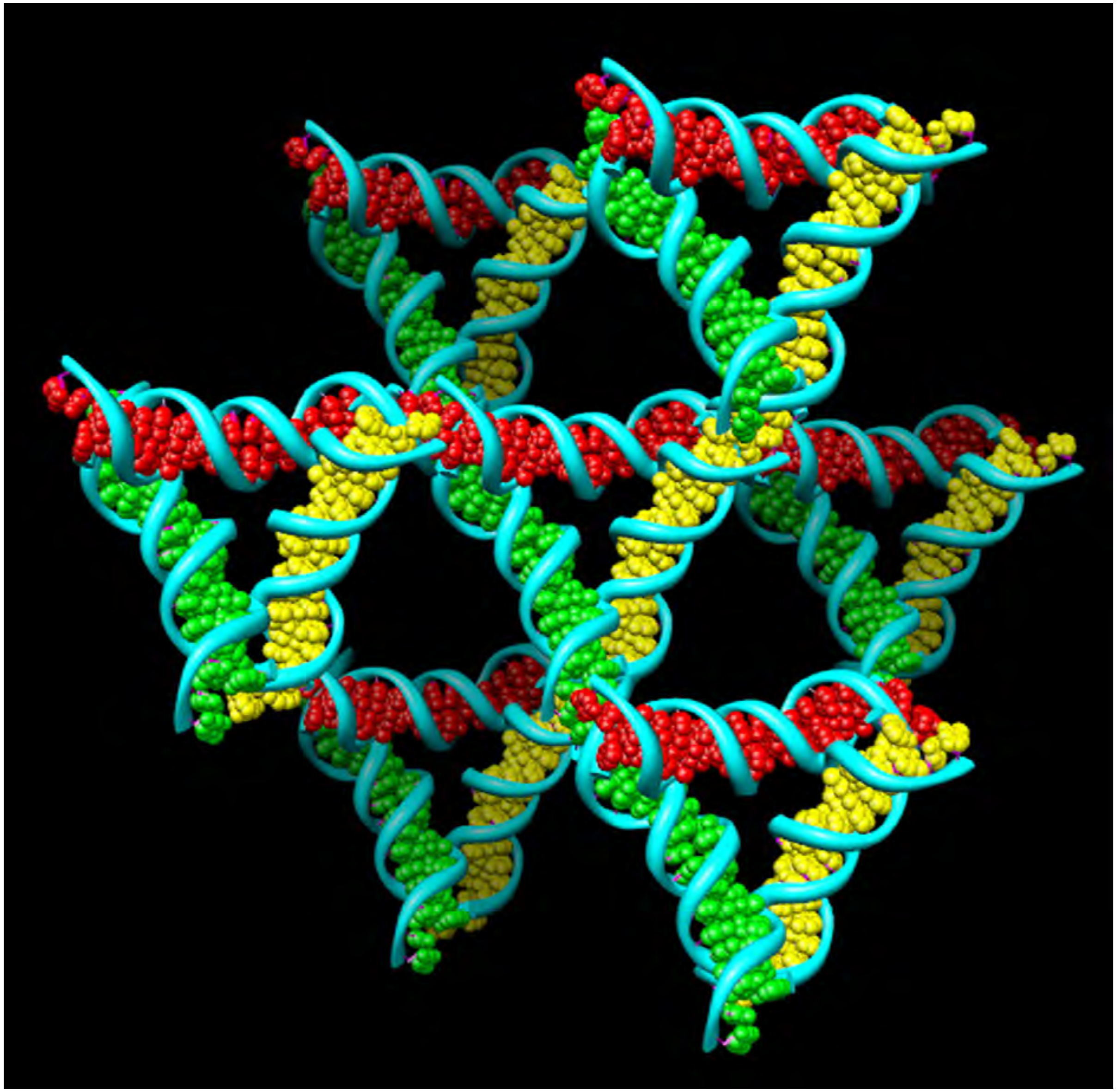
J. Zheng, J.J. Birktoft, Y. Chen, T. Wang, R. Sha,
P.E. Constantinou, S.L. Ginell, C. Mao & N.C. Seeman, *Nature* 461, 74-77 (2009).

4 Å [APS] Map Perpendicular to a Helix



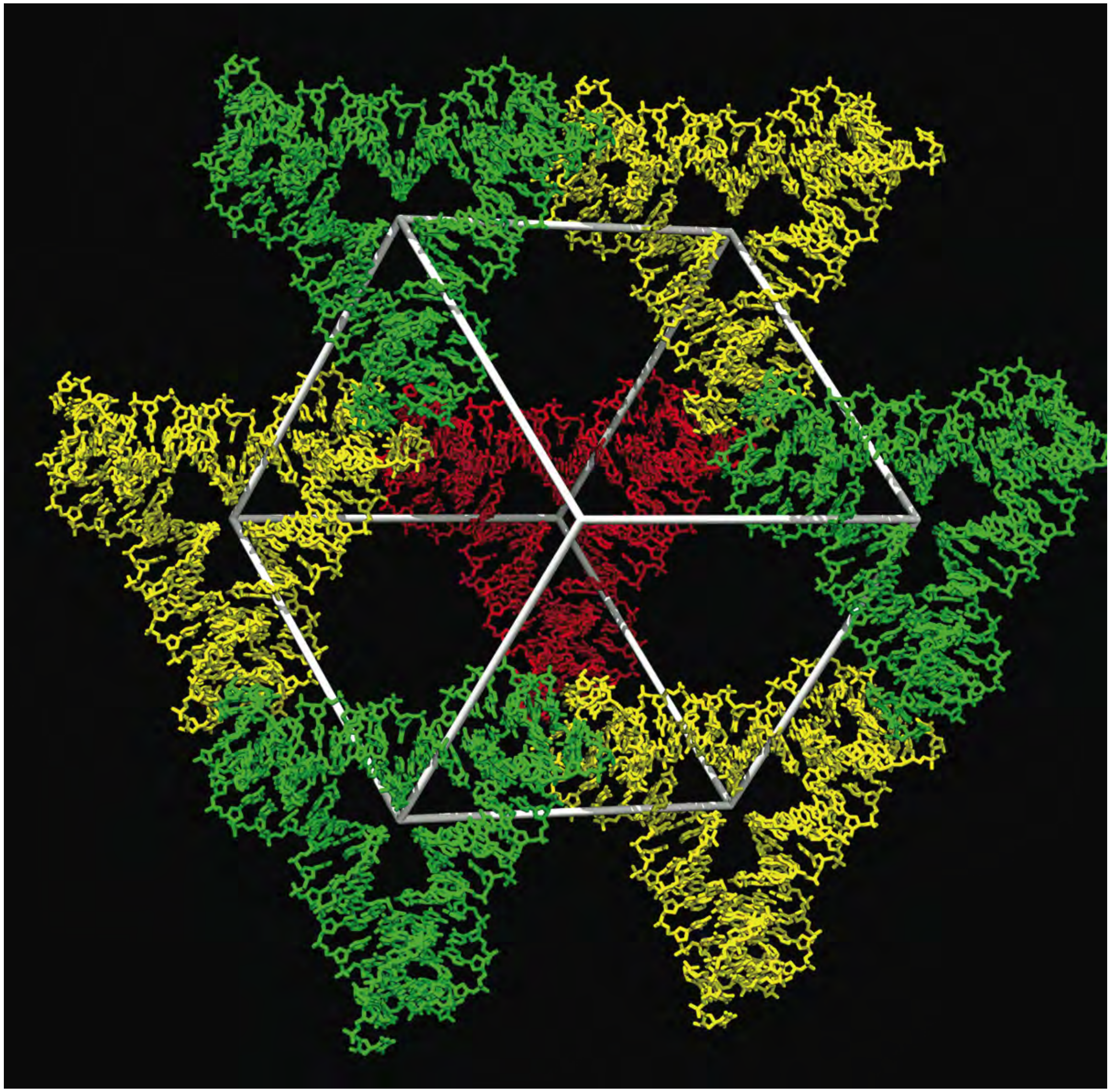
**J. Zheng, J.J. Birktoft, Y. Chen, T. Wang, R. Sha,
P.E. Constantinou, S.L. Ginell, C. Mao & N.C. Seeman, *Nature* 461, 74-77 (2009).**

Environment of a Single Triangle



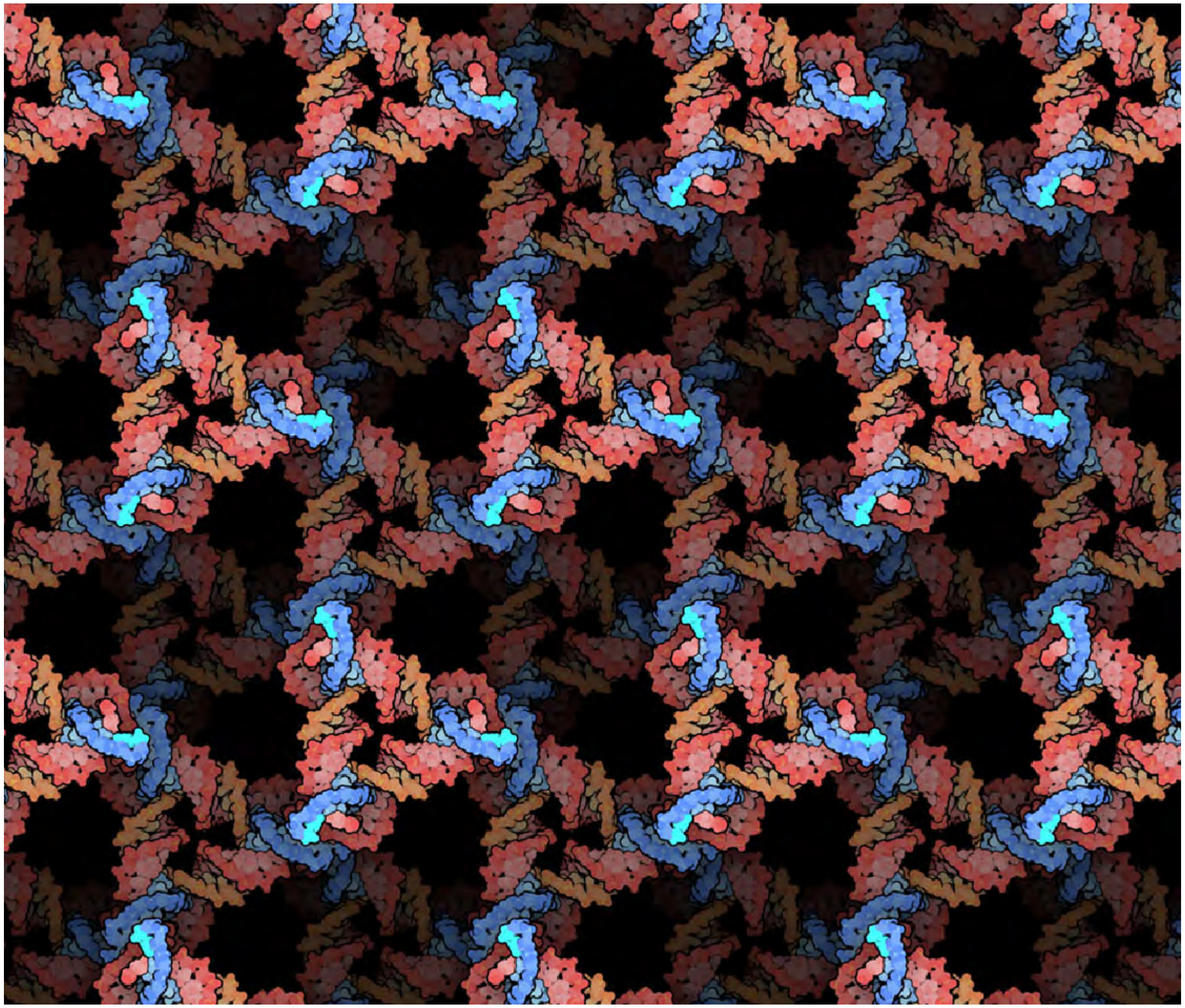
J. Zheng, J.J. Birktoft, Y. Chen, T. Wang, R. Sha,
P.E. Constantinou, S.L. Ginell, C. Mao & N.C. Seeman, *Nature* 461, 74-77 (2009).

The Rhombohedral Cavity



J. Zheng, J.J. Birktoft, Y. Chen, T. Wang, R. Sha,
P.E. Constantinou, S.L. Ginell, C. Mao & N.C. Seeman, *Nature* 461, 74-77 (2009).

Mono View Down 3-Fold Axis



R3; **a** = 68.28 Å; α = 102.44°

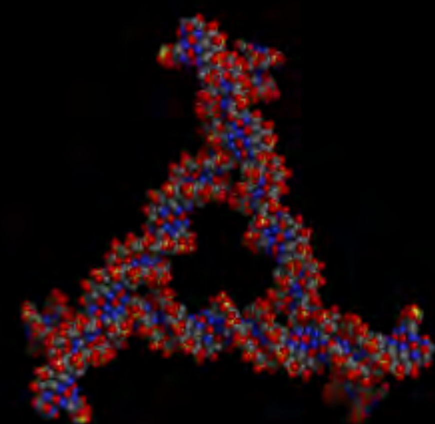
Image Courtesy of
David Goodsell

J. Zheng, J.J. Birktoft, Y. Chen, T. Wang, R. Sha,
P.E. Constantinou, S.L. Ginell, C. Mao & N.C. Seeman, *Nature* 461, 74-77 (2009).

Table 1. Crystalline Tensegrity Triangles

Edge Length	Symmetry	Inter-junction Pairs	Rhombohedral Cell Dimensions		Resolution (Å)	Cross Section (nm^2)	Cavity Size (nm^3)
21	+	7	a = 68.3,	$\alpha = 102.4^\circ$	4.0	23	103
21	-	7	a = 68.0,	$\alpha = 102.6^\circ$	5.0	23	101
31	+	17	a = 102.0,	$\alpha = 112.7^\circ$	6.1	62	366
31	-	17	a = 100.9,	$\alpha = 111.6^\circ$	6.3	61	373
32	+	18	a = 103.6,	$\alpha = 113.6^\circ$	6.5	64	367
32	-	18	a = 103.3,	$\alpha = 112.2^\circ$	6.5	64	395
42	+	17	a = 134.9,	$\alpha = 110.9^\circ$	11.0	123	1104
42	-	17	a = 133.7,	$\alpha = 111.3^\circ$	14.0	120	1048
42	+	28	a = 134.9,	$\alpha = 117.3^\circ$	10.0	117	643

J. Zheng, J.J. Birktoft, Y. Chen, T. Wang, R. Sha,
P.E. Constantinou, S.L. Ginell, C. Mao & N.C. Seeman, *Nature* 461, 74-77 (2009).

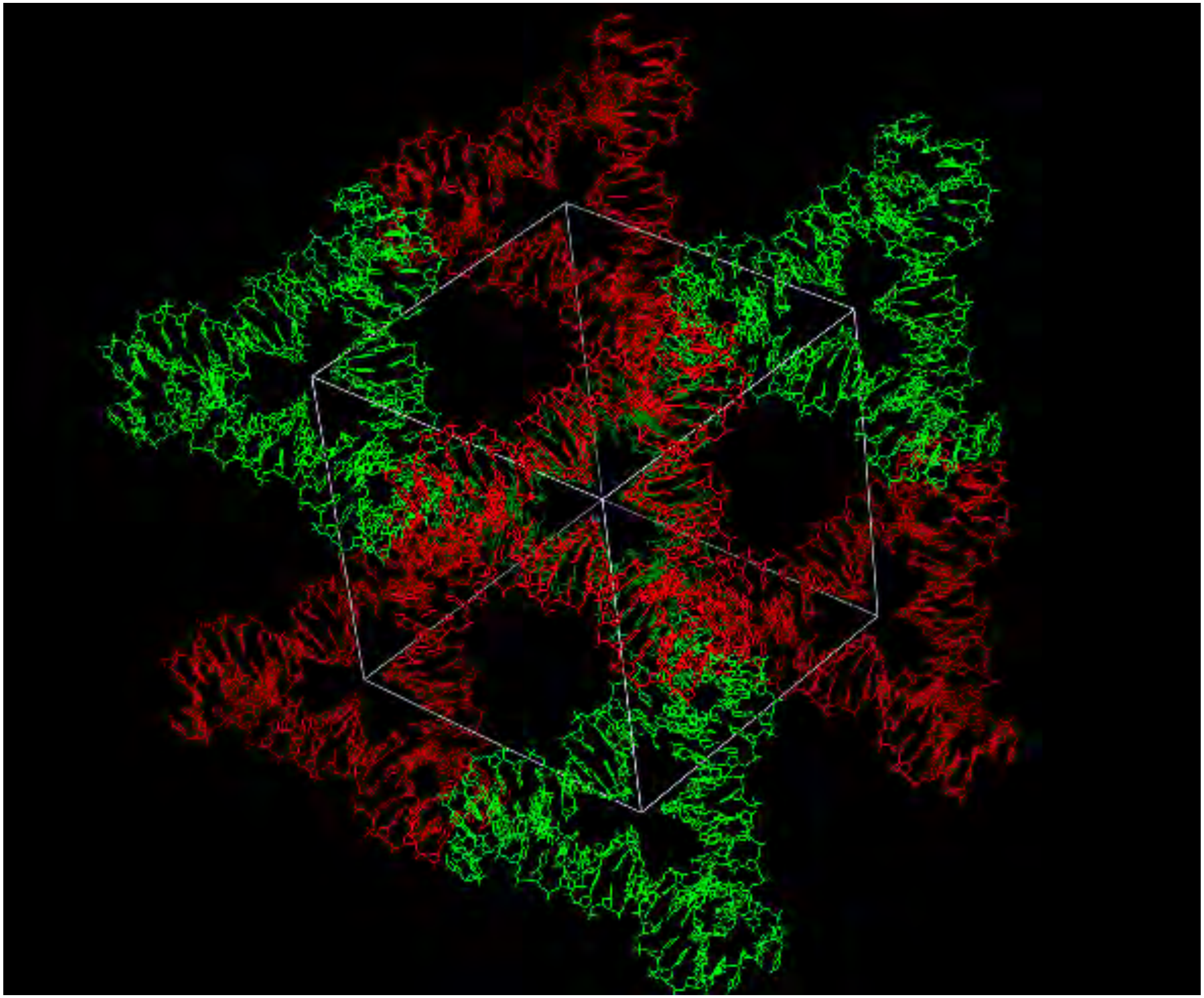


Movie Courtesy of Kevin Drew

A Two-Turn Tensegrity Triangle Designed Lattice with Two Components

Tong Wang
Ruojie Sha
Jens Birktoft
Jianping Zheng
Chengde Mao (Purdue)

Movie of the Rhombohedral Cavity

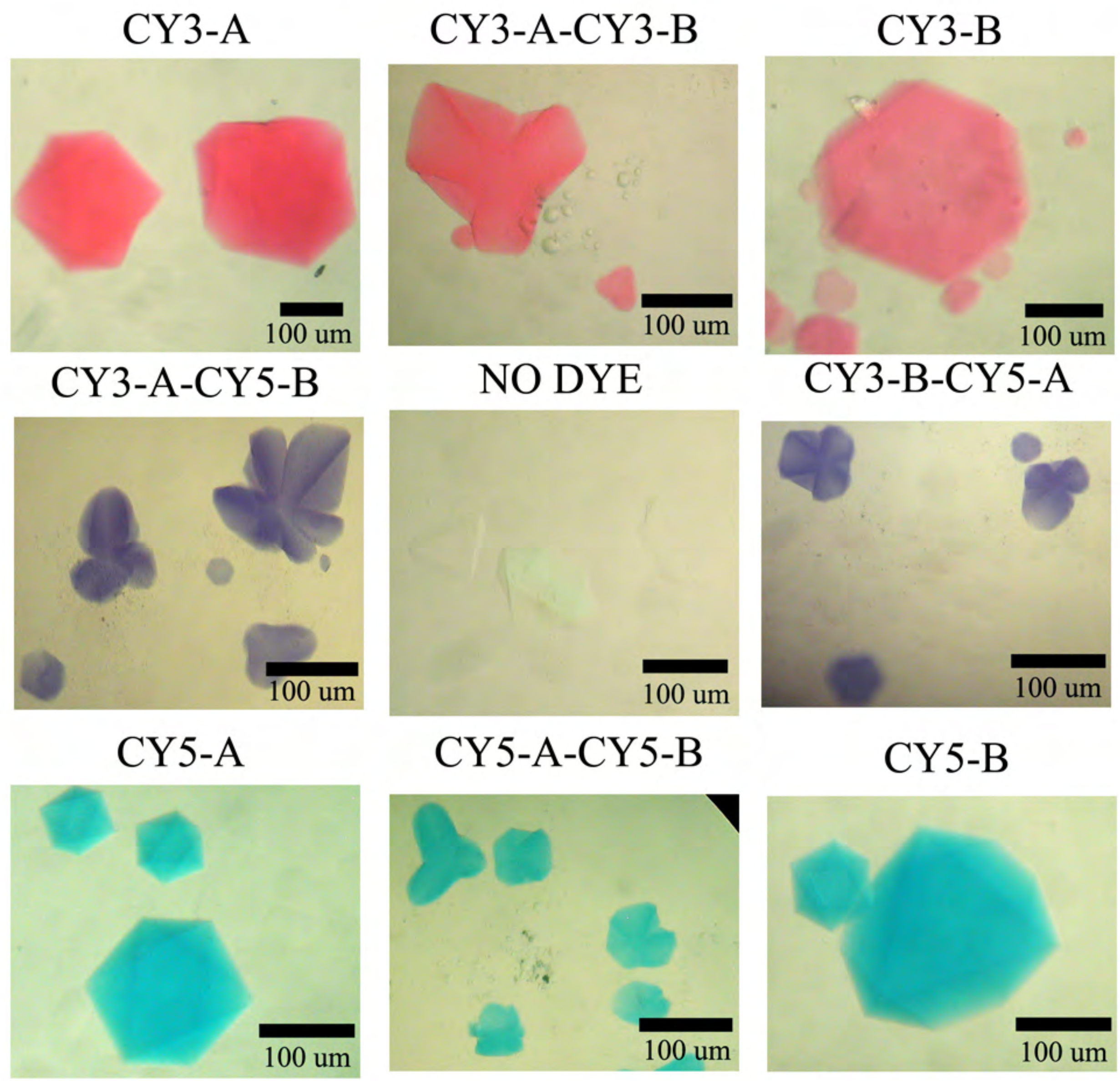


T.Wang, R. Sha, J.J. Birktoft, J. Zheng, C. Mao, N.C. Seeman, *J. Am. Chem. Soc.*, in press (2010).

