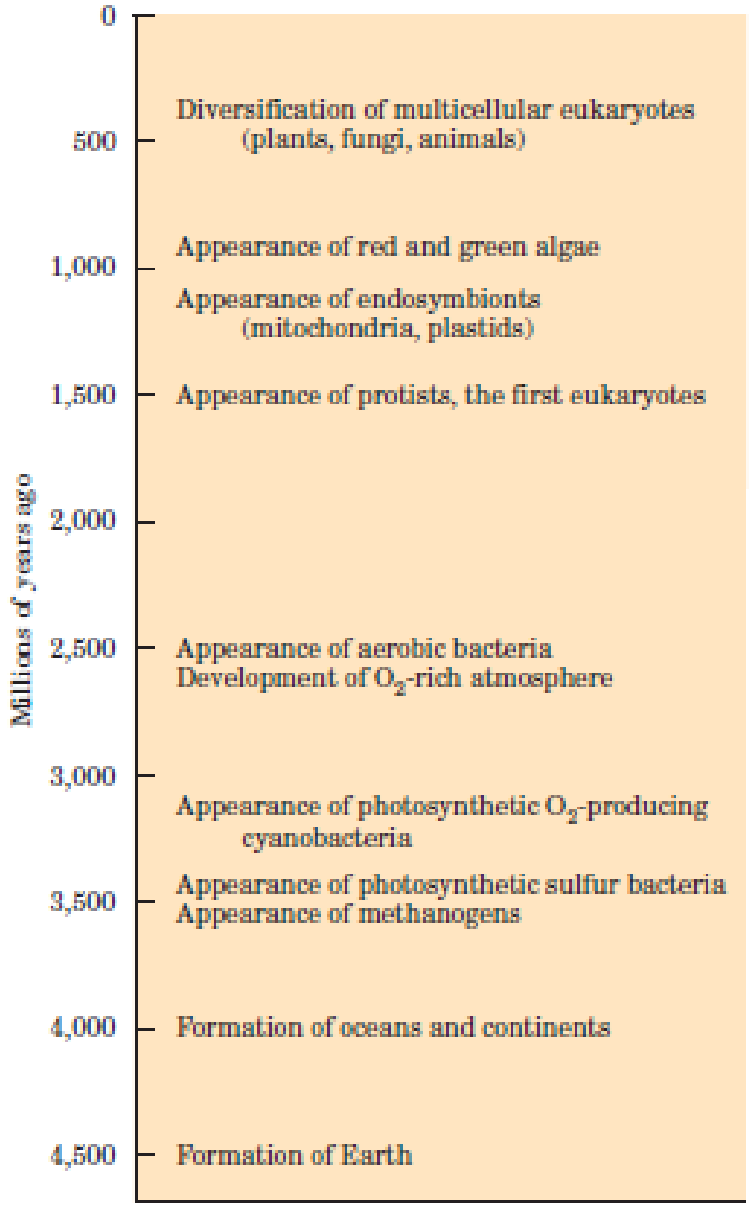
What is Life?

What are the principles of Biology ?

Landmarks in the evolution of life on Earth



Life's Origins

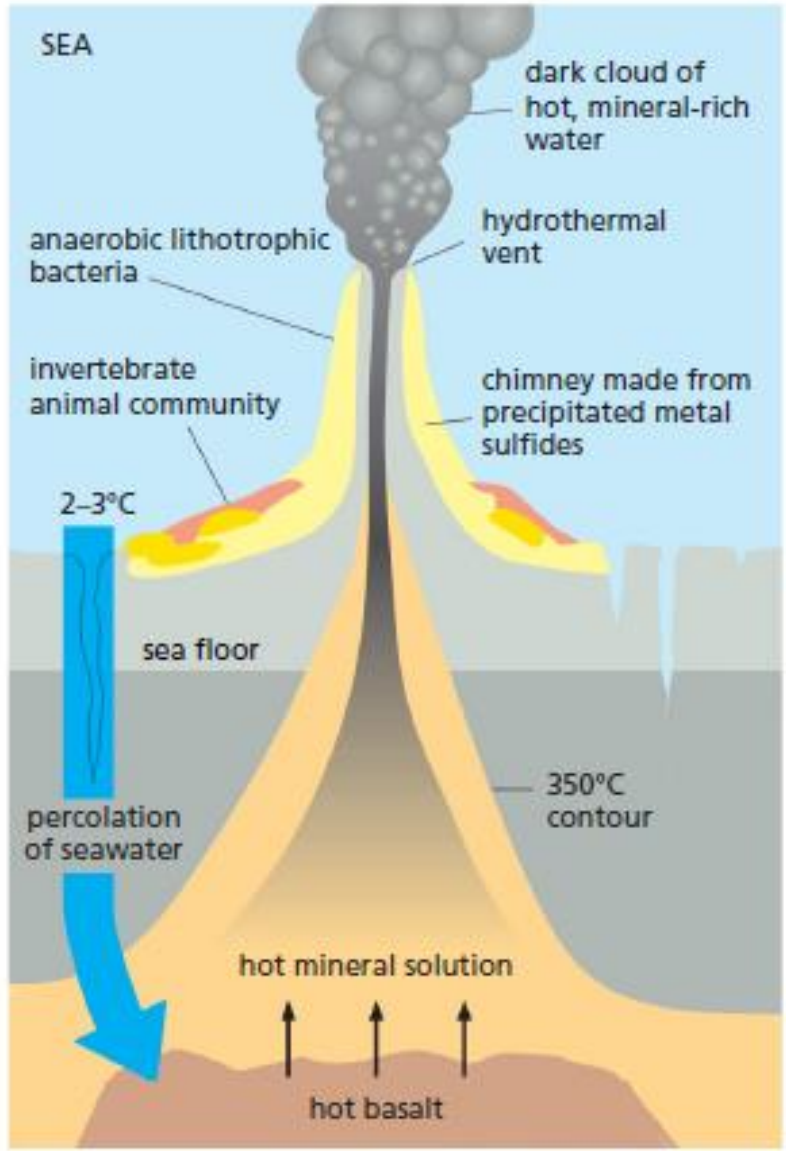
Today, research into the origin of life is interdisciplinary with workers trying to answer four main questions:

1. What was the Earth's physical environment like when life first evolved?

2.What sorts of chemical reactions could produce the building blocks of life and could these occur naturally in the early Earth's environment?

