Oct. 20, 2021

Bio-integrated Materials Science (Online Lectures)

Biomolecules

Lecture 6

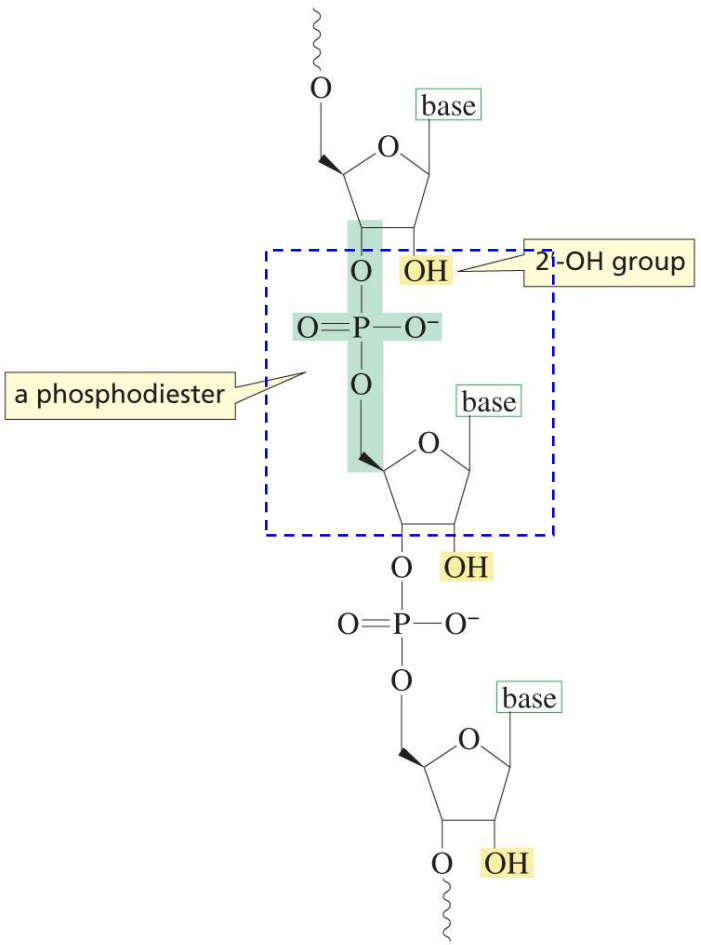
Prof. Jung Heon Lee

Nucleic acid

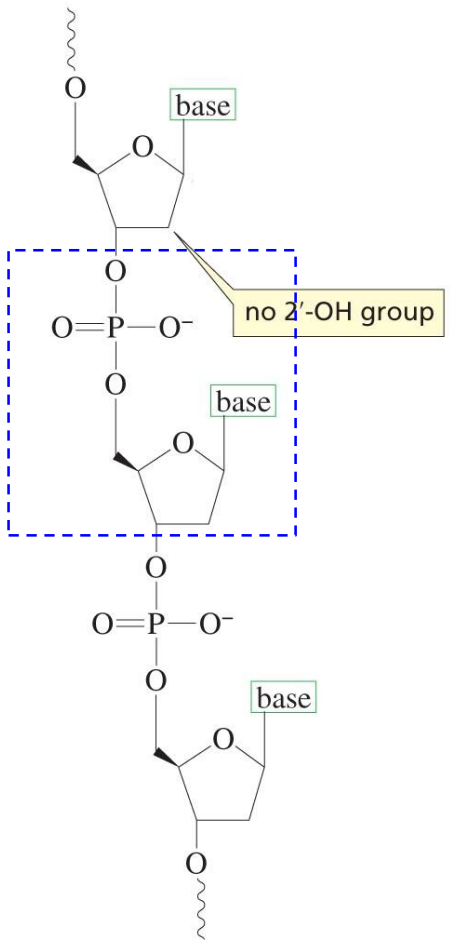
Nucleic + acid

$HA \leftrightarrow H^+ + A^-$

Nucleic acid



single stranded RNA

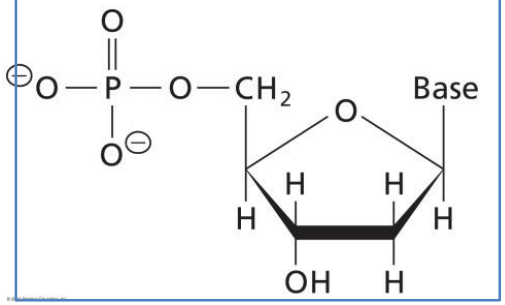


single stranded DNA

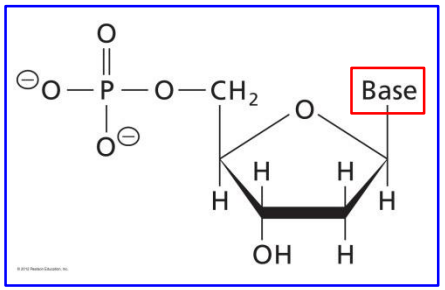
Both RNA and DNA are

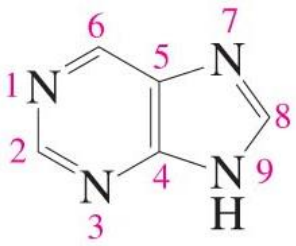
- Polymers of
- A single nucleotide
  - a nitrogenous base
  - a pentose sugar
  - a phosphate group

A nucleotide: unit element of DNA

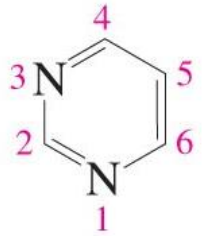


Bases

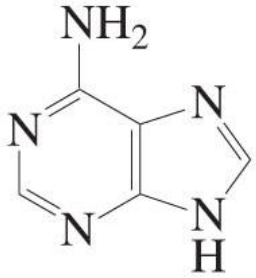




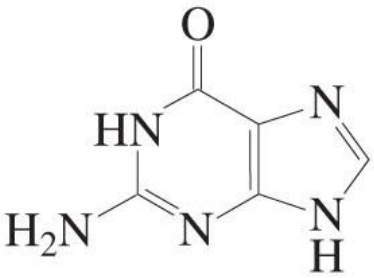
purine : Two rings with four “N”



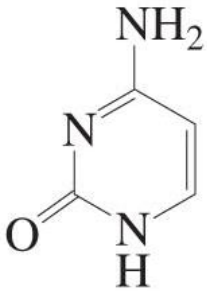
pyrimidine : One ring with two “N”



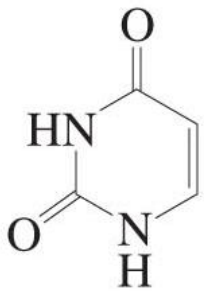
adenine



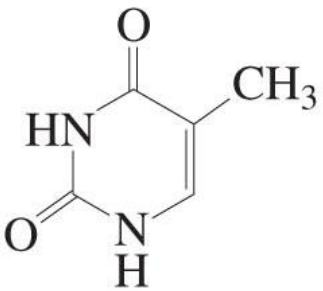
guanine



cytosine



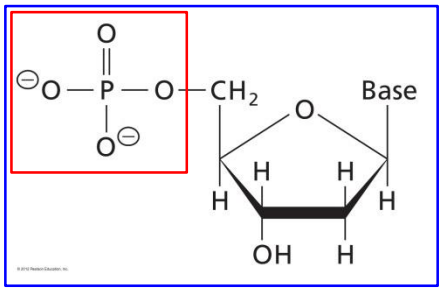
uracil



thymine

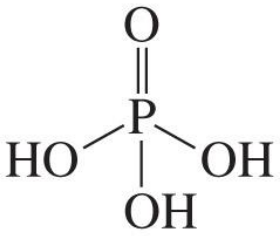
- Adenine (A), guanine (G), cytosine (C), and thymine (T) are found in .
- Adenine, guanine, cytosine, and uracil (U) are found in RNA
- Bases have ring structure →

Phosphate group

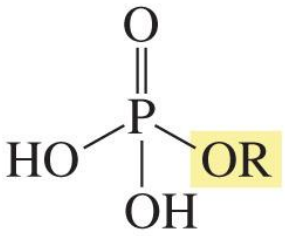


In nucleic acids, the phosphate group is a phosphodiester

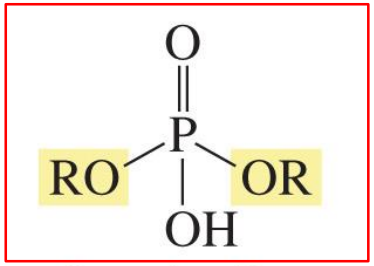
Phosphate group is highly charged →



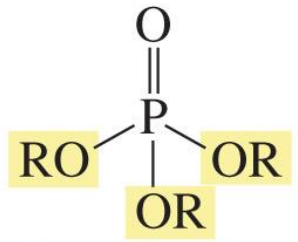
phosphoric acid



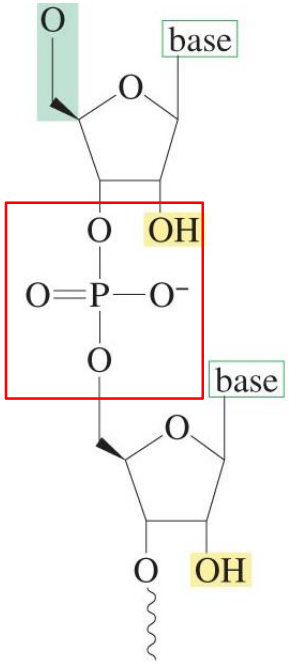
a phosphomonoester



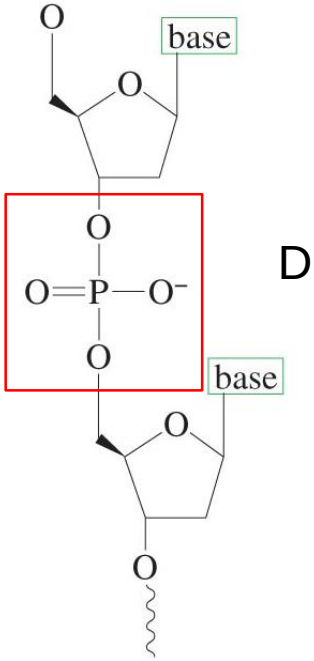
a phosphodiester



a phosphotriester



RNA

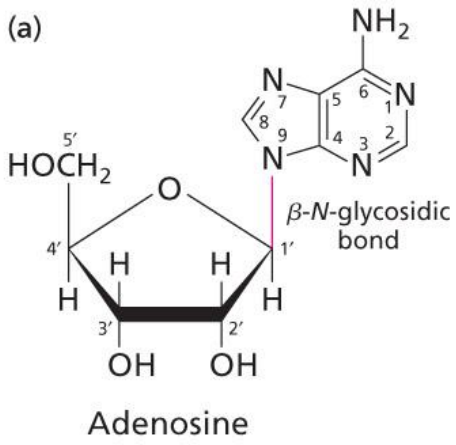


DNA

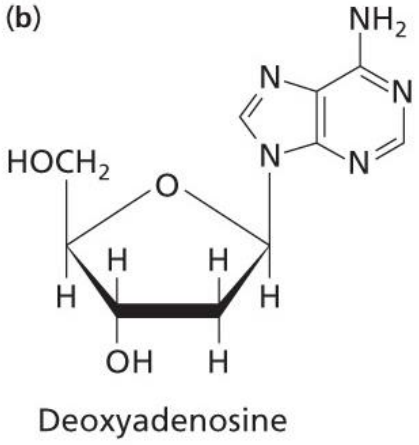
Nucleosides / Nucleotides

= base + sugar

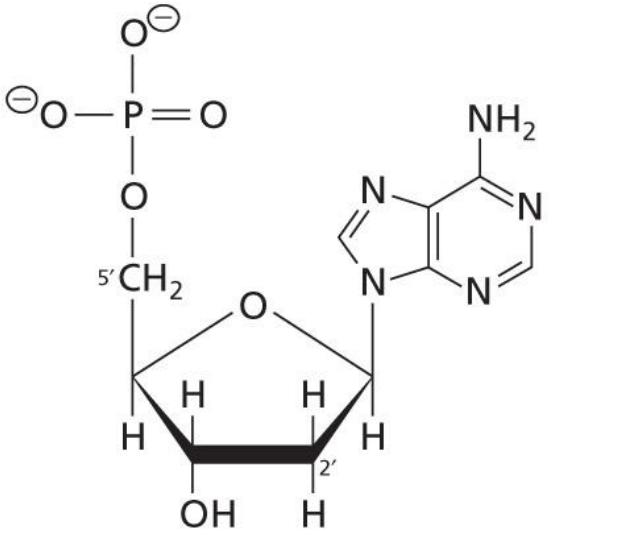
Nucleotide = base + sugar + phosphate



Adenosine



Deoxyadenosine



2′-Deoxyadenosine 5′-monophosphate (Deoxyadenylate, dAMP)

RNA

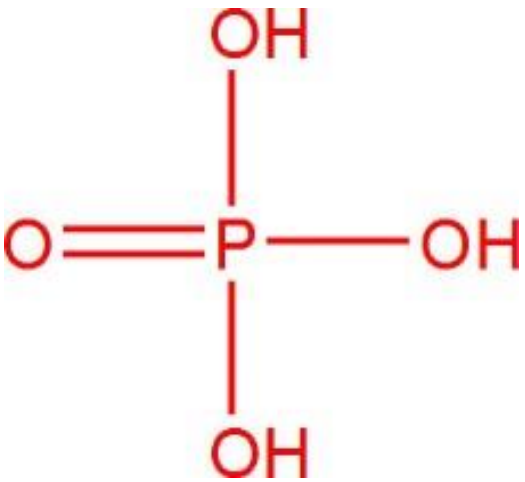
DNA

Nucleoside

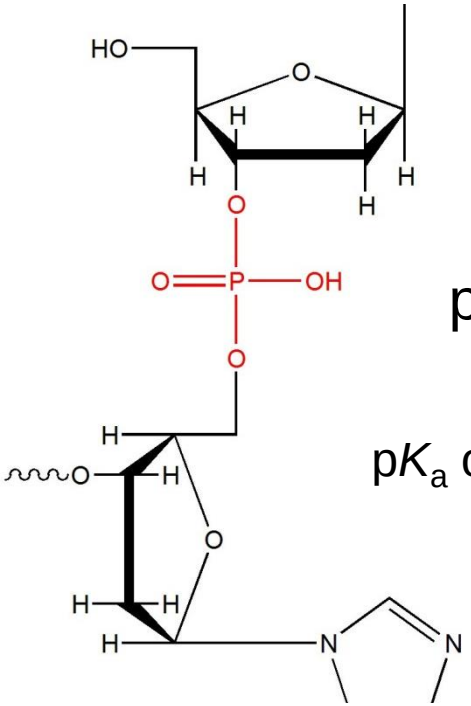
Nucleotide

Nucleic acid - overall

- Why is it called nucleic acid?
  - their initial discovery within the [ ]
  - the presence of phosphate groups (related to phosphoric acid)
  - under neutral conditions, DNA is deprotonated at this site, and the oxygen atom bears a negative charge



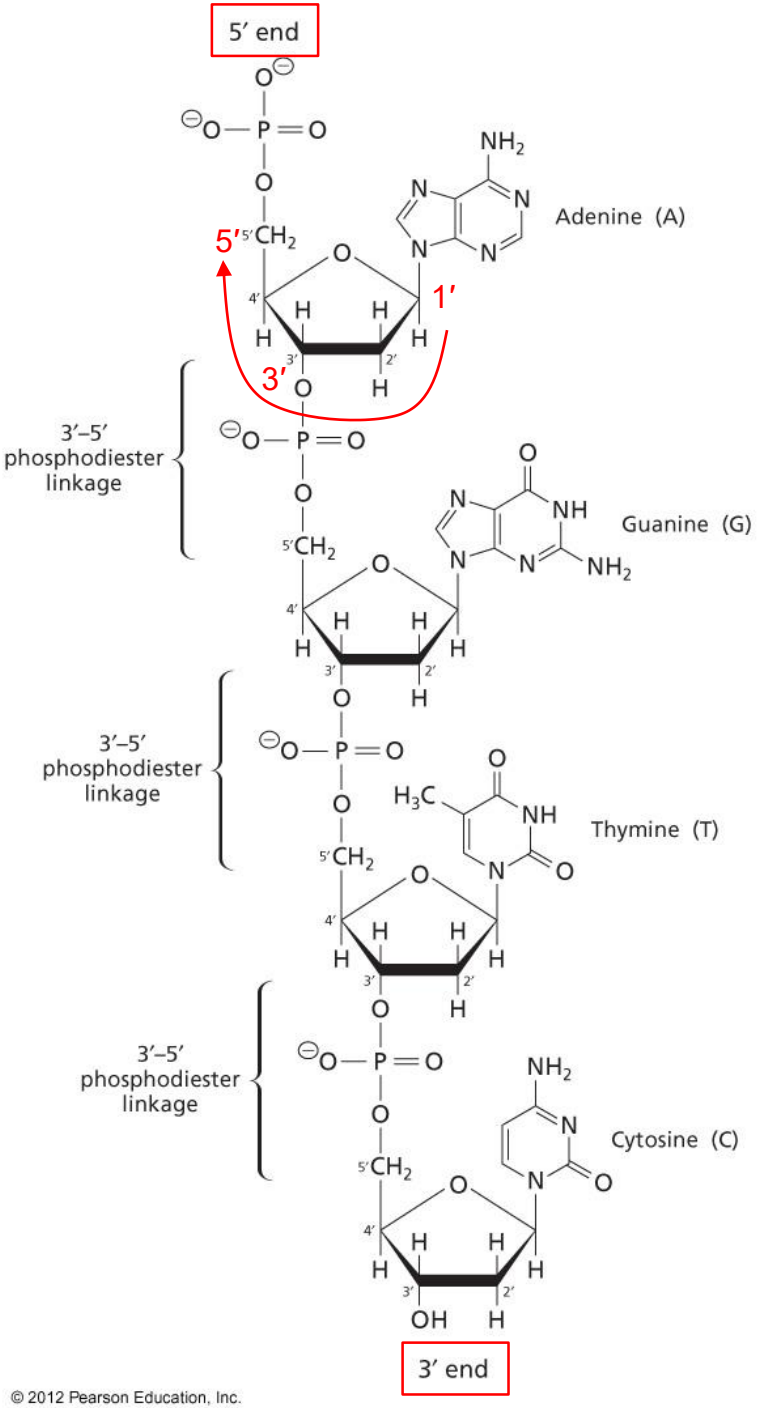
phosphoric acid



phosphate group on DNA

pK_a of phosphate group = [ ]

[ ] acid!



Expressing ssDNA

The left DNA can be represented as

→ Just write BASE without sugar and phosphate (Why?): called

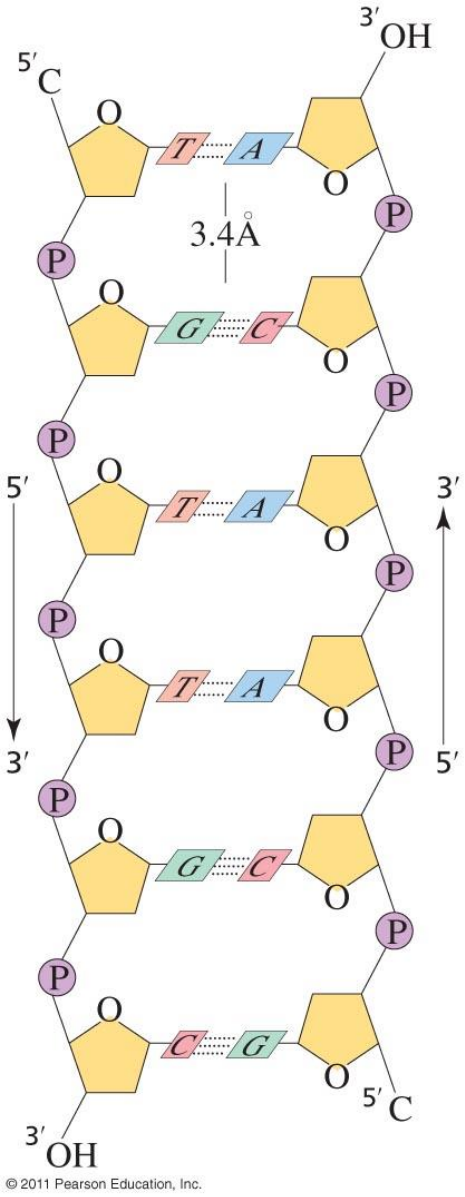
→ DNA sequences are referred from the 5’ to the 3’ end, which corresponds to the direction in which they are synthesized and read by other molecules

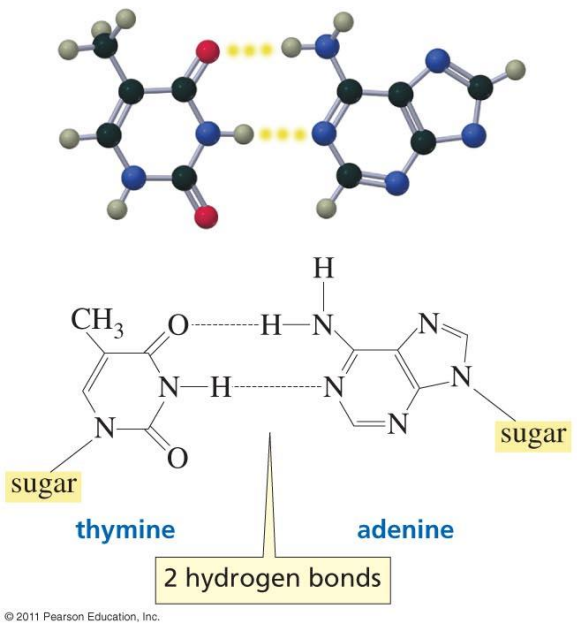
Question, is there any relationship between the two following strands, 5′ - AGTC - 3′ and 5′ - CTGA - 3′?