Covalent Attachment of Fluorescent Dyes to One or Two Triangles in the A•B Crystal

Ruojie Sha

Attachment of Cy3 & Cy5 to Triangles

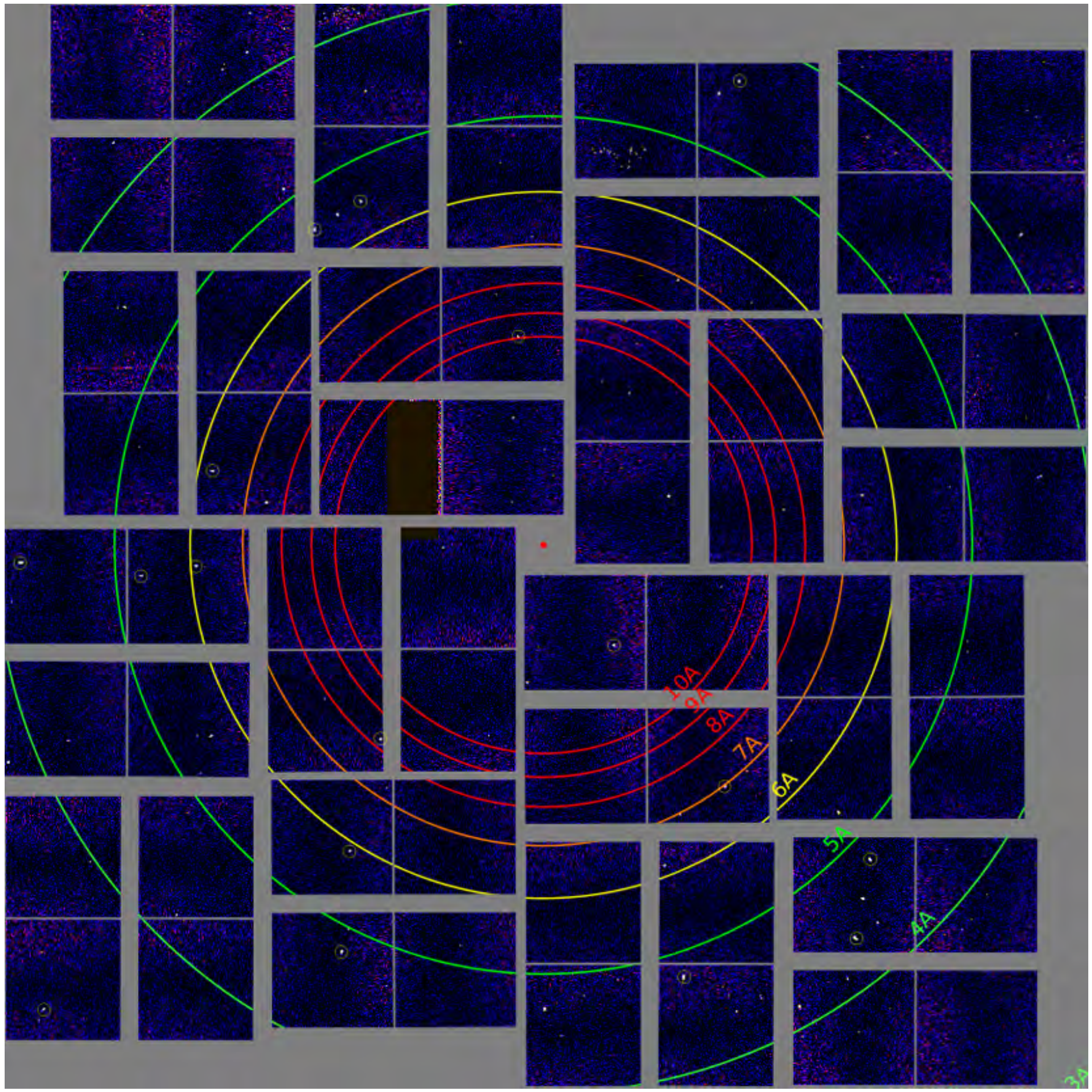


T.Wang, R. Sha, J.J. Birktoft, J. Zheng, C. Mao, N.C. Seeman, *J. Am. Chem. Soc.*, **132**, 15471-15473 (2010).

Nanocrystals Diffract Better than 4Å

Arun Richard Chandrasekaran
Yoel Ohayon
Ilme Schlichting
Petra Fromme
Henry Chapman
+ 30 Others

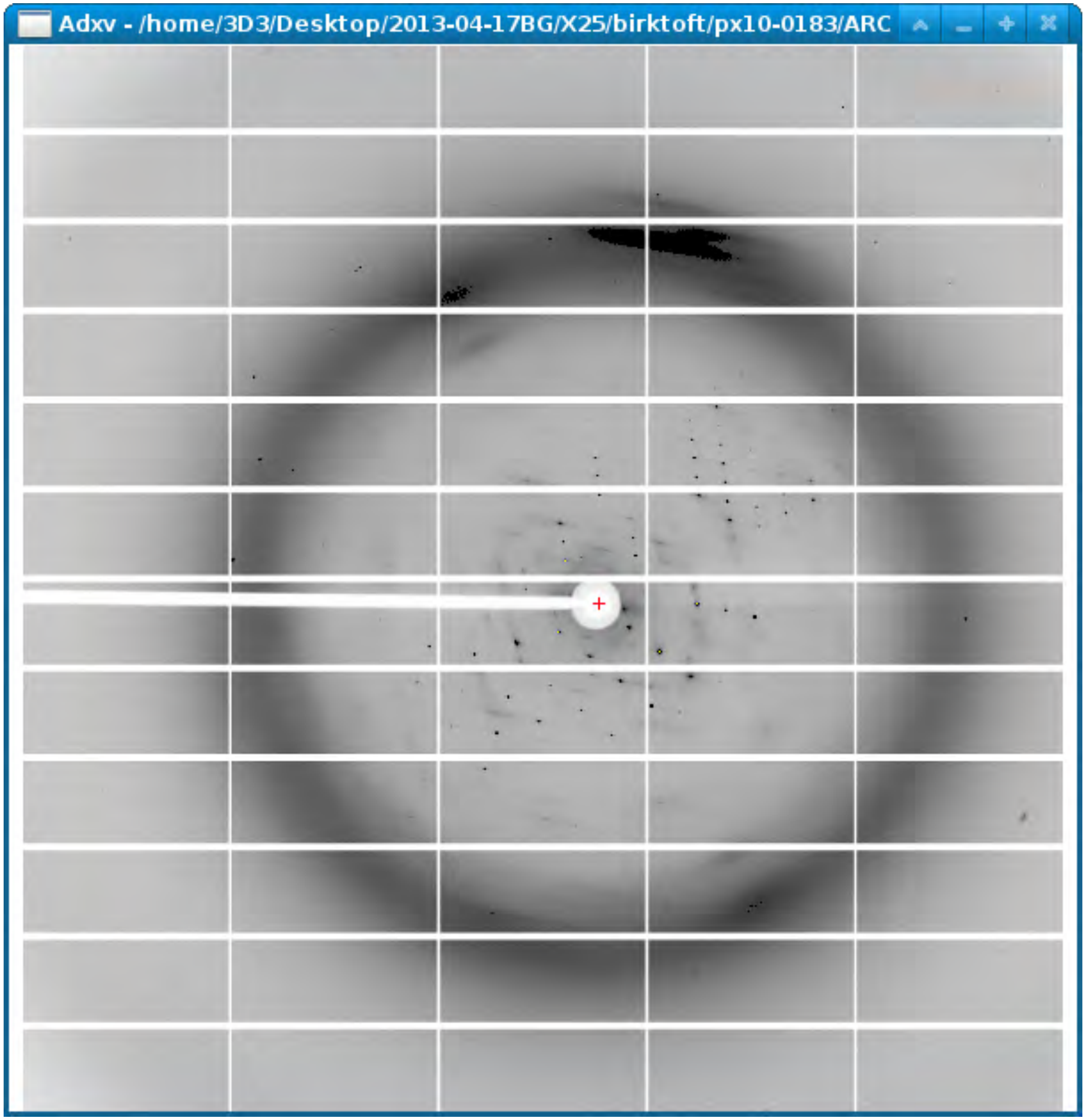
SE = 1, No PO_4



Modifying Contacts Improves Resolution to 3.0 Å at NSLS

Arun Richard Chandrasekaran
Yoel Ohayon
Nam Nguyen
Jens Birktoft
Ruojie Sha

SE = 1 G:C, All Strands Contain 5' PO_4



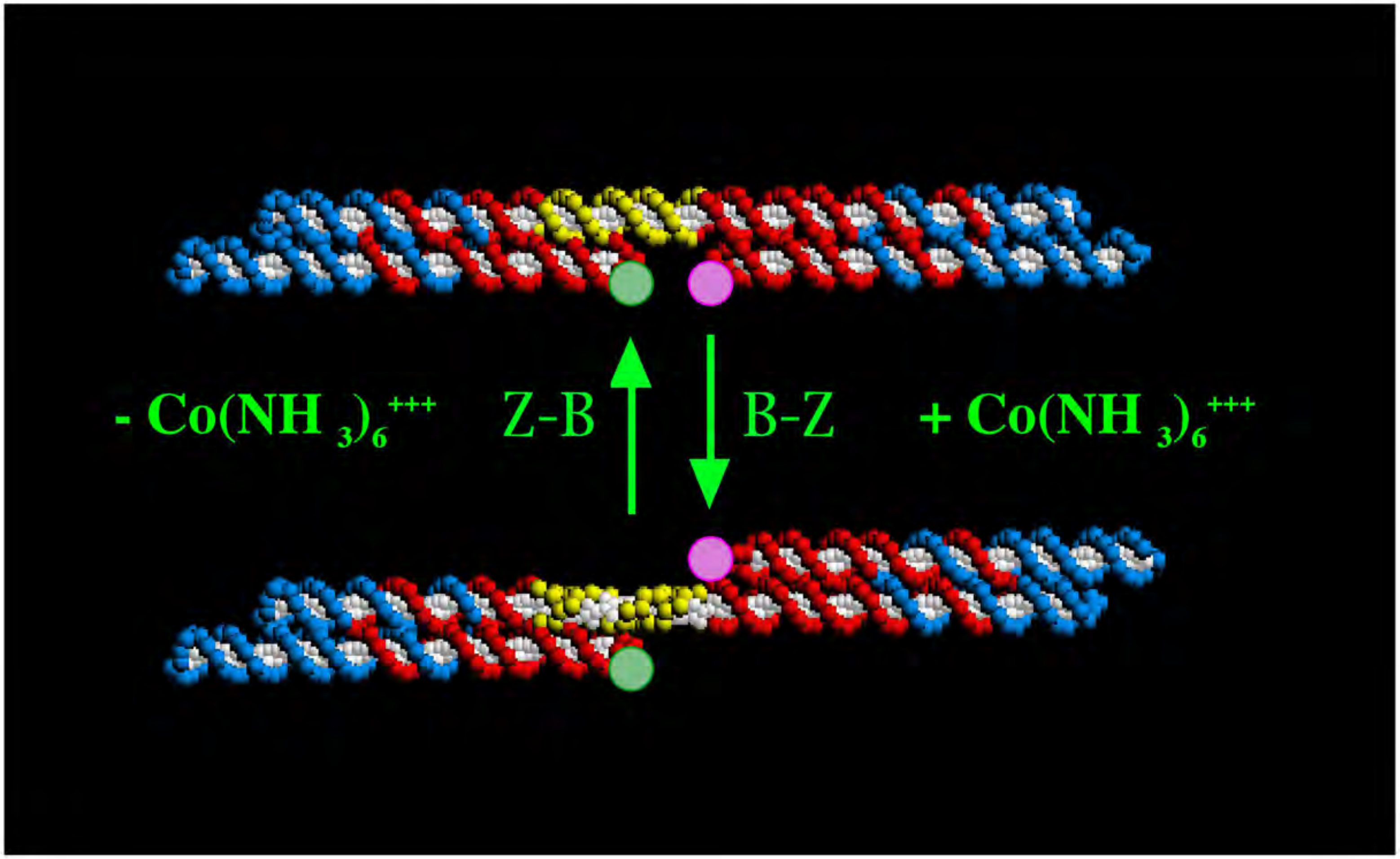
FROM GENES TO MACHINES

SHAPE-SHIFTERS

B-Z Device

Chengde Mao

A Device Based on the B<-->Z Transition

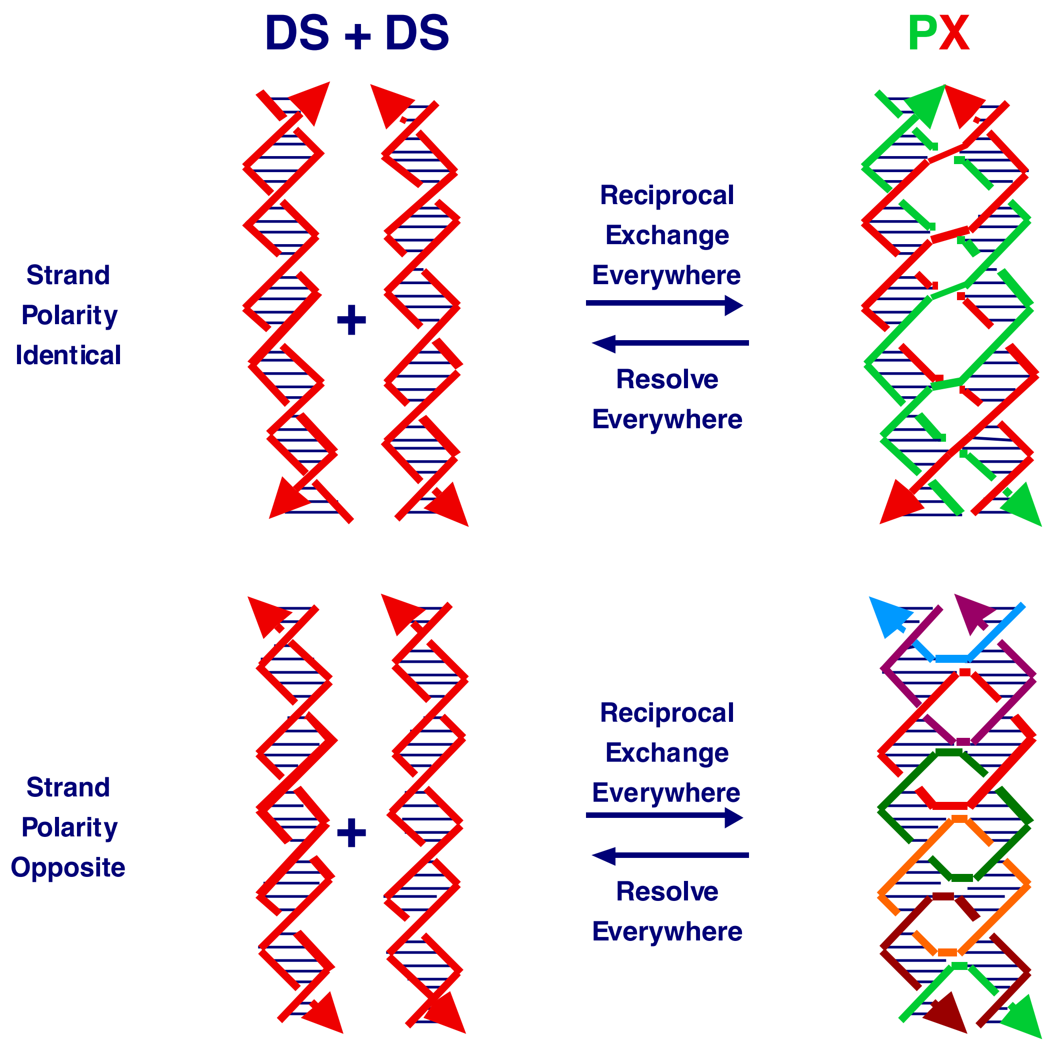


Mao, C., Sun, W., Shen, Z. & Seeman,N.C. (1999), *Nature* **397**, 144-146.

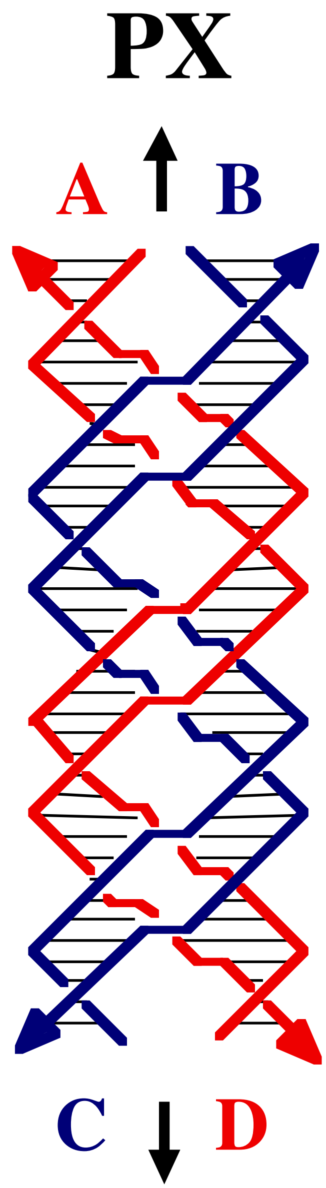
A Sequence-Dependent Device

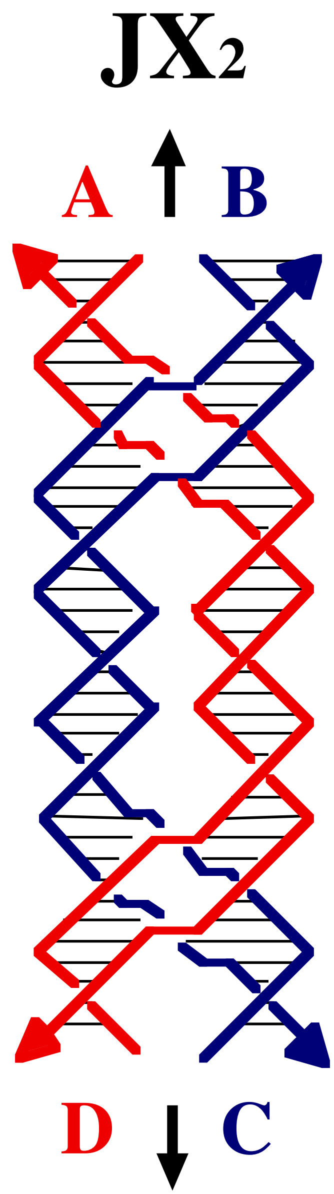
Hao Yan

Derivation of PX DNA



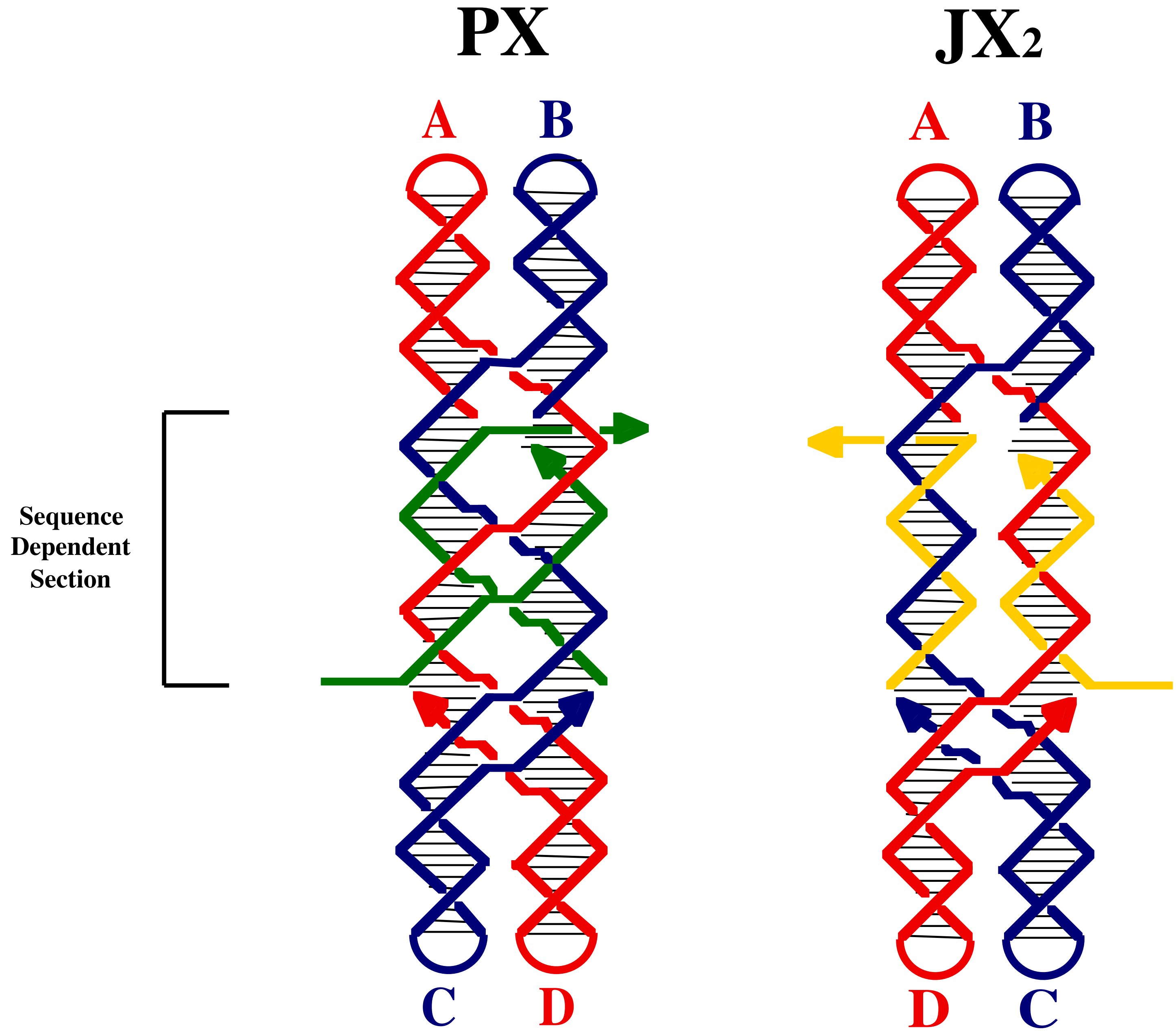
Seeman, N.C. (2001) *NanoLetters* **1**, 22-26.



