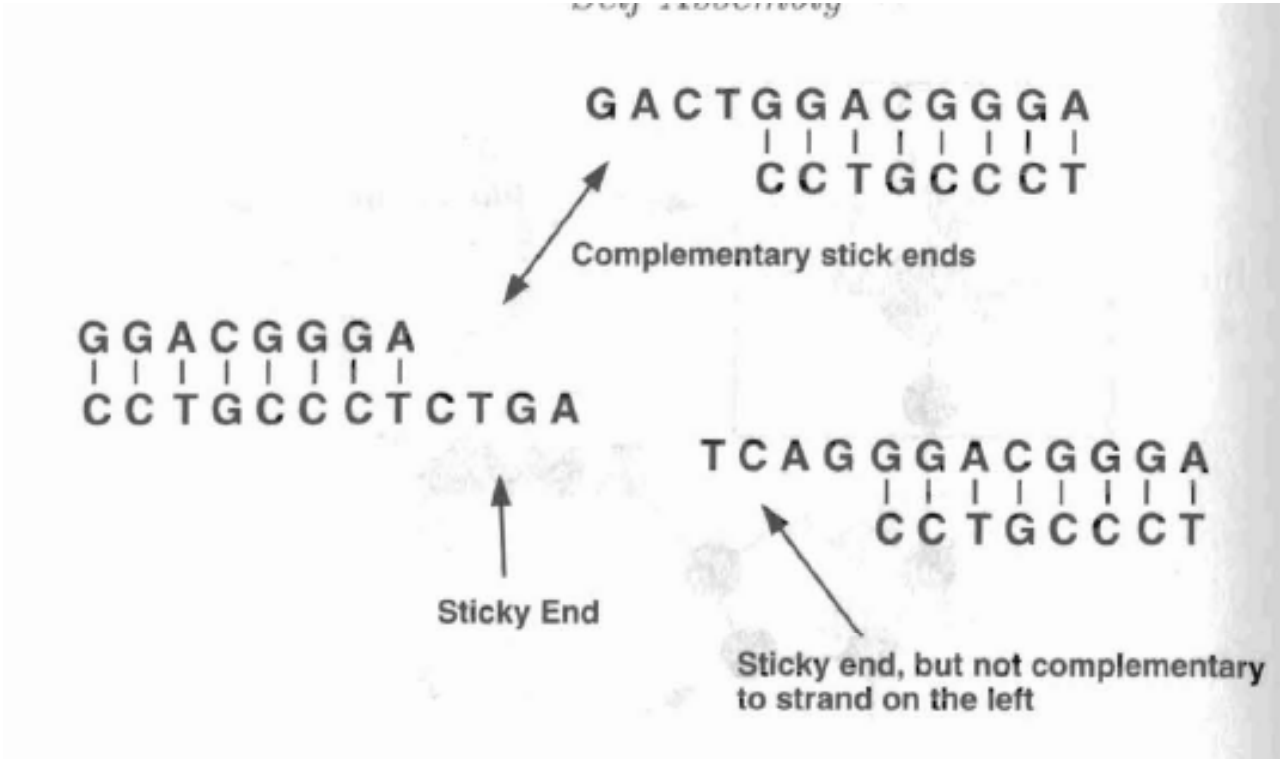
Self-Assembly

Lecture 8
DNA Self-Assembly

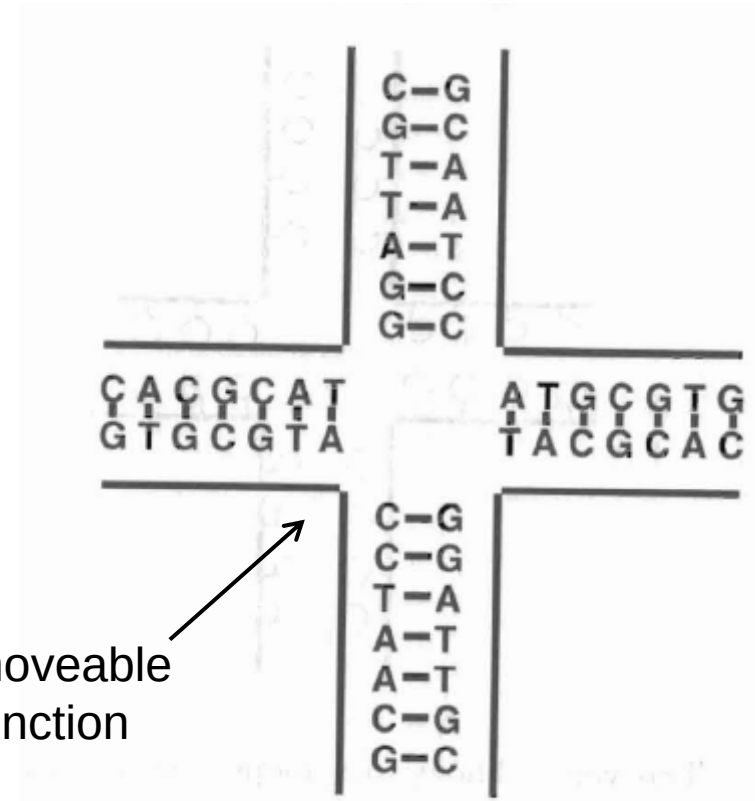
DNA self-assemby motifs

- Sticky ends: allow specific binding in DNA self-assembly



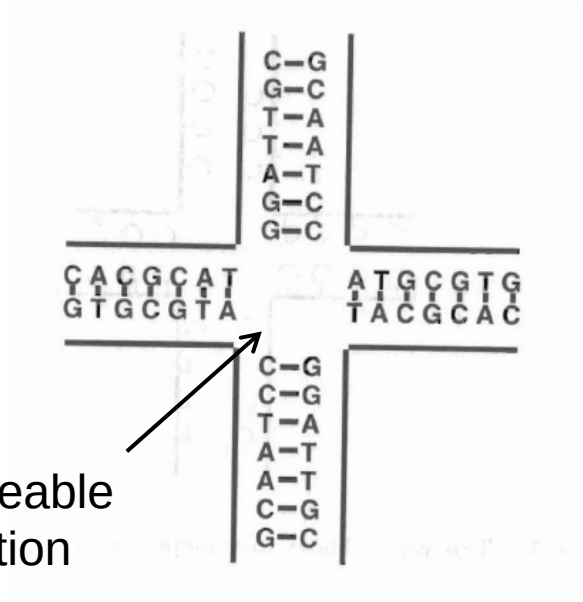
DNA self-assemby motifs

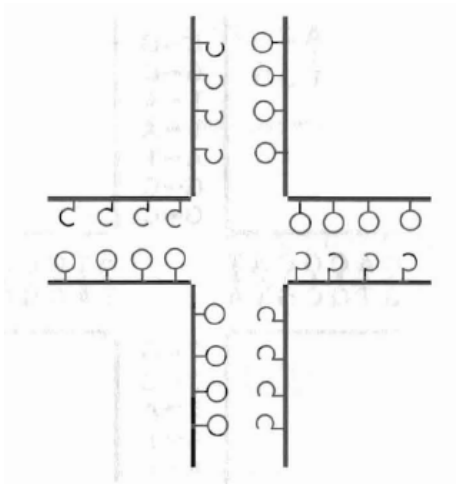
- Branched junction (Holliday junction):
  - discovered by Robin Holliday in 1964 to explain mechanism of genetic recombination
  - found to be involved in DNA replication and repair

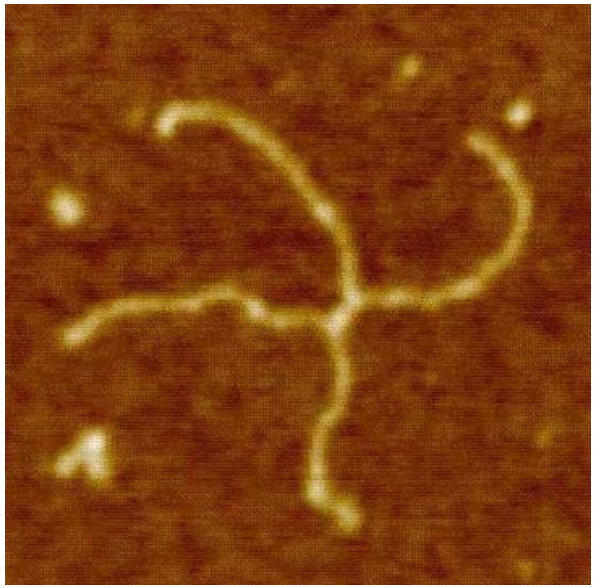


DNA branched junctions

- Holliday junctions in nature are **moveable** like a zipper, however in nanotechnology the structure designers are primarily interested in **stable** junctions





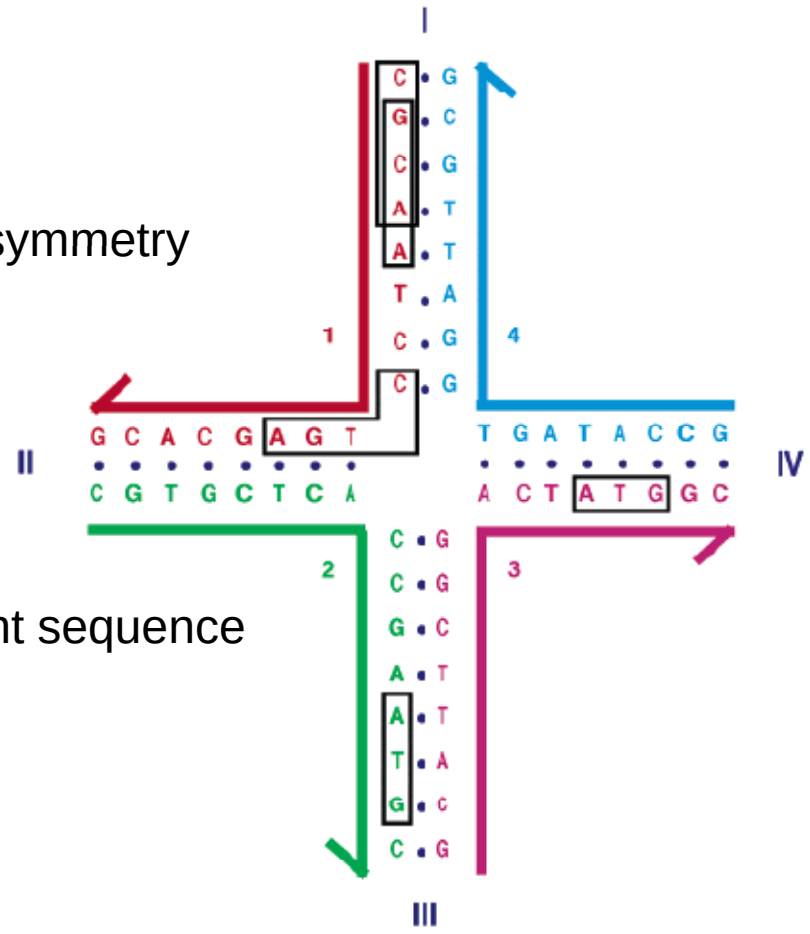


DNA branched junctions

- The symmetry should be broken to achieve a stable junction

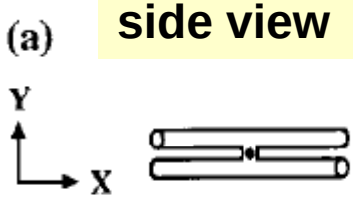
No Axis of seq. symmetry

No complement sequence in corners

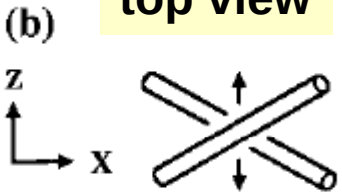


Holliday junctions as a constructing element

- Holliday junctions provide a construction set that can be used to build a 2D or 1D arrays