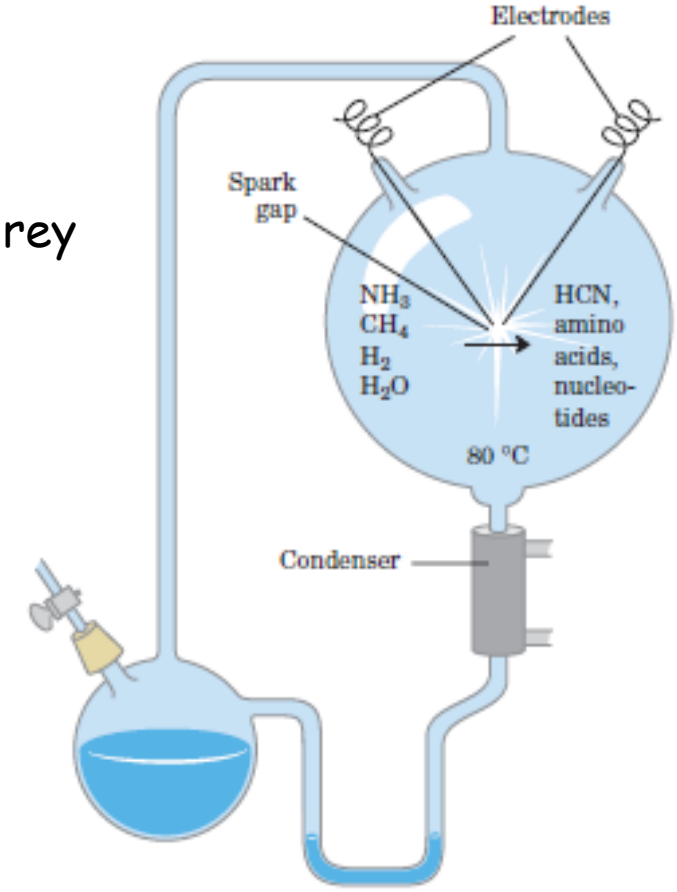
3. How could the complex organic molecules be compartmentalized into a contained unit?

4. How did the genetic code evolve?


SEA
dark cloud of hot, mineral-rich water
hydrothermal vent
anaerobic lithotrophic bacteria
invertebrate animal community
chimney made from precipitated metal sulfides
2–3°C
sea floor
350°C contour
percolation of seawater
hot mineral solution
hot basalt

How did the first living organisms acquire their characteristic organic building blocks?

Miller and Urey Experiment



Hypothesis:

Effects of powerful atmospheric forces—ultraviolet irradiation, lightning, or volcanic eruptions—on the gases in the prebiotic Earth's atmosphere, and on inorganic solutes in superheated thermal vents deep in the ocean.

The appearance of the first living cell???

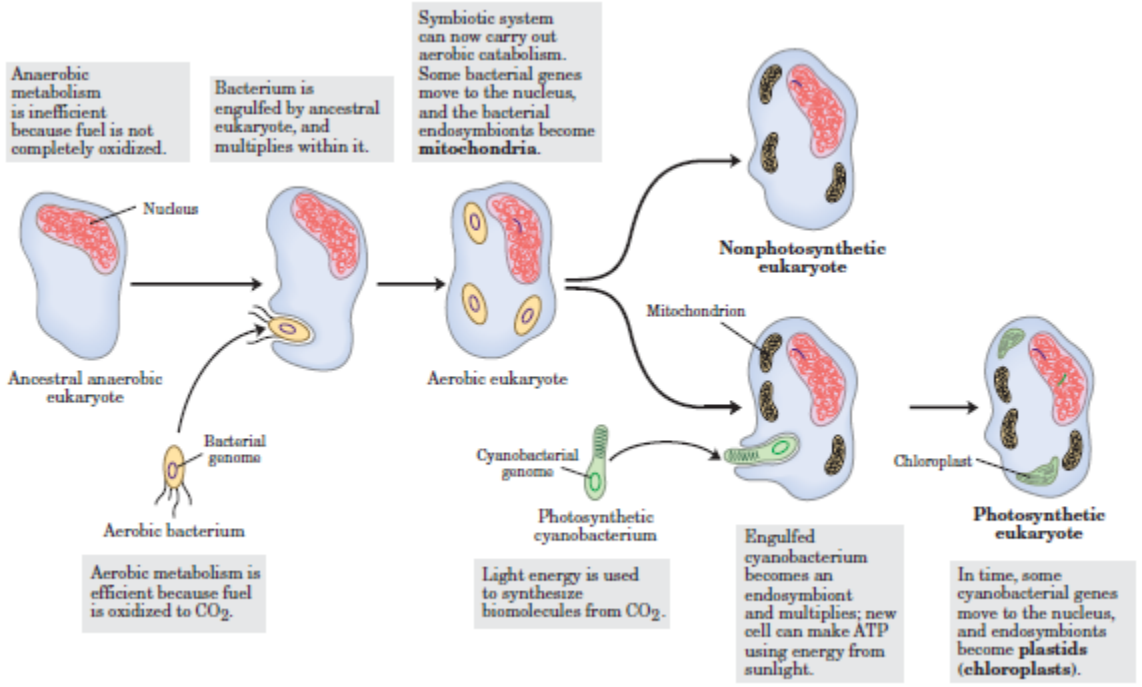
The First Cell Used Inorganic Fuels???