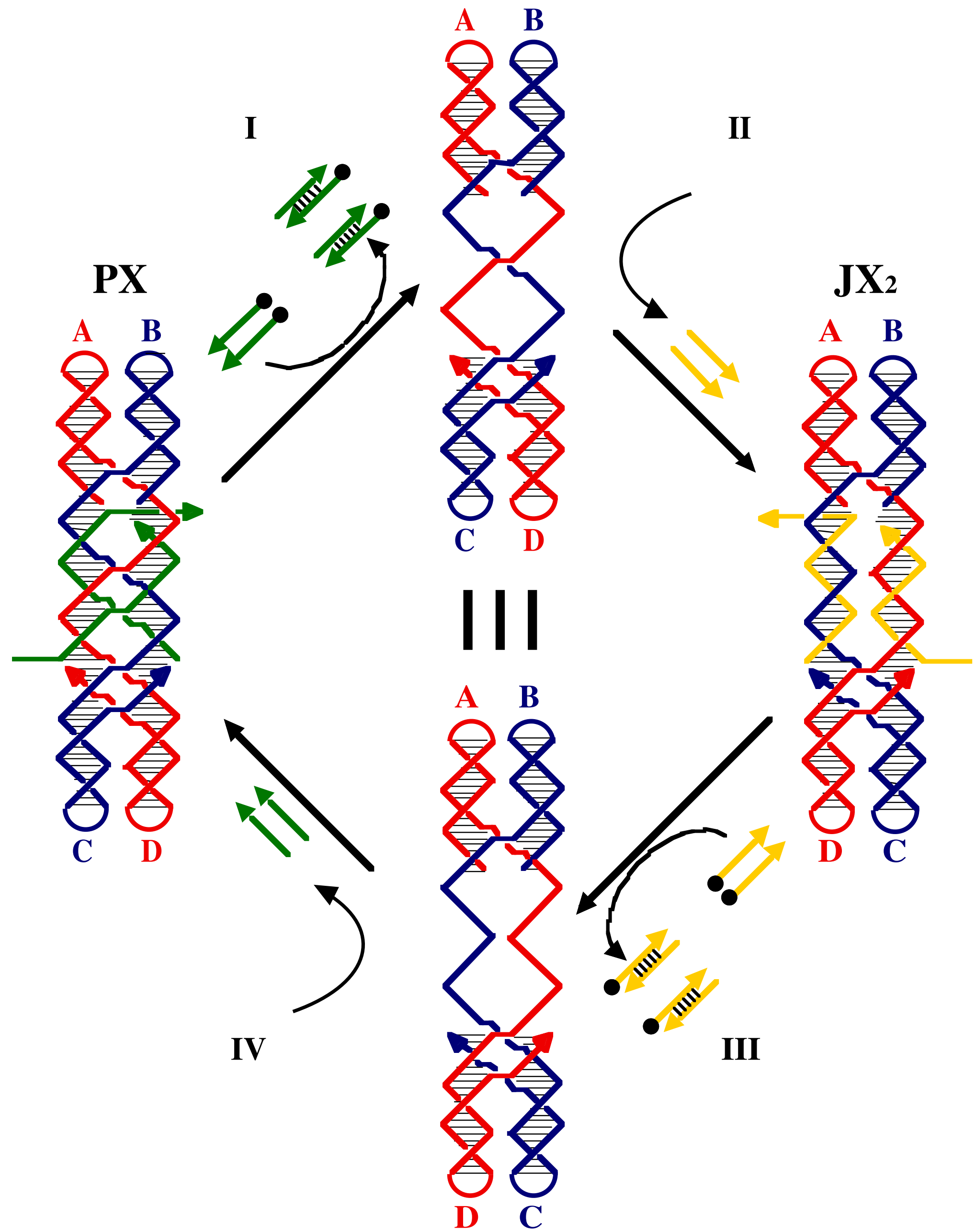


Yan, H., Zhang, X., Shen, Z. & Seeman, N.C. (2002), *Nature* **415**, 62-65..

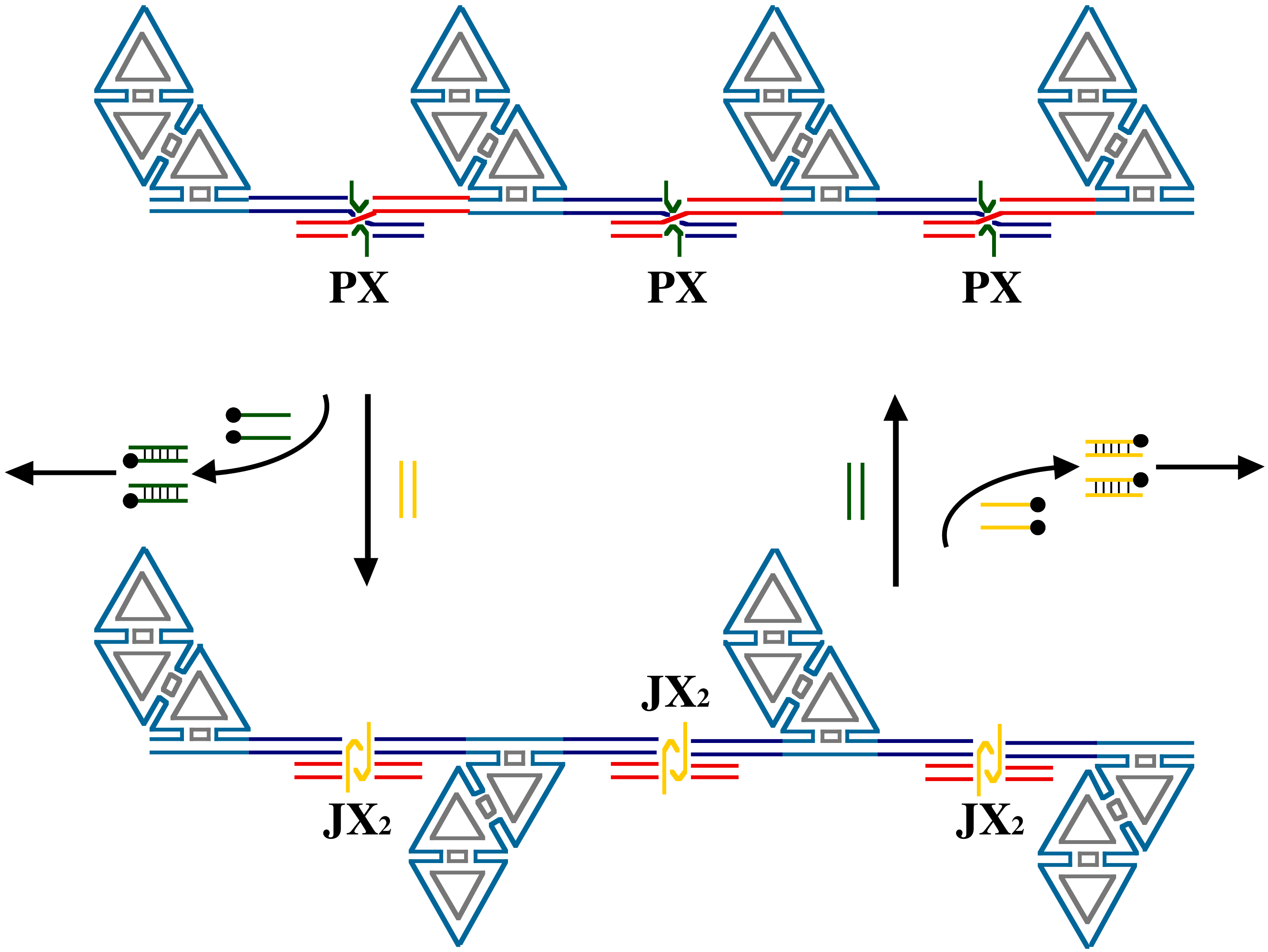
Switchable Versions of PX and JX_2



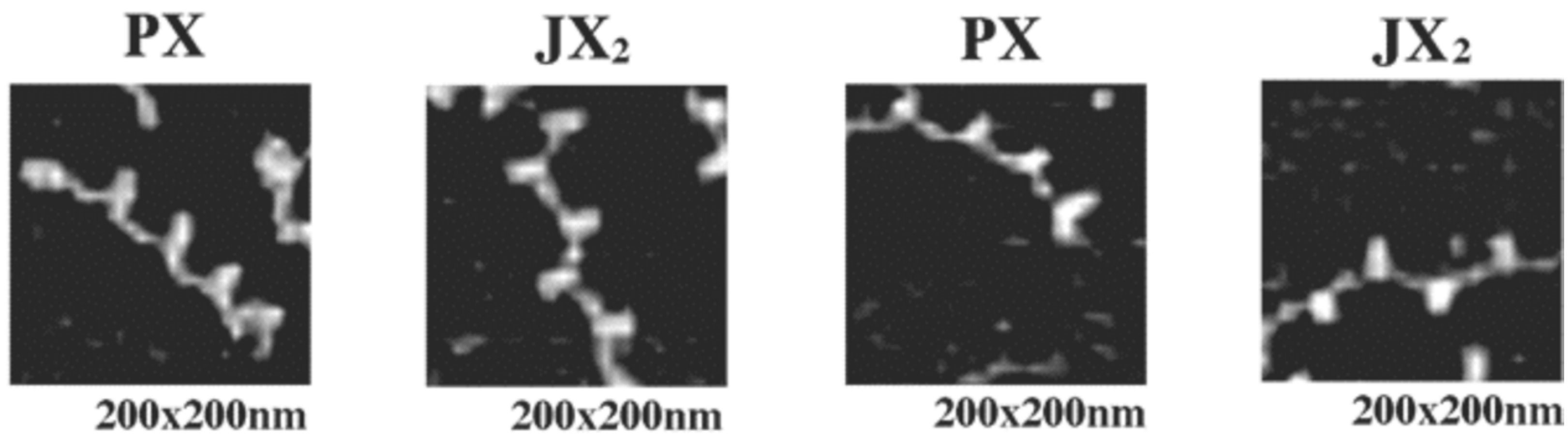
Machine Cycle of the PX-JX$_2$ Device



System to Test the PX-JX$_2$ Device



AFM Evidence for Operation of the PX-JX_2 Device



Yan, H., Zhang, X., Shen, Z. & Seeman, N.C. (2002), *Nature* **415**, 62-65.

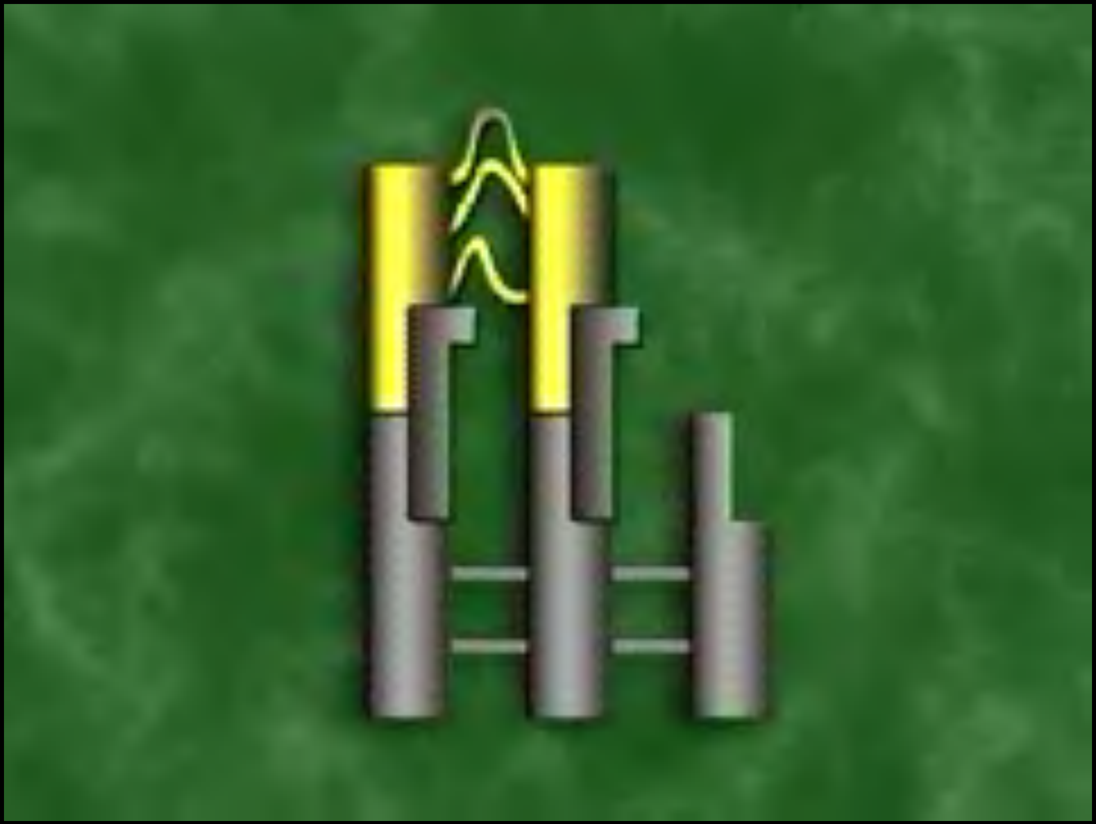
WALKERS

DNA Walking Biped

Bill Sherman

INCHWORM

Animation of the Biped Walker

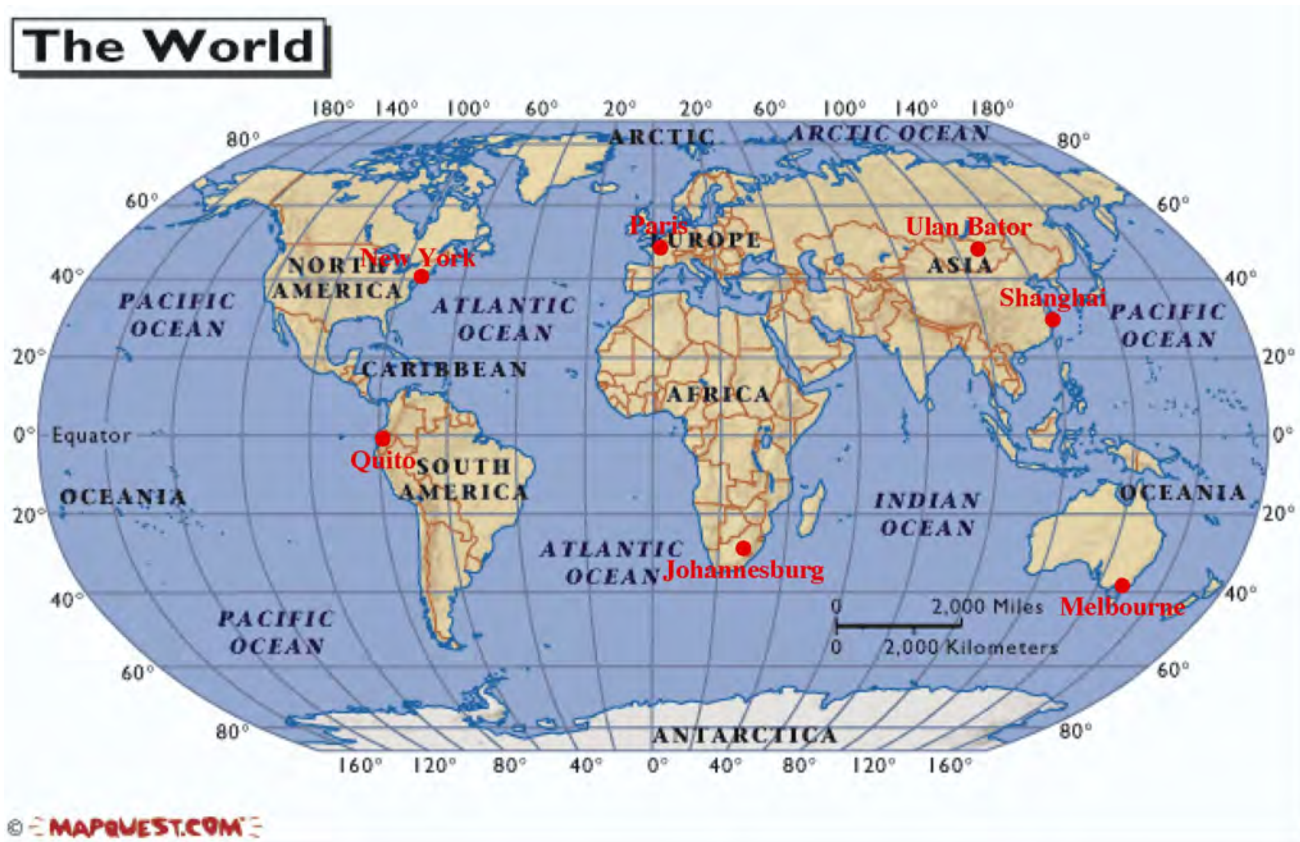


Courtesy of Ann Marie Cunningham and Donna Vaughn of ScienCentral News

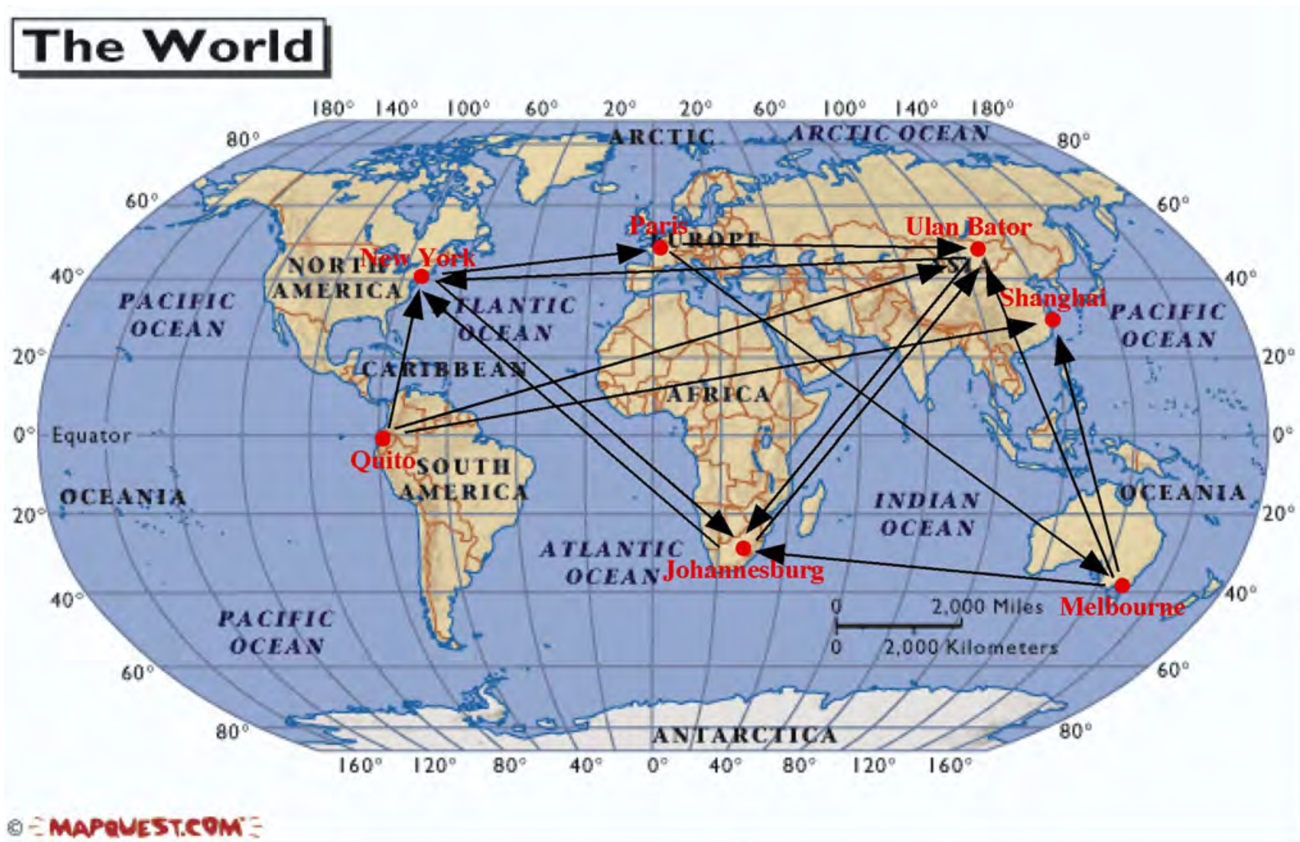
DNA-BASED COMPUTATION

The Adleman Hamiltonian Path Experiment (1994)