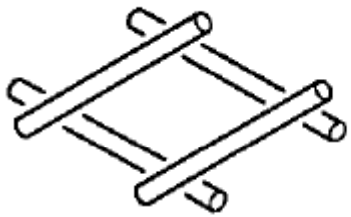
side view

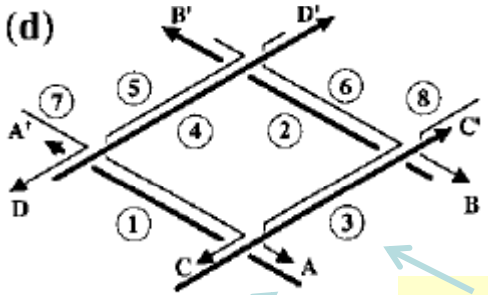


top view

63.5 deg angle

combination of 4 junctions assemble in a rhombus motif





one full turn

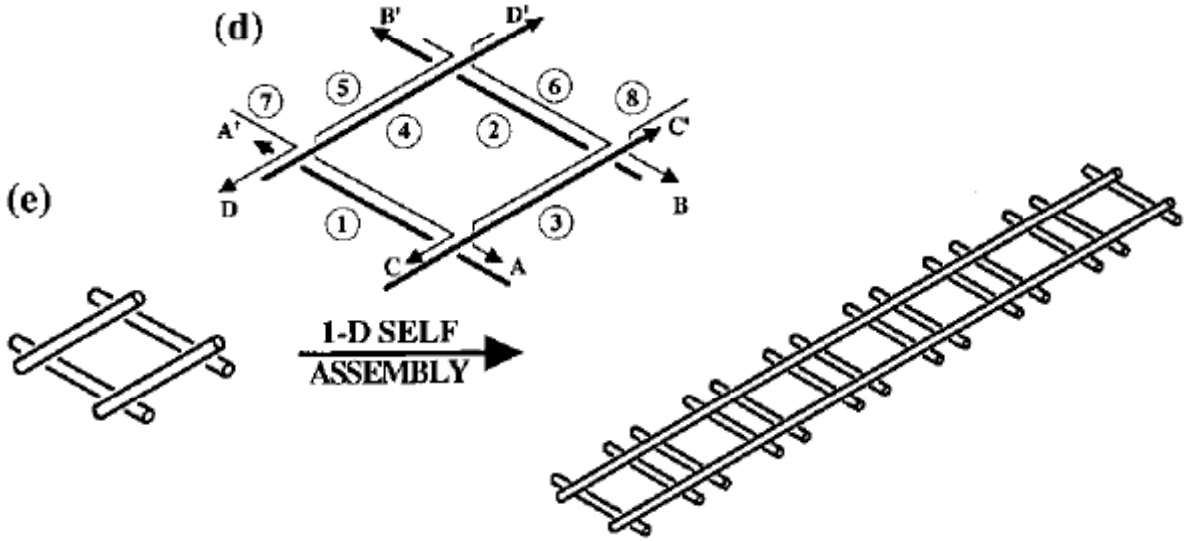
four full double helical turns (42 bp)

Ned Seeman et al, JACS 121, 5437 (1999)

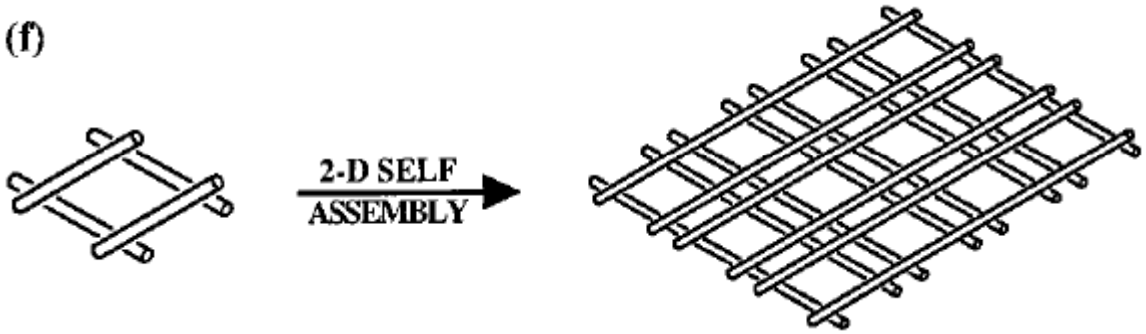
Holliday junctions as a constructing element

- Depending on the sticky ends in the rhombus, different arrays can be created

1D self assembly producing rail road track, sticky ends C, C', D, D' are eliminated



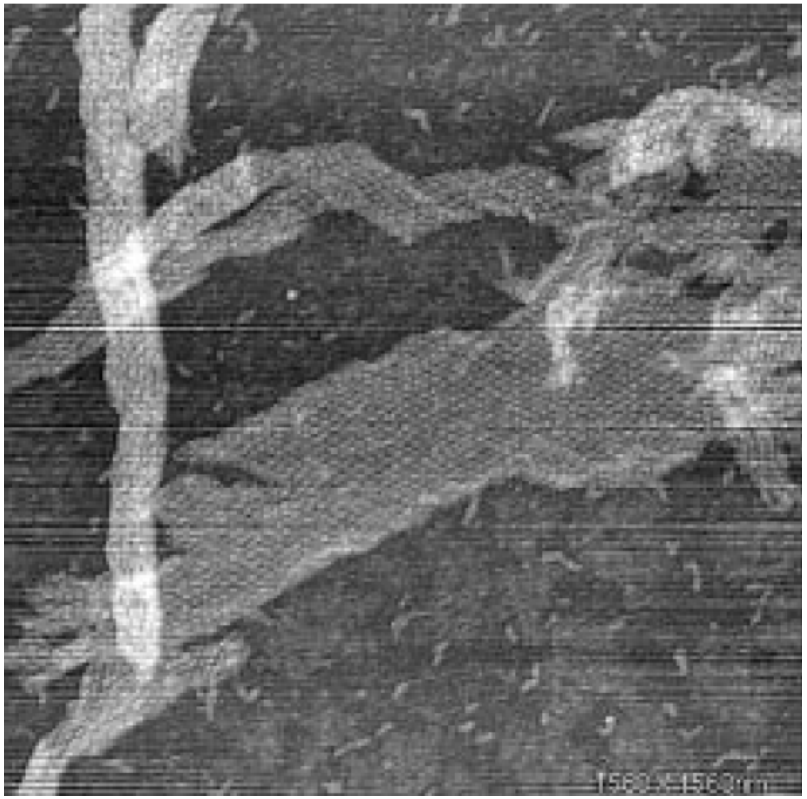
2D self assembly, all sticky ends used

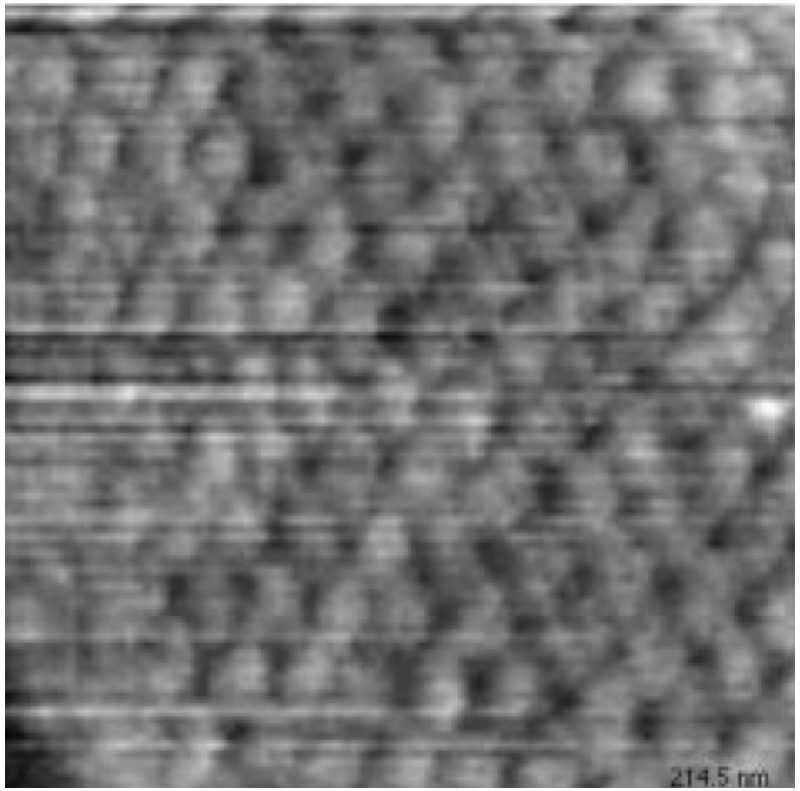


Ned Seeman et al, JACS 121, 5437 (1999)

Holliday junctions as a constructing element

- AFM imaging results assembled rhombus-shaped component (4 + 2 helices per repeat in each direction). (left) An image of dimensions 1568 1568 nm. The unit cell is 20.5 x 21.1nm.
- Imaging condition: sample deposited on mica, rinsed, blow dried and imaged under iso-propanol.

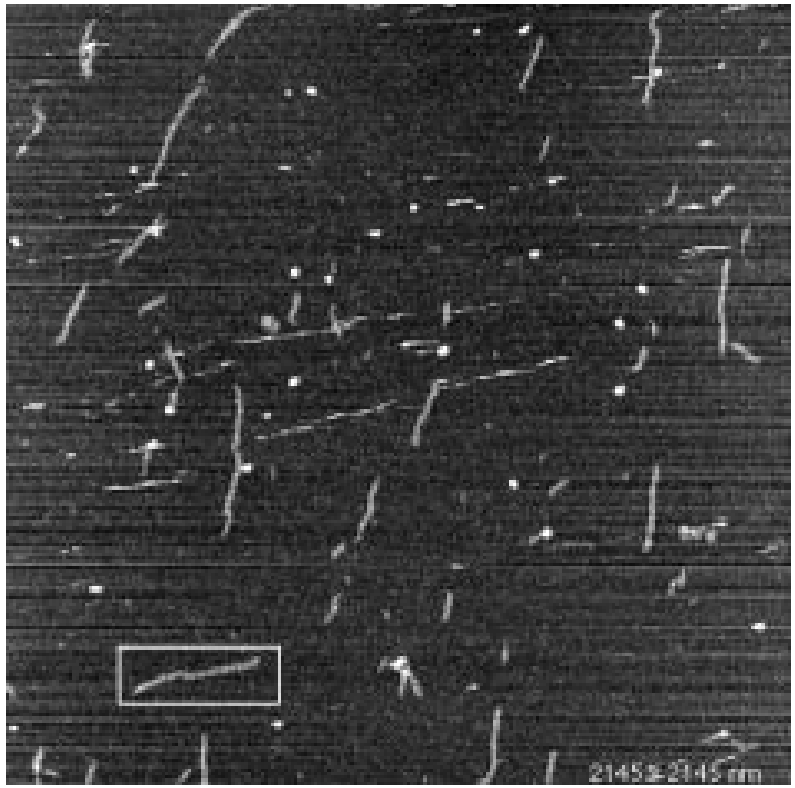


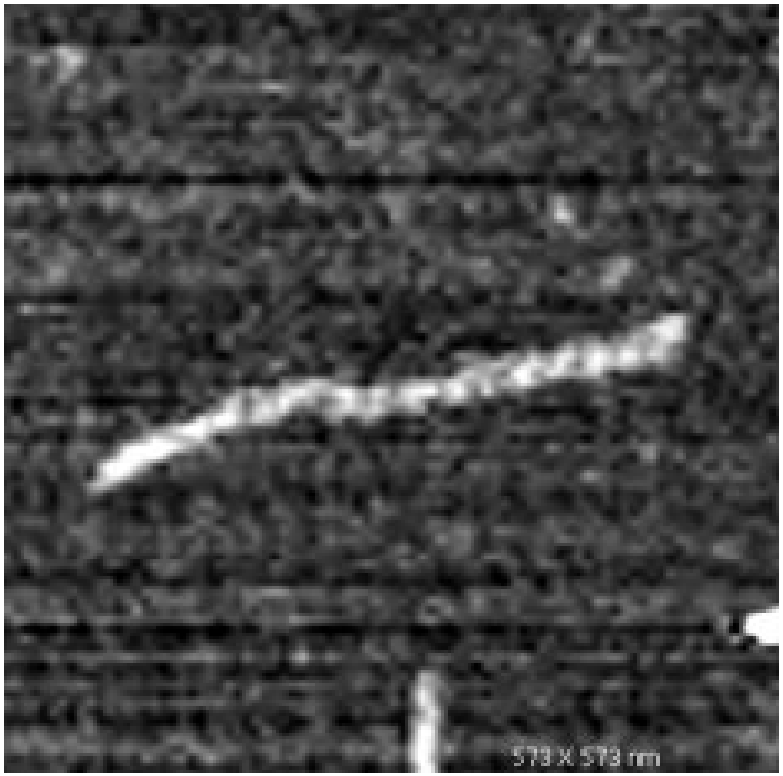


Ned Seeman et al, JACS 121, 5437 (1999)

Holliday junctions as a constructing element

- AFM image of 1D assembly.