Lynn Margulis and the Theory of Endosymbiosis

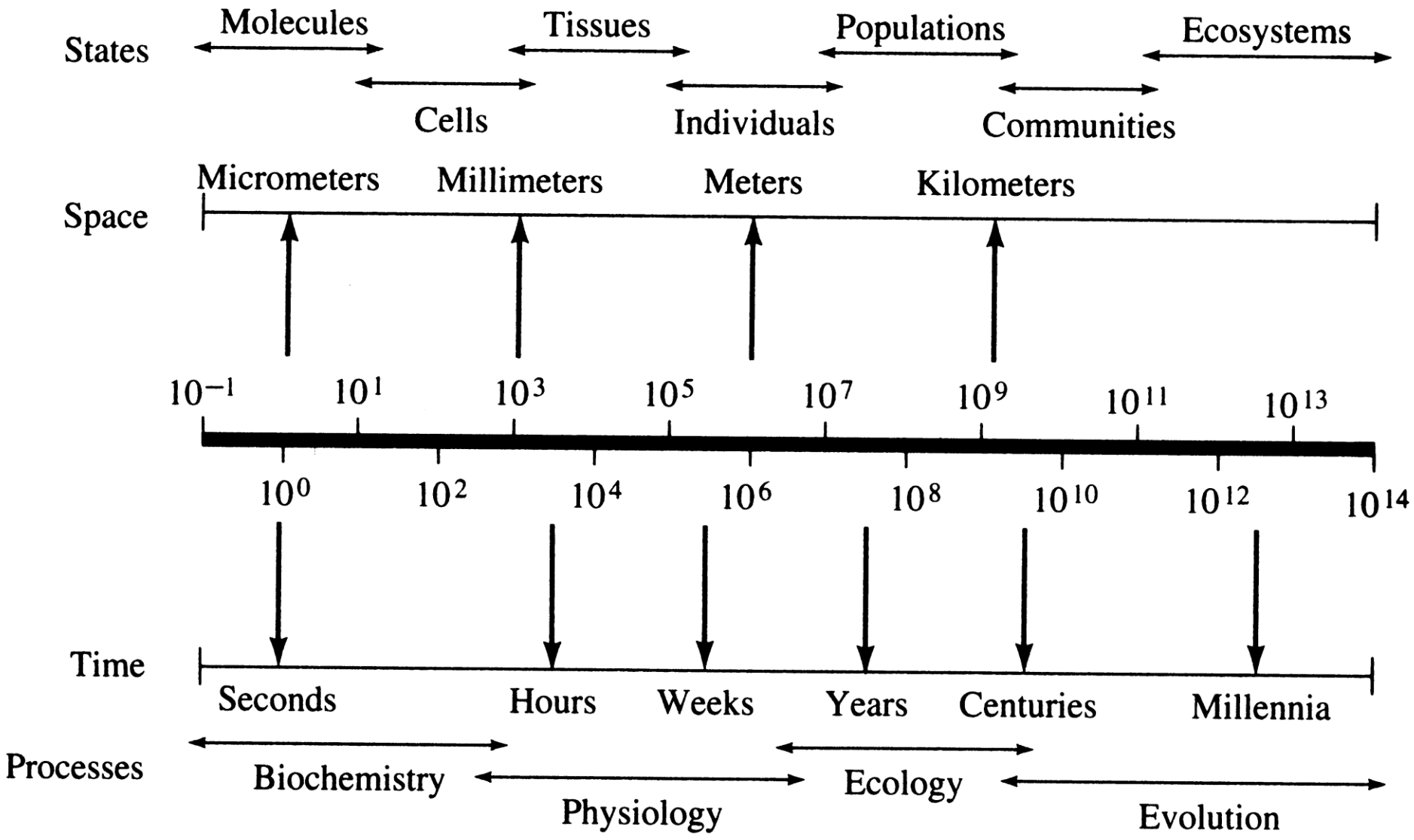
- Eukaryotic cells originated from a series of endosymbiotic events involving multiple prokaryotes

- This idea was considered outrageous at the time (1967), but many of Margulis's ideas have since become widely accepted

- Mitochondria are the descendants of oxygen-respiring bacteria and chloroplasts were originally photosynthetic bacteria, are almost universally accepted

