DNA-based (nano)technologies

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Outline

I. DNA molecular structure and properties
- *DNA and RNA chemical structures*
- *Biological functions of nucleic acids*
- *DNA (un)stability*
- *DNA synthesis (chemical and PCR-based)*

II. Design of new functionalities for DNA
- *Few words on biosensors and biochips*
- *Aptamers*
- *Biosensing with aptamers*
- *Data storage with DNA*

III. DNA as a nanometric tunable object
- *Seeman's work*
- *DNA origamis, structures & design*
- *DNA based origamis for sensing*
- *DNA bricks*
- *DNA machines*
- *DNA multi-enzyme catalysts*

IV. Some work completed in Grenoble
- *DNA based nano-electronics*

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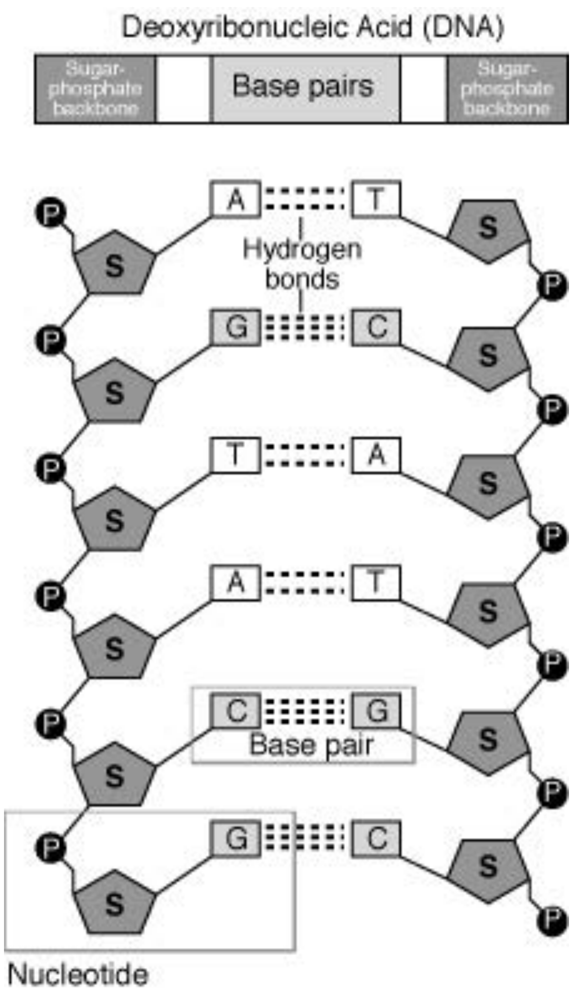
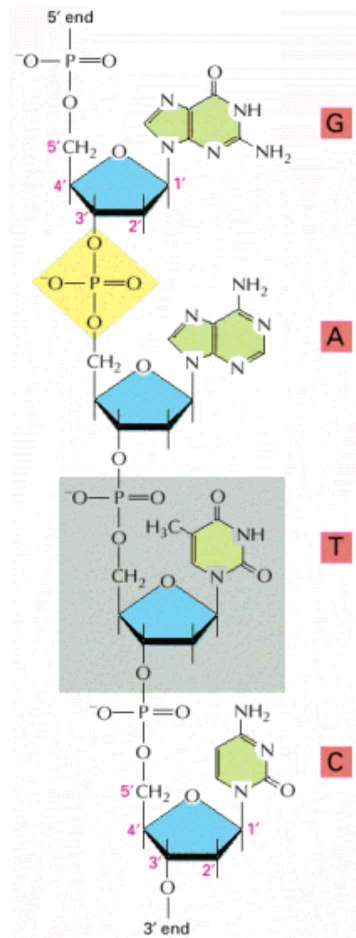
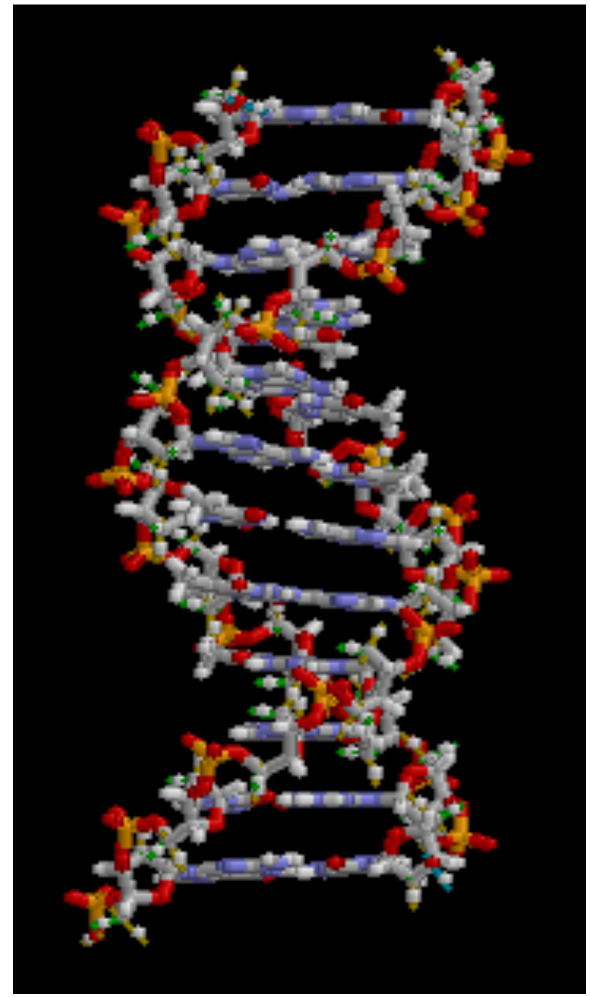
DNA, nucleotides and nucleotides

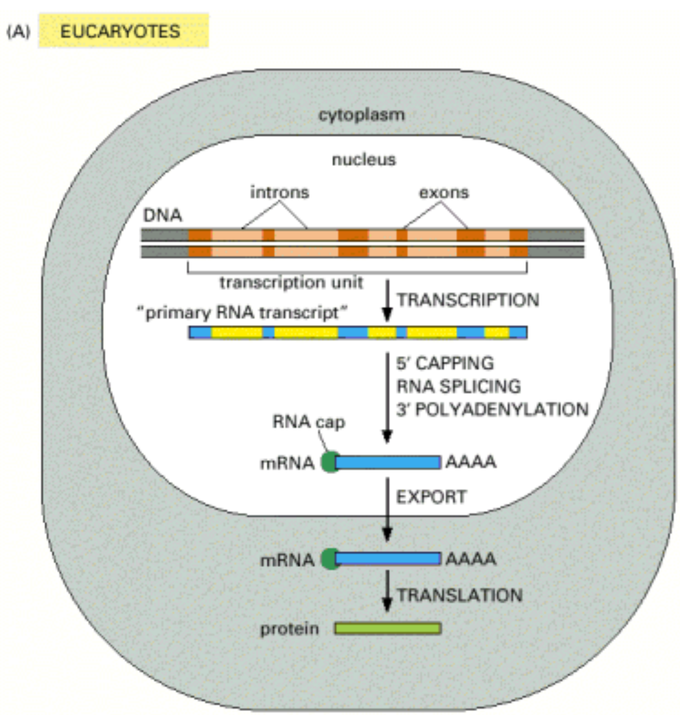


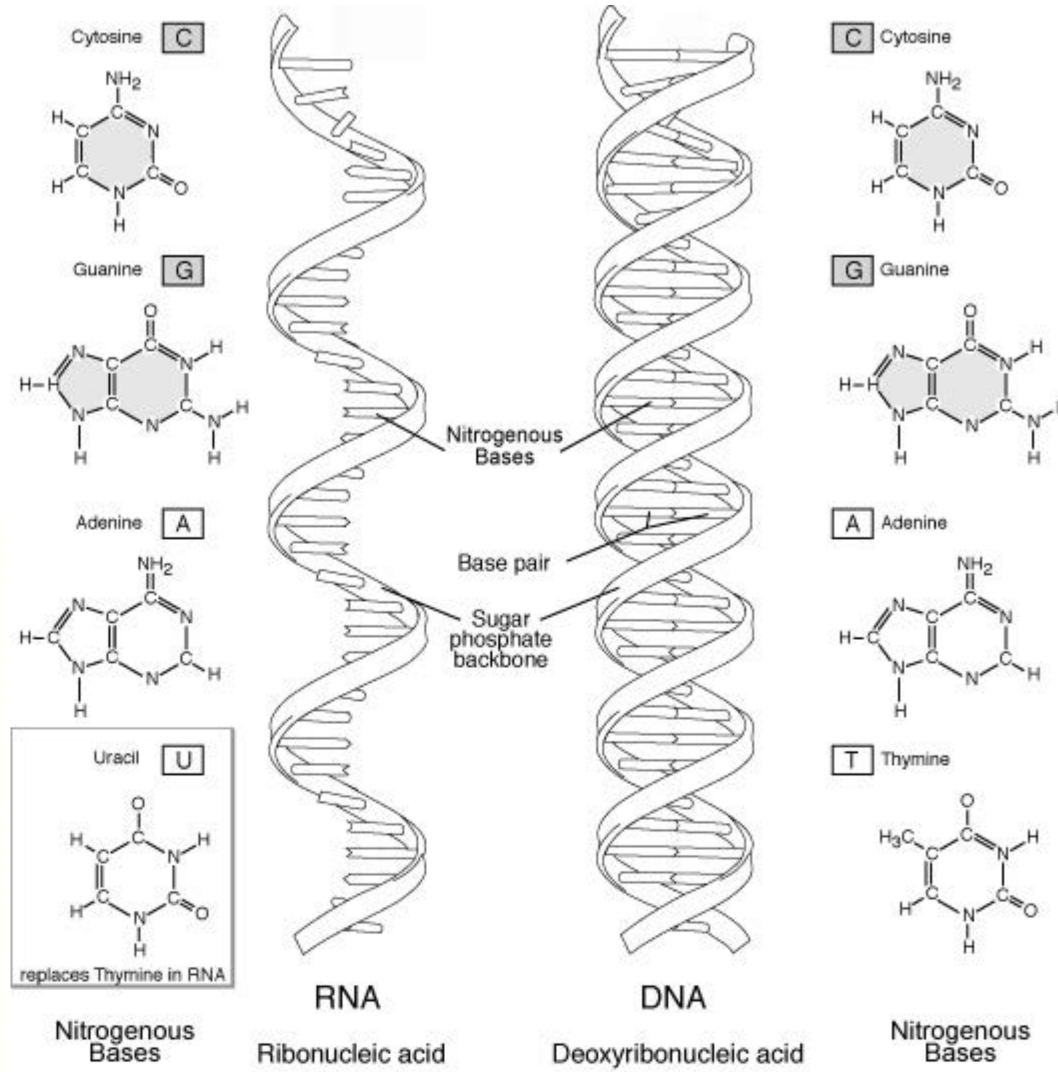




RNA structure and functions

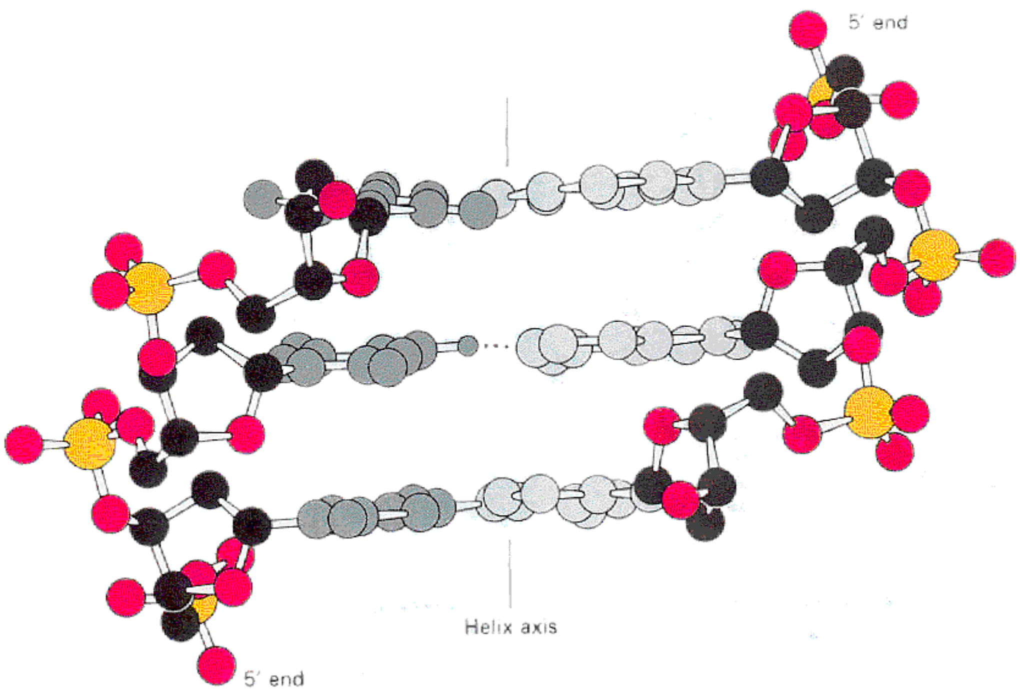
RNA looks like DNA but:
-single strand
-Uracile
-biological and chemical unstability
-many different functions!

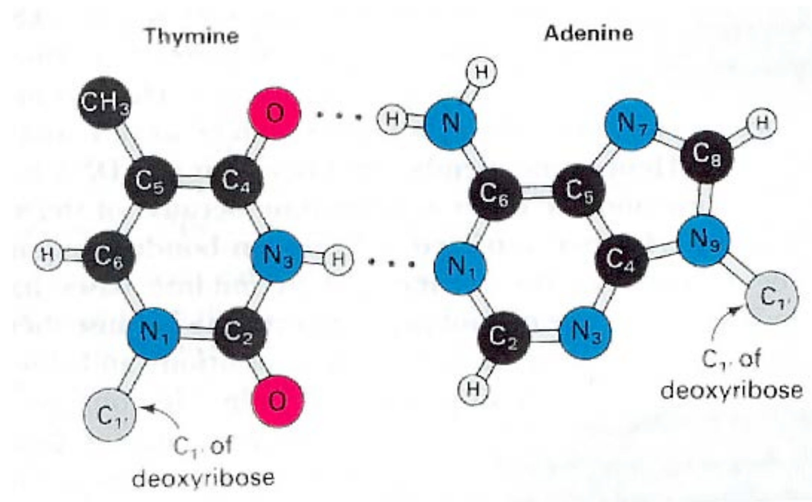


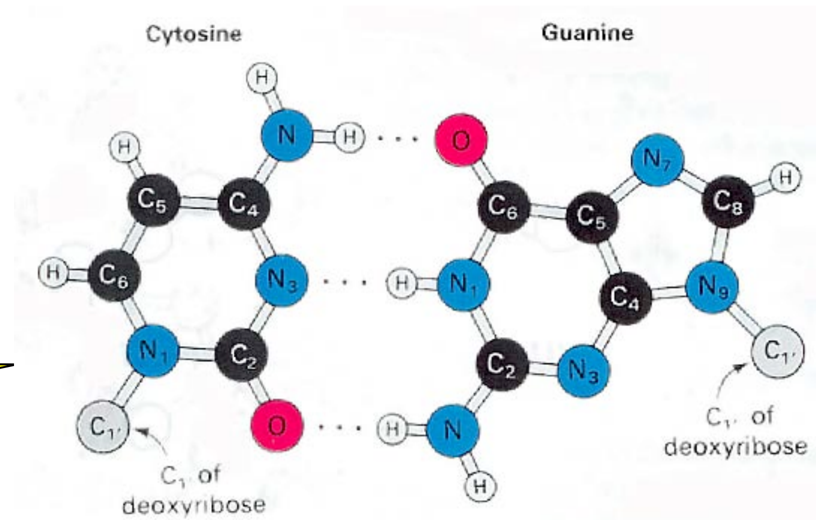


RNA may have different functions (transfert, ribosomal, expression regulation, interference)

Base pairing in a DNA double helix

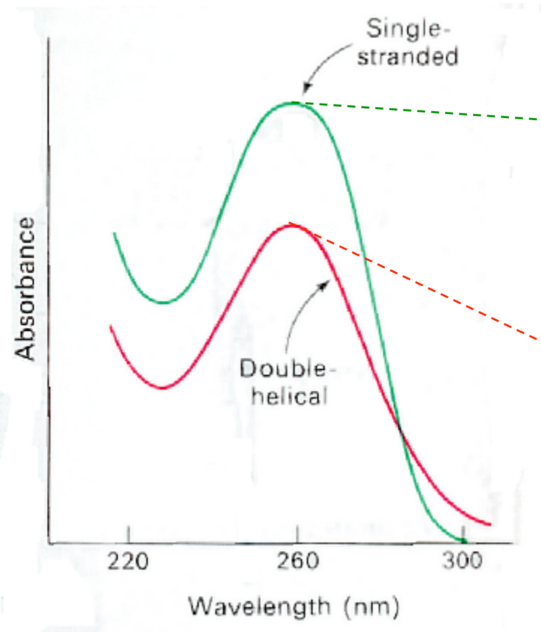




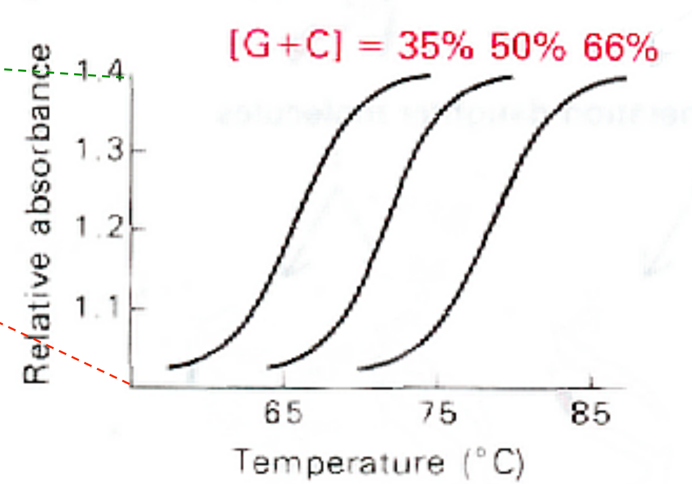


This is fundamental!!

Melting of a double stranded DNA

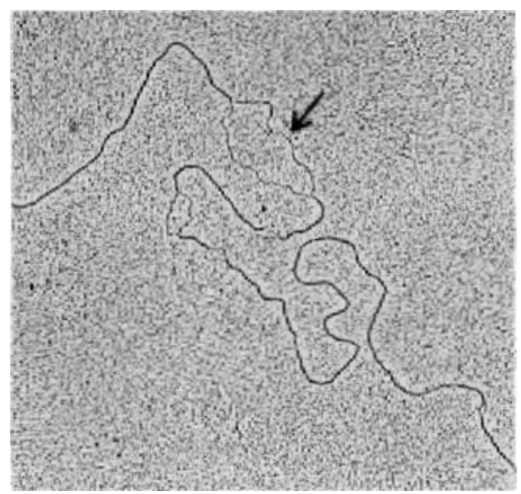


thermal denaturation



A,T : 2 H bonds
C, G: 3 H bonds

Hypochromism: dsDNA has a lower extinction coefficient than ssDNA or free nucleotides



Alkaline denaturation of a AT rich domain

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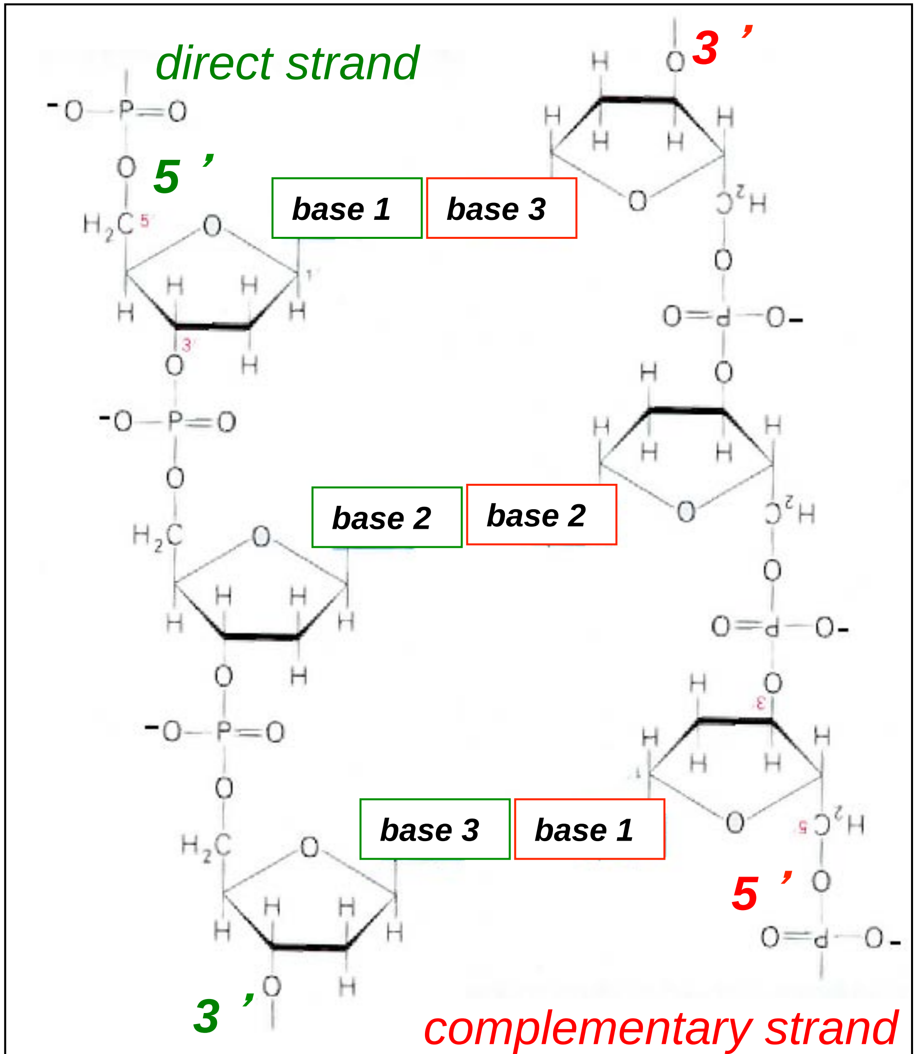
How naming a double stranded DNA?



Naming of a ‘direct’ strand:

$^{5'}$ AACTGGGTCAATTCCG $^{3'}$

Naming of the ‘complementary’ st:

$^{3'}$ TTGACCCAGTTAAGGC $^{5'}$ ou
$^{5'}$ CGGAATTGACCCAGTT $^{3'}$

which is different to:

$^{5'}$ TTGACCCAGTTAAGGC $^{3'}$

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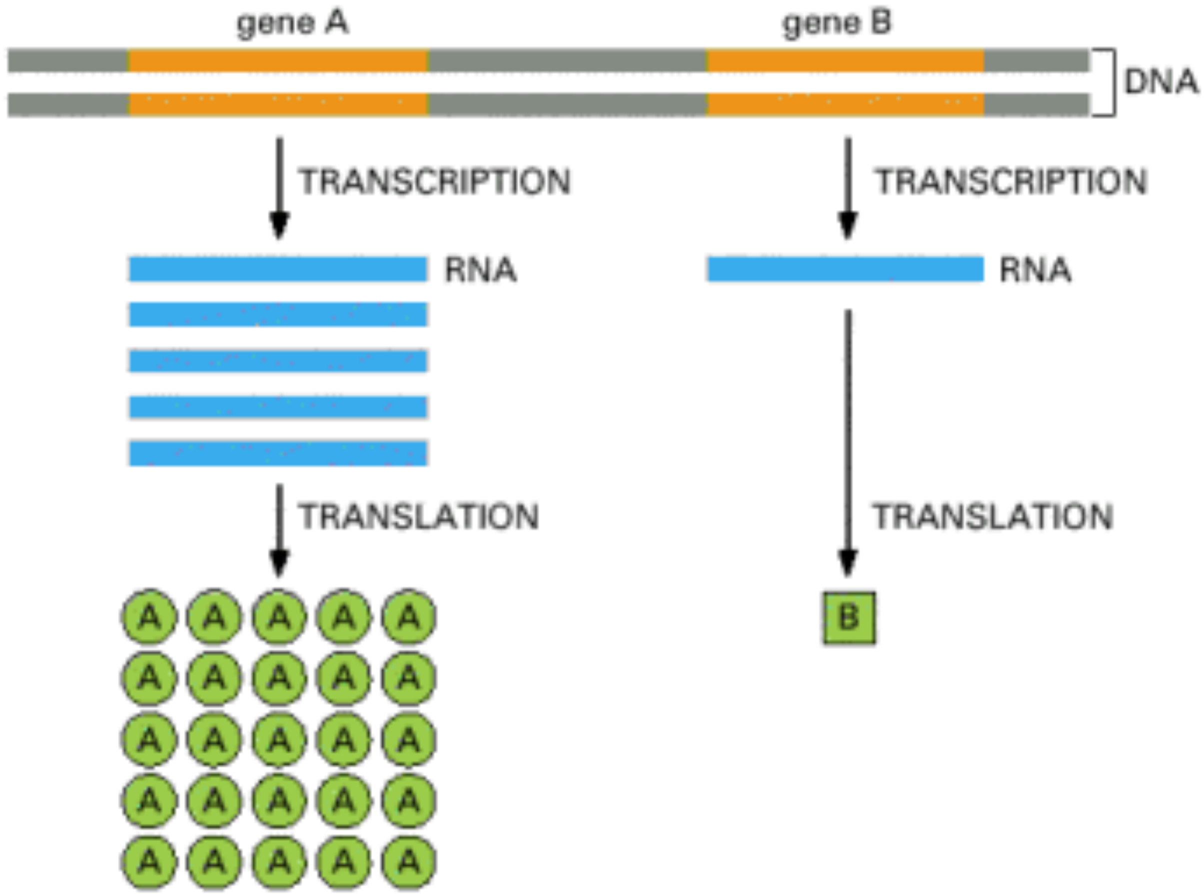
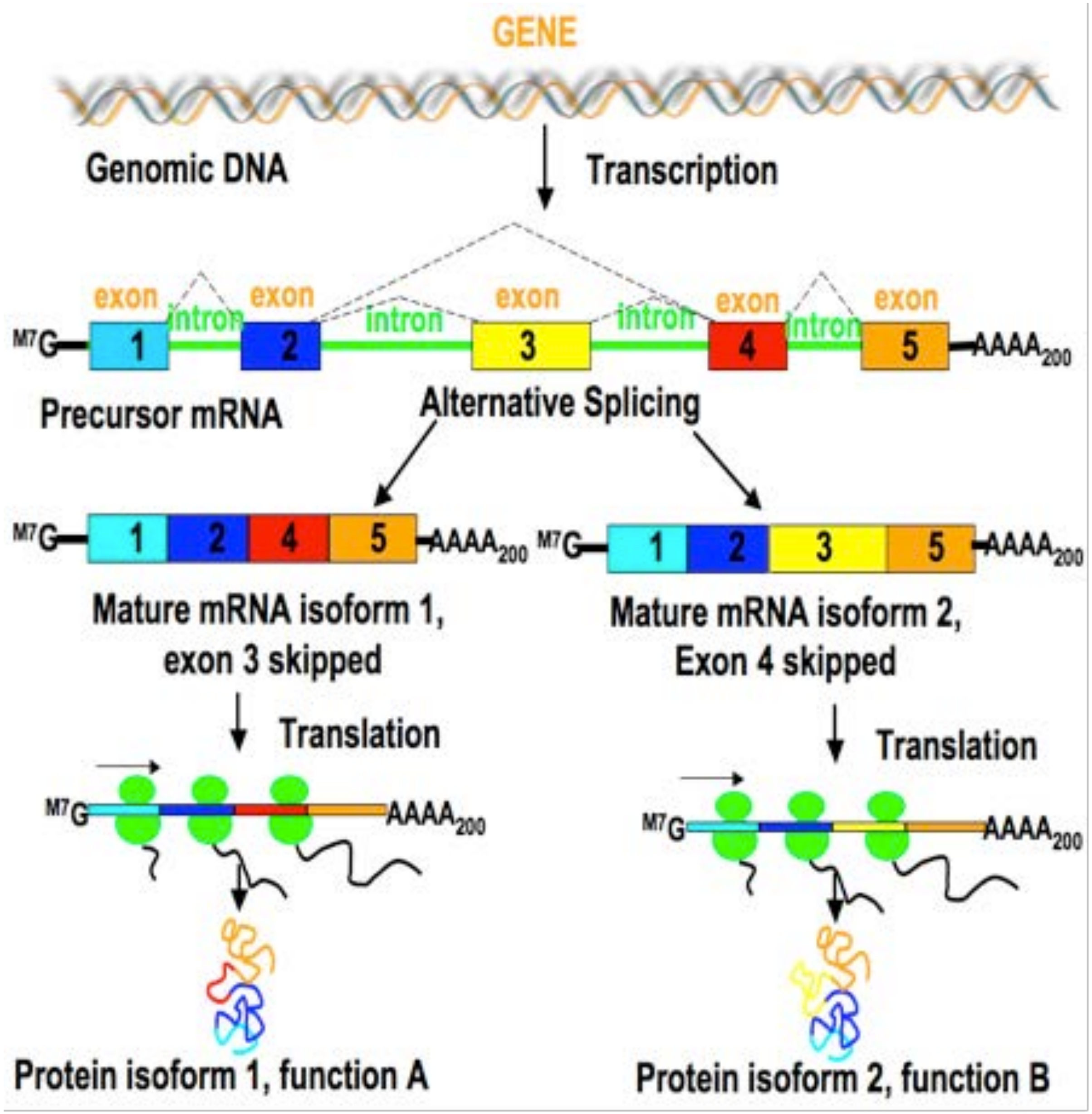
The central dogma in Molecular Biology



Gene structure and function



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POUR L'ÉNERGIE ET LA SANTÉ

Comparison of few genome sizes

ORGANISMES	Genome sizes (paires de bases)		Redondance (% unique copy)	Number of genes
VIRUS:				
SV40	5243			6
phage l	48502			20
phage T2	166000			
vaccinia	190000			240
BACTERIA:				
mycoplasma	$7.6\ 10^{5}$			
Escherichia coli	$4.7\ 10^{6}$			3000
EUCARYOTES:				
Saccharomyces cerevisiae	$1.5\ 10^{7}$	$7\ 10^{4}$	89	6800
Dictyostelium discoideum	$5.4\ 10^{7}$		70	10000
Arabidopsis thaliana	$7.0\ 10^{7}$			11000
Caenorhabitis elegans	$8.0\ 10^{7}$			11000
Drosophila melanogaster	$1.4\ 10^{8}$	$1.9\ 10^{4}$	60	13000
Gallus domesticus	$1.2\ 10^{9}$		80	
Mus musculatus	$2.7\ 10^{9}$	$1.6\ 10^{4}$	70	
Rattus norvegicus	$3.0\ 10^{9}$			
Xenopus laevis	$3.1\ 10^{9}$	$1.8\ 10^{4}$	75	
Homo sapiens	$3.3\ 10^{9}$	$1.6\ 10^{4}$	64	25000
Zea mays	$3.9\ 10^{9}$	$2+2\ 10^{5}$		
Nicotiana tabacum	$4.8\ 10^{9}$			
Bufo bufo	$6.6\ 10^{9}$		20	
Lilium davidii	$4.0\ 10^{10}$		36	

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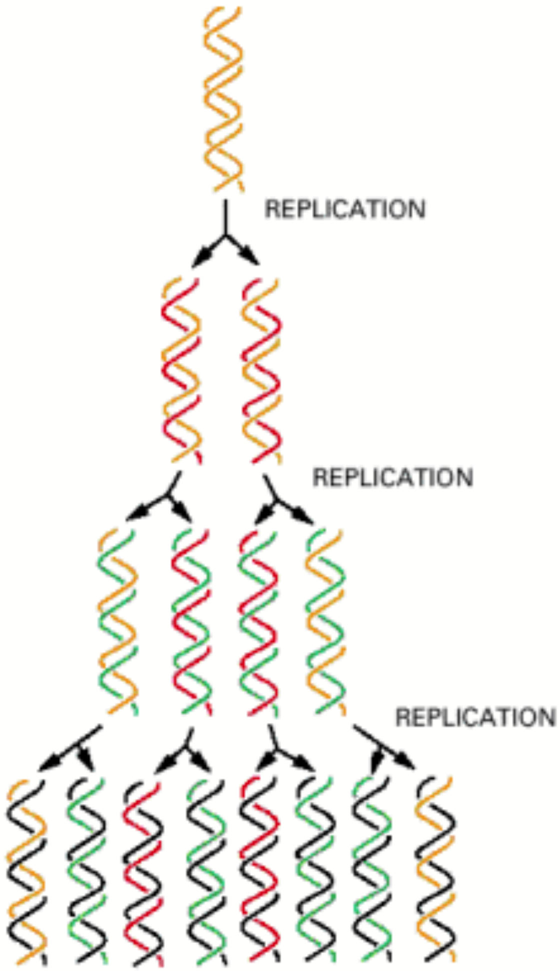
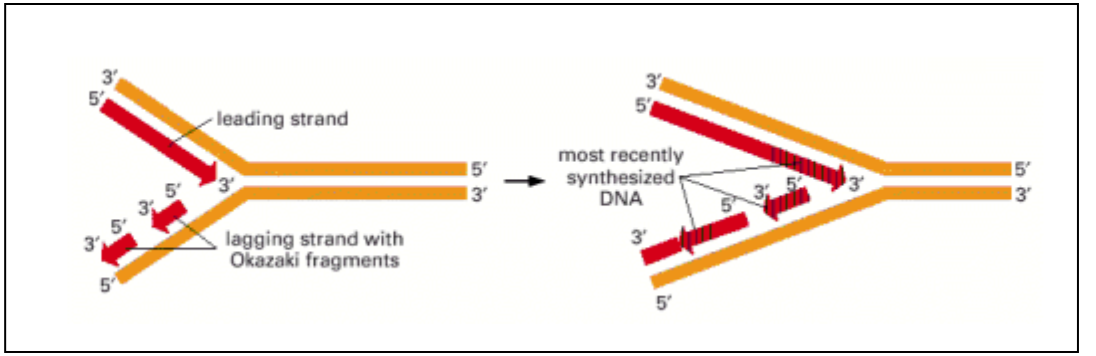
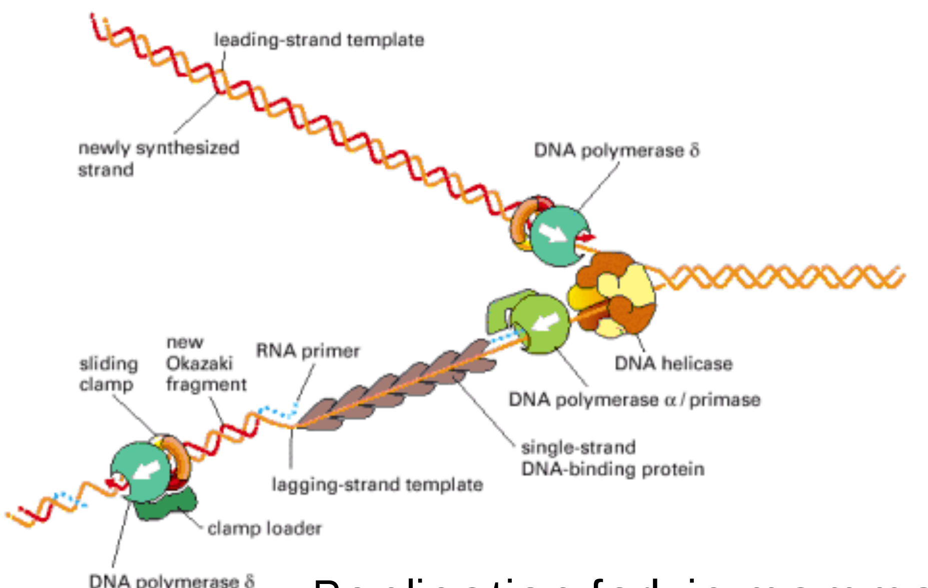
Duplication of DNA and genetic information storage



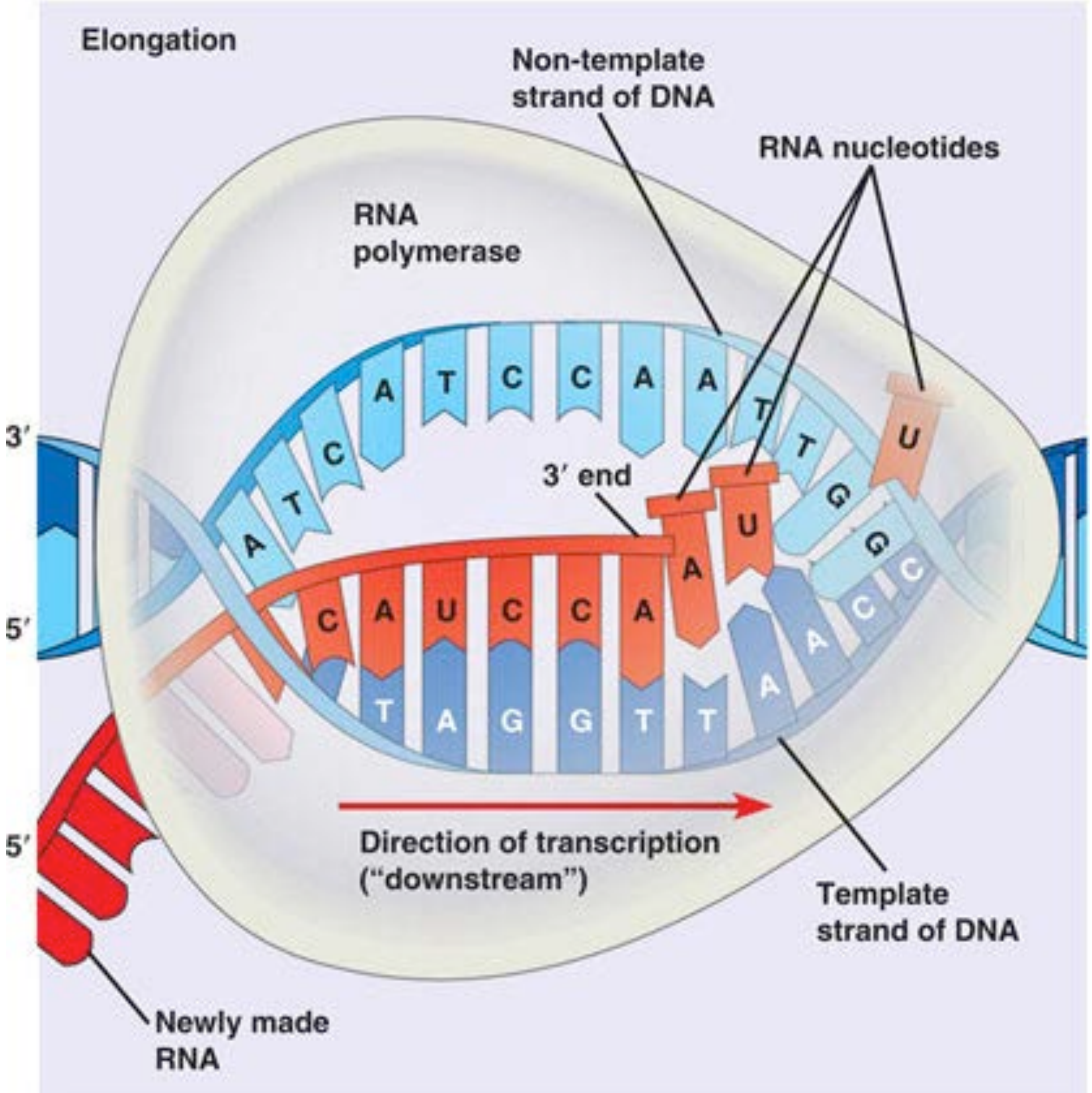
semi-replicative process





Replication fork in mammals

Gene transcription in RNA



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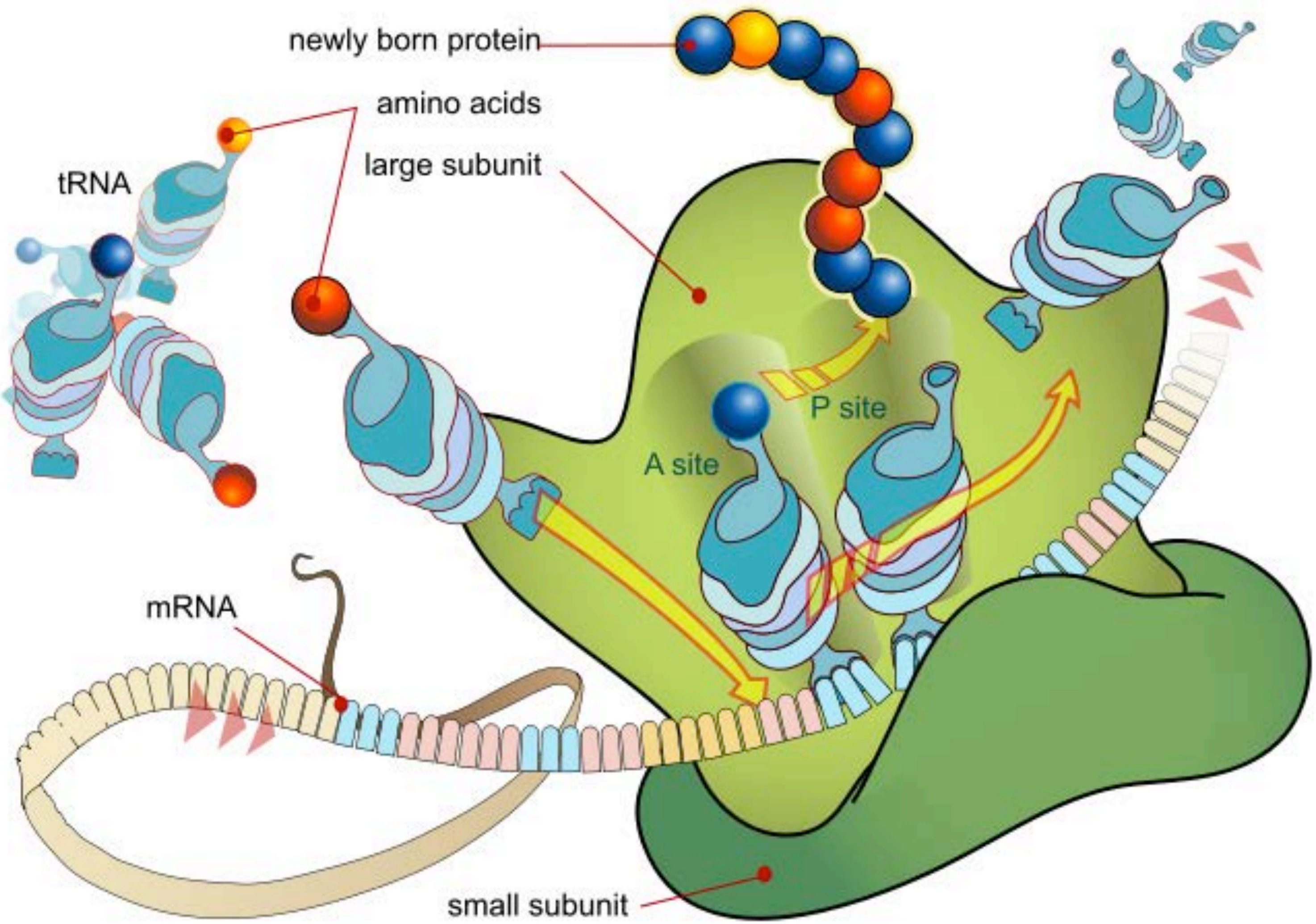
Traduction of mRNA into proteins



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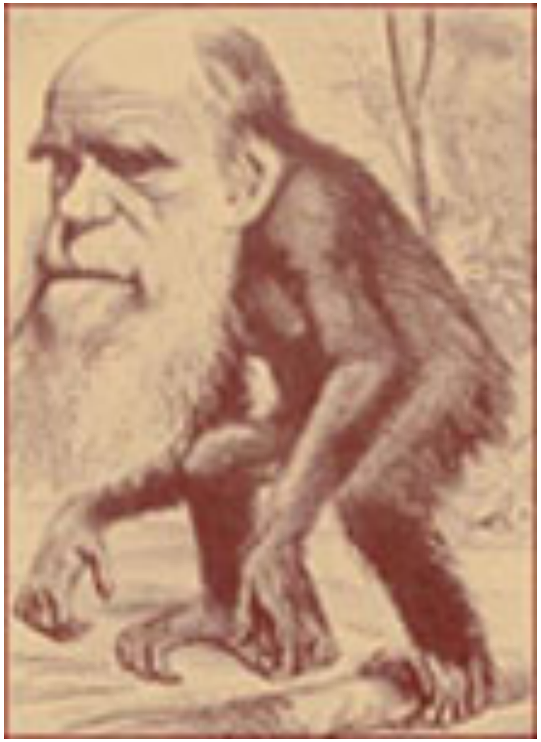
Nucleic acid unstability - Darwinian origin of life



At the very beginning (few billions years): Only some small organic molecules (such as urea), then more complex molecules: amino-acids, RNA then lipids, vesicles and eventually cells (Procaryotes)

Evolution from simple systems, unicellular to more and more complex objects

Principles of Darwinism:
-Evolution is ineluctable
-Natural selection generates evolution
-Possible thanks to genetic variability

Darwin argued that since offspring tend to vary slightly from their parents, mutations that make an organism better adapted to its environment will be encouraged and developed by the pressures of natural selection, leading to the evolution of new species differing widely from one another and from their common ancestors. Darwinism was later developed by the findings of Mendelian genetics (see **neo-Darwinian**).