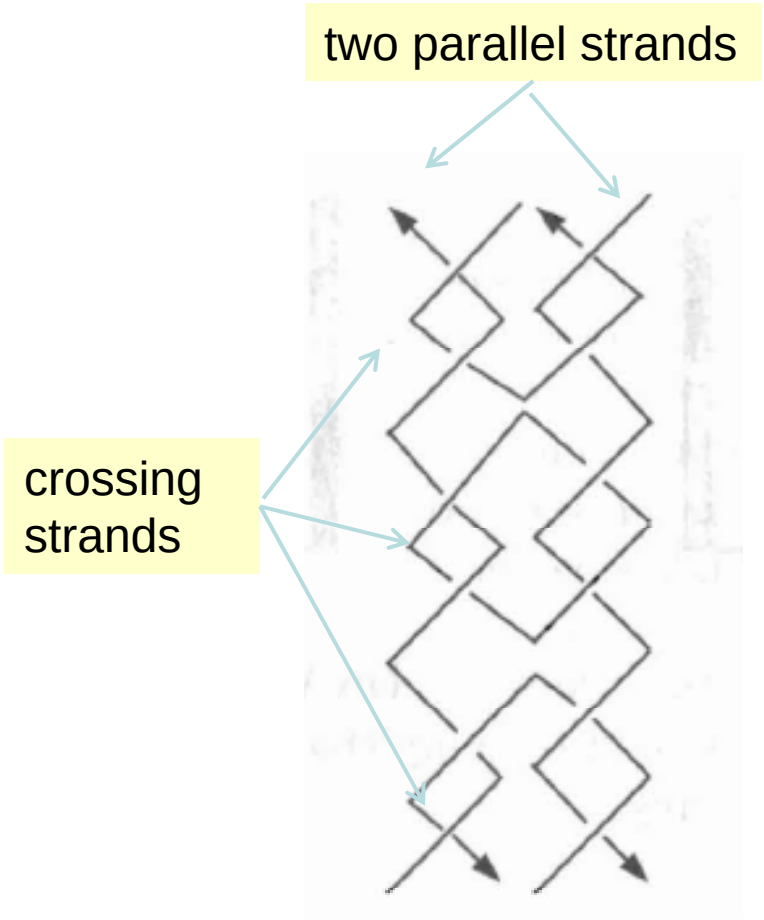




Ned Seeman et al, JACS 121, 5437 (1999)

DNA self-assemby motifs

- Double cross-over DNA molecules allow to more rigid construction kit



Tsu-Ju Fu and Nadrian C. Seeman, Biochemistry 32, 3211 (1993)

DNA self-assemby motifs

- Molecule containing multiple crossovers must be “phased”, there are 5 possibilities:

A – anti-parallel strands, stable

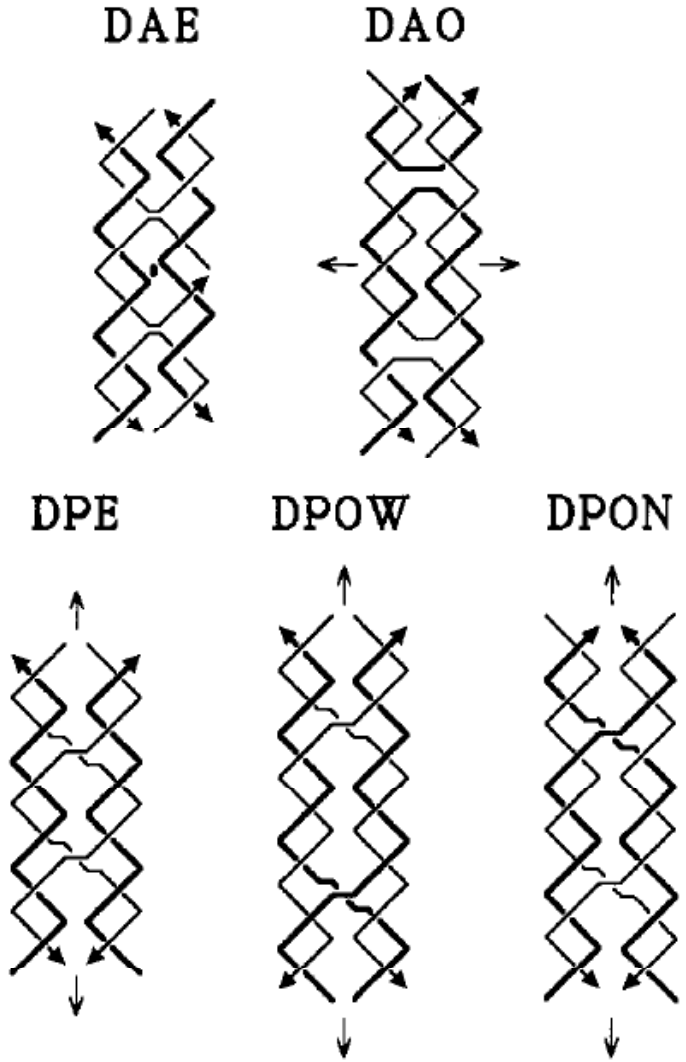
E – even number of half helical turns

O – odd number of half helical turns

P - parallel strands, unstable

OW – odd number of half helical turns, extra half turn corresponds to major grove separation (wide)

ON – odd number of half helical turns, extra half turn corresponds to minor grove separation (narrow)



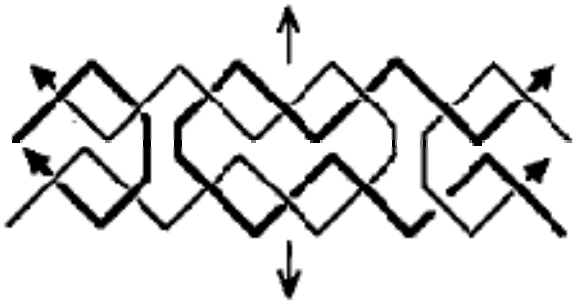
Tsu-Ju Fu and Nadrian C. Seeman, Biochemistry 32, 3211 (1993)

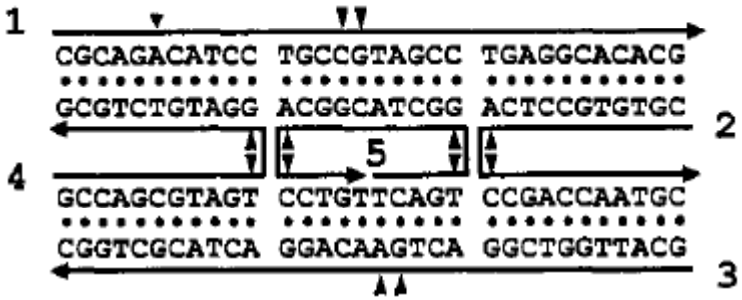
DNA self-assemby motifs

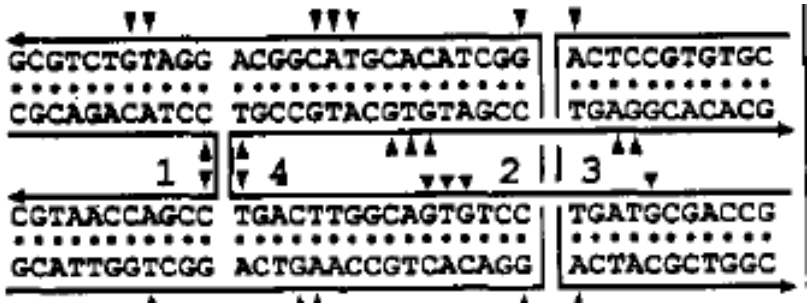
- Construction example

DAE

DAO



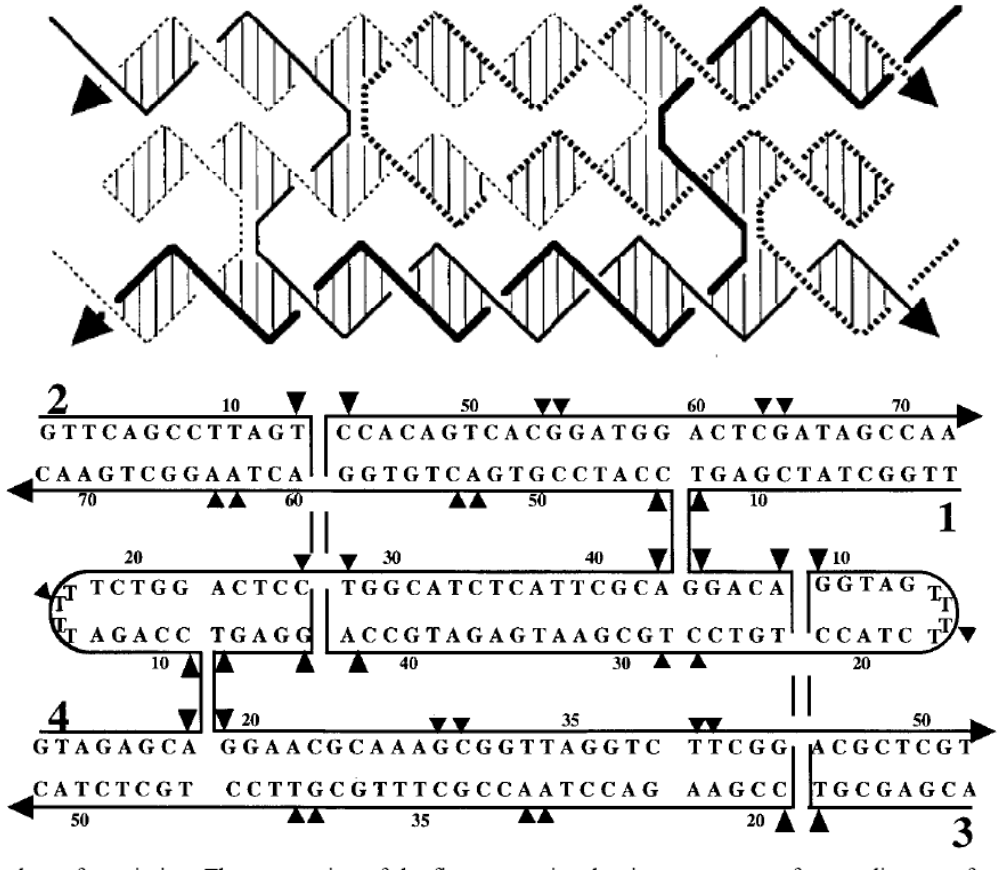




Tsu-Ju Fu and Nadrian C. Seeman, Biochemistry 32, 3211 (1993)