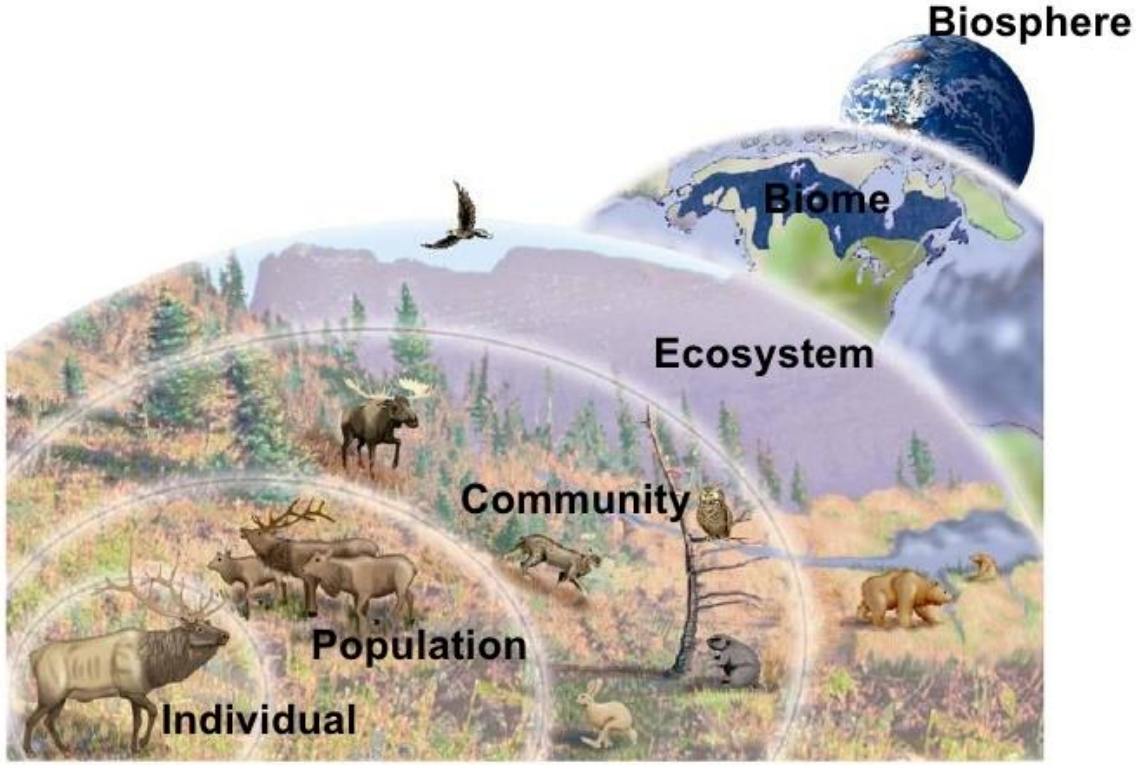


Biology is a vast discipline



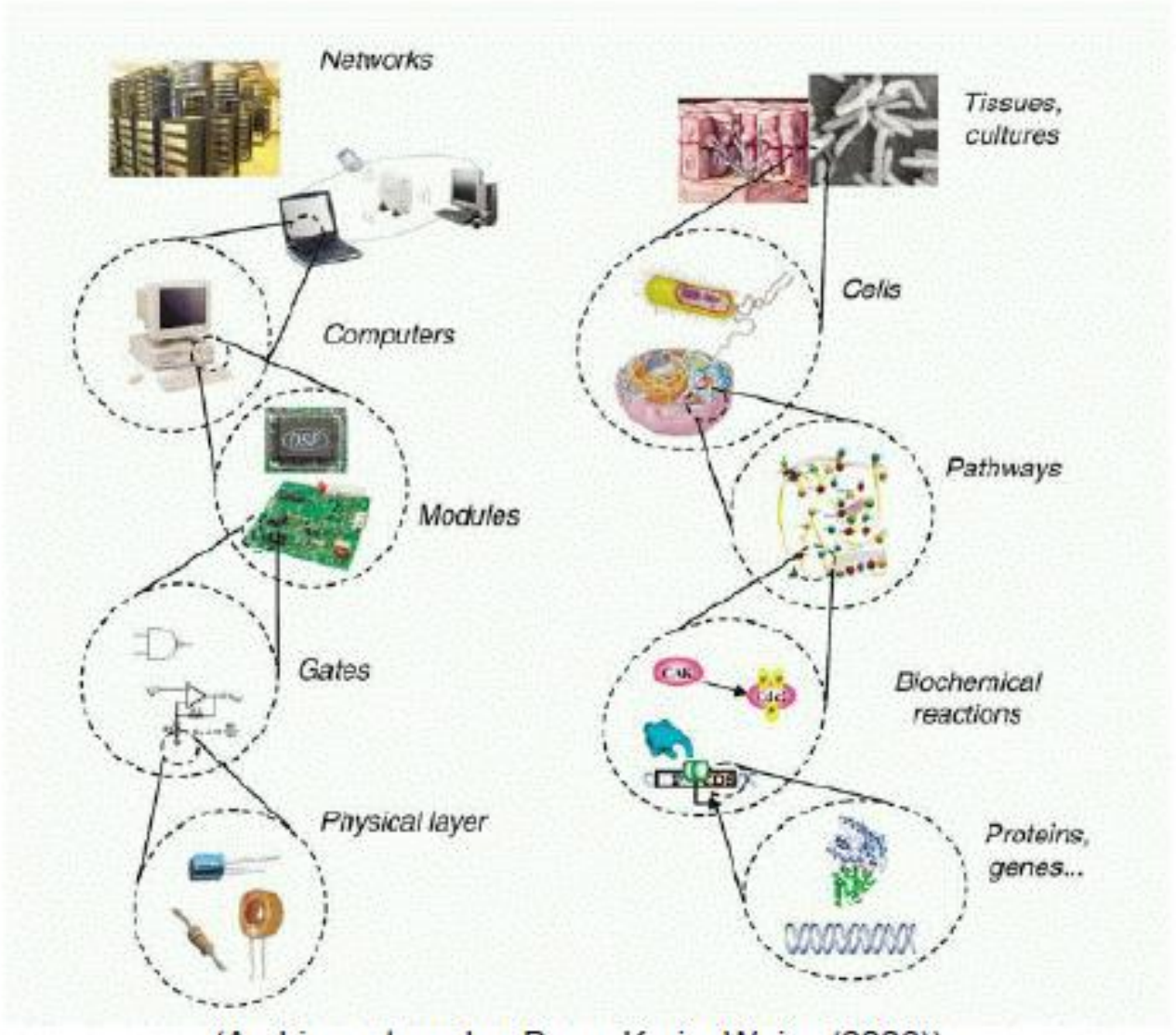
The Hierarchical Structure of Life

Levels of Organization



Individual = 1 Species
Population = Many of the same species
Community = Different populations (Biotic Factor = living)
Ecosystem = Various populations along with abiotic factors (non-living) coexisting.
Biome = Many ecosystems (Tundra, Tropical Rain Forest, Desert, etc...)
Biosphere = Many biomes

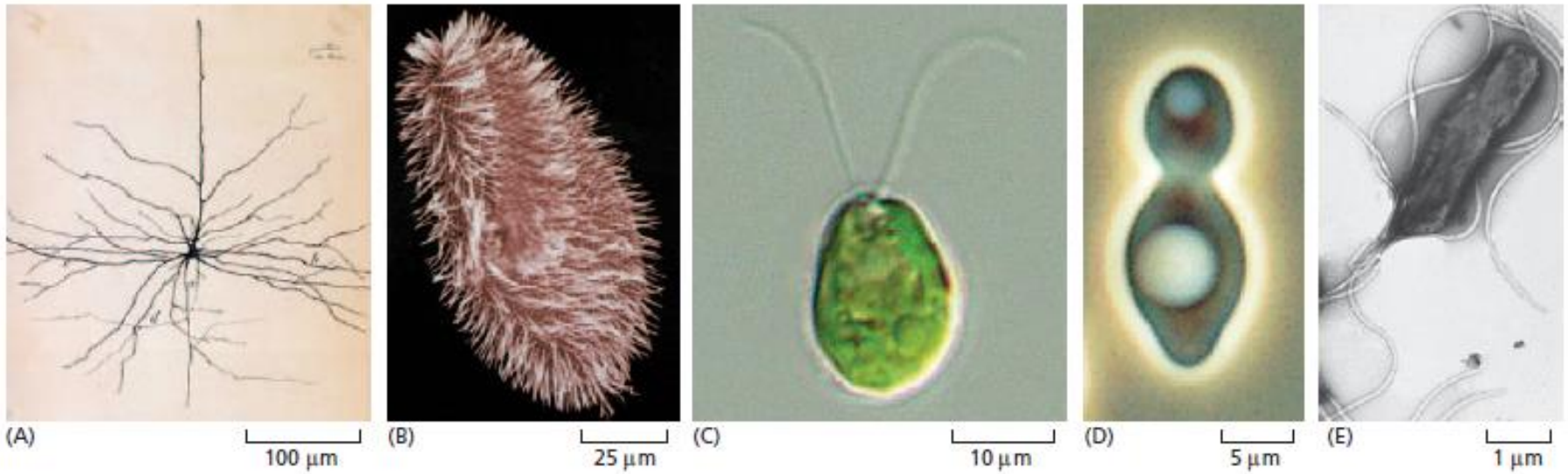
Cells compute?