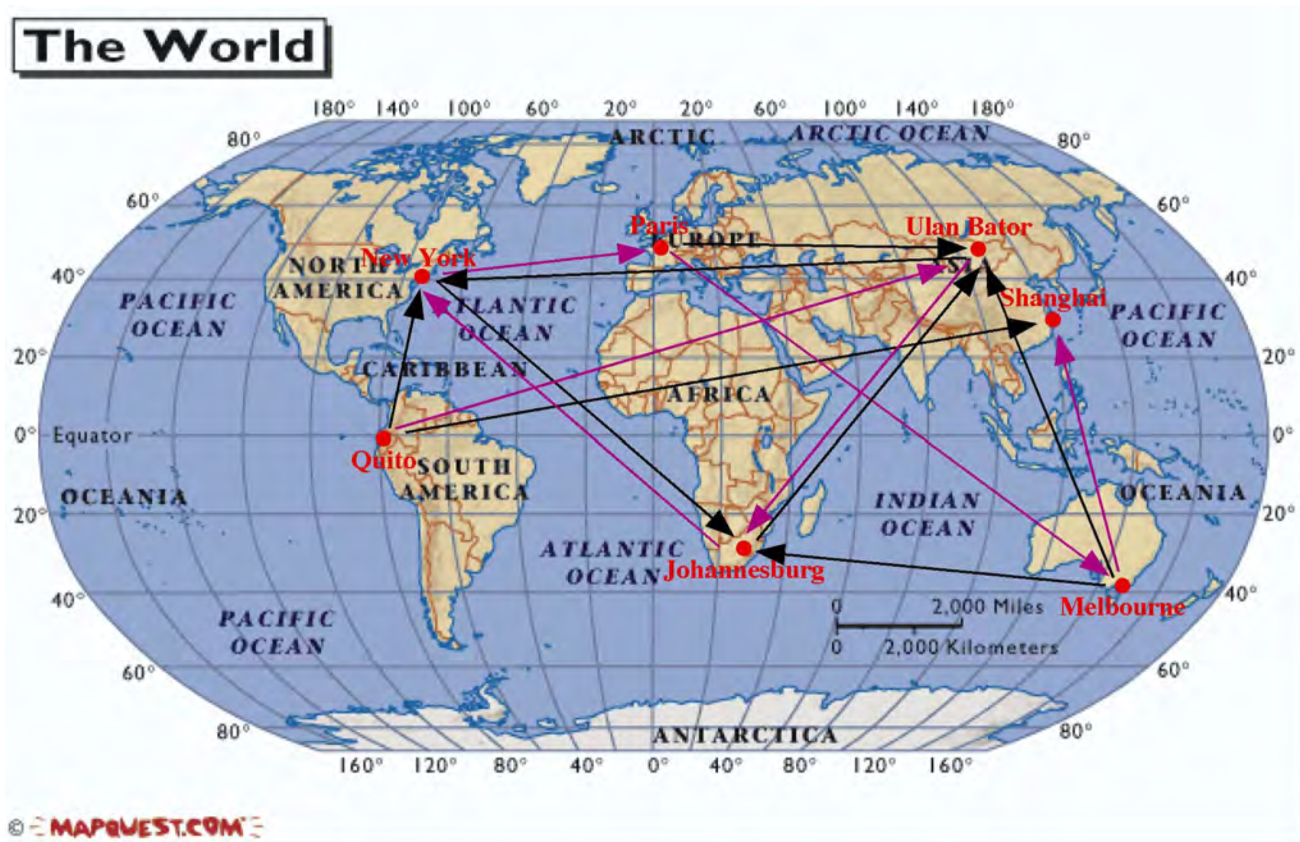
Seven Cities for a Hamiltonian Path Experiment



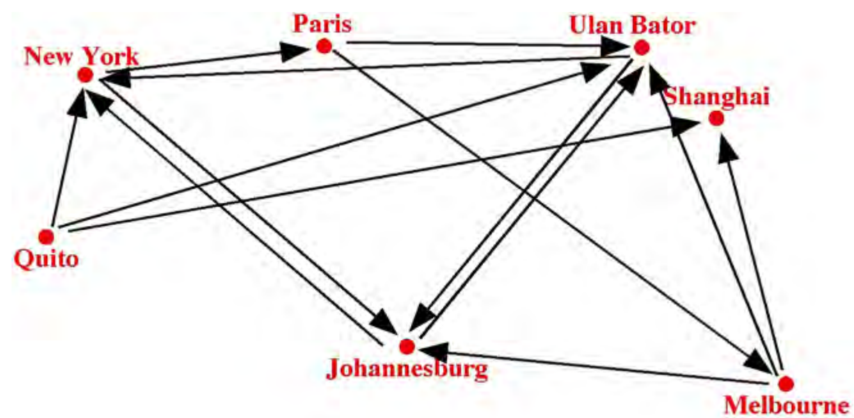
Routes for the Hamiltonian Path Experiment

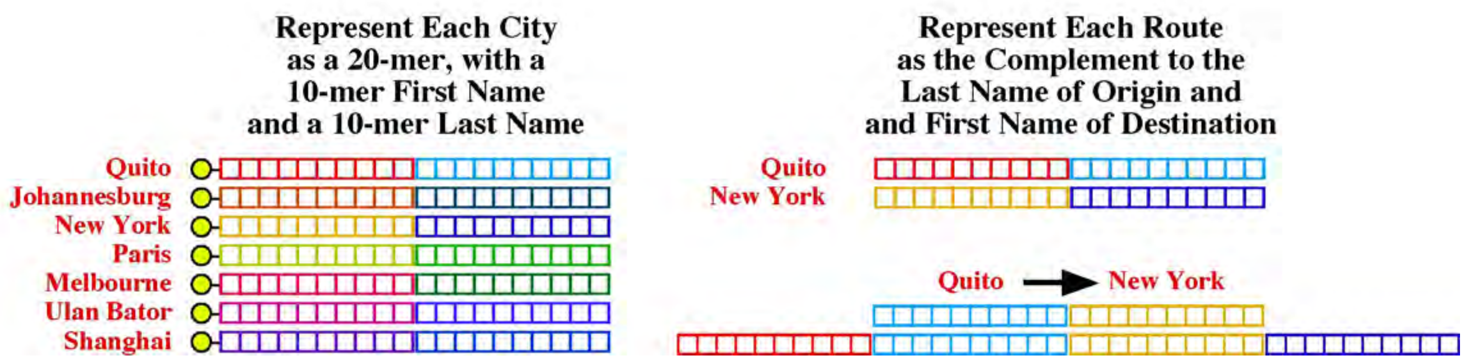


The Hamiltonian Path

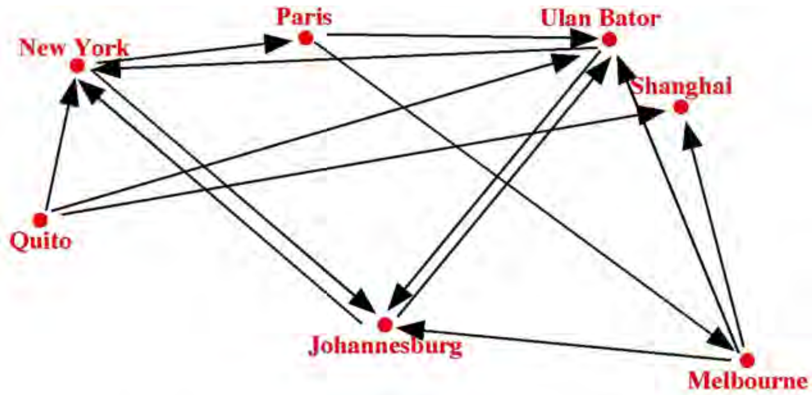


Assignment of Sequences





Strategy of the Hamiltonian Path Experiment



[1] Add All Cities (Phosphorylated) and All Routes (as Catalysts) to the Solution and Ligate.

[2] Targets are all 140-mers, so Run the Products on a Gel and Select 140-mers.

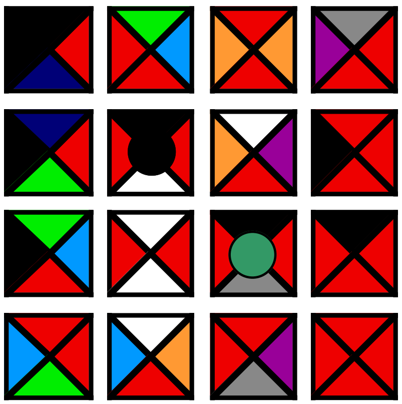
[3] To Select Routes that Start in Quito and End in Shanghai, Run PCR with Primers Complementary Quito and Shanghai.

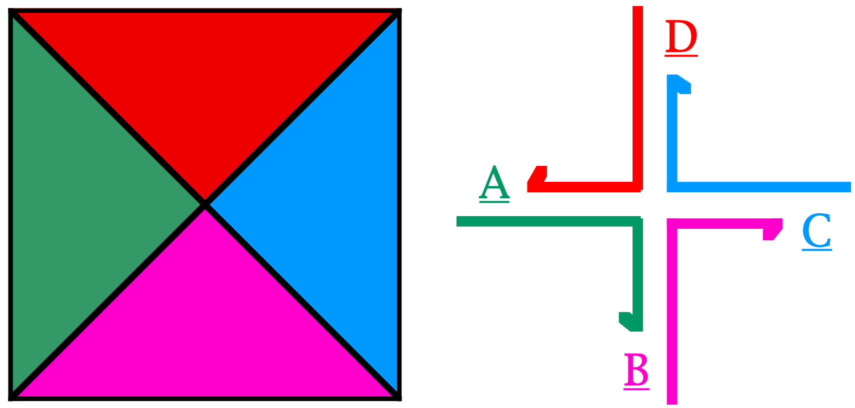
[4] Demonstrate All Intermediate Cities by Selecting for Each of Their Complements on Magnetic Beads.

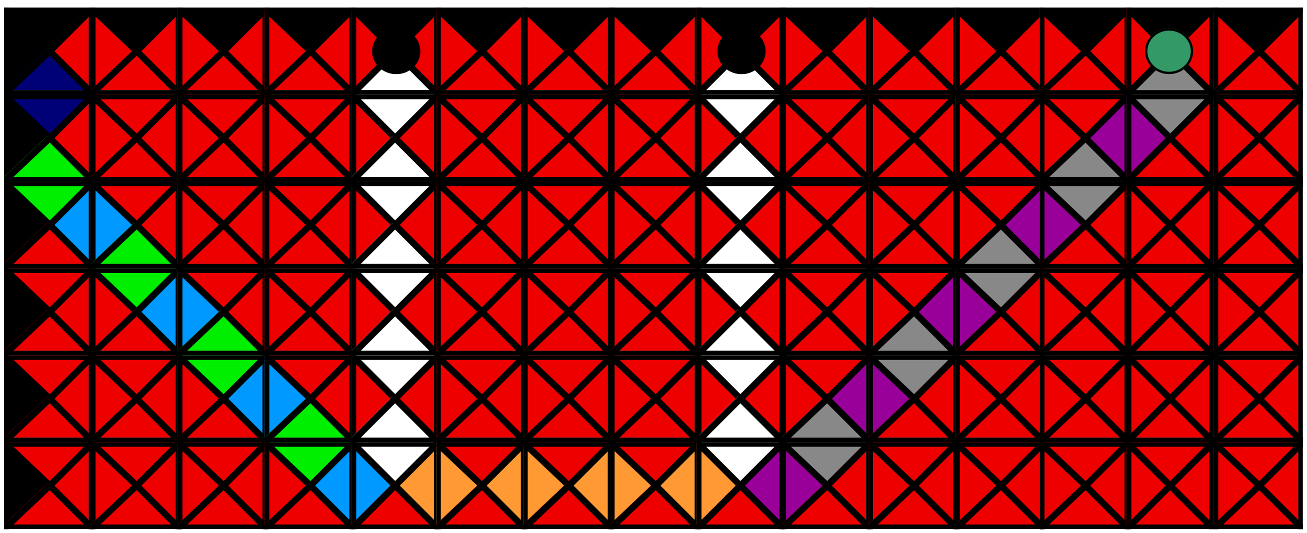
Algorithmic Assembly: A Cumulative XOR Calculation

Chengde Mao
Thom LaBean (Duke)
John Reif (Duke)

Wang Tiles



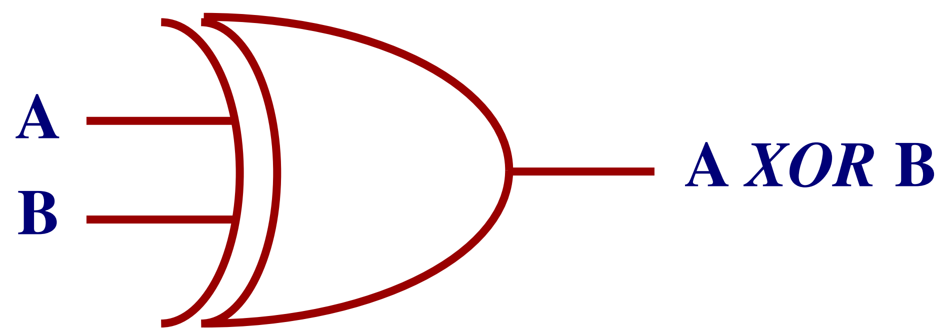




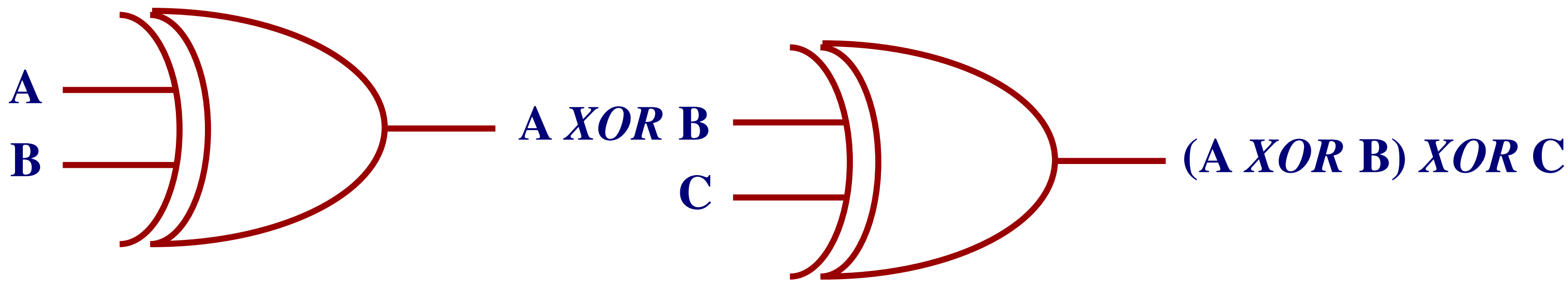
Grünbaum, B. & Shephard, G.C. *Tilings & Patterns*,
W.H. Freeman & Co., New York, 1987 pp. 583-608.

The *XOR* Operation

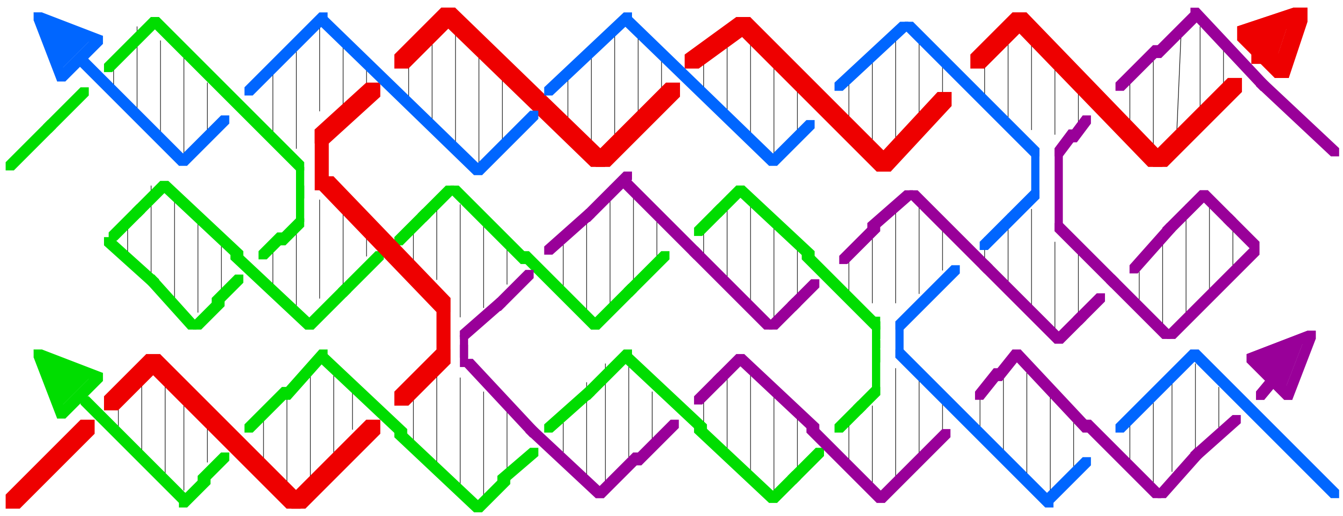
A	B	A *XOR* B
0	0	0
0	1	1
1	0	1
1	1	0



Cumulative *XOR*



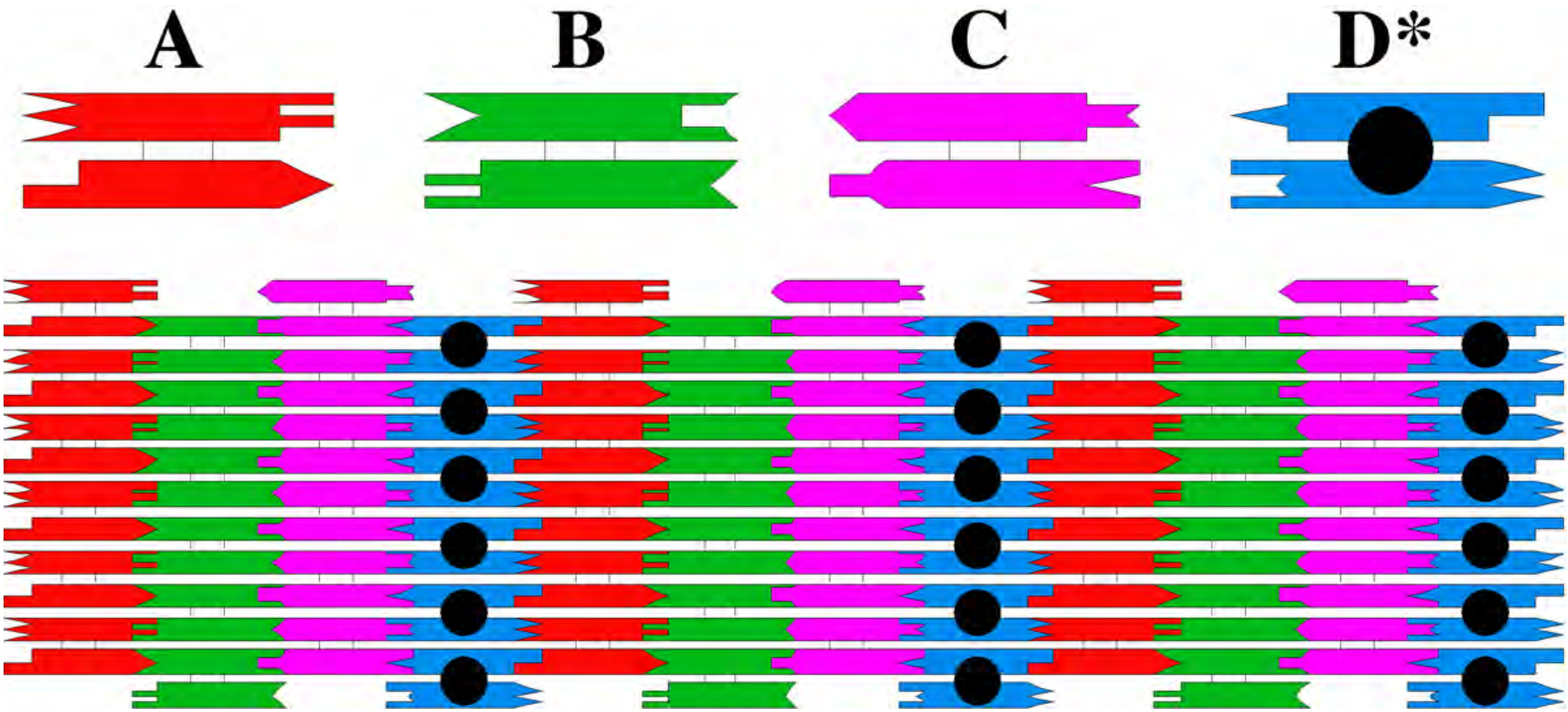
A Cumulative XOR Calculation: Tiles



Mao, C., LaBean, T.H., Reif, J.H. &
Seeman, N.C. (2000), *Nature* **407**, 493-496.