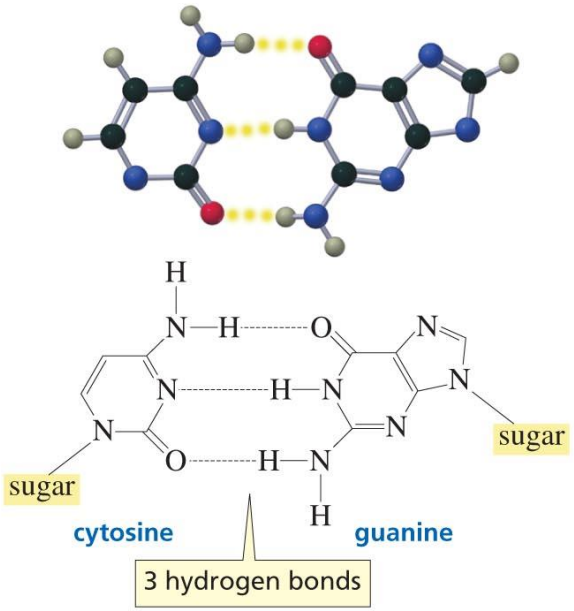
No, they are totally different strands

There is polarity in the direction of NA

Complementary base pairing in DNA

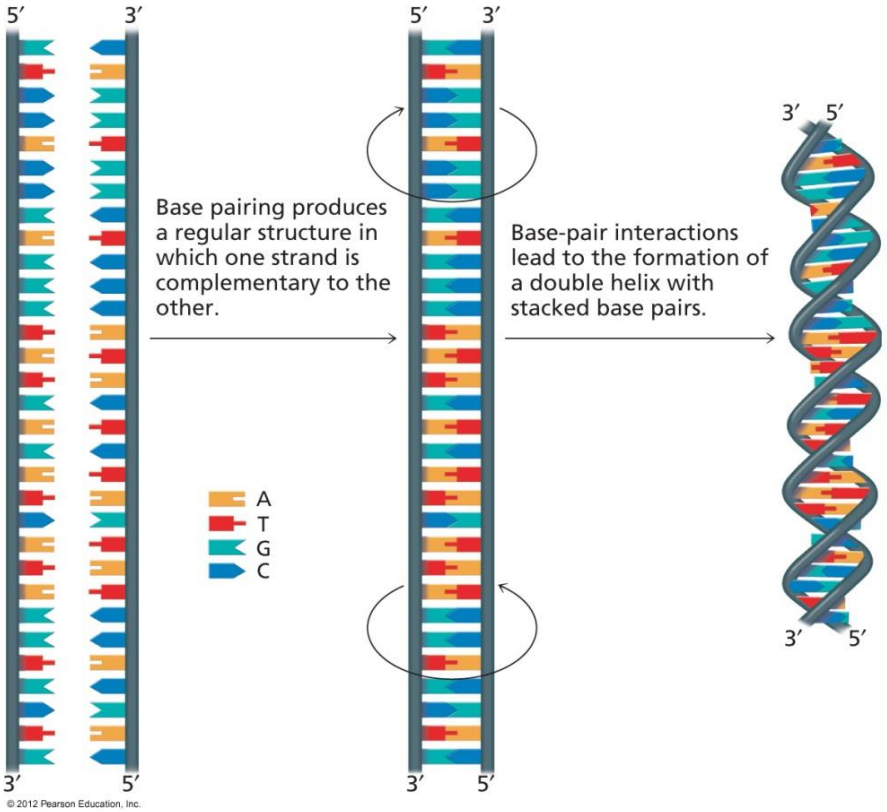






- Adenine and thymine forms [ ] hydrogen bonds
- Cytosine and guanine forms [ ] hydrogen bonds

Bases



Sugar–phosphate: hydro

Base: hydro

(sort of amphiphilic structure)

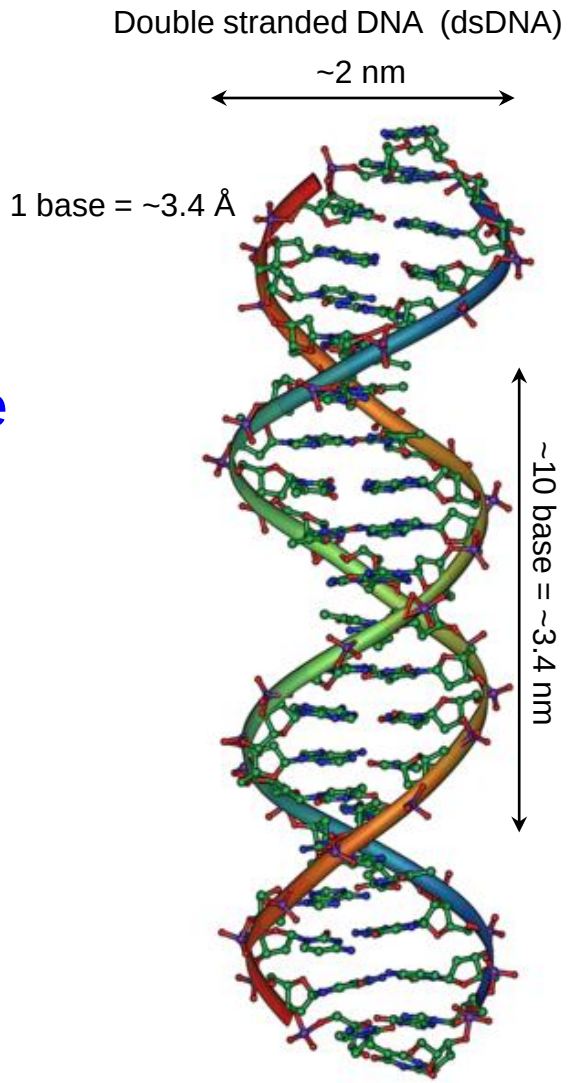
What will happen?

The base will try to minimize its exposure to water

How?

By making a helical structure

Structure of dsDNA



The sugar–phosphate backbone is on the outside, and the bases are on the inside:

- hydrophilic backbone is exposed outside
- hydrophobic base buried inside

→ DNA is [ ] and water soluble

→ DNA is [ ] charged

Interactions affecting the conformation of dsDNA

- [redacted] interactions: The stacked base pairs form van der Waals contacts.
- Hydrogen bonds: Hydrogen bonding between base pairs
- [redacted] effects: Burying hydrophobic purine and pyrimidine rings in the interior of the double helix
- Charge-charge interactions: electrostatic repulsion of the negatively charged phosphate groups of the backbone is a potential source of instability of DNA helix. However, they can be minimized by the presence of cations

Table 19.3 Stacking interactions for the ten possible combinations in double-stranded DNA

Stacked dimers		Stacking energies (kJ mol^{-1})
↑C-G G-C↓		–61.0
↑C-G A-T↓	↑T-A G-C↓	–44.0
↑C-G T-A↓	↑A-T G-C↓	–41.0
↑G-C C-G↓		–40.5
↑G-C G-C↓	↑C-G C-G↓	–34.6
↑T-A A-T↓		–27.5
↑G-C T-A↓	↑A-T C-G↓	–27.5
↑G-C T-A↓	↑T-A C-G↓	–28.4
↑A-T A-T↓	↑T-A T-A↓	–22.5
↑A-T T-A↓		–16.0

Arrows designate the direction of the sugar-phosphate backbone and point from C-3′ of one sugar unit to C-5′ of the next.

[Adapted from Omstein, R. L., Rein, R., Breen, D. L., and MacElroy, R. D. (1978). An optimized potential function for the calculation of nucleic acid interaction energies: I. Base stacking. *Biopolymers* 17: 2341–2360.]

Hybridization of DNA

- Under physiological conditions, [ ] stranded DNA is thermodynamically more stable than separated strands
- [ ] temperature (T_m): The temperature at which half the DNA has become single stranded

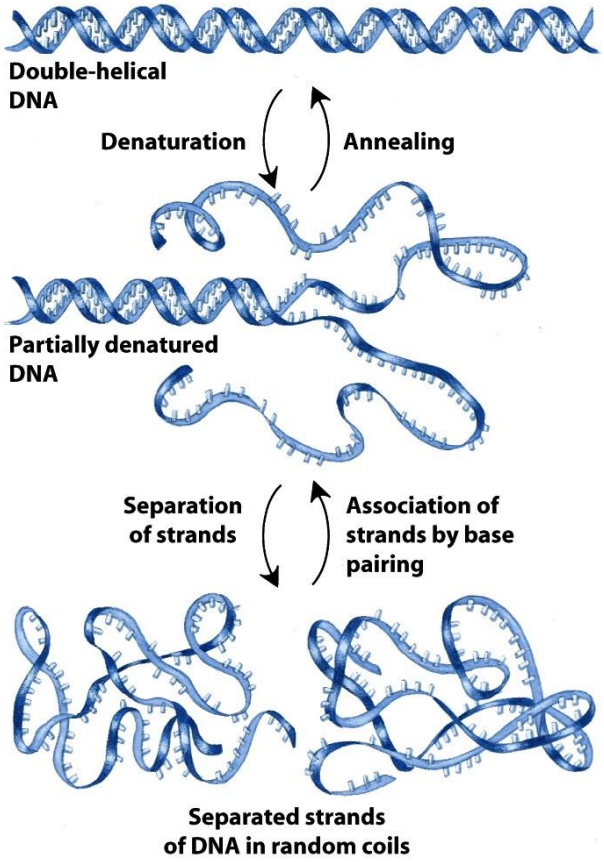


Figure 8-26
Lehninger Principles of Biochemistry, Fifth Edition

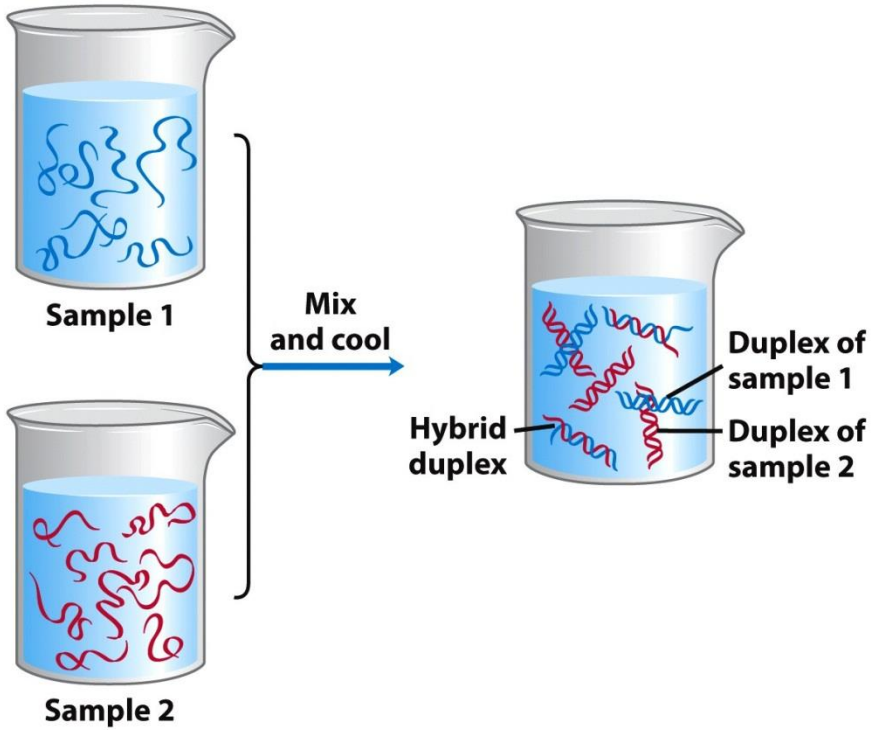
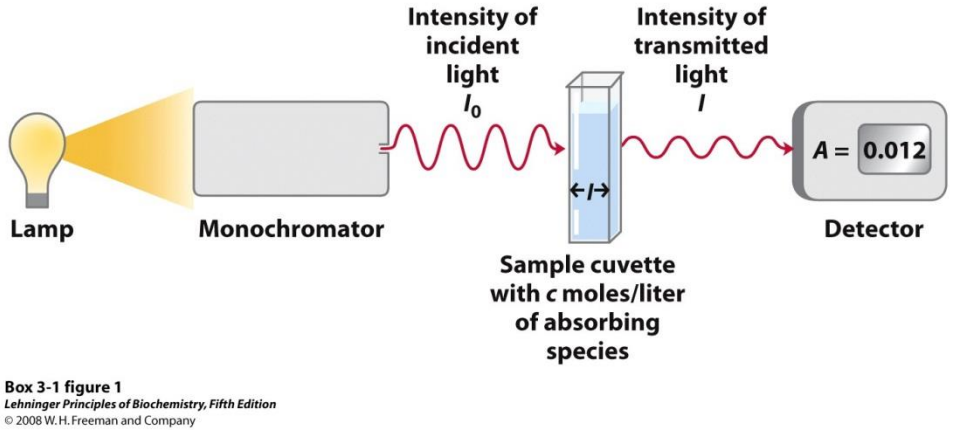


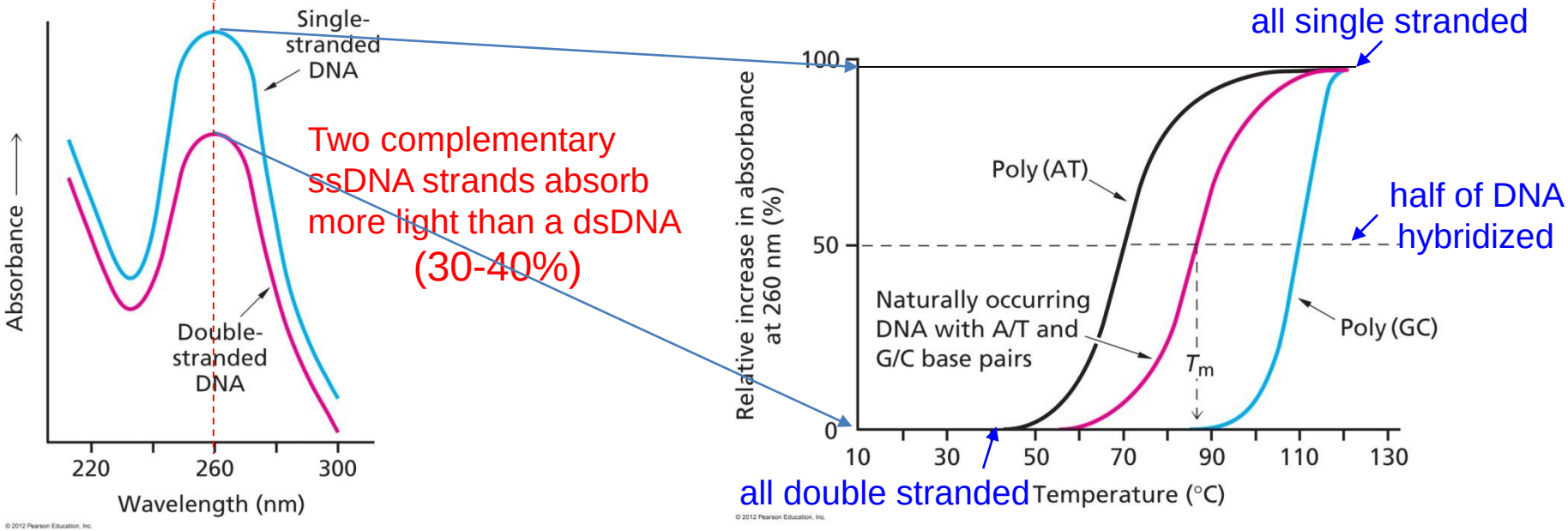
Figure 8-29
Lehninger Principles of Biochemistry, Fifth Edition

Melting temperature

UV-vis spectrophotometer



DNA has absorbance at 260 nm



Two complementary ssDNA strands absorb more light than a dsDNA (30-40%)

all single stranded

half of DNA hybridized

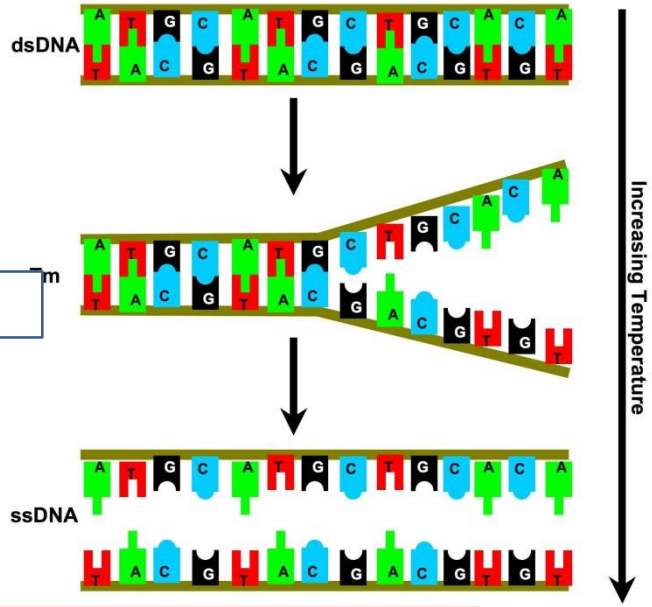
all double stranded

Melting temperature

Melting temperature variation

- Ionic strength [Na^+] ↑ → T_m ↑
- Length of DNA (n) ↑ → T_m ↑
- Sequence composition (%[G+C]) ↑ → T_m ↑
- Missmatch between ssDNA molecules:

  P ↑ → T_m ↓



$$T_m = 16.6 \log_{10}\left(\frac{[Na^+]}{1.0 + 0.7\,[Na^+]}\right) + 0.41\,(\%\,[G + C]) - \frac{500}{n} - P$$

T_m = melting temperature in ^oC

[Na^+] = Molar concentration of sodium ions in solution

%[G+C] = percent of G+C bases in DNA sequence

n = length of DNA sequence in bases

P = temperature correction for % mismatched base pairs (~1^oC per 1% mismatch)

Three conformations of DNA

- DNA can have structures other than common B form
- The conformation that DNA adopts depends on the hydration level, DNA sequence, the amount and direction of supercoiling, chemical modifications of the bases, the type and concentration of metal ions, as well as the presence of polyamines in solution

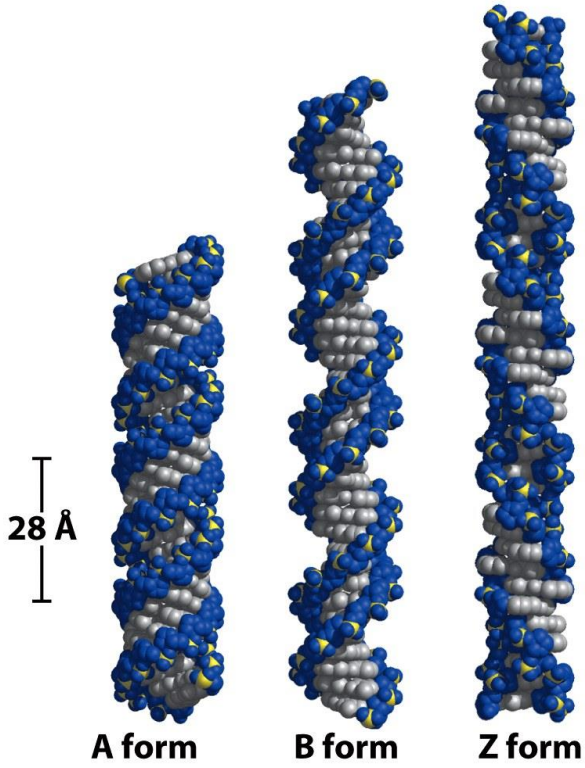


Figure 8-17 part 1
Lehninger Principles of Biochemistry, Fifth Edition

Feature	B-DNA	A-DNA	Z-DNA
Type of helix	Right-handed	Right-handed	Left-handed
Helical diameter (nm)	2.37 (or 2.0)	2.55	1.84
Rise per base pair (nm)	0.34	0.29	0.37
Distance per complete turn (pitch) (nm)	3.4	3.2	4.5
Number of base pairs per complete turn	10	11	12
Topology of major groove	Wide, deep	Narrow, deep	Flat
Topology of minor groove	Narrow, shallow	Broad, shallow	Narrow, deep

A form: under non-physiological conditions in partially dehydrated DNA

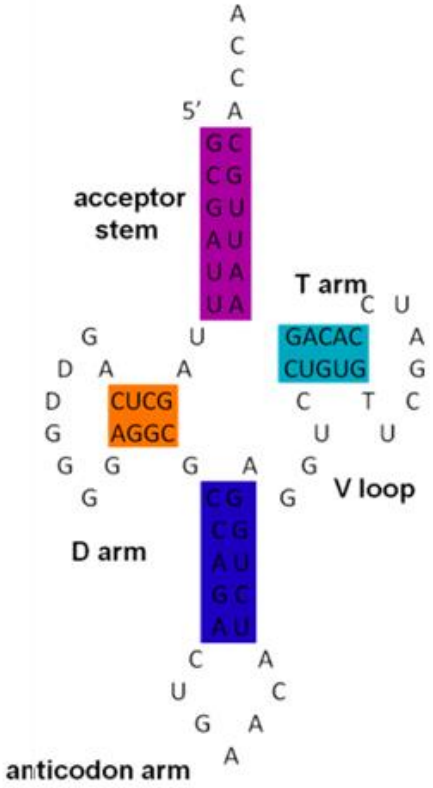
Z form: segments of DNA where the bases have been chemically modified by methylation

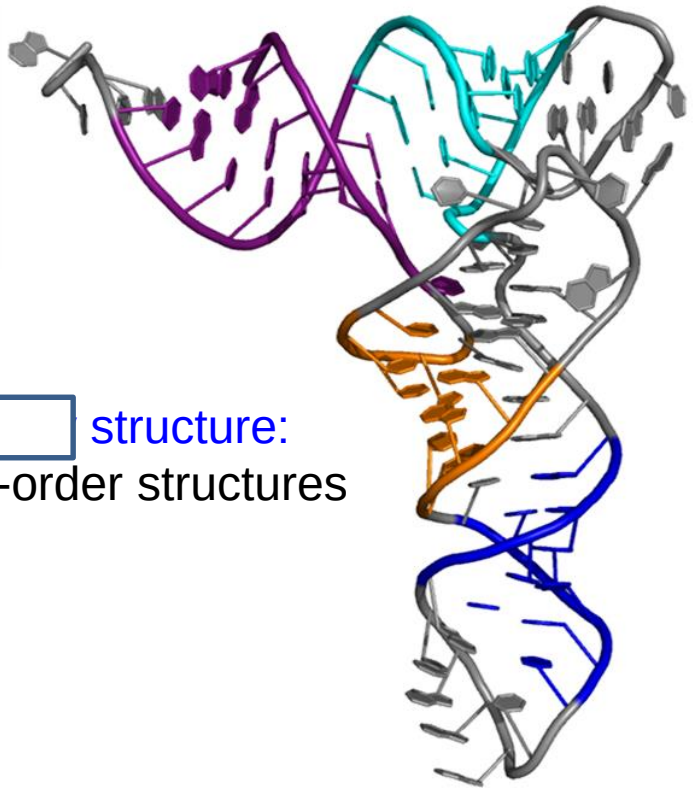
Primary, secondary, and tertiary structure of nucleic acids

[ ] structure: the linear sequence of nucleotides

5′-GCGAUUUAGCUCAGDDGGGGAGGCGCAGACUGAACAUCUGGAGGU
CUGUGTUCGAUCCACAGAAUUGCACCA-3′

Secondary structure: the different helical arrangements adopted by the molecule



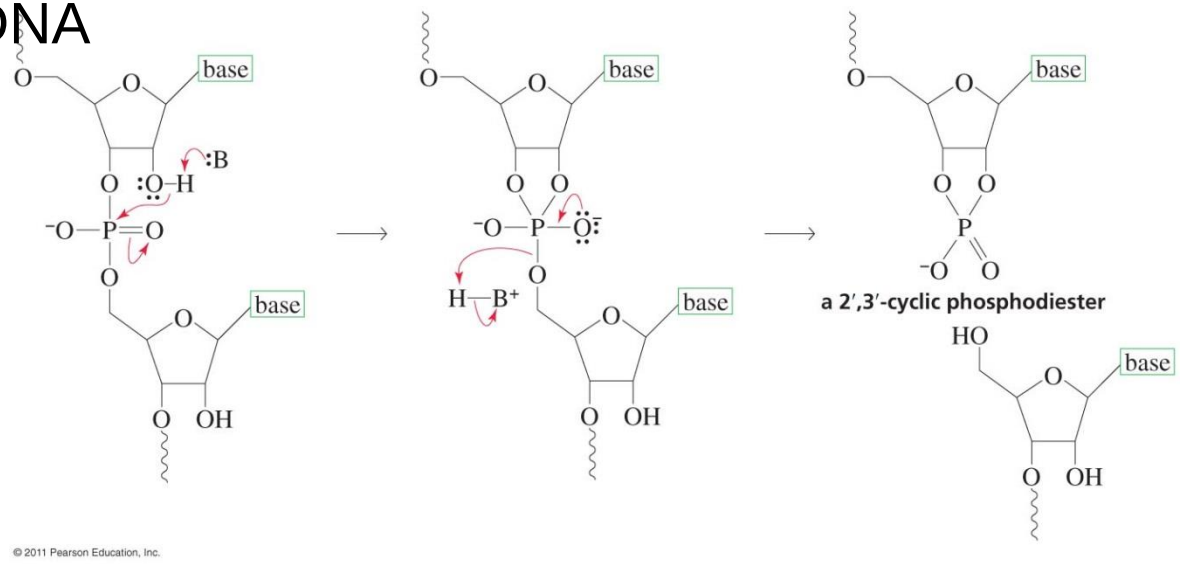


[ ] structure: higher-order structures

Stability of nucleic acids

- DNA is relatively stabile
  - at acidic or basic pH ranges DNA can be denatured
  - at high temperatures DNA can be denatured

  However, DNA can be [ ] at physiological conditions
  - RNA can be easily hydrolyzed and is much less stable than DNA



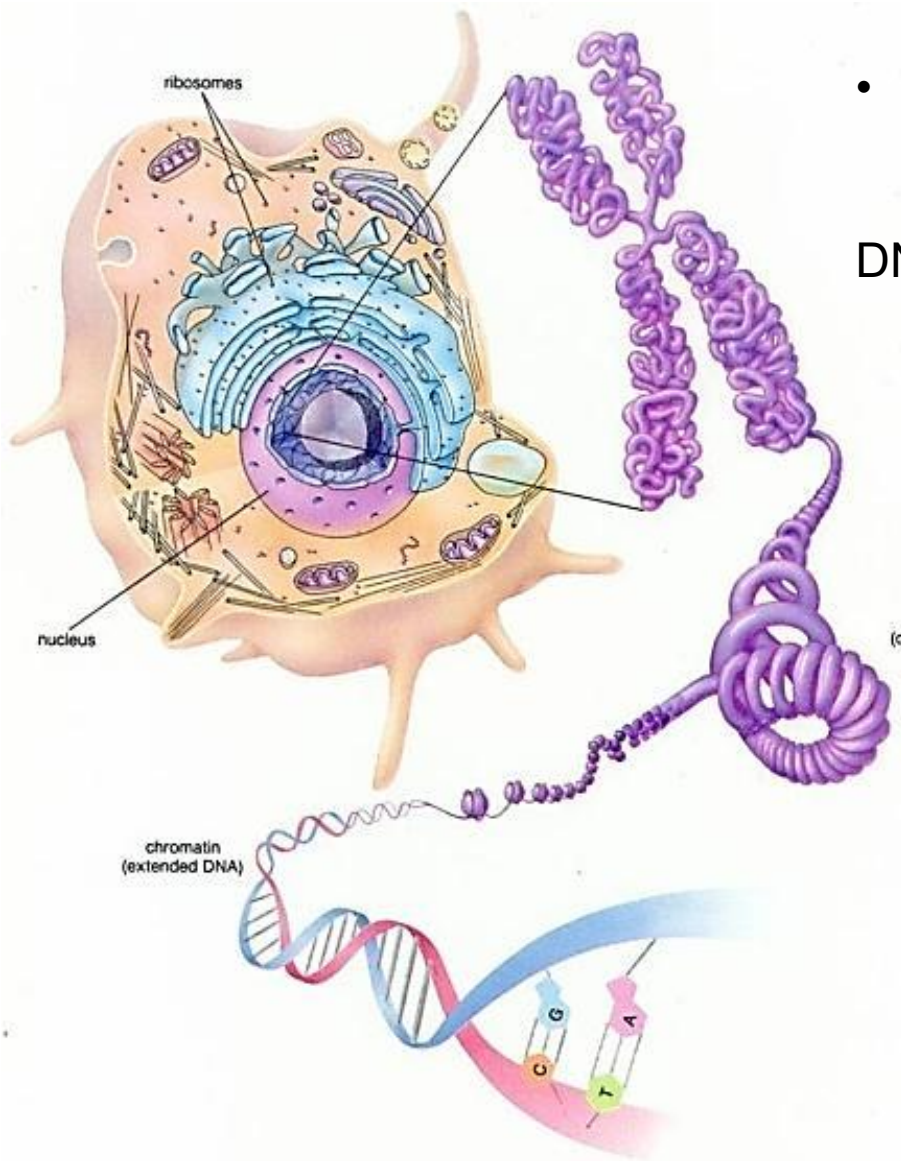
- In cellular conditions, both DNA or RNA can be degraded easily due to the presence of various nucleases.