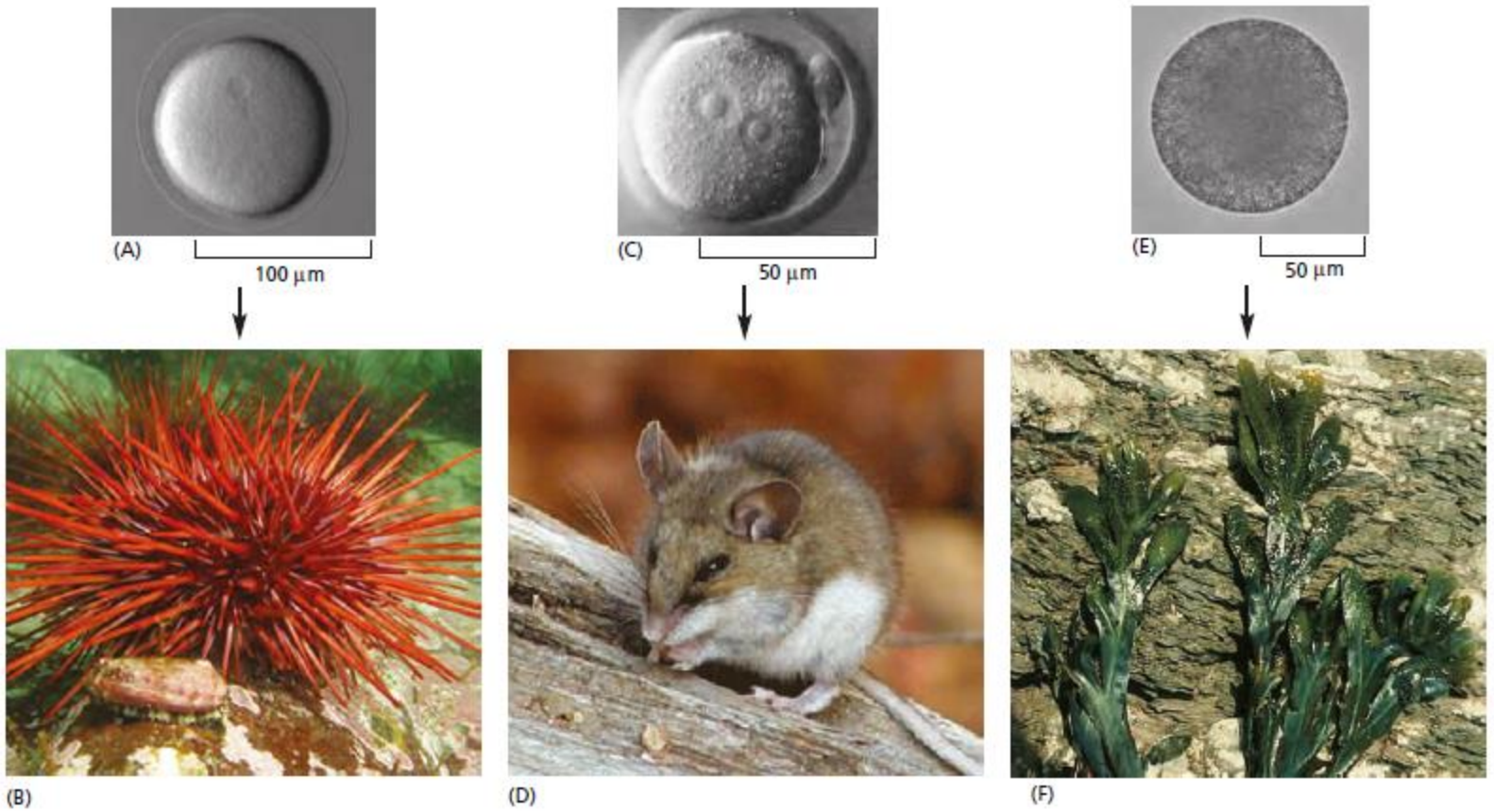
(Andrianantoandro, Basu, Karig, Weiss (2006))

Can we decipher the biological hardware and software?

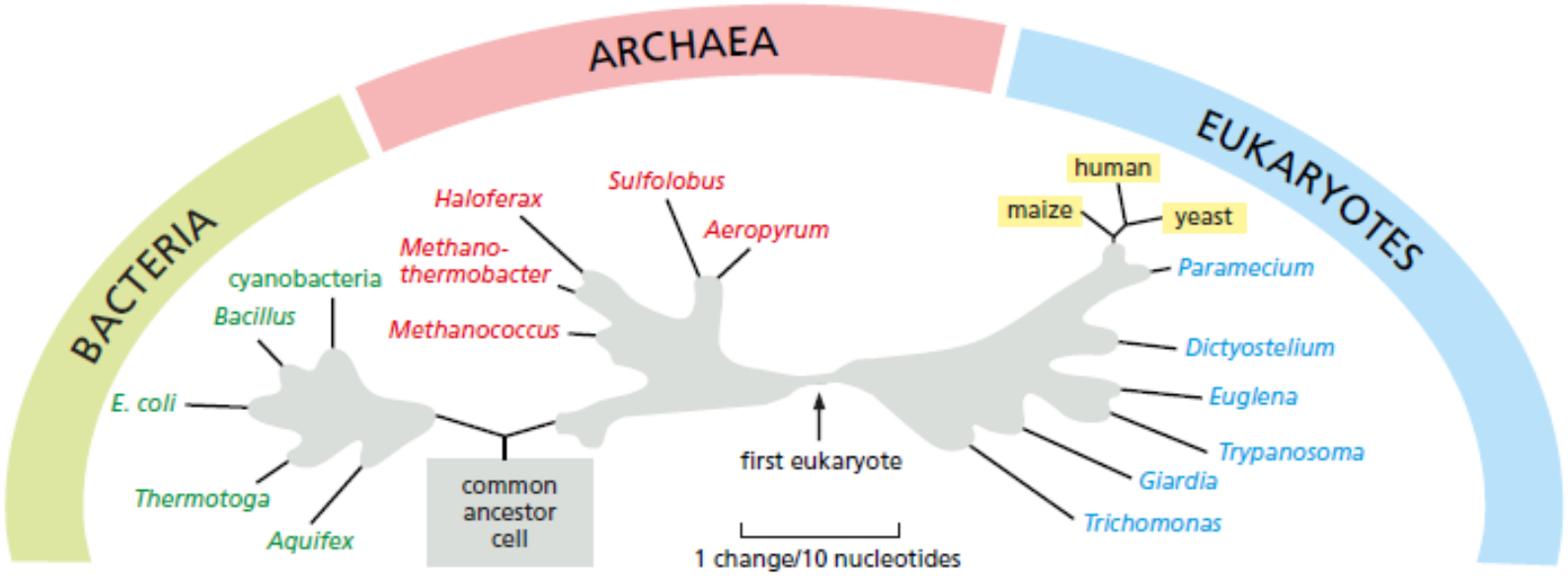
Cells come in variety of shapes and sizes