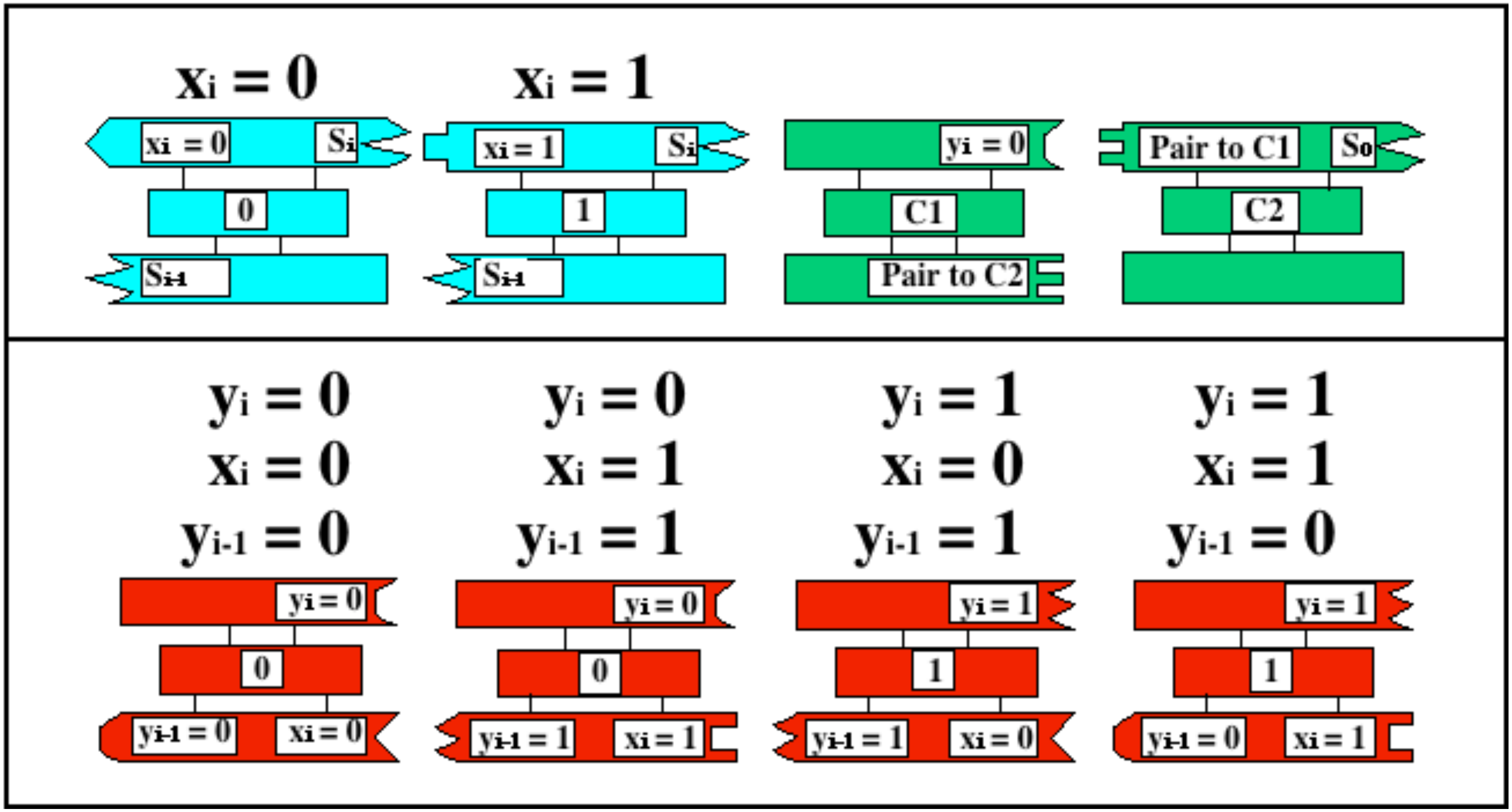
Schematic of a Lattice Containing 3 DX Tiles and 1 DX+J Tile

Correct Tiles Compete Against Incorrect Tiles



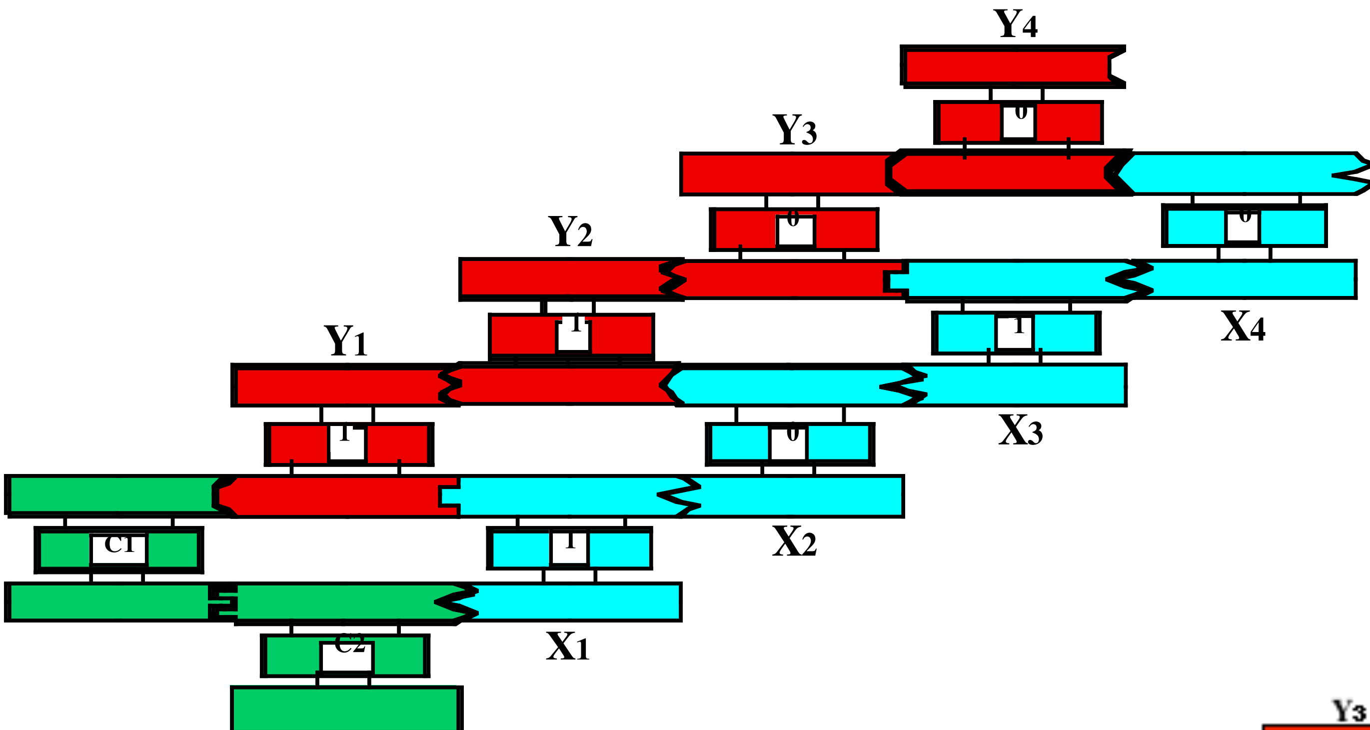
Tiles for the Cumulative XOR Calculation

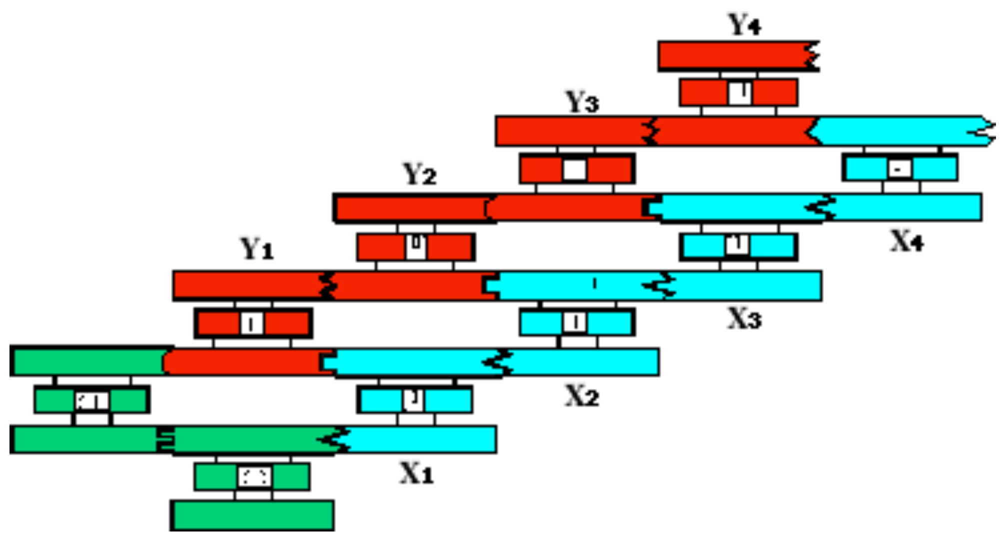
Correct Tiles Compete Against Half-Correct Tiles



Mao, C., LaBean, T.H., Reif, J.H. &
Seeman, N.C. (2000), *Nature* **407**, 493-496.

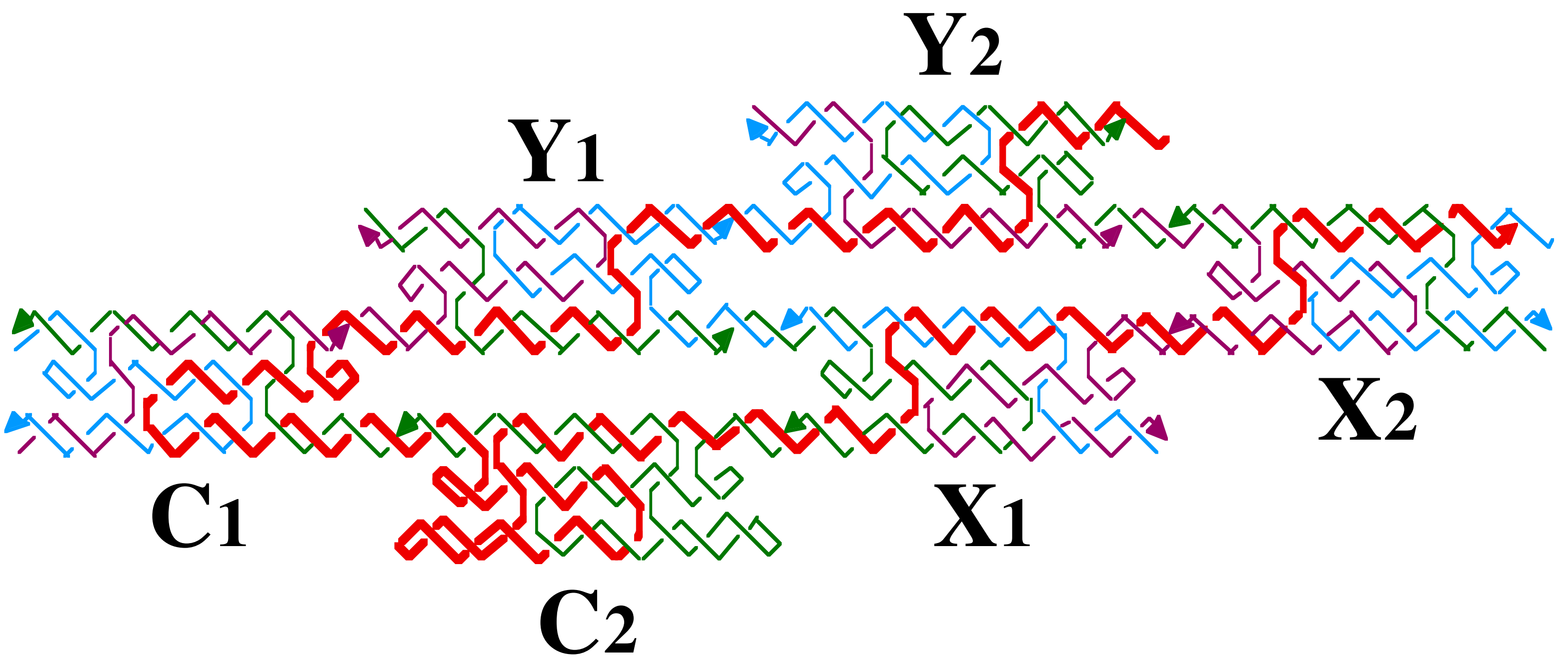
A Cumulative XOR Calculation: Assembly





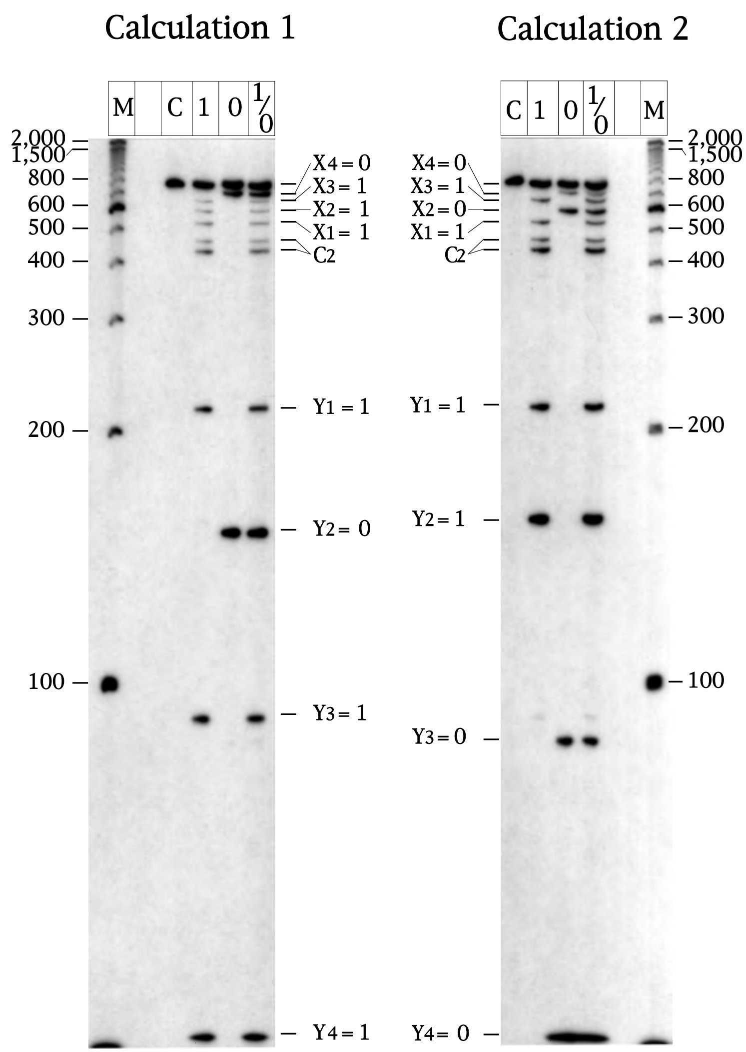
Mao, C., LaBean, T.H., Reif, J.H. &
Seeman, N.C. (2000), *Nature* **407**, 493-496.

A Cumulative XOR Calculation: Extracting the Answer



Mao, C., LaBean, T.H., Reif, J.H. &
Seeman, N.C. (2000), *Nature* **407**, 493-496.

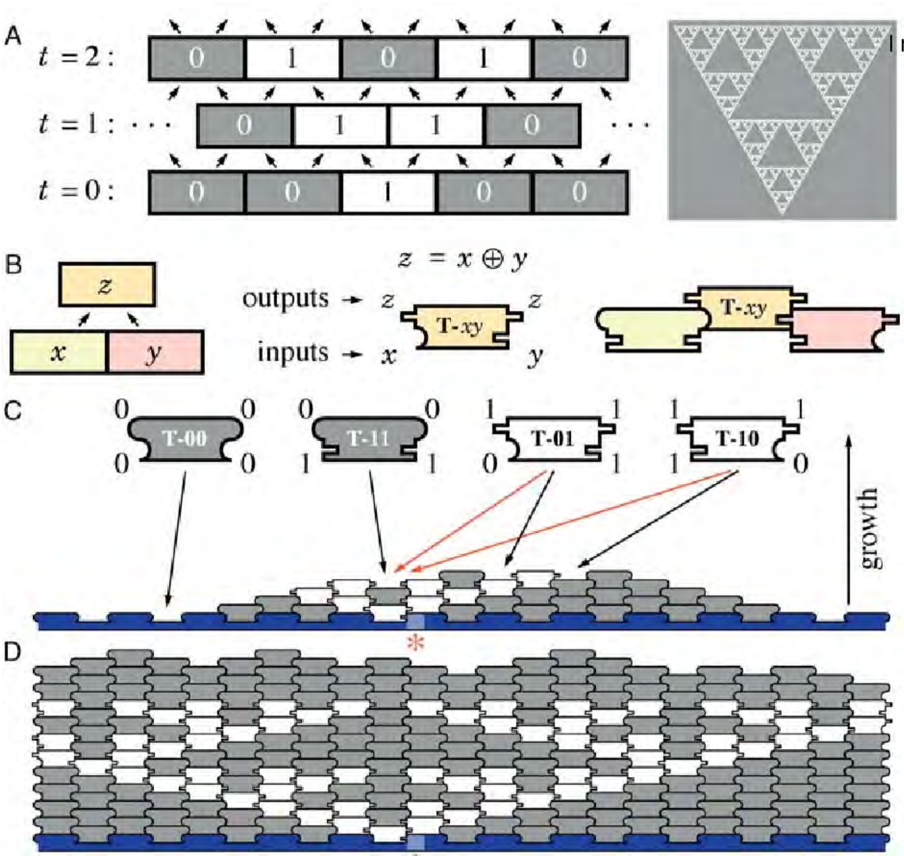
A Cumulative XOR Calculation: Data

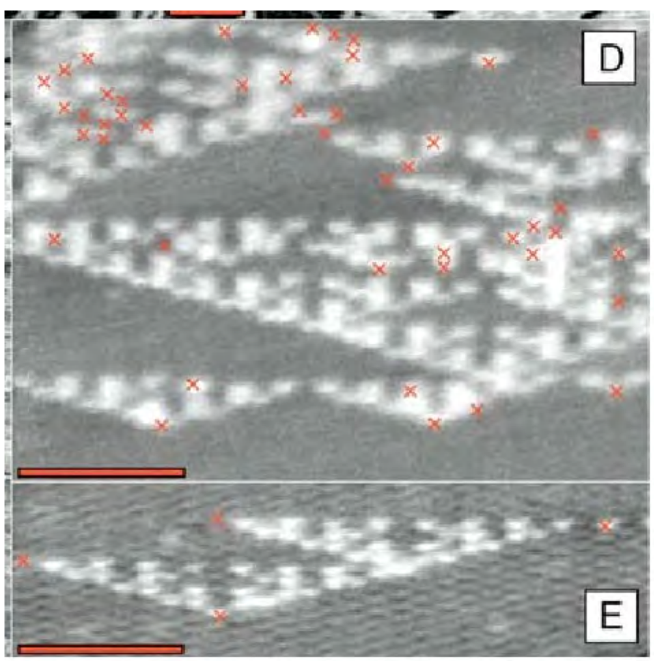


Mao, C., LaBean, T.H., Reif, J.H. &
Seeman, N.C. (2000), *Nature* **407**, 493-496.