Phylogenesis

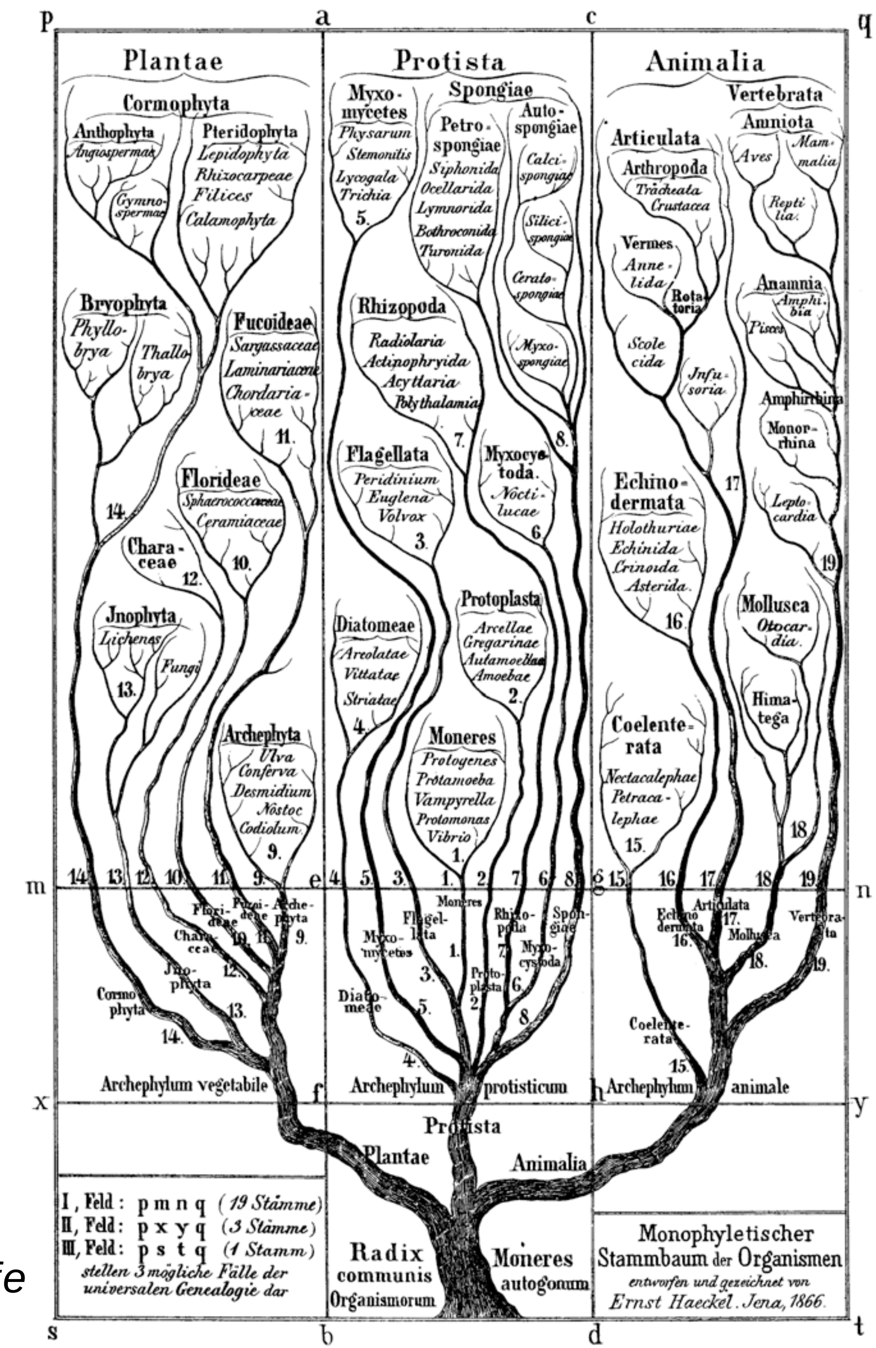
- Molecular phylogeny builds the story of evolution for the living organisms

- <u>The dogma:</u>

« the closer are two living organisms, the closer are the sequences of their biomolecules (DNA, RNA and proteins).»

- <u>Most used sequences:</u>

rRNA >> DNA > proteins



Tree of Life

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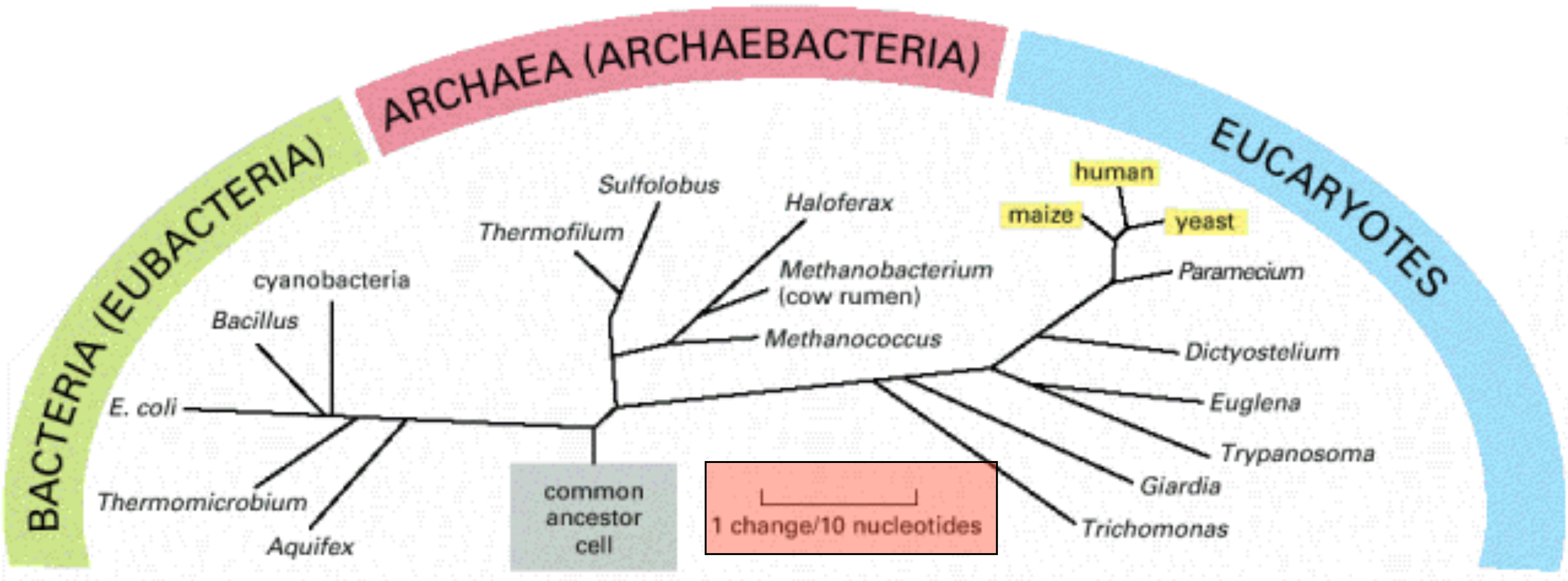
The branches of the Tree of Life



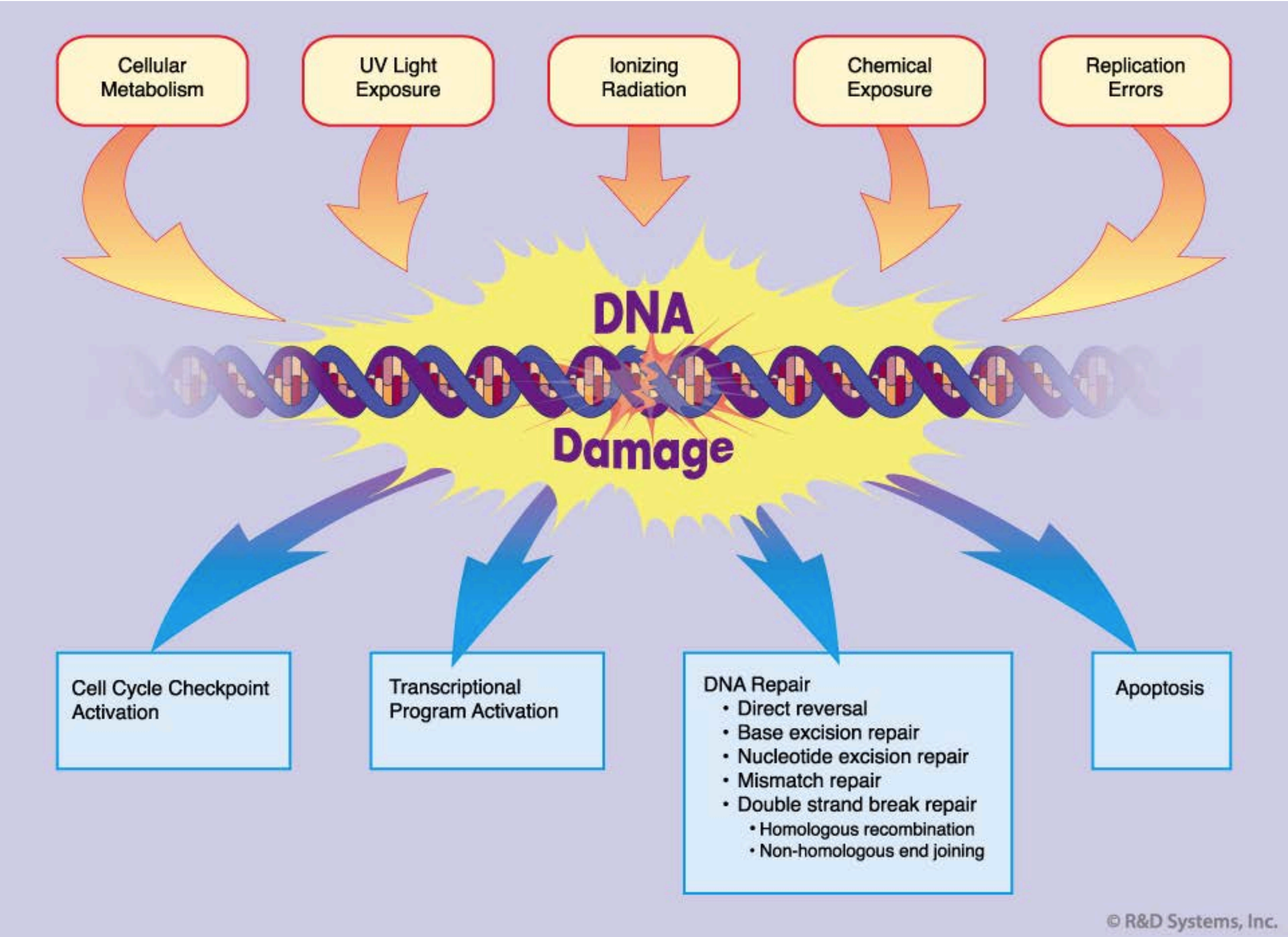
Procaryotes (Eubacteria et Archeobacterai) vs Eucaryotes

Univellular, large variety but only few genes (1000-4000), fed with inorganic salts

Unicellular or multicellular organisms
More complex biological objects, DNA stored as chromosomes
Four regna: mycetes, animals, vegetals and protists

Eubacteria vs Archaebacteria

Extreme conditions (temperature, high pressure, salts)


Cellular Metabolism
UV Light Exposure
Ionizing Radiation
Chemical Exposure
Replication Errors
DNA
Damage
Cell Cycle Checkpoint Activation
Transcriptional Program Activation
DNA Repair
• Direct reversal
• Base excision repair
• Nucleotide excision repair
• Mismatch repair
• Double strand break repair
• Homologous recombination
• Non-homologous end joining
Apoptosis
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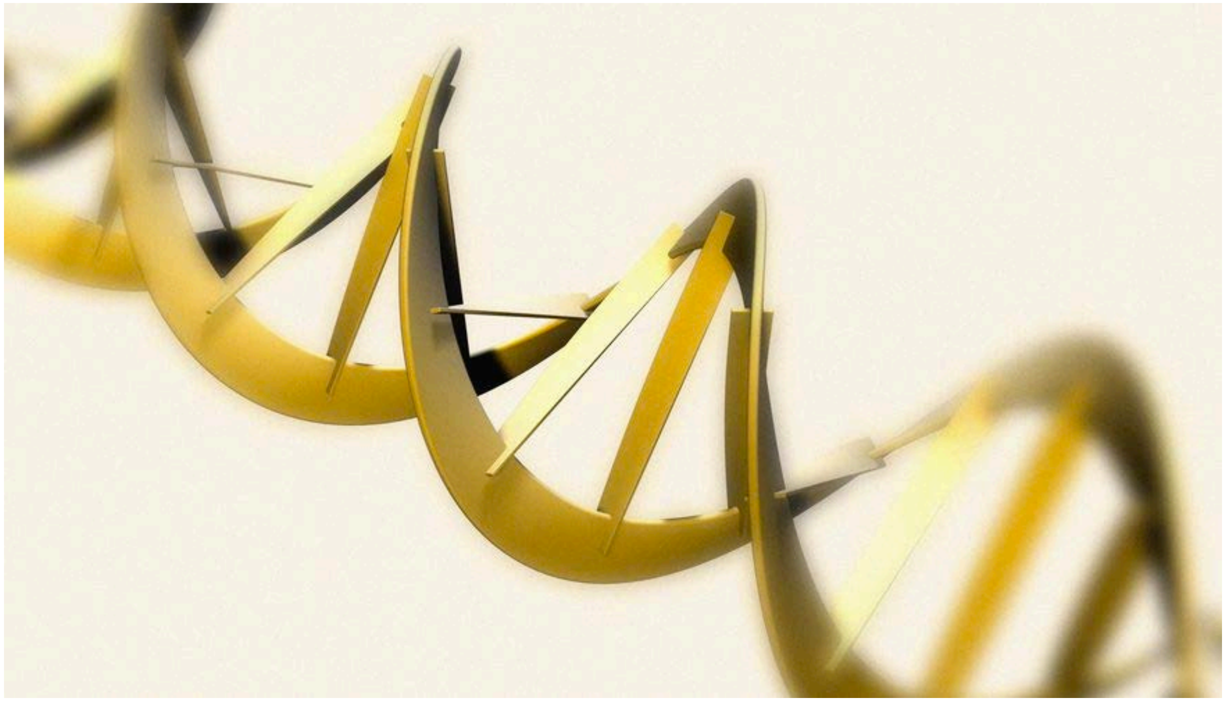
Time and physio-chemical conditions...

... are critical issues for DNA stability over centuries, or millenium.

Otherwise, DNA is a very stable compound on a « human » time scale.

Then DNA can be used as a building block for « non natural » purposes



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DNA solid phase synthesis

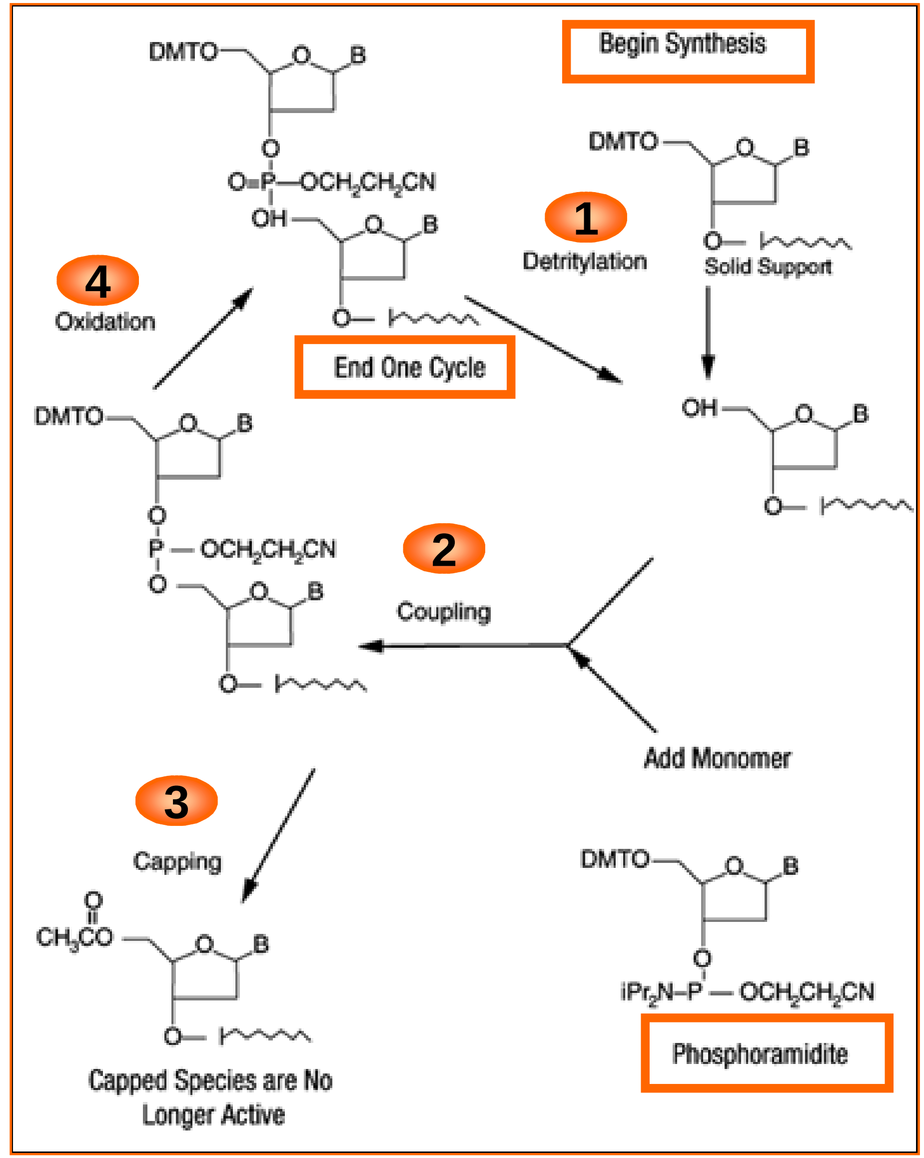
-short fragments (<100 bases)

-RNA and DNA, and NA analogs as well ! All single stranded

-modifications can be incorporated everywhere (fluorescent labeling, biotin, amines, carboxylic acids, thiols, etc)

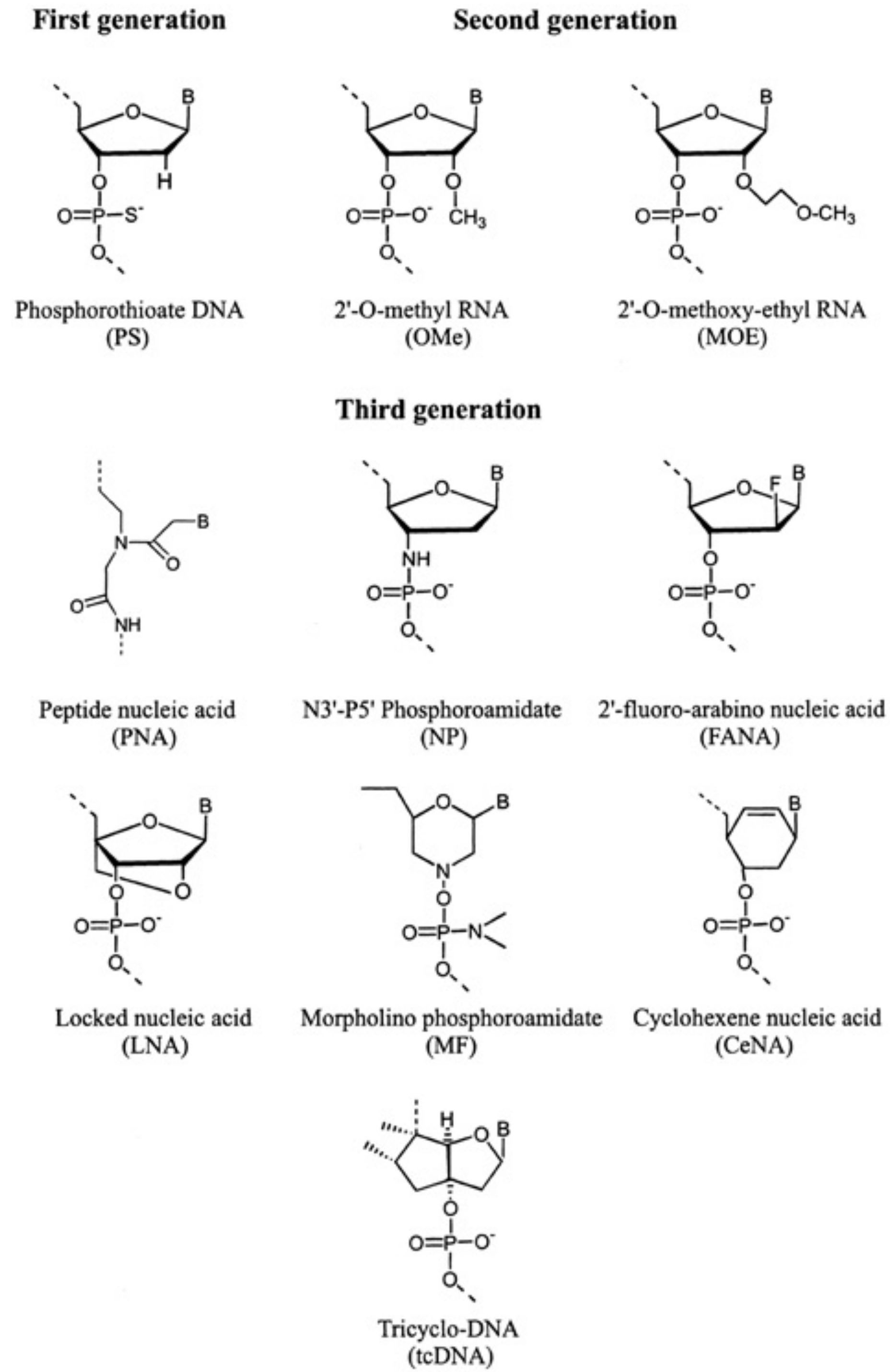
-many suppliers, cheaper and cheaper

-quality control required



DNA synthesis

nucleic acids analogs



DNA PCR-based synthesis

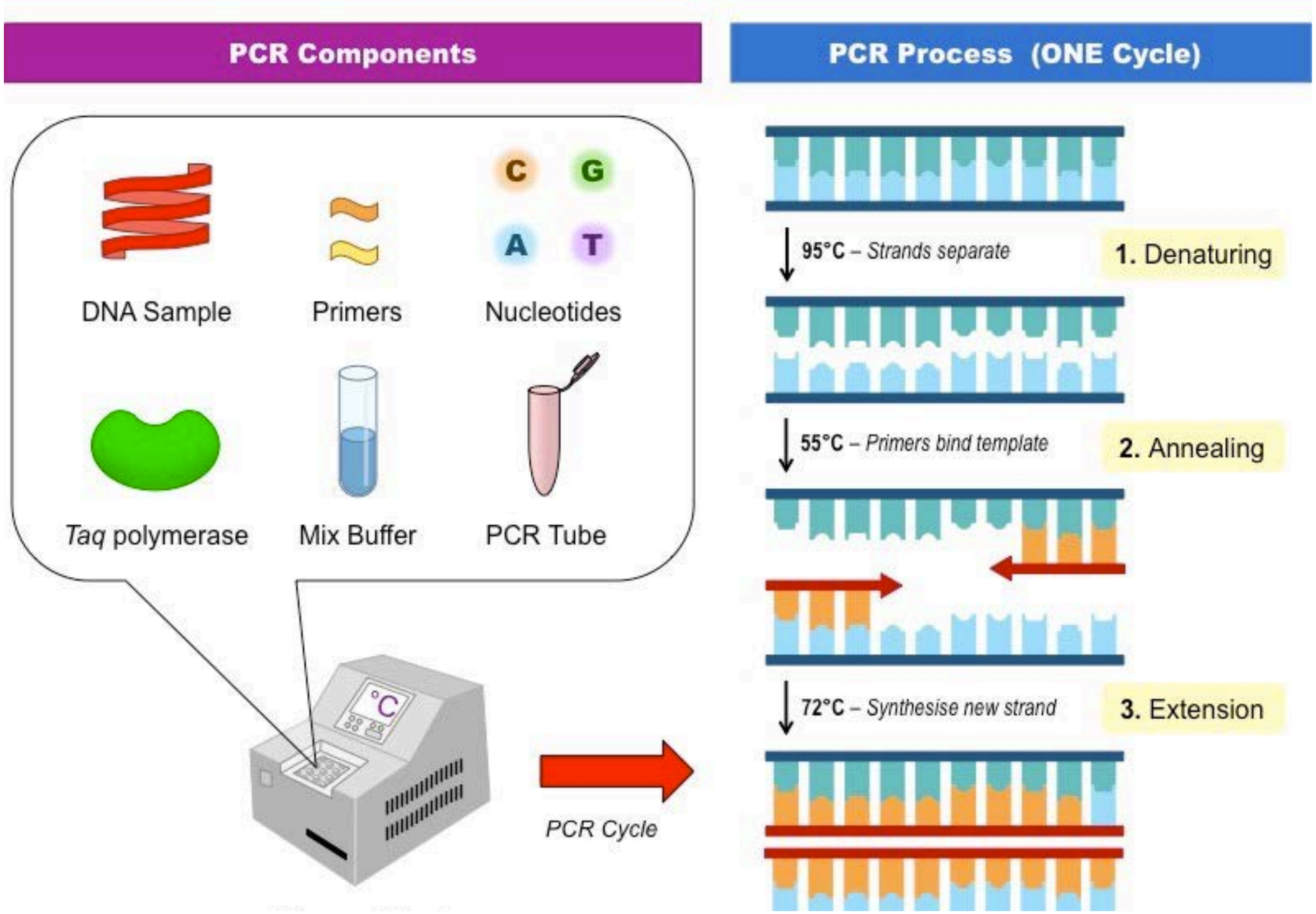
- PCR amplifies DNA
  - Makes lots and lots of copies of a few copies of DNA
  - Can copy different lengths of DNA, doesn't have to copy the whole length of a DNA molecule
    - One gene
    - Several genes

- Artificial process which imitates natural DNA replication

- Requires a DNA template and specific DNA primers

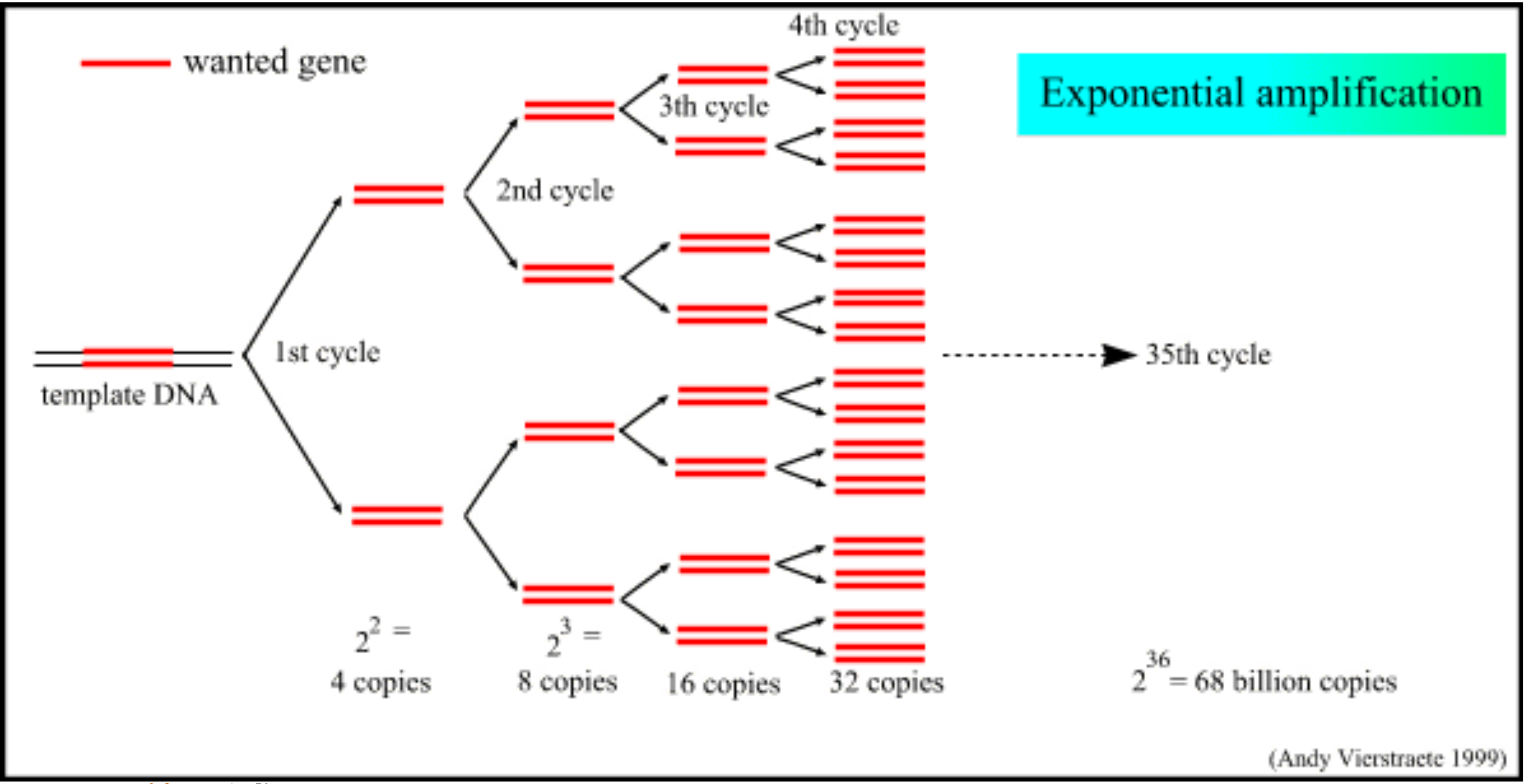
Routine techniques in molecular biology: NUCLEIC ACIDS

Biological synthesis: PCR - Polymerase Chain Reaction

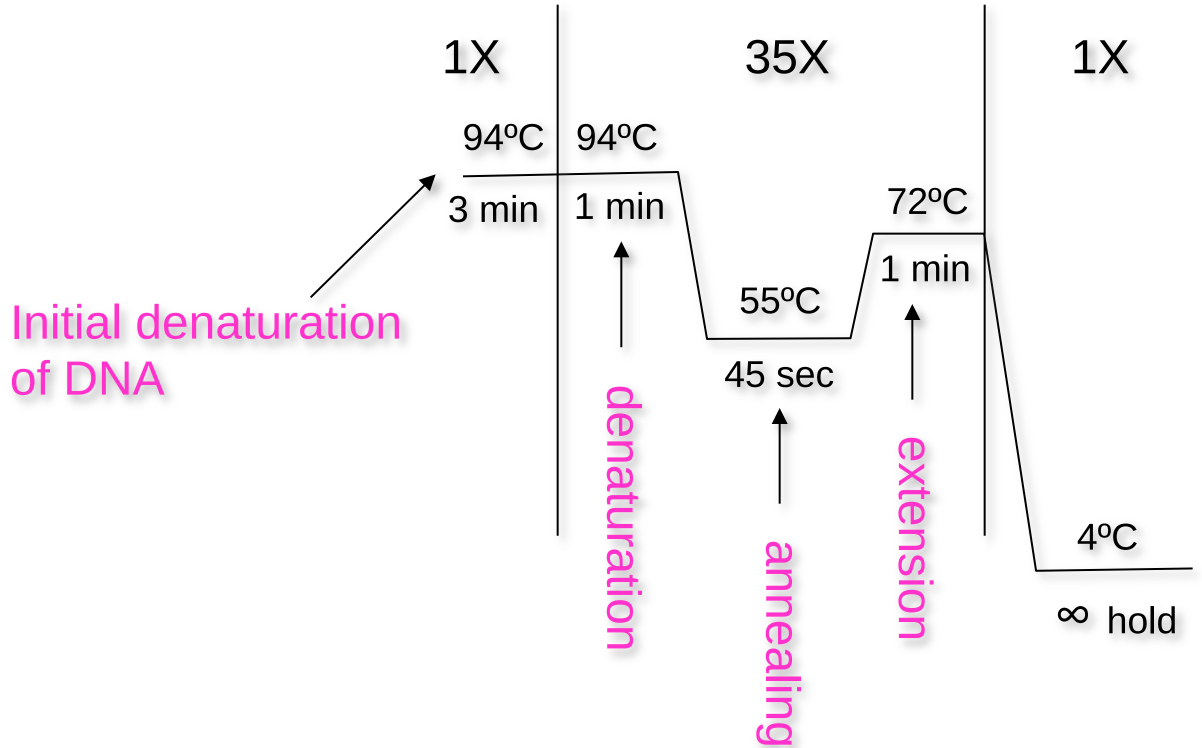


-requires starting material (DNA or RNA sequence)
-primer design needed. They are obtained by solid phase synthesis
-fully automated, pretty affordable
-yields double stranded DNA
-no incorporation of modifications (except in the primers)

Routine techniques in molecular biology: NUCLEIC ACIDS
Polymerase Chain Reaction



A simple thermocycling protocol



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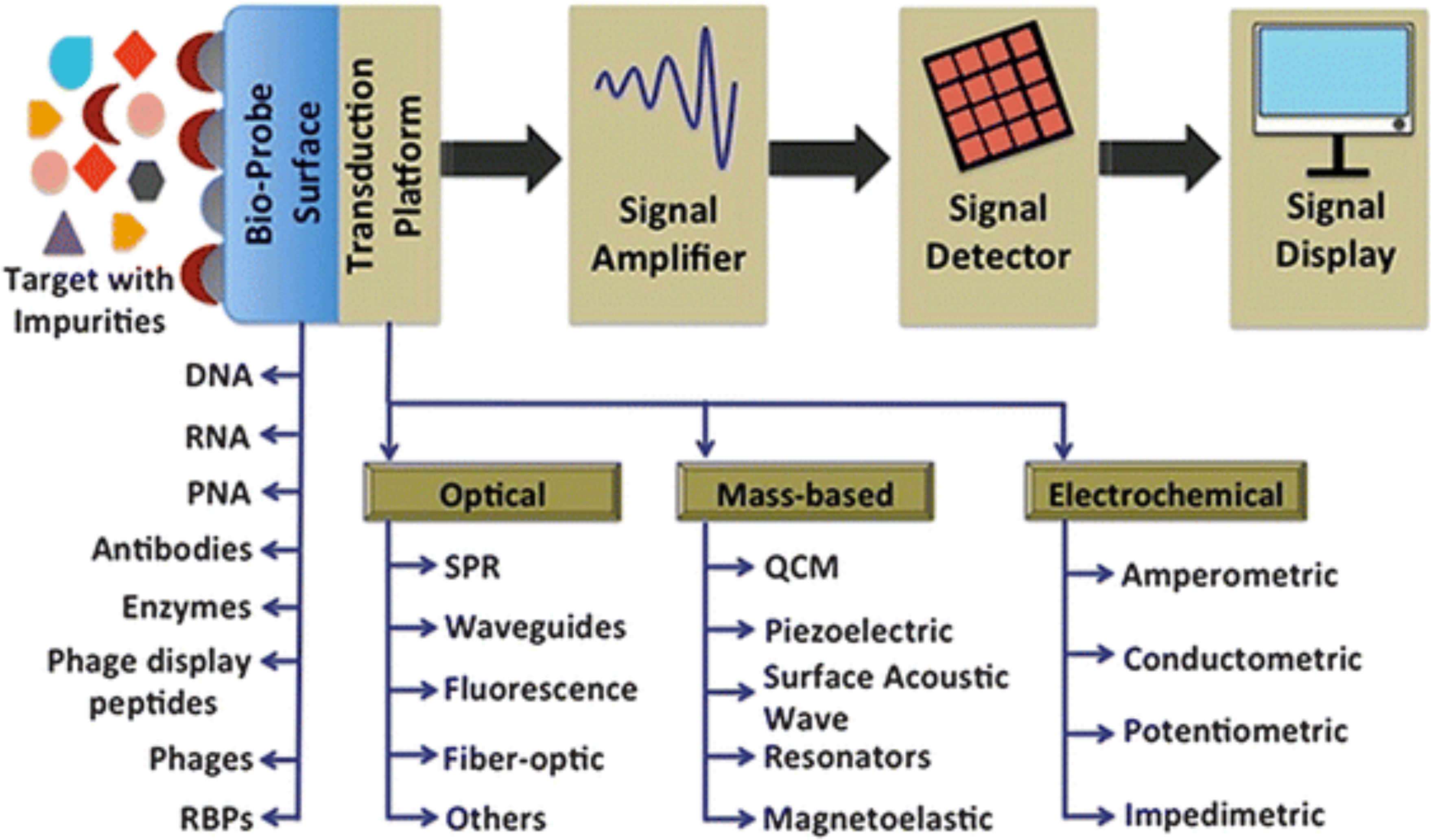
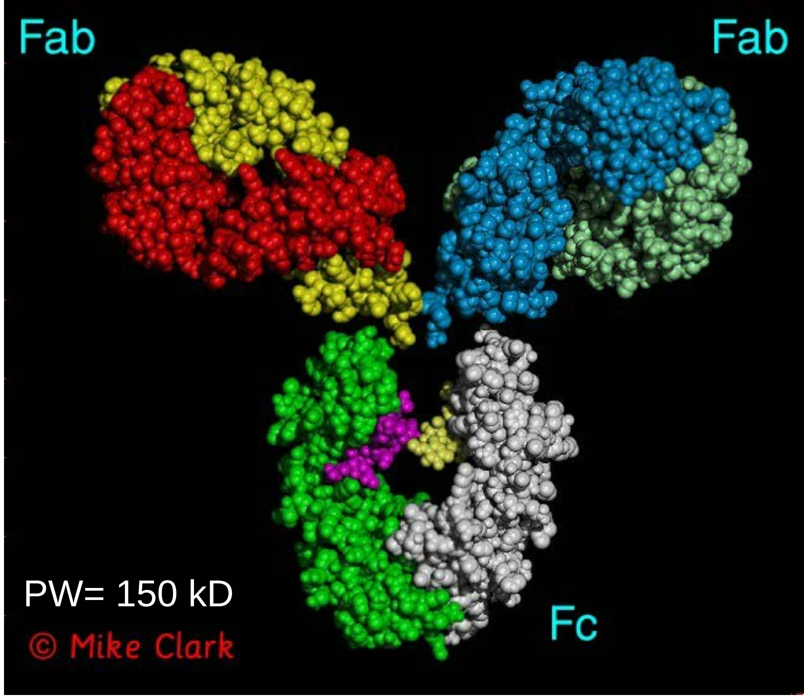
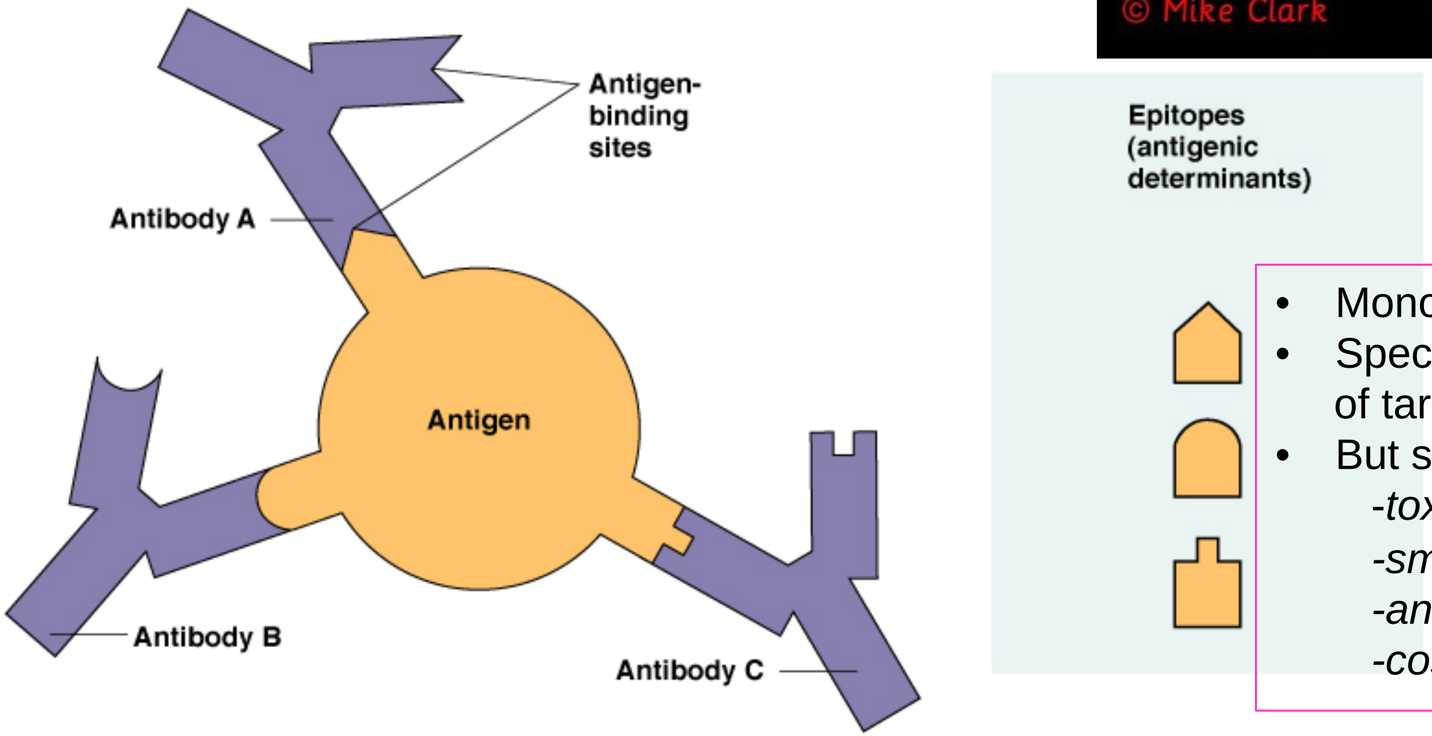
Biosensors & Microarrays