Origin from single cell

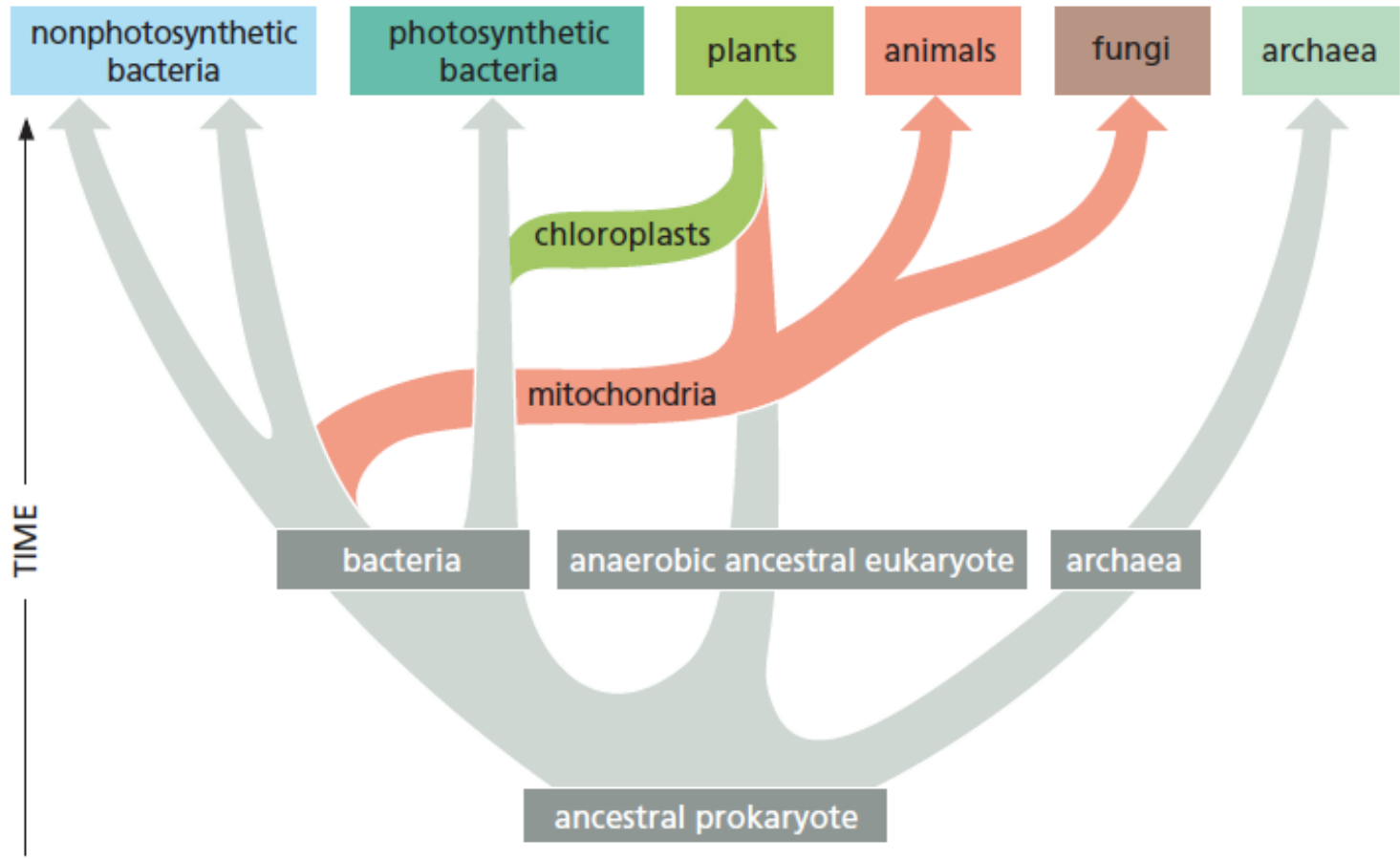


The Tree of Life

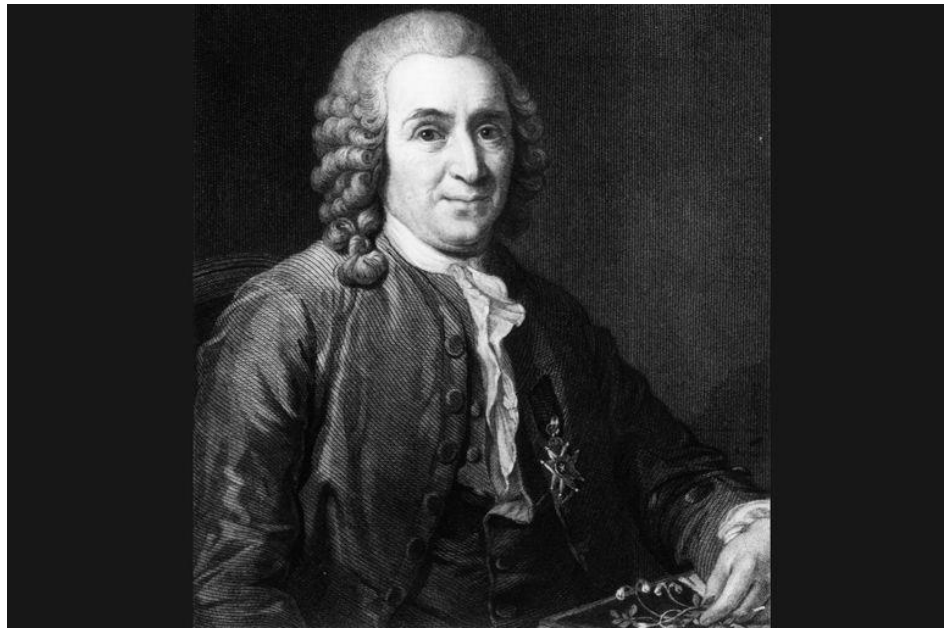


The domain system of classification was developed by Carl Woese and places organisms under three domains: **Archaea**, **Bacteria**, and **Eukarya**.

