Engineering Application of Nanoscale Biology

Lecture 7: DNA-based nanosystems

Kaustubh D. Bhalerao
bhalerao@uiuc.edu
217.244.6569

What can we do with DNA?

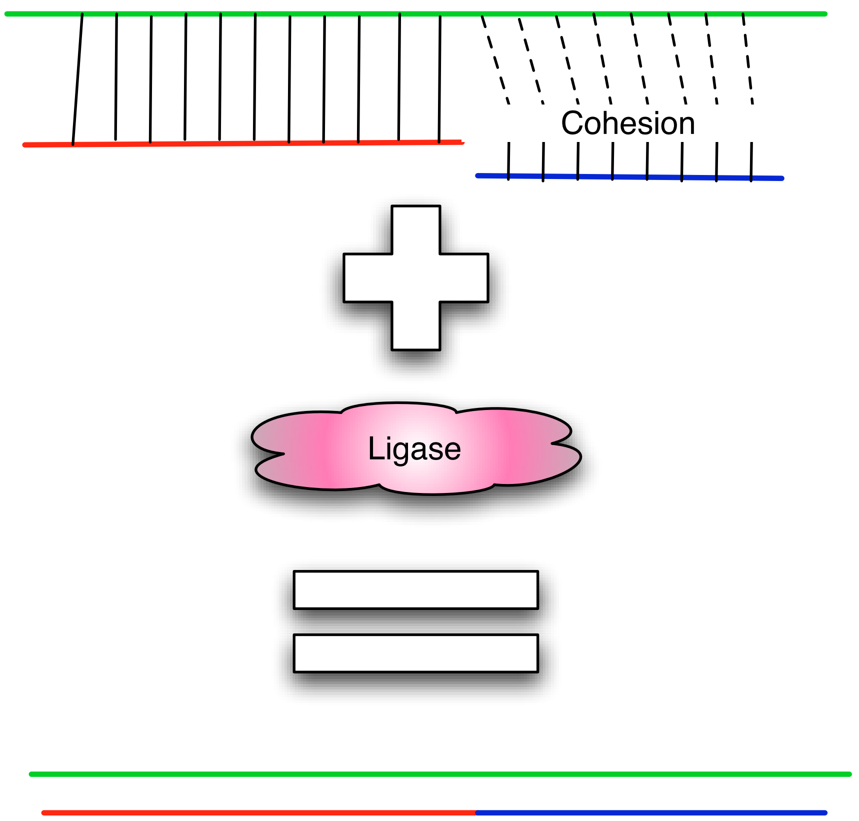
- Using its physical-chemical properties (size, shape, charge etc)
- Using its biological properties (sequence specificity, biomolecular interaction)
- How to manipulate DNA - or how to use DNA to manipulate other things

What can we do with DNA?

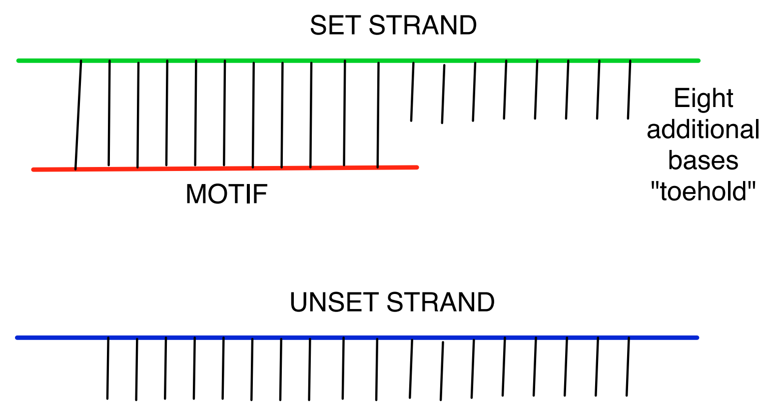
- Biotechnology uses: (not today's lecture)
  - Genetic Engineering, PCR, plasmid technology
- Bionanotechnology uses: (What we want to learn from)
  - DNA Structures
  - Molecular probes (molecular beacons)
  - Nanoelectronics
  - DNA lithography
  - DNA biochips