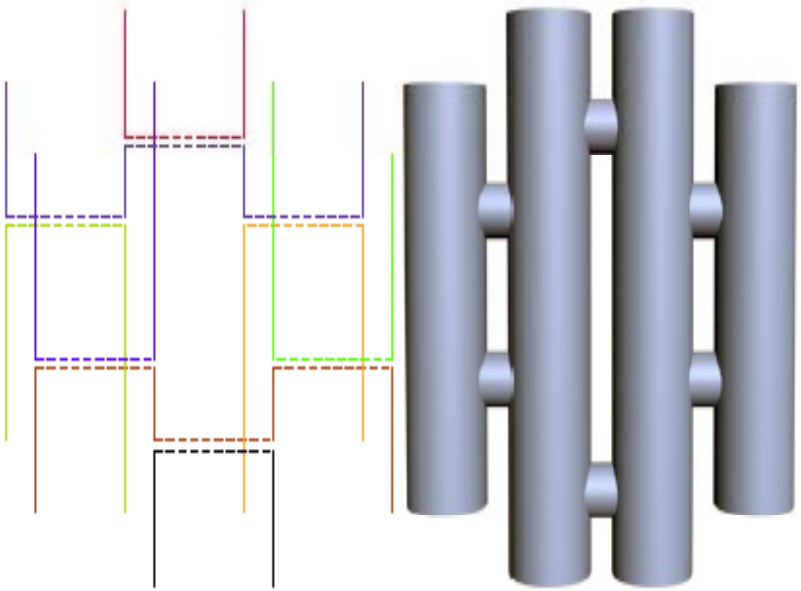
DNA self-assemby motifs

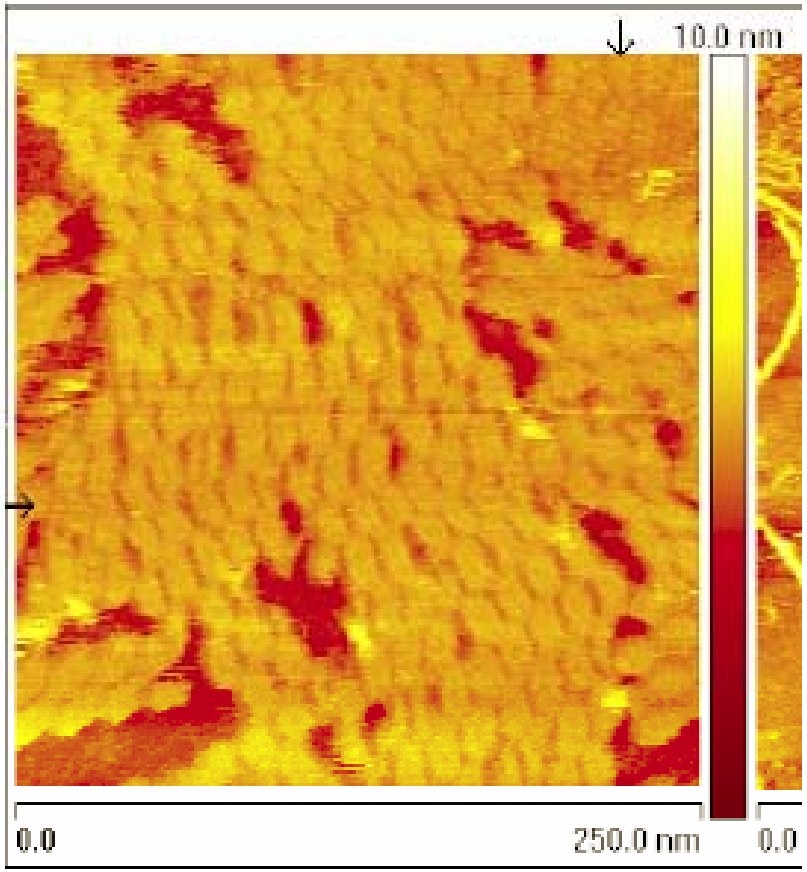
- **Triple crossover (TX)**: the molecule contains three helices, designed to have their axes coplanar. The molecule is composed of four strands (arrow indicate 3’ ends). The three helical domains are indicated by horizontal stripes.



Motif formed by quadruple cross-over (QX) & Lattice

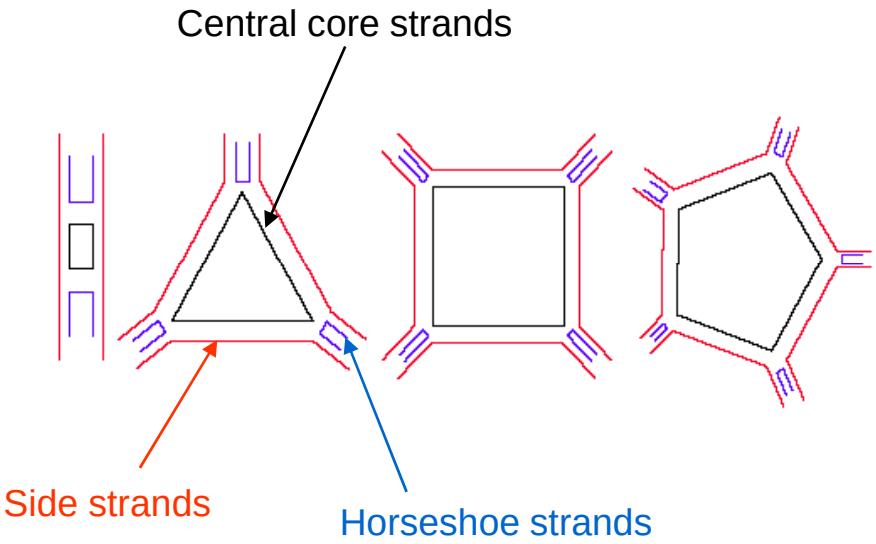
Quadruple crossover consists of eight strands, interweaving to form four parallel double helices. Note that there is no base pairing along the dashed lines; all base pairing occurs along the solid lines. Two adjacent solid lines represent B-form double stranded DNA

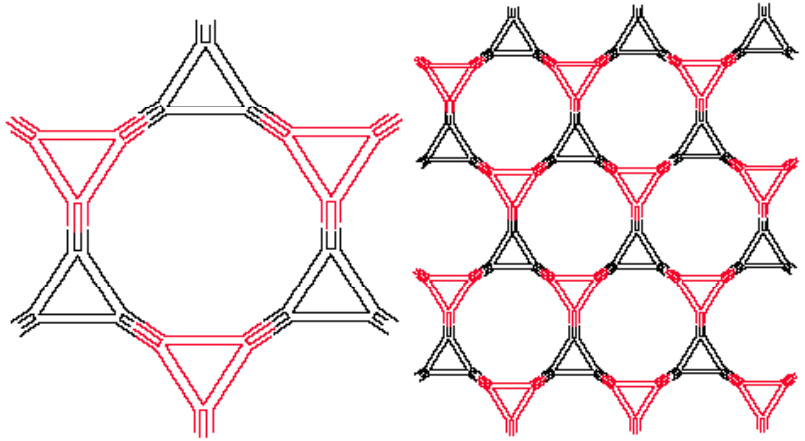


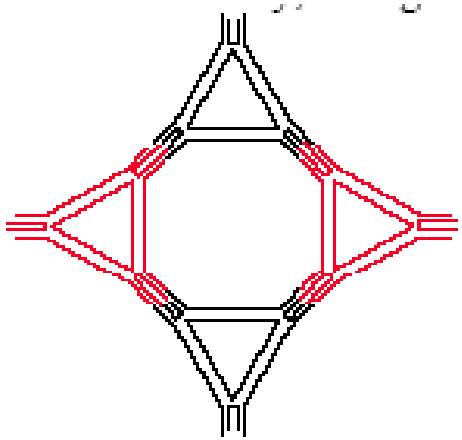


Polygon DNA tiles

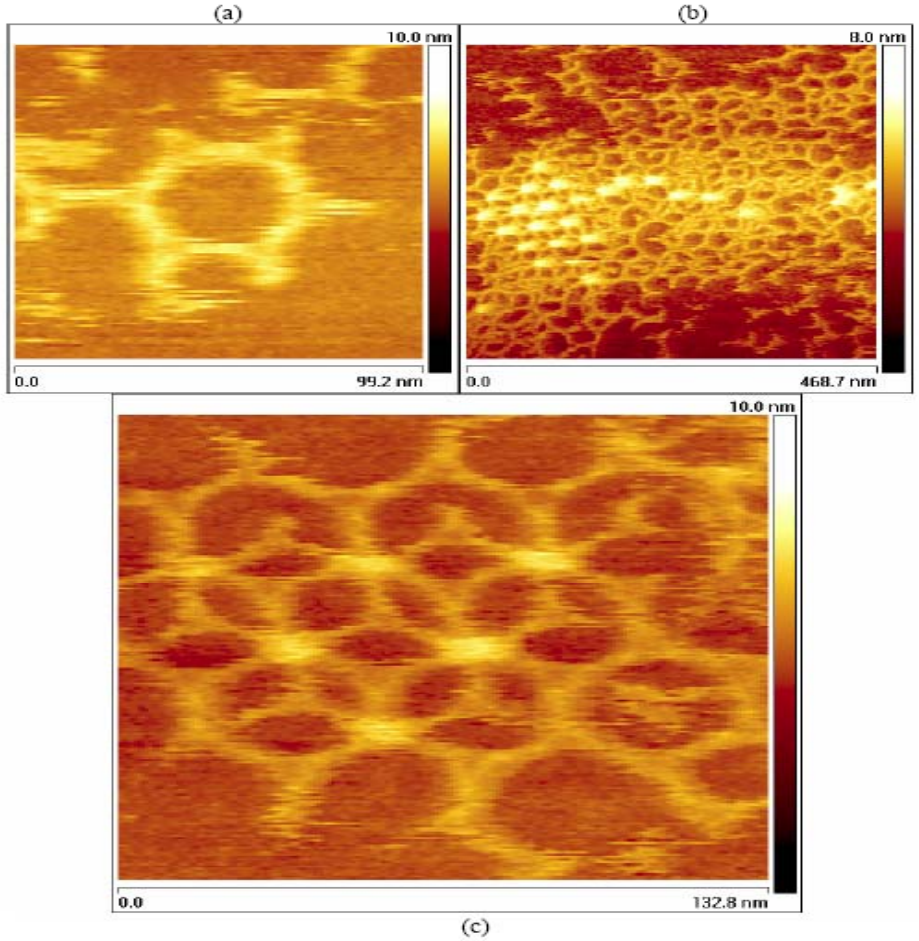
- Polygon paradigm designs for n = 2, 3 (triangle), 4 (square), and 5 (pentagon).