2D Algorithmic Assembly: A Sierpinski Triangle by Paul Rothemund, Nick Papadakis & Erik Winfree

The Sierpinski Triangle is Pascal's Triangle, Mod 2
It can be Generated by XOR in 2 Dimensions



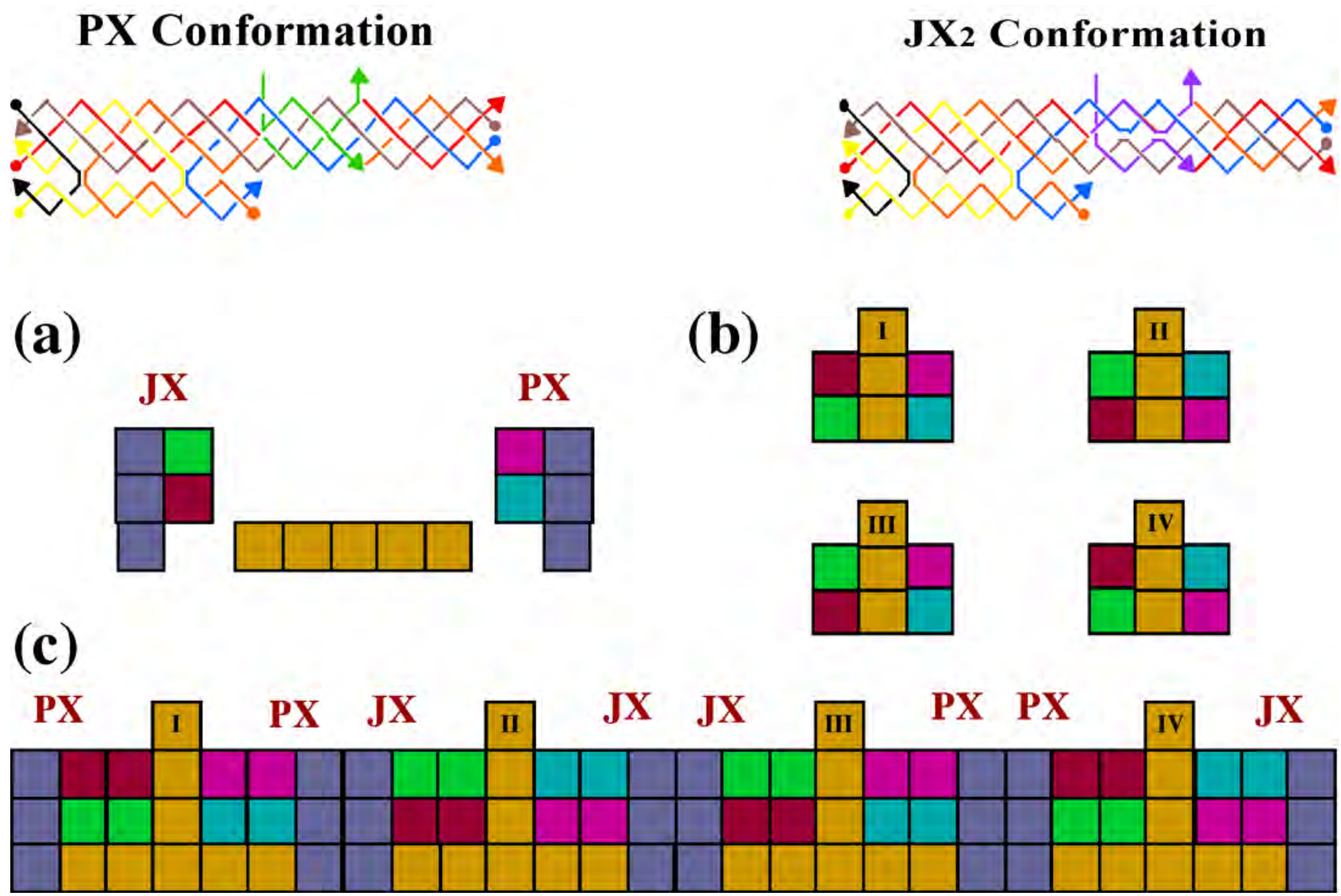


P.W.K. Rothemund, N. Papadakis & E. Winfree, *PLOS Biology* **2**, 2041-2053 (2004)

Pairs of Inserted $PX\text{-}JX_2$ Devices Used to Program a Pattern

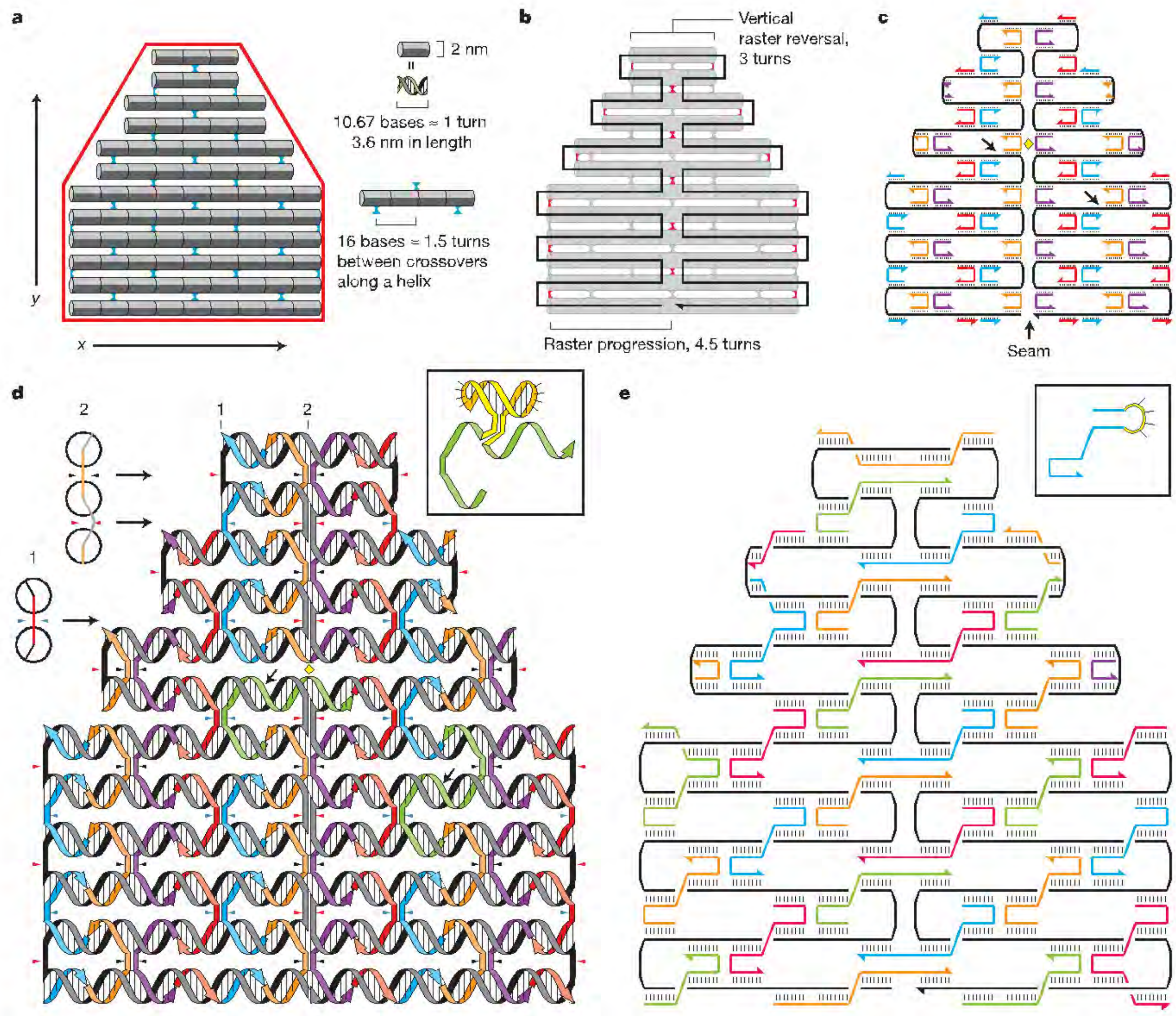
Hongzhou Gu
Jie Chao

Programming an Array for Assembly



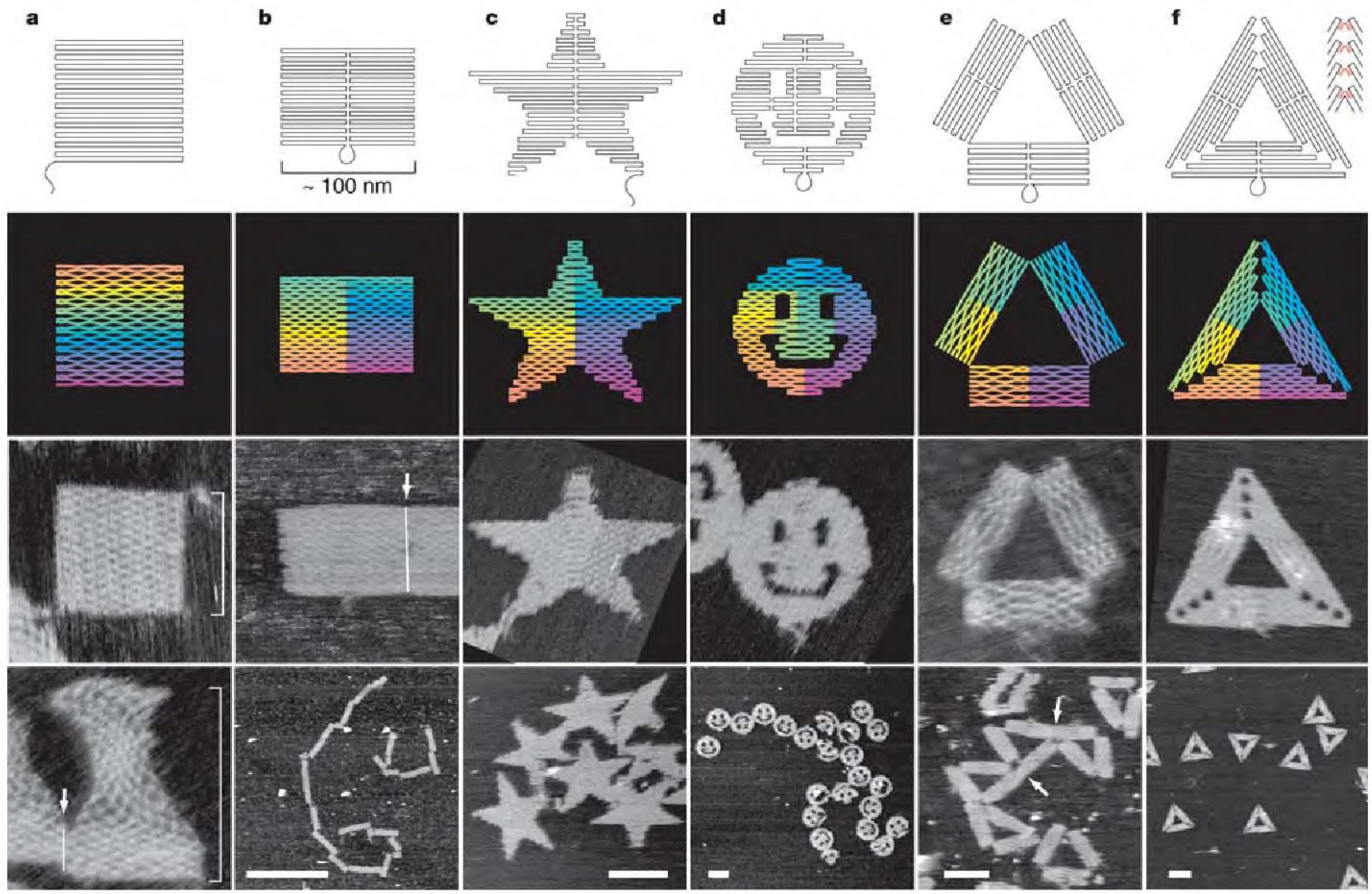
A. Carbone & N.C. Seeman, *Proc. Nat. Acad. Sci. (USA)* **99** 12577-12582 (2002).

Producing Patterns from Long Viral Strands



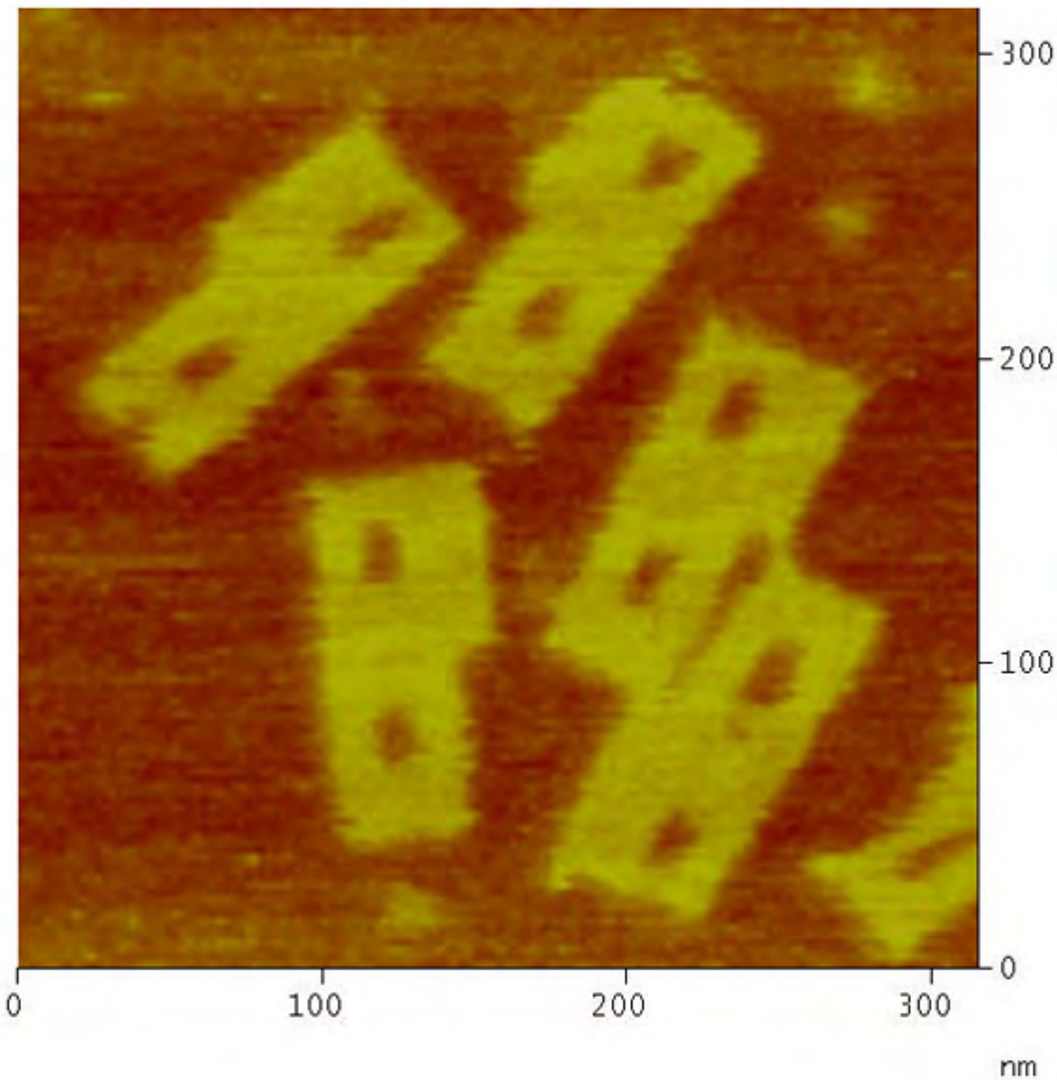
P.W.K.Rothemund, *Nature* **440**, 297-302(2006).

Various Shapes from Long Viral Strands



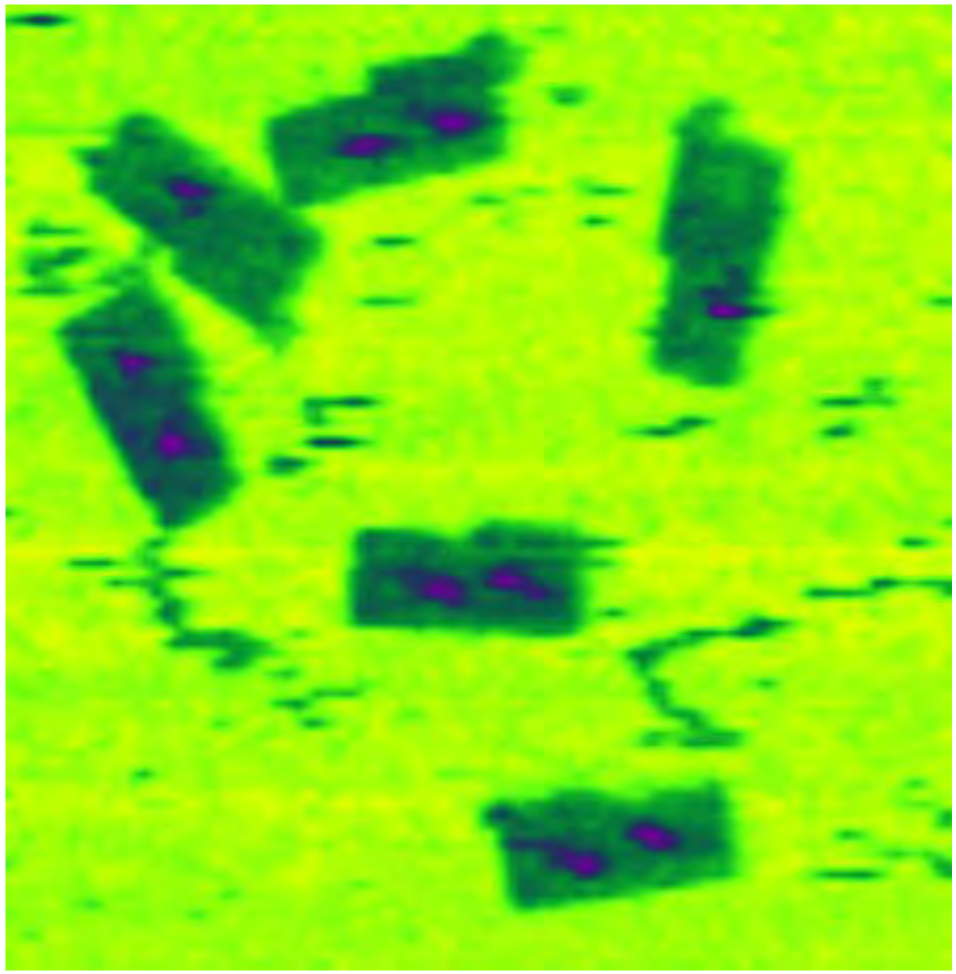
P.W.K.Rothemund, *Nature* **440**, 297-302(2006).

AFM Image of Blank Origami Arrays for Insertion



H. Gu, J. Chao, S-J. Xiao & N.C. Seeman, *Nature Nanotech*. **4**, 245-249 (2009).

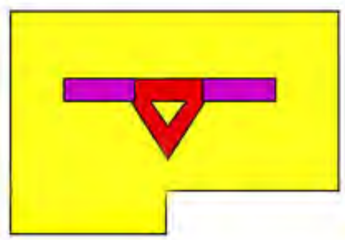
AFM Image of Origami Arrays with Inserted Cassettes



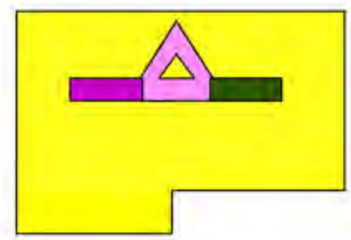
H. Gu, J. Chao, S-J. Xiao & N.C. Seeman, *Nature Nanotech*. **4**, 245-249 (2009).