DNA Structures

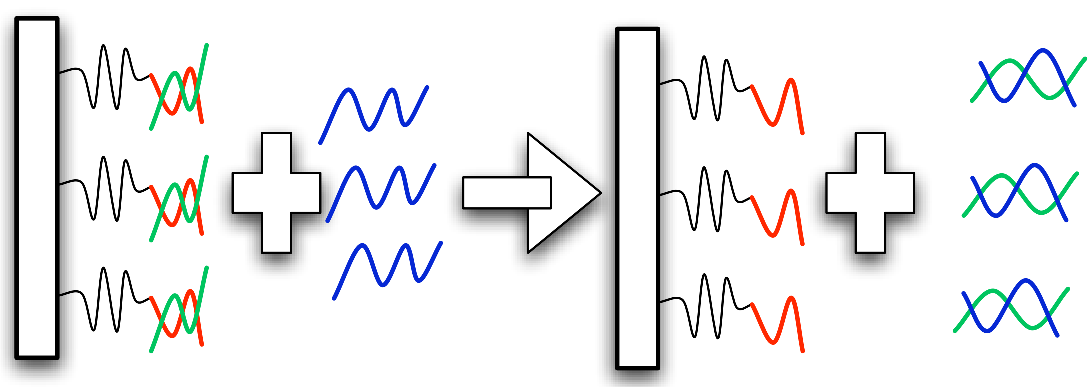
- Principle:
  - Sticky ends for cohesion (base pair matching)
  - Ligase enzyme assisted ligation (fixing the strand)



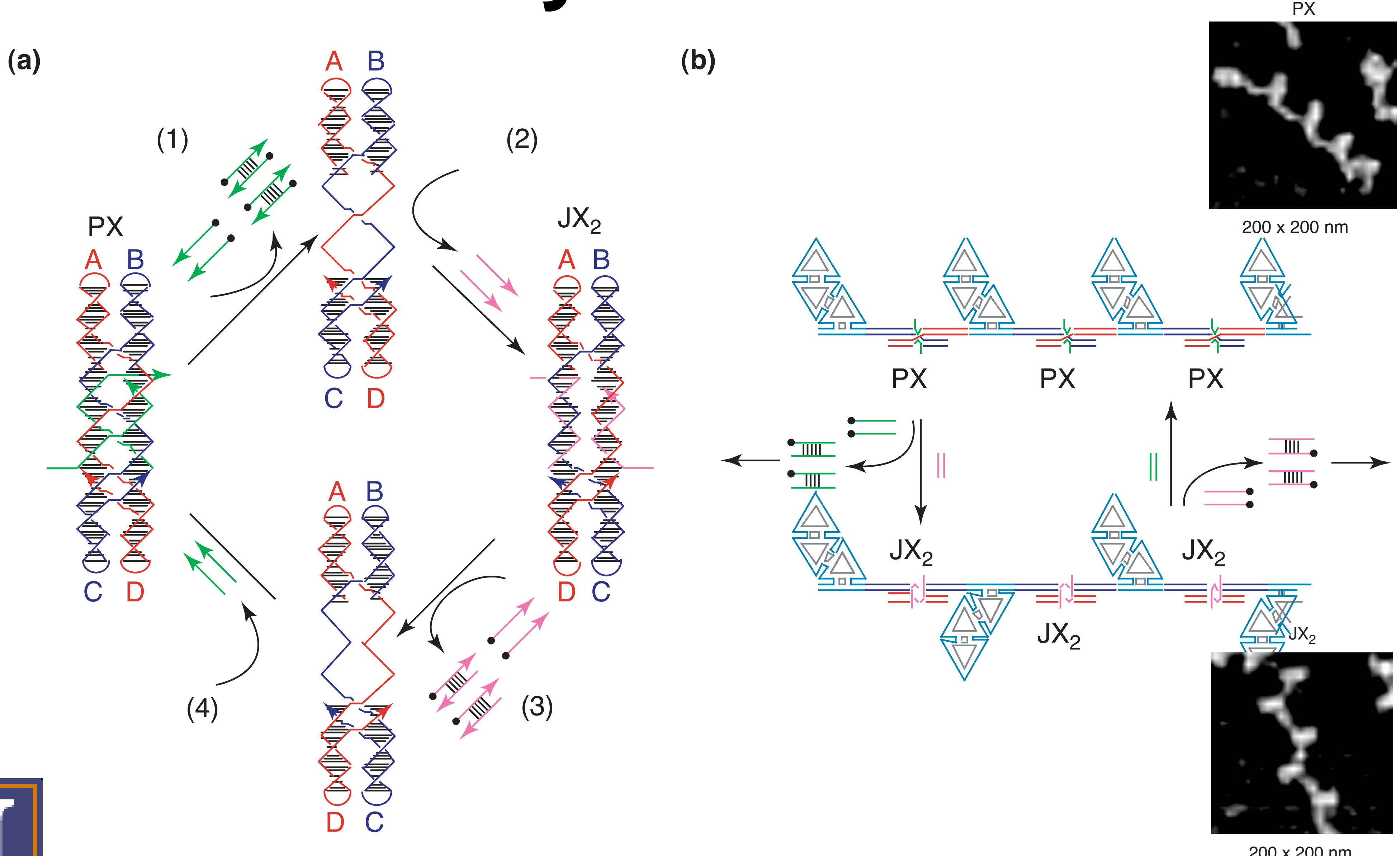
Sticky ends



- Hybridization based device
- Simple idea: (from Nature, 406, pp. 605-608)
- Set Strand
- Unset Strand