Lattices from SA of triangle motifs

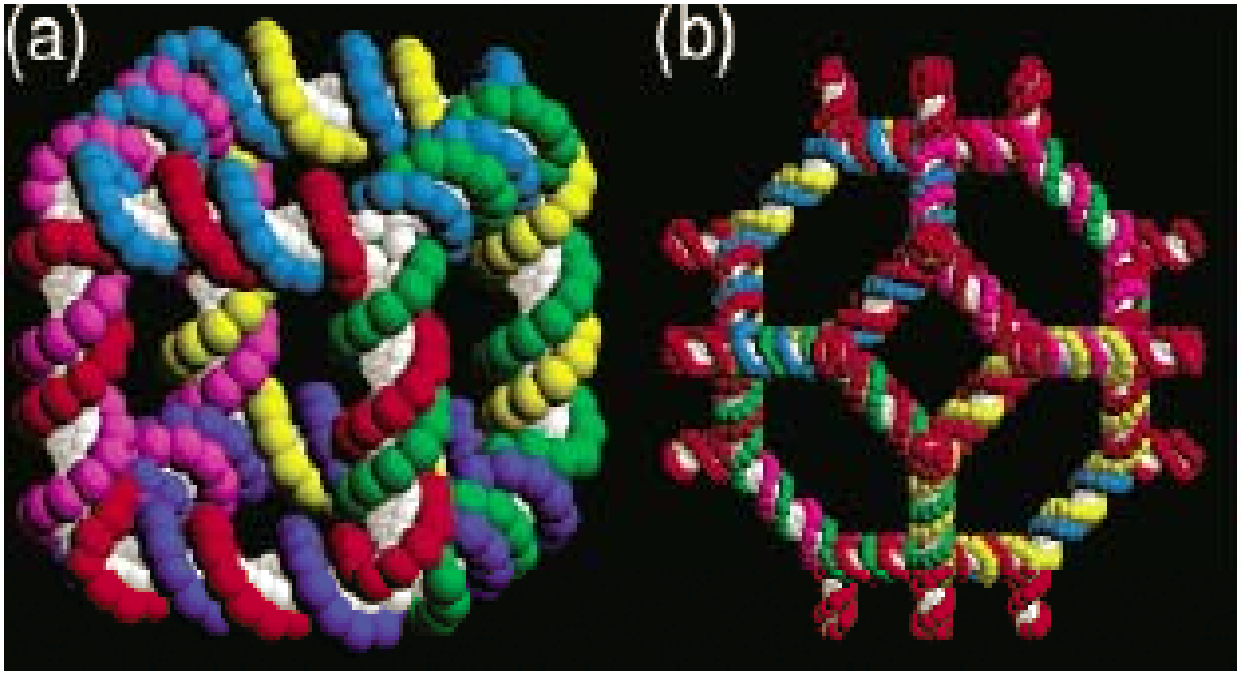


Brun et al, 2006

DNA self-assemby motifs

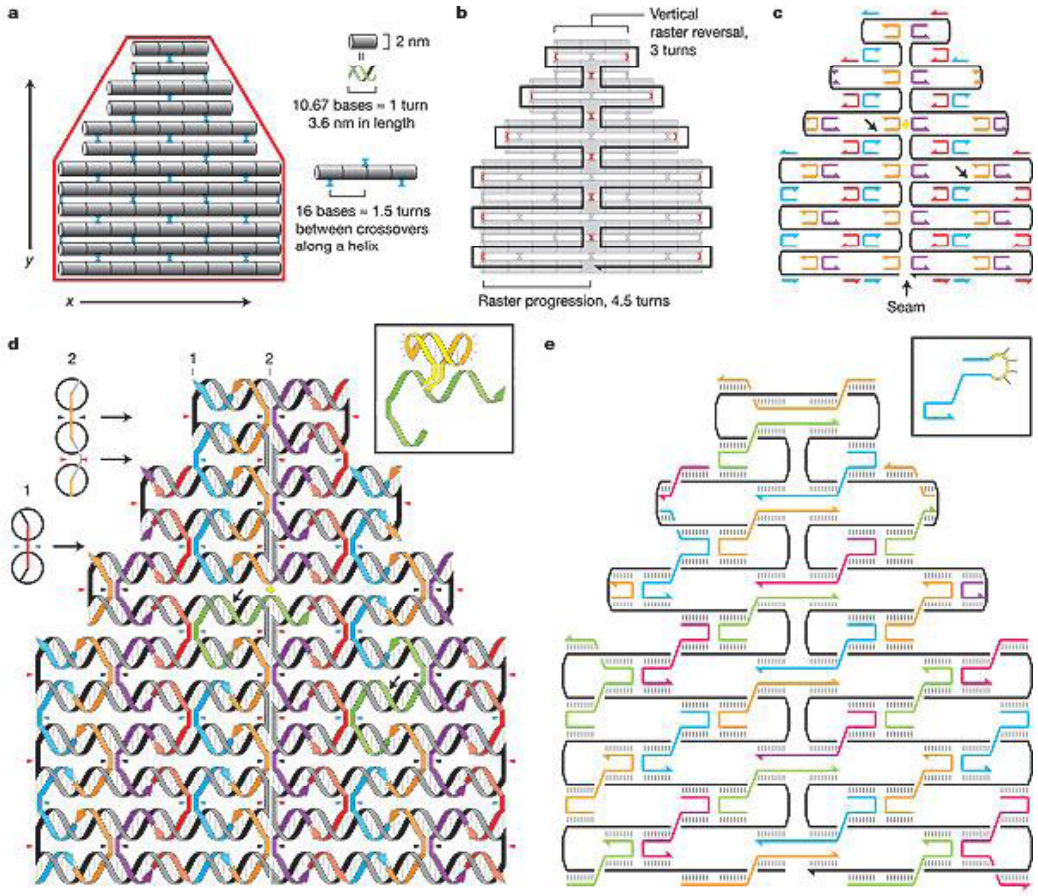
- Complicated 2D and 3D structures can be assembled from DNA tiles due to their rigidity

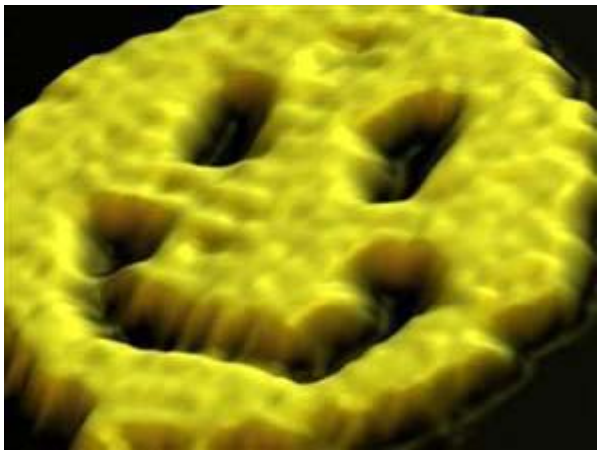
cube **truncated octahedron**



DNA Origami

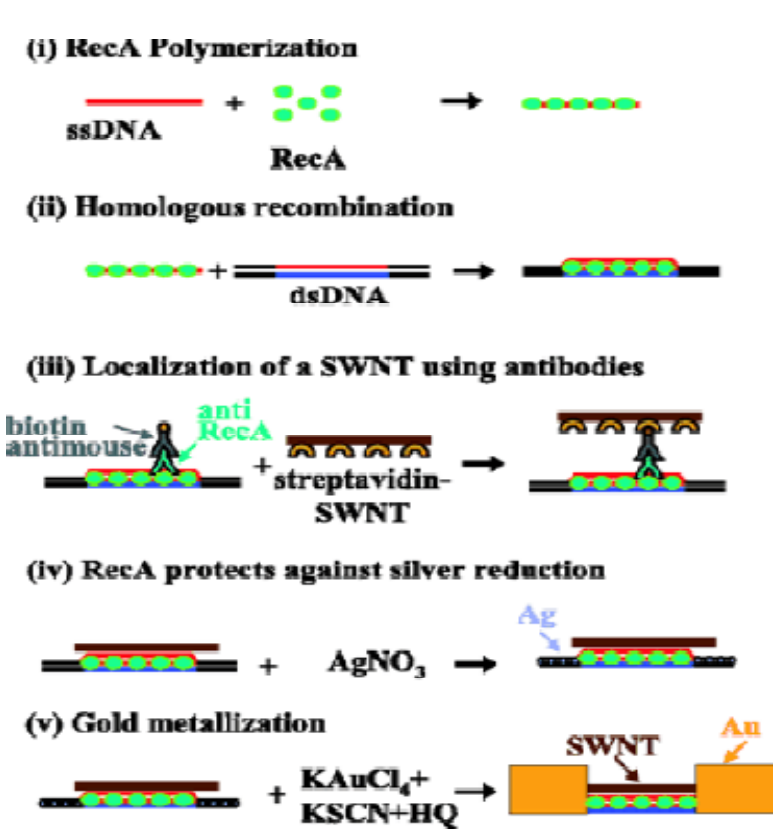
- **DNA Origami** concept: distant parts of DNA match together and lead to stable 2D objects, to give structure rigidity short helper strands (“staples”) attach strand together

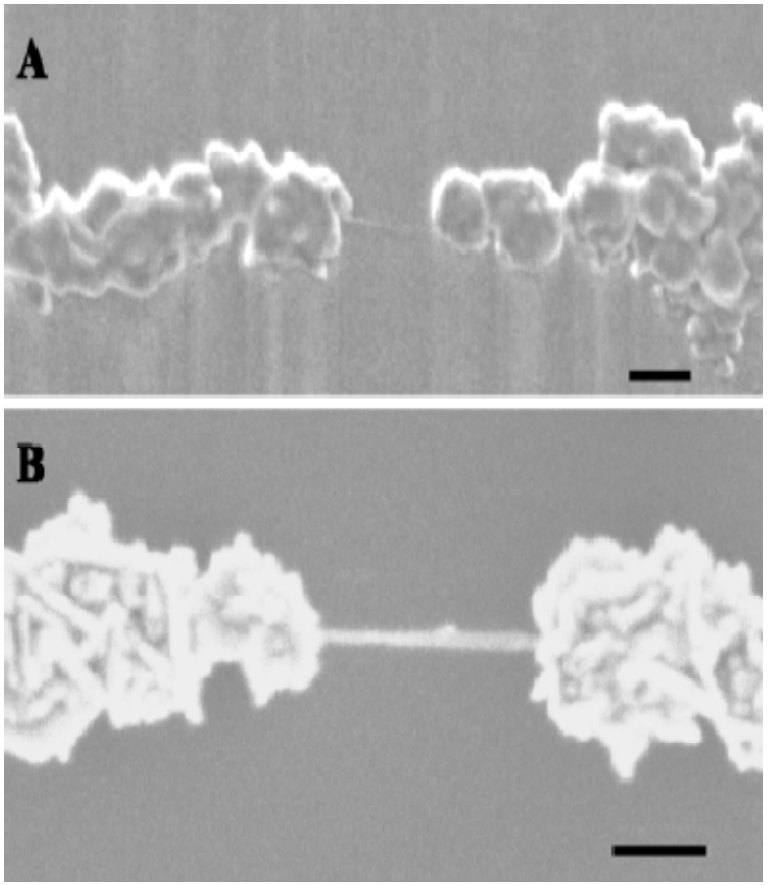




Rothemund , PNAS 440, 297 (2006)