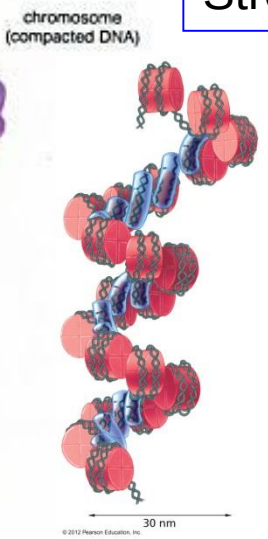
DNA in cells

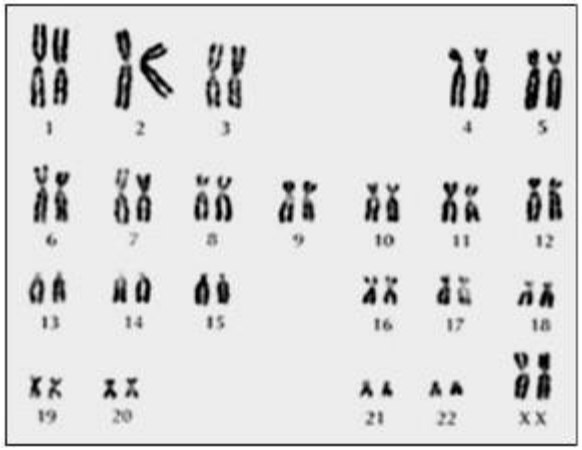
- Total length of DNA in a single cell
  = 3.4 Å × 6 × 10^9 bps = [ ]
- Total length of DNA in your body
  = 2 m × 10^{13} cells = [ ]
  = 70 trips from the earth to the sun

DNA is tightly packed in each cell. It's wrapped around proteins called histones, then coiled into the familiar X chromosome shape.

Size of nucleus ~ 6 μm
Size of chromosome ~ 5 μm
Stretched chromosome ~ few cm





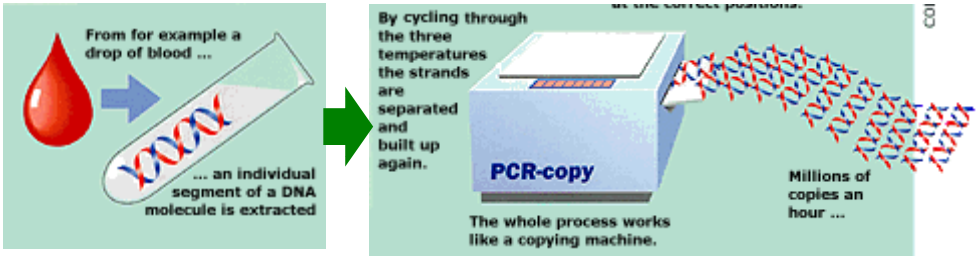


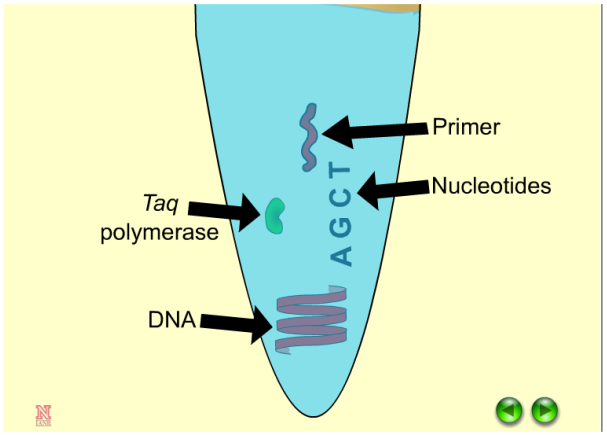
23 pairs of chromosomes

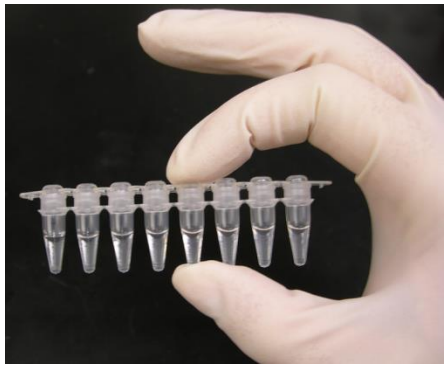
Earth ↔ sun: 149,597,870,700 m

Polymerase Chain Reaction (PCR)

PCR: a biochemical technology to [ ] a single or a few copies of a piece of DNA across several orders of magnitude



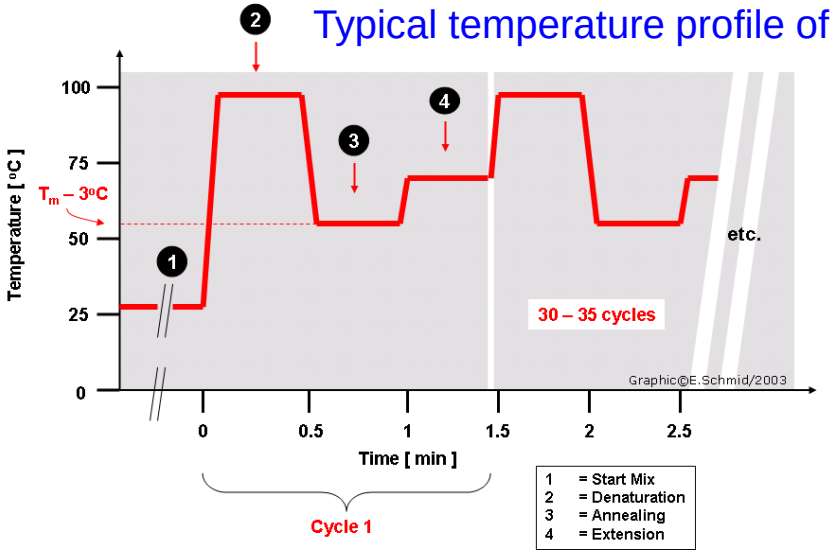




Four basic components for PCR

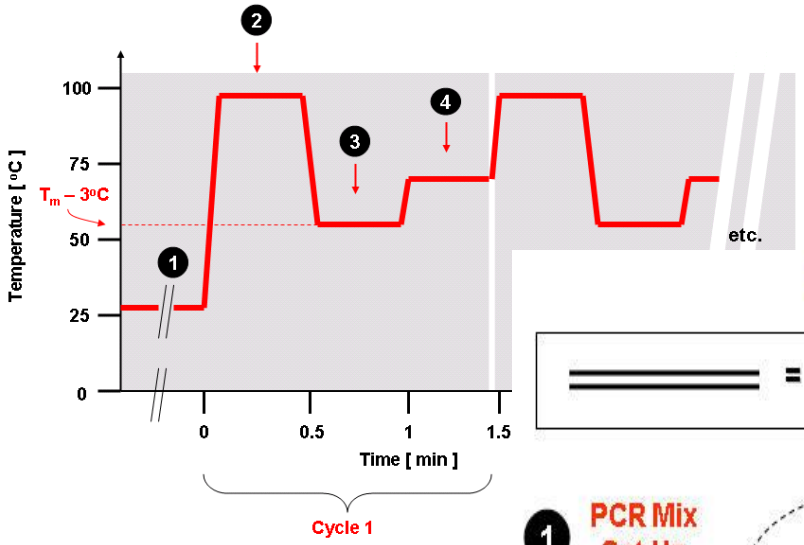
- A DNA template
- Primers
- A heat-stable DNA-polymerase
- Free nucleotides

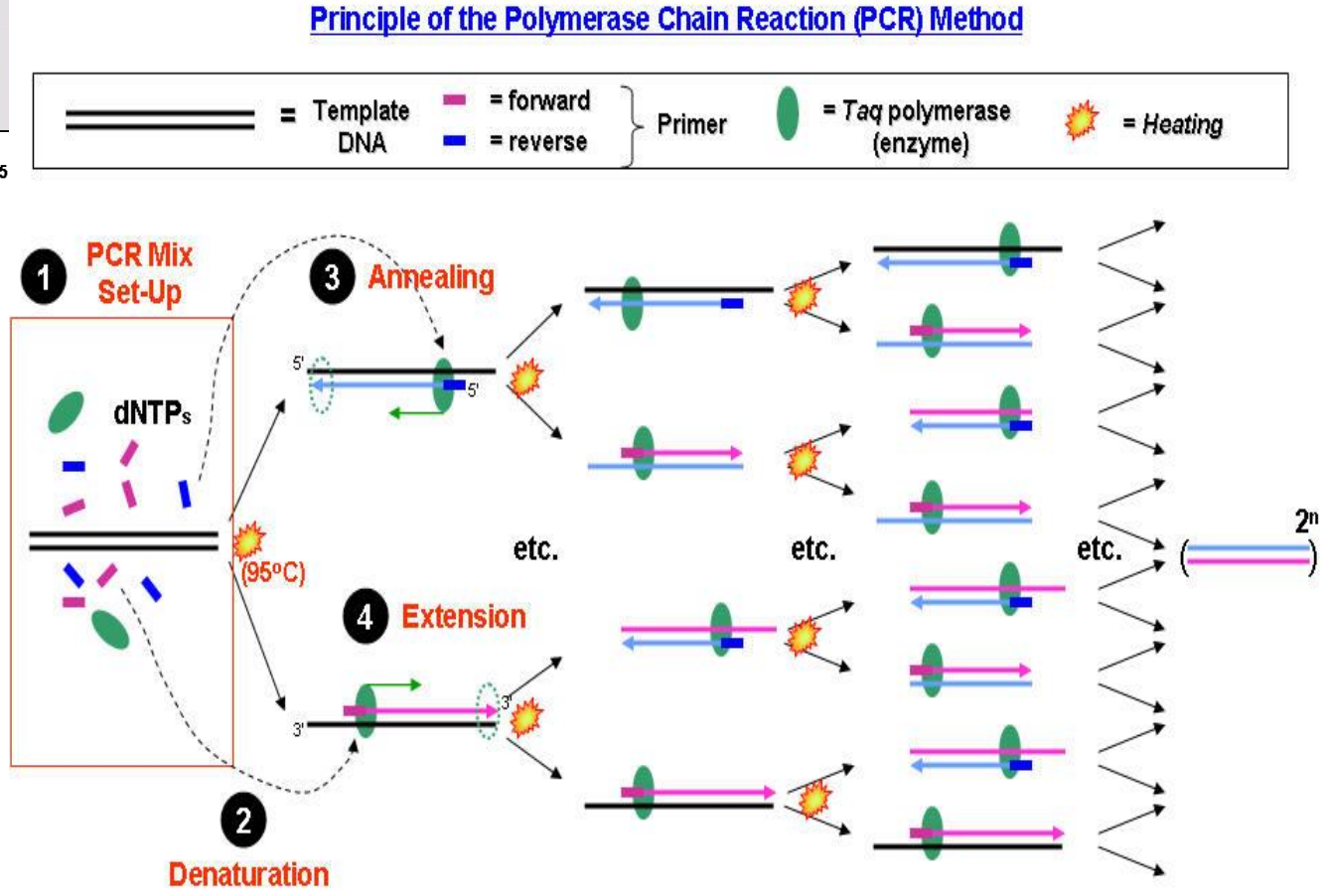
Typical temperature profile of PCR



PCR

Capable to generate million copies an a few hours

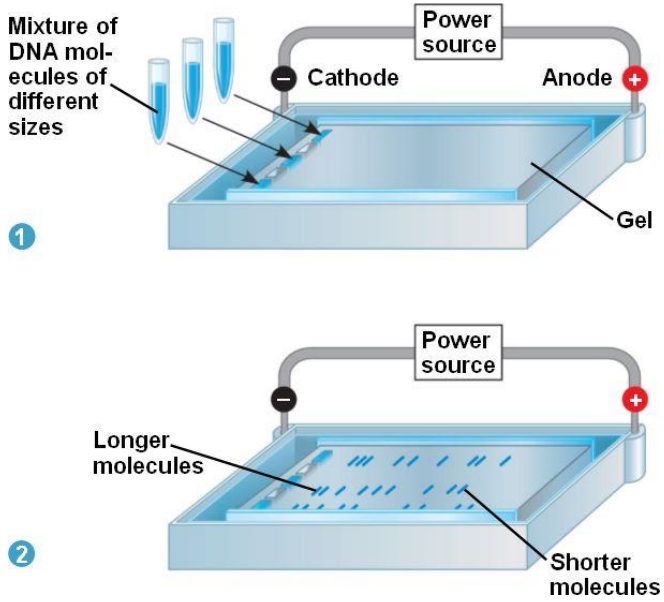


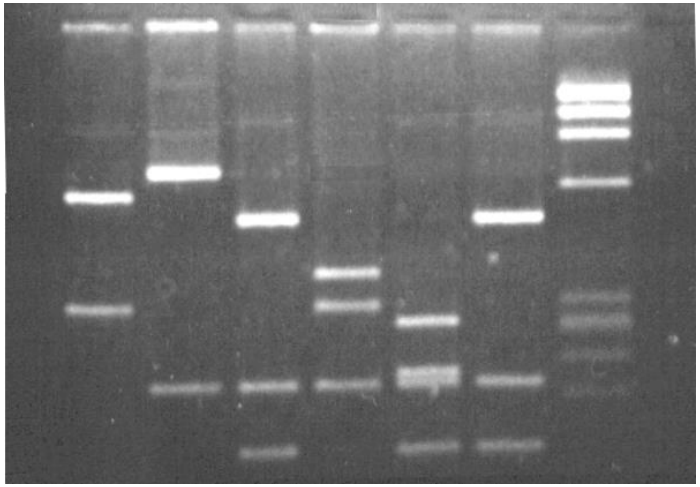


Start	1	2	3	n	Cycle No.
1	2	4 (= 2^2)	8 (= 2^3)	2^n	DNA No.

Gel electrophoresis

- Gel electrophoresis is a method that can _____ nucleic acids that differ in _____
- How far a DNA molecule travels is _____ proportional to its length.
- After the current is turned off, a dye is added; this reveals the separated bands by fluorescing in ultraviolet light.
- Used for DNA purification and analysis

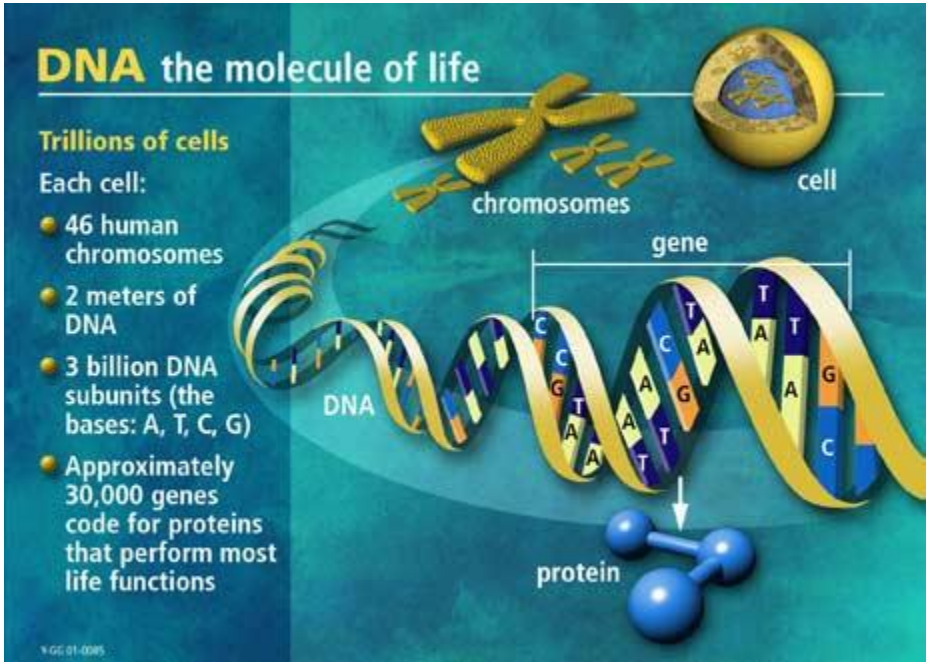




Human genome project

Overview:

- Initiated in 1990 by US Department of Energy.
- International scientific research project from groups from US, UK, Japan, France, Germany, China, and India
- Largest single investigative projects in modern science. ($3 billion)



Objective:

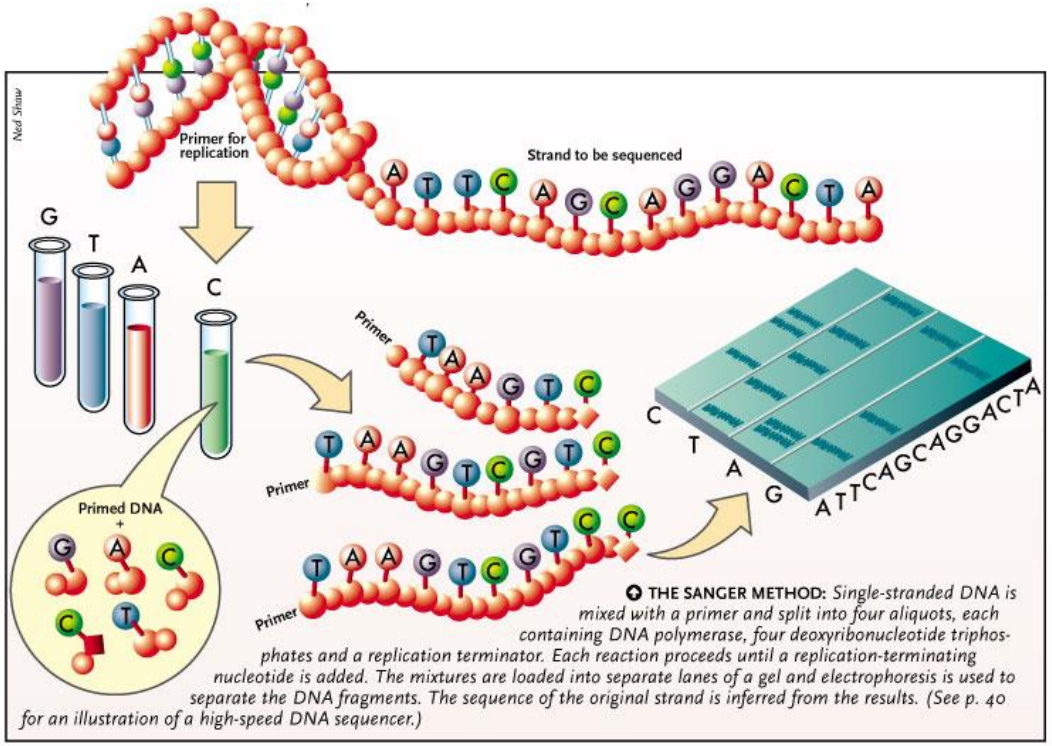
- Find the complete sequence of A, C, G, T's in human genome DNA
- To understand the genetic makeup of the human species

Benefit:

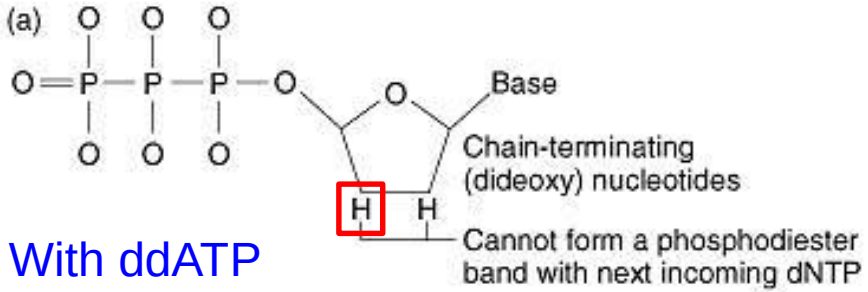
- Knowledge of the effects of variation of DNA among individuals can revolutionize the ways to diagnose, treat and even prevent a number of diseases that affects the human beings.
- It provides clues to the understanding of human biology.