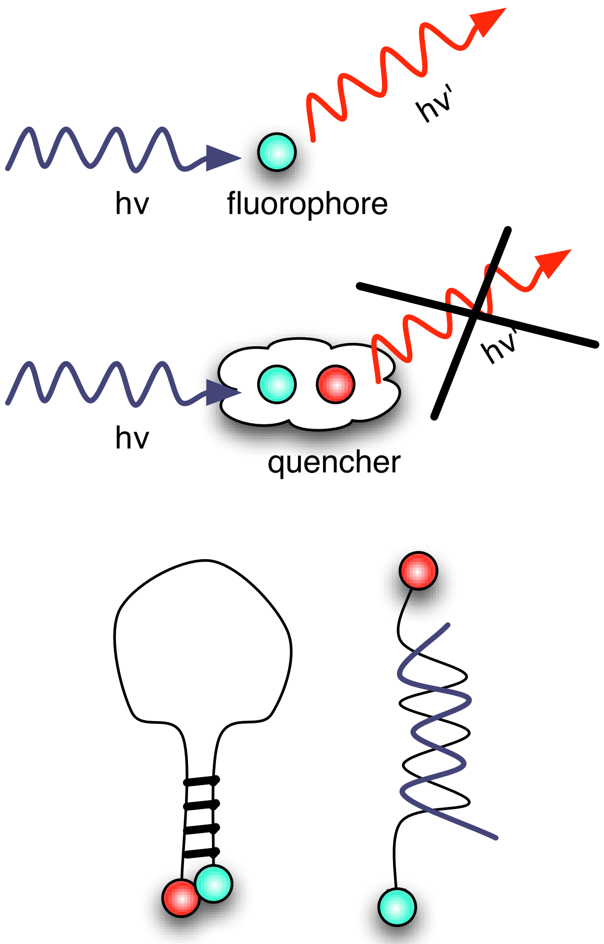


PX-JX2 device



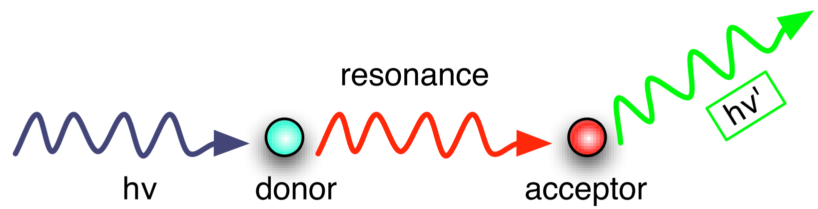
Molecular probes / beacons

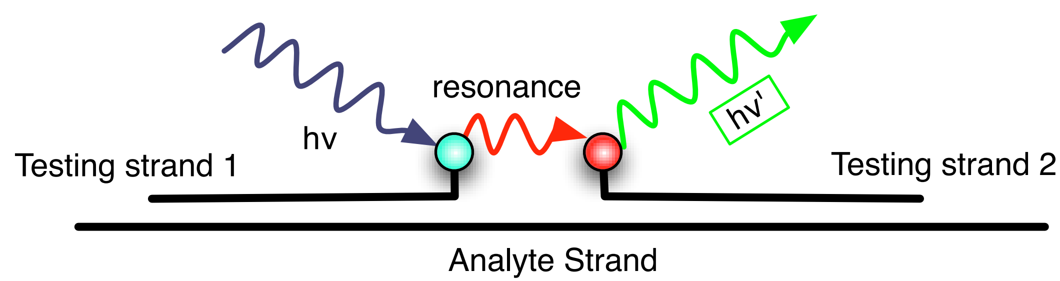
- Probe is normally in the hairpin configuration - i.e. fluorescence is quenched
- When hybridized the quencher and fluorophore are separated restoring fluorescence