Antibodies used as bioprobes



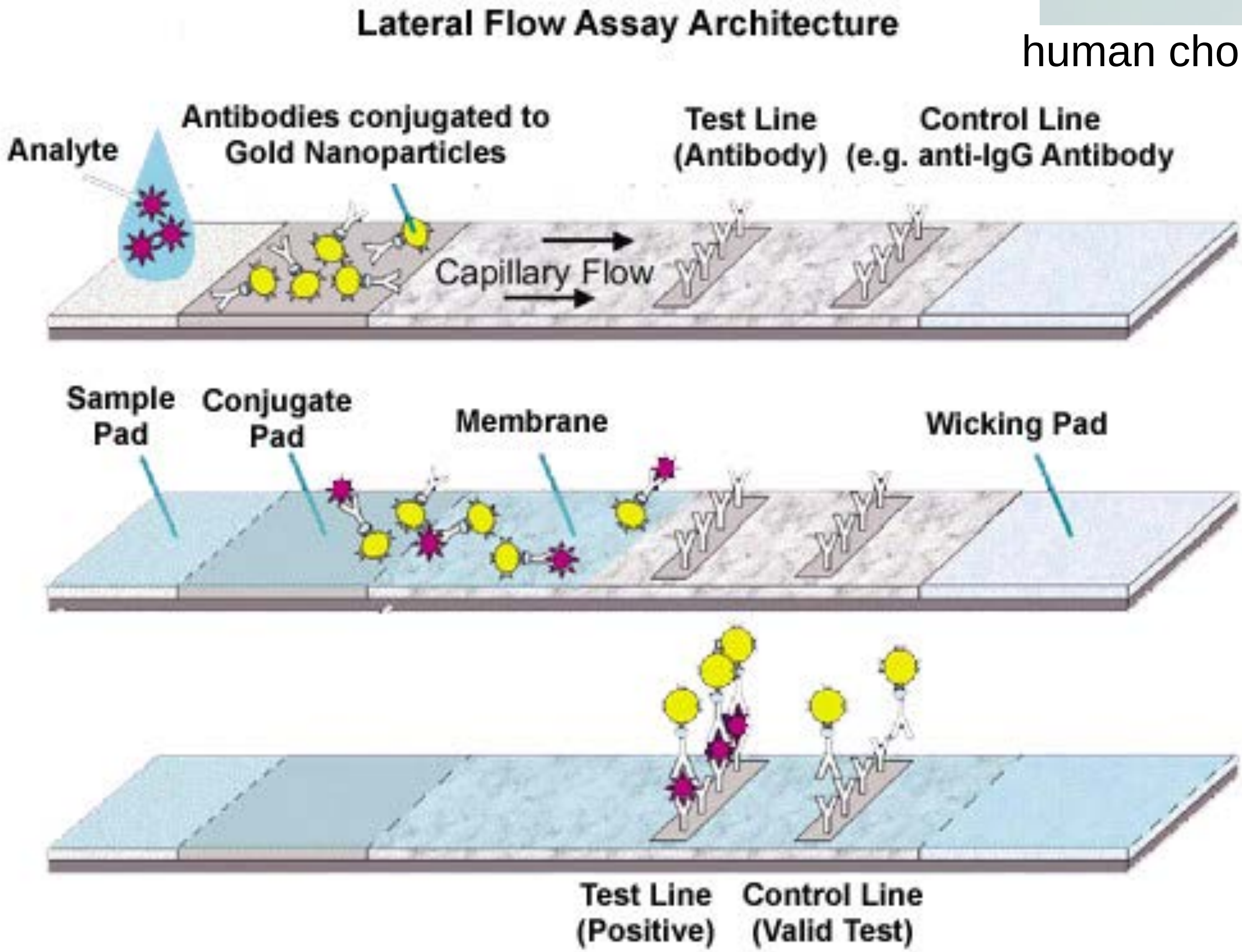
Capable of specific binding to a dedicated molecular structure (epitope) to neutralize/eliminate a pathogen



- Monoclonal vs Polyclonal
- Specific to a large variety of targets
- But some limitations:
  - *-toxins*
  - *-small molecules*
  - *-antibody stability*
  - *-cost*

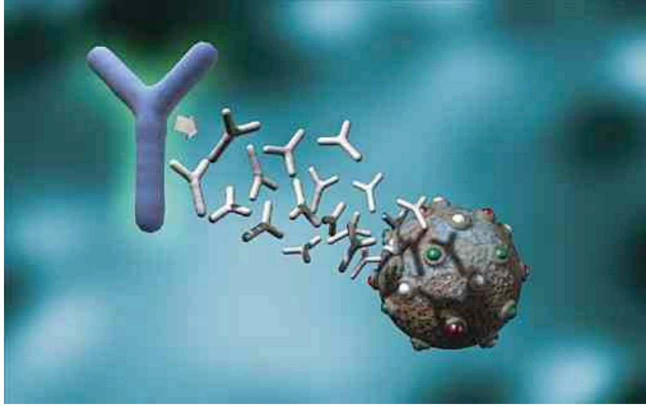
Biosensor with antibodies: immunoassays

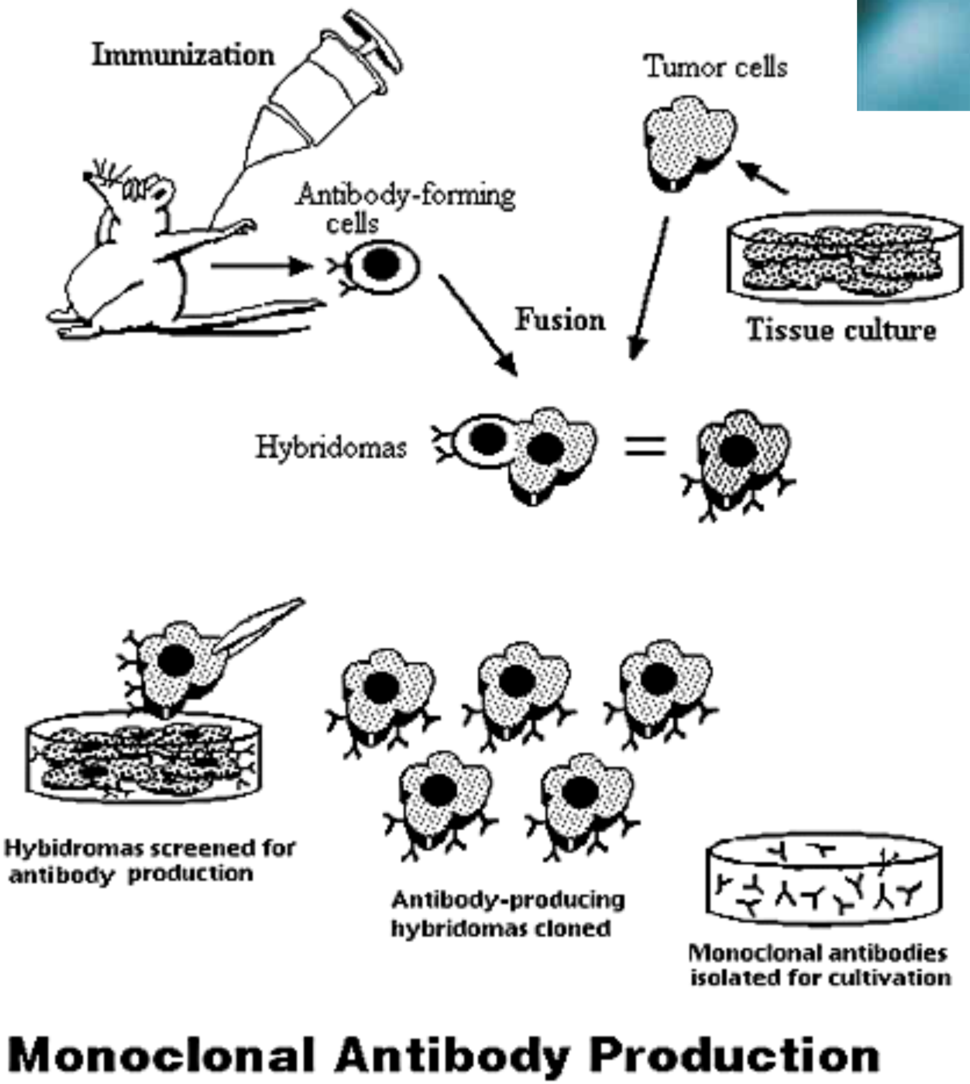
human chorionic gonadotropin



TARGET
PROBE
TRANSDUCER

Antibody production:
a long and expensive process!





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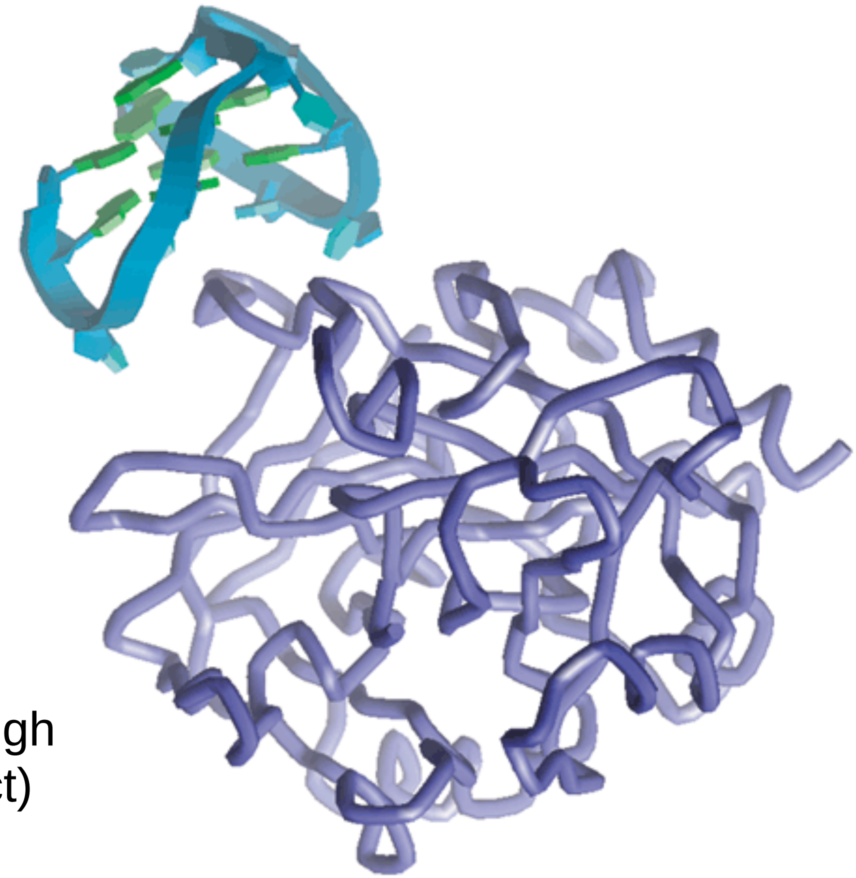
Toward new ARN/DNA functionalities: aptamers



- Aims at mimicking antibodies

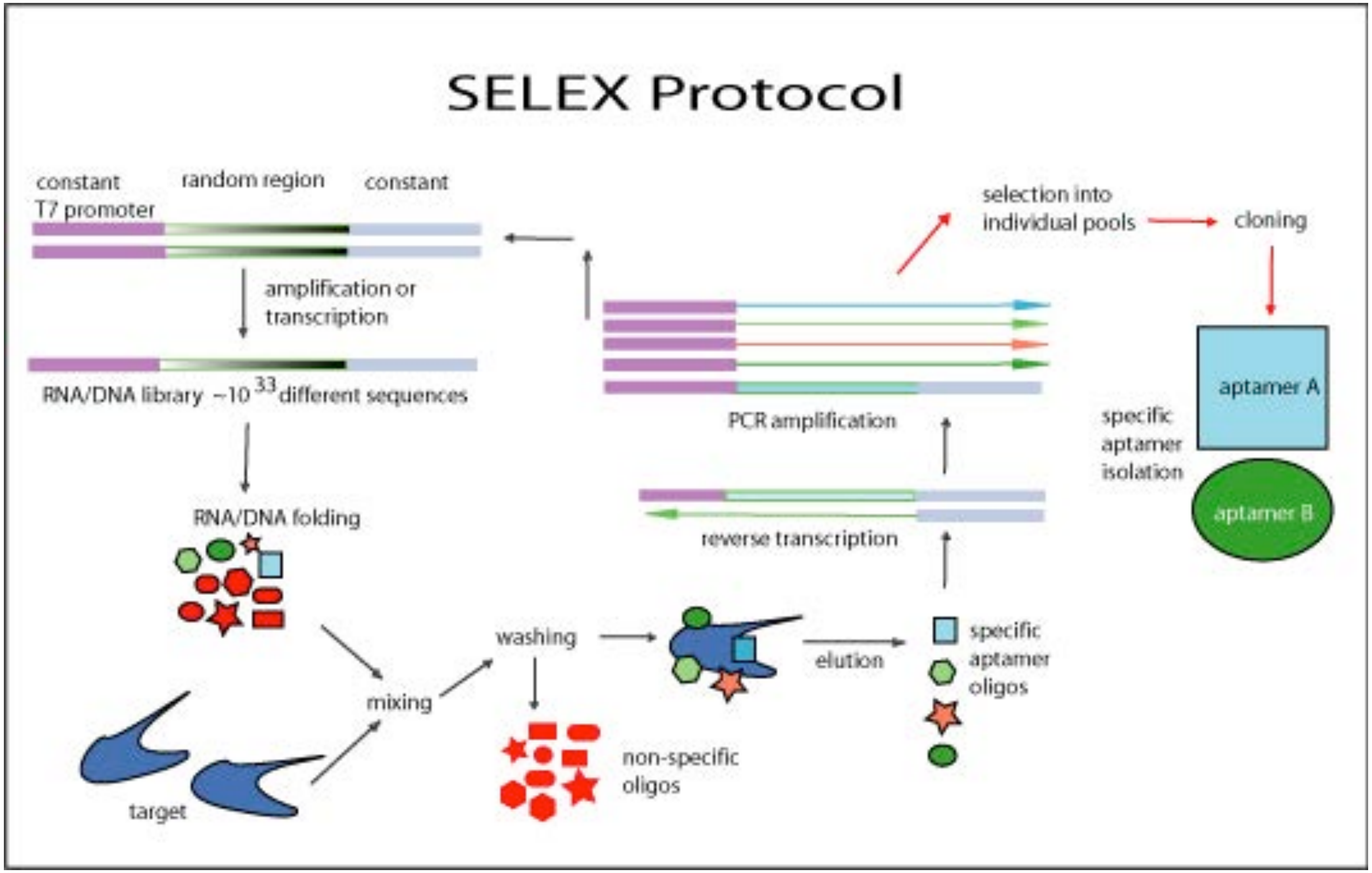
- NA are more stable than proteins,
they are cheaper and easier of synthesize

- Might be used against several targets

- Selection using the SELEX strategy although this approach remains challenging (artefact)

The thrombin aptamer (aqua) forms a specific binding surface with the thrombin protein (blue).
Thiel, Nature Biotechnology 22, 649 - 651 (2004)

Toward new ARN/DNA functionalities: the SELEX



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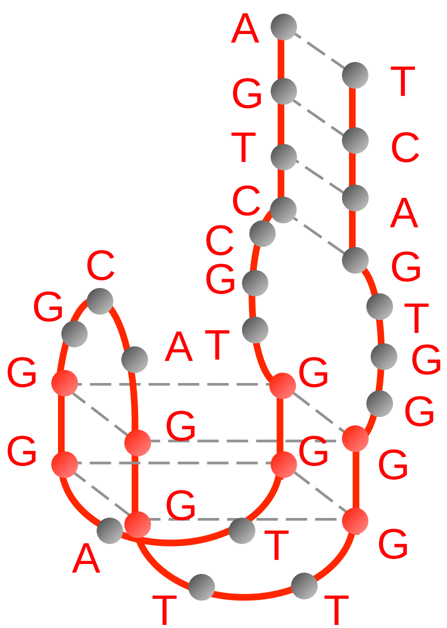
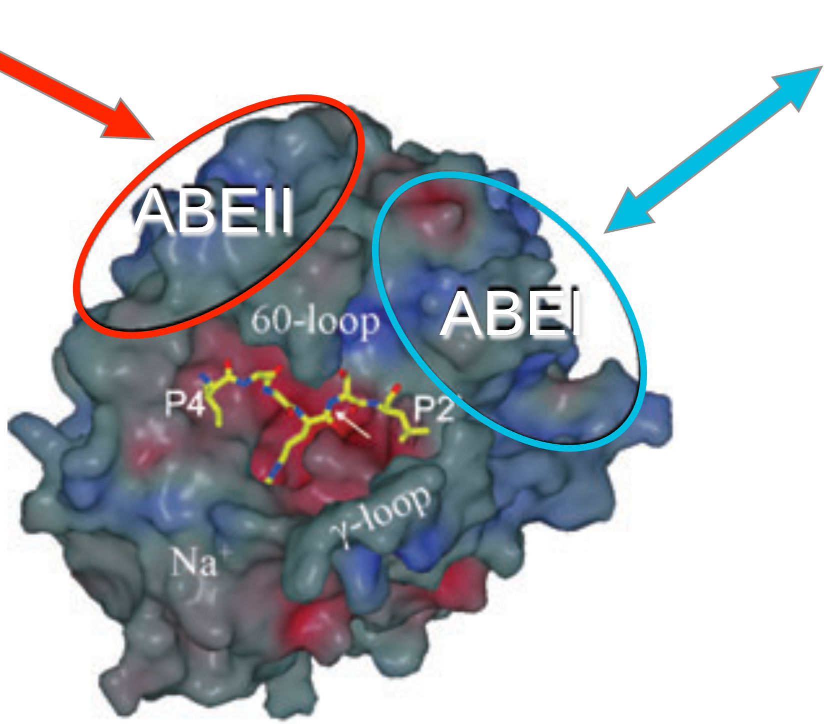
Aptamers raised againt a targeted protein

Thrombin = first protein targeted for DNA aptamer recognitio

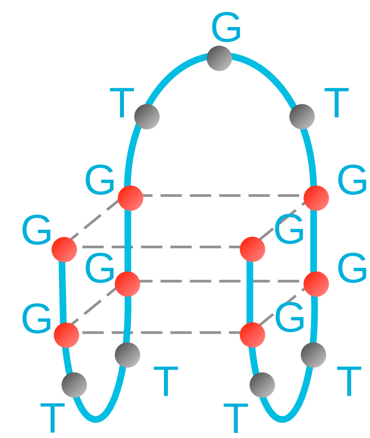


APT 2
(Tasset, 1997)

29 bases
K_D : 0.5 – 250 nM



Source : Huntington, Nature, 2000



APT 1
(Bock, 1992)

15 bases
K_D : 2 – 200 nM

Huang *et al.*, Talanta, 2010
Zhao *et al.*, Biosens. Bioelectron., 2011
Edwards *et al.*, Anal. Bioanal. Chem., 2010…

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Small molecule detection

- *Antibodies can hardly be raised against small molecules*
- *Aptamers may address this issue*

Target	Binding affinity (K_d)	Year
Adenosine TriPhosphate	6 µM	1995
Dopamine	700 nM	2009
Bisphenol A	8.3 nM	2011
Kanamycin	78.8 nM	2011
Ampicillin	9.4–13.4 nM	2012
Cellobiose	600 nM	1998
Cholic acid	5–67.5 µM	2000

Examples of small molecules reported in the literature that have been confirmed to bind specific aptamers.

M. McKeague, M. DeRosa, *Journal of Nucleic Acids*, vol. 2012.

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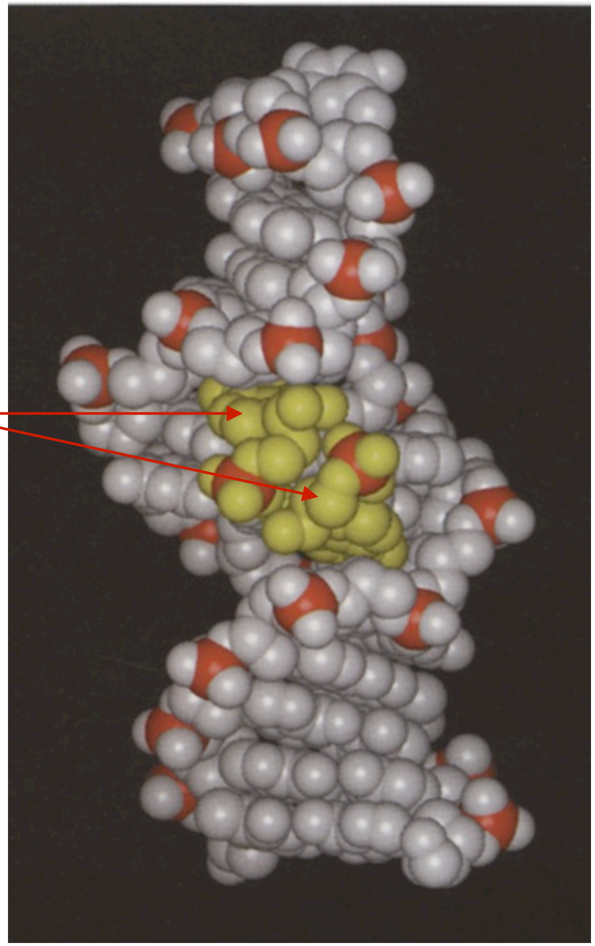
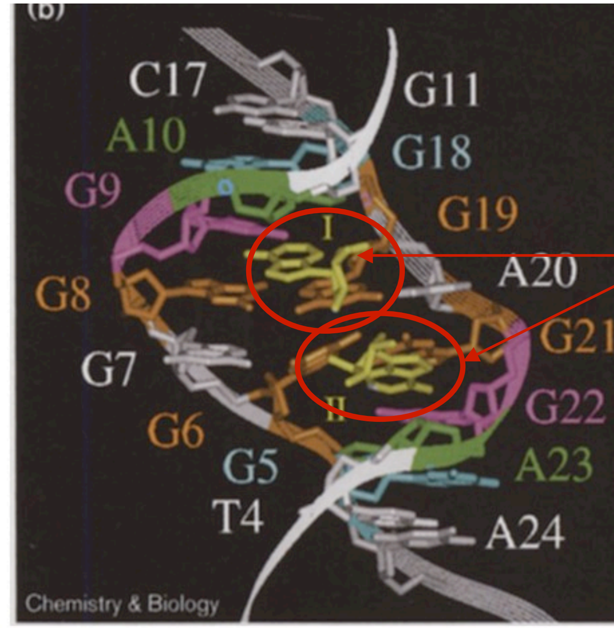
The most famous aptamer against small targets

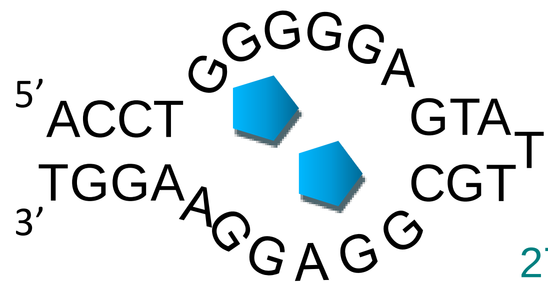
2 Adenosines molecules



Lin et al., *Chemistry & Biology*, 1997.



Adenosine



27 bases

K_D : 6 µM

Huizenga et al., *Biochemistry*, 1995.

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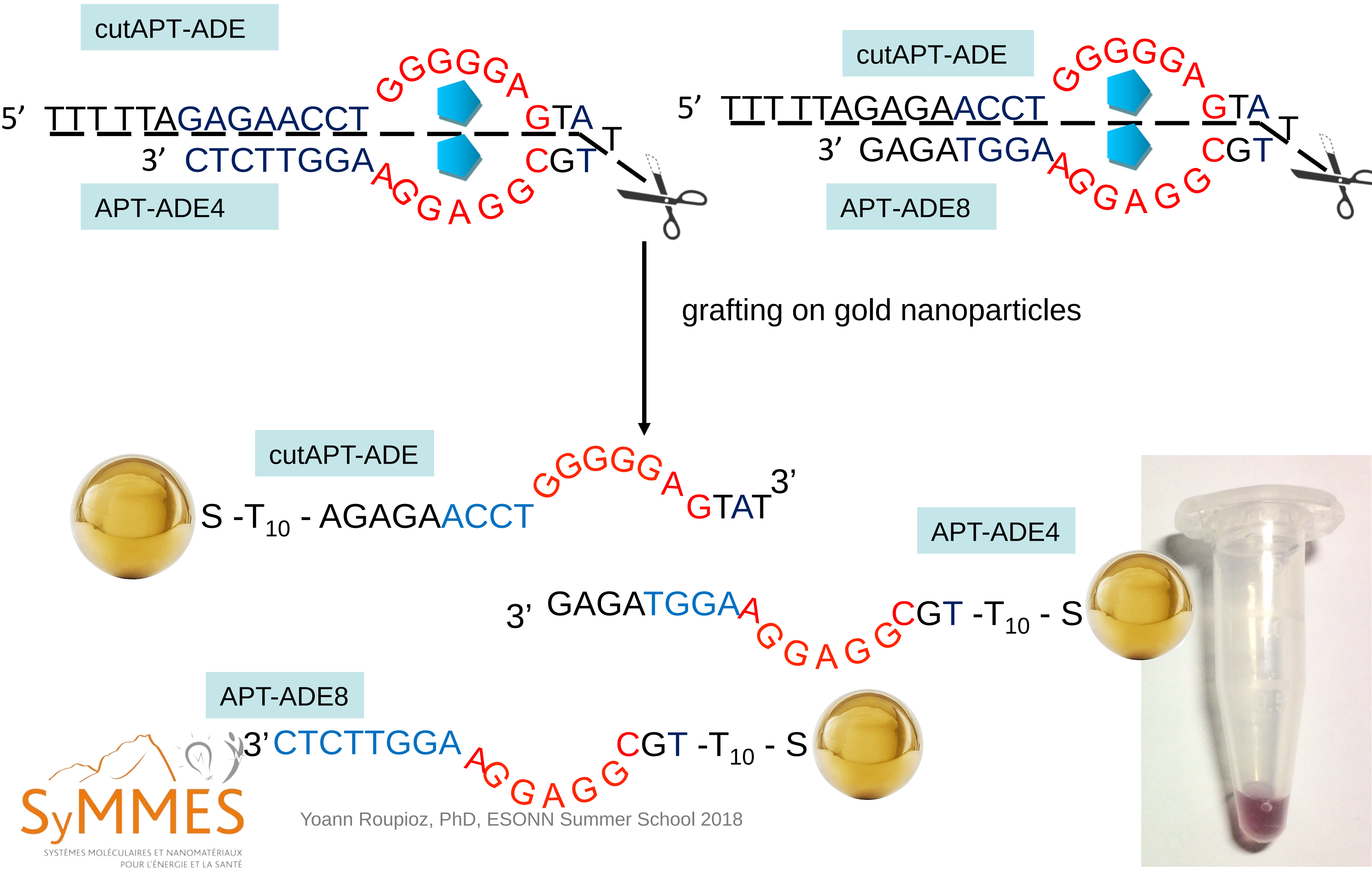
Biosensors made of DNA and gold nanoparticles



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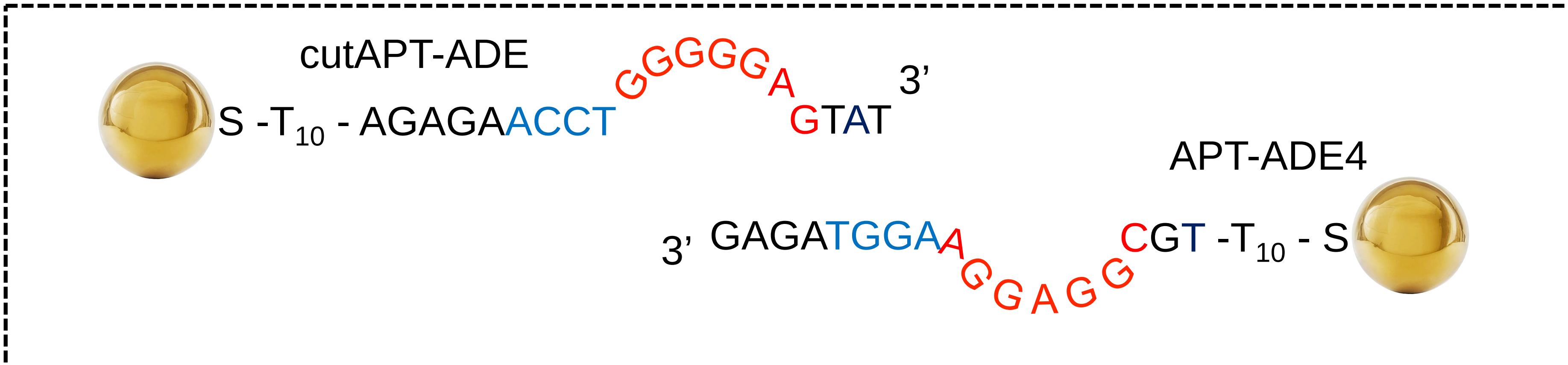

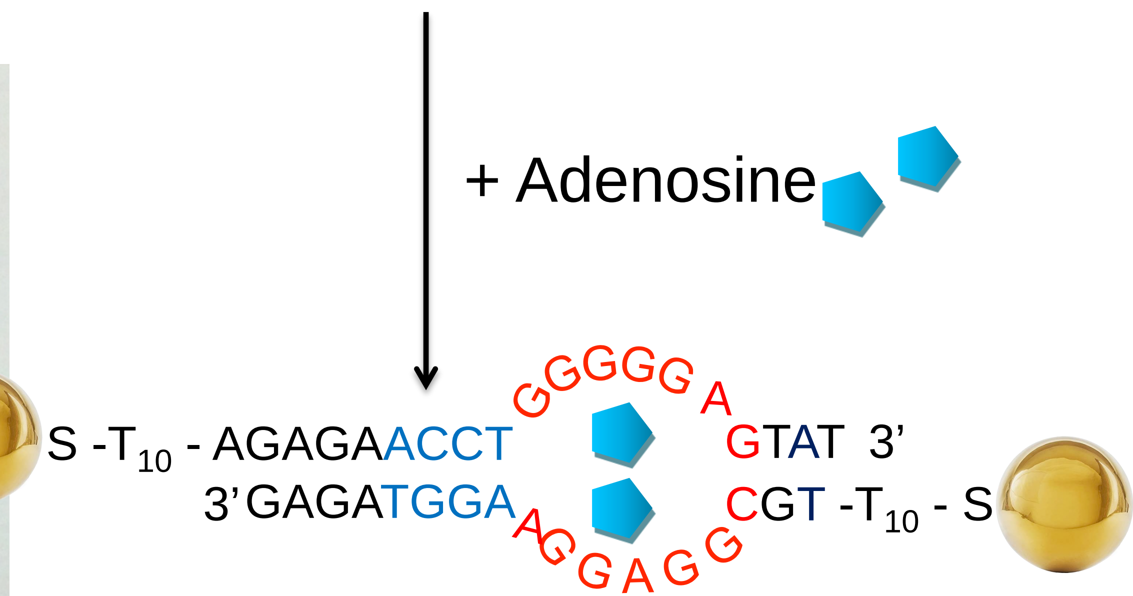

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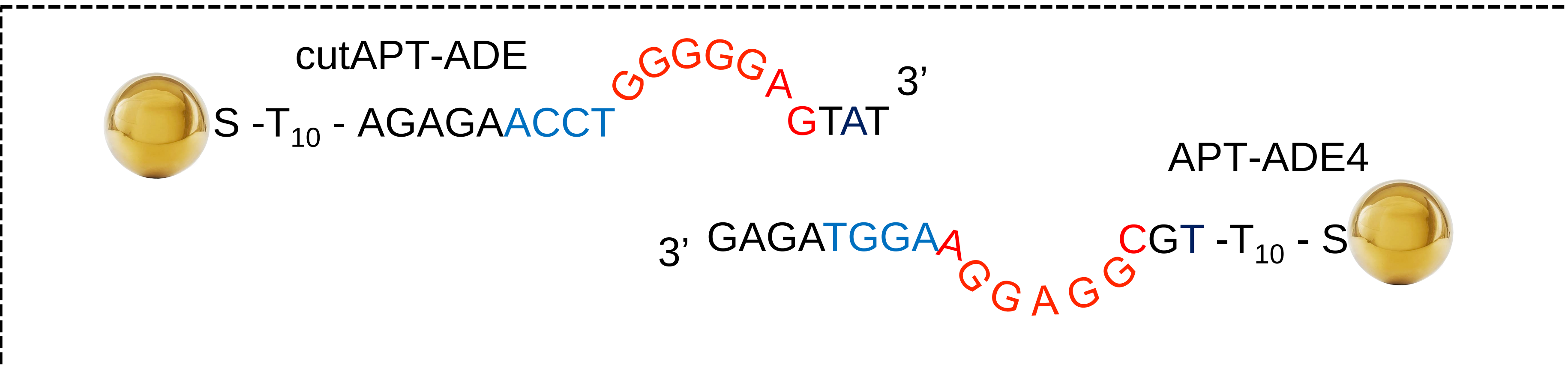

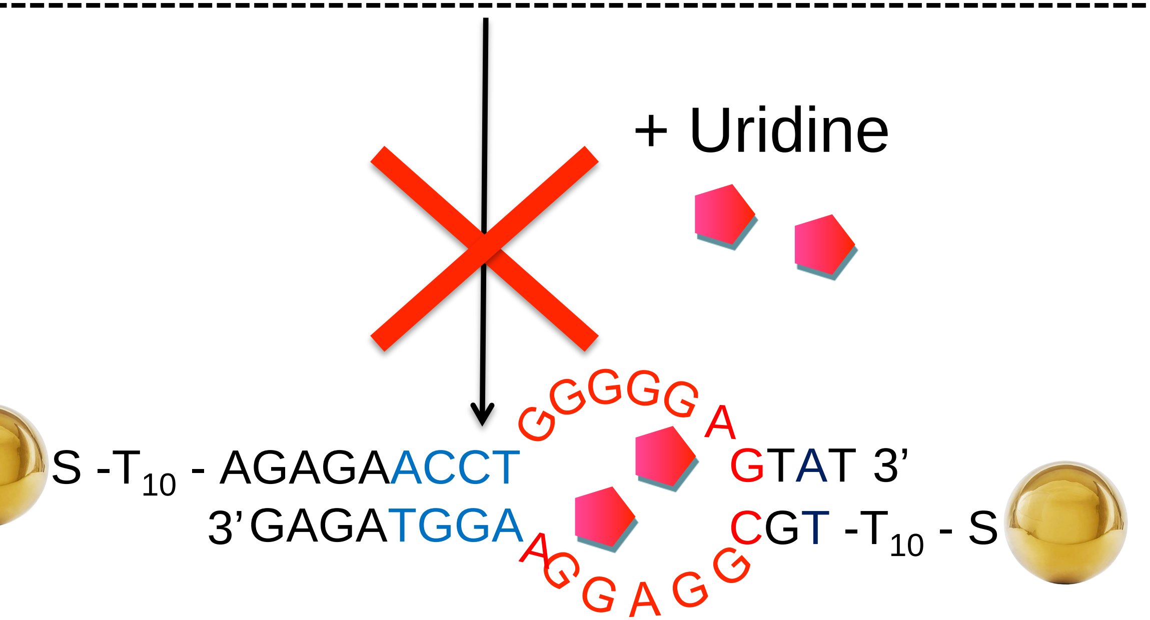

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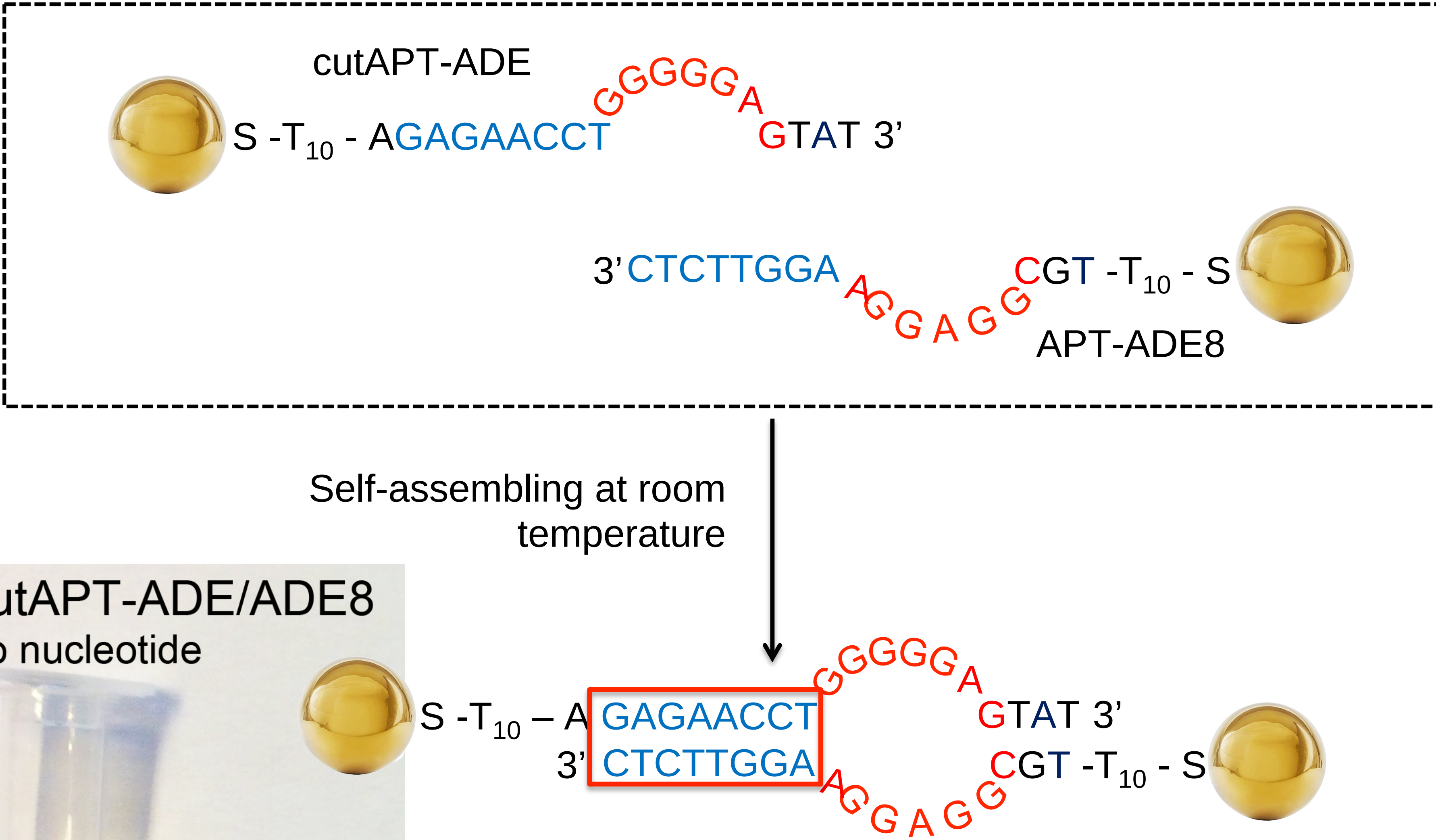

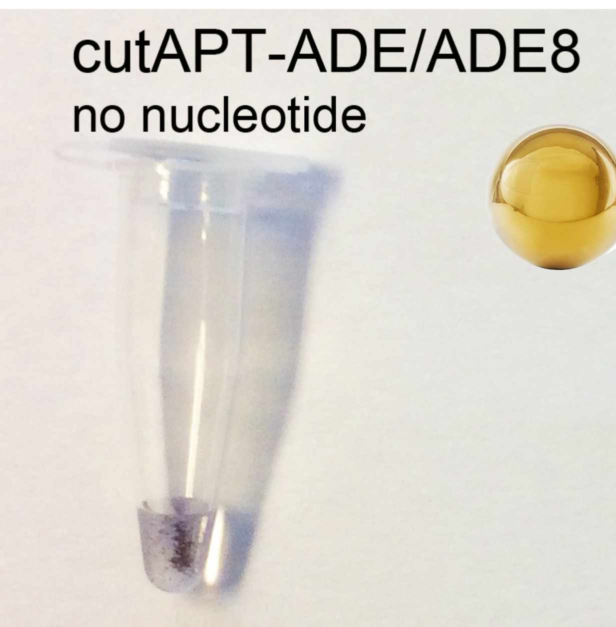

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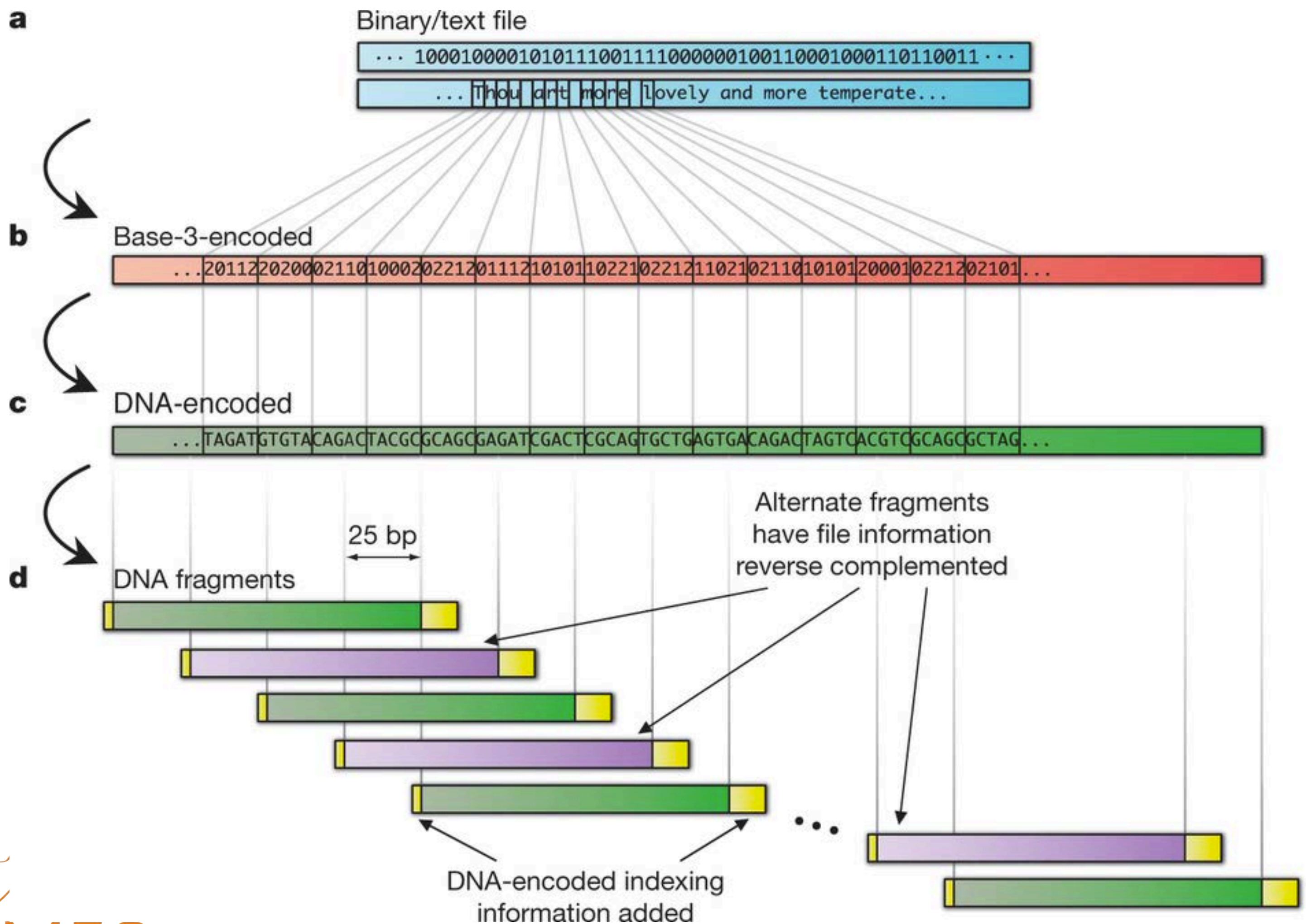
Data storage using DNA

Encoding of all 154 of Shakespeare's sonnets, a classic scientific paper, a medium-resolution colour photograph (JPEG 2000 format), a 26-s excerpt from Martin Luther King's 1963 'I have a dream' speech (MP3 format) and a Huffman code in DNA (739 kilobytes)

Goldman, N. et al. Nature 494, 77–80 (2013).