DNA sequencing

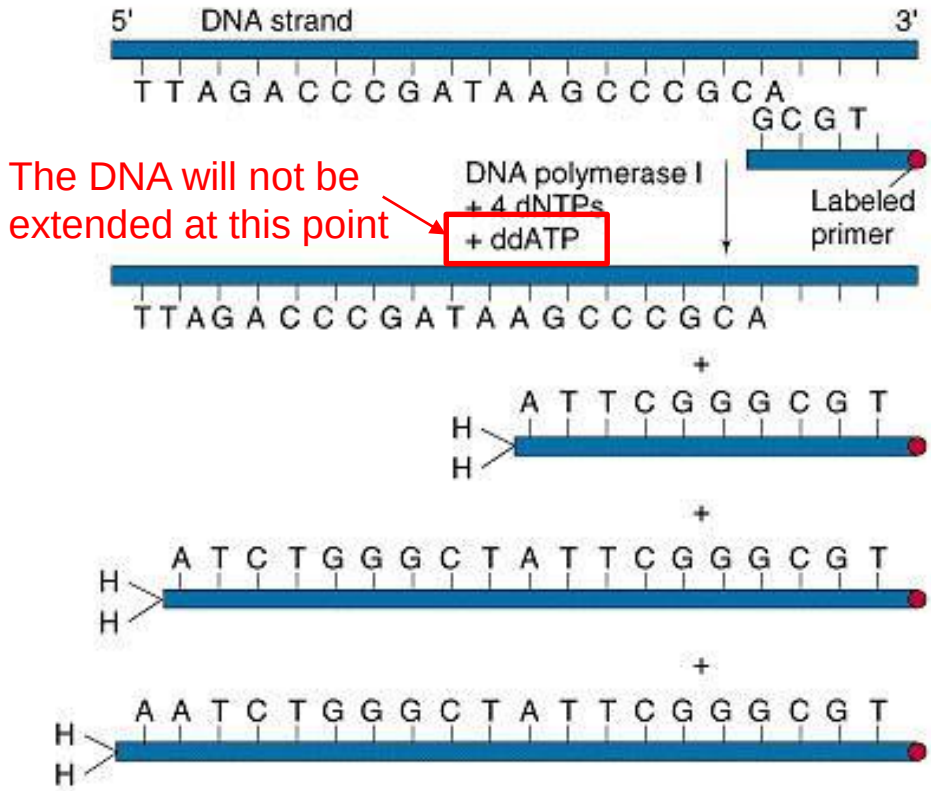
- A standard way to do DNA sequencing
- Use modified nucleotide as well as regular DNA to amplify DNA. Use gel electrophoresis to separate amplified DNA and do sequencing.
- Problem: limitation in the length of the DNA to be sequenced, laborious, expensive.



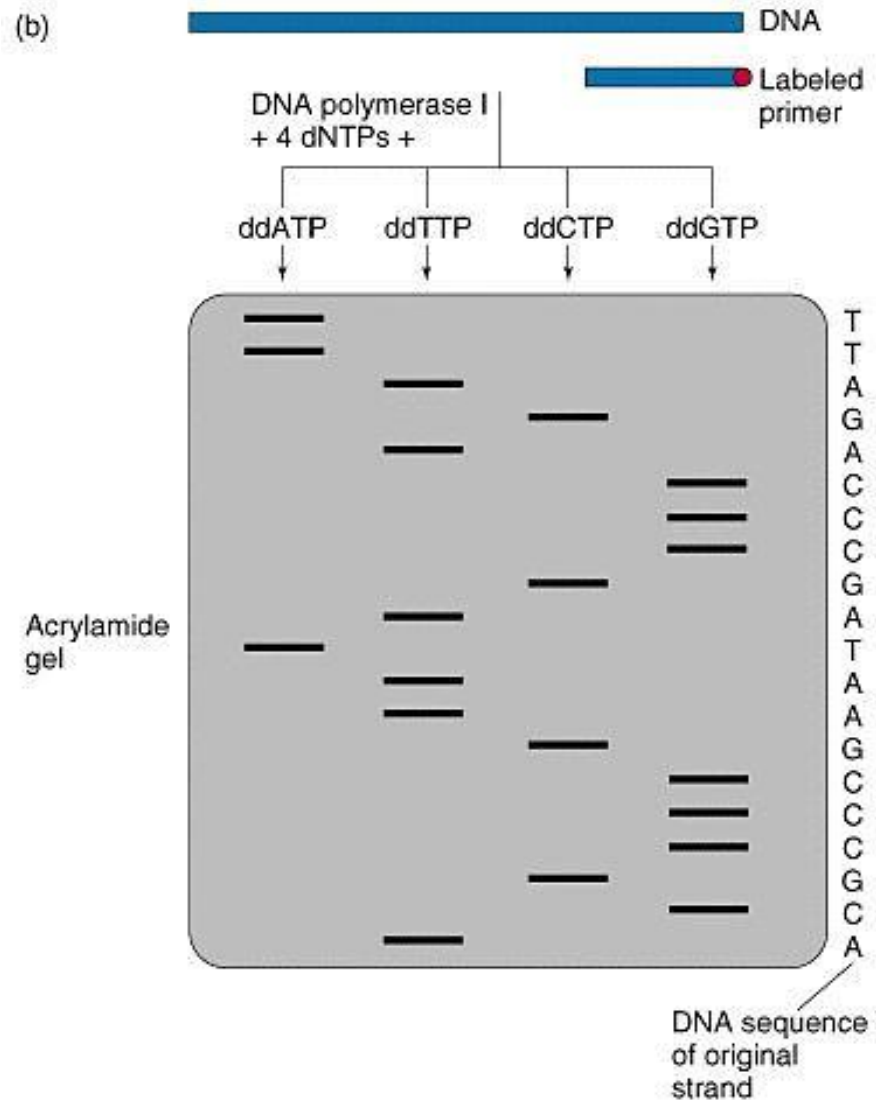
Sanger method



With ddATP



DNA strands with different lengths (all discontinued at ddATP) will be generated



Crystal structures in materials

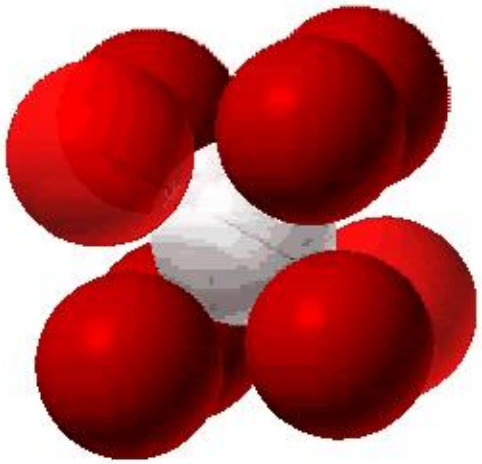
Body Centered Cubic Structure (BCC)

- Atoms touch each other along cube diagonals.

  --Note: All atoms are identical; the center atom is shaded differently only for ease of viewing.

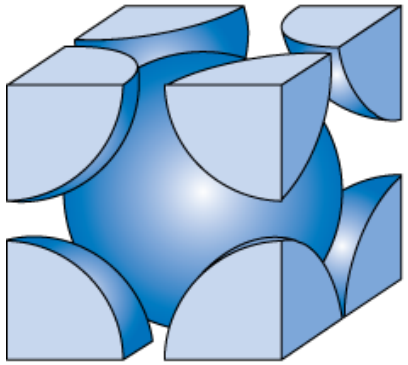
ex: Cr, W, Fe (α), Tantalum, Molybdenum

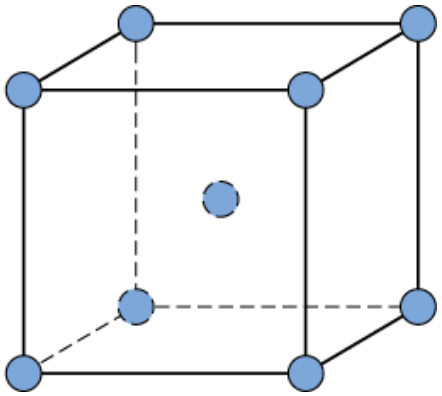
- Coordination # = 8



Click once on image to start animation

(Courtesy P.M. Anderson)





Adapted from Fig. 3.2, *Callister & Rethwisch 4e.*

Crystal structures in materials

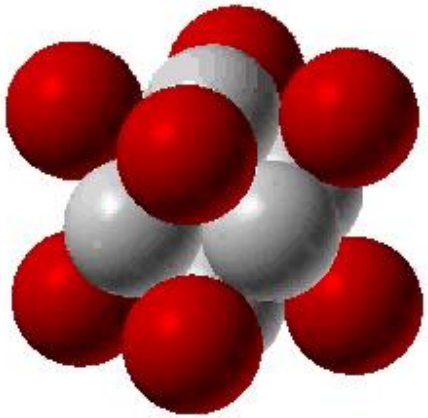
Face Centered Cubic Structure (FCC)

- Atoms touch each other along face diagonals.

  --Note: All atoms are identical; the face-centered atoms are shaded differently only for ease of viewing.

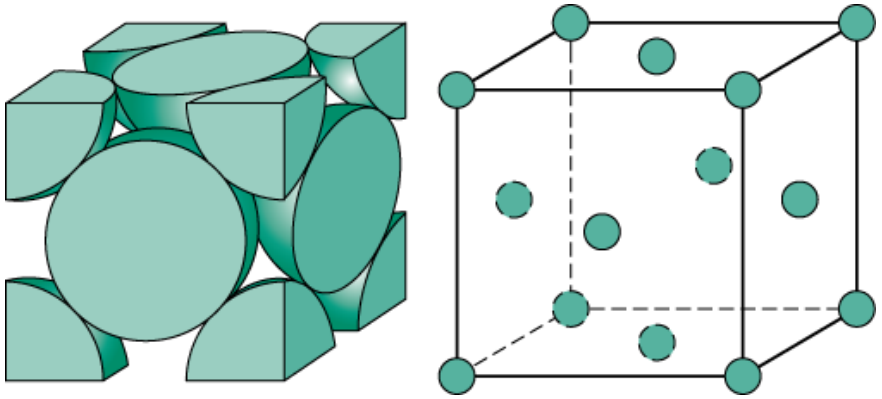
ex: Al, Cu, Au, Pb, Ni, Pt, Ag

- Coordination # = 12



Click once on image to start animation

(Courtesy P.M. Anderson)

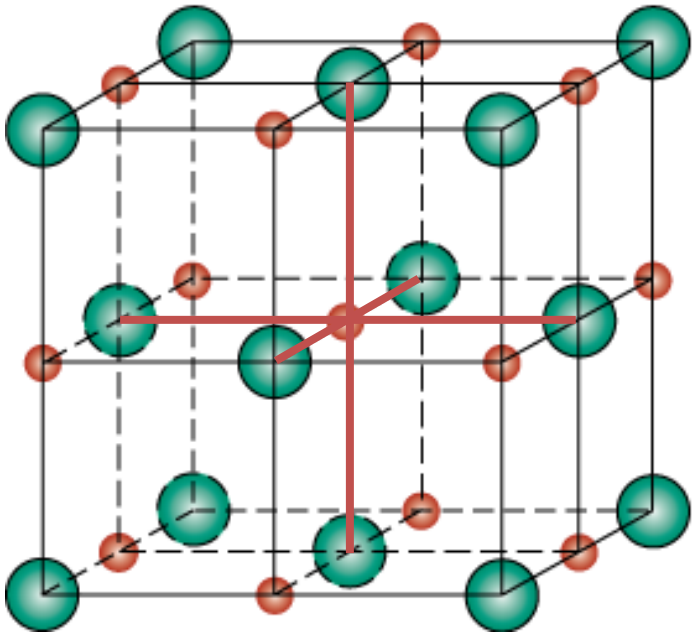


Adapted from Fig. 3.1, *Callister & Rethwisch 4e.*

Crystal structure of NaCl

Same concepts can be applied to ionic solids in general.

Example: NaCl (rock salt) structure



Adapted from Fig. 3.5,
Callister & Rethwisch 4e.

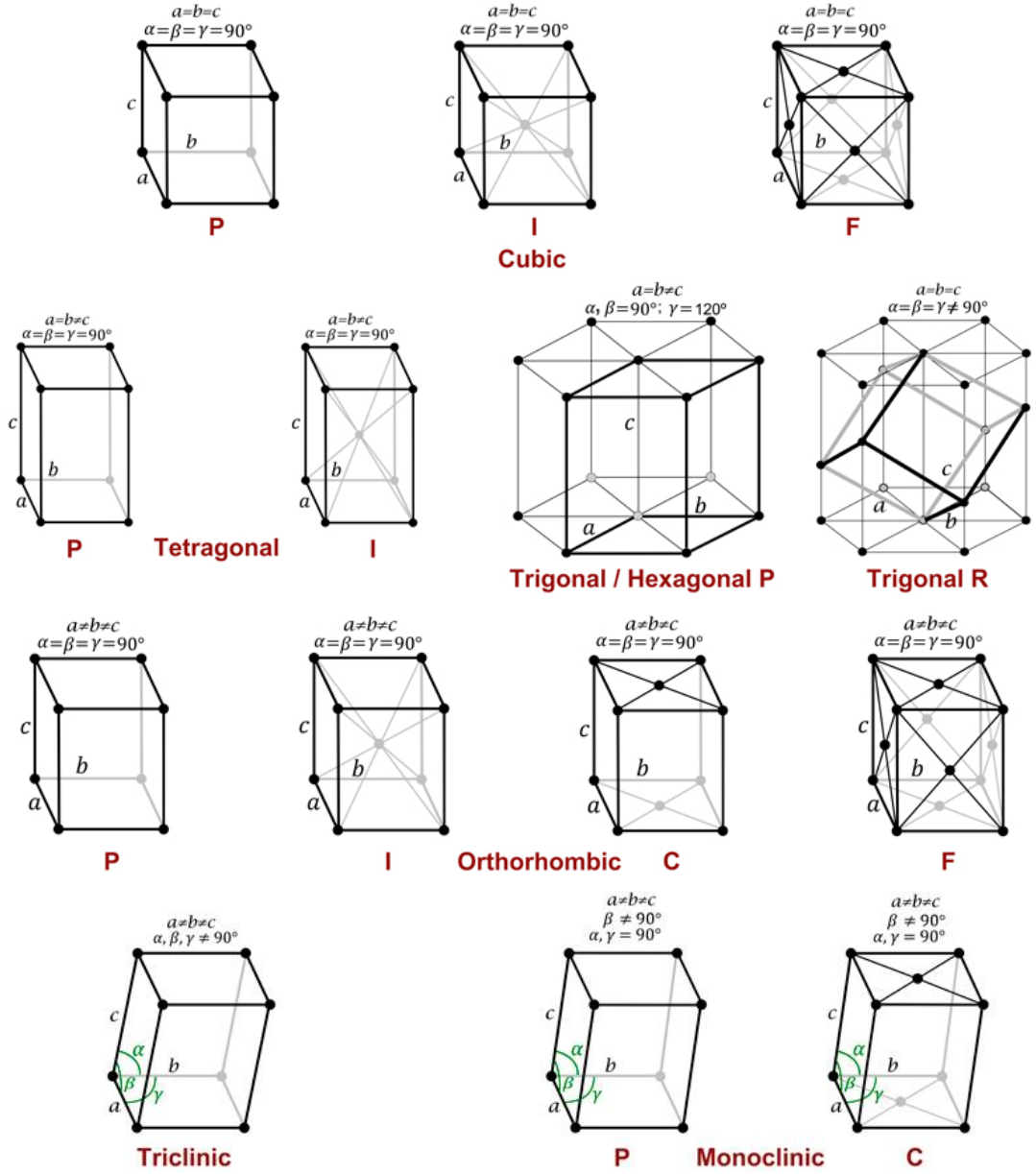
Na^+ $r_{Na} = 0.102$ nm

Cl^- $r_{Cl} = 0.181$ nm

$r_{Na}/r_{Cl} = 0.564$

$\therefore$ cations (Na^+) prefer octahedral sites

14 Bravais lattices



Symbols P C I F R refer to the different lattice types:

P = primitive (there is only one reticular point inside the cell (1 point in each of the 8 corners of the cell means 8/8=1 points in the cell)

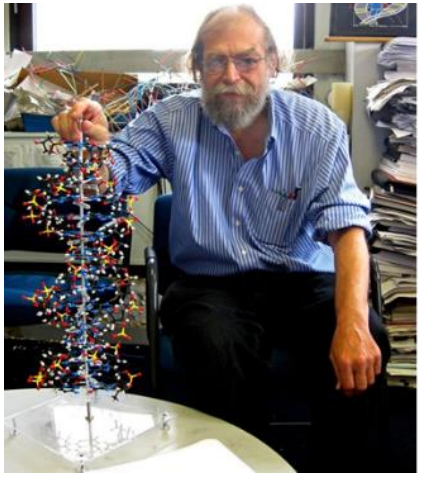
C = centered in the faces perpendicular to the cell c axis (+ 1/8 of reticular point in each corner)

I = centered in the body of the cell (+ 1/8 of reticular point in each corner)

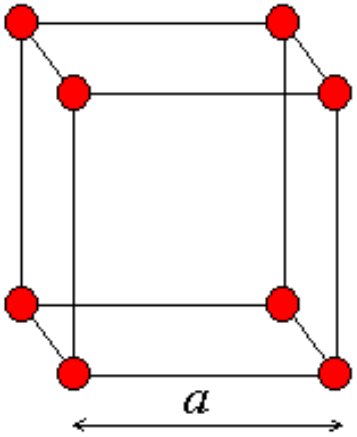
F = centered in all faces of the cell (+ 1/8 of reticular point in each corner)

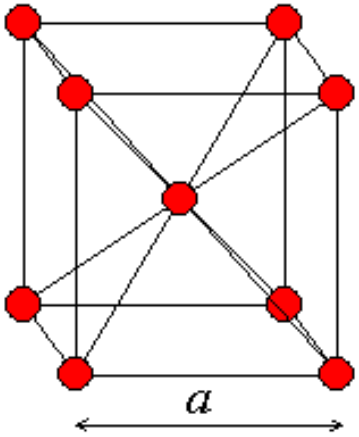
R = primitive, identical cell axes and cell angles, or hexagonal two times body centered (+ 1/8 of reticular point in each corner)

DNA nanotechnology



Nadrian Seeman





- Field opened by Prof. Seeman at NYU (early 1980's)
- Use DNA as building blocks for synthesis of crystalline structures

Stiffness of DNA

Typical Young's modulus (Pa) of materials

Steel: 2×10^{11}

Glass: 1×10^{11}

Bone: 2×10^{11}

Wood: 1×10^{11}

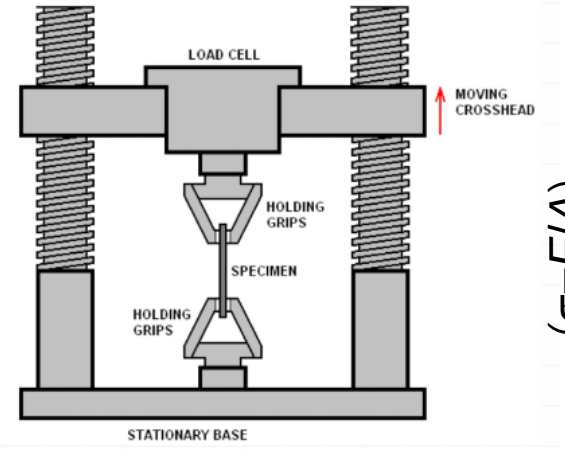
Single folded protein: ~10^9

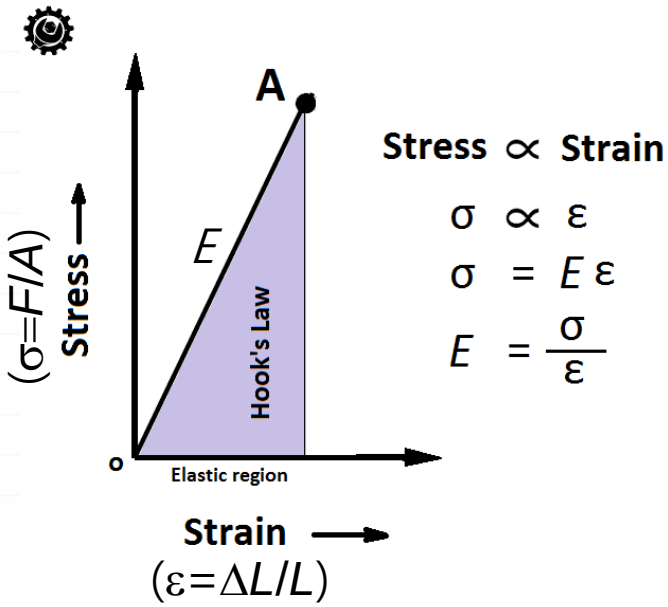
Plexiglas: 4×10^8

Double stranded DNA: 3×10^8

Polymer rubber: ~10^6

Polymer gel: ~10^4





Bustamante *et al*., 1994. Science, 265, 1599-1600

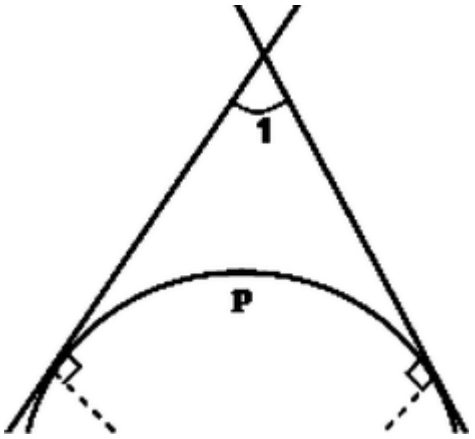
Persistence length

Definition:

- a basic mechanical property quantifying the stiffness of a material
- the average length required to bend a material 1 radian (= 180/π = 57.3˚)

1 mm steel wire

1 mm rubber band



Persistence length

Definition:

•a basic mechanical property quantifying the [ ] of a polymer (or DNA).