FRET systems

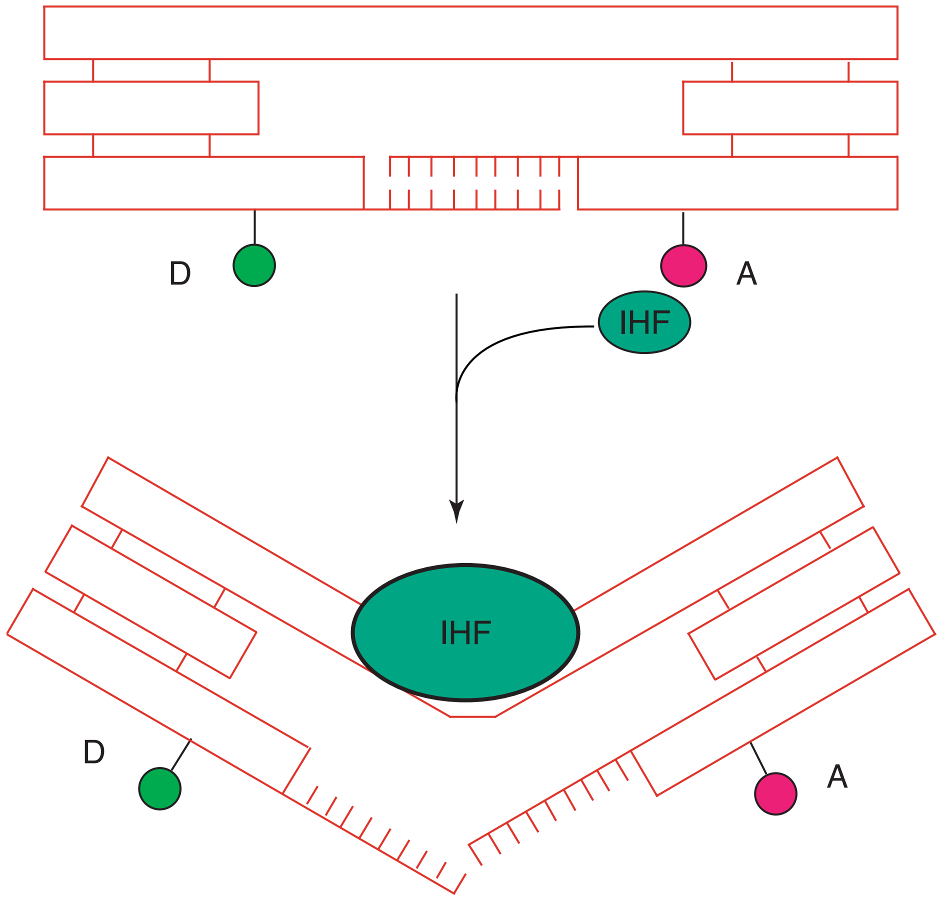
- How do you know your beacon is not dead?
- Forster / fluorescence resonance energy transfer
- Emission of donor = absorption of acceptor
- Distance between donor and acceptor is critical