Schematics of Programmed Patterns Made By Capturing Different Molecules

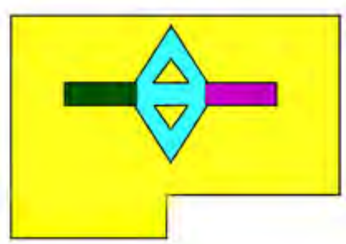
JX-JX



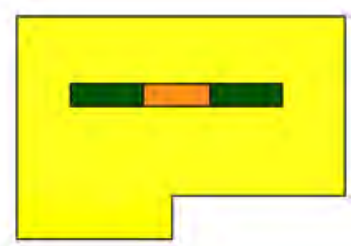
JX-PX



PX-JX

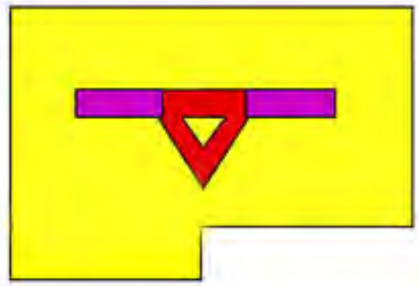


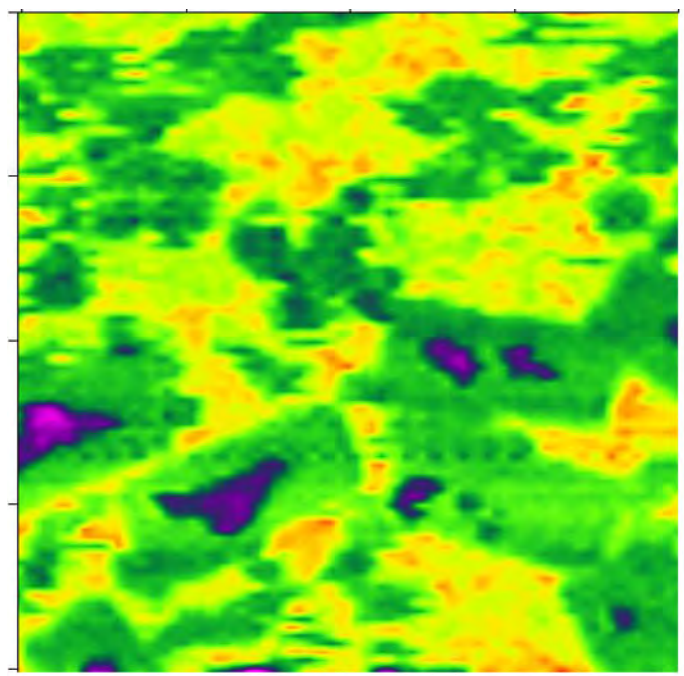
PX-PX



H. Gu, J. Chao, S-J. Xiao & N.C. Seeman, *Nature Nanotech*. **4**, 245-249 (2009).

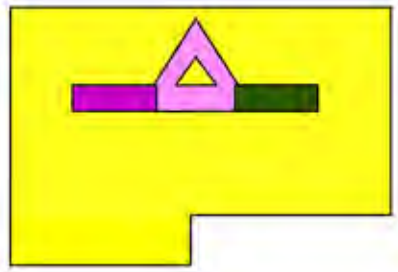
AFM Images of JX-JX Patterns

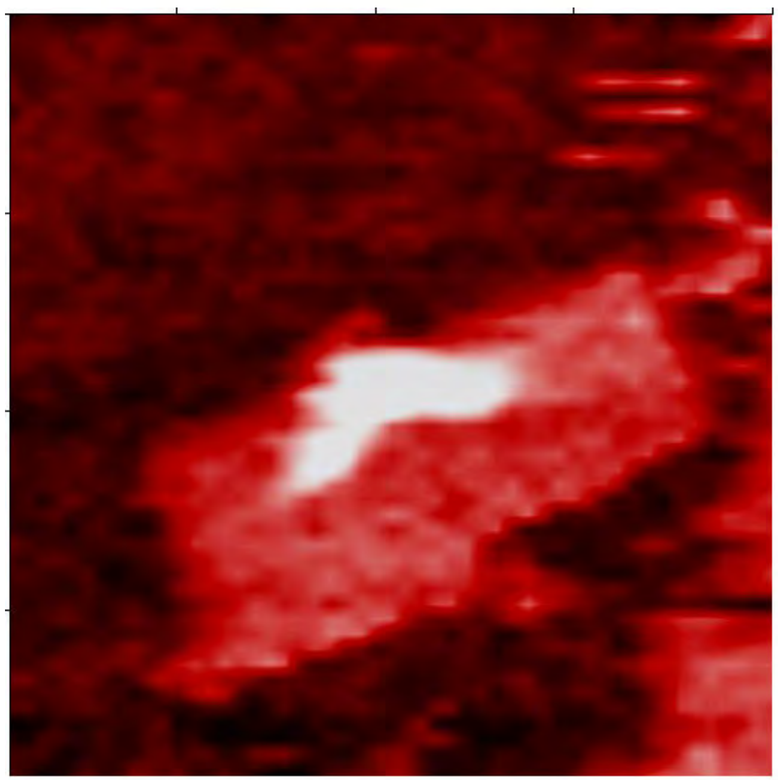




H. Gu, J. Chao, S-J. Xiao & N.C. Seeman, *Nature Nanotech*. **4**, 245-249 (2009).

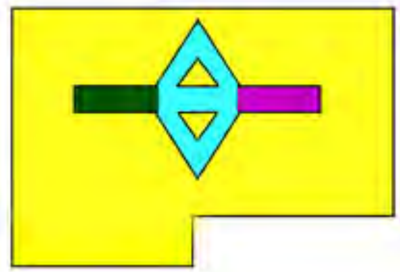
AFM Images of JX-PX Patterns

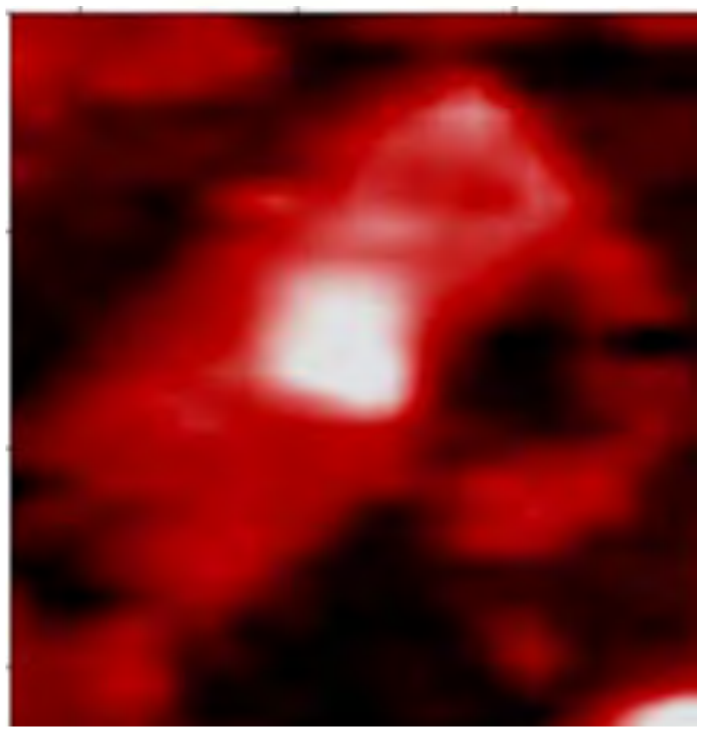




H. Gu, J. Chao, S-J. Xiao & N.C. Seeman, *Nature Nanotech*. **4**, 245-249 (2009).

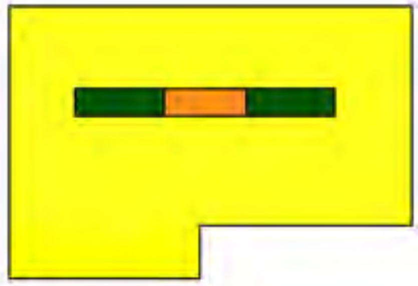
AFM Images of PX-JX Patterns

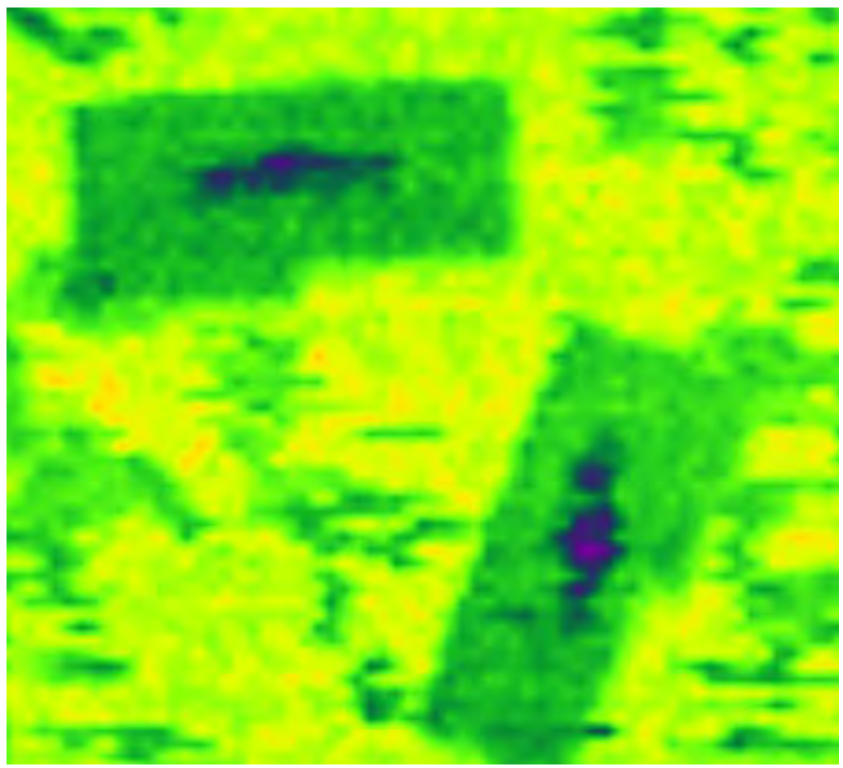




H. Gu, J. Chao, S-J. Xiao & N.C. Seeman, *Nature Nanotech*. **4**, 245-249 (2009).

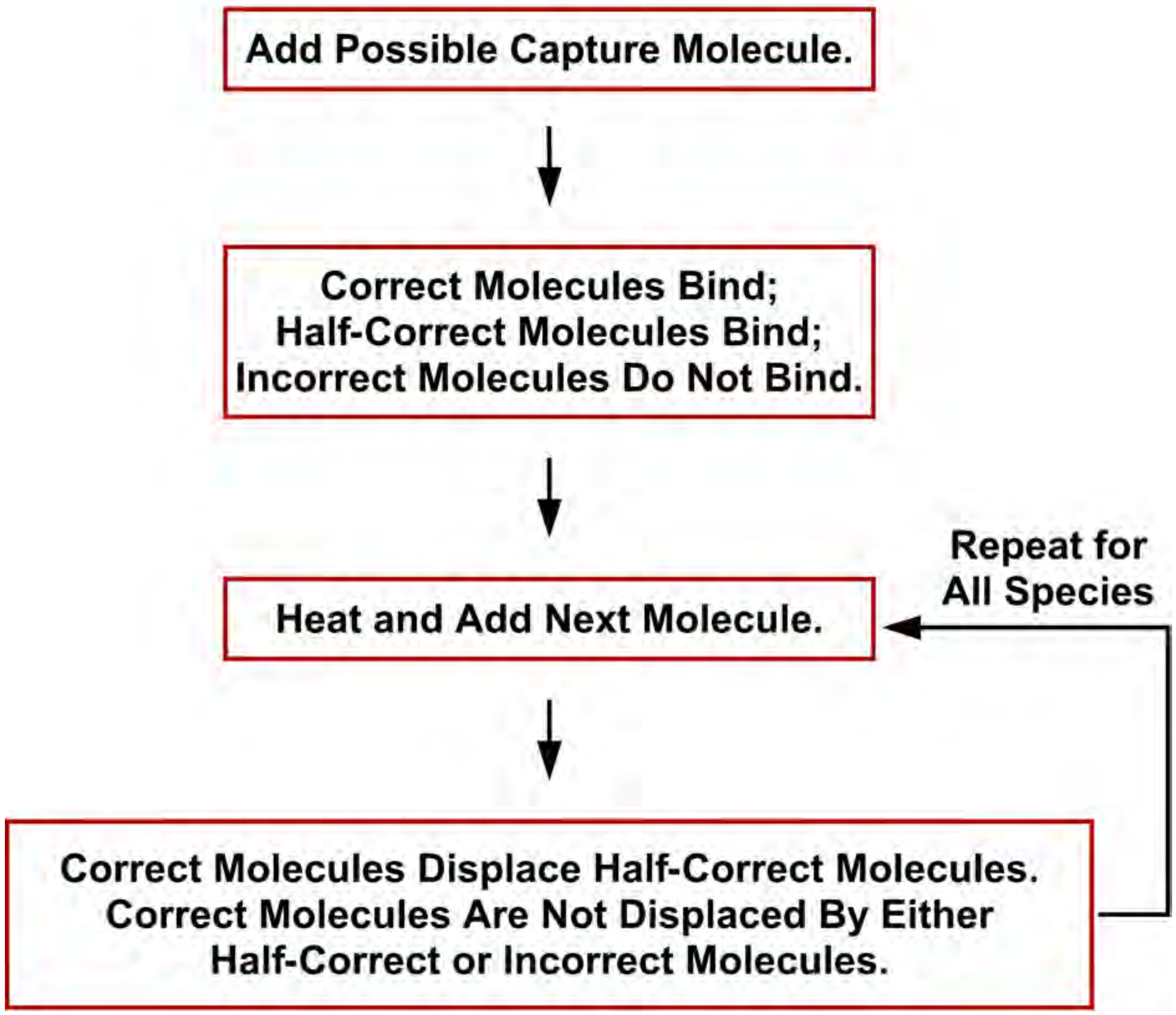
AFM Images of PX-PX Patterns





H. Gu, J. Chao, S-J. Xiao & N.C. Seeman, *Nature Nanotech*. **4**, 245-249 (2009).

Error-Free Binding Protocol

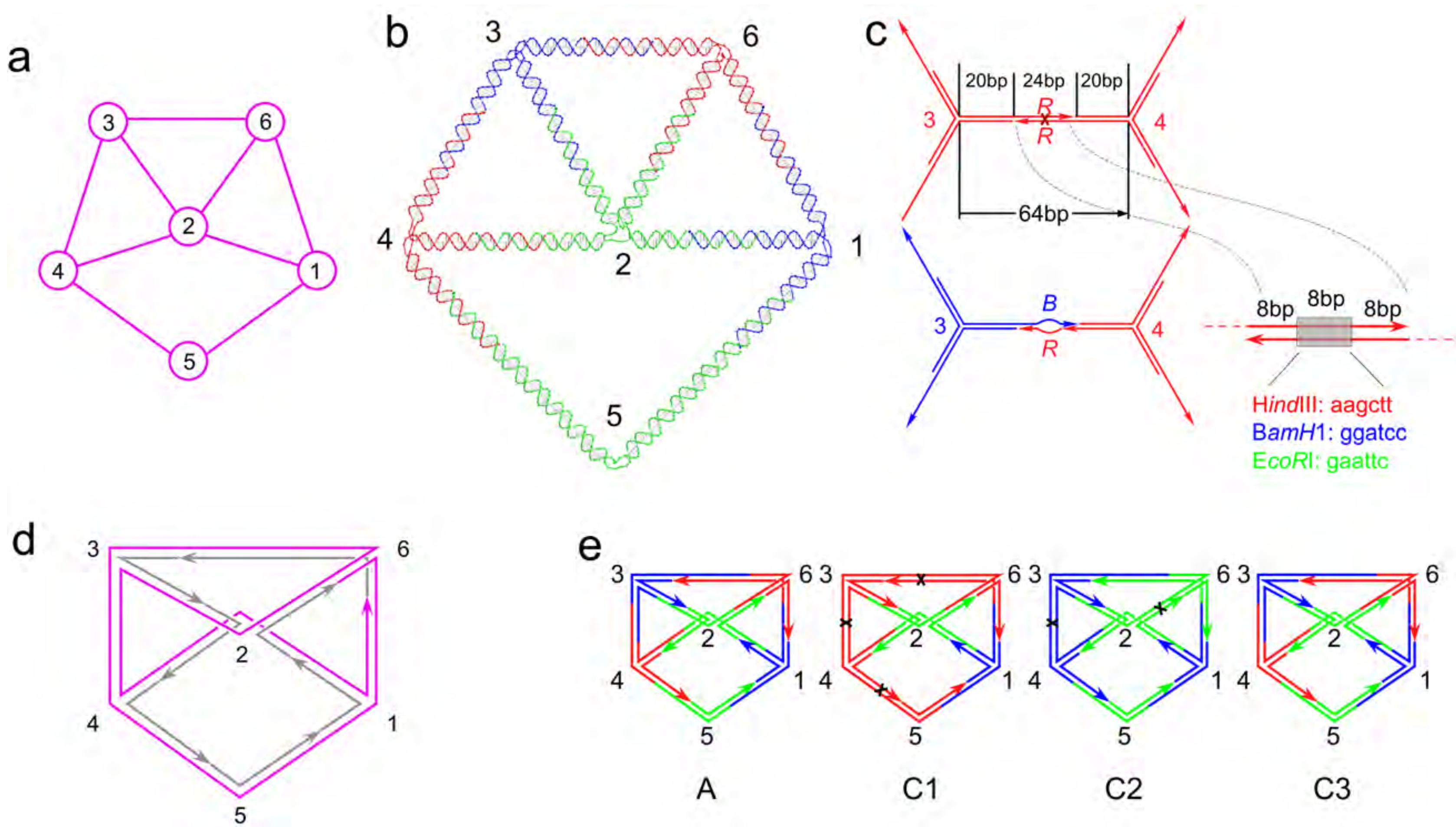


DNA SELF-ASSEMBLY AS COMPUTATION

Assembly of a DNA Nano-Object Solves a Graph Theory Problem

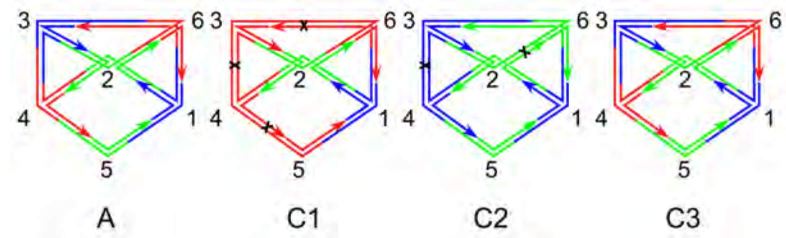
Gang Wu
Natasha Jonoska (U. South Florida)

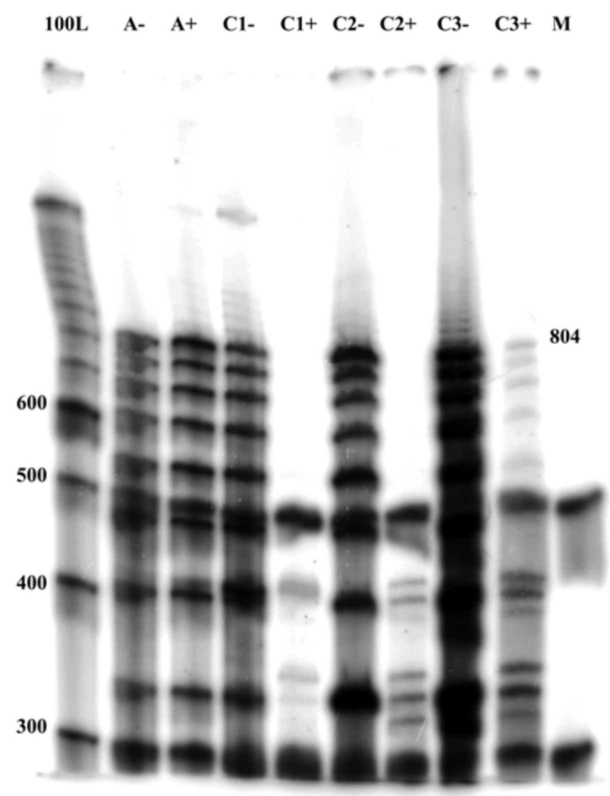
System to Determine Graph 3-Colorability



G.Wu, N.Jonoska and N.C. Seeman, *Biosystems* **98**, 80-84 (2009).

Result of 3-Colorability Experiments





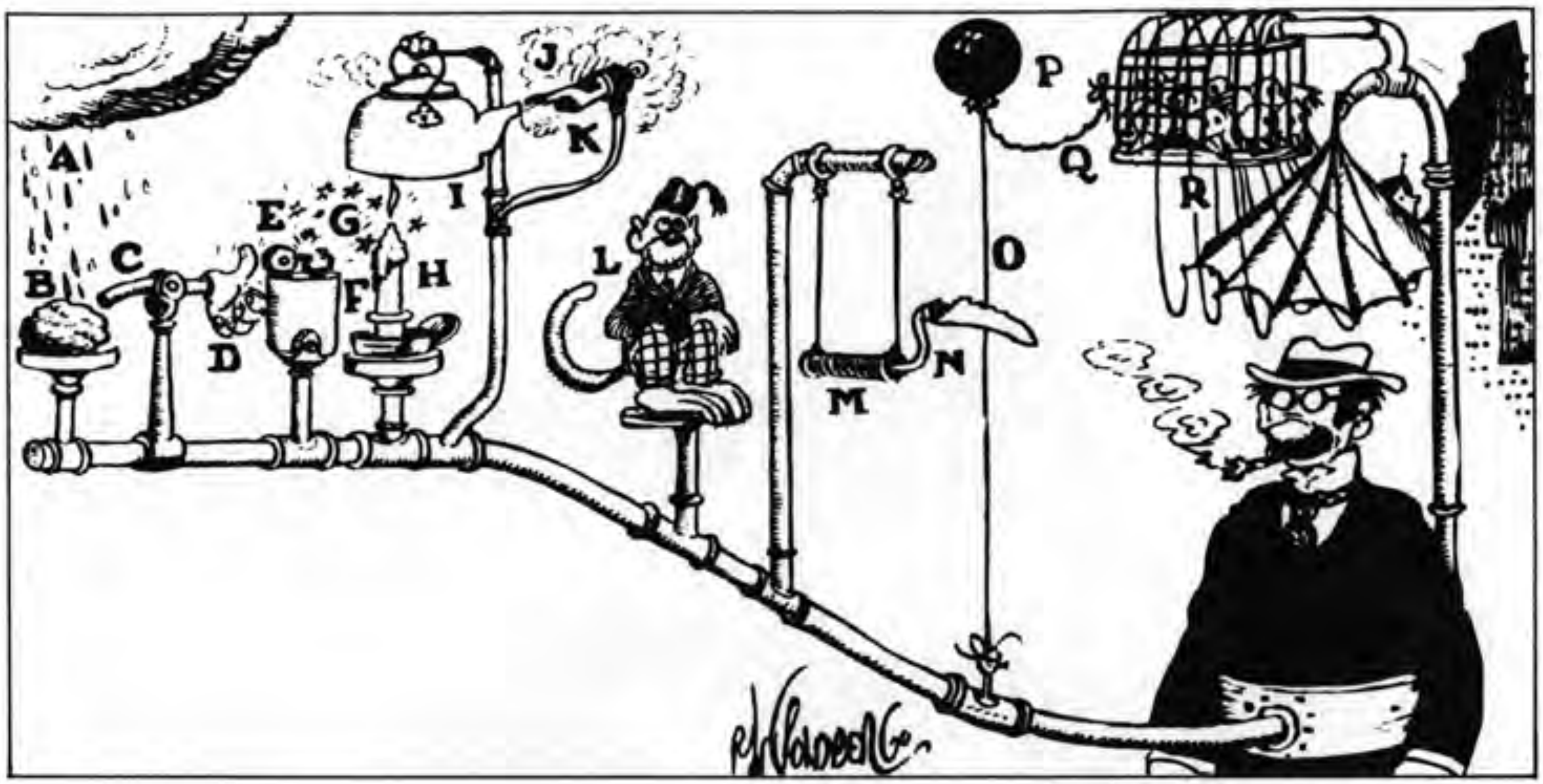
G.Wu, N.Jonoska and N.C. Seeman, *Biosystems* **98**, 80-84 (2009).