•the average length of DNA required for the helix backbone to bend 1 radian (= 180/π = 57.3˚)

-for pieces of the polymer that are shorter than the persistence length, the molecule behaves rather like a flexible [ ] rod

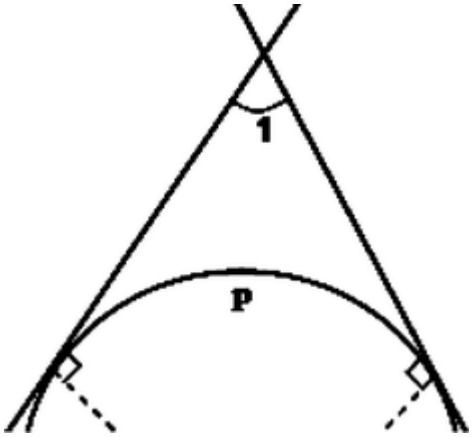
-for pieces of the polymer that are much longer than the persistence length, the properties can only be described statistically, like a three-dimensional random walk

→ Persistence length of dsDNA:

[ ]

→ Persistence length of ssDNA:

1.5-3 nm (4-9 bps)



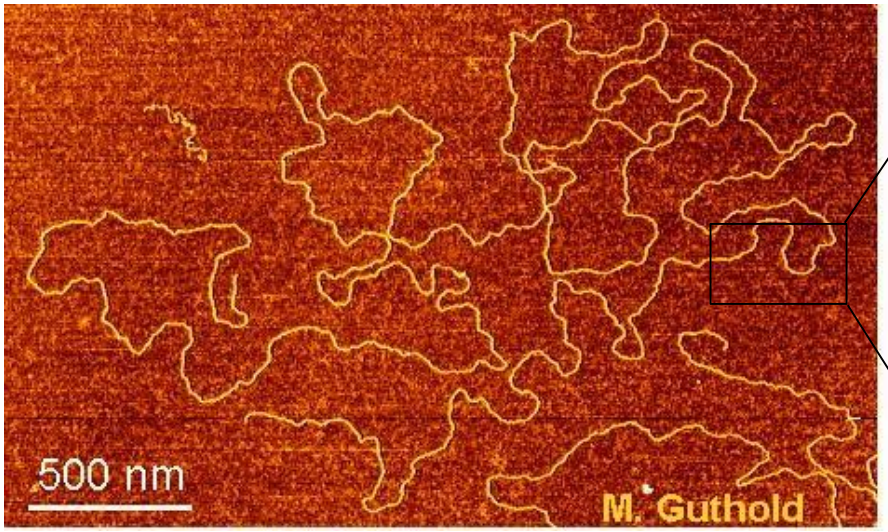
Persistence length

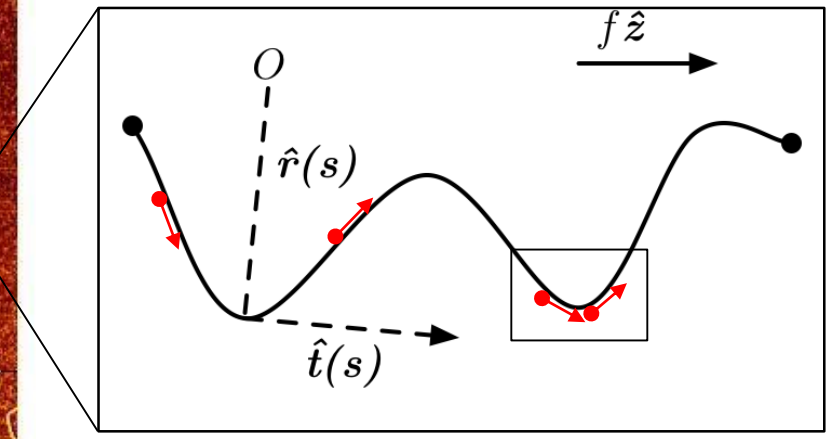
Definition:

- a basic mechanical property quantifying the stiffness of a DNA.
- the average length of DNA required to bend 1 radian

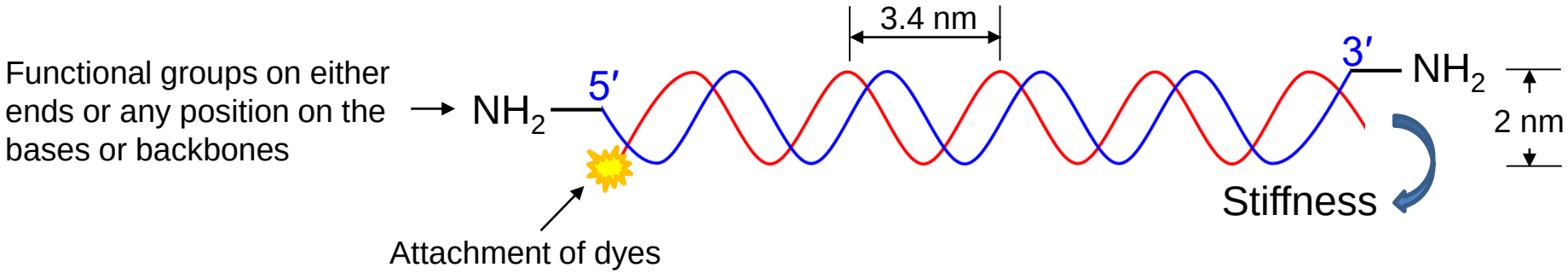
→ Persistence length of dsDNA: 50 nm (150 bps)
→ Persistence length of ssDNA: 1.5-3 nm (4-9 bps)

- DNA < 50 nm → rigid, elastic rod
- DNA >> 50 nm → flexible molecule



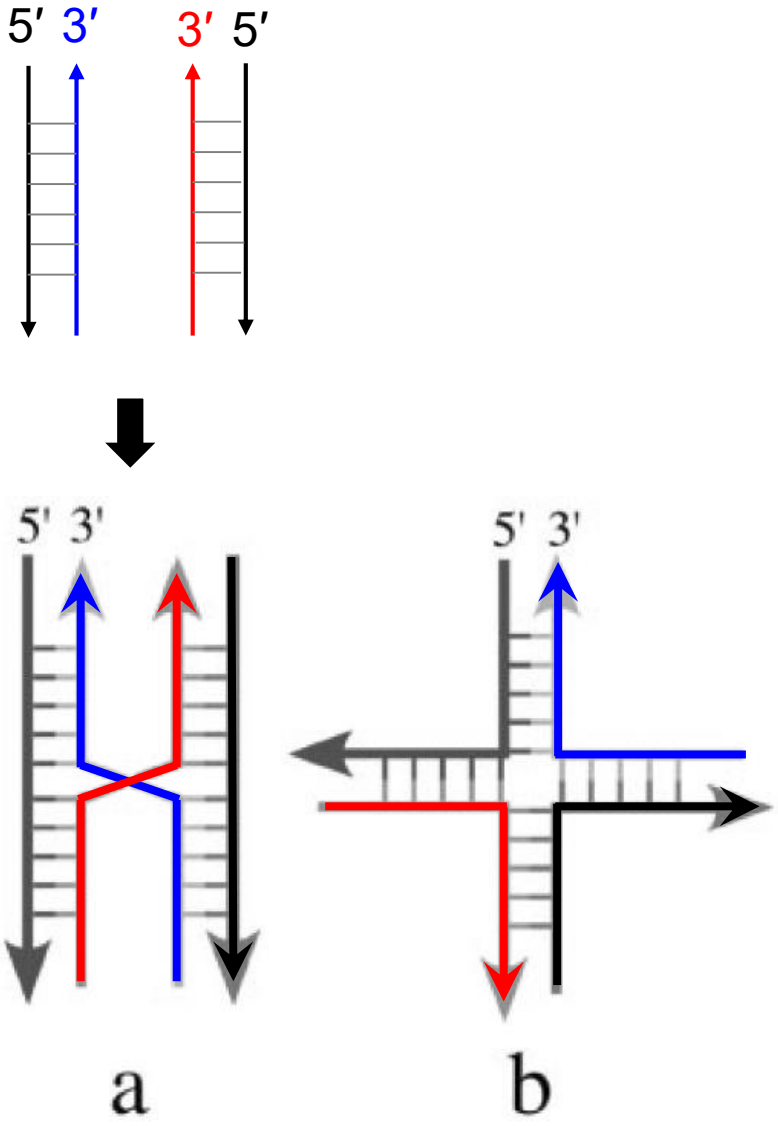


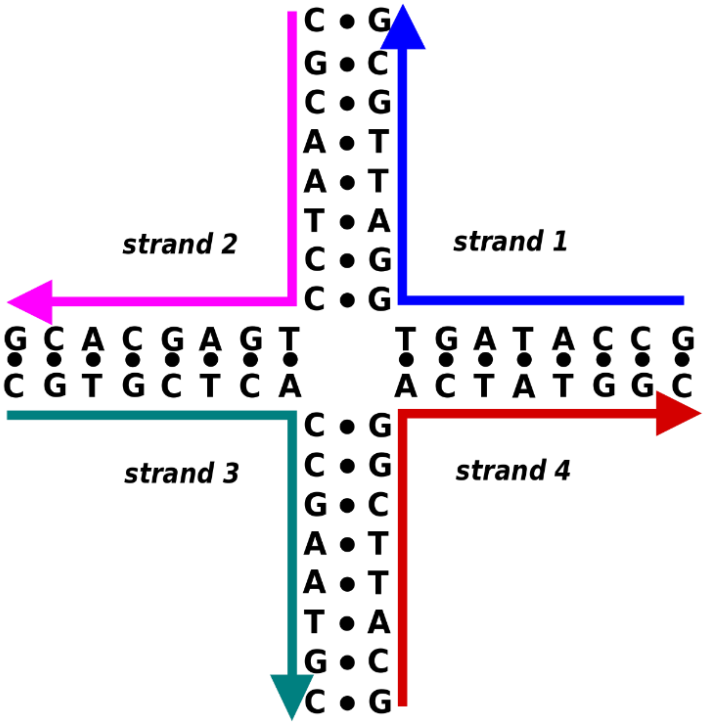
Unique properties of DNA



- The rigorous Watson-Crick base pairing makes the hybridization between DNA strands highly predictable and programmable.
- The structure of the B-form DNA double helix is well-understood.
- DNA possesses combined structural stiffness and flexibility. The rigid DNA double helices can be linked by relatively flexible single-stranded DNA (ssDNA) to build stable motifs with desired geometry.
- Modern organic chemistry and molecular biology have created a rich toolbox for readily synthesizing, modifying, and replicating DNA molecules.
- DNA is a biocompatible material, making it suitable for the construction of multicomponent nanostructures made from heterobiomaterials.

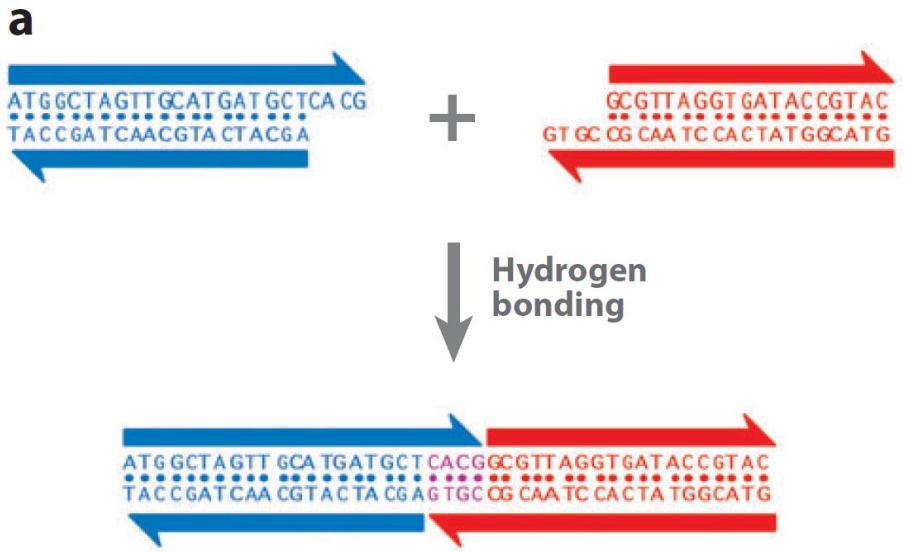
Structural forms of DNA Holliday junction



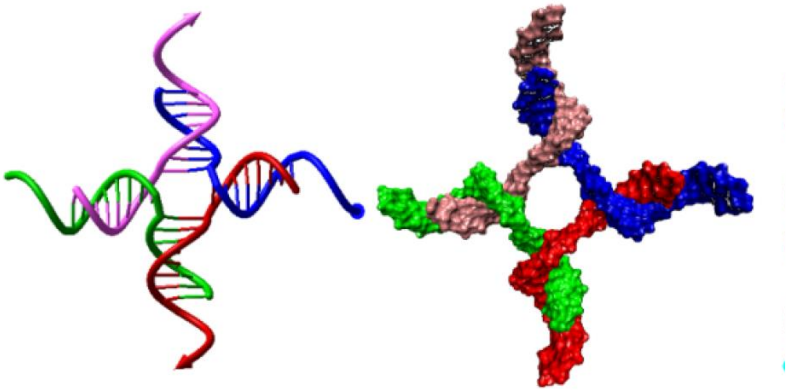


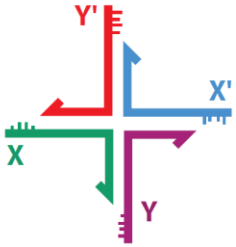
J Mol Recognit. 2006, 19(3), 234–242

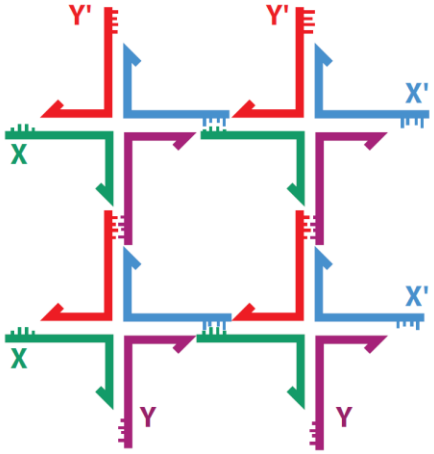
DNA sticky ends



Sticky end of DNA
→ Connect each unit by designing DNA sequence

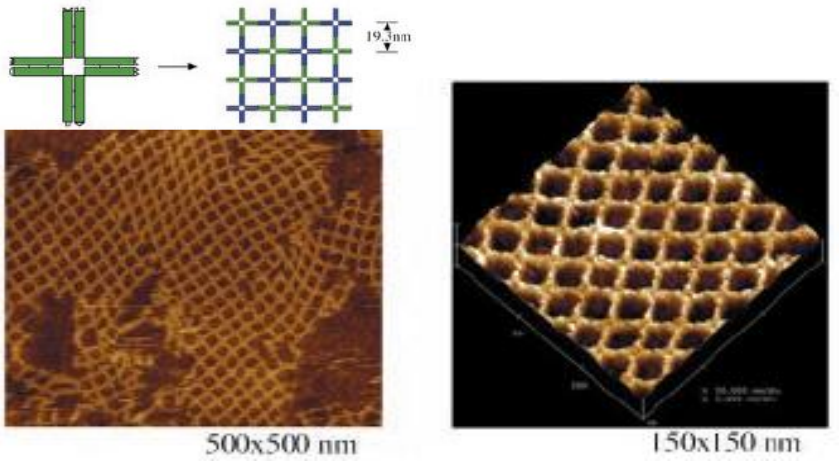




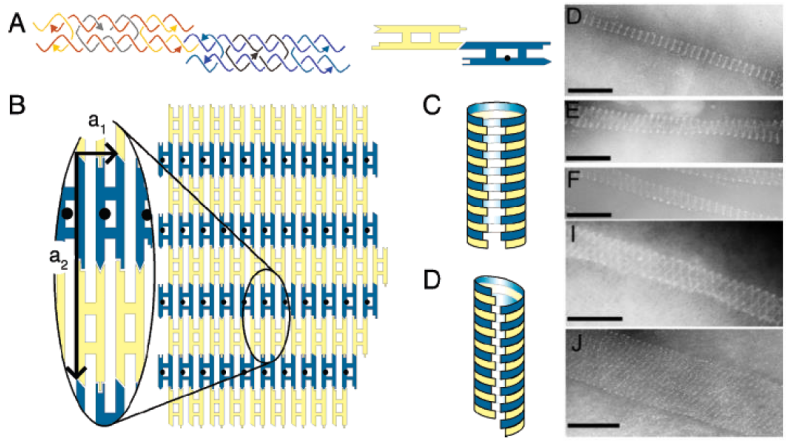


DNA nanostructures

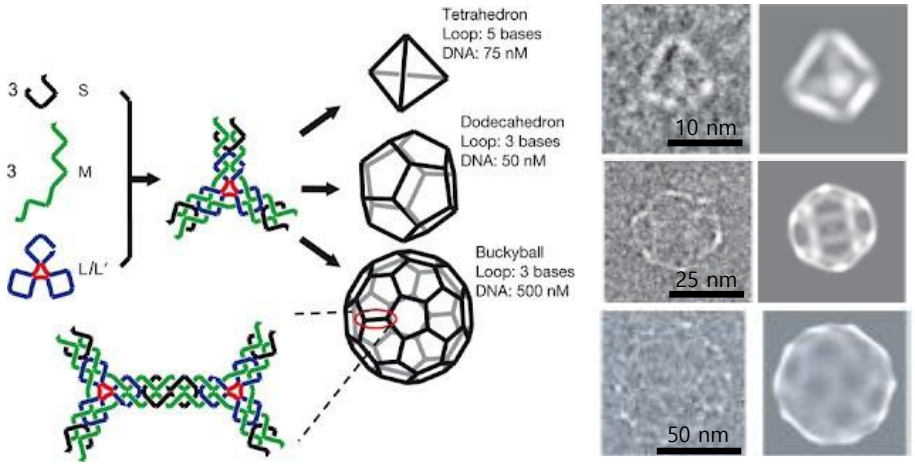
- It is possible to make 1D, 2D and 3D structured nanoscale materials using DNA
- Still very difficult to design structures we want (elegant work)



H. Yan *et al*., *Science*, 2003, *301*, 1882

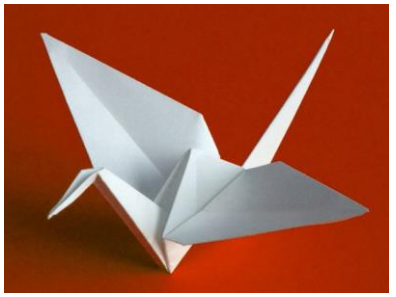


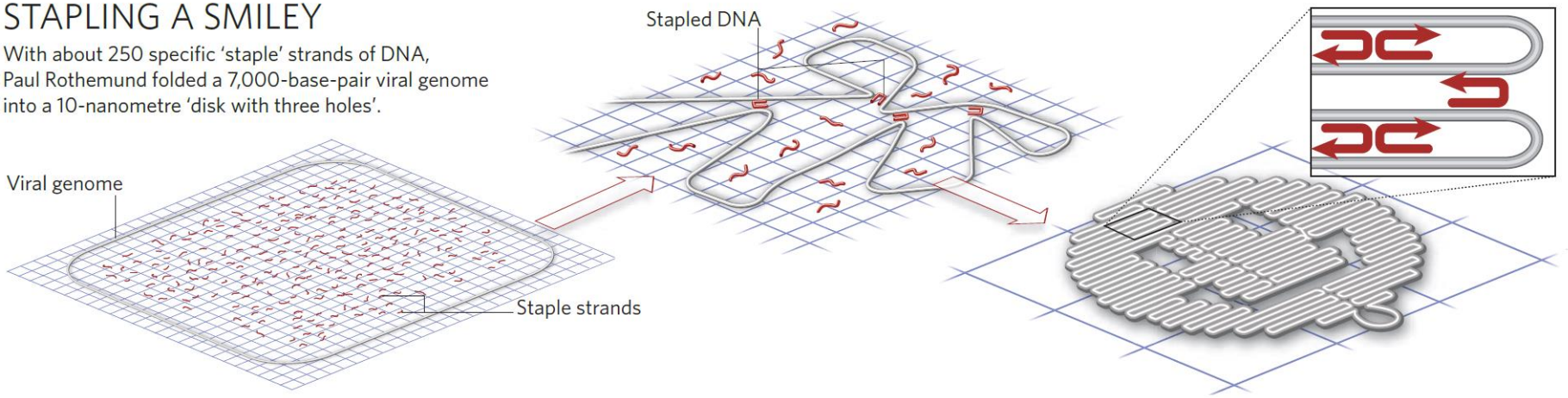
A. J. Turberfield et al. *JACS* 2004, 126, 16342



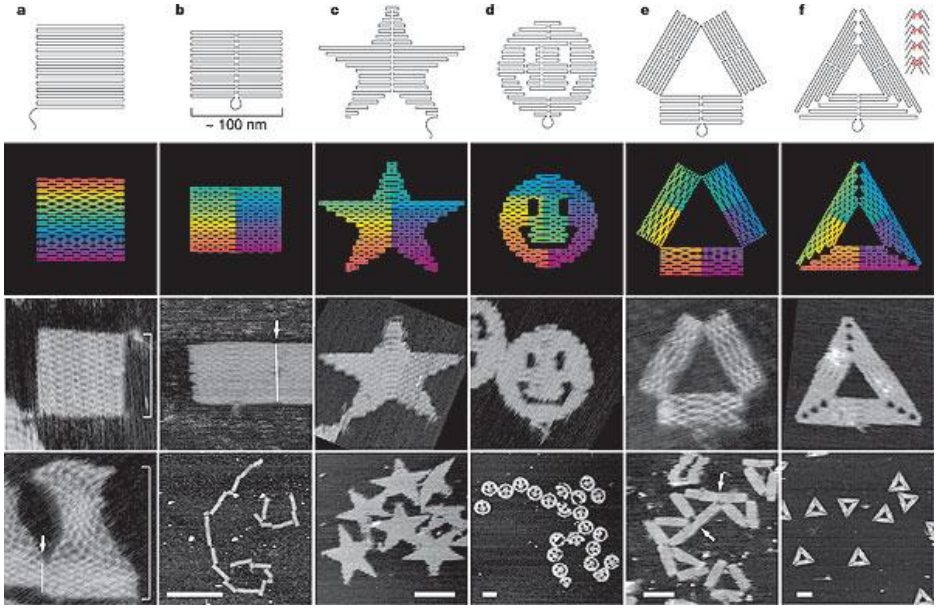
C. Mao *et al*., *Nature*, 2008, *452*, 198

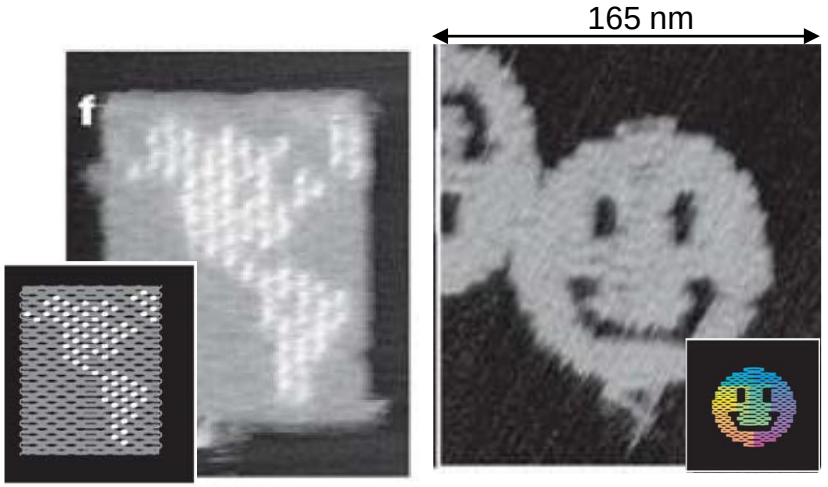
DNA origami





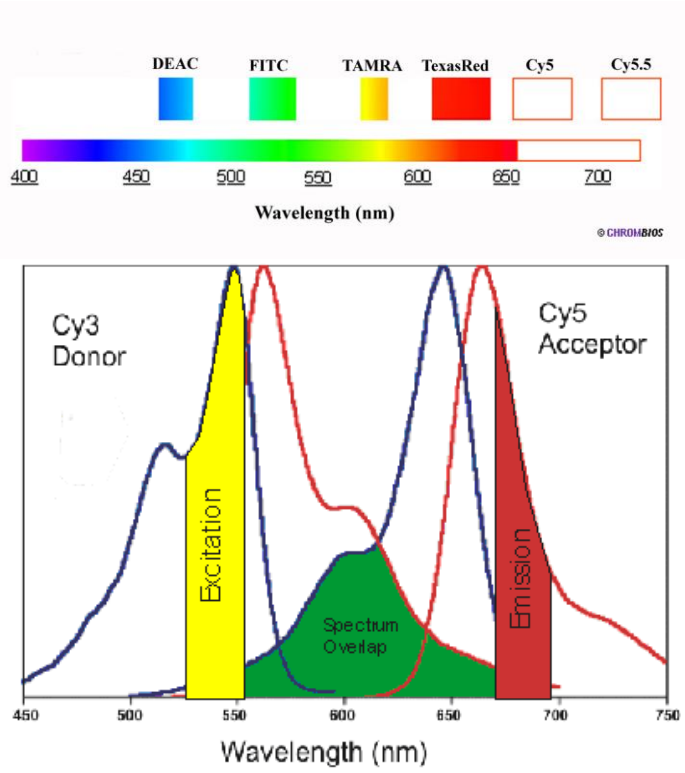
Nature 464, 11, 158, 2010





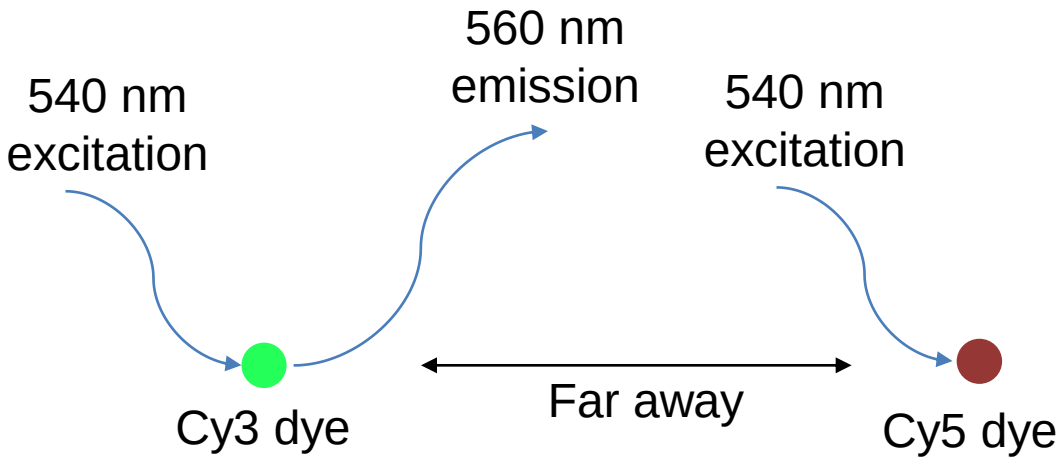
P WK Rothemund, *Nature,* 2006

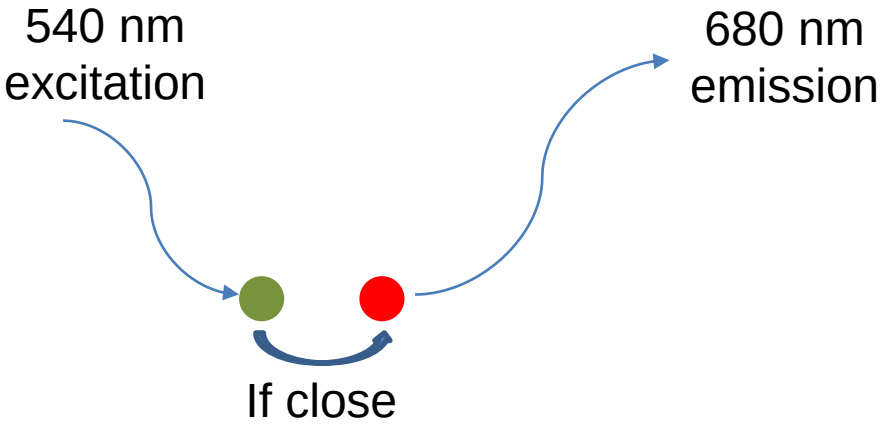
FRET (Förster resonance energy transfer)