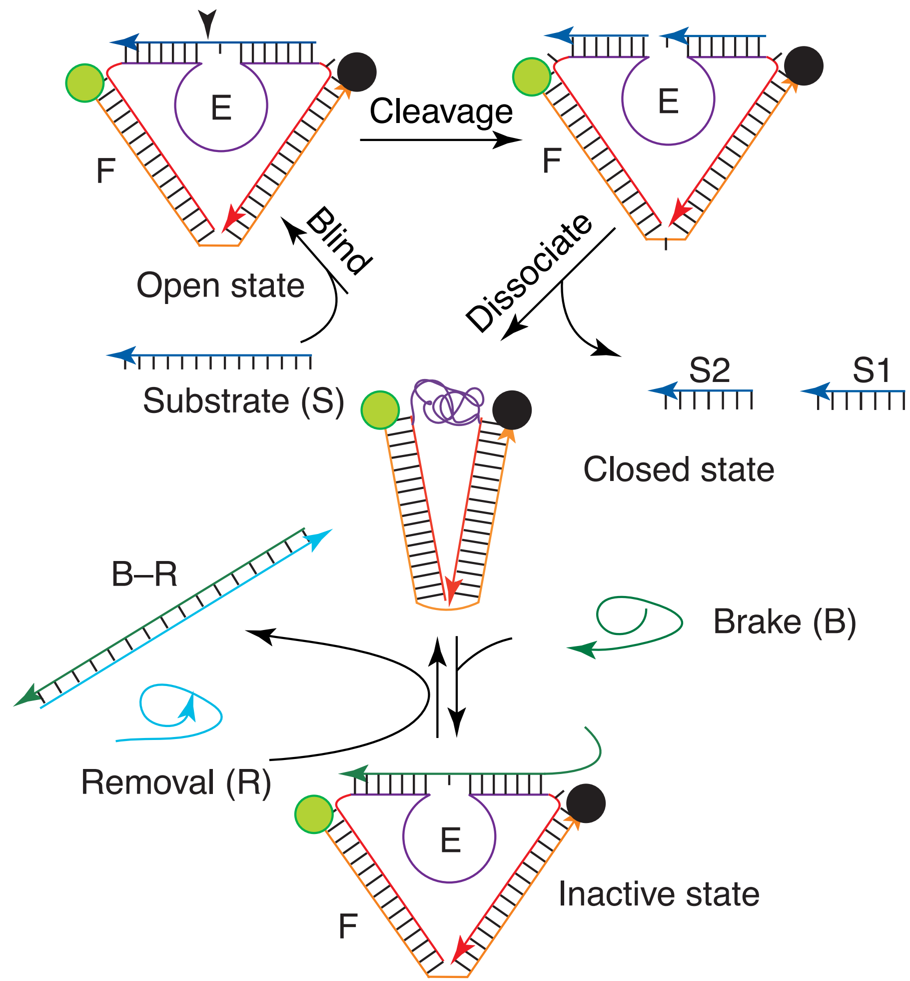
DNA stress gauge

- IHF - a protein bends a DNA molecule.
- Connecting a sticky end FRET system one can estimate the bending force of IHF



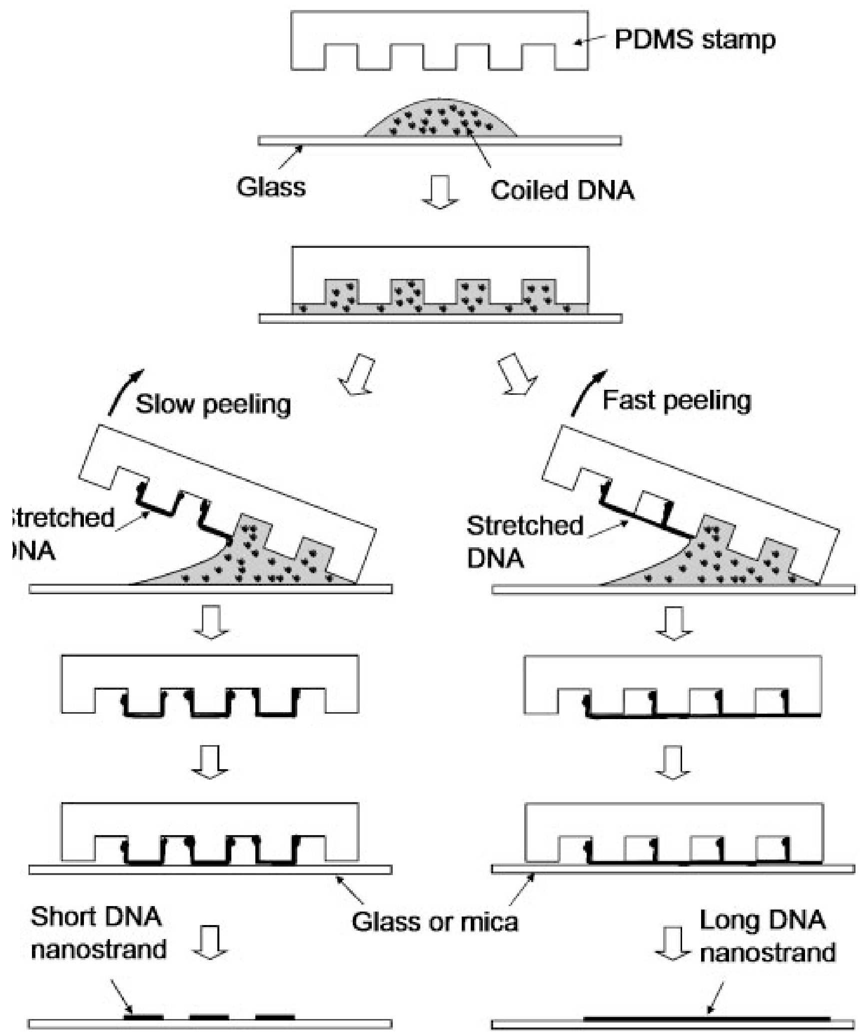
An autonomous device

- Long RNA substrate (S) binds to device (FRET signal disappears)
- Enzyme cleaves RNA - shorter strands dissociate
- Device closes (FRET appears)
- DNA 'brakes' can be applied