Data storage using DNA

In all, the five files were represented by a total of 153,335 strings of DNA, each comprising 117 nucleotides



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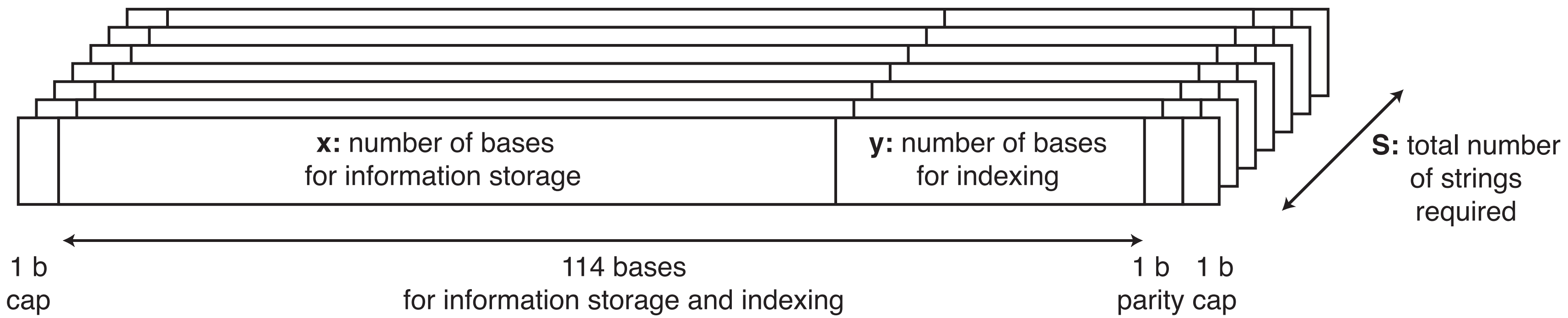
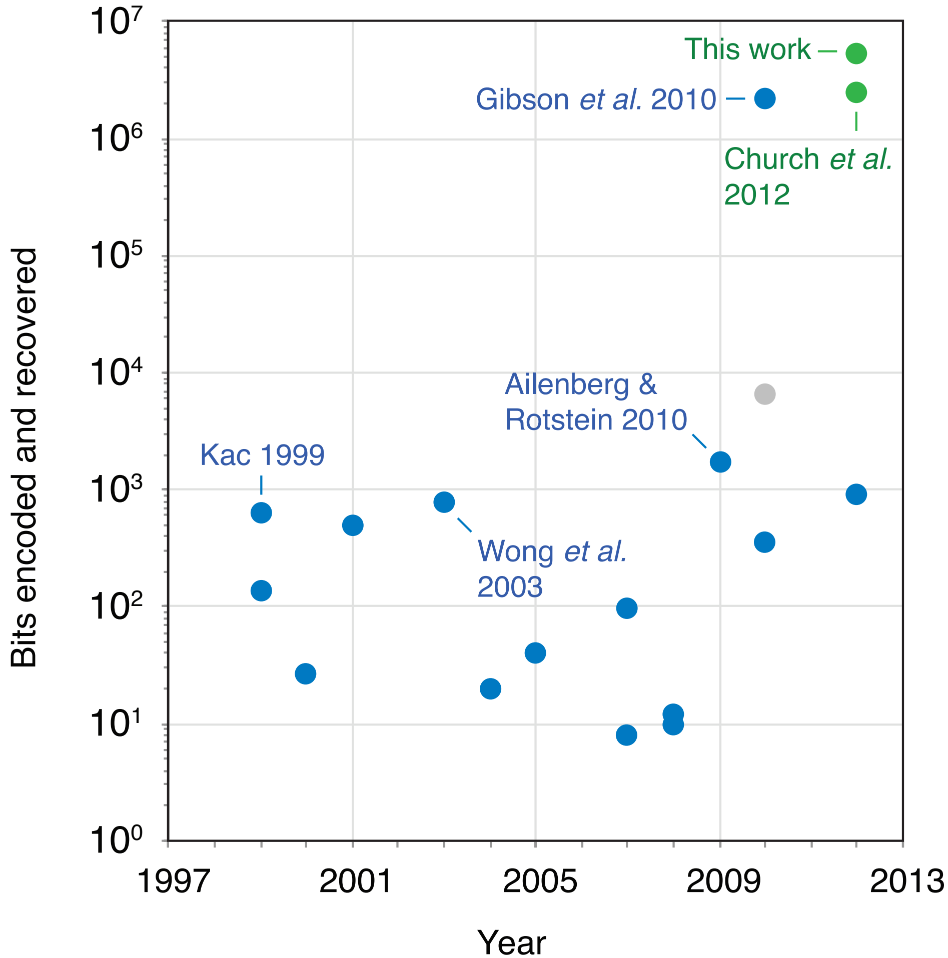
Data storage using DNA

Synthesis of about 1.2 x10^7 copies of each DNA string
Errors occurred only rarely (about 1 error per 500 bases)
In all, the five files were represented by a total of 153,335 strings of DNA, each comprising 117 nucleotides
Then shipping from the USA to Germany, via the UK, resuspension, amplification and purification followed by sequencing at the EMBL Genomics Core facility



Supplementary Figure 4 | Schematic representation of information encoding in DNA. Multiple strings are used, each comprising 117 bases of which x may be used for storing information and y for indexing, with $x + y = 114$.

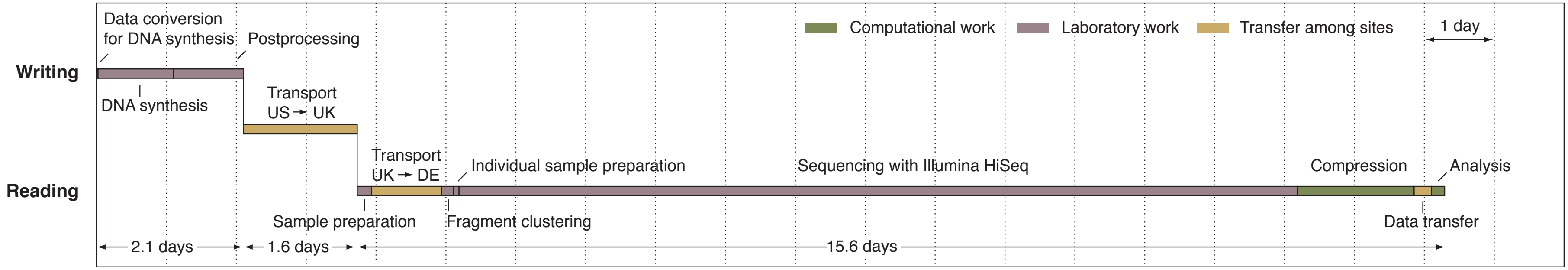
Data storage using DNA



Supplementary Figure 1 | Amounts of human-designed information stored in DNA and successfully recovered. Information content is measured in bits; note the logarithmic scale on the *y*-axis. Blue points indicate studies not adapted to high-throughput data storage; green indicates high-throughput methods. The grey point indicates that part of the Gibson *et al*. (2010) experiment[8] that encoded information of non-biological origin.

Goldman, N. et al. Nature 494, 77–80 (2013).

Data storage using DNA



Supplementary Figure 9 | Timeline of DNA-storage experiment. We report only periods of active work on the experiment. We have omitted time taken to devise repairs for the file with two information gaps (above).

Information storage density. We recovered 757,051 bytes of information from 337 pg of DNA (above), giving an information storage density of ~2.2 PB/g (= $757{,}051/337 \times 10^{-12}$). We note that this information density is enough to store the US National Archives and Records Administration's Electronic Records Archives' 2011 total of ~100 TB (ref. 55) in < 0.05 g of DNA, the Internet Archive Wayback Machines's 2 PB archive of web sites[56] in ~1 g of DNA, and CERN's 80 PB CASTOR system for LHC data[25] in ~35 g of DNA.

Goldman, N. et al. Nature 494, 77–80 (2013).

Data storage using DNA

« If information could be packaged as densely as it is in the genes of the bacterium Escherichia coli, the world's storage needs could be met by about a kilogram of DNA »

	Hard disk	Flash memory	Bacterial DNA
Read–write speed (µs per bit)	~3,000–5,000	~100	<100
Data retention (years)	>10	>10	>100
Power usage (watts per gigabyte)	~0.04	~0.01–0.04	$<10^{-10}$
Data density (bits per cm^3)	$\sim10^{13}$	$\sim10^{16}$	$\sim10^{19}$

WEIGHT OF DNA NEEDED TO STORE WORLD'S DATA

~1 kg

©nature

Nature **537,** 22–24 , 2016 doi:10.1038/537022a

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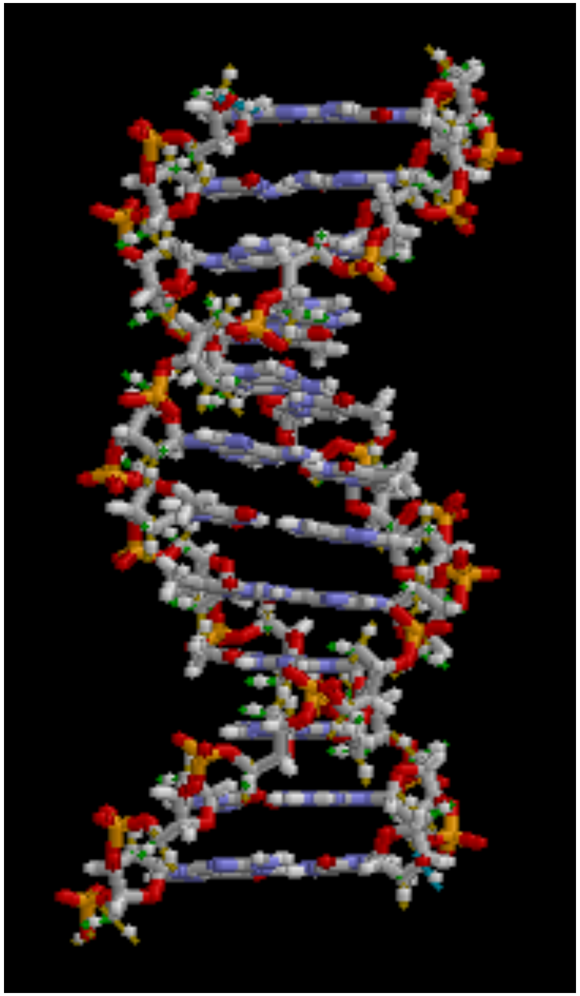
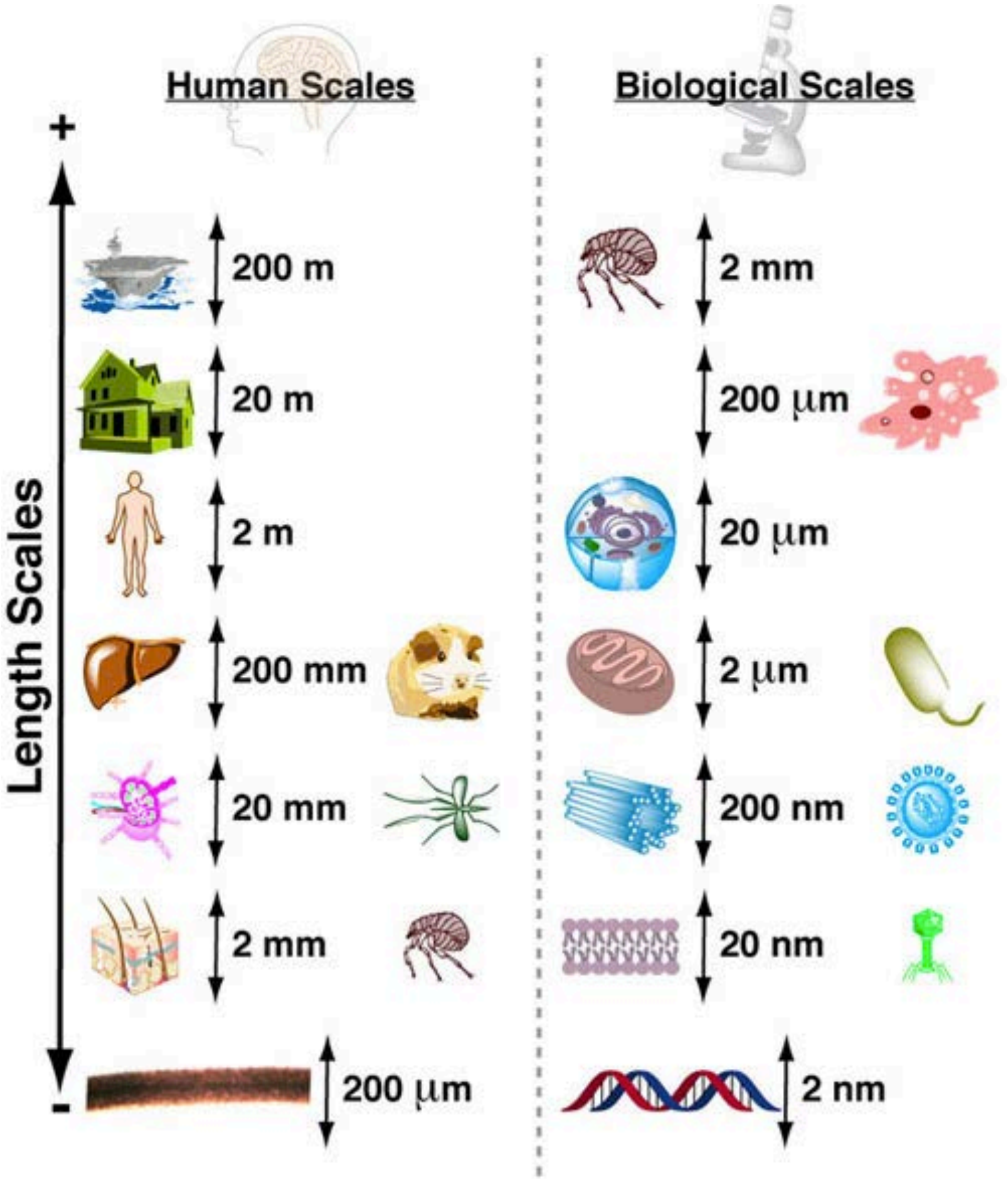
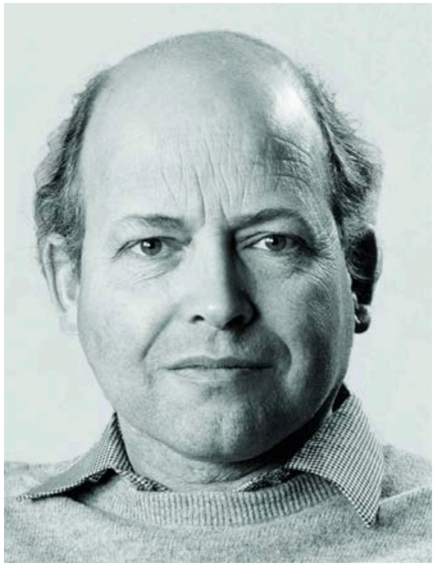
DNA unique self-assembling properties





DNA Four-ways junctions
« Holliday junctions »



PNAS | **April 11, 2000** | vol. 97 | no. 8 | **3971–3976**

- *These structures have been described in 1964 by Robin Holliday*
- *Key intermediate structures in many types of genetic recombination, as well as in double-strand break repair mechanisms*
- *Natural 4-ways junctions have a symmetrical sequence and are thus mobile, meaning that the four individual arms may slide through the junction*

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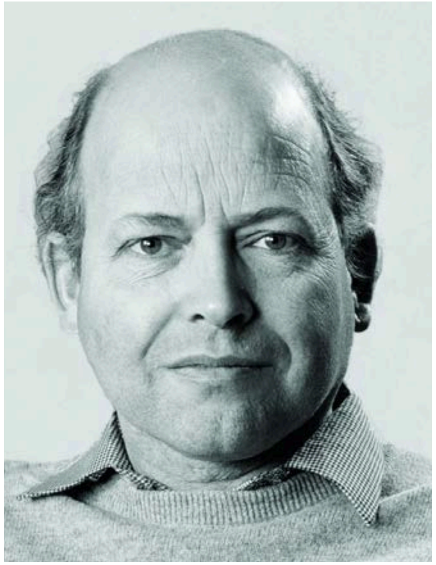
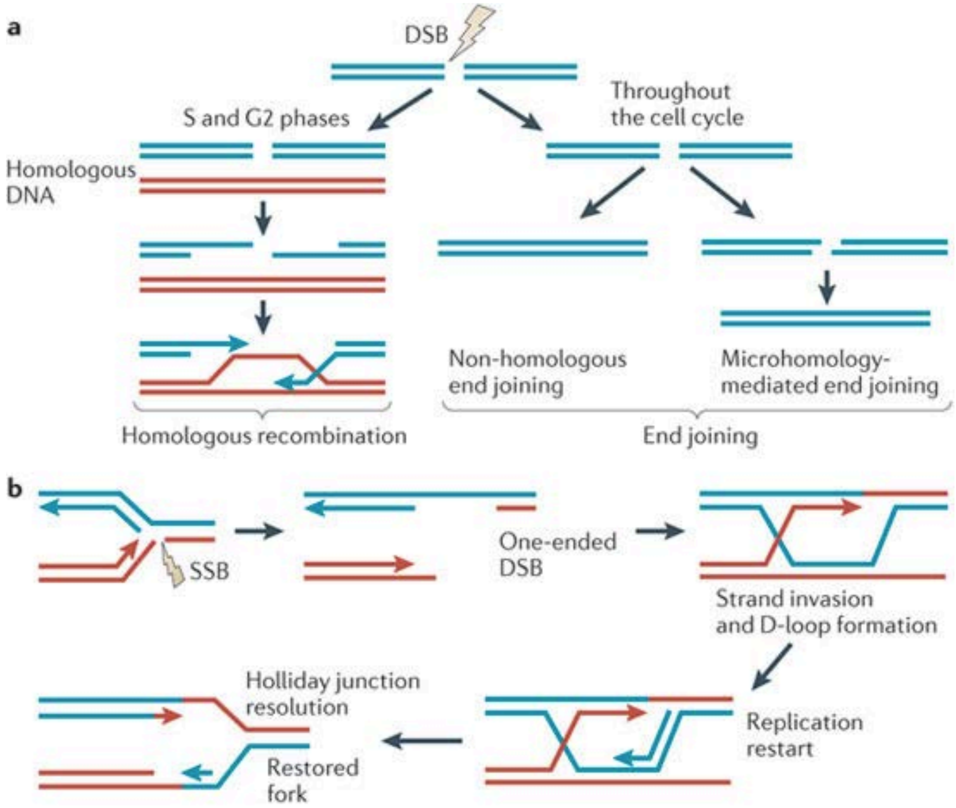
« Holliday junctions »





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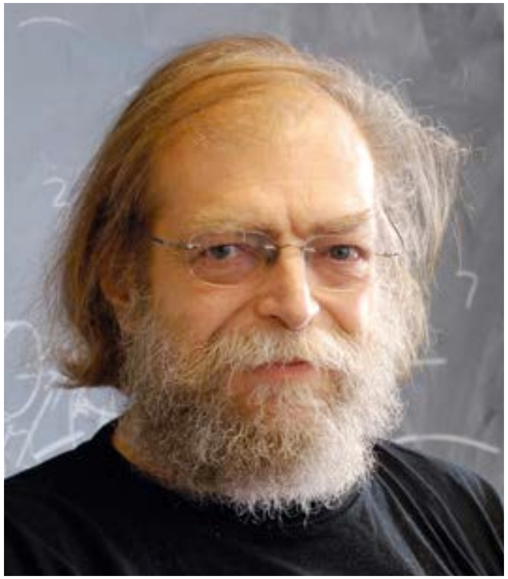
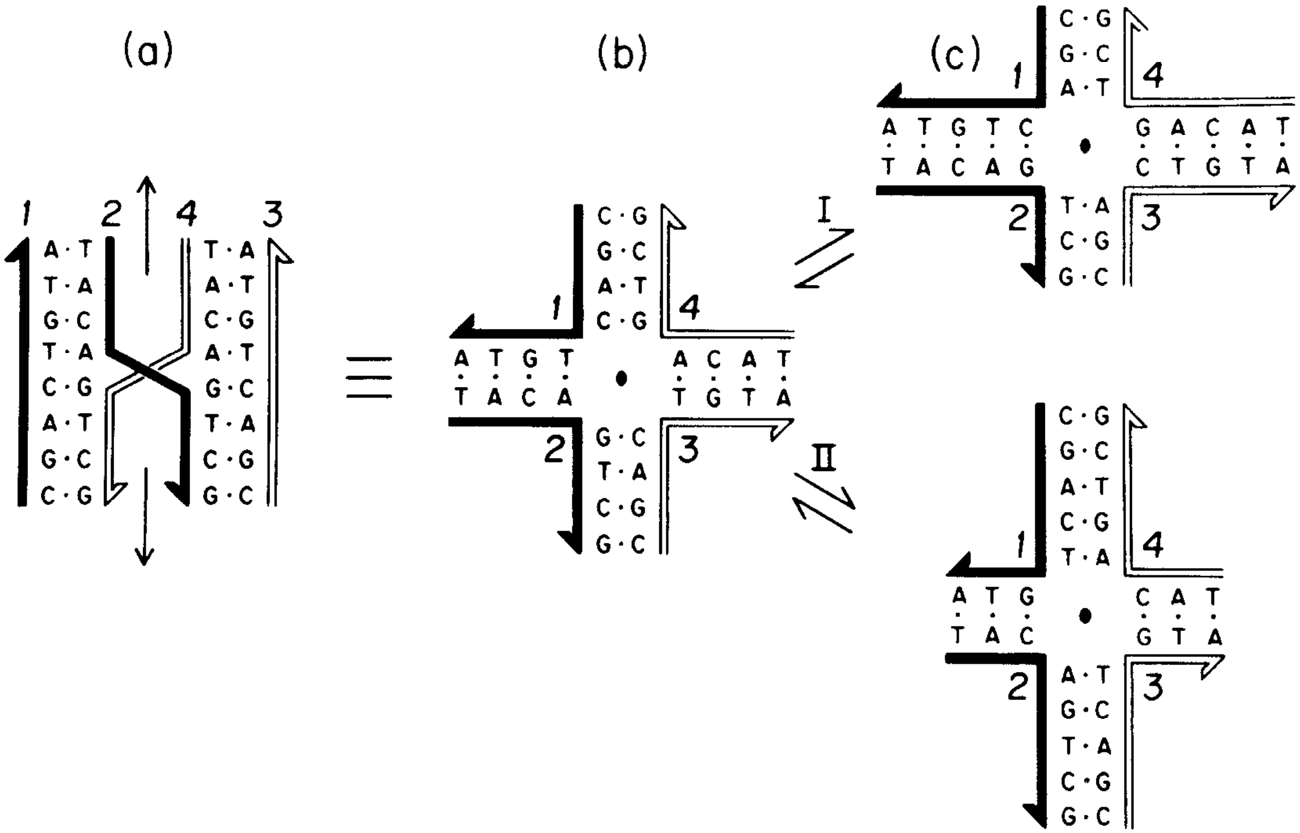
DNA six-ways junctions



- *These structures have been designed and produced in the early 1980s by Nadrian Seeman, State Univ. New York*
- *Inspiration from 4-ways junctions and protein troubles for cristallography*
- *He got the initial idea while he was drinking a beer in a bar and looking at this painting of flying fishes...*

Mobile Holliday junction



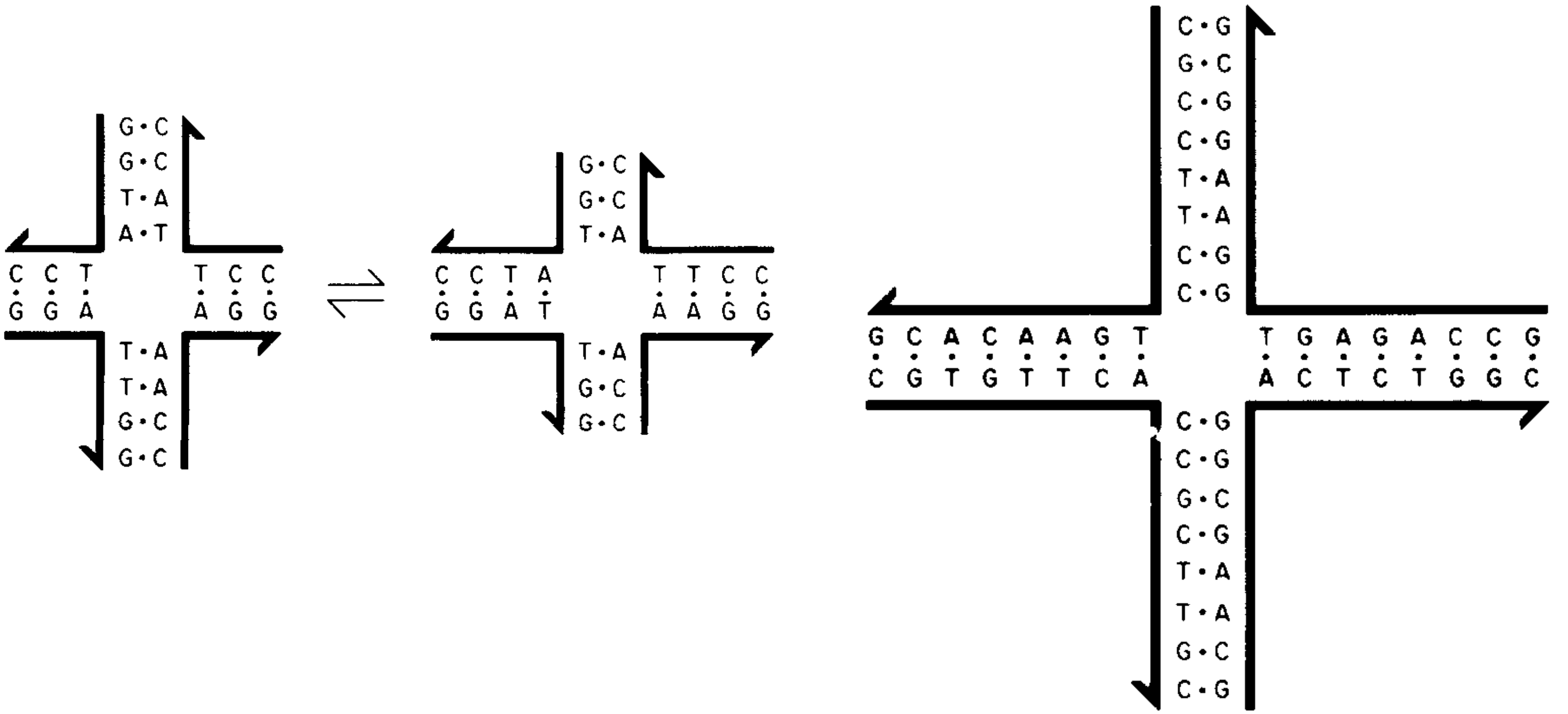
J. theor. Biol. (1982) **99,** 237–247

Nucleic Acid Junctions and Lattices

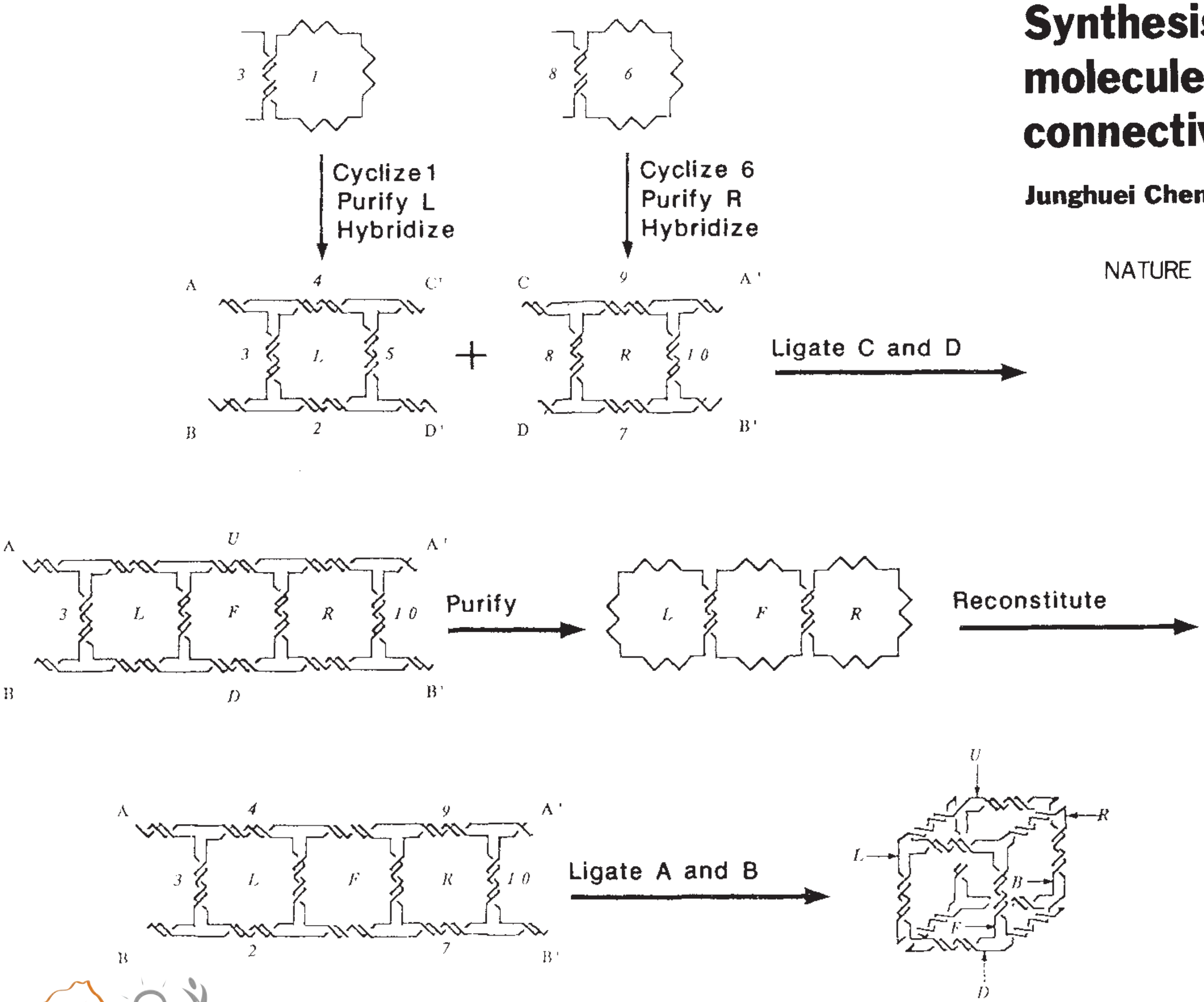
NADRIAN C. SEEMAN

Center for Biological Macromolecules, State University of New York at Albany, Albany, New York 12222, *U.S.A.*

Semi-mobile and immobile Holliday junction



The first 3D objects built from DNA 3-ways junctions

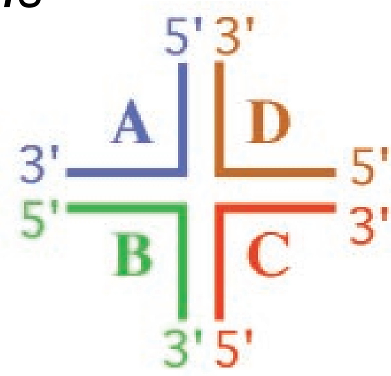


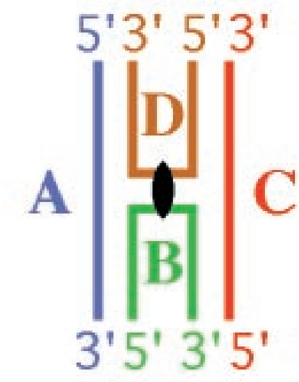
Synthesis from DNA of a molecule with the connectivity of a cube

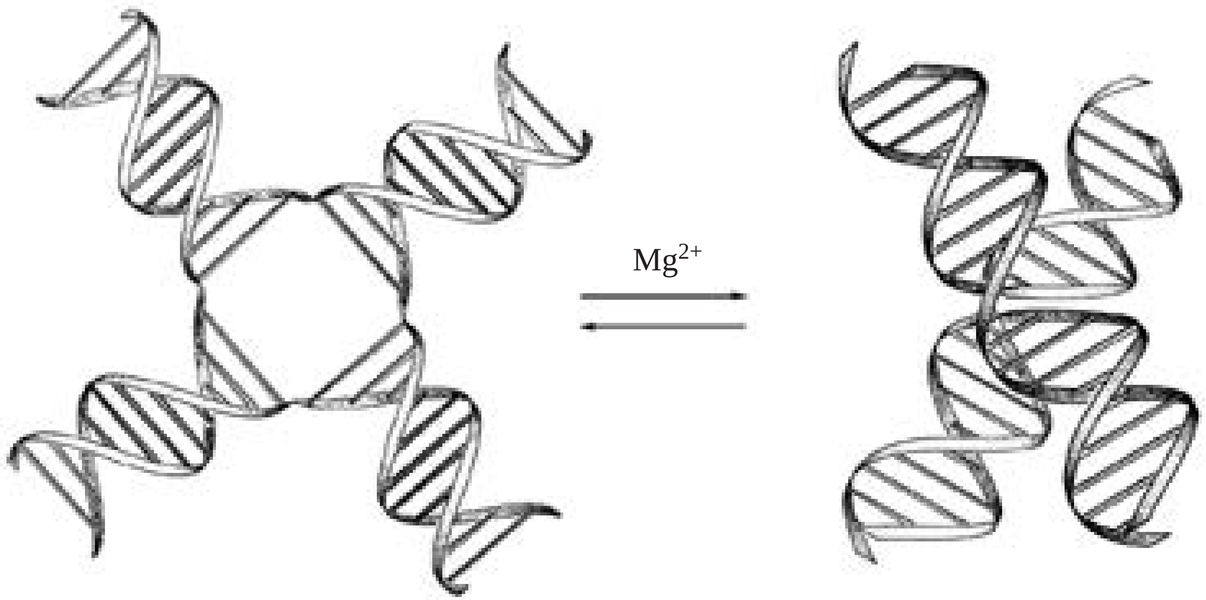
Junghuei Chen & Nadrian C. Seeman

NATURE · VOL 350 · 18 APRIL 1991

Holliday junction conformations







Several possible conformations (extended X-form if Mg^{2+}<0.1µM; left or stacked X-form if Mg^{2+}>0.1µM, right)

PNAS | **April 11, 2000** | vol. 97 | no. 8 | **3971–3976**

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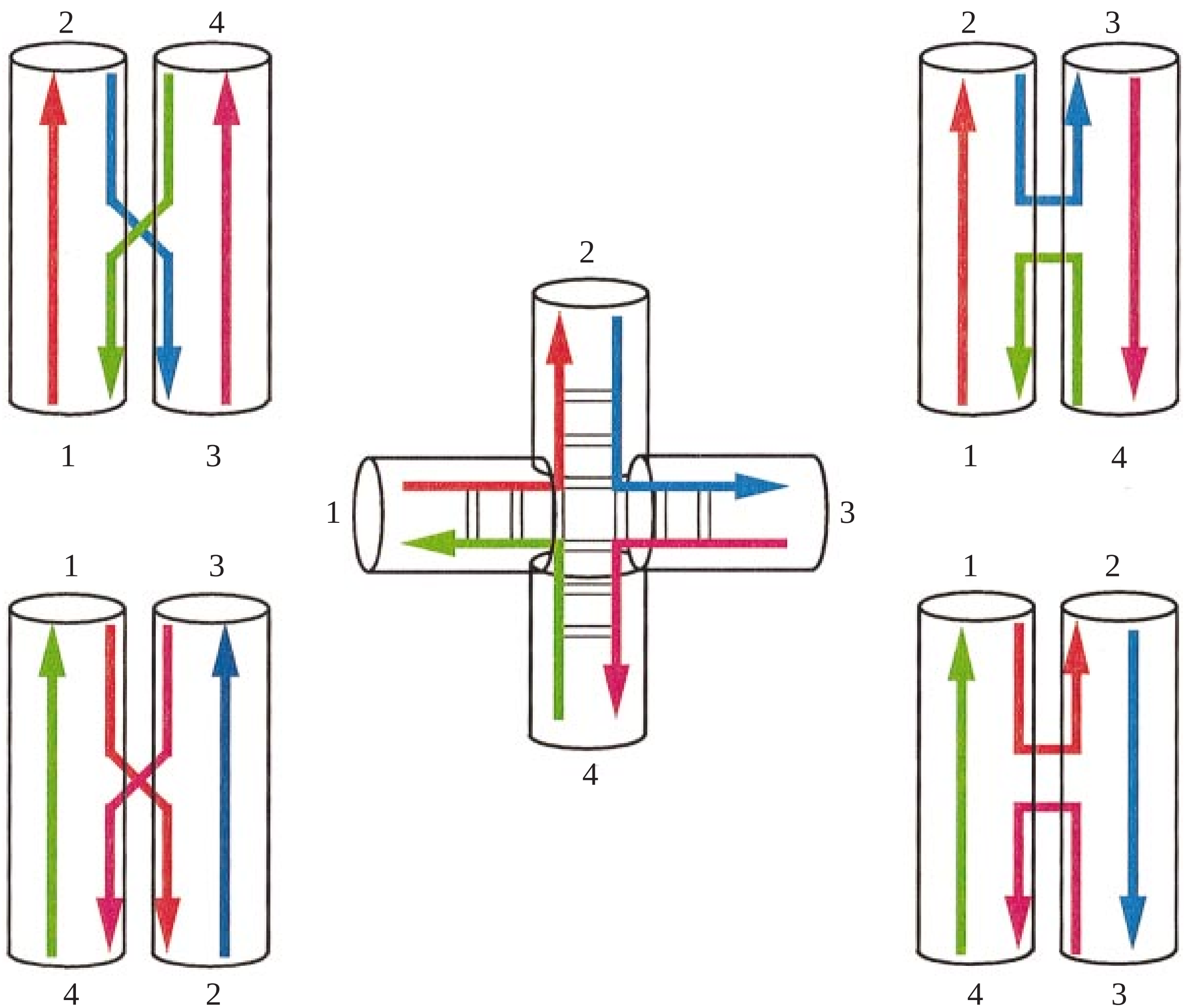

Parallel *Anti-parallel*

PNAS | April 11, 2000 | vol. 97 | no. 8 | 3971–3976

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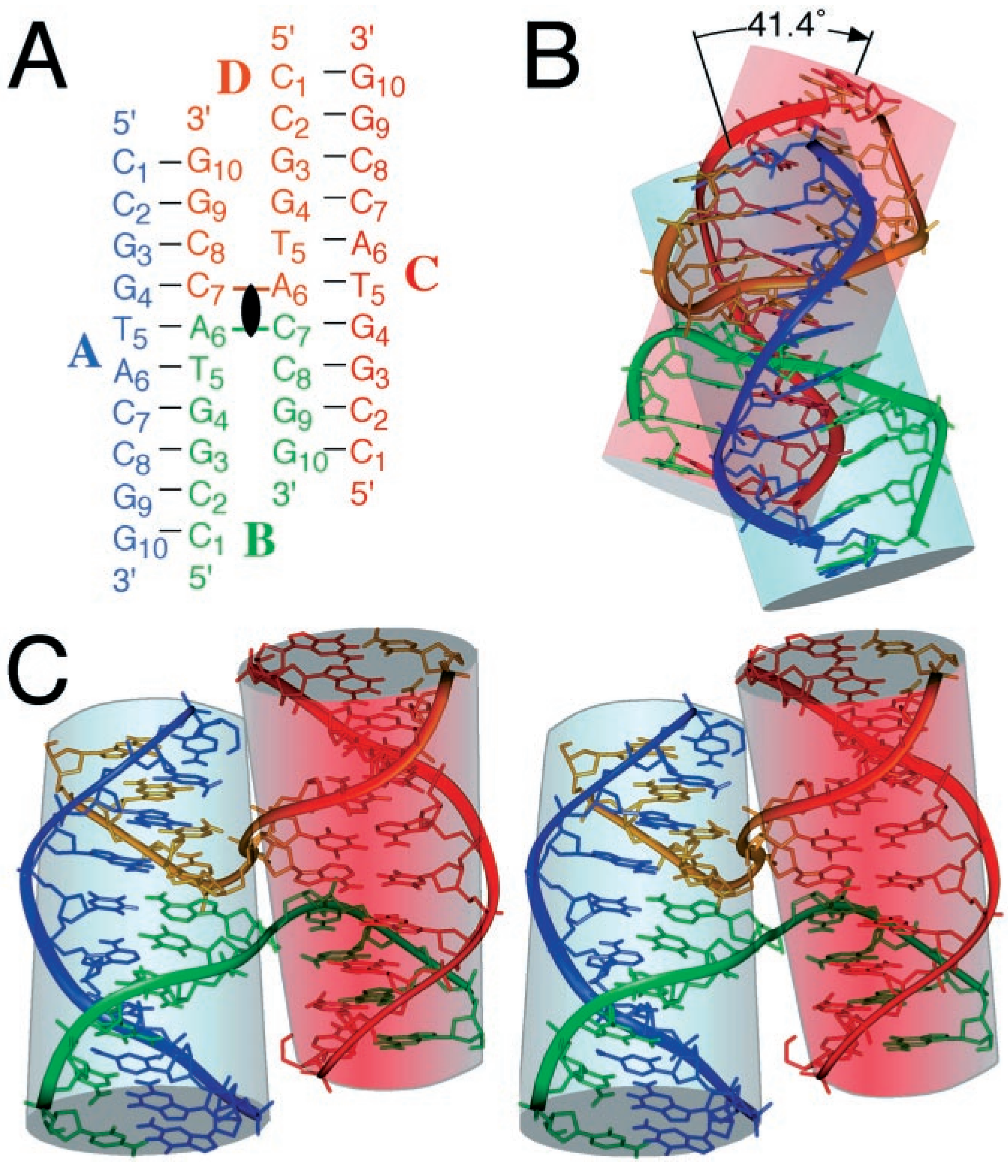