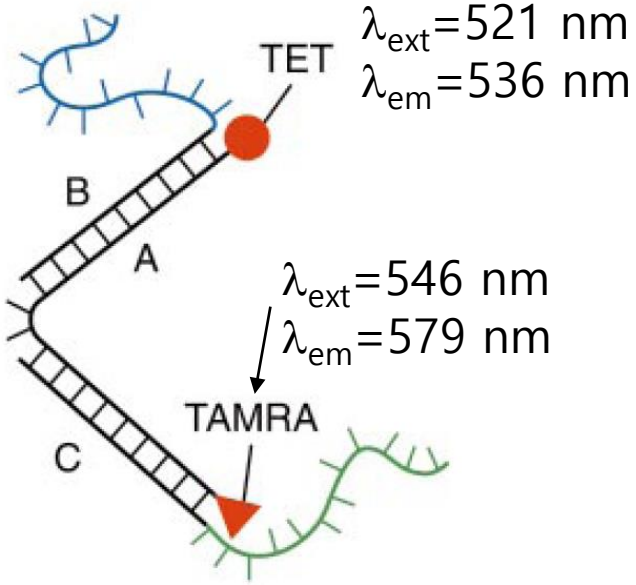
$$E = \frac{1}{1 + (r/R_0)^6}$$

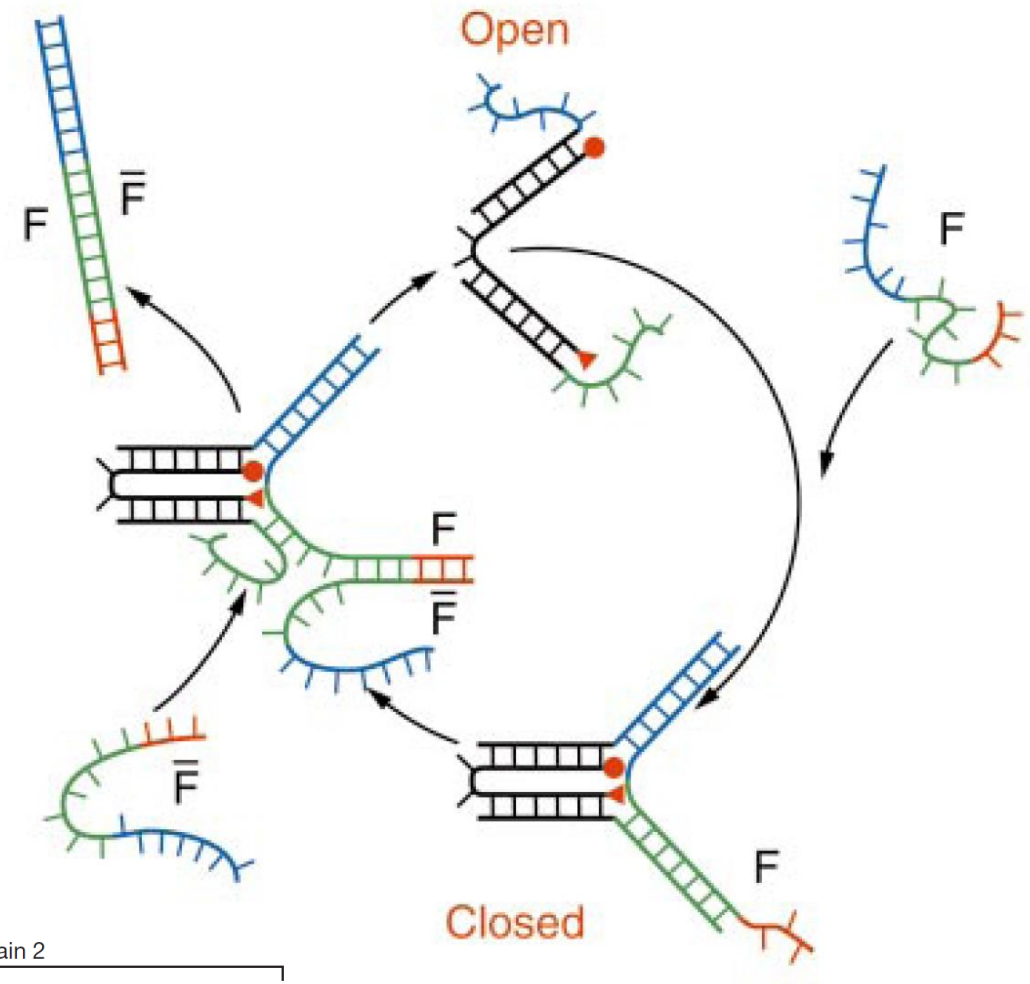
R_0 : Förster distance of this pair of donor and acceptor, (the distance at which the energy transfer efficiency is 50%)





First molecular machine-DNA tweezer





Name	Sequence: Domain 1	Domain 2
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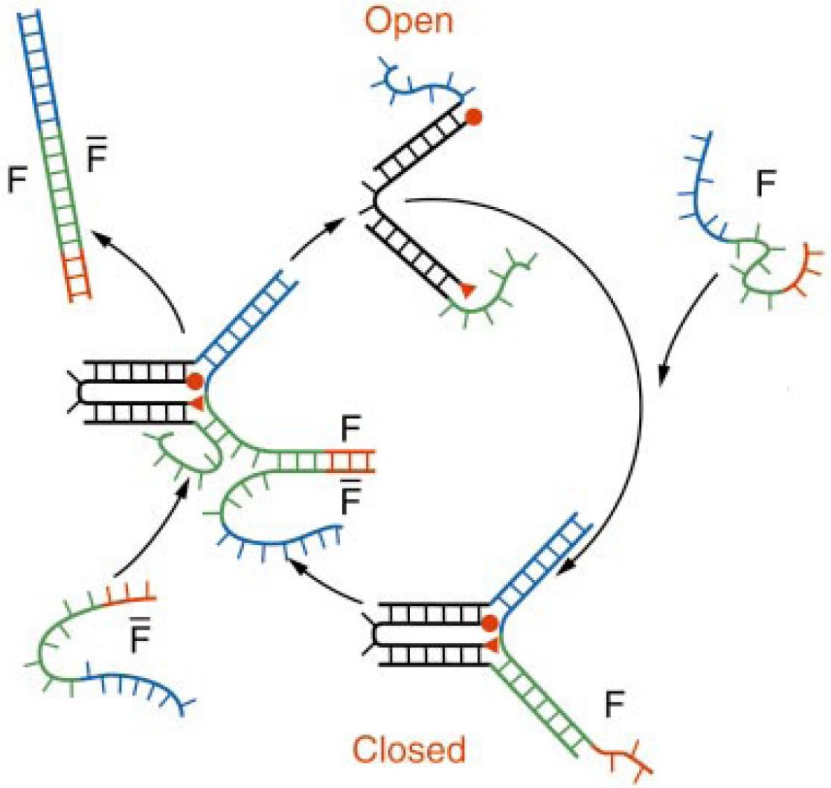
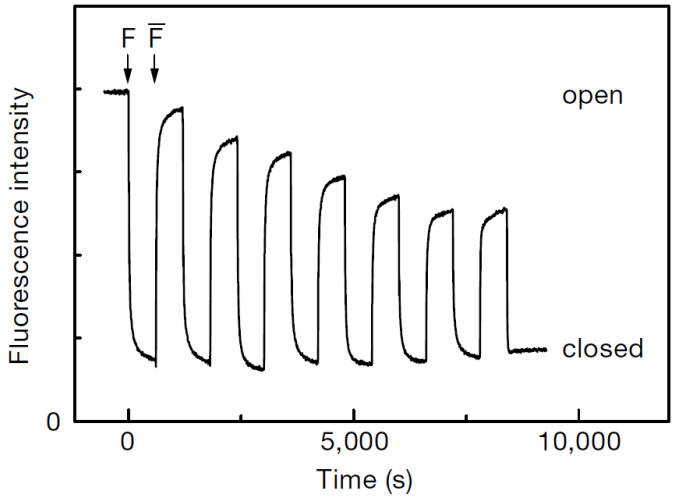
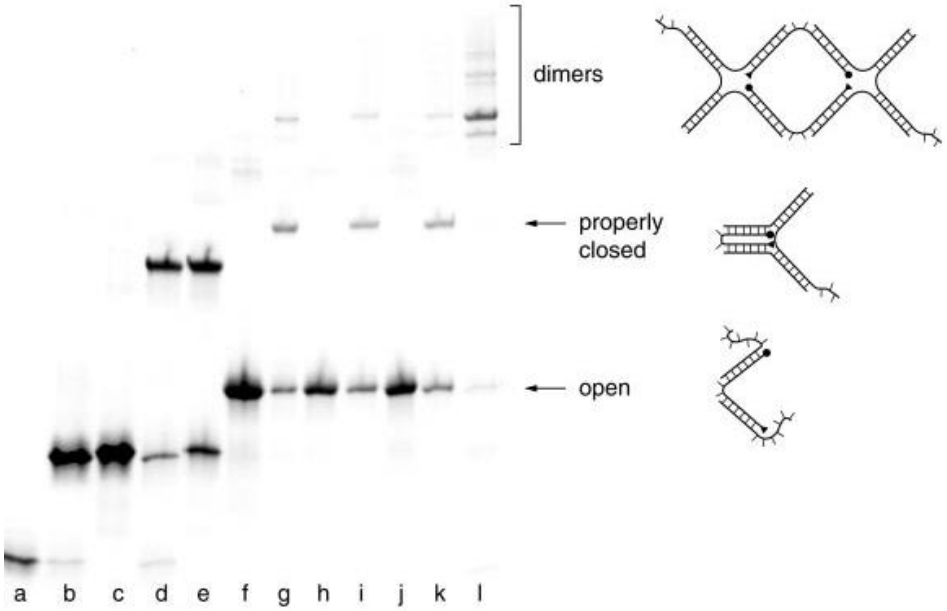
B	5′ GGTCGCTCTTACAAGGCA	CTGGTAACAATCACGGTCTATGCG 3′
C	5′ GGAGTCCTACTGTCTGAACTAACG	ATCCGAAGCATTCCAGGT 3′
F	5′ CGCATAGACCGTGATTGTTACCAG	CGTTAGTTCAGACAGTAGGACTCCTGCTACGA 3′
β	5′ GGTCGCTCTTACAAGGCA	CAGCTAGTTTCACAGTGGCAAGTC 3′
γ	5′ GCAGGCTTCTACATATCTGACGAG	ATCCGAAGCATTCCAGGT 3′
$F_{B\gamma}$	5′ CGCATAGACCGTGATTGTTACCAG	CTCGTCAGATATGTAGAAGCCTGC ACGTCGAT 3′
$F_{C\beta}$	5′ GACTTGCCACTGTGAAACTAGCTG	CGTTAGTTCAGACAGTAGGACTCC TGTCCAGA 3′

Nature **2000**, *406*, 605

First molecular machine-DNA tweezer

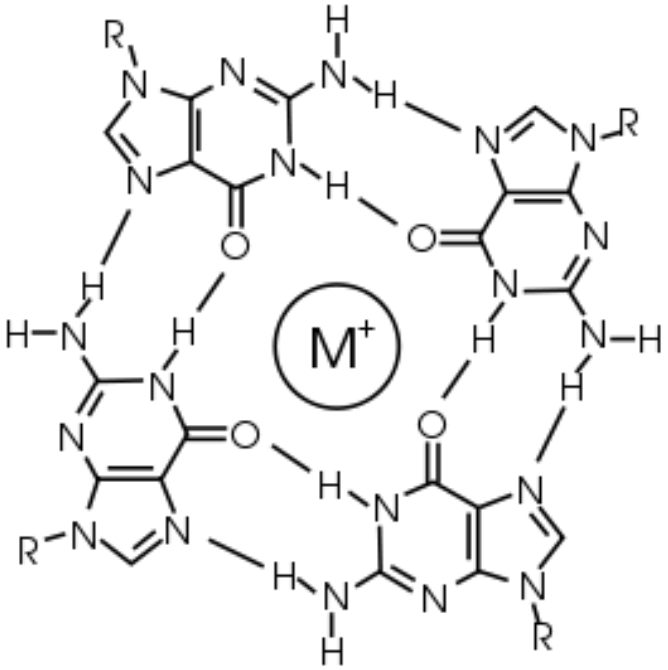


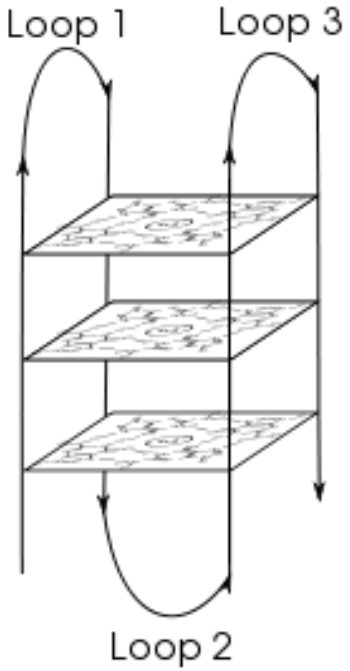




Nature **2000**, *406*, 605

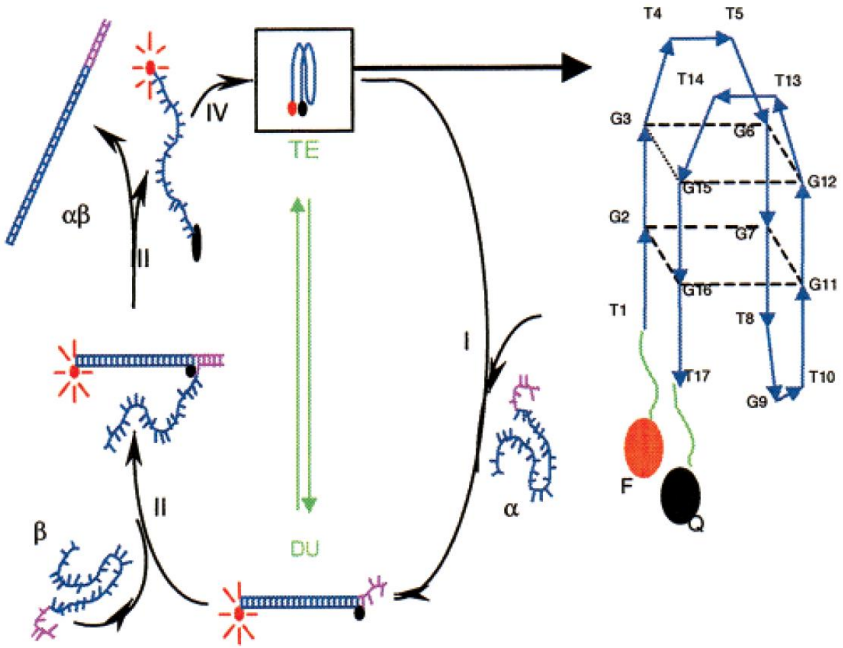
G-quadruplex

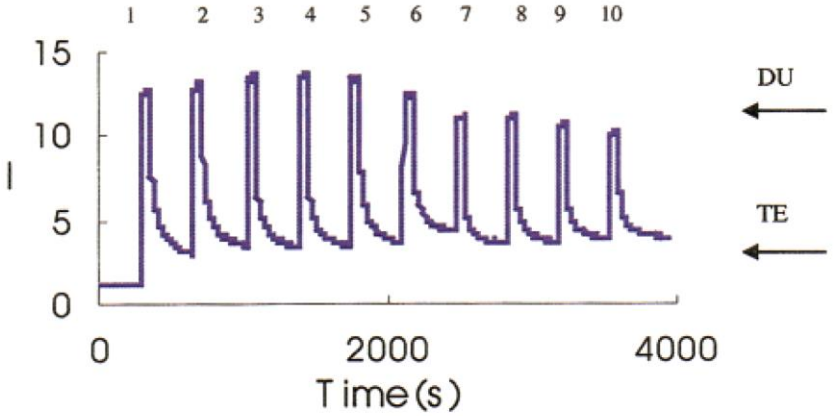


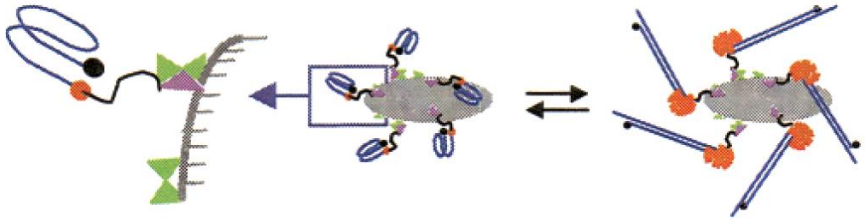


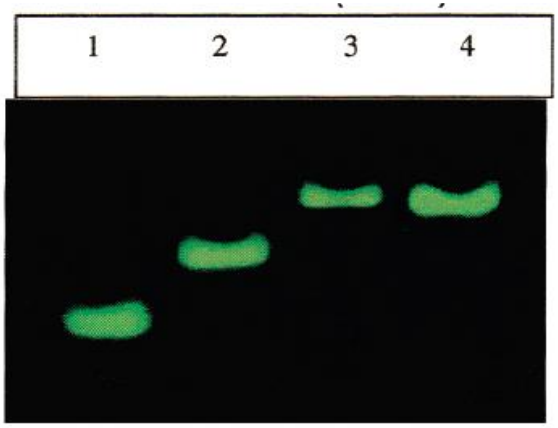
- DNA structures formed in nucleic acids by sequences that are rich in guanine.
- The quadruplex structure is further stabilized by the presence of a cation, especially potassium, which sits in a central channel between each pair of tetrads.

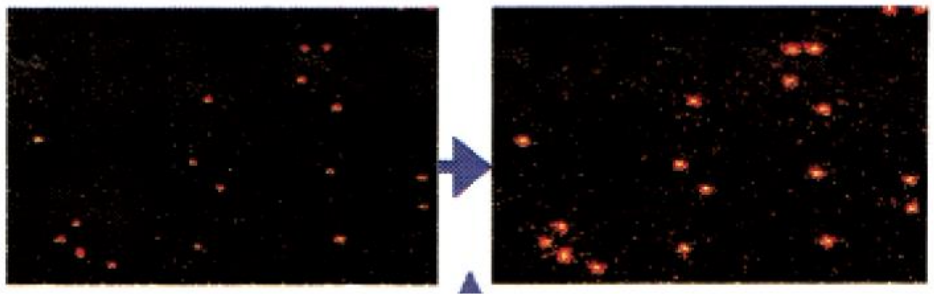
A single DNA molecule nanomotor







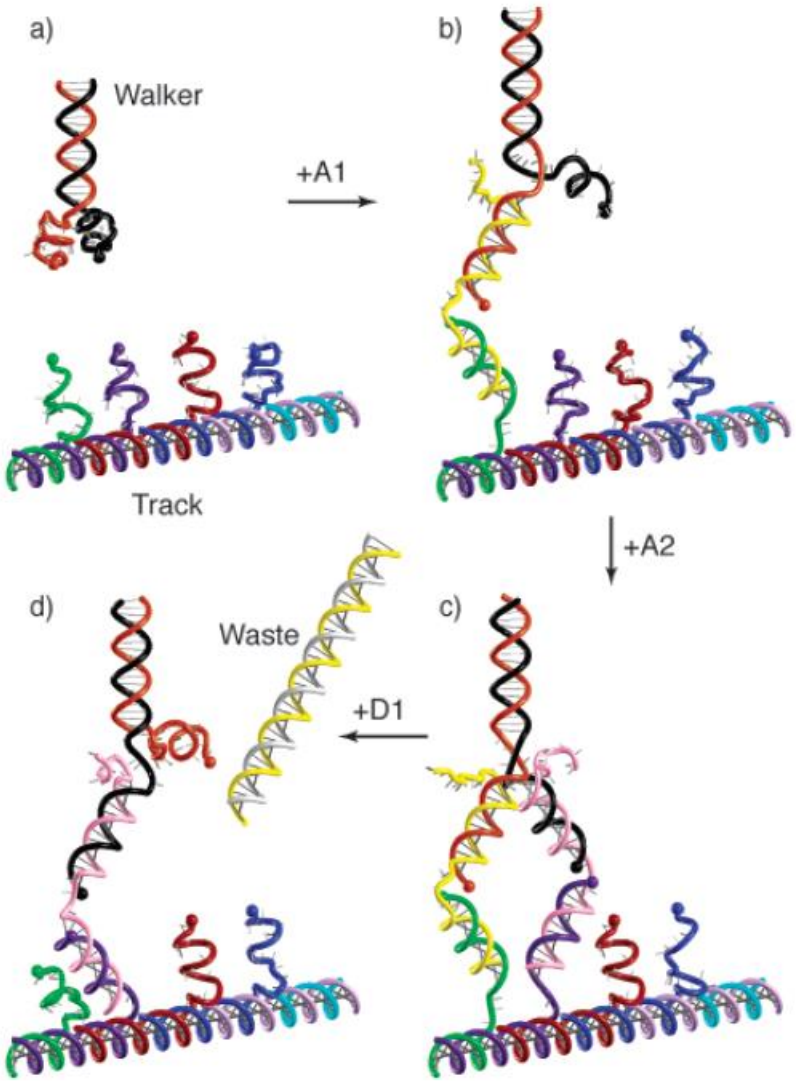




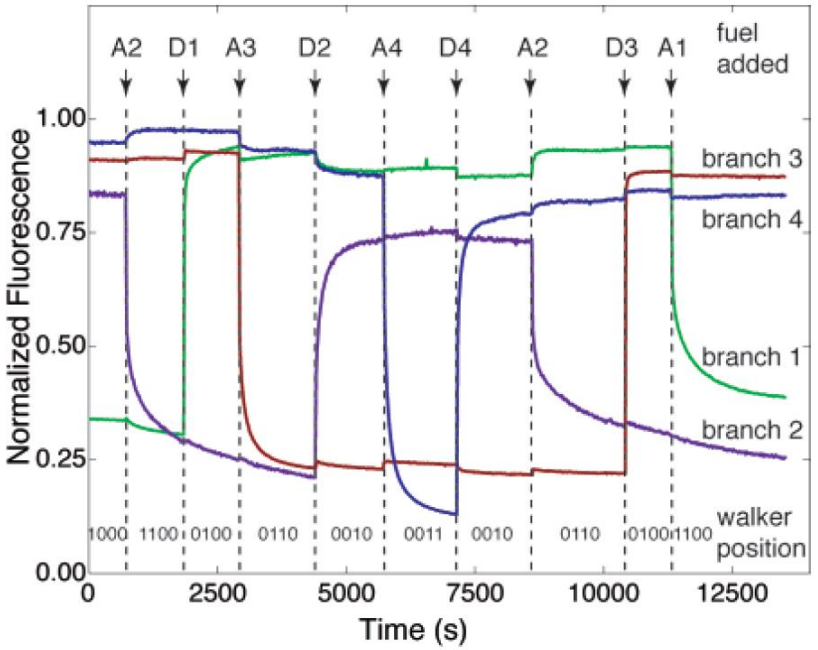
Gel electrophoresis: 1, nanomotor; 2, S17mer; 3, nanomotor plus R; 4, S17mer plus its complementary sequence.