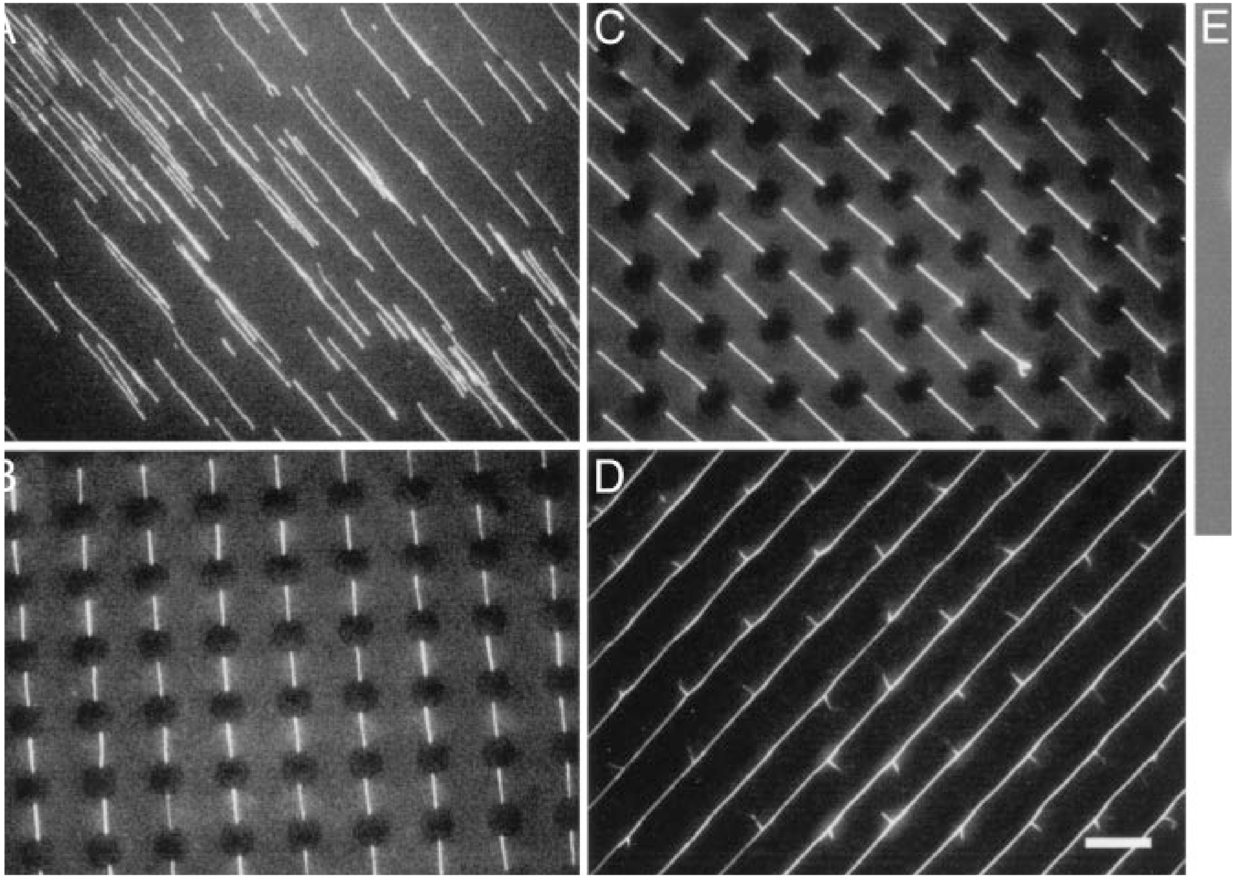
Organizing DNA

- Polydimethyl siloxane (PDMS) stamp is made
- DNA is "combed" using the stamp
- DNA sticks to glass as PDMS is hydrophobic
- Guan and Lee, 2005, PNAS 102, 51, pp 18321-18325



g. 1. Schematic of generating and transferring DNA nanostrand arrays.