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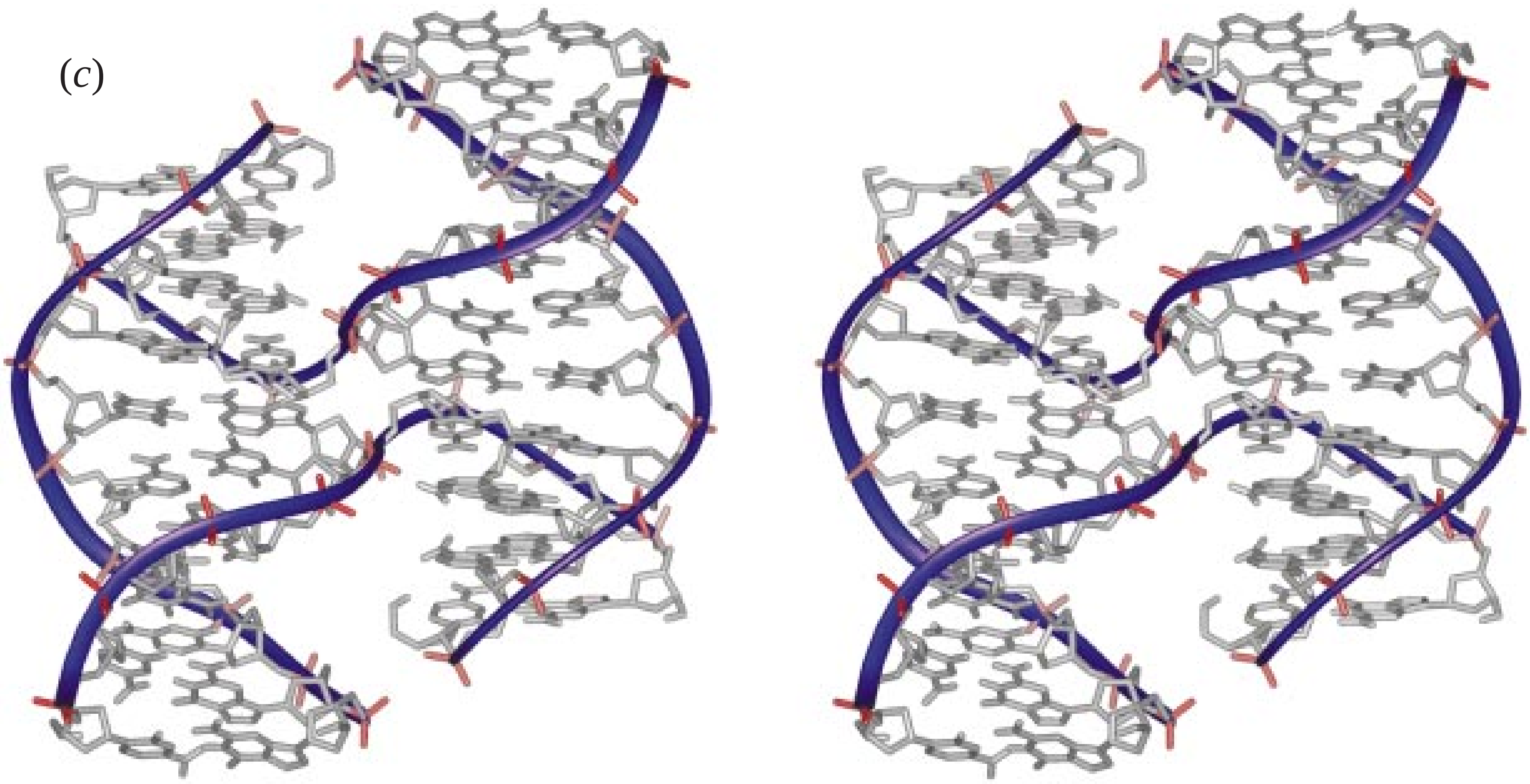

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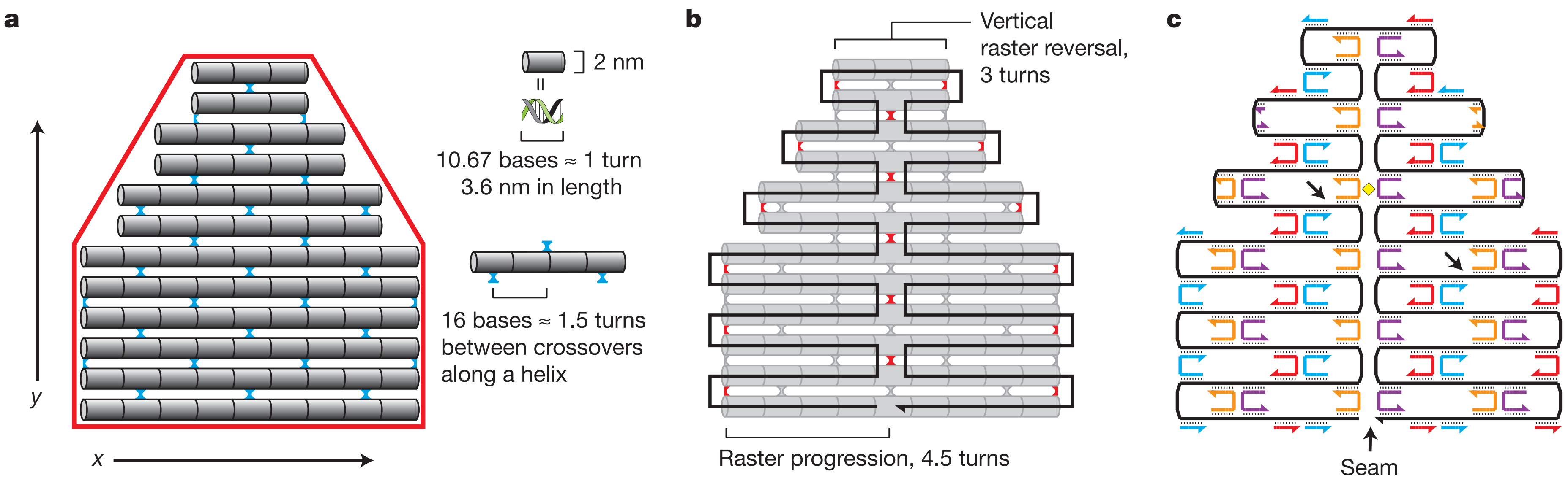
Folding DNA to create nanoscale shapes and patterns

Vol 440|16 March 2006|**doi:10.1038/nature04586**

Paul W. K. Rothemund[1]

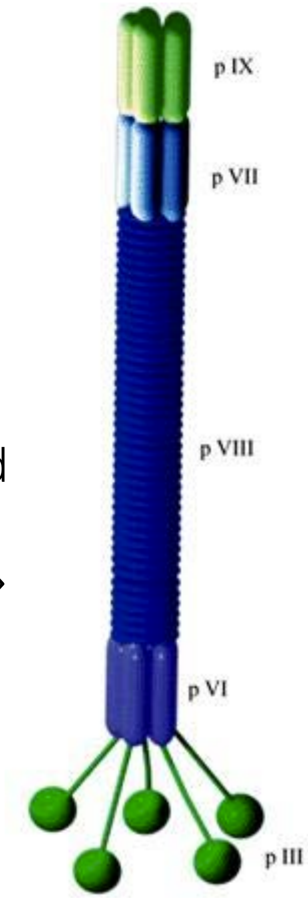


DNA origami

Bacteriophage M13

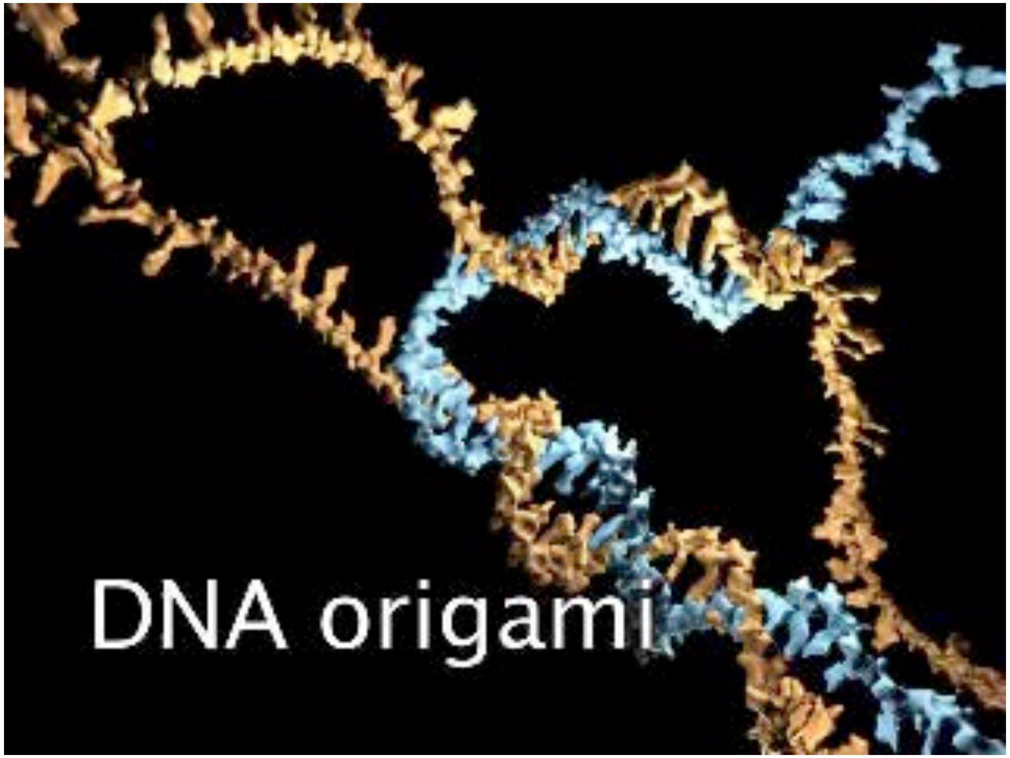
« M13 is a virus that infects the bacterium *Escherichia coli*. It is composed of **a circular single-stranded DNA molecule** encased in a thin flexible tube made up of about 2700 copies of a single protein called P8, the major coat protein. The ends of the tube are capped with minor coat proteins. »

Source: Wikipedia



http://2010.igem.org/wiki/images/e/ed/P3_image.jpg

DNA origami



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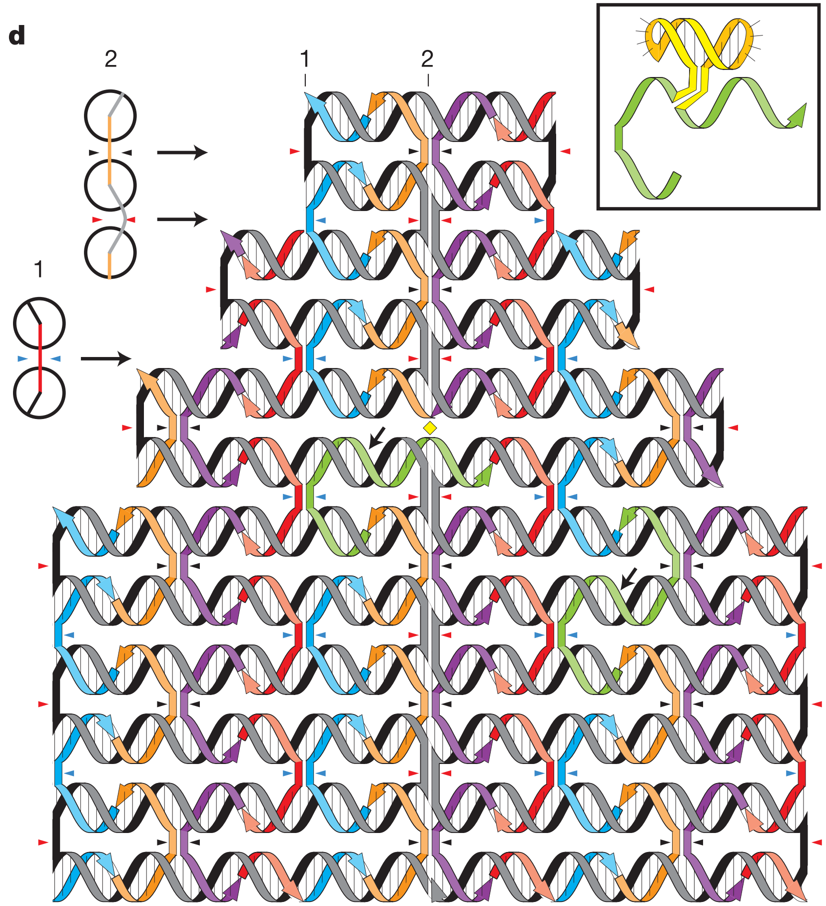

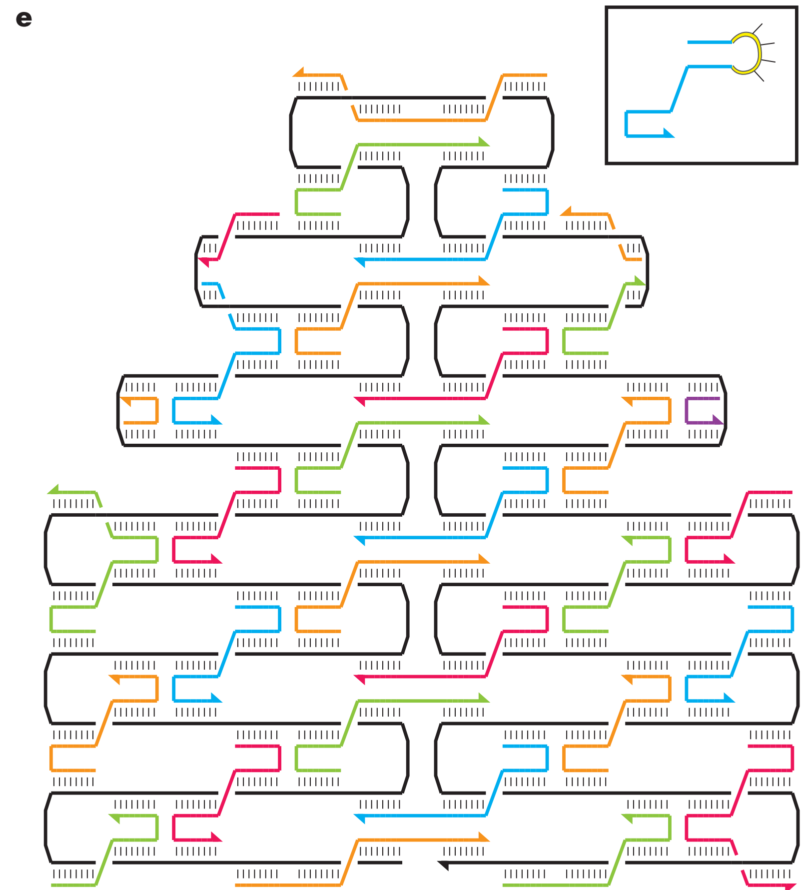

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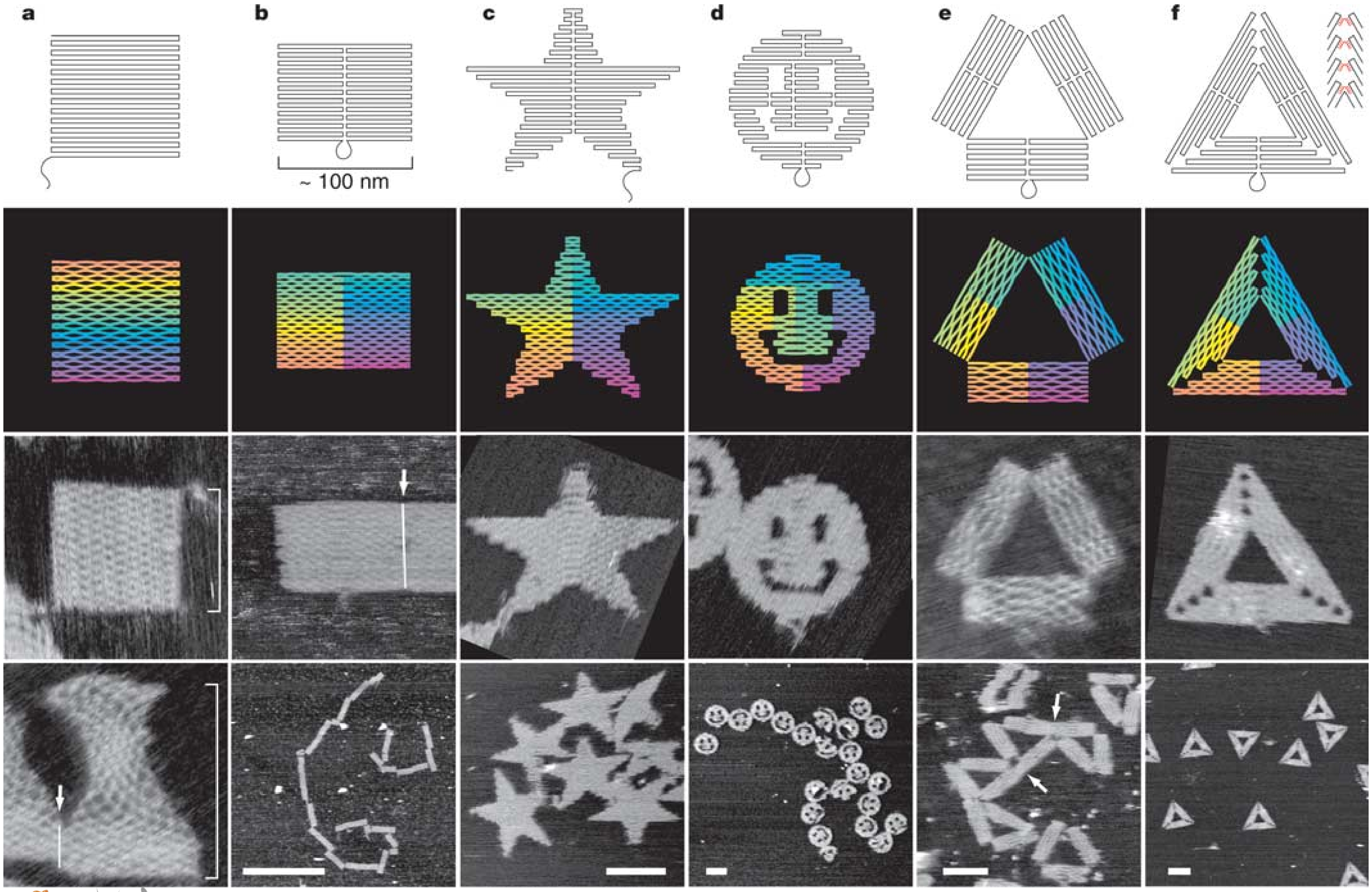
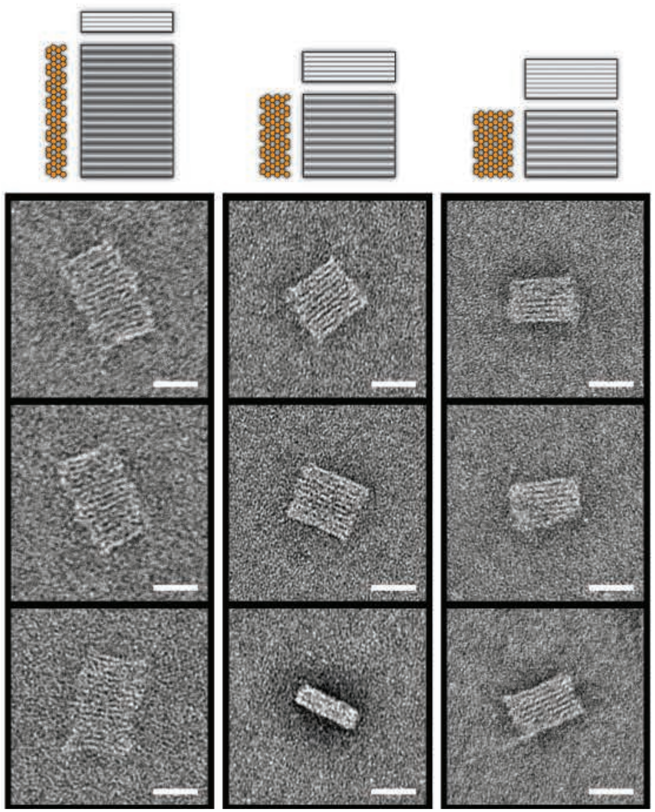


Dedicated softwares for DNA origami designs

Who to design 2D or 3D objects??



scale bars: 25 nm

Nucleic Acids Research, 2009, Vol. 37, No. 15 ***5001–5006***
doi:10.1093/nar/gkp436

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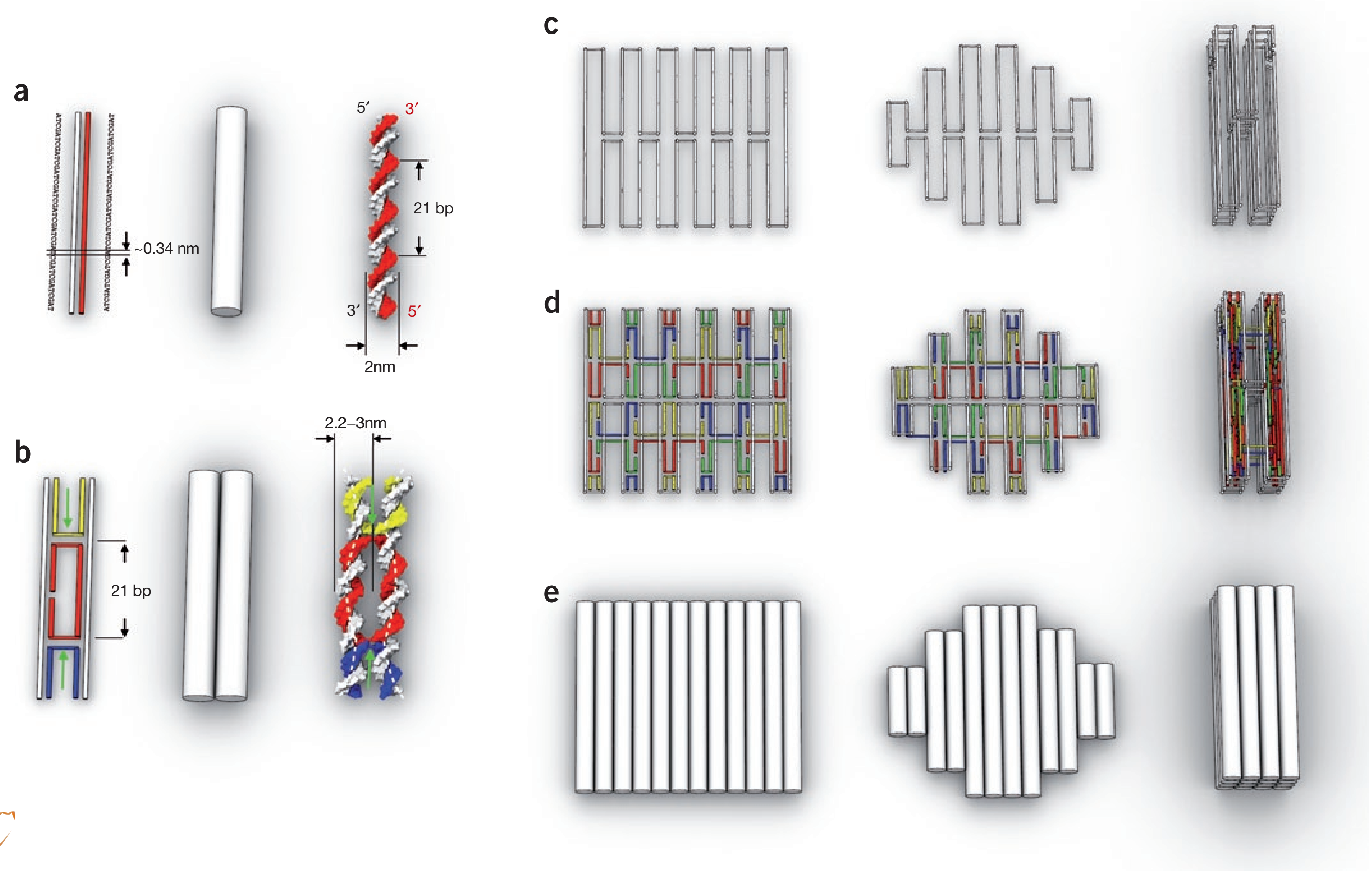
CanDo (https://cando-dna-origami.org/examples/)

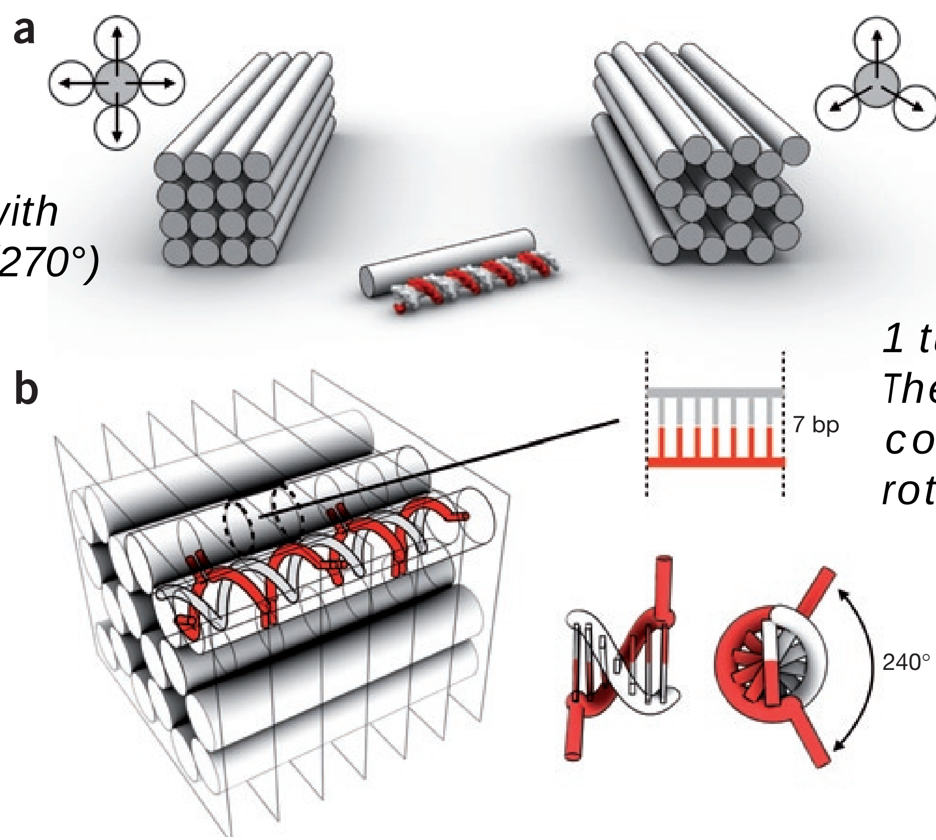


Castro et al., Nature Meth, 2011,DOI:10.1038/NMETH.1570

Dedicated softwares for DNA origami designs

CanDo (https://cando-dna-origami.org/examples/)

1 turn = 10.67 bp
Then, fourfold symetry with cross-overs every 8 bp (270°)



1 turn = 10.67 bp
Then, every 7 bp correspond to a 240° rotation

Castro et al., Nature Meth, 2011,DOI:10.1038/NMETH.1570

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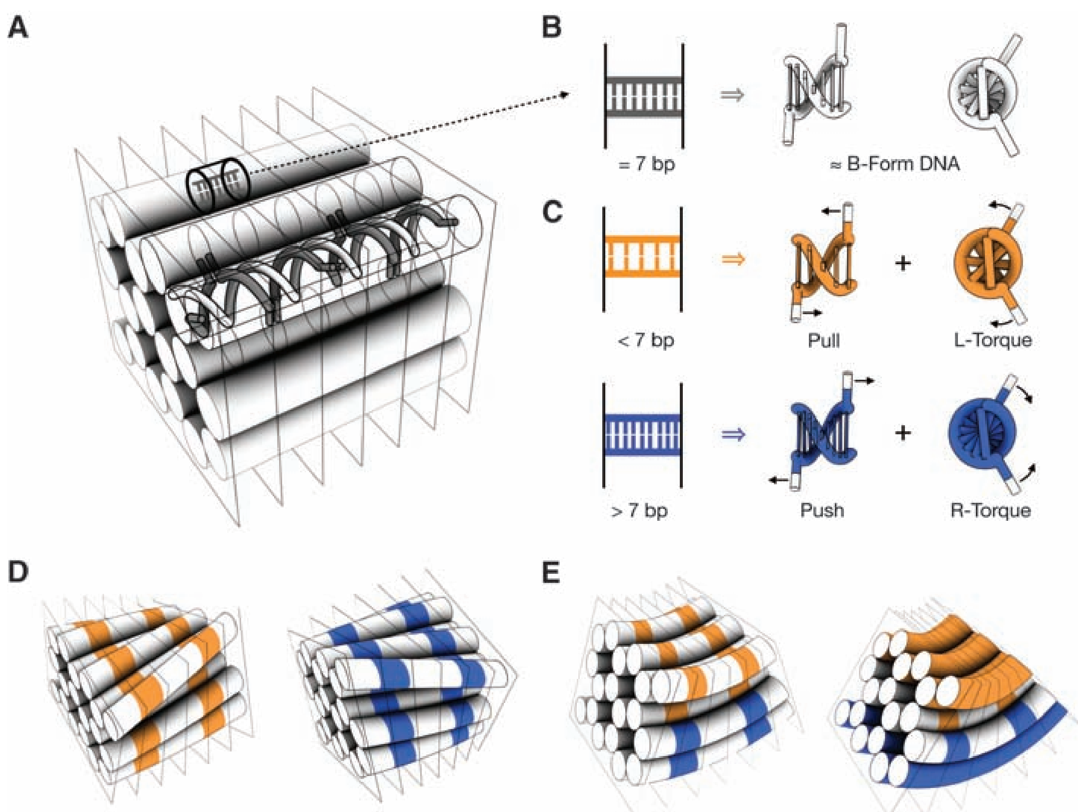
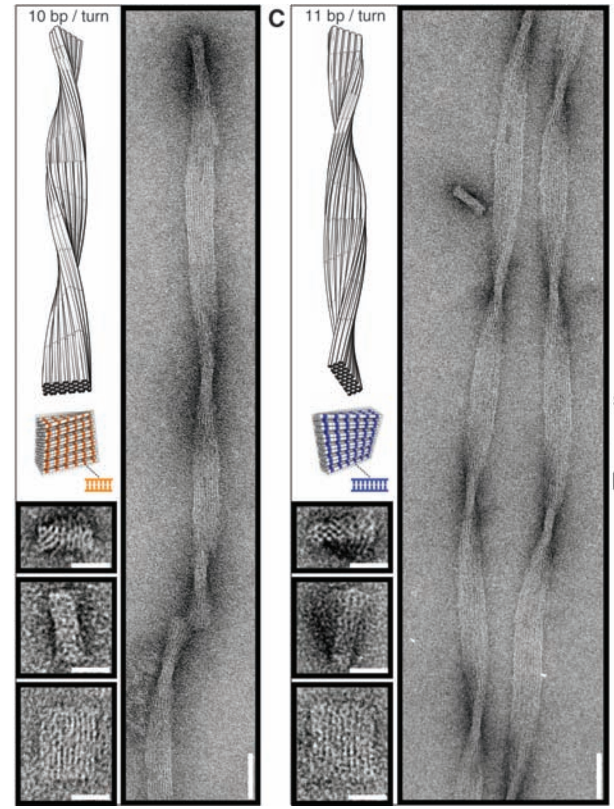
Twisted and curved structures





scale bars: 50 nm

Dietz et al., Science, (2009), 325, p725

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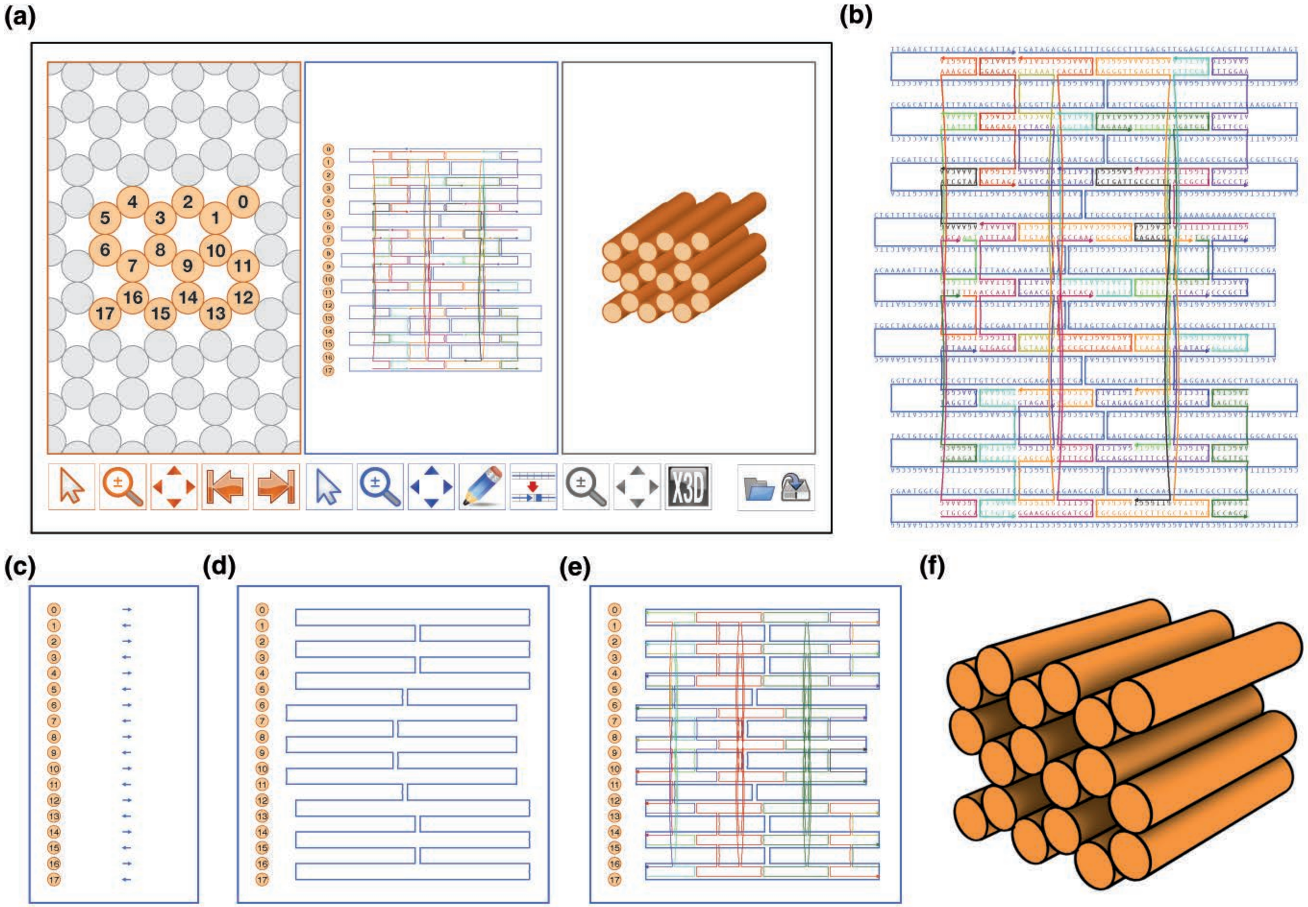
caDNAno (Shi's group, MIT)



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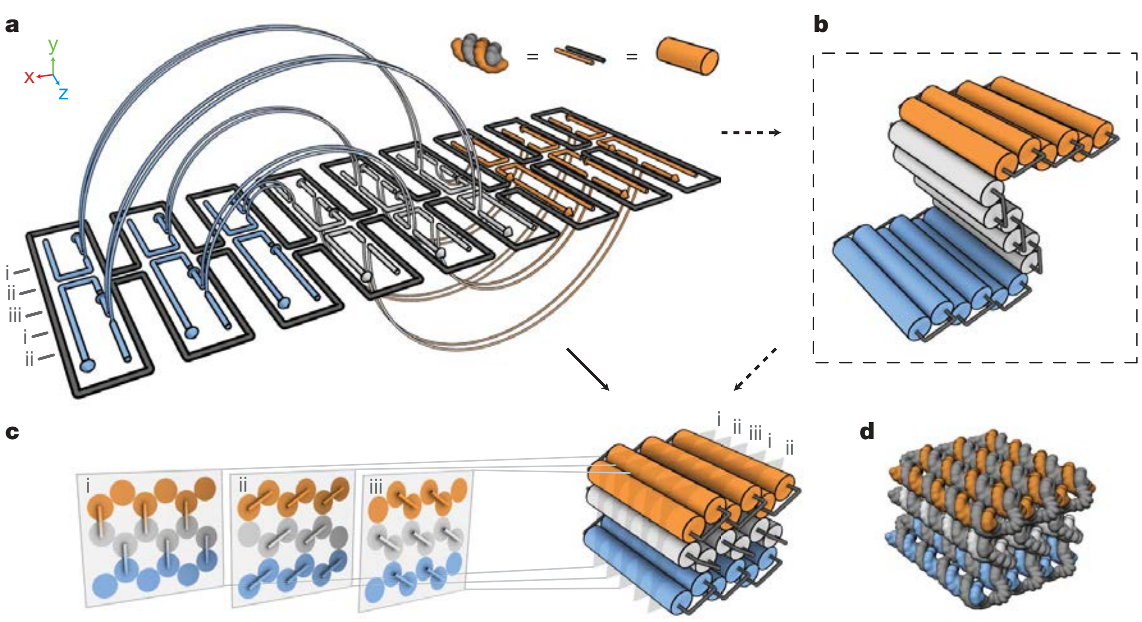

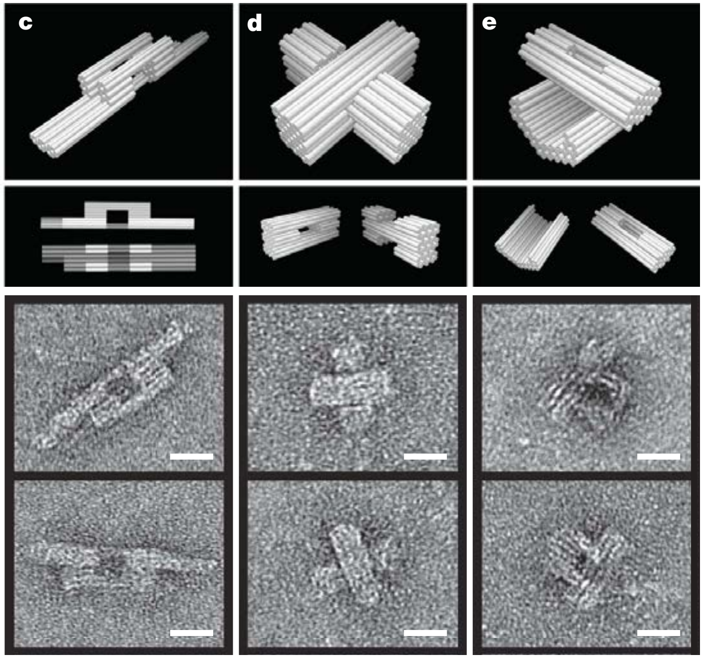

scale bars: 20 nm

Vol 459 | 21 May 2009 | **doi:10.1038/nature08016**

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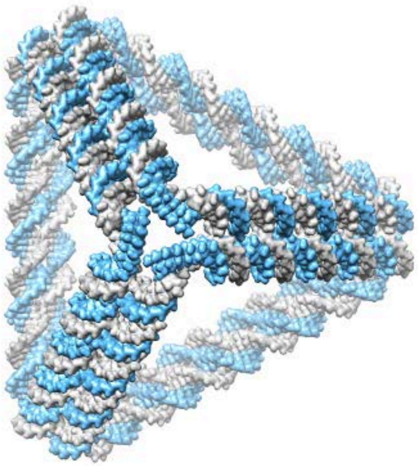
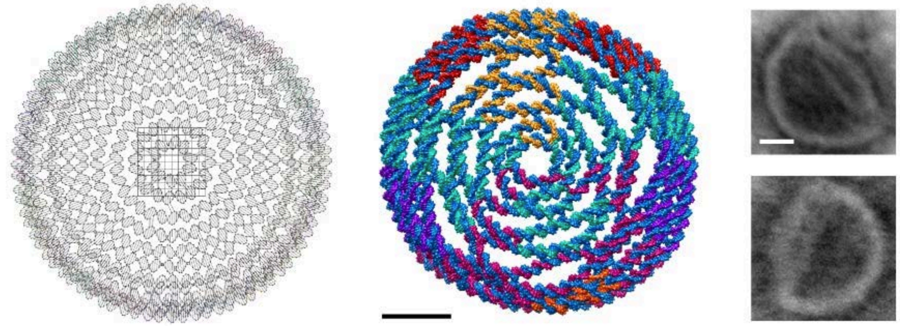
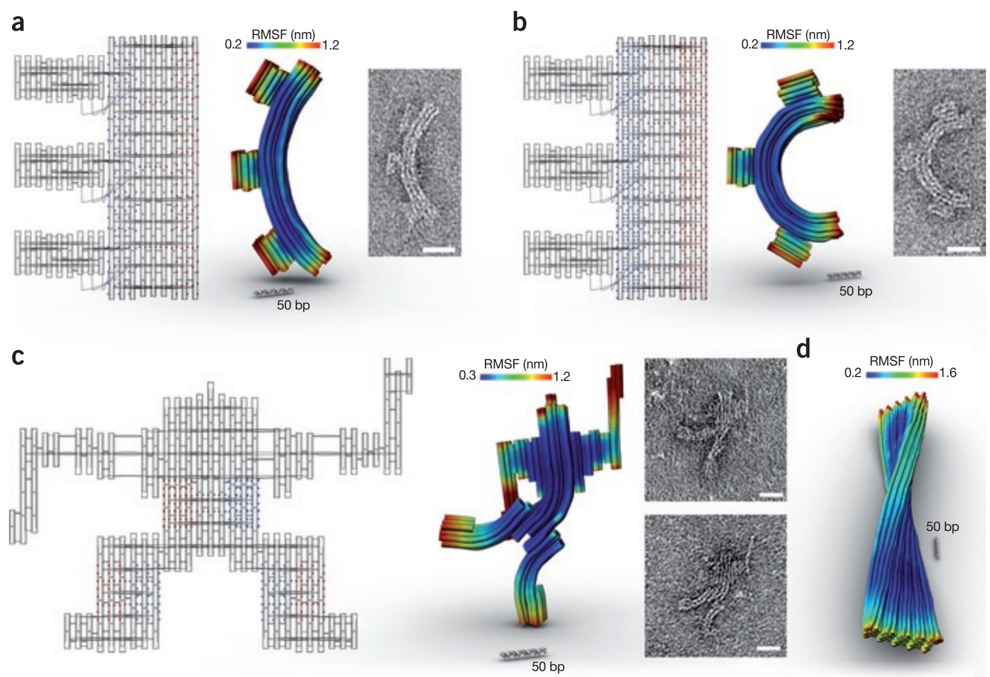
CanDo *(https://cando-dna-origami.org/examples/)*