Nano Lett. **2002**, *4*, 315

DNA walker

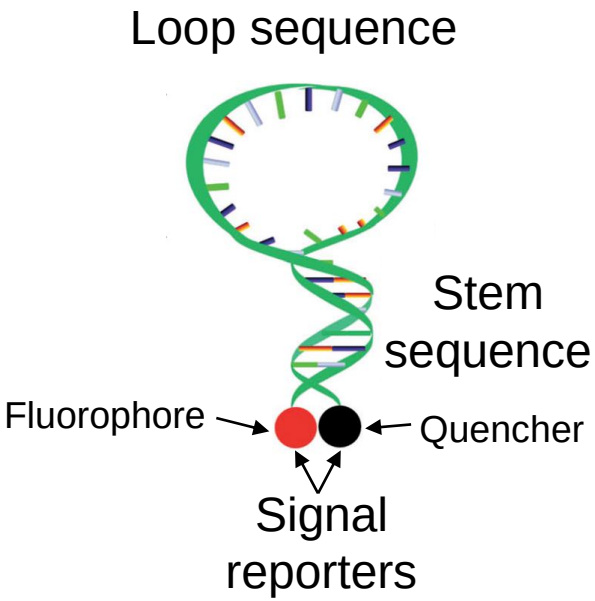


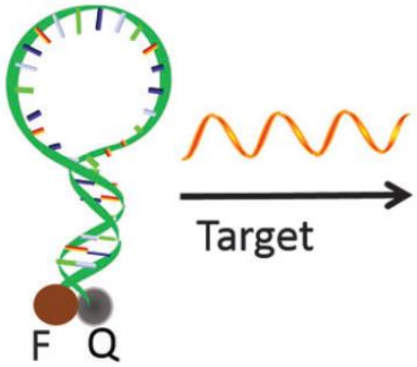
Walker strands (W)	
W1	5′-GGCTGGTTTCTGCTCTCTAGTTCGCGAGGTGCAATCTCCTATC-3′-BHQ1
W2	IBRQ-5′-GTCTGGGATGCTGGATACTGAACCTAGAGAGCAGAAACCAGCC-3′
Track strands (T)	
T1	HEX[c]-5′-GCTGTACTTTGGTTACTGAAAGGGAGTGGCTCGGA-3′
T2	5′-TCCGAGCCACTCCCTGGACACCATCTACAAACTTGTATGGGACGTAGCGT-3′-Cy5
T3	FAM[d]-5′-TCCACATCGGACTCTGTAATGCAAAGACACGTTACTTGTAGATGGTGTCC-3′
T4	5′-GTAACGTGTCTTTGCTCTCAAACATACGCTCTTCATGGCATTCGTCACCA-3′-Texas Red
T5	5′-AACTCTTAGCCAAGATCGTAAGCGTATGTTTGAGA-3′
T6	5′-TACGATCTTGGCTAAGAGTT-3′
Attachment strands (A)	
A1	5′-AGTAACCAAAGTACAGCACTGCGATAGGAGATTGCACCTCCAATTTACCC-3′
A2	5′-GACTGTTACGGTATCCAGCATCCCAGACGGTCAACGCTACGTCCCATACA-3′
A3[e]	5′-ACAGAGTCCGATGTGGAAGTCAGATAGGAGATTGCACCTCATCATTGTCG-3′
A4[e]	5′-GGATCAGTTAGTATCCAGCATCCCAGACCTAAGTGGTGACGAATGCCATG-3′



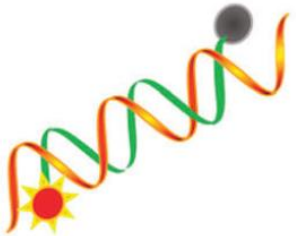
JACS **2004**, 126, 10834

DNA molecular beacon





Unbound beacon with quenched fluorescence

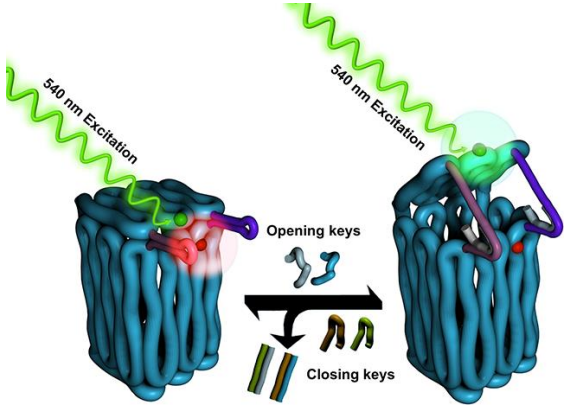


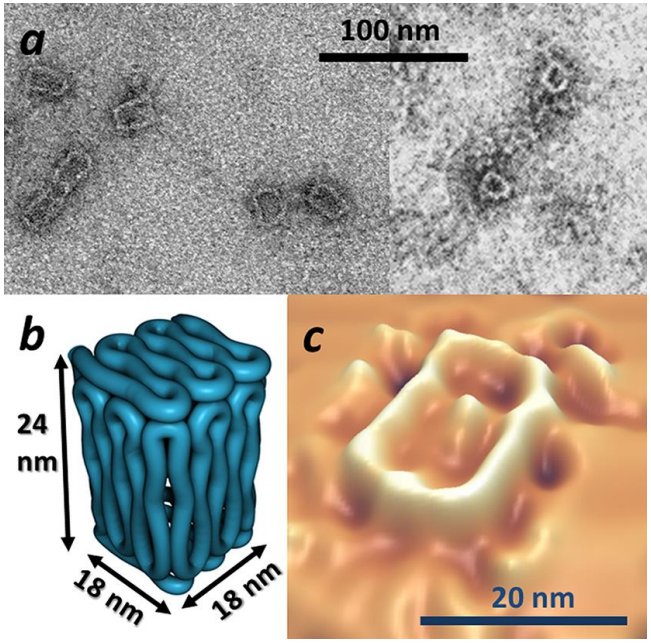
Bound beacon with unquenched fluorescence

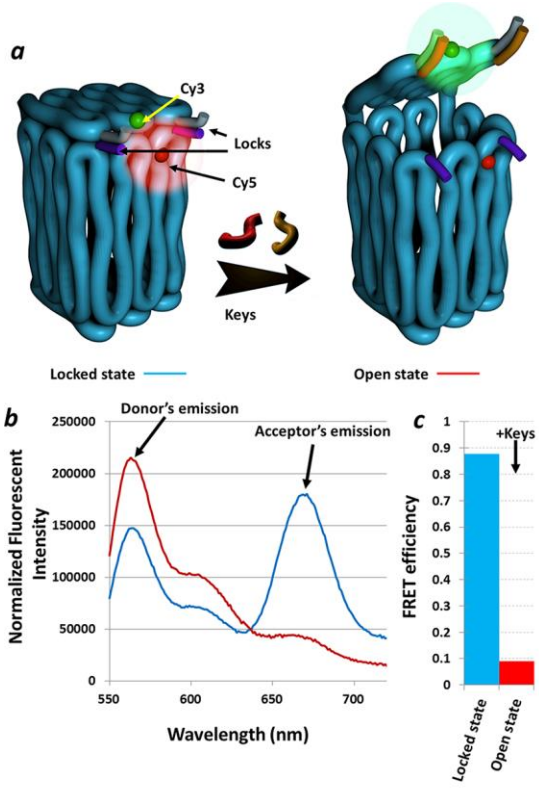
- Molecular beacons are oligonucleotide hybridization probes that can report the presence of specific nucleic acids in homogenous solutions.
- Molecular beacons are hairpin shaped molecules with an internally quenched fluorophore whose fluorescence is restored when they bind to a target nucleic acid sequence.

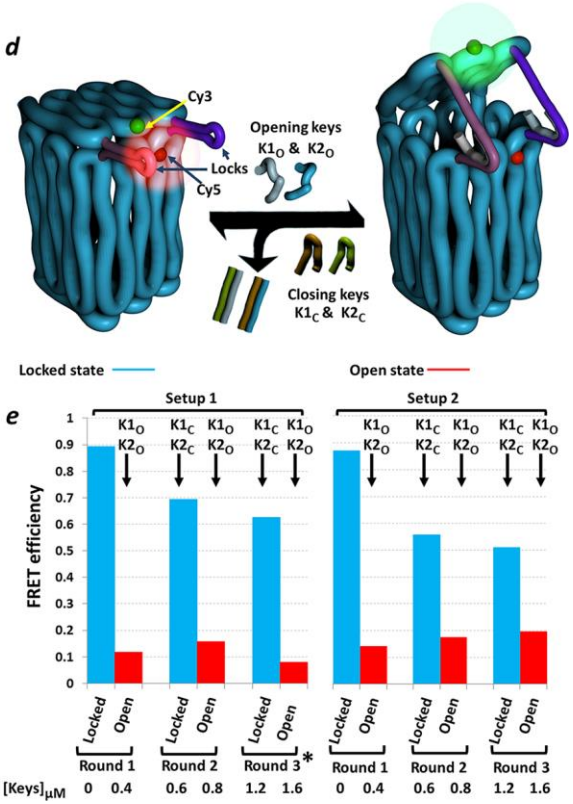
Chem. Soc. Rev., **2015**, 44, 3036

3D DNA Box Origami





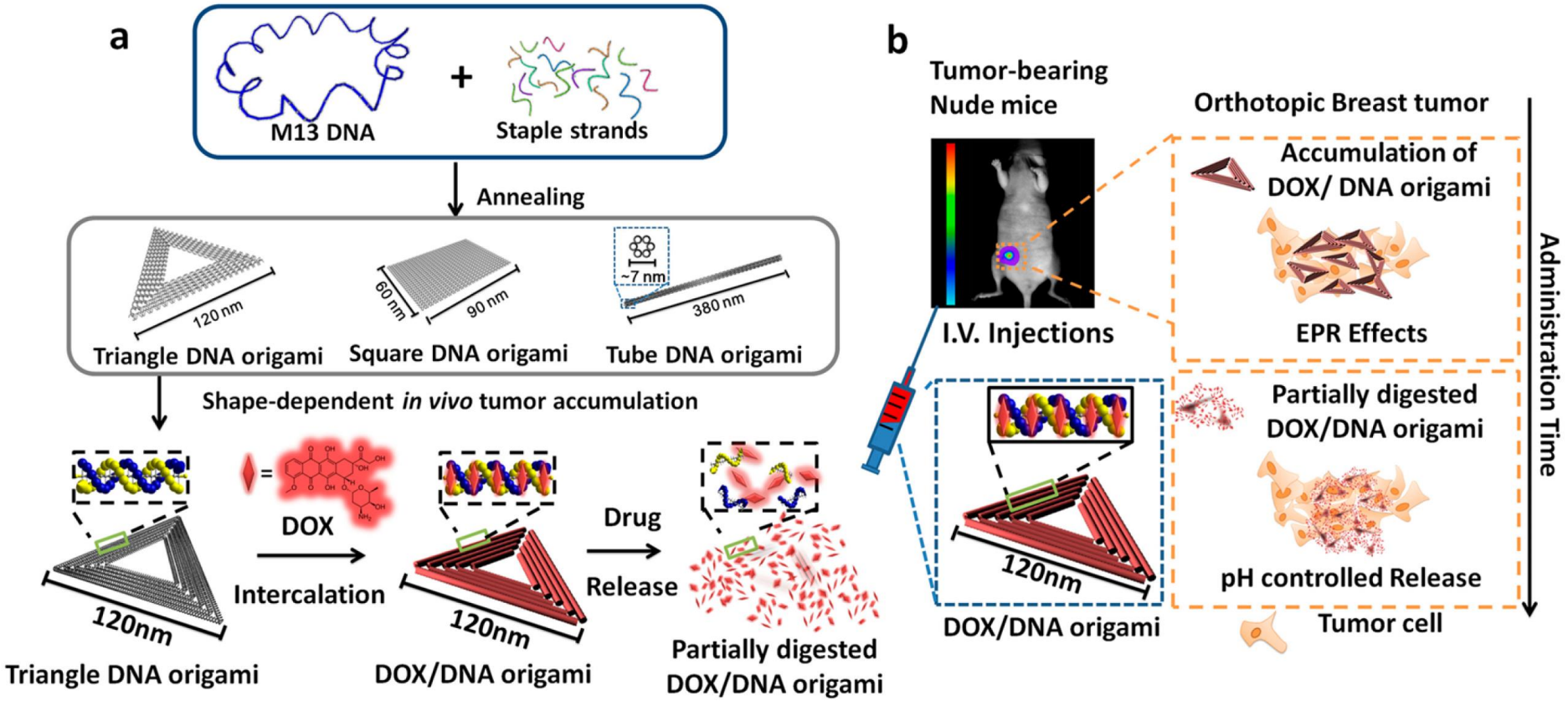




4 Zeptoliters Switchable
3D DNA Box Origami

ACS Nano, **2012**, *6*, 11, 10050

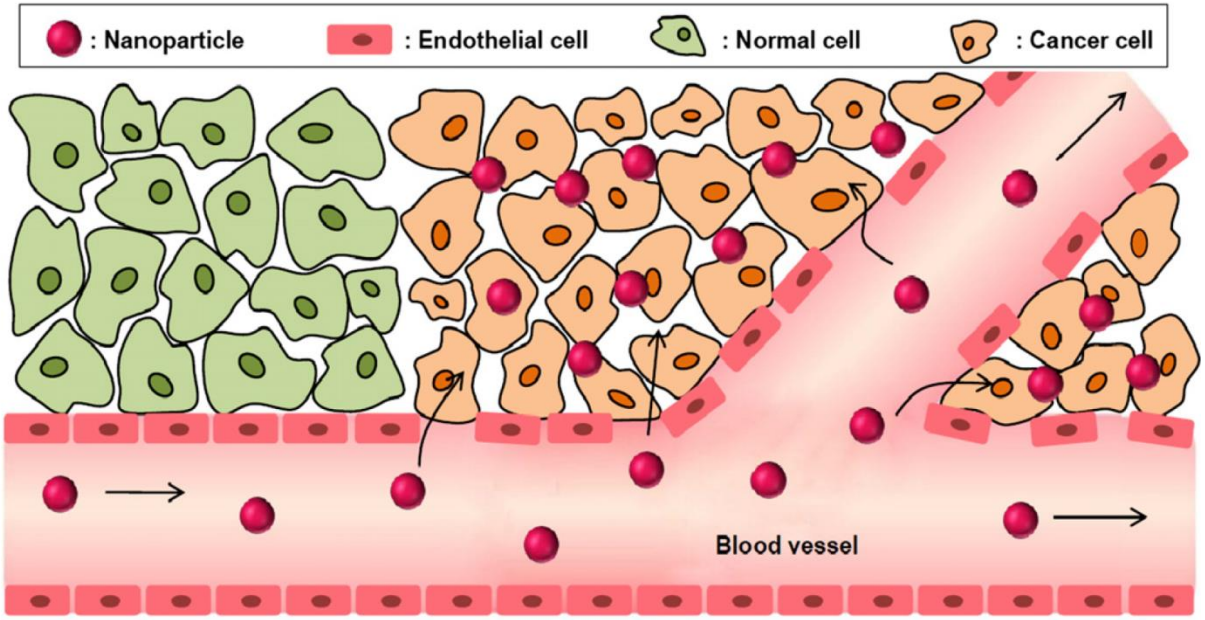
DNA origami as a drug delivery vehicle



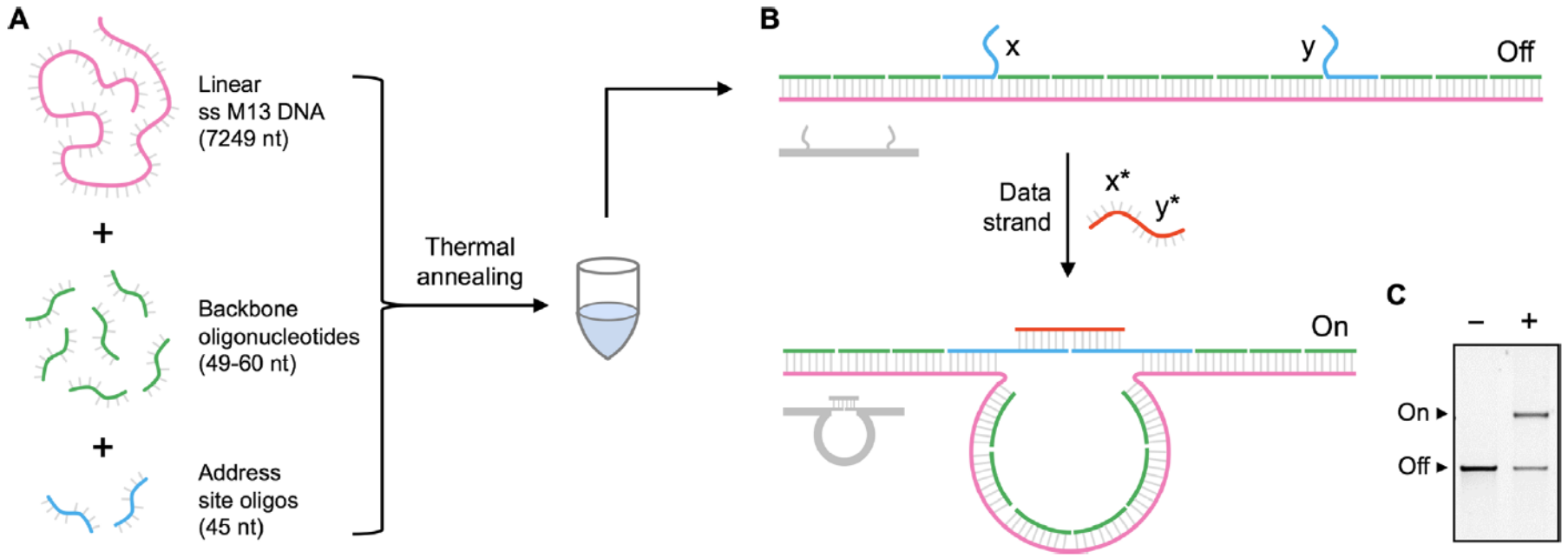
ACS Nano, **2014**, *8* (7), pp 6633–6643

Enhanced permeability and retention (EPR) effect

- In most cases, endothelial cells are tightly bounded to each other and limit the penetration of cells
- Significant uptake of NPs can occur in tissues with a leaky blood vasculature (e.g. tumor) → called “enhanced permeability and retention (EPR)” effect
- EPR effect is the most popular strategy for ***passive tumor targeting*** method
- Size of typical transvascular pore: 100~200 nm
- The highest accumulation of NP in tumor occurs when NPs ~ 60 nm