Ordered nanostrands



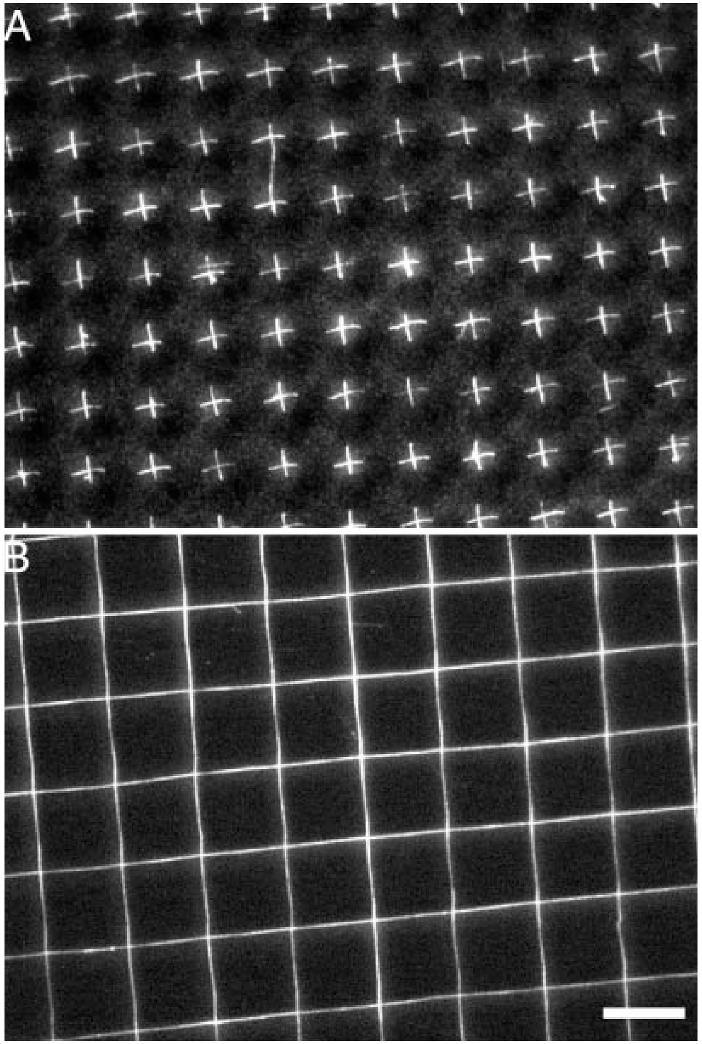
Scale bar: 10 microns

More complex structures

- Depending on the length of the DNA strands, DNA grids can be created

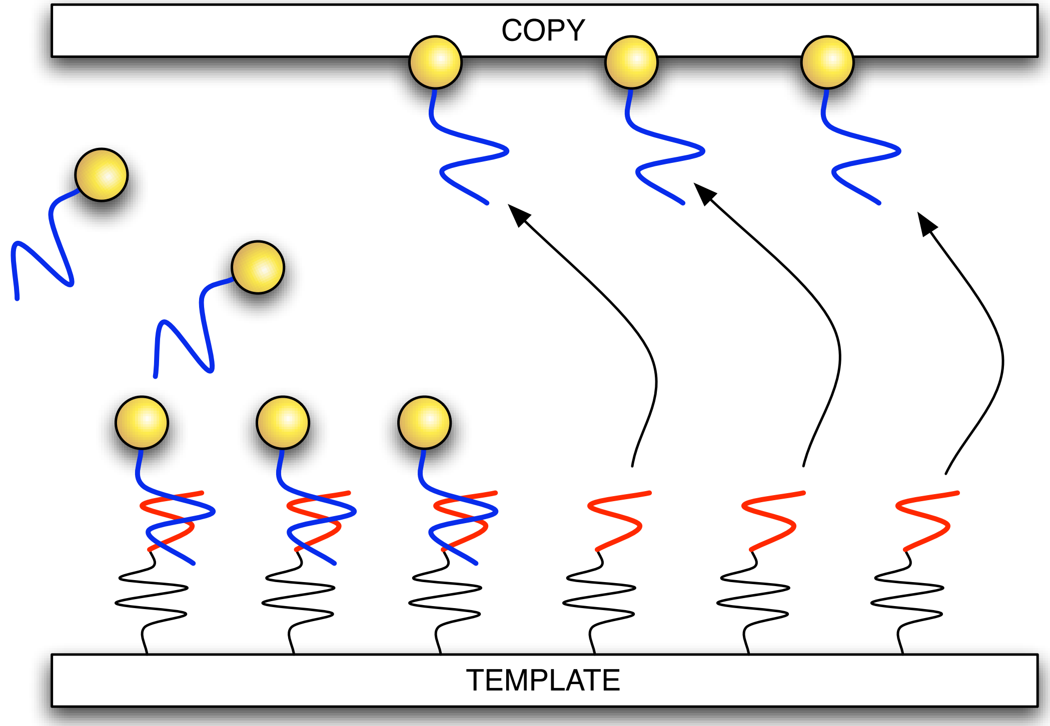
- What do you think this enables?

- What are its limitations?