Under the domain system, organisms are further grouped into six Kingdoms. The Kingdoms include: **Archaebacteria** (ancient bacteria), **Eubacteria** (true bacteria), **Protista**, **Fungi**, **Plantae**, and **Animalia**.


nonphotosynthetic bacteria
photosynthetic bacteria
plants
animals
fungi
archaea
chloroplasts
mitochondria
TIME
bacteria
anaerobic ancestral eukaryote
archaea
ancestral prokaryote

Taxonomy and Organism Classification



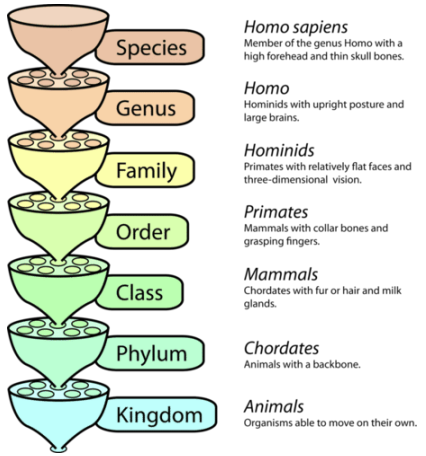
Botanist Carl von Linnaeus (1707-1778), founder of the modern system of binomial nomenclature for plants

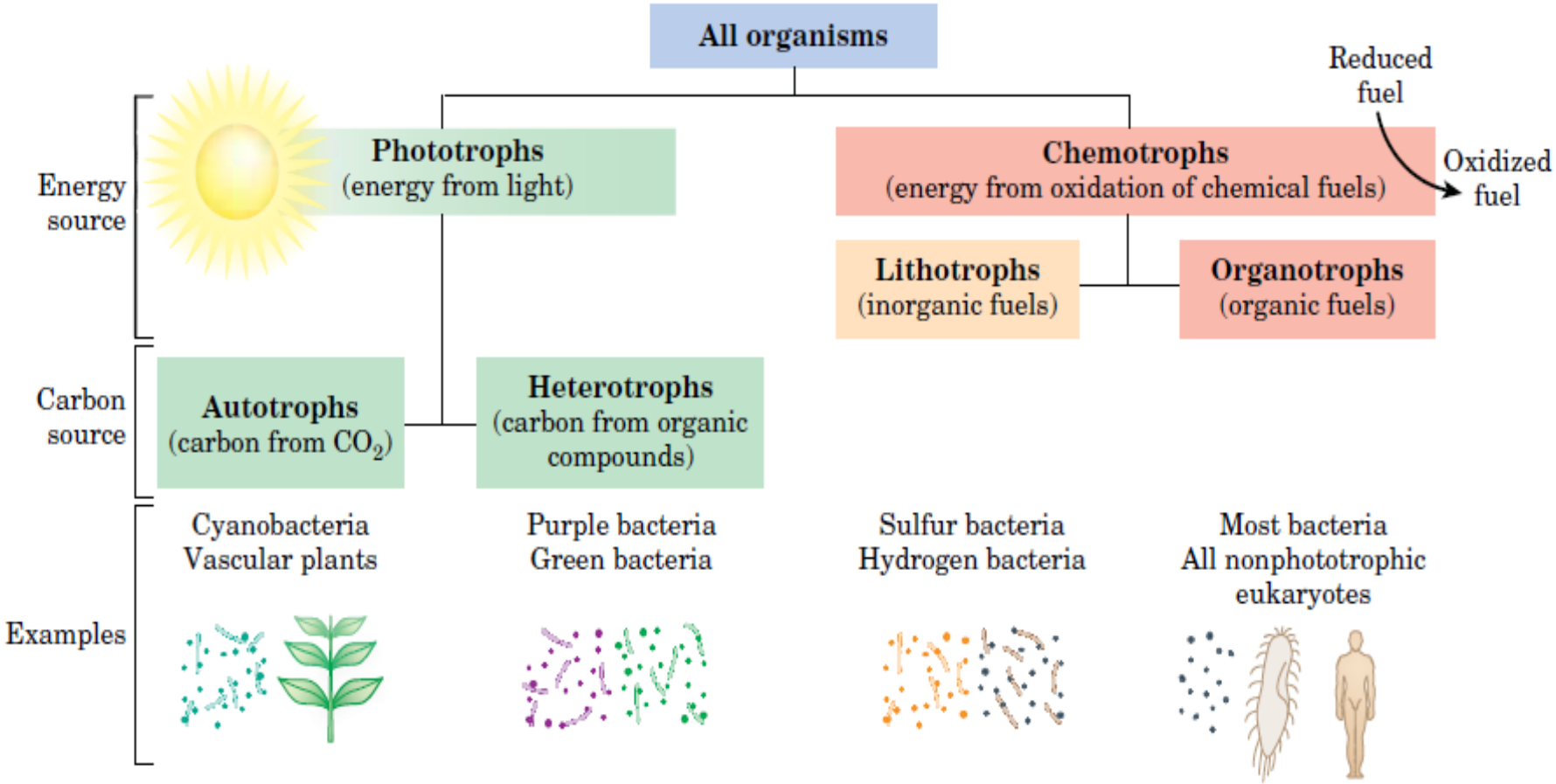
Kingdom, **Phylum**, **Class**, **Order**, **Family**, **Genus**, and **Species**.

A helpful aid for remembering the taxonomic categories:

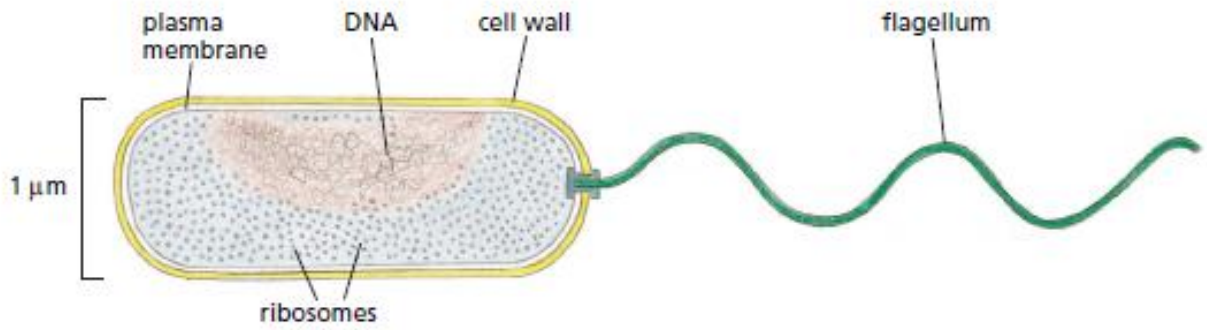
Domain, **Kingdom**, **Phylum**, **Class**, **Order**, **Family**, **Genus**, and **Species** is the mnemonic device:

Do **K**eep **P**lates **C**lean **O**r **F**amily **G**ets **S**ick.