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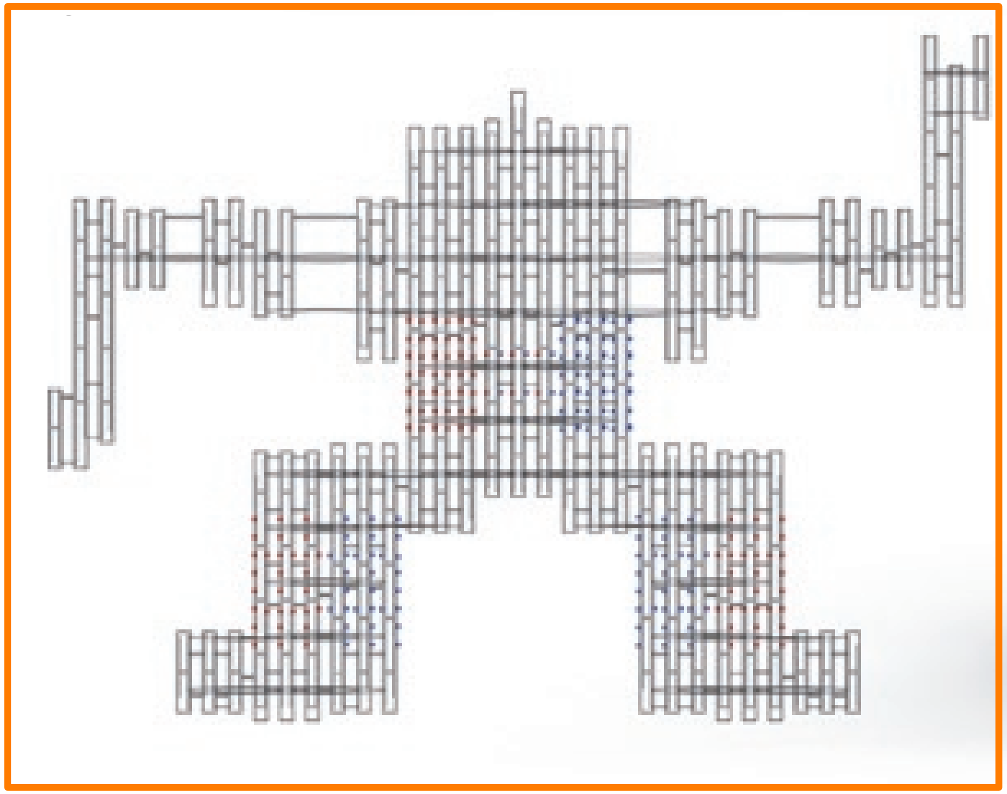
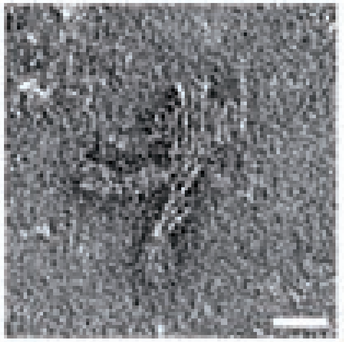
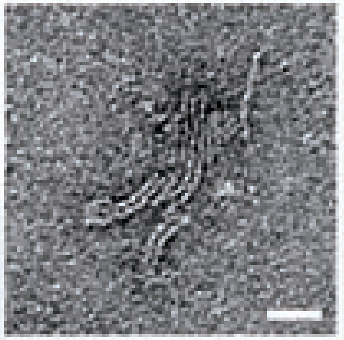
Dedicated softwares for DNA origami designs

cADNano



CanDo





Castro et al., Nature Meth, 2011,DOI:10.1038/NMETH.1570

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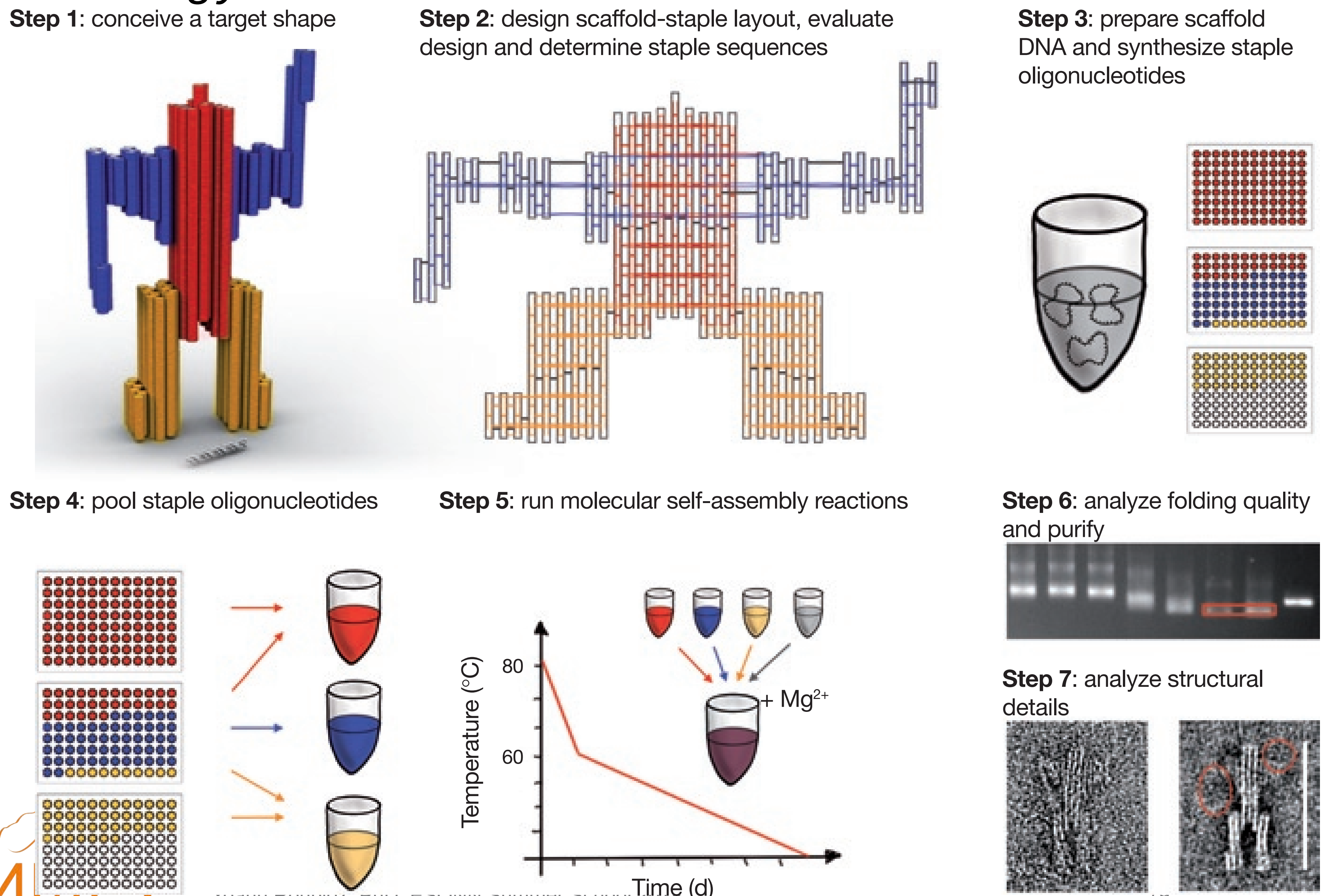
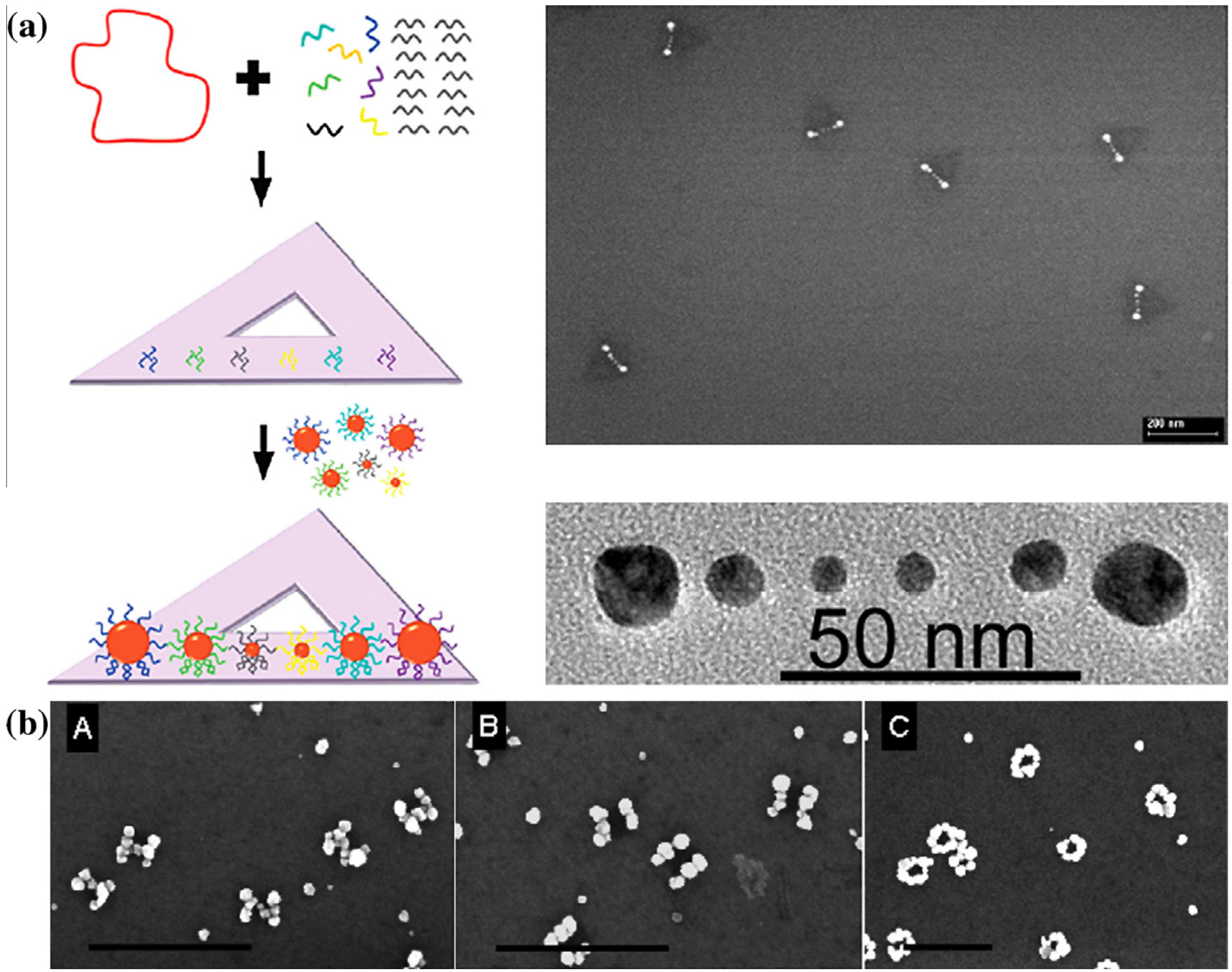
Methodology



Castro et al., Nature Meth, 2011,DOI:10.1038/NMETH.1570

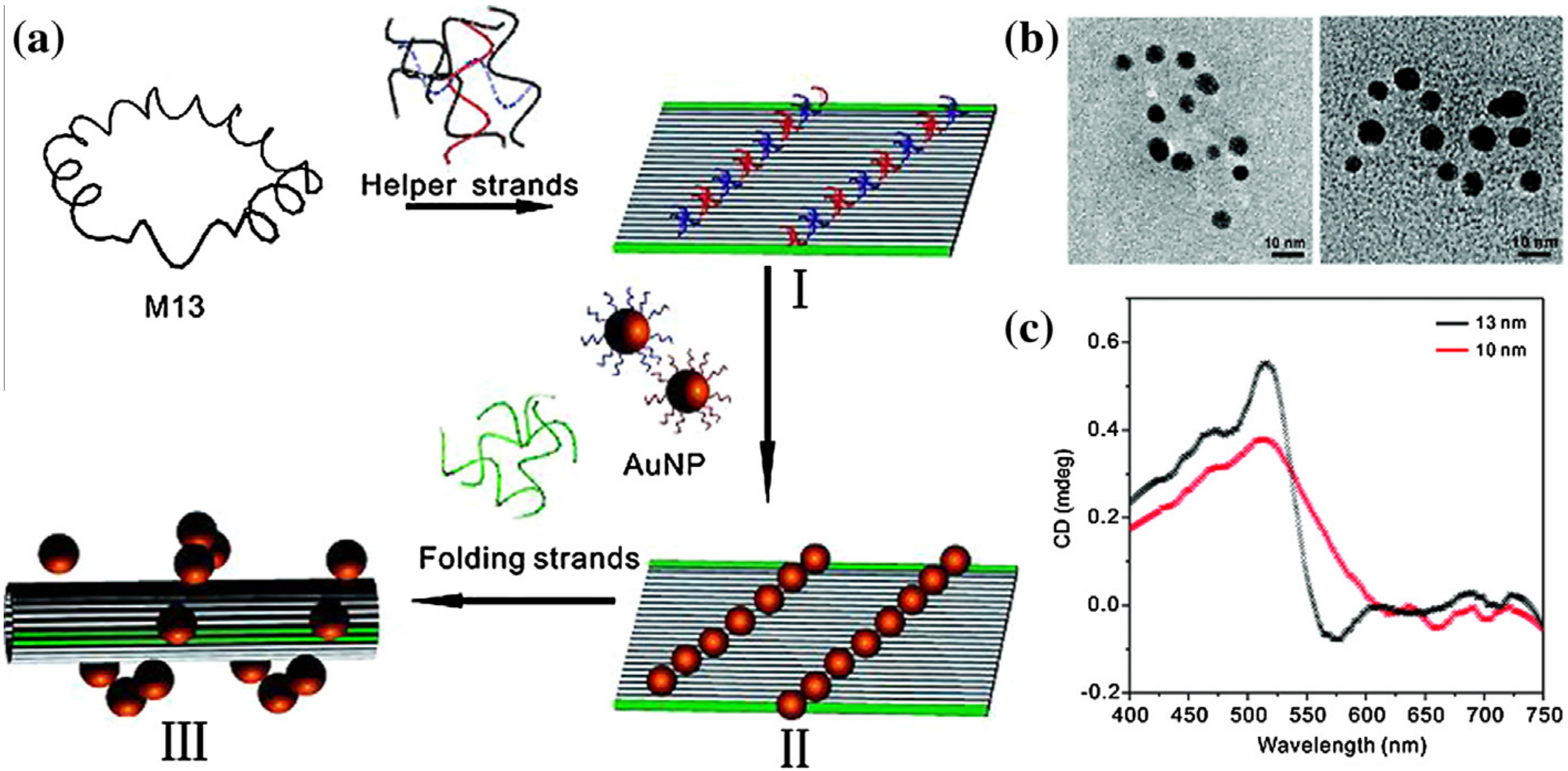
DNA origami decorated with nanoparticles
2D nanostructures



Q. Liu et al., Methods (2013), http://dx.doi.org/10.1016/j.ymeth.2013.10.006

DNA origami decorated with nanoparticles

3D helical nanostructures



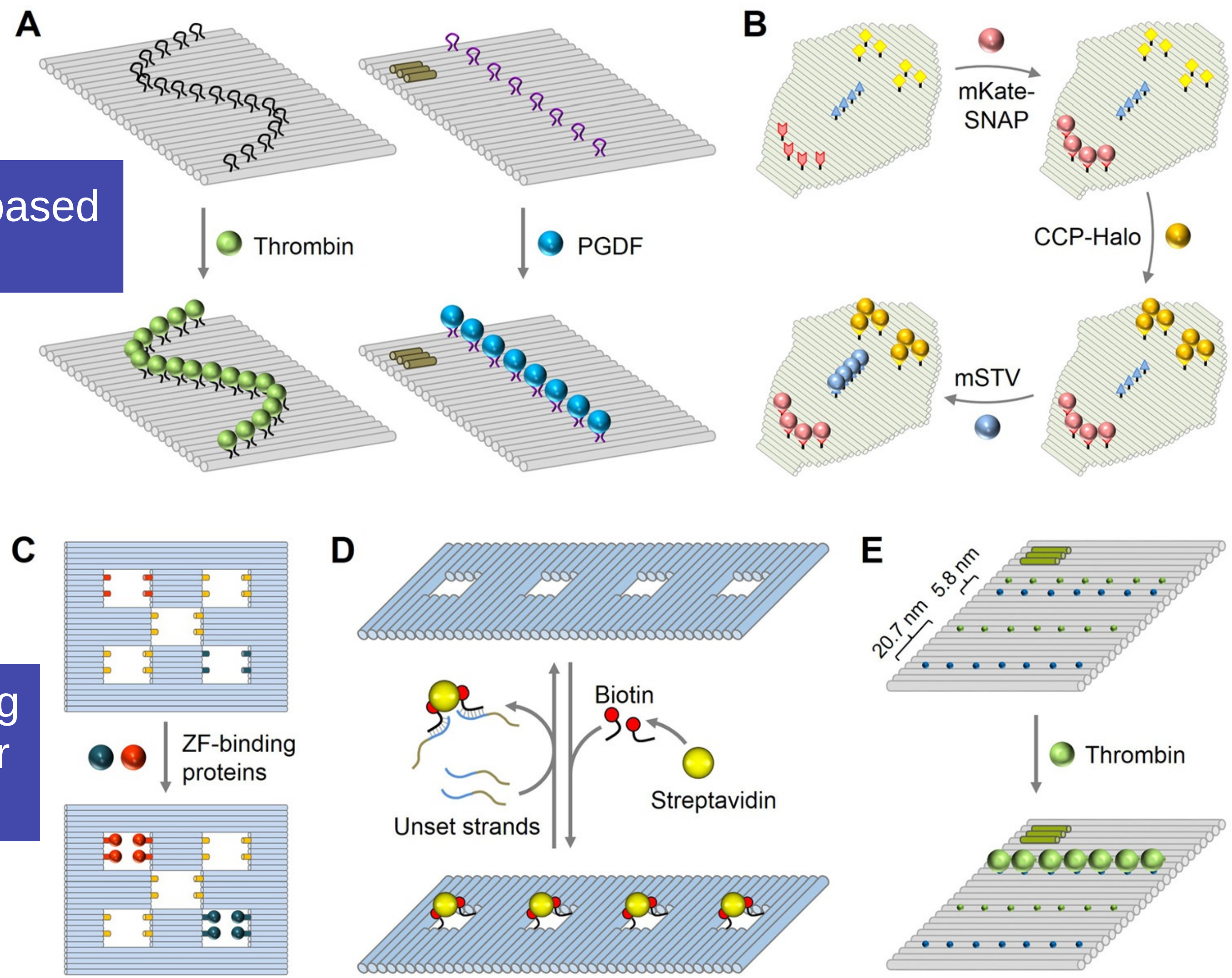
Q. Liu et al., Methods (2013), http://dx.doi.org/10.1016/j.ymeth.2013.10.006

DNA origami decorated with proteins

site-specific coupling w/ chemical ligands

Aptamer-based binding

DNA binding by Zn-finger proteins



toehold-mediated strand displacement

analysis of distance specific apt-protein interactions

ChemBioChem 2016, 17, 1081 – 1089

DNA nanocage decorated with proteins

DOI: 10.1002/anie.200603392

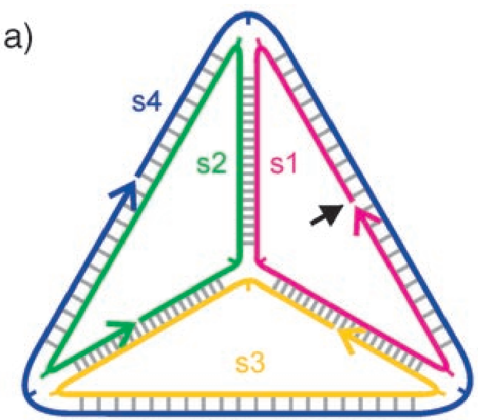
Single-Molecule Protein Encapsulation in a Rigid DNA Cage**

*Christoph M. Erben, Russell P. Goodman, and Andrew J. Turberfield**

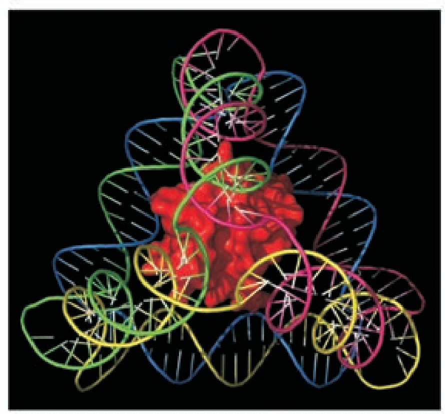
Central cavity of the tetrahedron could accommodate a sphere of radius of approximately 2.6nm,corresponding to a globular protein with a molecular weight of 60 kDa.

cytochrome c (12.4 kDa)

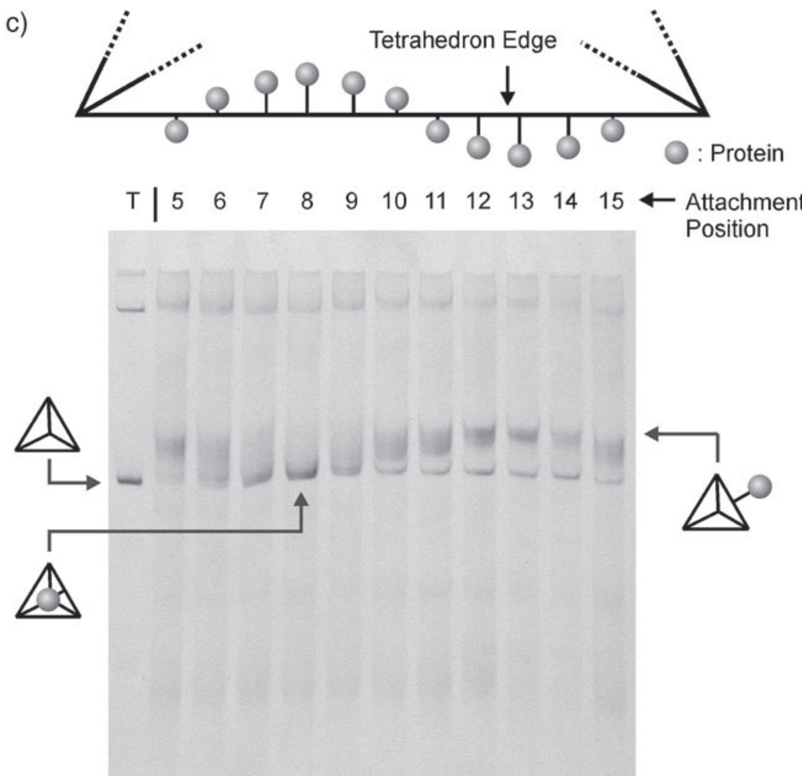
a)



b)

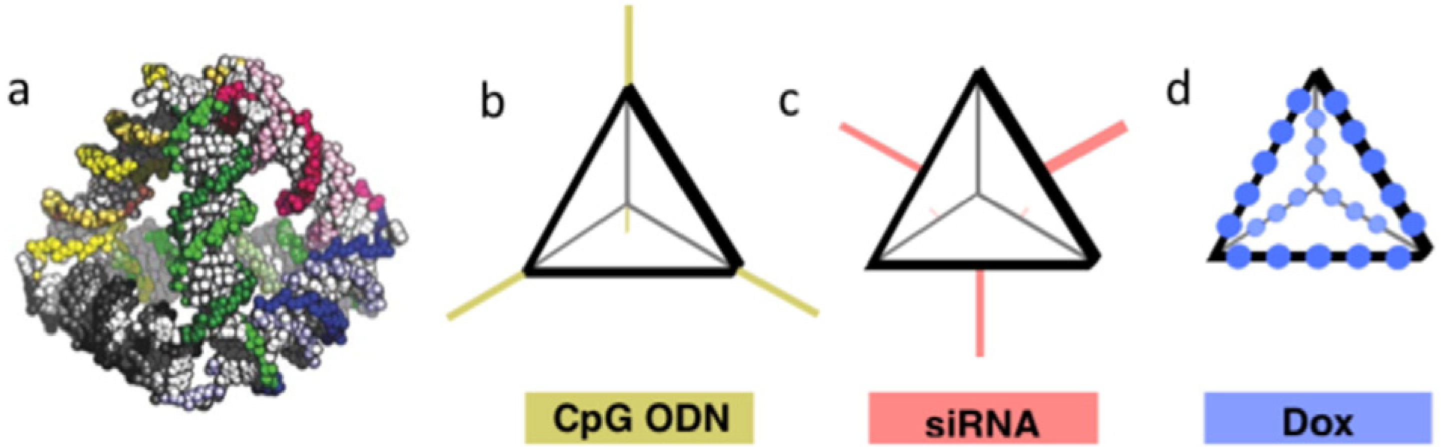


c)



DNA-based drug delivery

« Particles below 25 nm are subject to filtration in the kidney or uptake in the liver, and particles above 150 nm experience increased filtration in the spleen and phagocytosis by macrophages » => DNA nanocages are the perfect « nanovehicles »



a) The DNA tetrahedron is assembled by annealing of 4 ODNs. It consists of three 20 bp sides and three 30 bp sides making it approximately 7.5 nm or 10.5 nm high
b) CpG ODNs attached to the vertices of the tetrahedron
c) siRNA attached to the sides of the tetrahedron
d) Doxorubicin interchelates dsDNA of the tetrahedron

A.H. Okholm, J. Kjems / Advanced Drug Delivery Reviews 106 (2016) 183–191

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- *DNA origamis, structures & design*
- *DNA based origamis for sensing*
- *DNA bricks*
- *DNA machines*
- *DNA multi-enzyme catalysts*

IV. Some work completed in Grenoble

- *DNA based nano-electronics*

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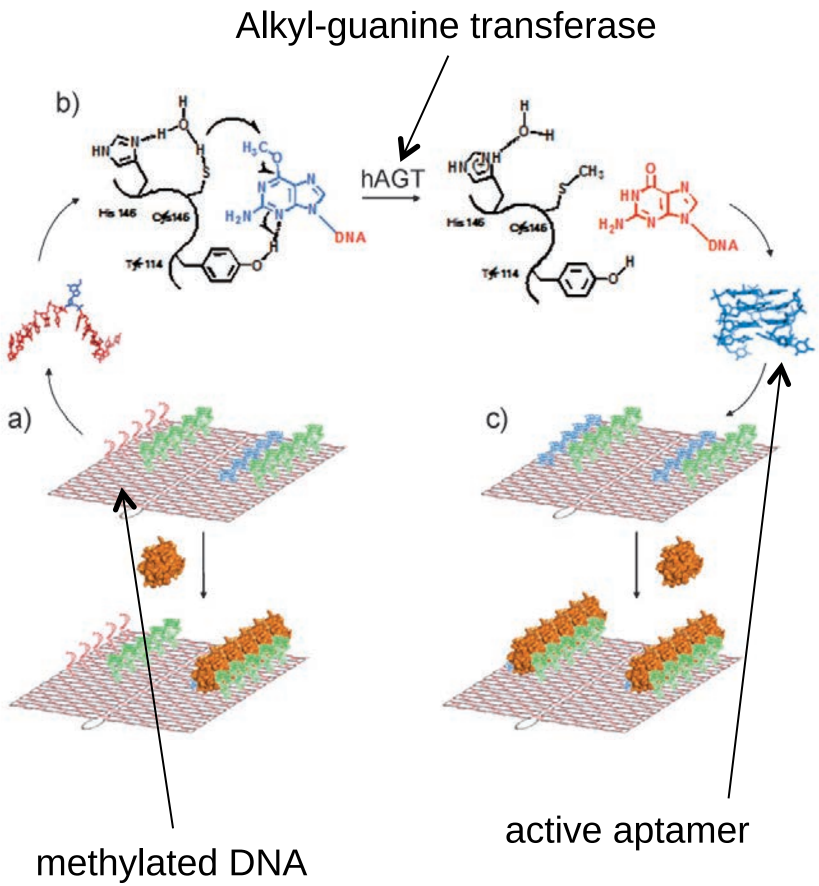
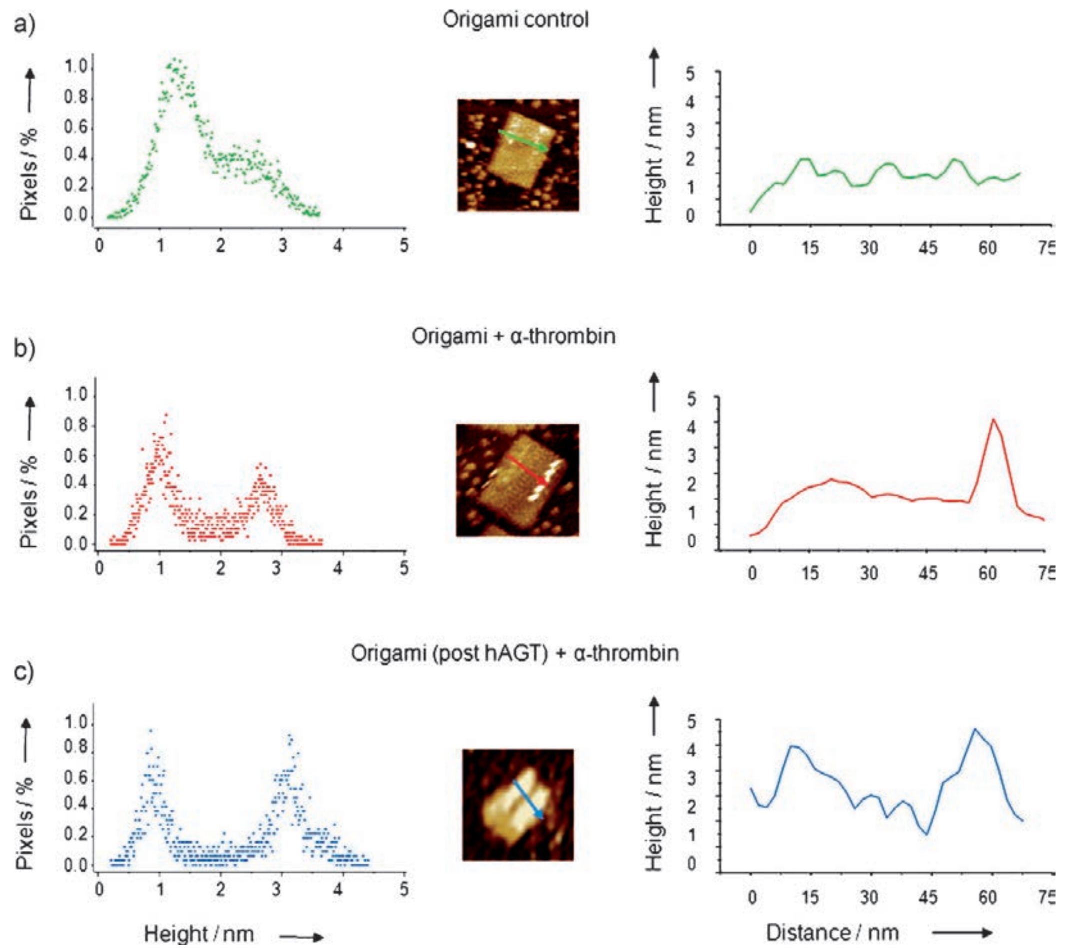
DNA origami for biosensing





Follow-up of enzymatic activity

Angew. Chem. Int. Ed. **2013**, 52, 1–5

Spatial addressability of DNA origami in combination with the change of conformation of a DNA G-quadruplex to visually detect by AFM the change in its binding affinity to a-thrombin.

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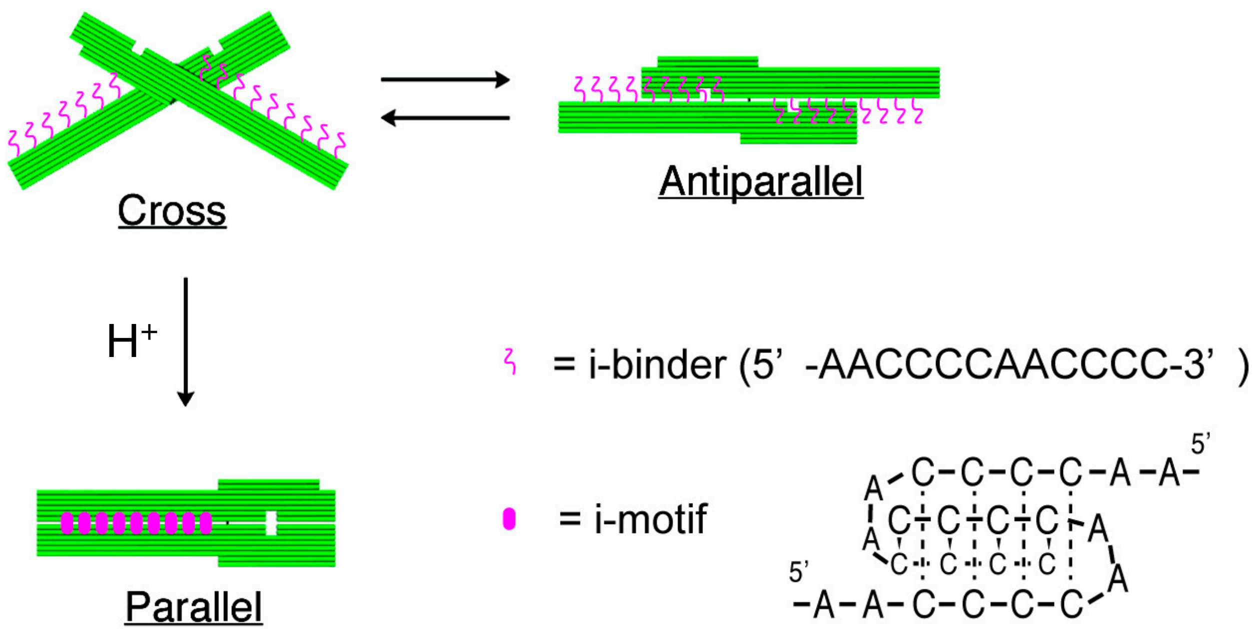
DNA origami as pH sensor

Under acidic conditions, nine pairs of 12-mer i-binders (5'-AACCCCAACCCC-3') attached to the levers of DNA Origami Pliers form i-motif quadruplexes by protonation of the cytidines.

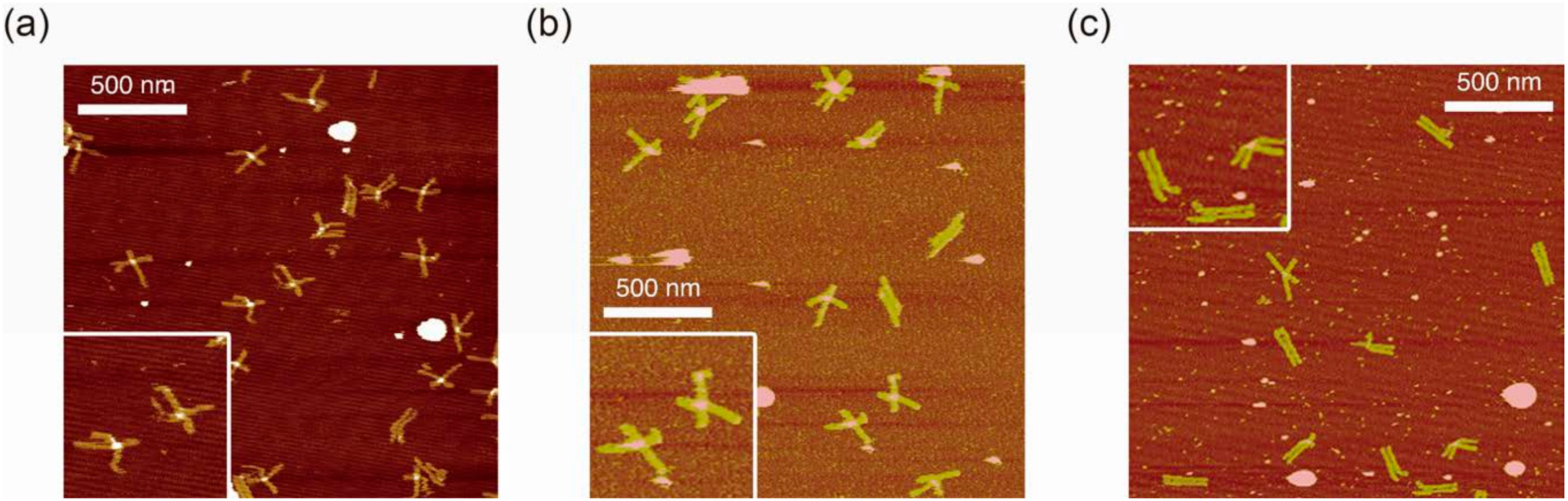


Formation of C-quadruplex

Sensors **2014**, *14*

DNA origami as pH sensor

Atomic force microscopy (AFM) images of DNA Origami Pliers deposited on mica at pH 8.2 (a); pH 7.0 (b); and pH 5.6 (c). Insets: 150% magnified view of typical motifs.



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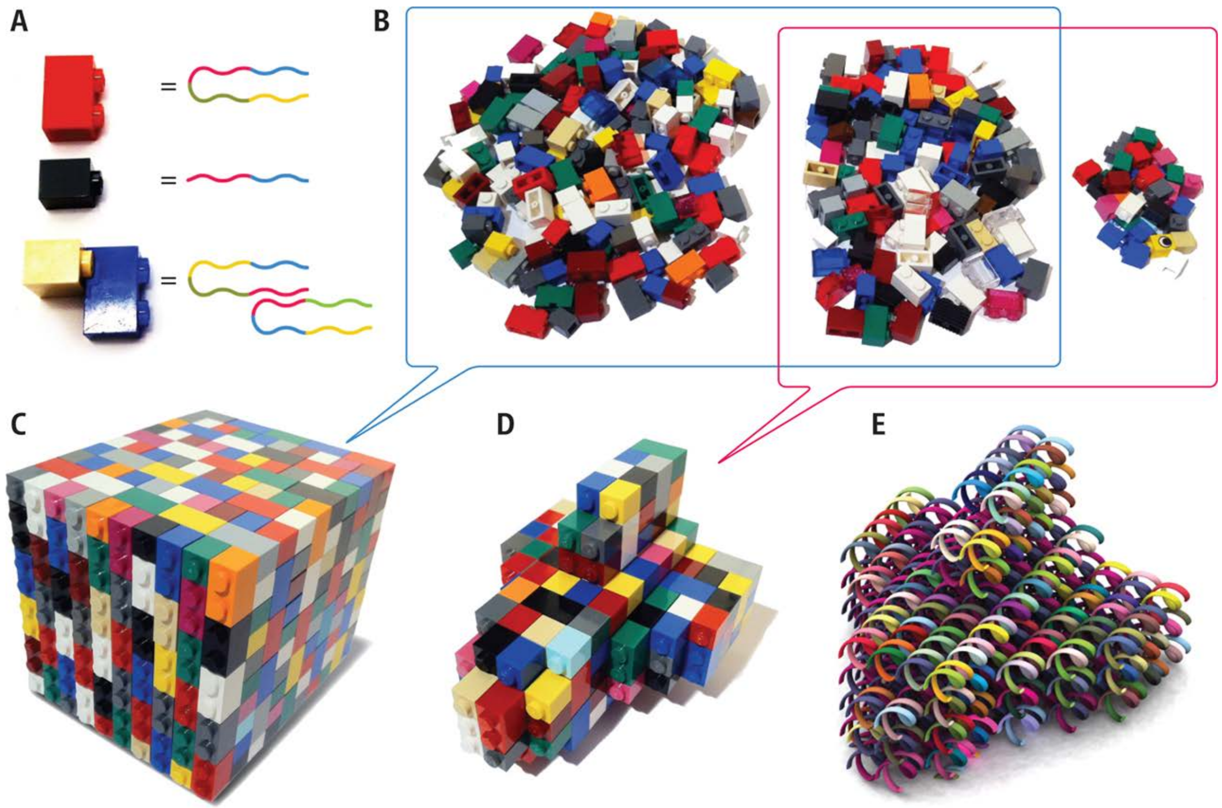
DNA based « lego »

Three-Dimensional Structures Self-Assembled from DNA Bricks

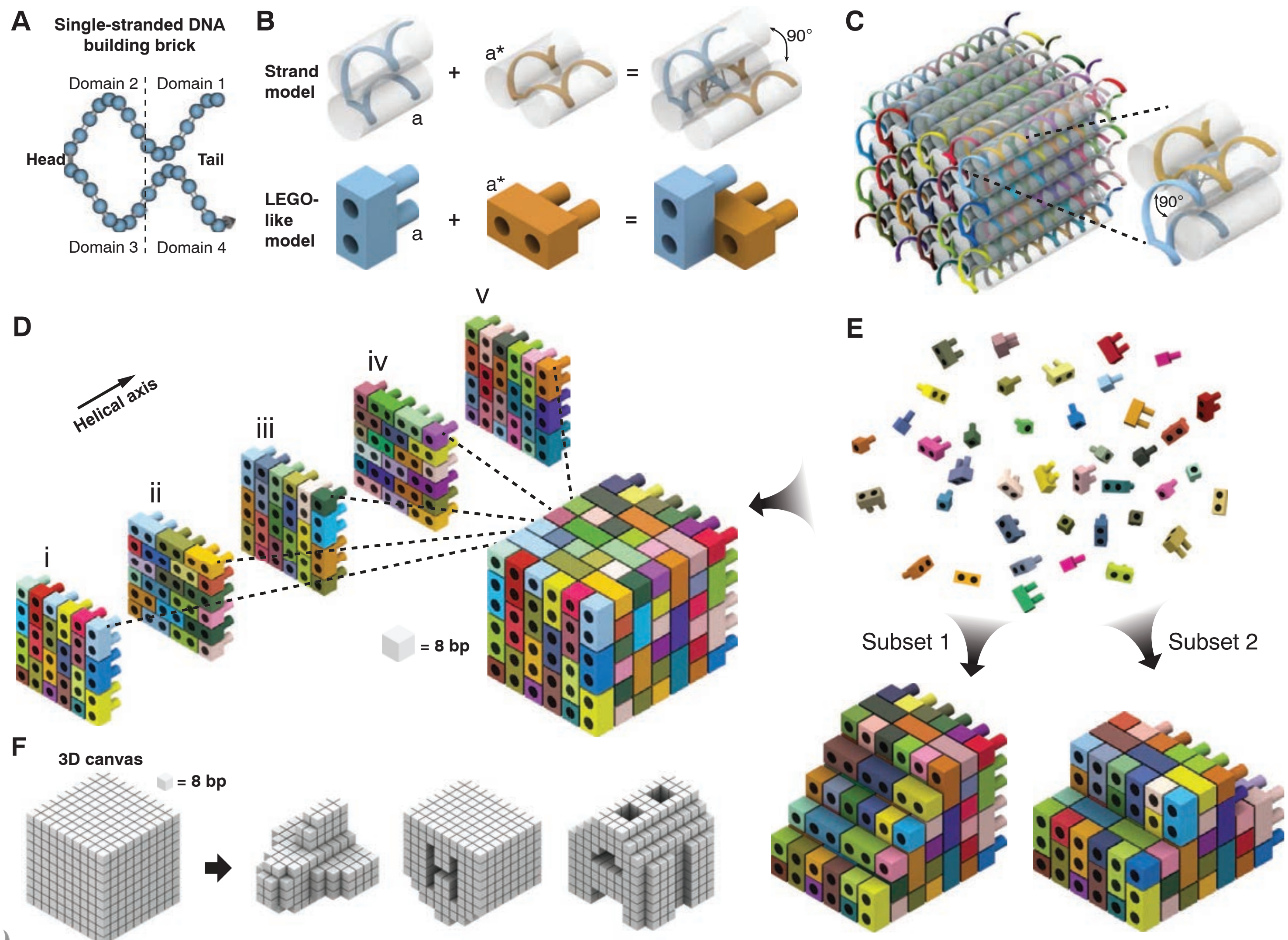
Yonggang Ke,[1,2,3] Luvena L. Ong,[1,4] William M. Shih,[1,2,3] Peng Yin[1,5]*



SCIENCE VOL 338 30 NOVEMBER 2012

DNA single stranded bricks

SCIENCE VOL 338 30 NOVEMBER 2012



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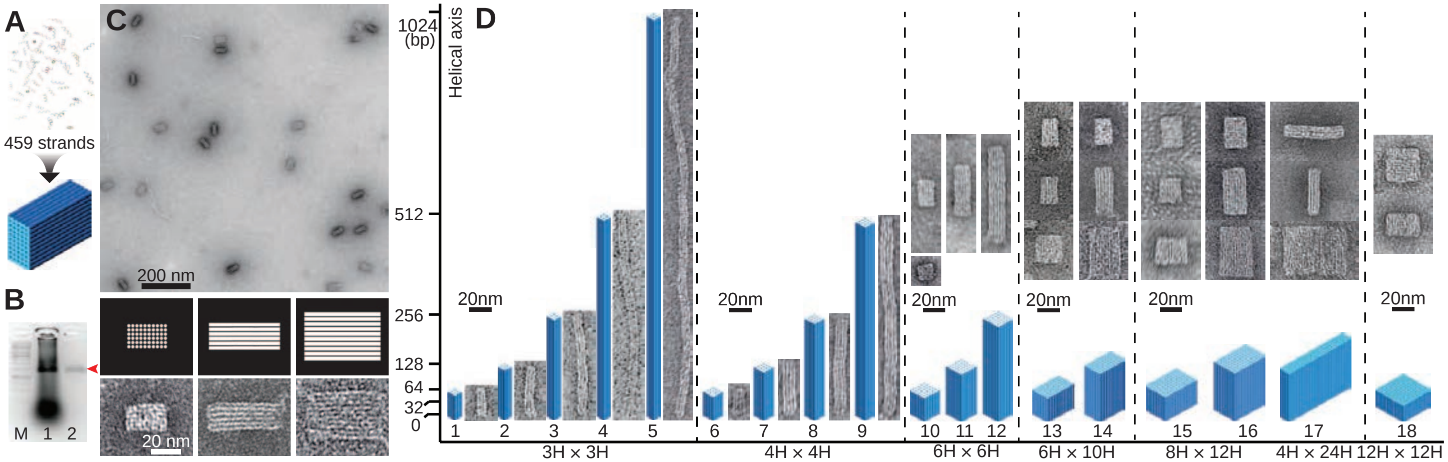

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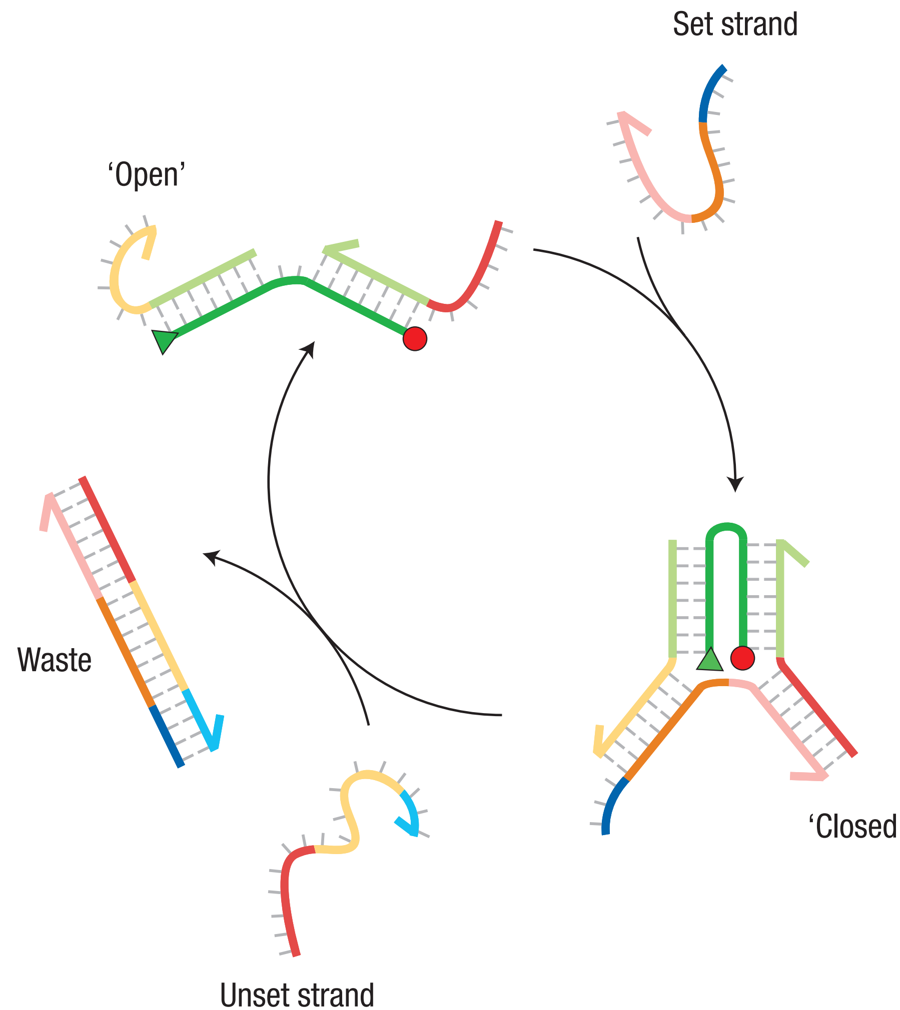
DNA machines

- DNA nanomachine driven by repeated sequential addition of DNA control strands
- DNA tweezers: two double-stranded arms connected by a flexible single-stranded hinge
- The 'set' strand pulls the arms into a closed conformation by hybridizing to single-stranded tails at the ends of the arms
- A short region of the set strand remains single-stranded even when it is hybridized to the tweezers: this region serves as a toehold that allows the 'unset' strand to hybridize to the set strand and strip it from the device, returning the tweezers to the open configuration and generating a double-stranded waste product.
- The state of the device can be determined by measuring the separation between donor and acceptor fluorophores (represented by the green triangle and red circle) using FRET.