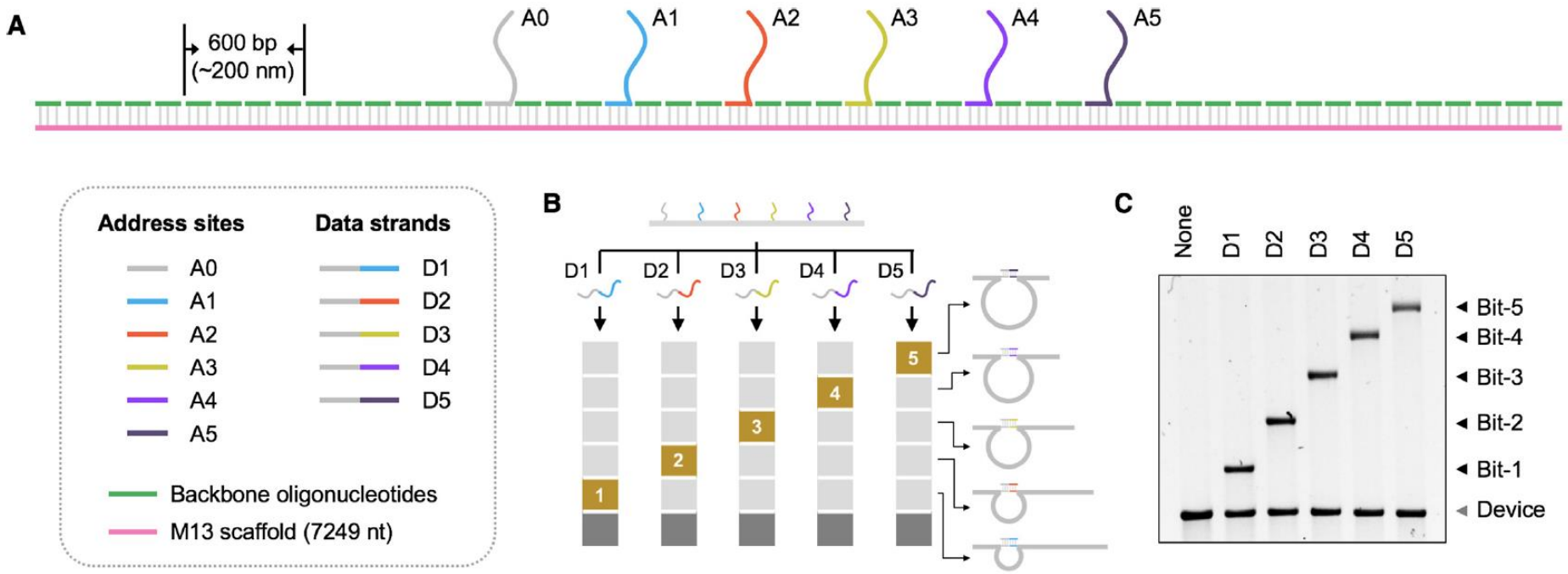


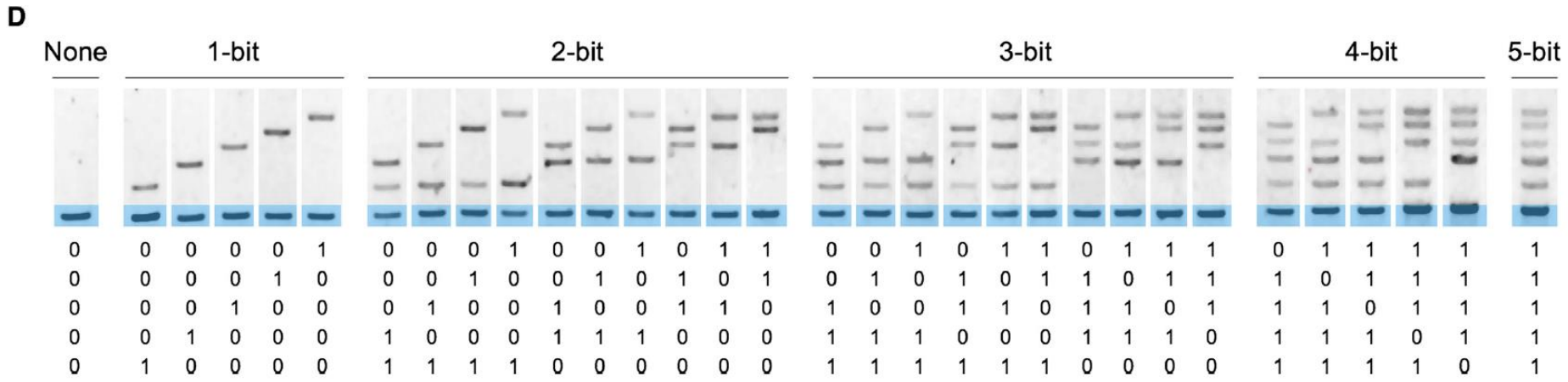
DNA based memory device



Nucleic Acids Research, **2017**, 45 (19), 11459

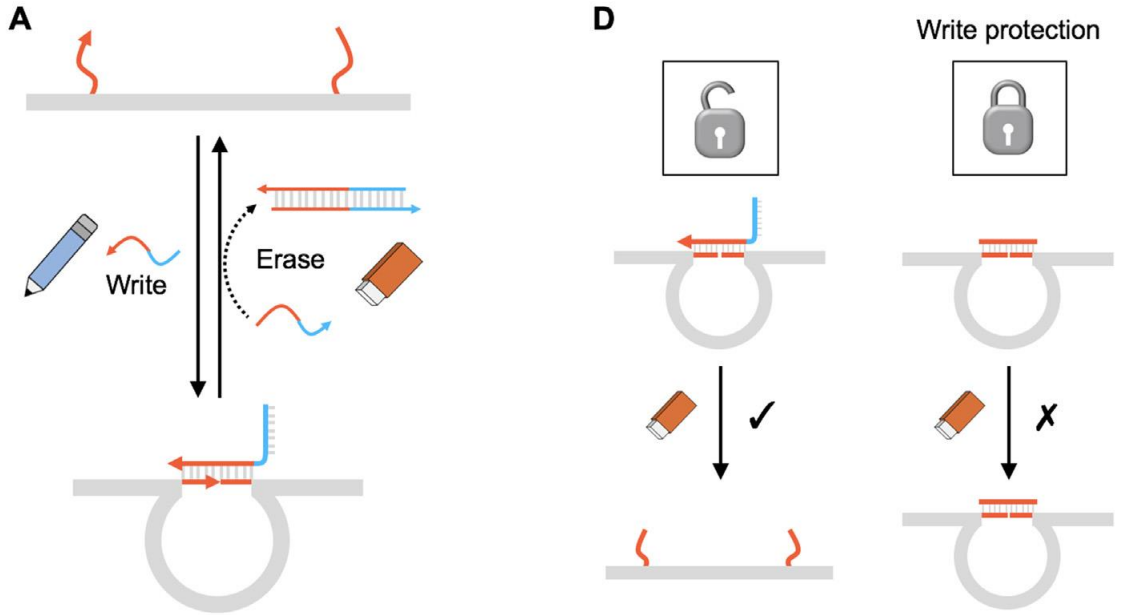
DNA based memory device

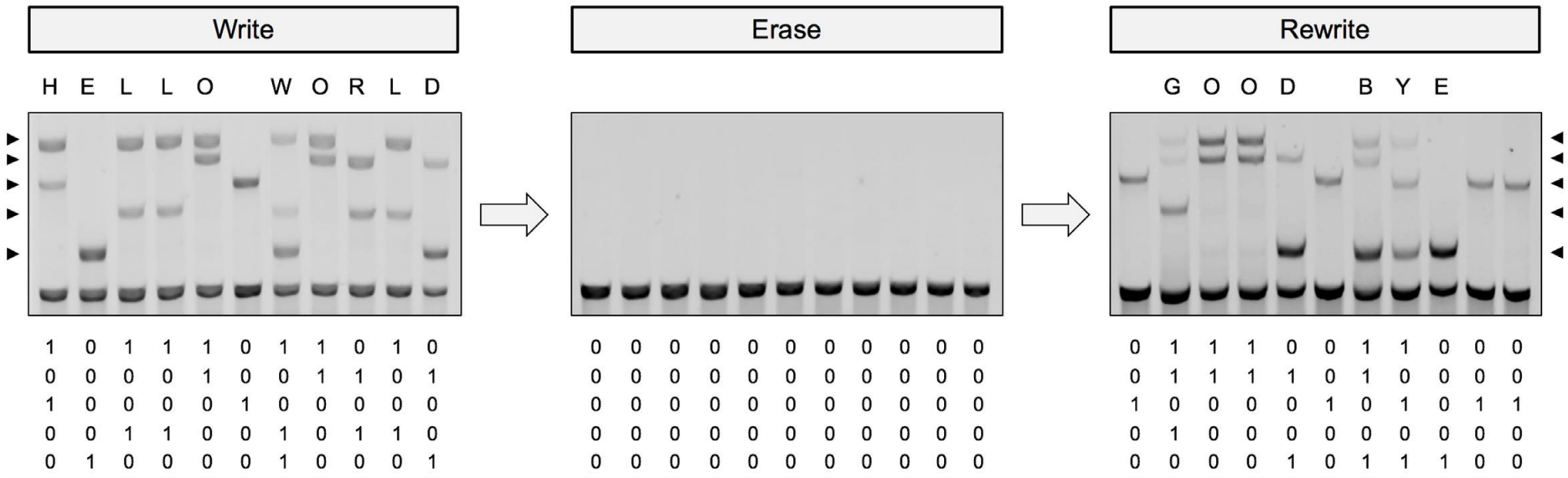




Nucleic Acids Research, **2017**, 45 (19), 11459

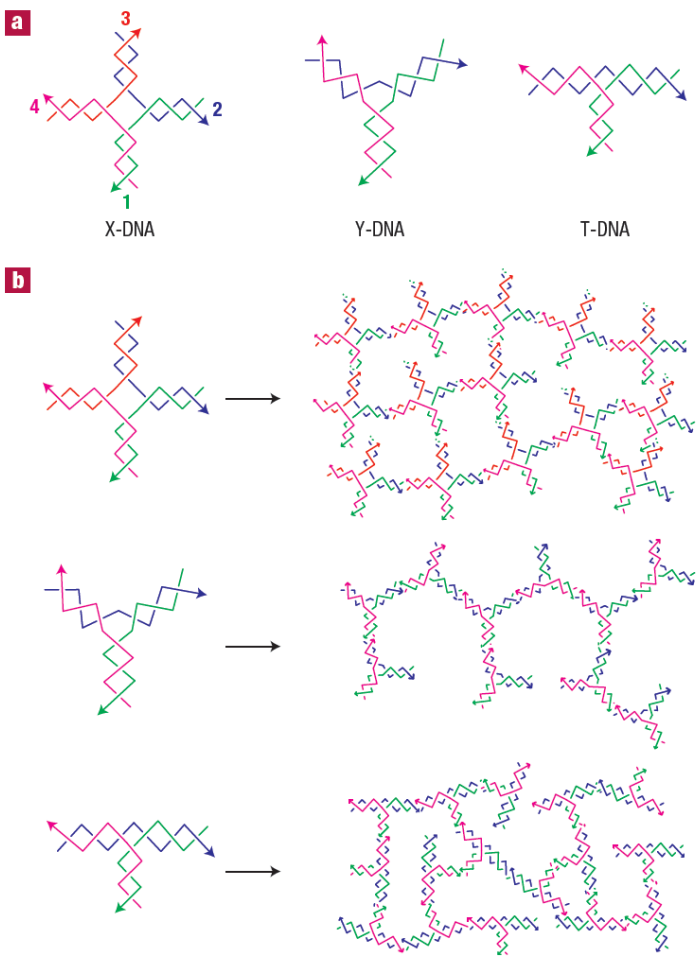
DNA based memory device

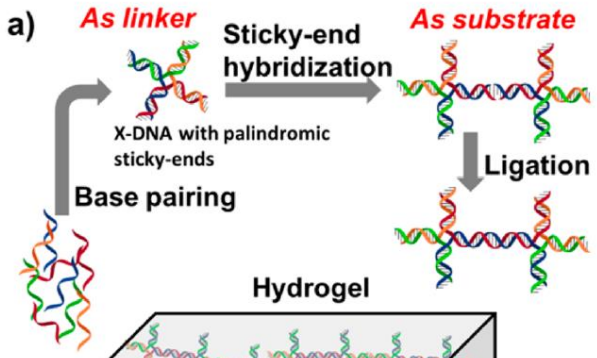


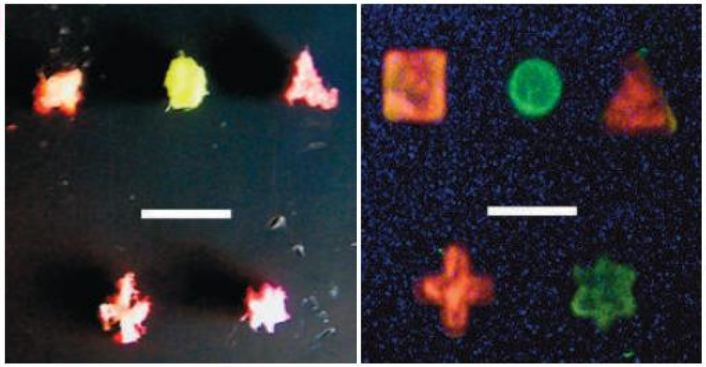


Nucleic Acids Research, **2017**, 45 (19), 11459

DNA Gels

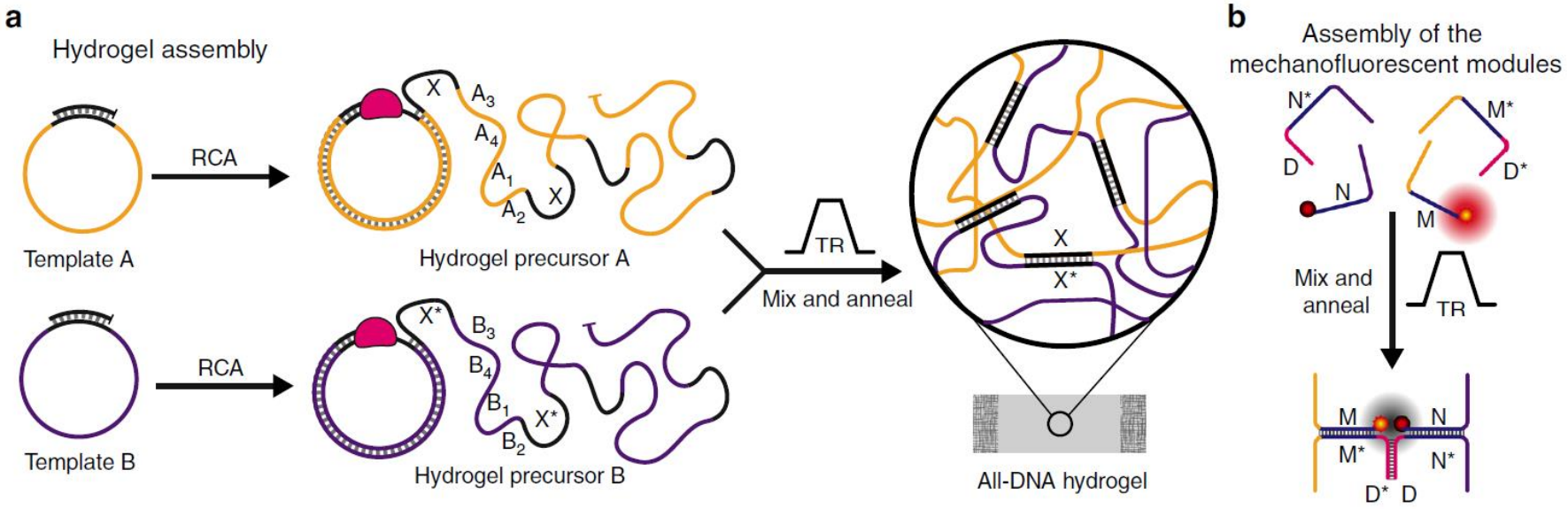


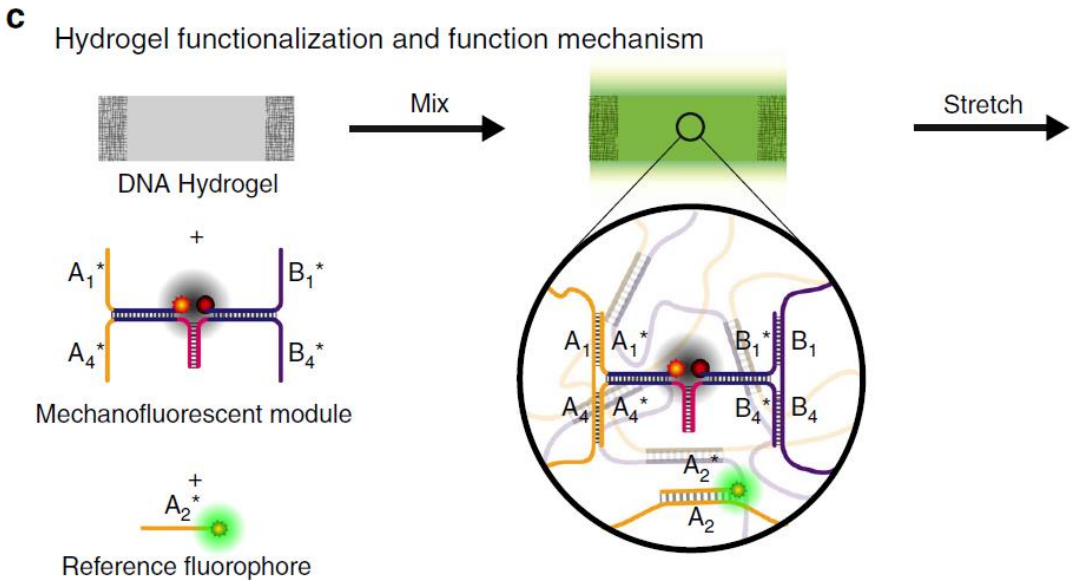


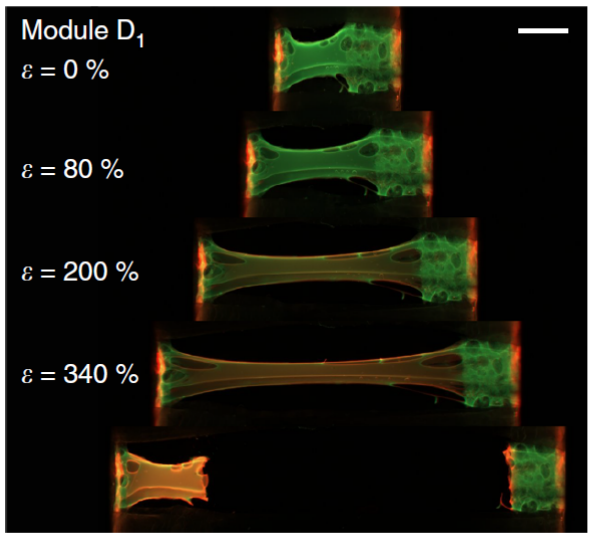


SH Um *et al.*, *Nature Materials*, **2006**, 5, 797

DNA gel-based mechano-sensor



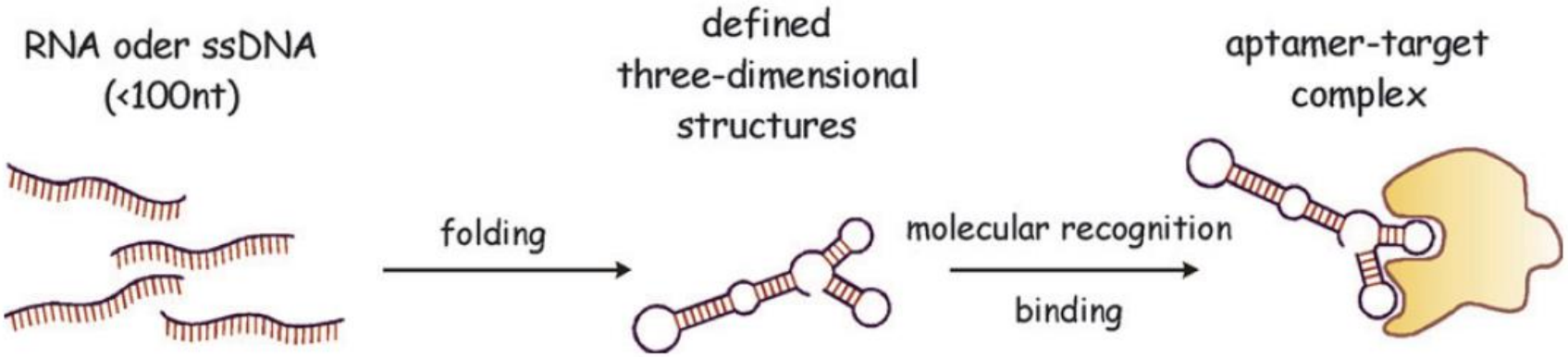




Nature Commun. **2019**, 10, 528

Aptamers: nucleic acid version of antibodies

Aptamer ["*aptus*"-fit (Latin); "*meros*"-region (Greek)]:
short single-stranded oligonucleic acid (ssDNA or RNA) that can bind to specific target molecule



"Chemical antibodies" with broad range of target molecules

- ions
- small molecules
- proteins
- whole organisms (cells)

Binding mechanism
- Induced fit
- Structure compatibility
- Electrostatic interactions
- Hydrogen bonds

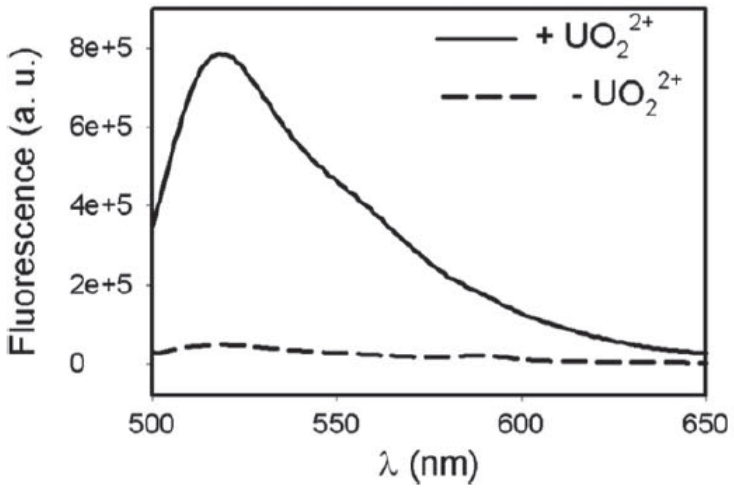
R. Stoltenburg et al., Biomolecular Engineering 24 (2007) 381

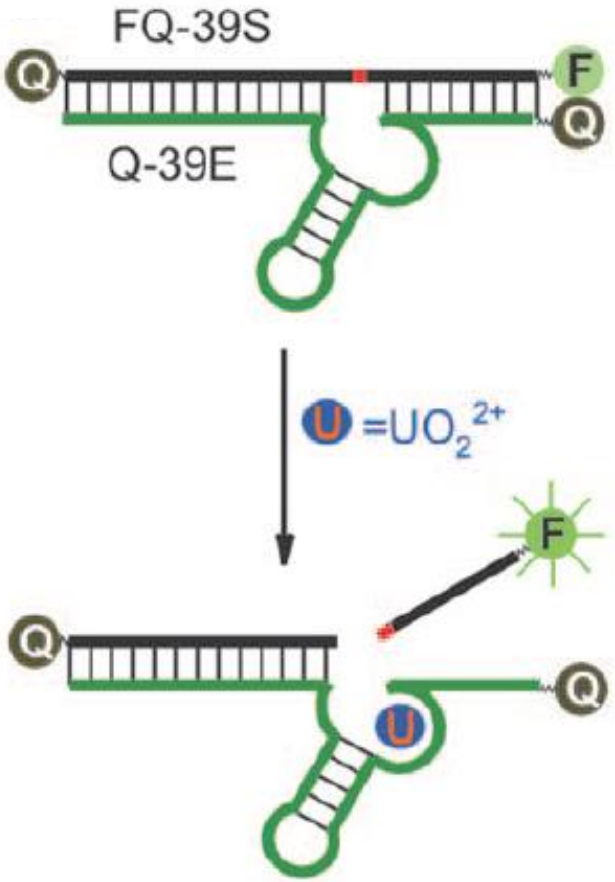
Aptamers

Partial list of targets with selected aptamers

Metal ions	K(I), Mg(II), Pb(II), Zn(II), Hg(II), UO_2(II)
Organic dyes	Malachite green, Cibacron blue, Reactive green 19
Small molecules	Ricin toxin, Cocaine, Dopamine
Nucleotides and derivatives	Adenine, Adenosine/ATP, Guanosine, Xanthine
Nucleic acids	TAR RNA element of HIV-1, Yeast phenylalanine *t*RNA, *E.coli* 5S RNA
Cofactors	Coenzyme A, FAD, NAD
Amino acids	L-Arginine, L-Tyrosinamide, L-Histidine, D-Tryptophan
Carbohydrates	Cellobiose, Chitin, Sephadex
Antibiotics	Streptomycin, Viomycin
Peptides and proteins	T4 DNA polymerase, a-Thrombin, Immunglobulin E, Streptavidin
Intact viral particles	Rous sarcoma virus
Pathogenic bacteria	Anthrax spores
Complex structures	Ribosomes/ribosomal protein S1, Differentiated PC12 cells, Leukemia cells CCRF-CEM
⋮	⋮

Uranyl (UO_2^{2+}) fluorescent biosensors

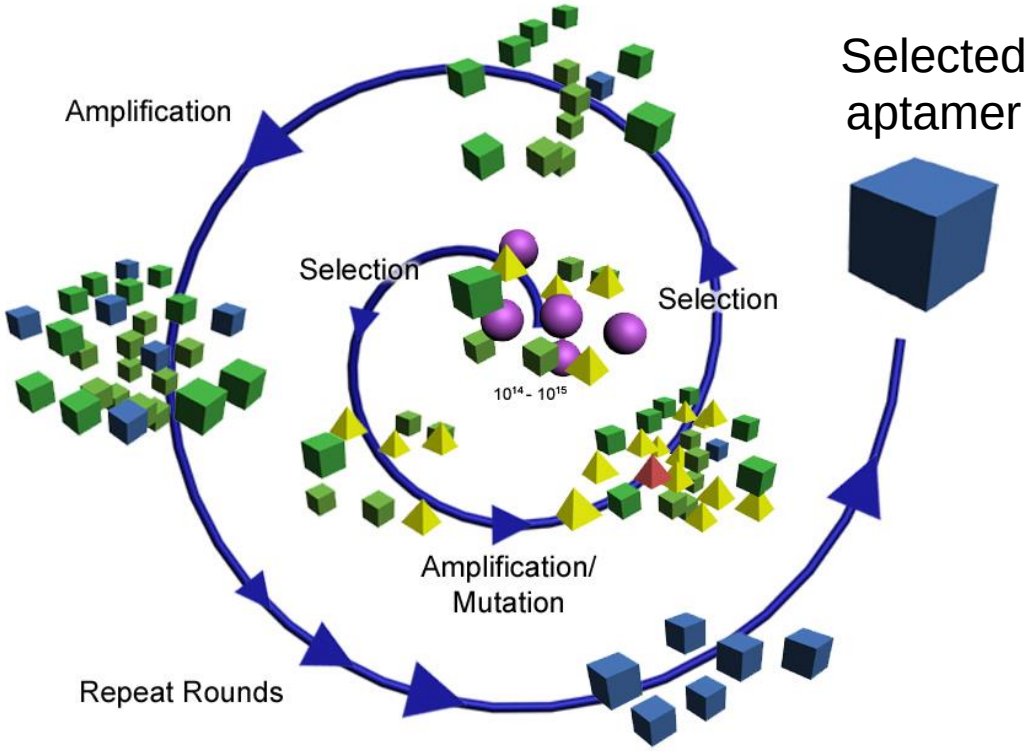




PNAS **2007** *104 (7)* 2056-2061

Selection of aptamers

Systematic Evolution of Ligands by Exponential Enrichment (SELEX)



- Process to find nucleic acid with the highest affinity and selectivity to target molecule
- Start with random sequence of nucleic acid
- 10-15 rounds of SELEX need to be repeated