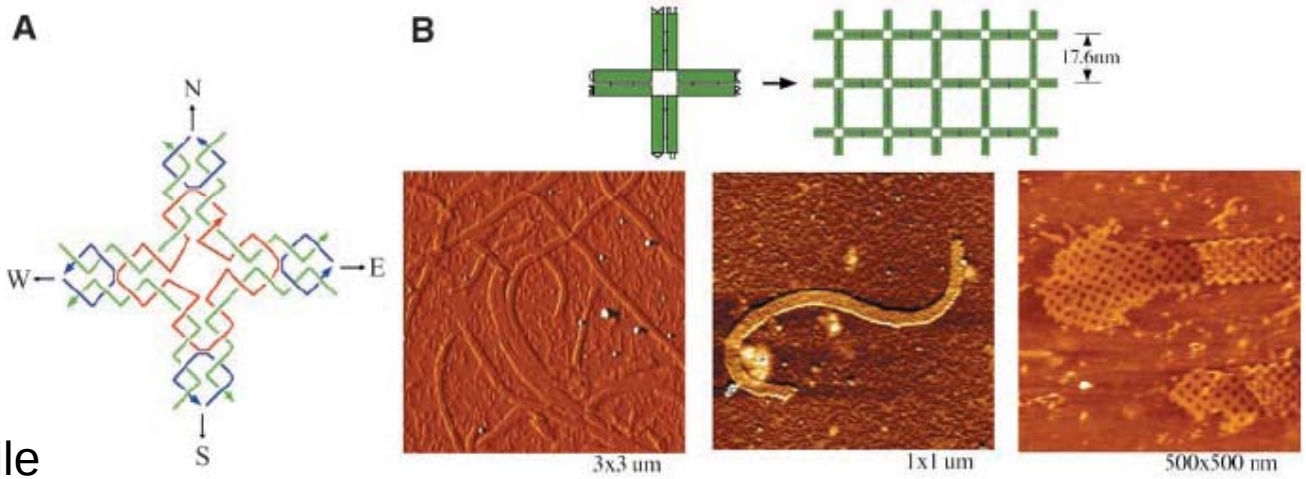
Nanowires templated on DNA





- **Fig. 1. Assembly of a DNA-templated FET and wires contacting it. Steps are as follows: (i) RecA monomers polymerize on a**
- ssDNA molecule to form a nucleoprotein filament. (ii) Homologous recombination reaction leads to binding of the nucleoprotein
- filament at the desired address on an aldehyde-derivatized scaffold dsDNA molecule. (iii) The DNA-bound RecA is used to localize
- a streptavidin-functionalized SWNT, utilizing a primary antibody to RecA and a biotin-conjugated secondary antibody. (iv) Incubation
- in an AgNO3 solution leads to the formation of silver clusters on the segments that are unprotected by RecA. (v) Electroless gold
- deposition, using the silver clusters as nucleation centers, results in the formation of two DNA-templated gold wires contacting the
- SWNT bound at the gap.

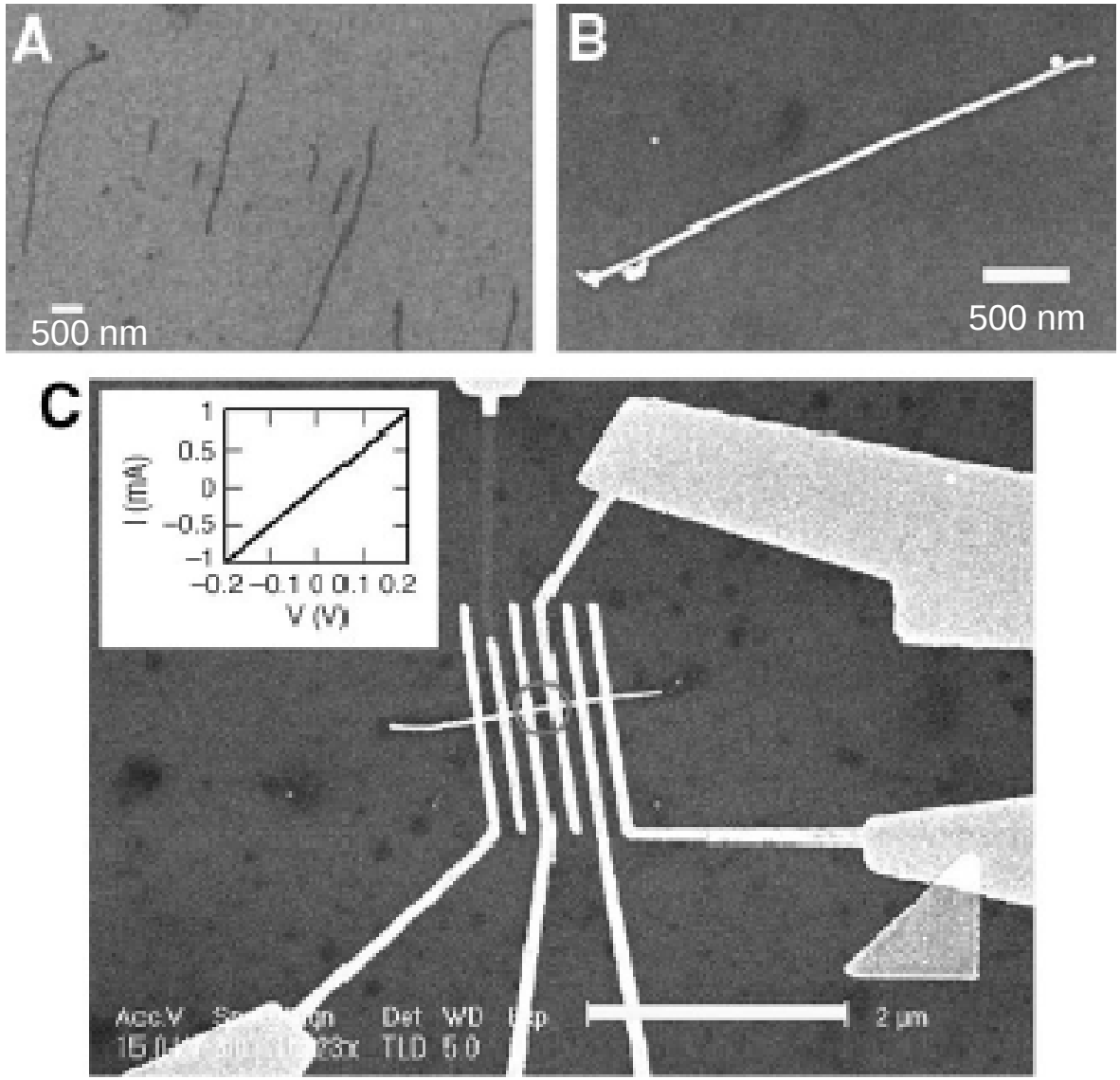
Templated DNA-nanowires



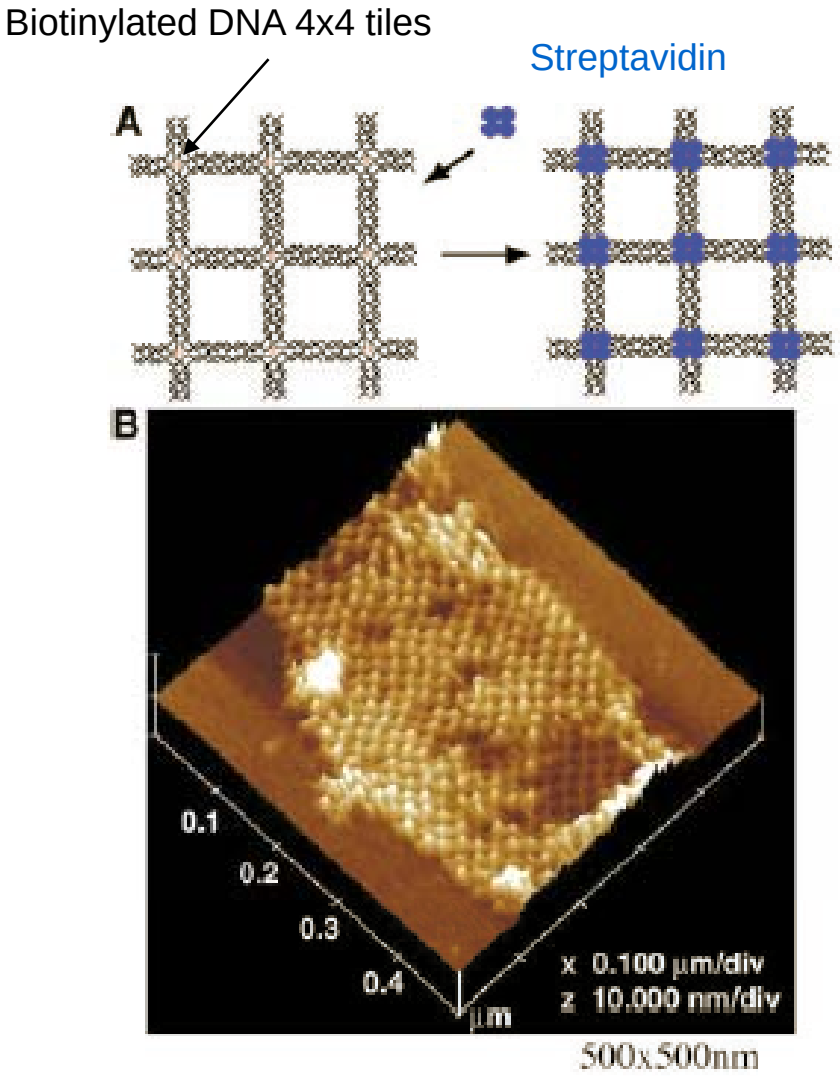
4x4 DNA tile

Yan et al, 2003. Science 301:1882-84

Metallization and conductivity measurements of DNA 4x4 tile ribbons



Templated array of proteins on 4x4 nanogrids

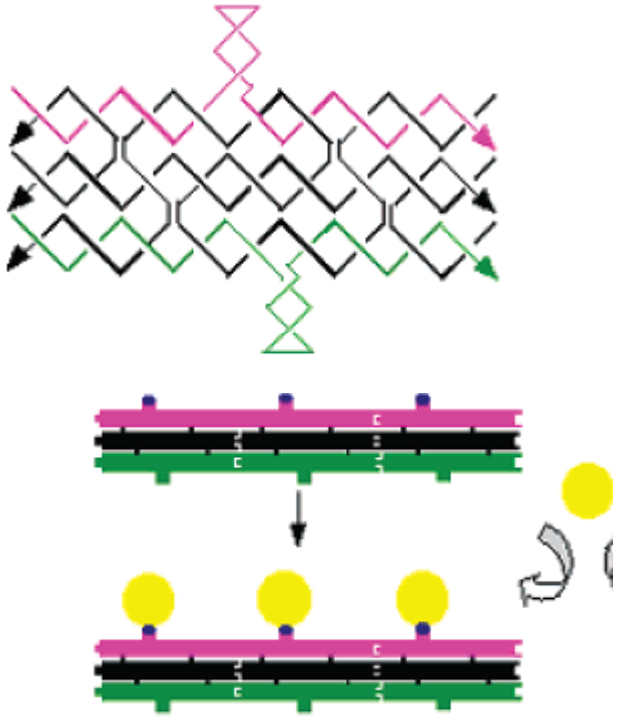


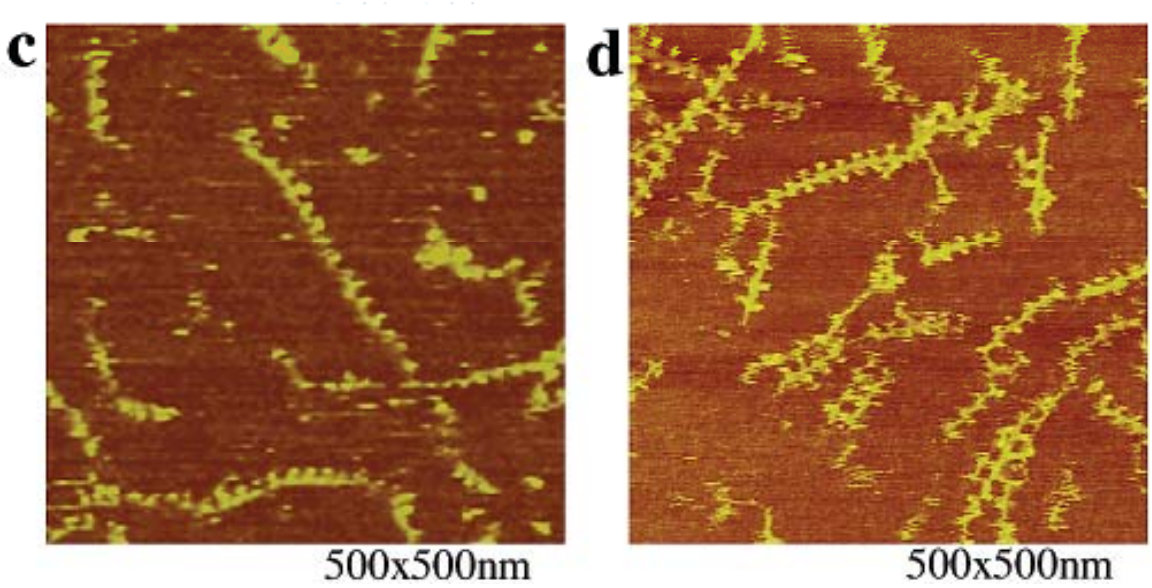
- In nano-electronics designs: possibility to self-assemble proteins on DNA grid