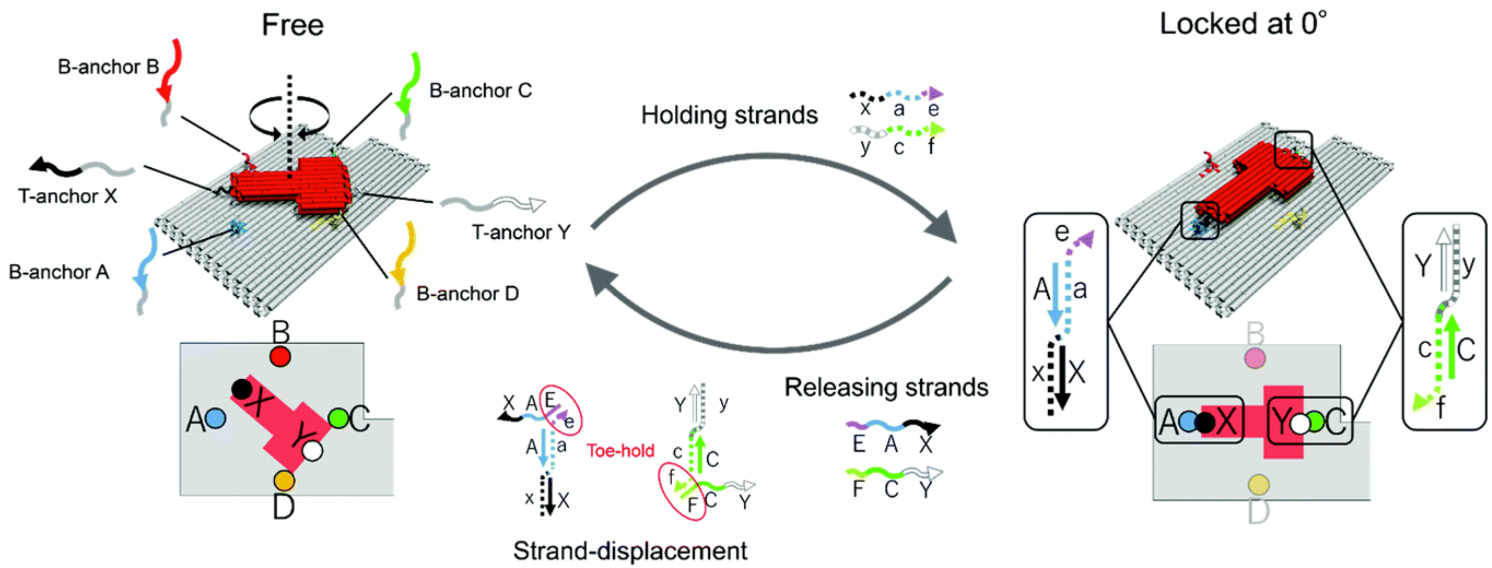


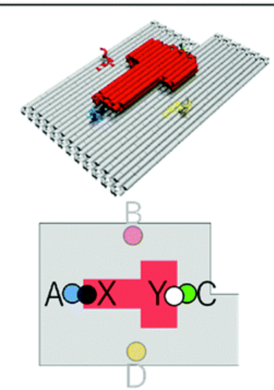
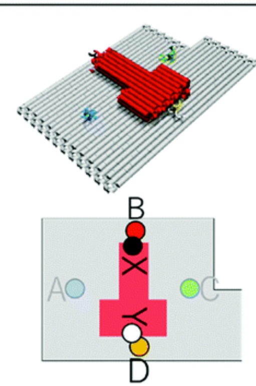
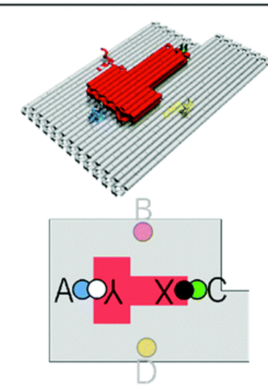
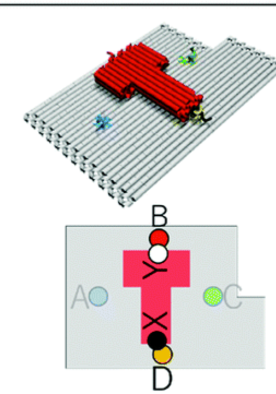
Yurke, B., Turber eld, A. J., Mills, A. P. Jr, Simmel, F. C. & Neumann, J. L. A DNA-fuelled molecular machine made of DNA. *Nature* **406,** 605–608 (2000).

DNA machine: rotor

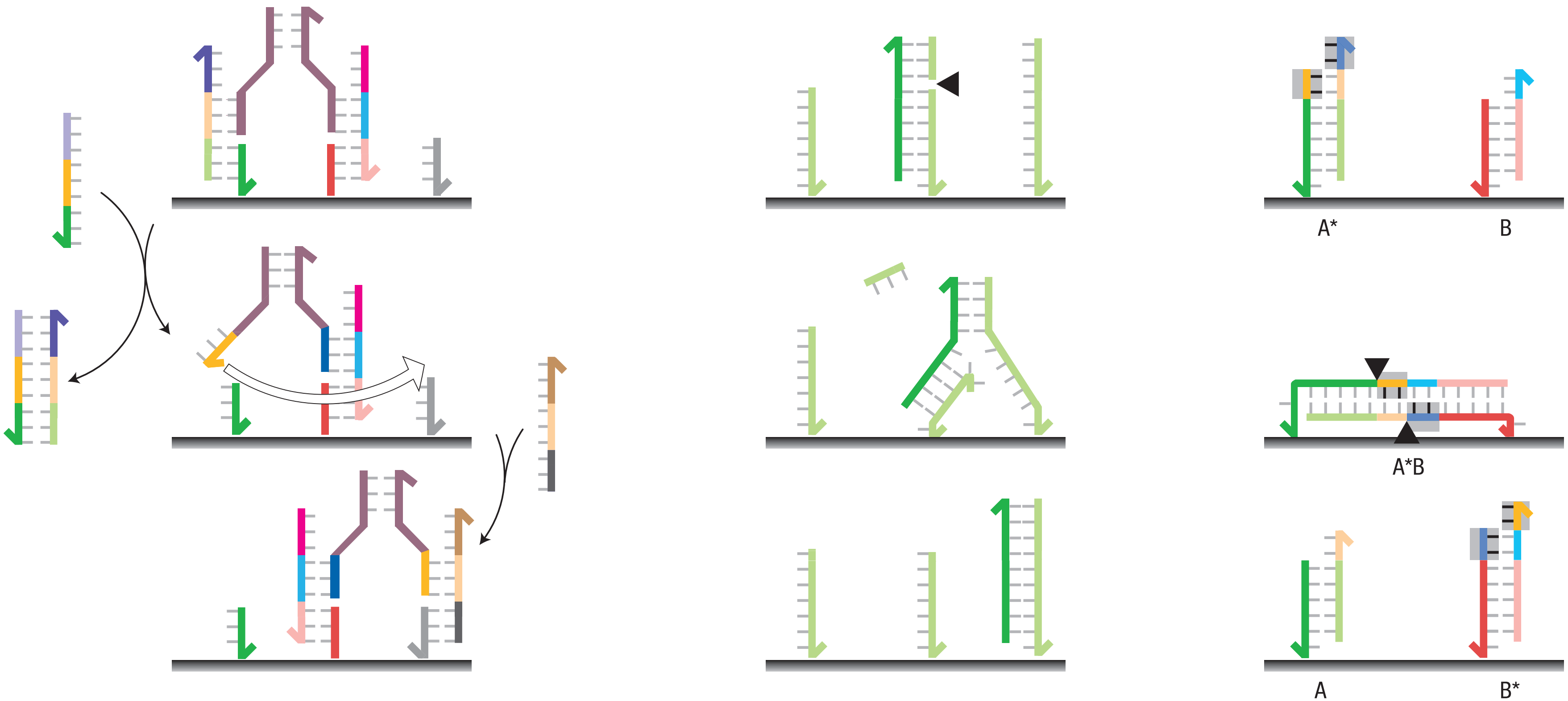
Stepping operation of a rotary DNA origami device†

DOI: 10.1039/c7cc03214e



State	Locked at 0°	Locked at +90°	Locked at 180°	Locked at -90°
Anchors	X-A , Y-C	X-B , Y-D	X-C,Y-A	X-D,Y-B
Holding strands	xae , ycf	xbg , ydh	xci , yaj	xdk , ybl
Releasing strands	EAX , FCY	GBX , HDY	ICX , JAY	KDX , LBY
				

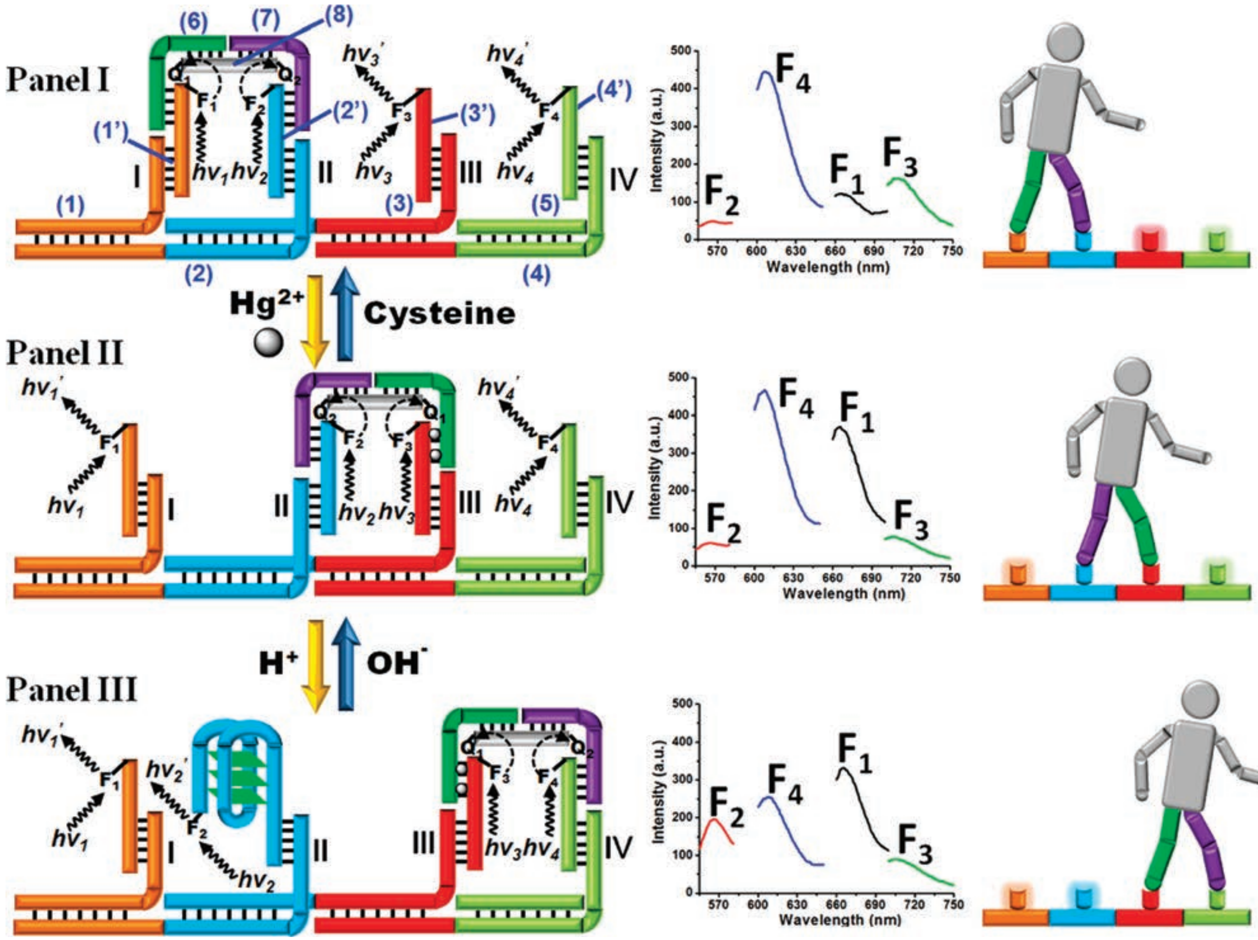
DNA walking machines



Tuberfield review, Nature Nanotechnology, vol 2, may 2007, p.275

DNA single stranded bricks

thymine-Hg2+-thymine complex
and i-motif structure as driving forces



NANO LETTERS

pubs.acs.org/NanoLet

DNA Machines: Bipedal Walker and Stepper

Zhen-Gang Wang,† Johann Elbaz,† and Itamar Willner*

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DNA-based drug delivery

ChemComm

COMMUNICATION

View Article Online
View Journal

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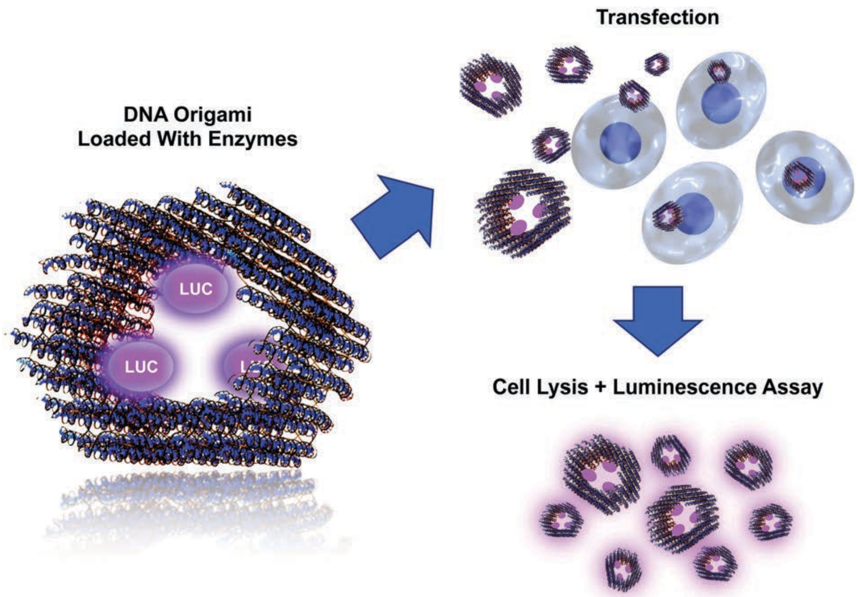
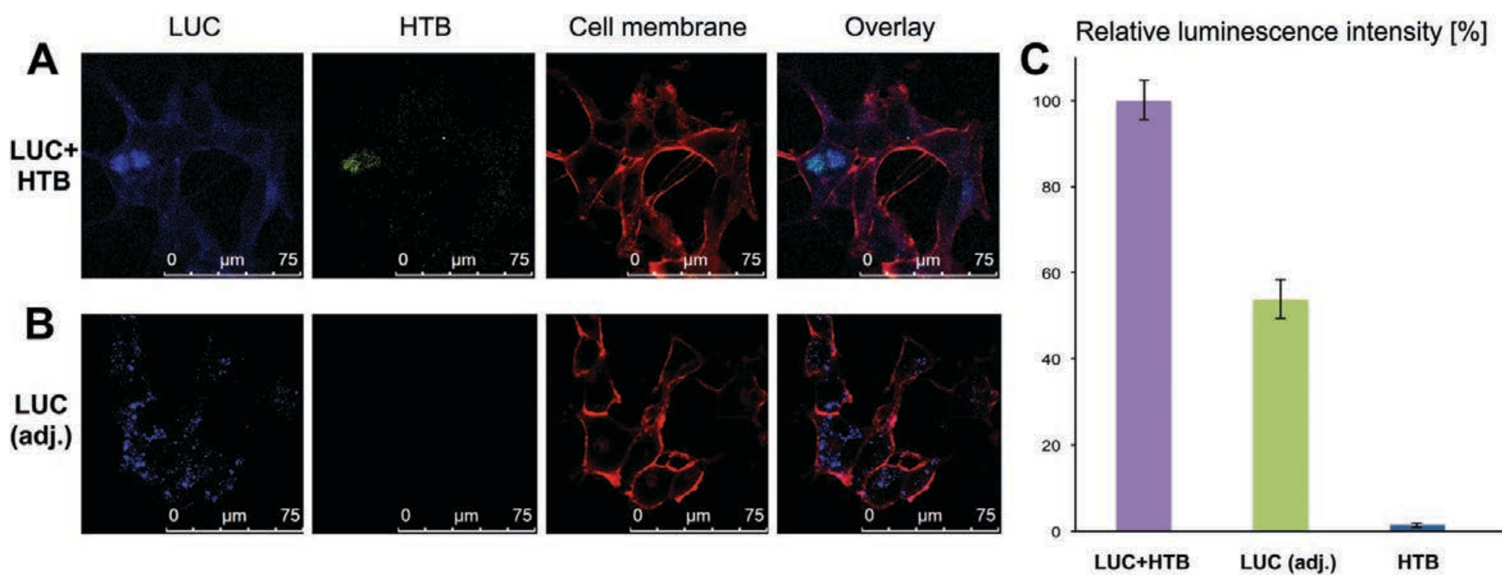
Cite this: DOI: 10.1039/c6cc08197e

Cellular delivery of enzyme-loaded DNA origami†

Ari Ora,‡[a] Erika Järvihaavisto,‡[a] Hongbo Zhang,[b] Henni Auvinen,[a] Hélder A. Santos,[b] Mauri A. Kostiainen*[a] and Veikko Linko*[a]





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POUR L'ÉNERGIE ET LA SANTÉ

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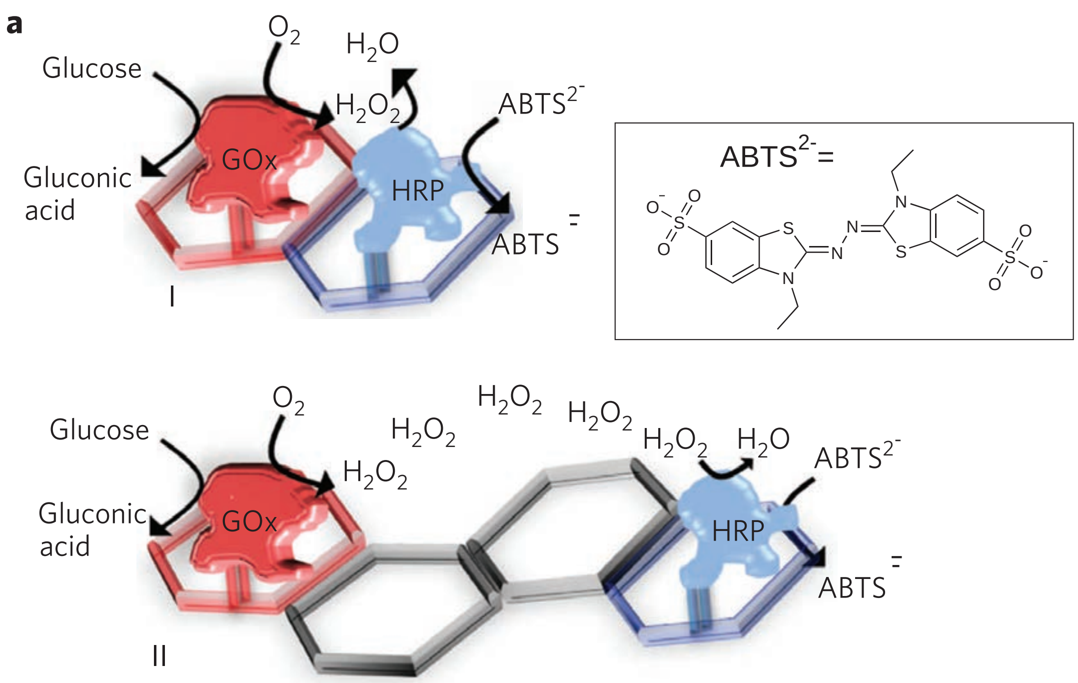
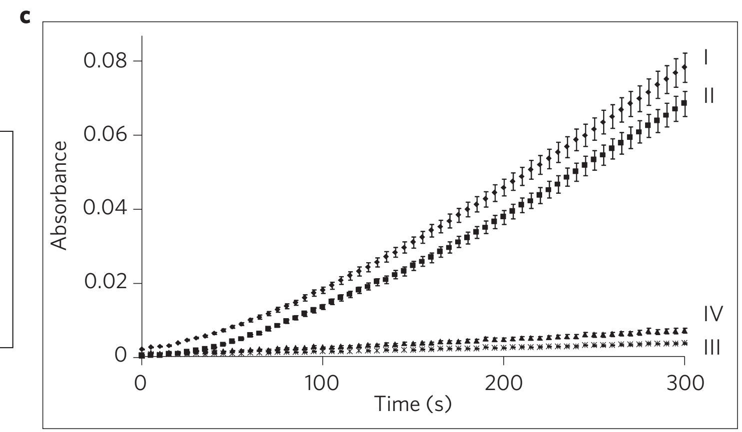
Enzyme cascades activated on topologically programmed DNA scaffolds

Ofer I. Wilner, Yossi Weizmann, Ron Gill, Oleg Lioubashevski, Ronit Freeman and Itamar Willner*





Time-dependent absorbance changes as a result of the oxidation of ABTS2- by the GOx–HRP cascade in the presence of (I) the two-hexagon scaffold, (II) the four-hexagon scaffold, (III) in the absence of any DNA, and (IV) in the presence of foreign calf thymus DNA

DOI: 10.1038/NNANO.2009.50

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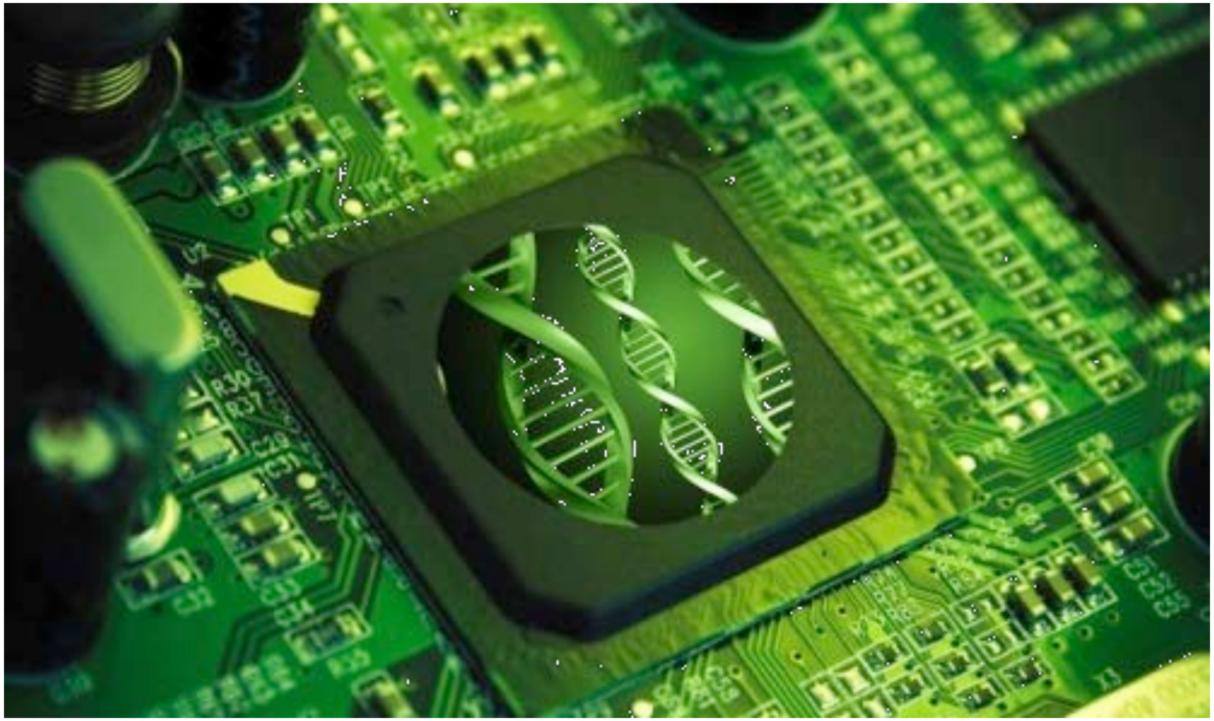
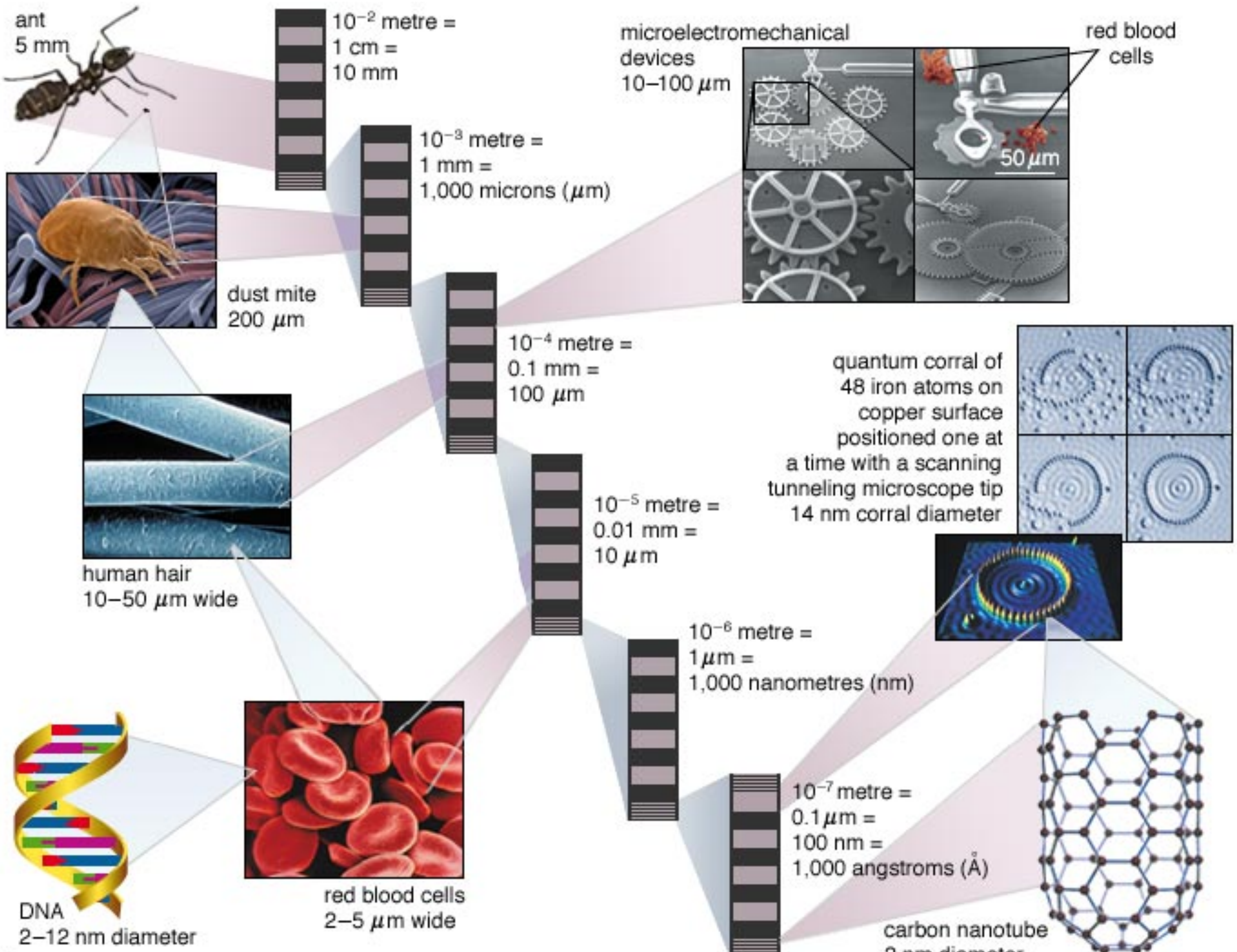
DNA and micro-nano(electronics)



prepared with Raluca Tiron,
CEA researcher (raluca.tiron@cea.fr)

Results from the A3DN project carried in Grenoble (R. Tiron & D. Gasparutto)

DNA and micro-nano(electronics)



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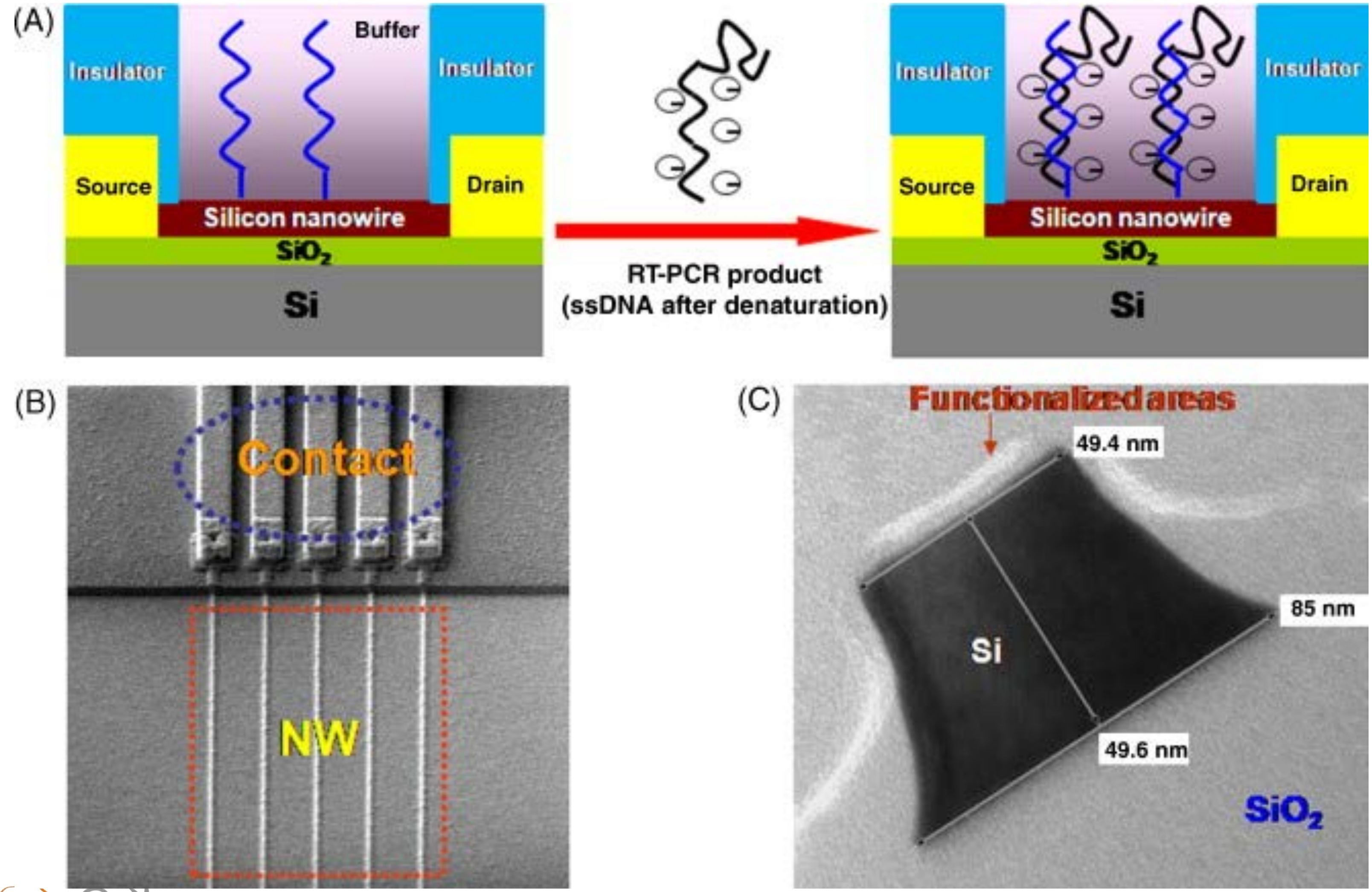
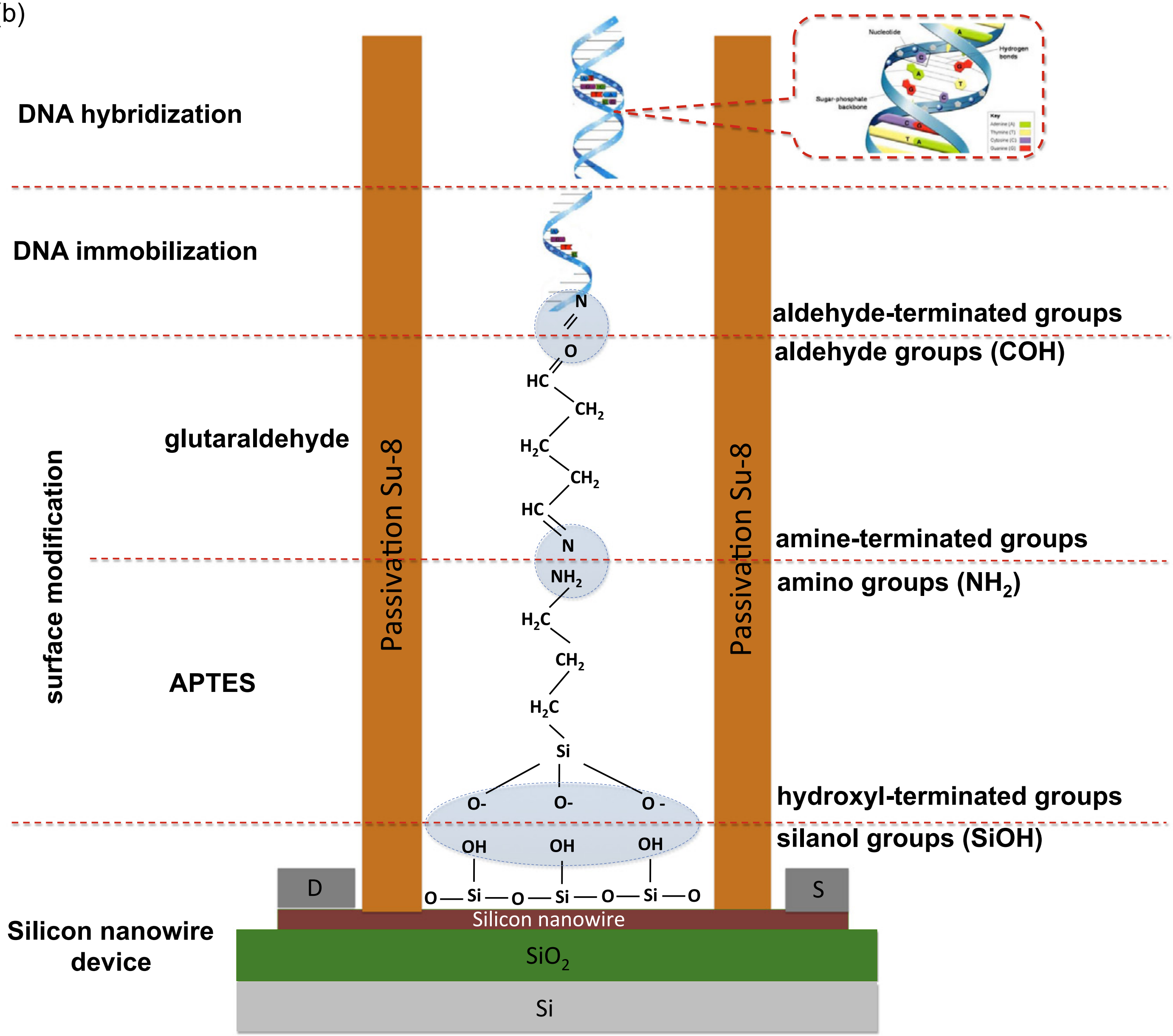
DNA and silicon nanowires



Sensors and Actuators B: Chemical, Volume 146, Issue 1, 8 April 2010, Pages 138–144

DNA and silicon nanowires

(b)



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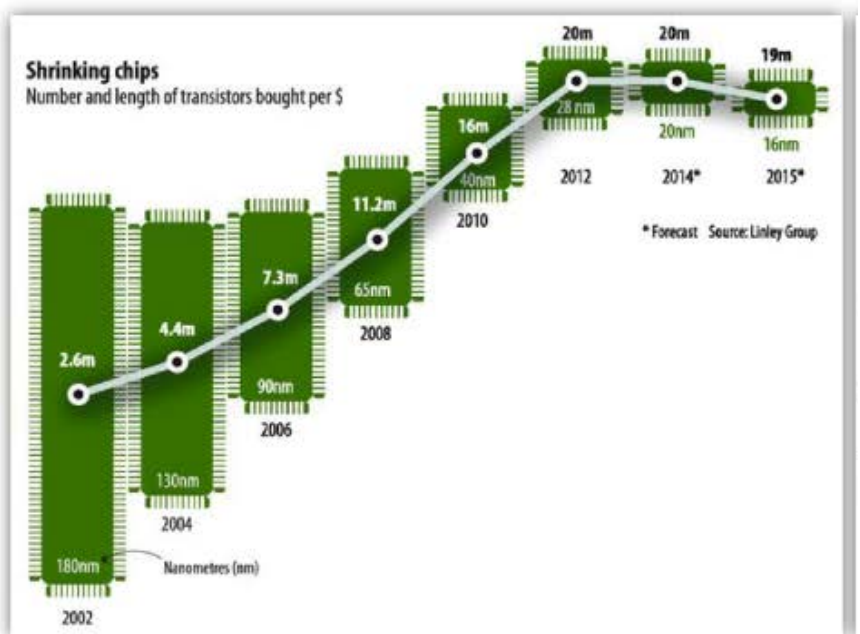
Micro- (nano-)electronics & Moore's law: a major issue

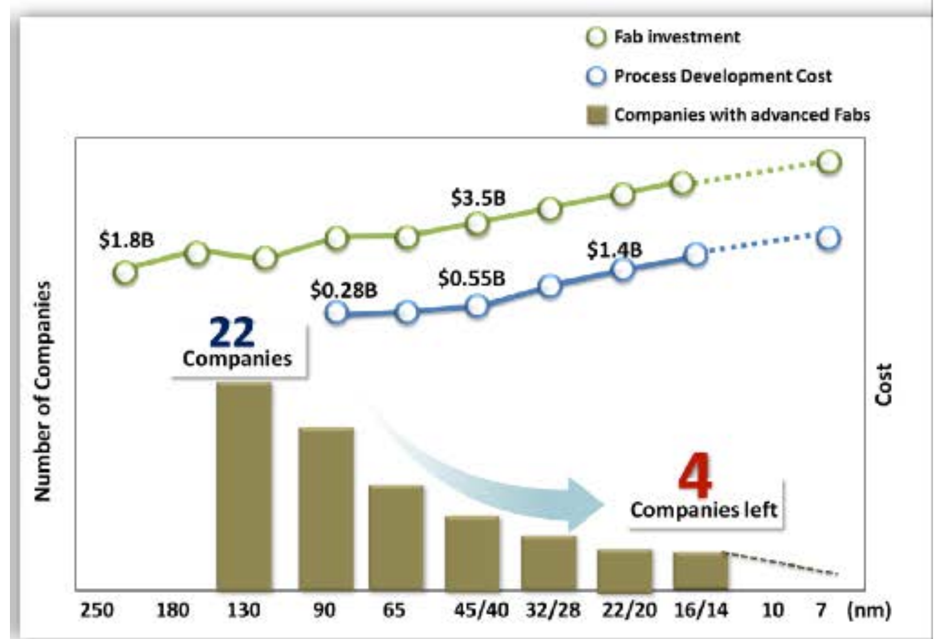
Moore's law, enounced in 1965 by Gordon Moore, the co founder of Intel, is the observation that the number of transistors in a dense integrated circuit doubles approximately every two years.