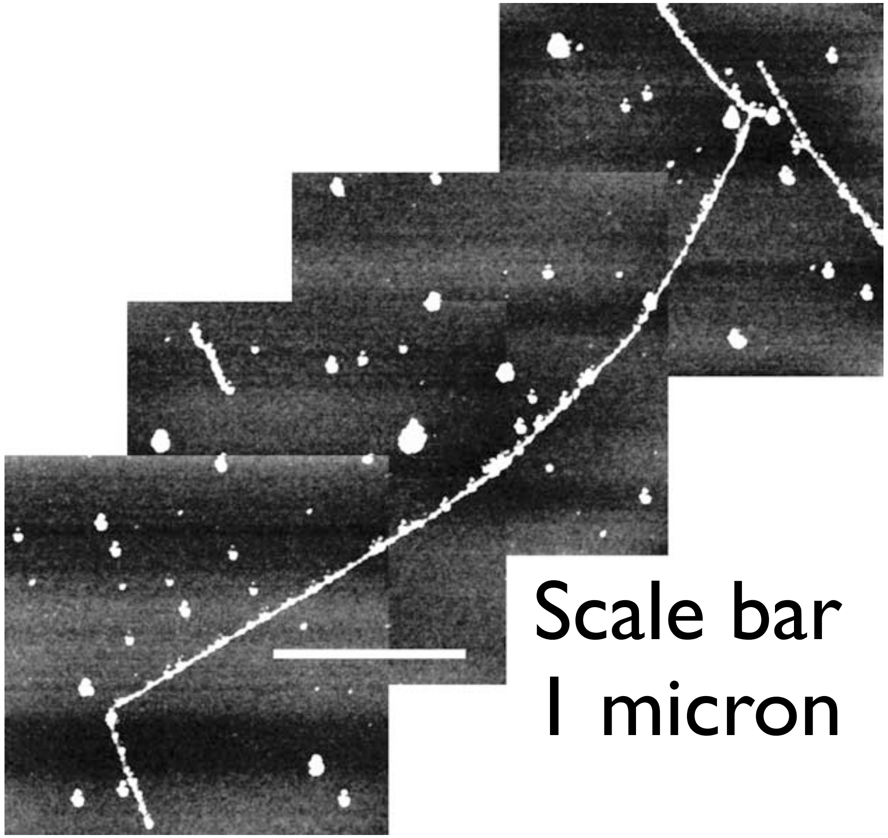
DNA lithography

- Create a master template
- Hybridize with (thiolated) complements
- Transfer complements to (gold) surface
- Repeat



DNA templated fabrication

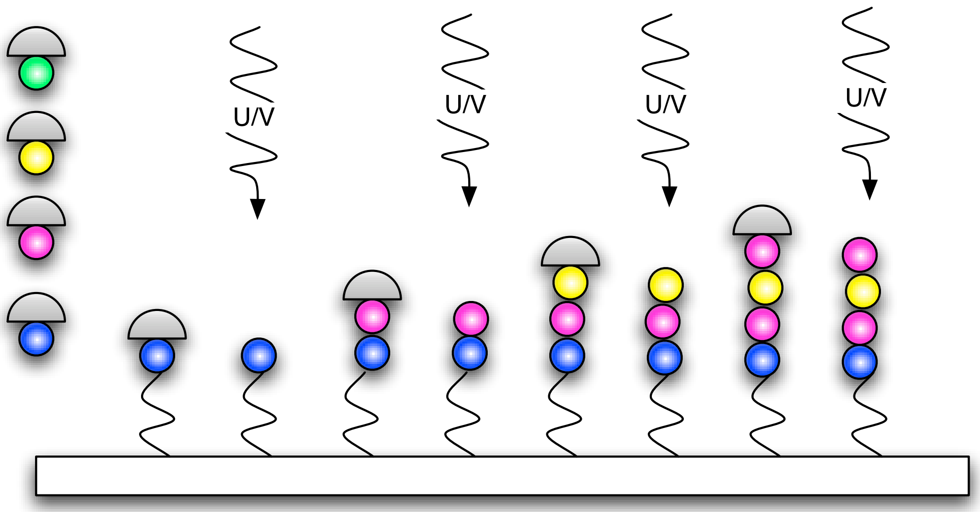
- Now we know how to control position of DNA
- DNA is negatively charged
- Use DNA as a template to lay down metal nanowires!



Scale bar
1 micron

Affymetrix GeneChip®

- 3' end of nucleotide is protected by a U/V labile cap
- Attach nucleotide through 5' end
- Deprotect using U/V
- Repeat



Reading List

- Seeman (2005) From genes to machines: DNA nanomechanical devices. *TRENDS in Biochemical Sciences* 30 (3)
- Guan and Lee (2005) Generating highly ordered DNA nanostrand arrays. *PNAS* 102(51) pp. 18321-25
- Stoltenberg and Woolley (2004) DNA-Templated Nanowire Fabrication. *Biomedical Microdevices* 6(2) 105-111

Questions and Feedback?