➢ Nano-electronics components

DNA templated linear arrays

- Linear arrays based on TX motif





single layer streptavidin

double layer streptavidin

Computing with tiles

- Rothemund's tiles:

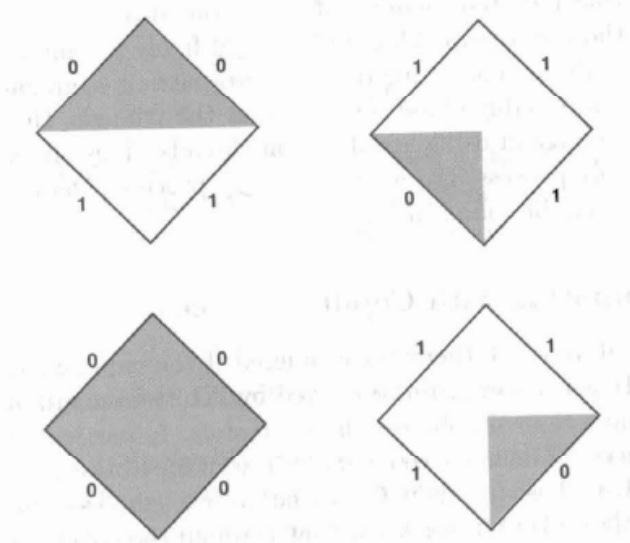
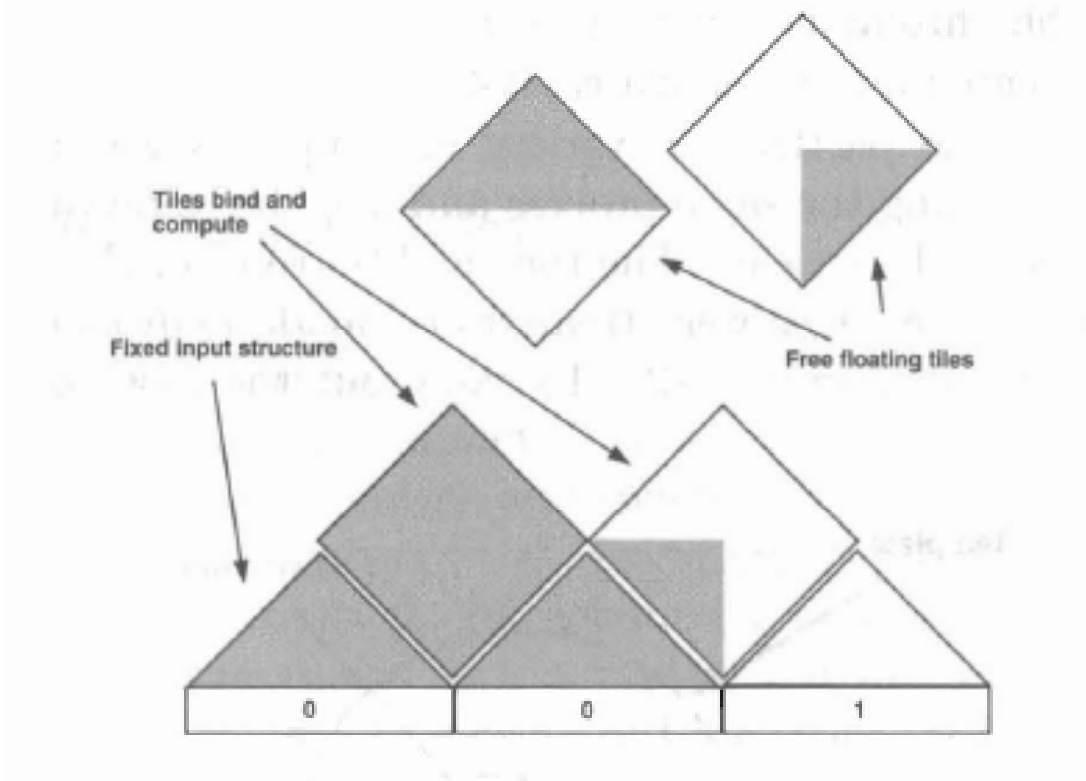


TABLE 6.1: The Logical Operation XOR

Input	Output
0 0	0
0 1	1
1 0	1
1 1	0



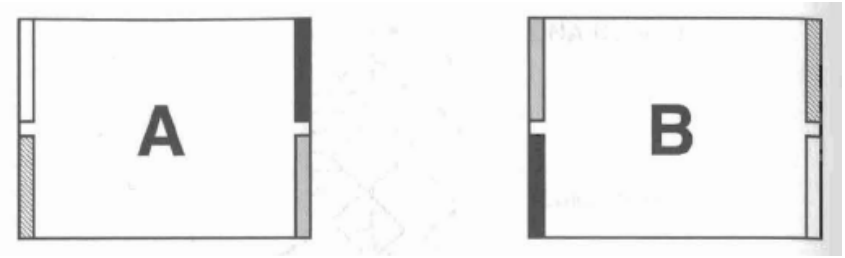
Computation by Self-assembly of DNA Tilings

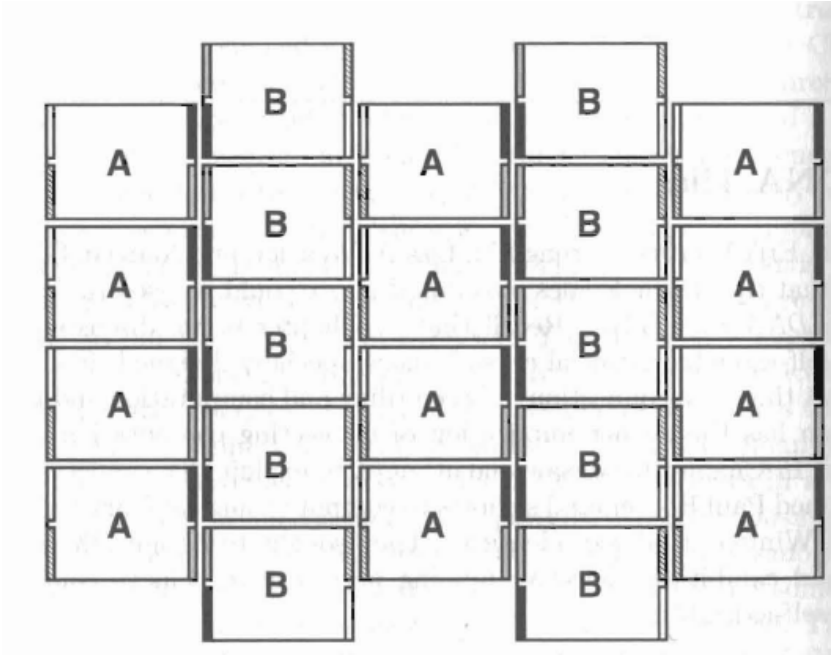
- Tiling Self-assembly can:
  - Provide arbitrarily complex assemblies using only a small number of component tiles.
  - Execute computation, using tiles that specify individual steps of the computation.

- Computation by DNA tiling lattices:
  - Fist proposed by Winfree (1998)
  - First experimentally demonstrated by Mao, et al (2000) and N.C. Seeman (2000).

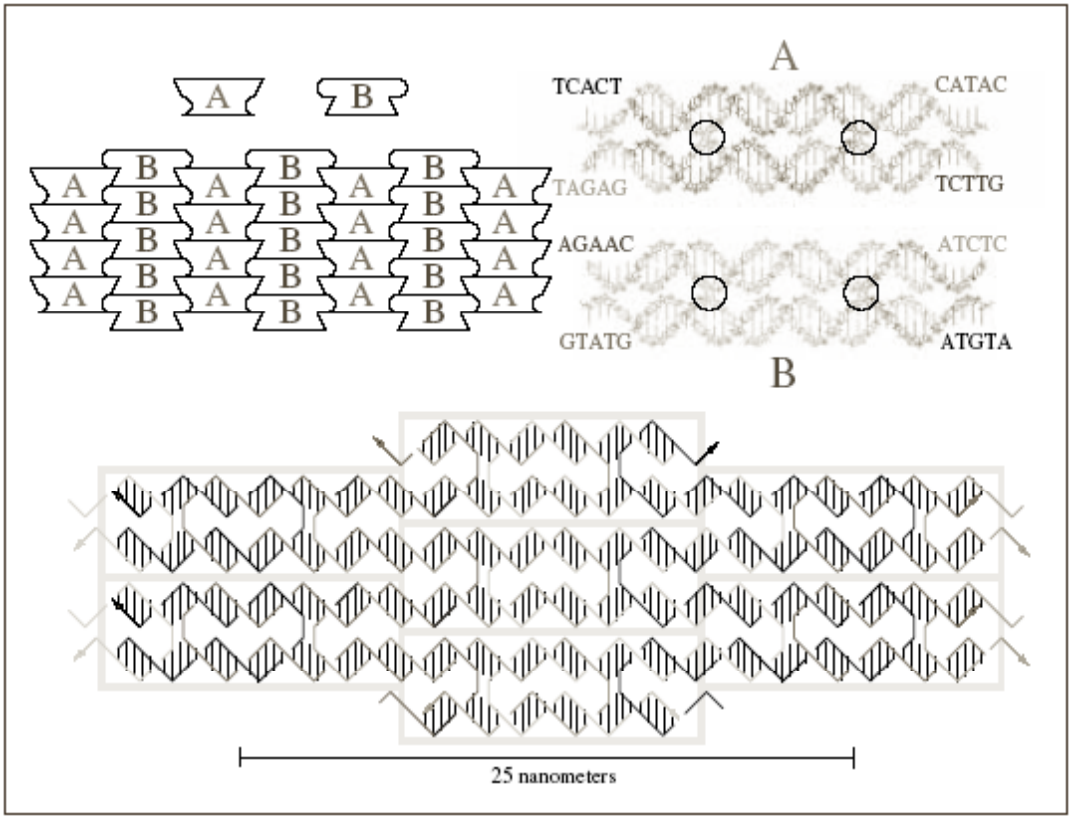
DNA tiles

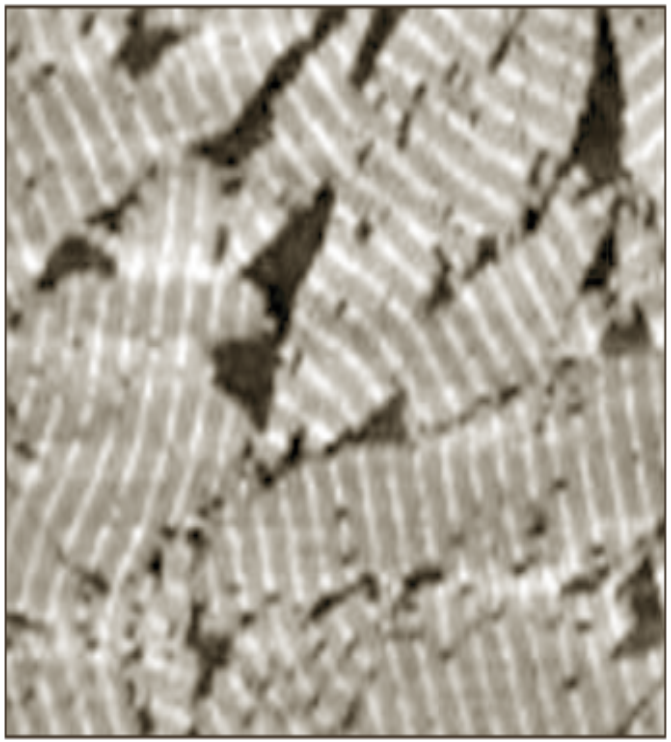
- DNA tiles can be designed based on DX motif