DNA Nanotechnology:

Combining Multiple Components

Combining Multiple Components: The Macroscopic Scale

Self-Opening Umbrella



A Proximity-Based Programmable Nanoscale Assembly Line

Hongzhou Gu
Jie Chao

Combining Components

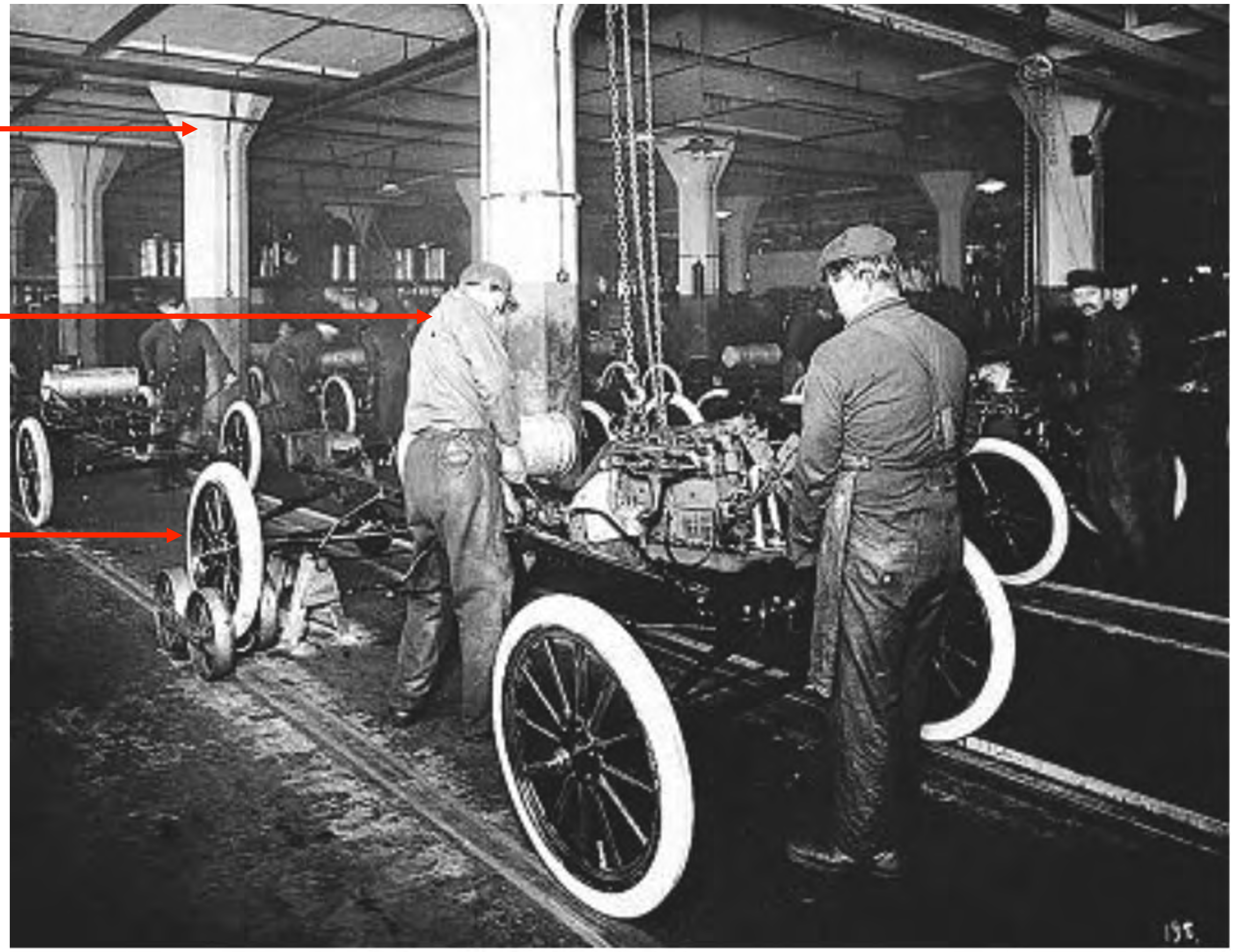
PX-JX_2 Cassettes
Clocked Walker
Nanoparticles
DNA Origami

Automobile Assembly Line (1920s)

Framework

Directable Assembler

Conveyor



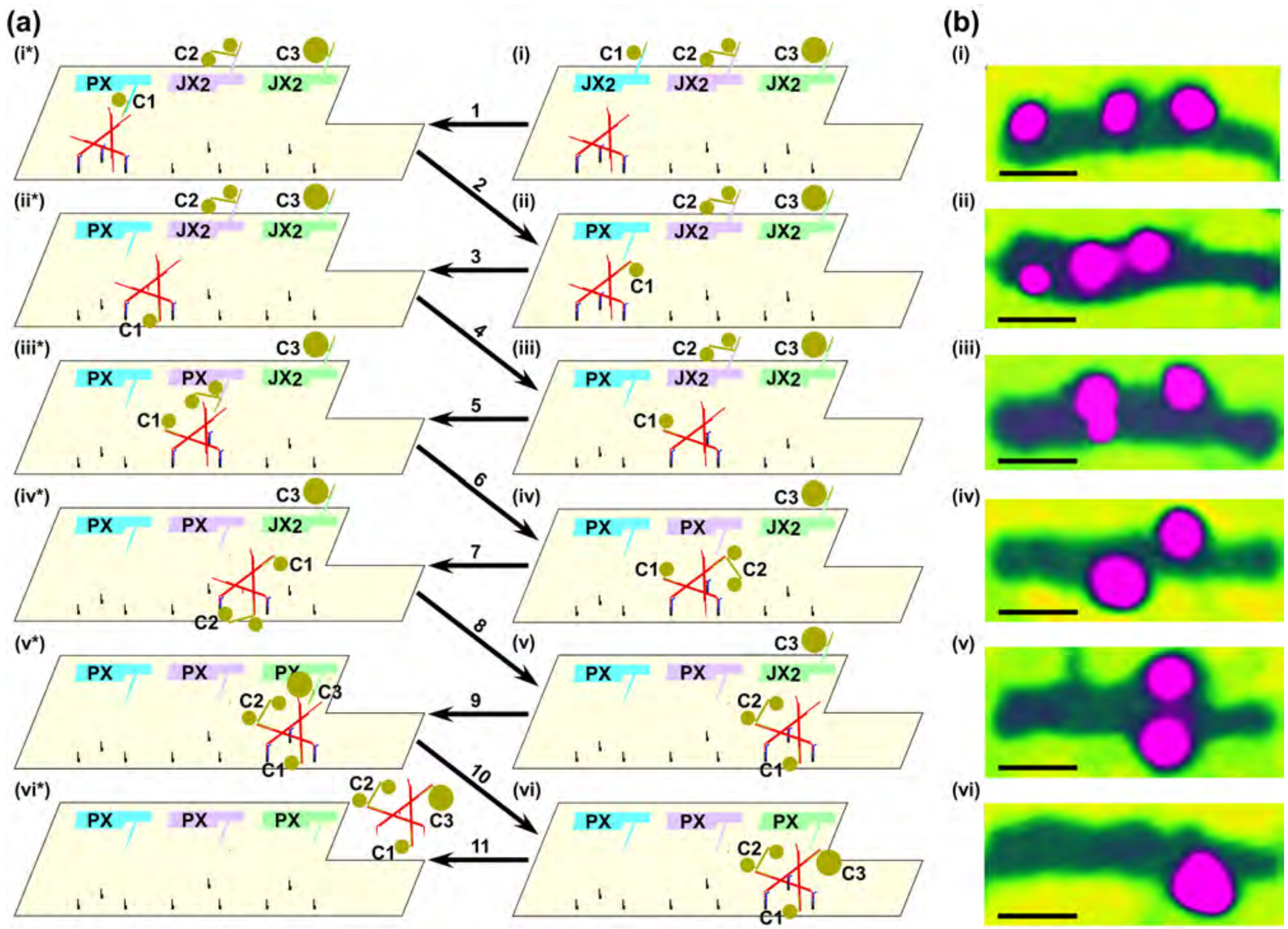
Requirements for this System

[1] Directable Assembler <--> PX-JX$_2$ Cassette

[2] Inter-Station Conveyer <--> Trigonal Walker

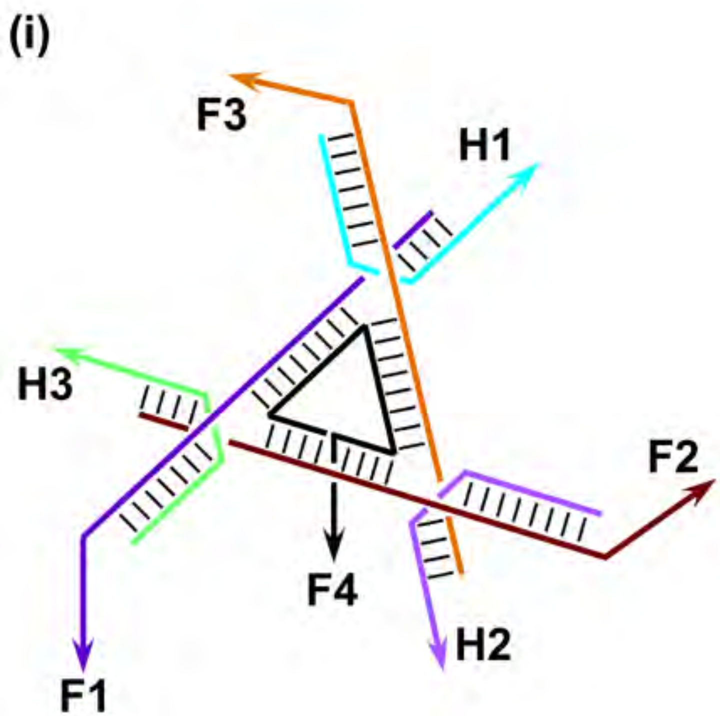
[3] Framework for the System <--> DNA Origami

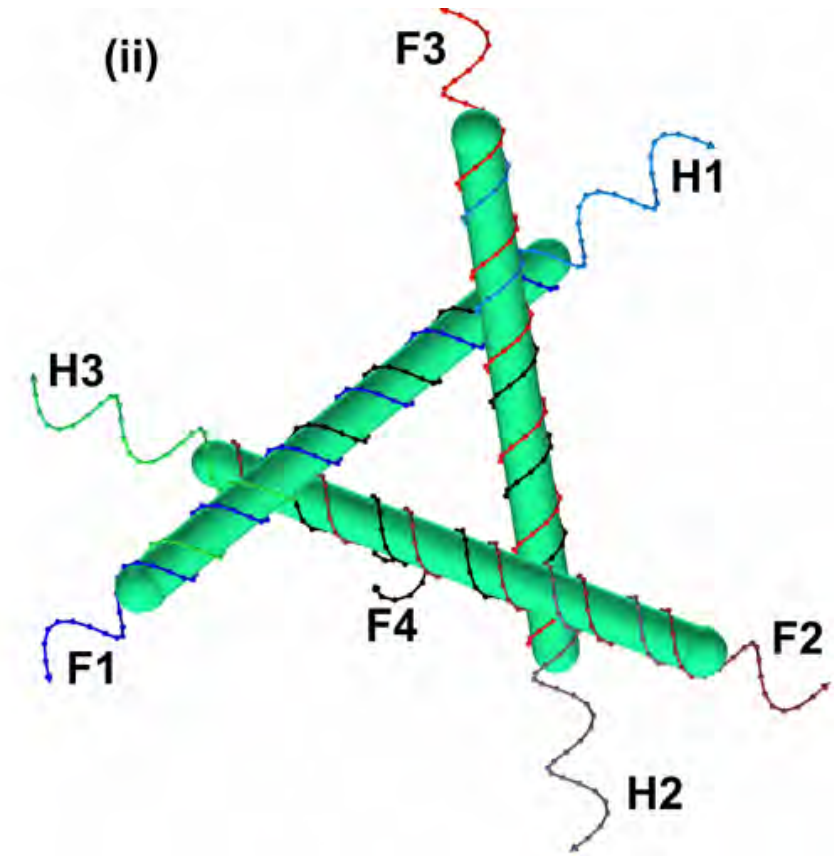
Mechanism of Assembly



H. Gu, J. Chao, S.J. Xiao & N.C. Seeman, *Nature* **465**, 202-205 (2010).

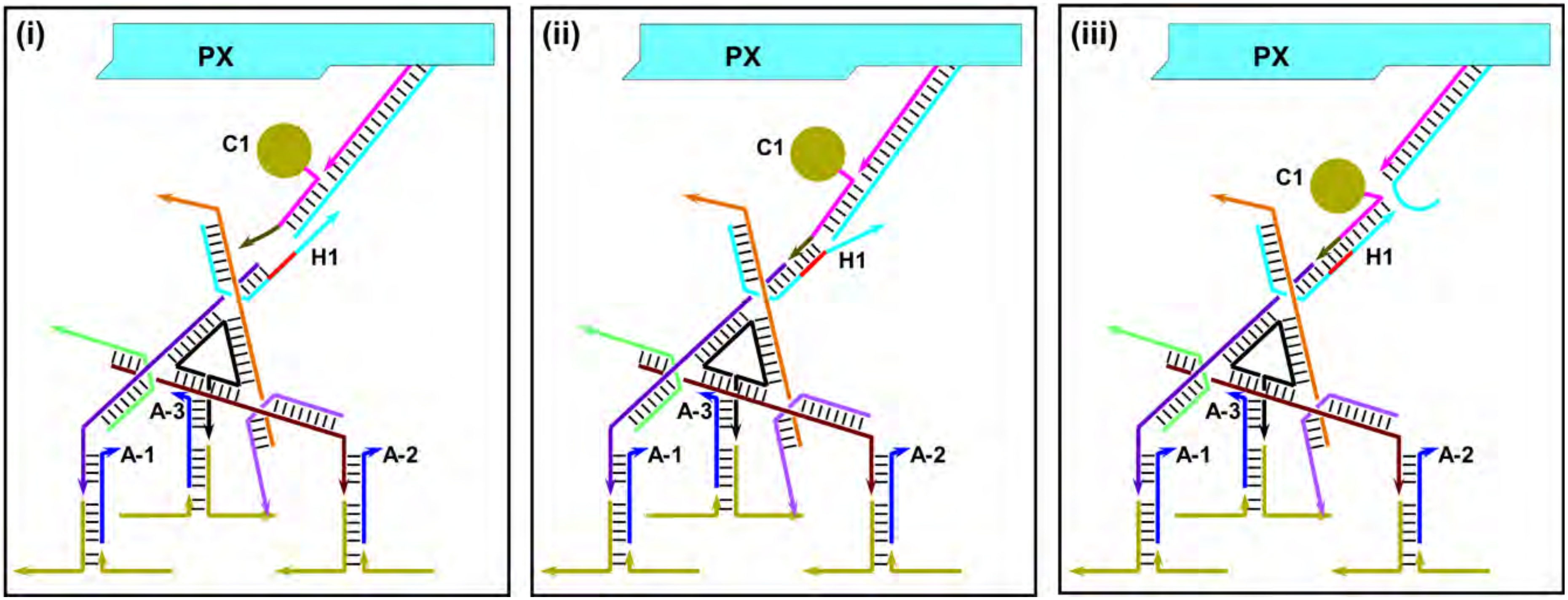
Walker Structure





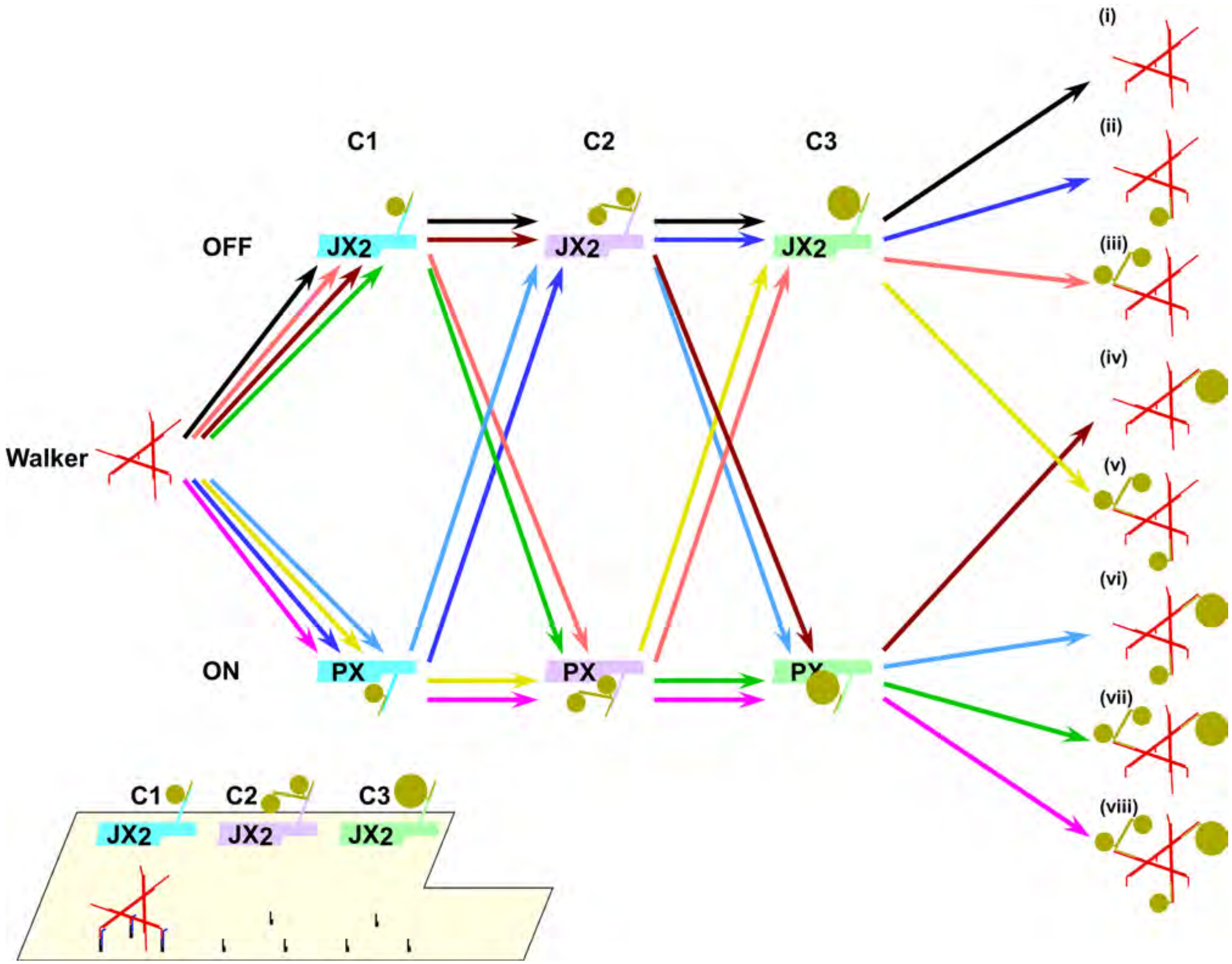
H. Gu, J. Chao, S.J. Xiao & N.C. Seeman, *Nature* **465**, 202-205 (2010).

Cargo Transfer



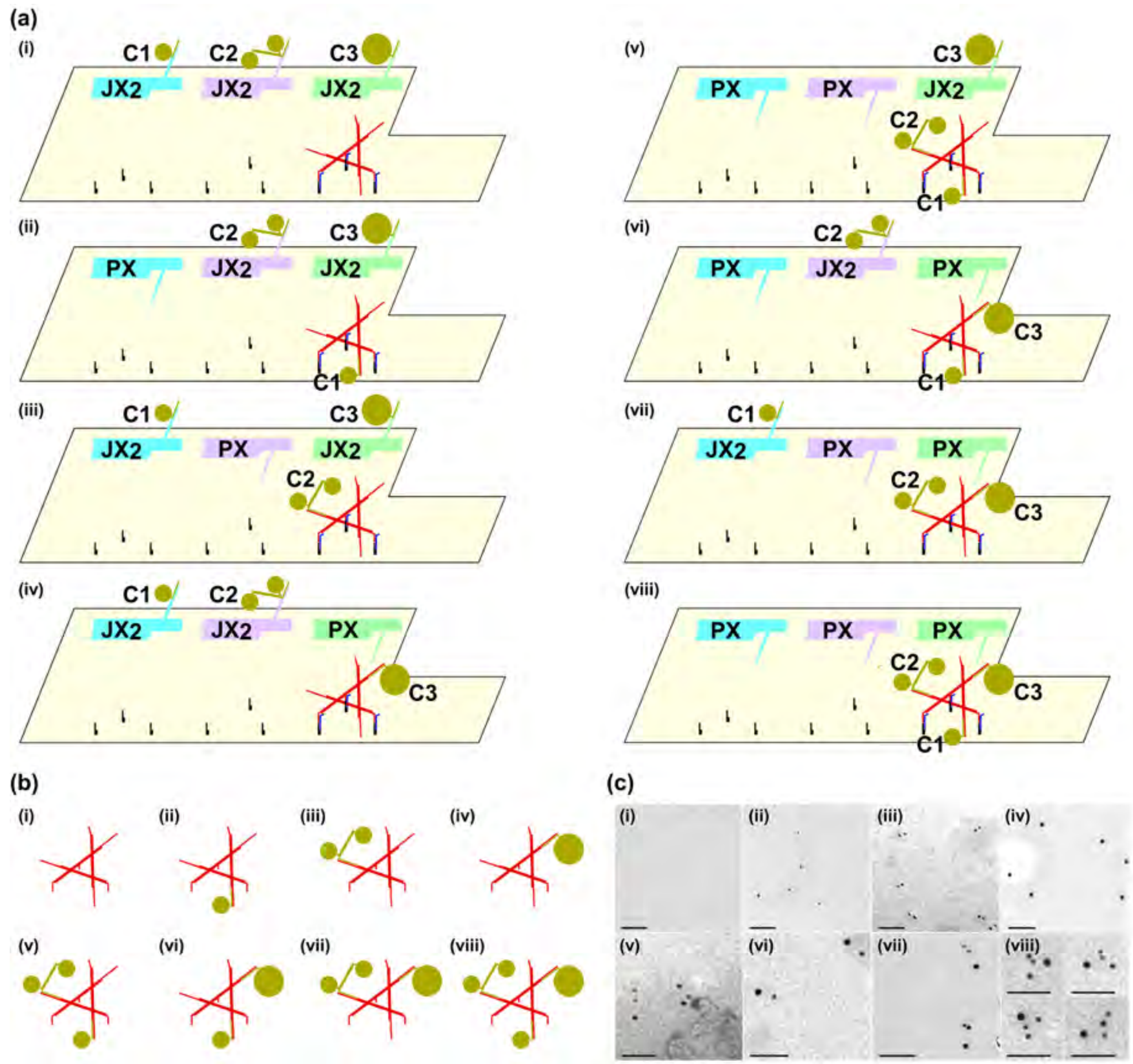
H. Gu, J. Chao, S.J. Xiao & N.C. Seeman, *Nature* **465**, 202-205 (2010).

Diversity of Products



H. Gu, J. Chao, S.J. Xiao & N.C. Seeman, *Nature* **465**, 202-205 (2010).

Distinct Programmed Products



H. Gu, J. Chao, S.J. Xiao & N.C. Seeman, *Nature* **465**, 202-205 (2010).

Summary of Results

- Polyhedral Catenanes, Knots and Borromean Rings can be Assembled from Branched DNA by Ligation.
- 2D Lattices with Tunable Features have been Made from DNA Tile and Origami Components.
- 3D Crystals with Tunable Properties have been Self-Assembled and their Structures have been Determined.
- Heterologous Species have been Included in DNA Nanoconstructs.
- Algorithmic Assembly has been Prototyped and its Problems have been Addressed.
- Nanomechanical Devices have been Assembled from Branched DNA, Including Shape-Shifters and Walkers. These have been Combined on an Origami Surface to Produce a Nano-Scale Assembly Line.

SUPPORT

National Institute of General Medical Sciences (1982-)
Office of Naval Research (1989-2004; 2009-)
National Science Foundation (1997-)
DARPA/AFOSR (2001-2003)
Army Research Office (2005-)
W. M. Keck Foundation (2006-2010)
Nanoscience Technologies, Inc. (2003-2006)
Department of Energy -- (2006-2008; 2012-)

WEB PAGE

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