Cost of technology increasing after 28nm



Source : http://www.economist.com, Linley Group

Lesser number of players for leading edge nodes



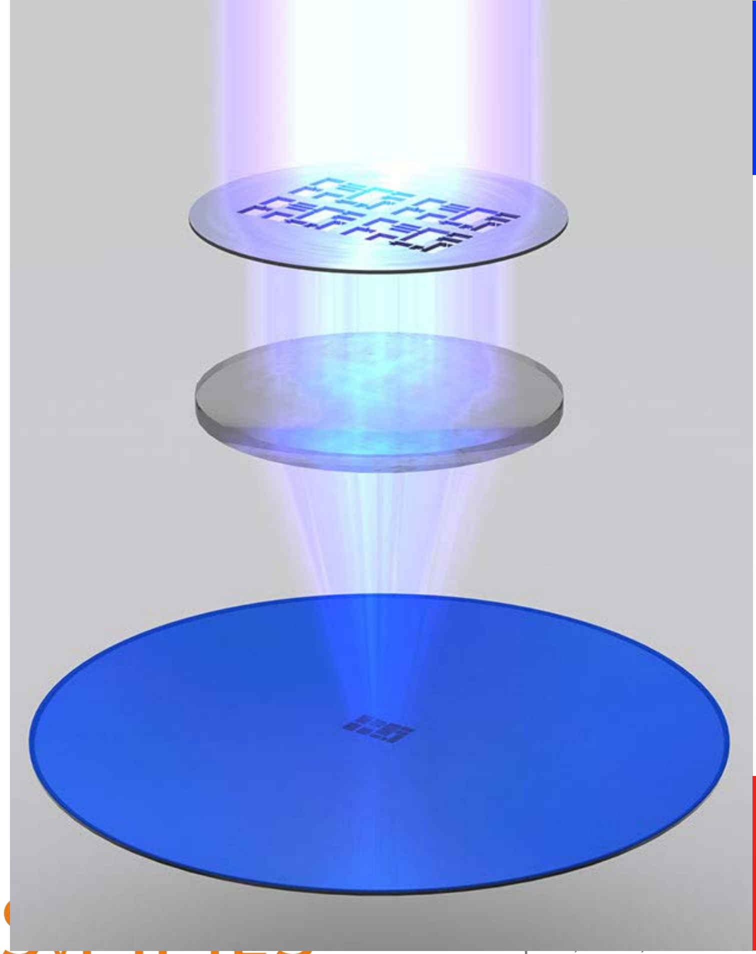
Source : Samsung Foundry data

Source: Semiconwest 2016

After the 28nm node, we can continue
to make transistors smaller, but not cheaper. *EETimes*

Feature processing by photo-lithography: a top-dow approach

<u>Photolithography</u> is a process used in microfabrication to pattern parts of a thin film. It uses light to transfer a geometric pattern from a photomask to a light-sensitive chemical "photoresist" (resist) on the substrate. *(wikipedia)*



Same mask used many times to print thousand of wafers

Mask

Exposure tool

Coated wafer

$$\boxed{\mathrm{CD} = k_1 \frac{\lambda}{\mathrm{NA}}.}$$

CD: pattern resolution
λ ***:*** exposure wavelenght
(193nm today in production)
k_1, NA: *constants*

Light wavelenght dictates patterning resolution (diffraction limits)

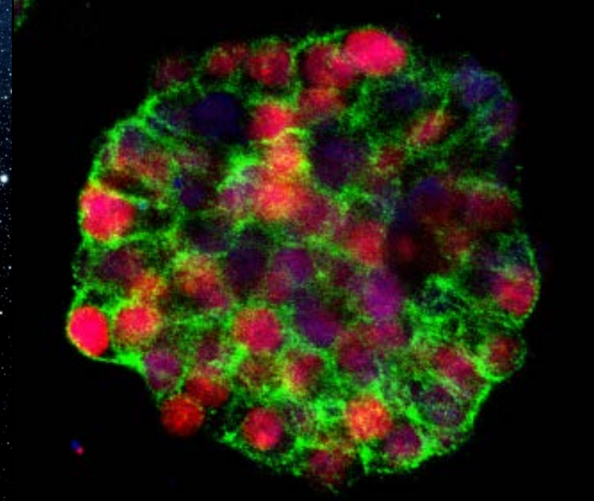
SYSTÈMES MOLÉCULAIRES ET NANOMATÉRIAUX POUR L'ÉNERGIE ET LA SANTÉ

Top-down versus bottom up approach

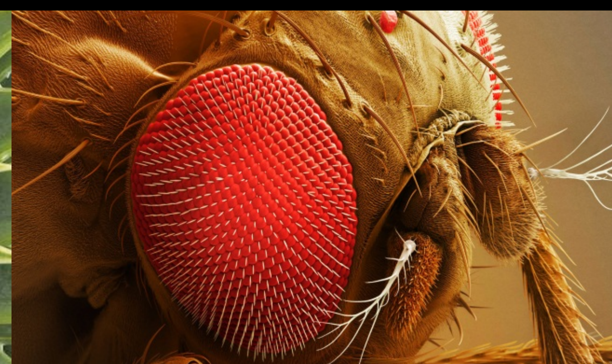
OPTICAL LITHOGRAPHY A TOP-DOWN APPROACH WITH SEVERAL LIMITATIONS: COST AND RESOLUTION

TO GO FORWARD NEED TO THINK DIFFERENTLY: SELF ASSEMBLY A BOTTOM-UP APPROACH

Self-assembly: a process in which a **disordered system** of pre-existing components **forms an organized structure** or pattern as a consequence of specific, local interactions among the components themselves, **without external direction**. *(wikipedia)*

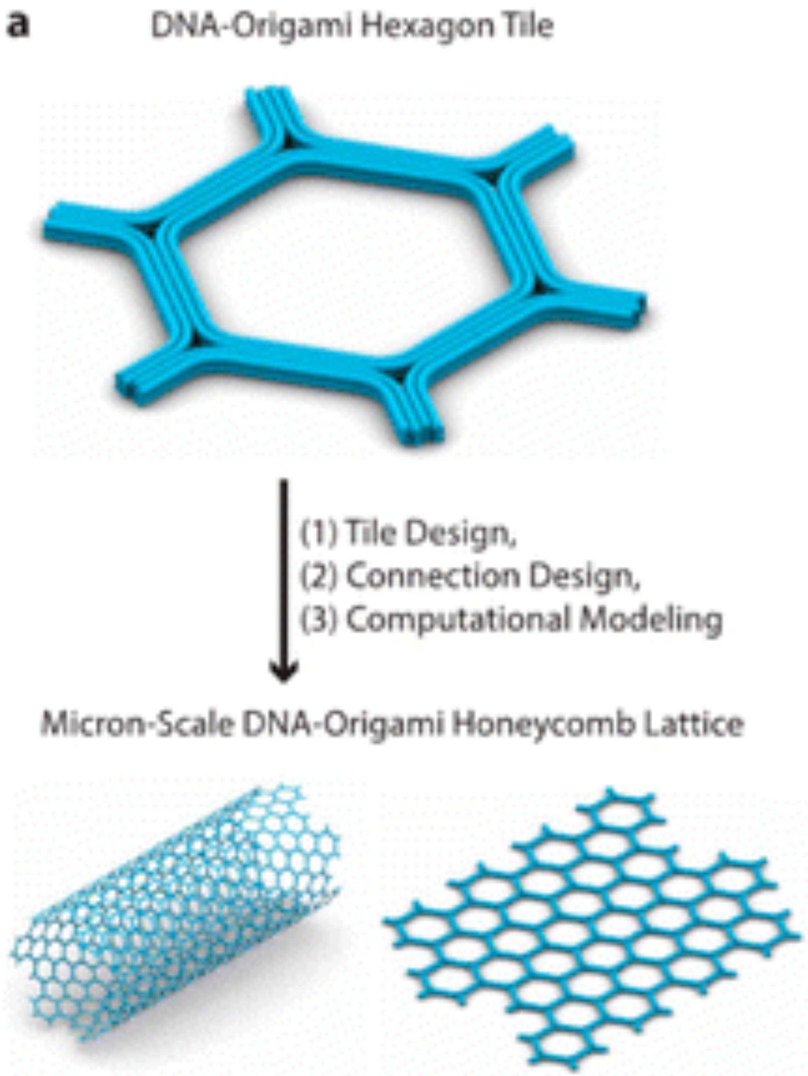

SELF-ASSEMBLY EVERYWHERE IN THE NATURE

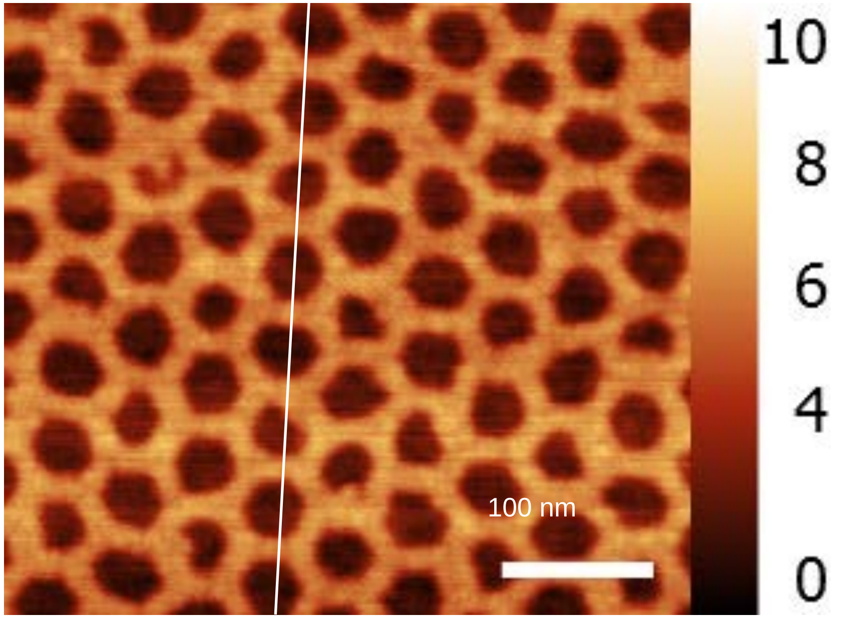




BUT KEEP IN MIND HIGH RESOLUTION



DNA origami honeycomb lattices



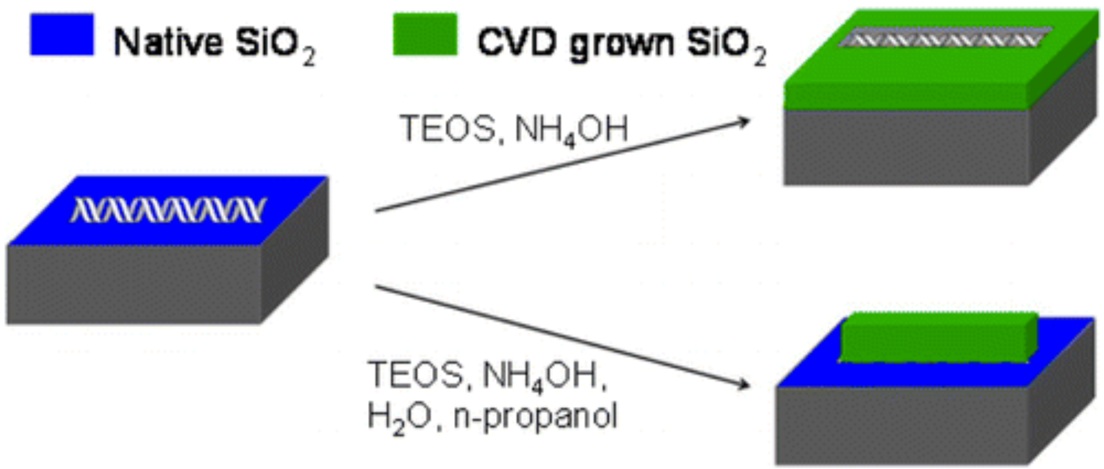


CD = 40nm
Pitch = 60nm

P.Wang et al, *J. Am. Chem. Soc.*, **2016**, *138* (24), pp 7733–7740

Oxide deposition (CVD) with DNA templates

When samples are exposed to a mixed vapor of $Si(OEt)_4$ (TEOS), H_2O, and NH_3, deposition of SiO_2 occurred selectively on the SiO_2 surface that was not covered by the DNA template, resulting in a negative-tone pattern of SiO_2



To reverse the area selectivity of the CVD, propanol vapor was introduced and the relative humidity of the reaction chamber was increased. In this case, the CVD reaction selectively deposited SiO_2 onto the DNA nanostructures to produce a positive-tone pattern

J. Am. Chem. Soc., 2013, 135, 6778–6781
DOI: 10.1021/ja401785h

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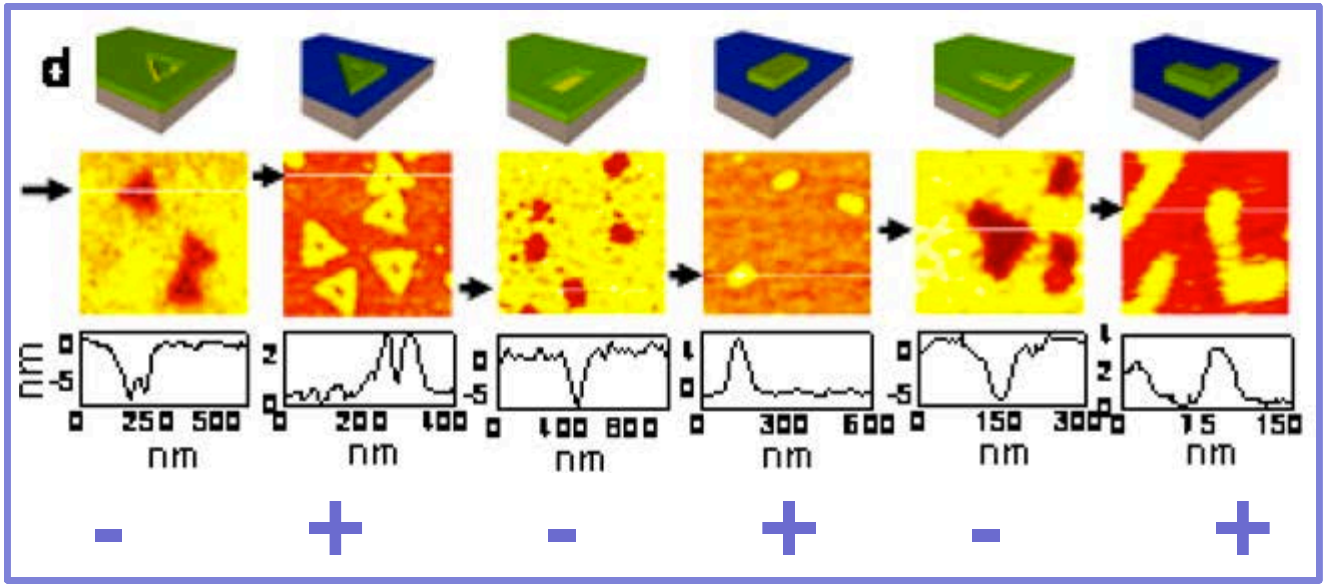
Oxide deposition (CVD) with DNA templates

selective deposition of inorganic oxide onto a DNA nanostructure in the presence of a SiO2 substrate



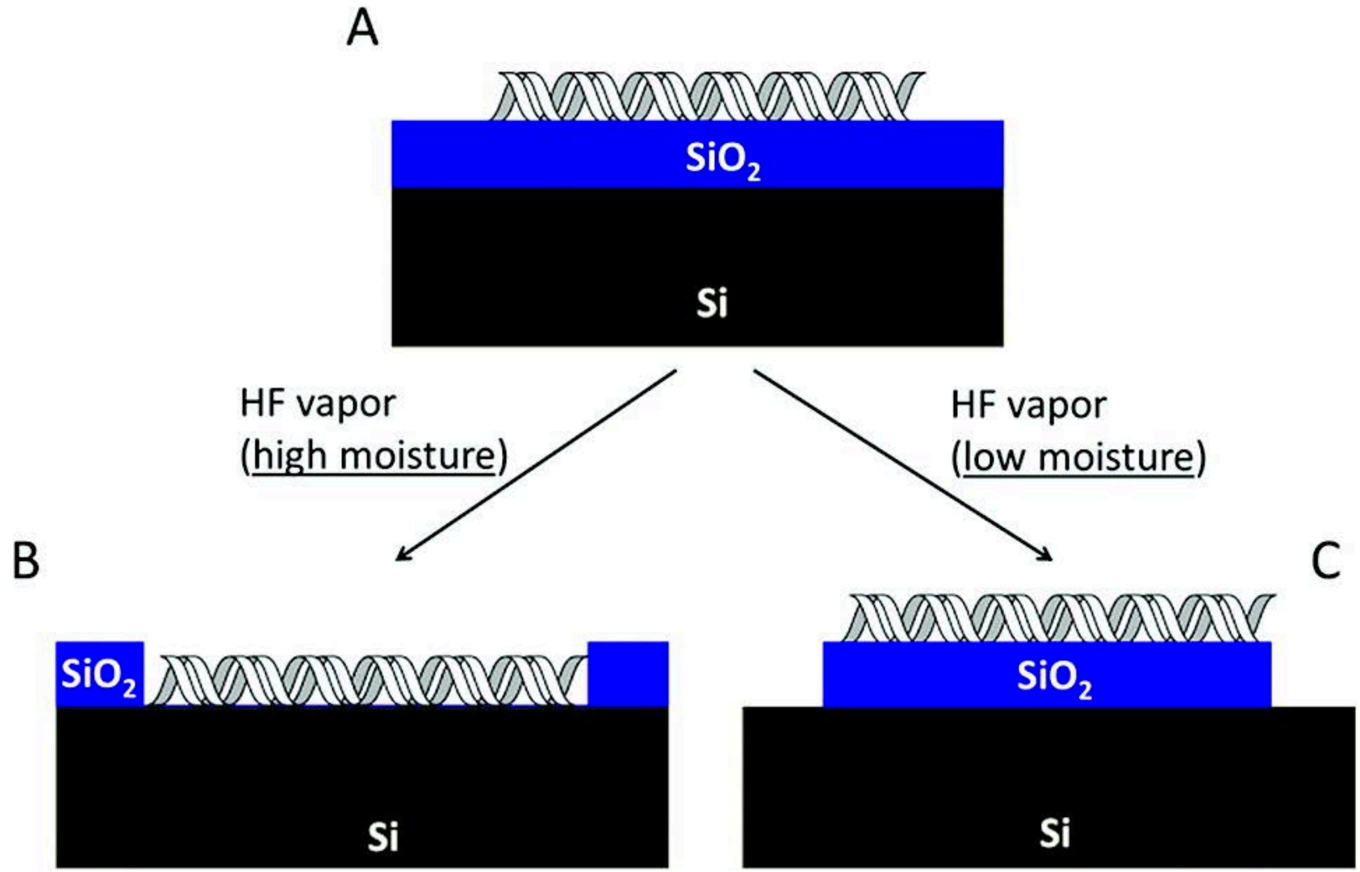
+/- presence of water/n-propanol

Oxide deposition on different substrates with <20nm lateral resolution

J. Am. Chem. Soc., 2013, 135, 6778–6781
DOI: 10.1021/ja401785h

HF « dry » etching of SiO_2 on DNA nanostructures

HF induced pattern transfer from DNA nanostructures



J. Am. Chem. Soc., 2011, 133 (31), pp 11868–11871

HF « dry » etching of SiO_2 on DNA nanostructures

HF induced pattern transfer from DNA nanostructures

$SiO_2(s) + 4\ HF(g) \rightarrow SiF_4(g) + 2\ H_2O(g)$

$6\ HF + 3\ H_2O \rightarrow 3\ HF_2^- + 3\ H_3O^+$ (deprotonation)

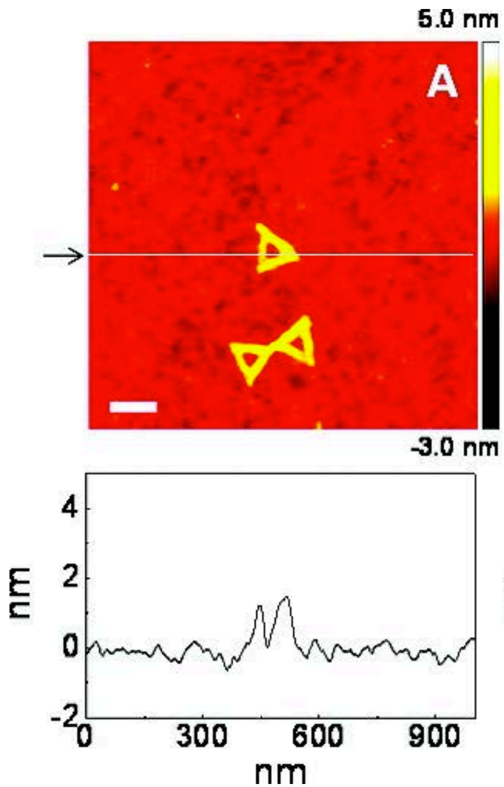
$3\ HF_2^- + 3\ H_3O^+ + SiO_2 \rightarrow 2\ HF + SiF_4 + 5\ H_2O$ (etching)

- DNA may absorb water (up to +100% w/w!) (phosphate groups)
- but DNA may also serve as a diffusion barrier after deposition on SiO_2…
- ... then H_2O content in SiO_2 adsorbed DNA may favor or inhibit **HF dry etching**

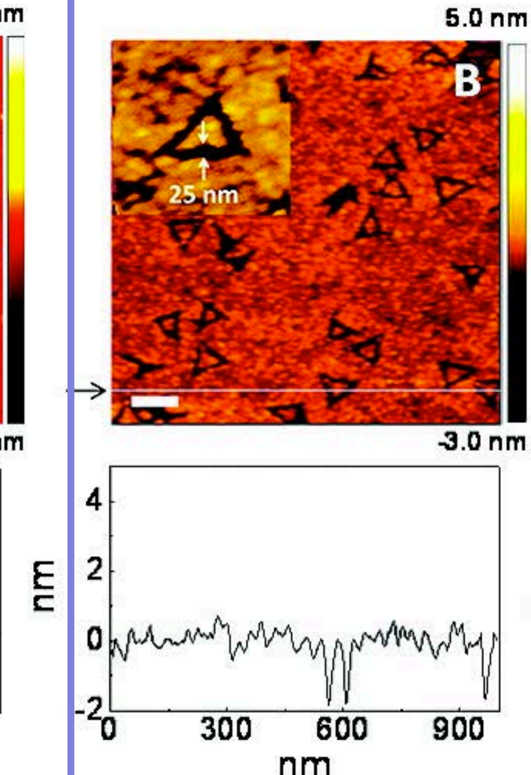
J. Am. Chem. Soc., 2011, 133 (31), pp 11868–11871

HF induced pattern transfer from DNA nanostructures

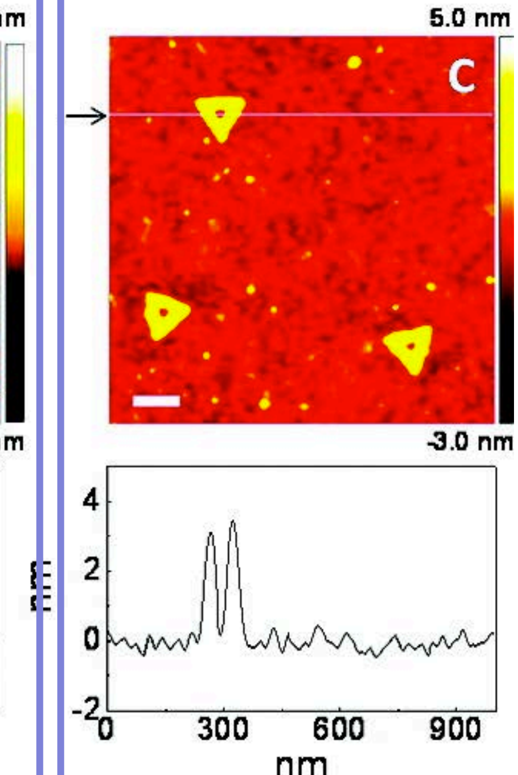
Triangular DNA origami on a SiO_2 surface



50% relative humidity, 5 min



34% relative humidity, 15 min



Scale bars represent 100 nm.

J. Am. Chem. Soc., 2011, 133 (31), pp 11868–11871

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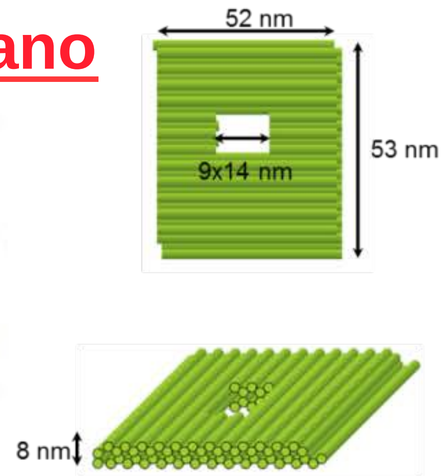
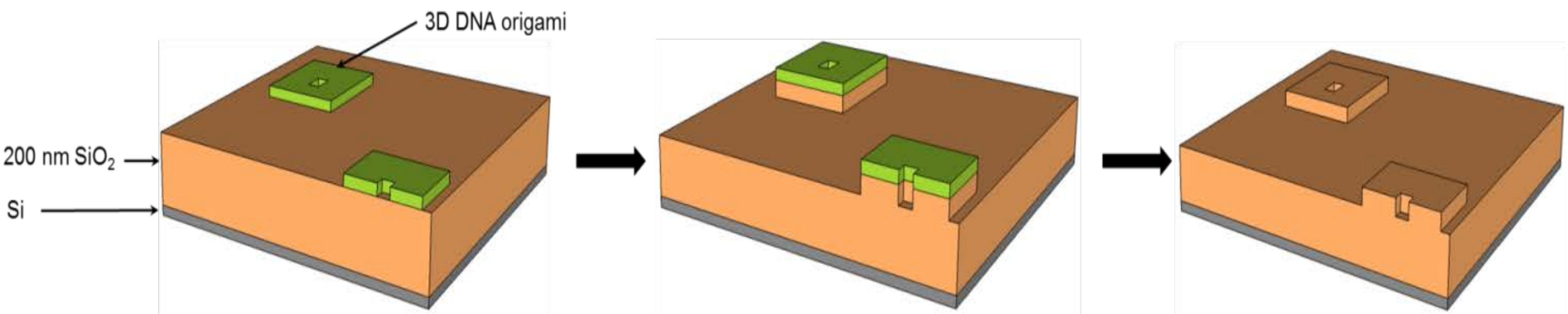
DNA Origami Mask for sub-10 nm lithography

I/ Design: cadnano



II/ Synthesis:

III/ Process :

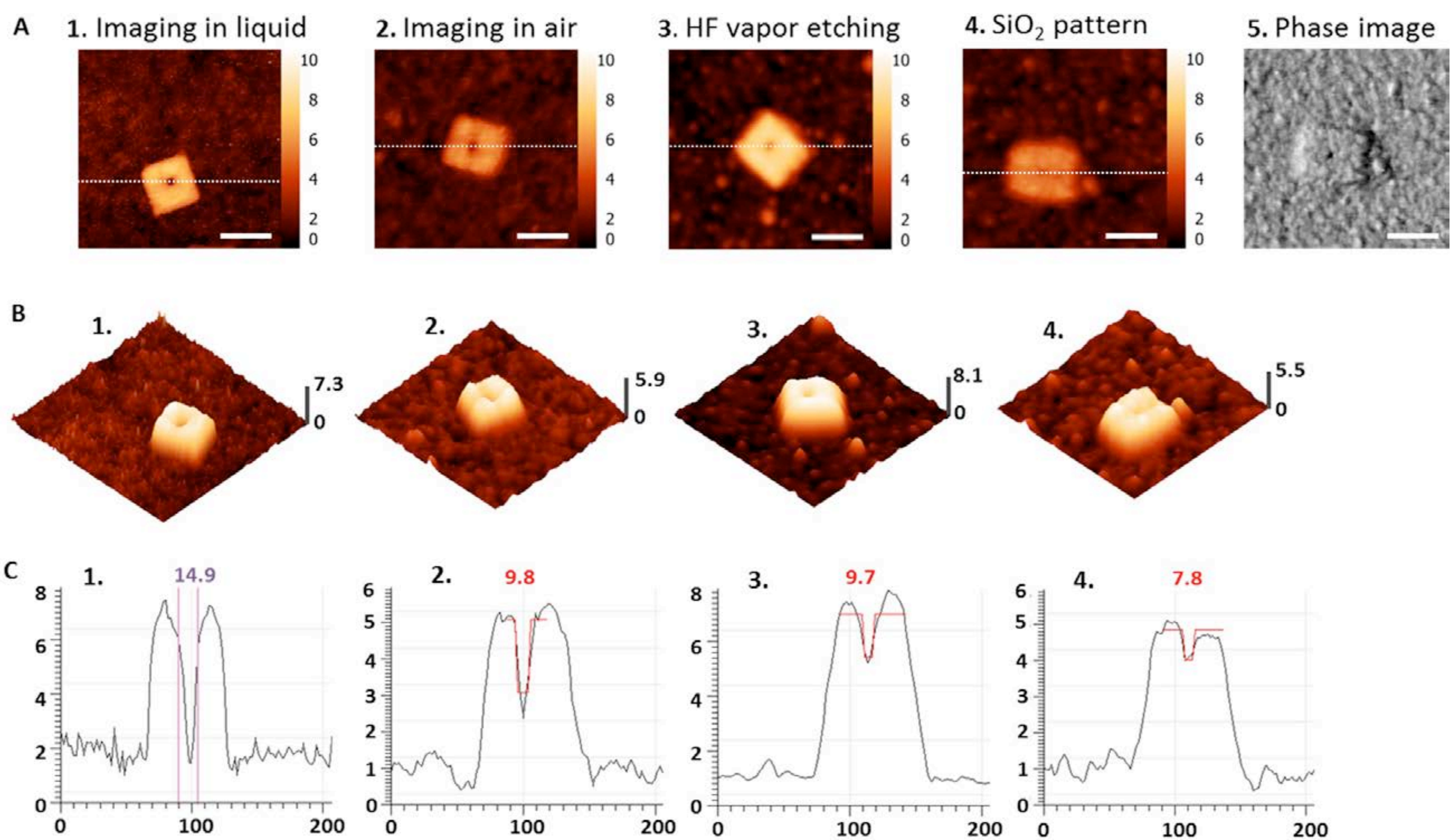


1- DNA adsorption on Si-SiO_2

2- DNA pattern transfer by HF vapor etching

3- DNA mask removal

Sub 10 nm-large patterns transferred onto SiO_2



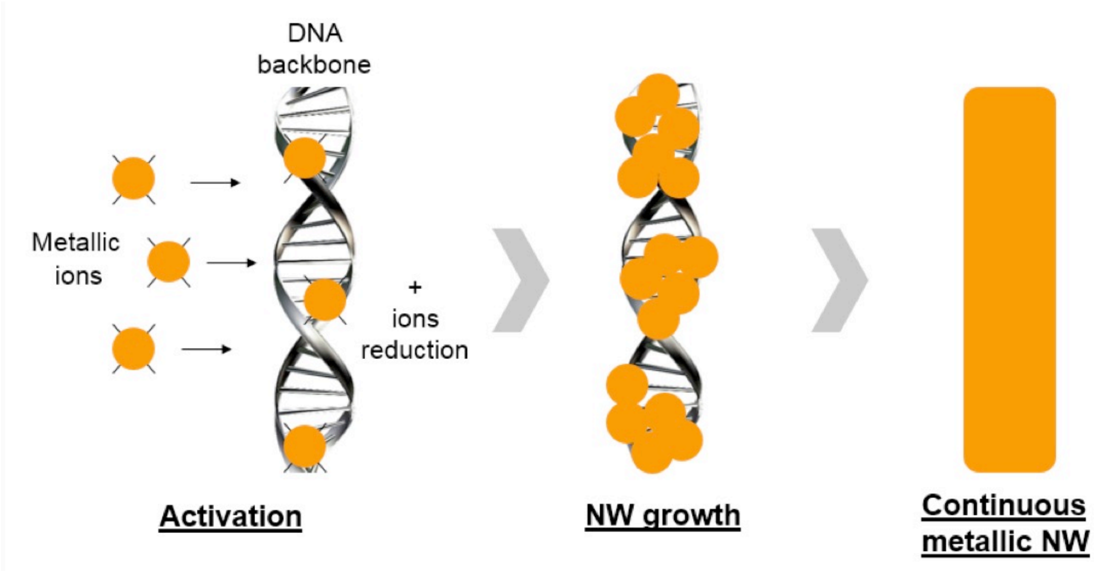
AFM images of DNA and SiO_2 substrate before and after HF vapor etching.

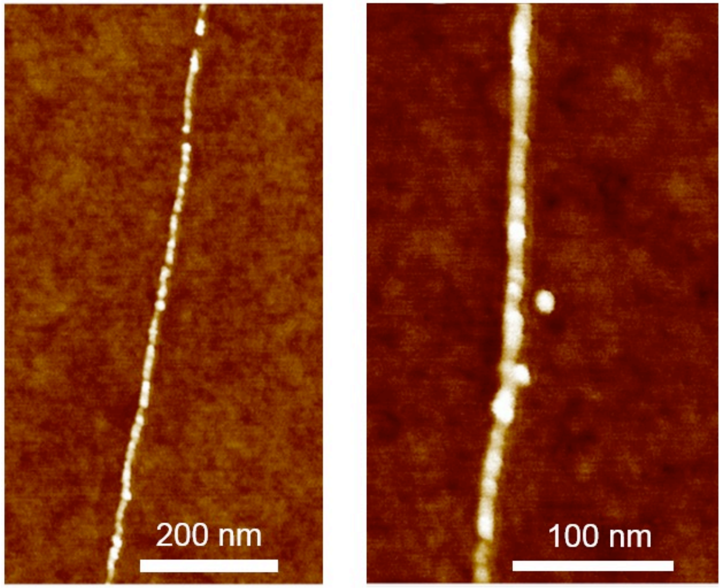
All values are given in nm. Scale bars: 50 nm.

Diagne C et all.

ACS Nano. 2016 Jul 26;10(7):6458-63

DNA used a conducting nanowire





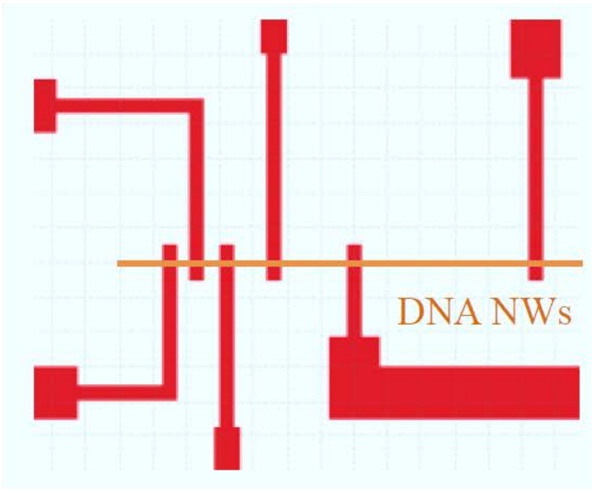
DNA metallization process:

- **activation** step consisting in an exchange of metallic cations on the DNA backbone,
- cluster **NW growth** by electroless plating process,
- achievement of a uniform and **continuous metallic nanowire**.

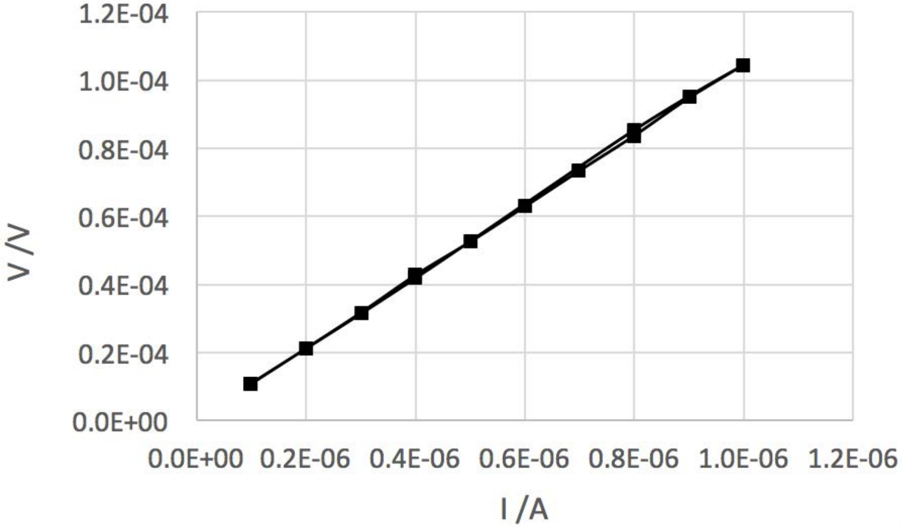
AFM images after metalization

C.Brun et al, IEEE Nanotechnology Magazine, Vol. 11 (1), 2017

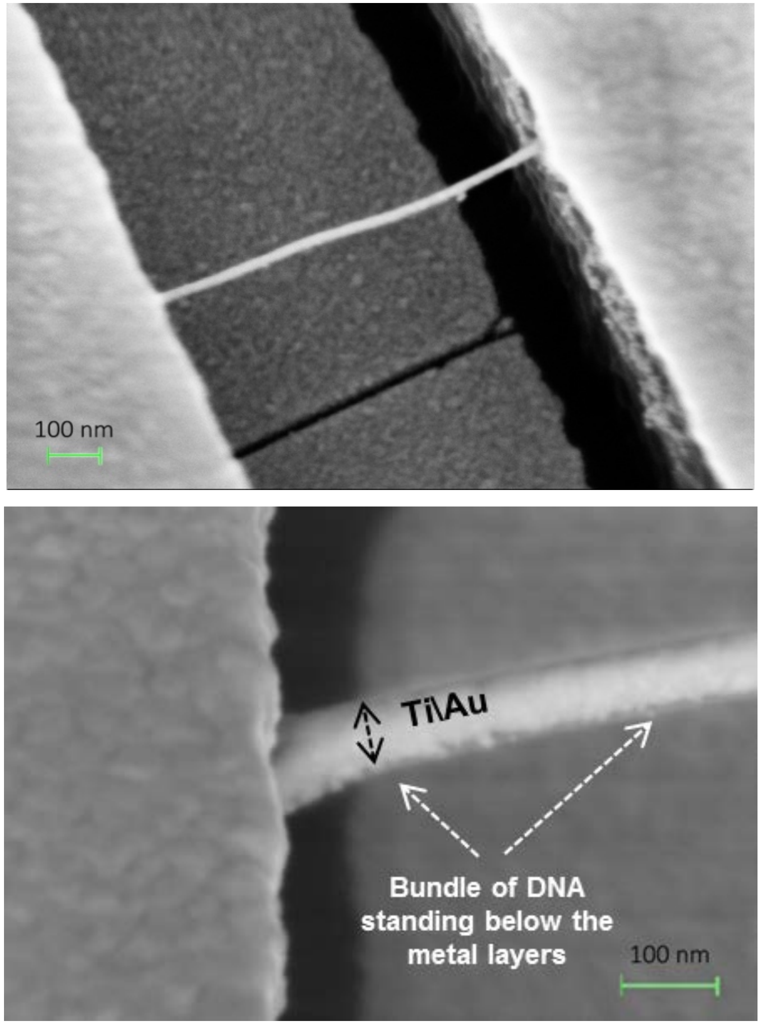
DNA used a conducting nanowire



I/V curve for 80-nm diameter metallic NWs

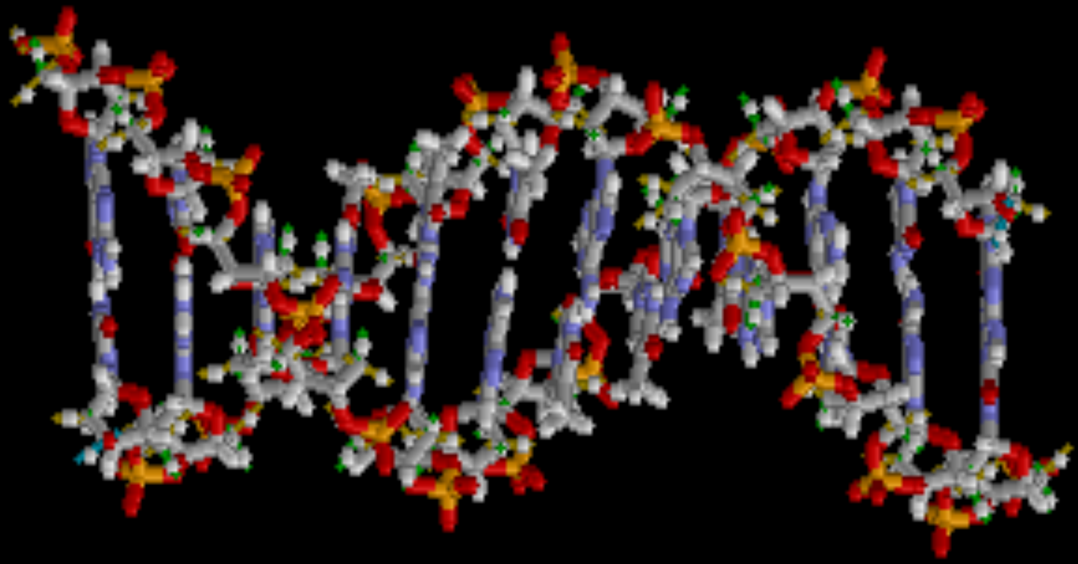


SEM images of the fabricated Ti/Au NWs from suspended DNA wires



C.Brun et al, IEEE Nanotechnology Magazine, Vol. 11 (1), 2017

Thank you for your attention, enjoy your stay in Grenoble!



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