Implementation of abstract Wang-tiles with DNA tiles

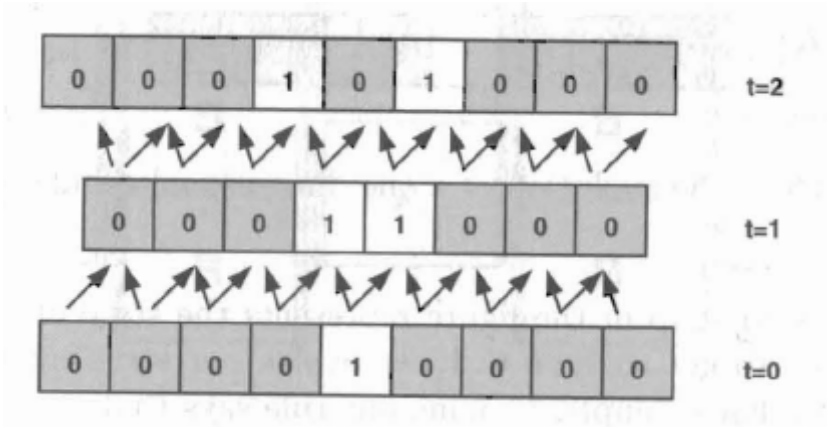




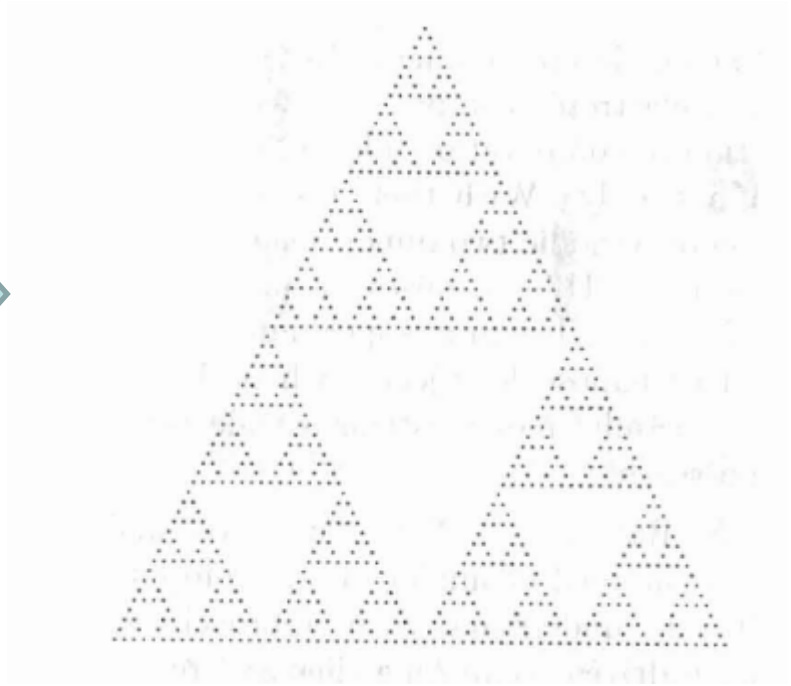
Winfree, 2003

DNA tiles

- Implementing computation with DNA tiles



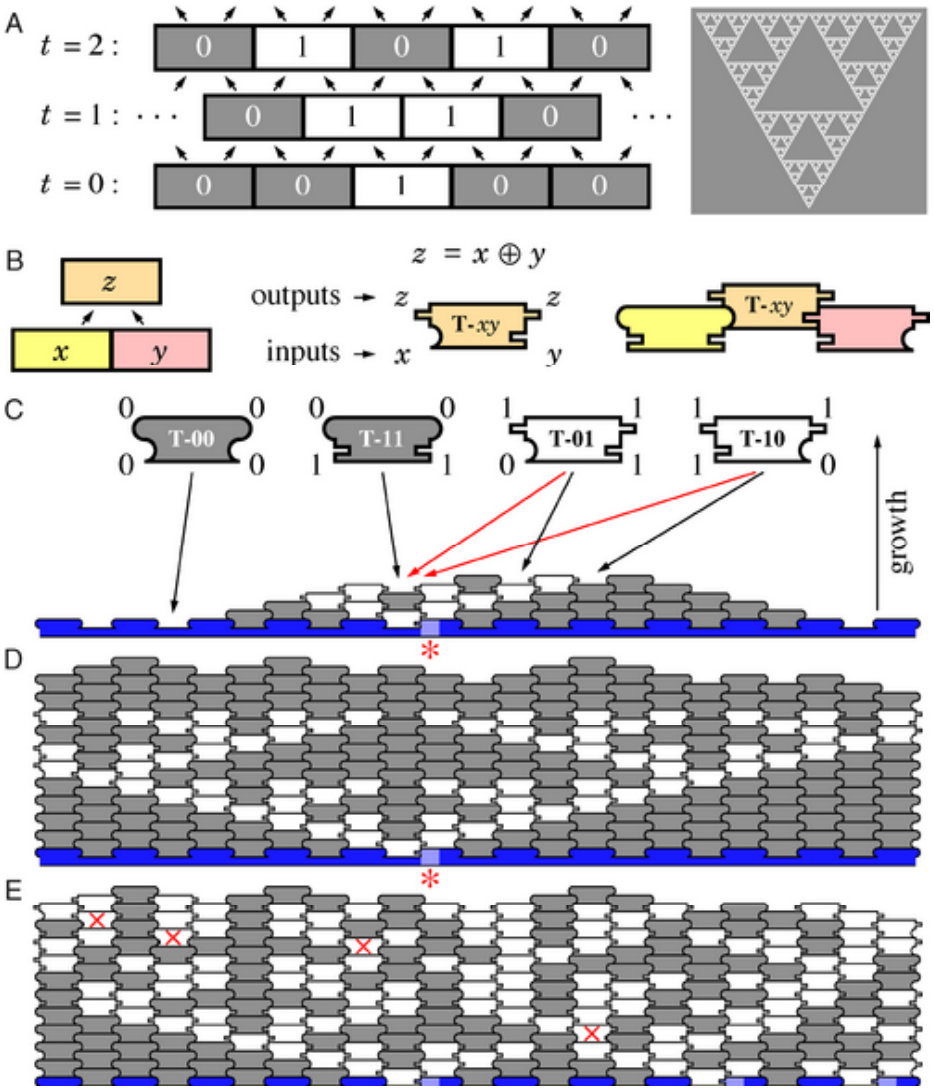
XOR computation

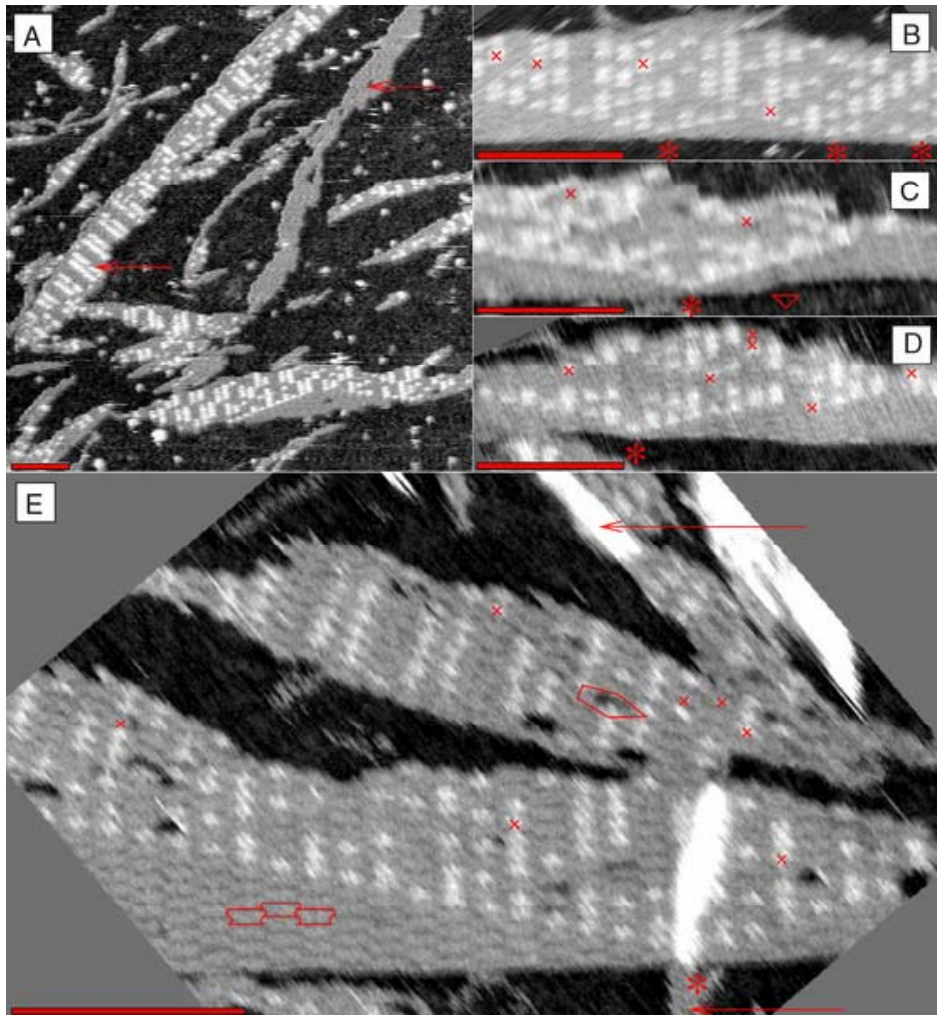


Sierpinski Gasket

DNA tiles

- Assembly of Sierpinski gasket
  (Rothemund et al, PLOS Biology, 2004)





Advantages of Biomolecular Computation

- **Ultra Scale:** each ”processor” is a molecule.
- **Massively Parallel:** number of elements could be 10^{18} to 10^{20}
- **High Speed:** perhaps 10^{15} operations per second.
- **Low Energy:**
  - example calculation ~10^{-19} Joules/op.
  - electronic computers ~10^{-9} Joules/op.
- **Existing Biotechnology:** well tested recombinant DNA techniques.

	DNA	Current computer
Information density (bits/nm^3)	~1	~10^{-11}
Parallelism (operations/sec)	~10^{18}	~10^{12}
Energy expediture (J/operation)	~10^{-19}	~10^{-9}

Potential Disadvantages of Biomolecular Computation:

- **Many Laboratory Steps Required:**
  - **is very much reduced by Self-Assembly !**

- **Error Control is Difficult:**
  - **may use a number of methods for error-resilient Self-Assembly**

Problems

- Construct a sequence of base pairs for real DNA that allows one to build a three armed junction. Choose your sequence so that the junction is fixed.
- It is possible to build junctions that have more than four arms. Show how to build a five armed junction.