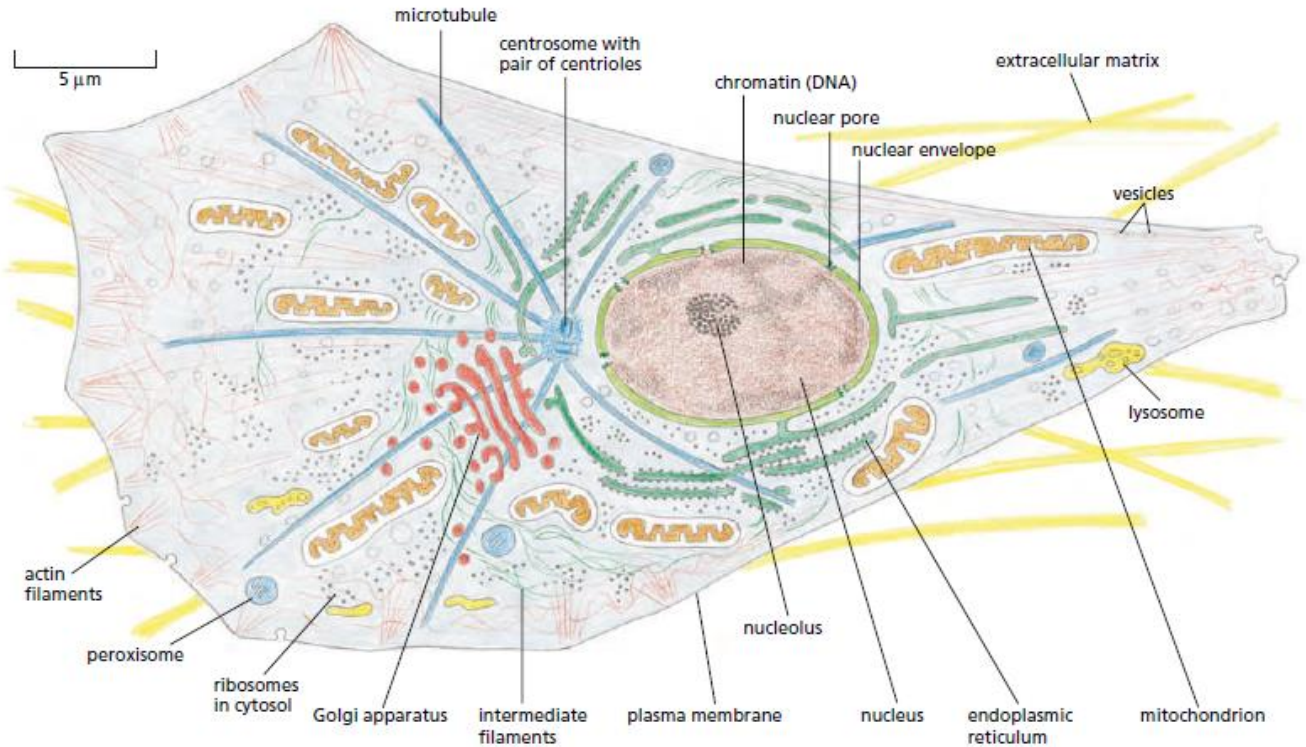



All organisms
Reduced fuel
Oxidized fuel
Energy source
Phototrophs
(energy from light)
Chemotrophs
(energy from oxidation of chemical fuels)
Lithotrophs
(inorganic fuels)
Organotrophs
(organic fuels)
Carbon source
Autotrophs
(carbon from CO_2)
Heterotrophs
(carbon from organic compounds)
Examples
Cyanobacteria
Vascular plants
Purple bacteria
Green bacteria
Sulfur bacteria
Hydrogen bacteria
Most bacteria
All nonphototrophic eukaryotes

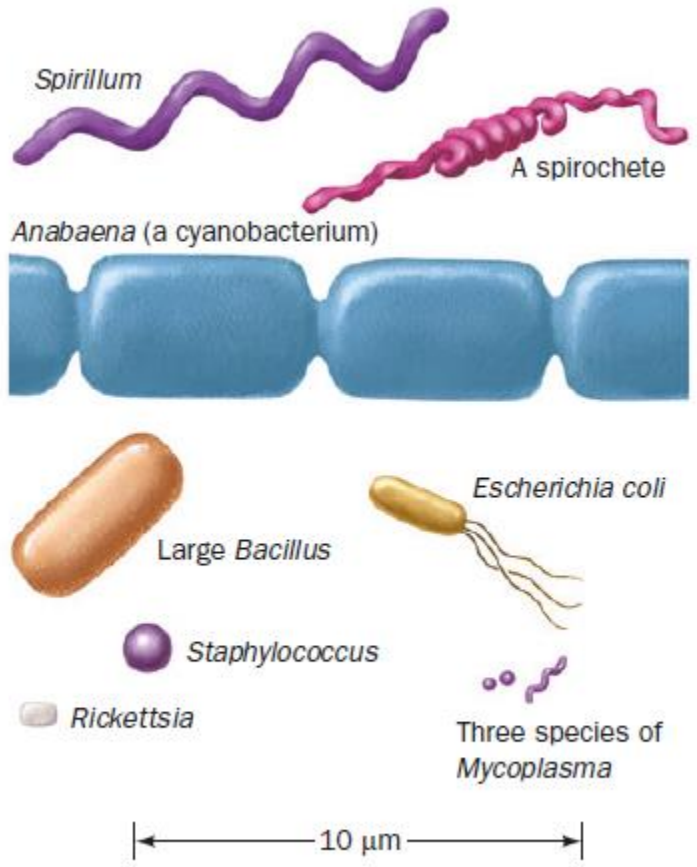
Bacterial cell



Animal cell



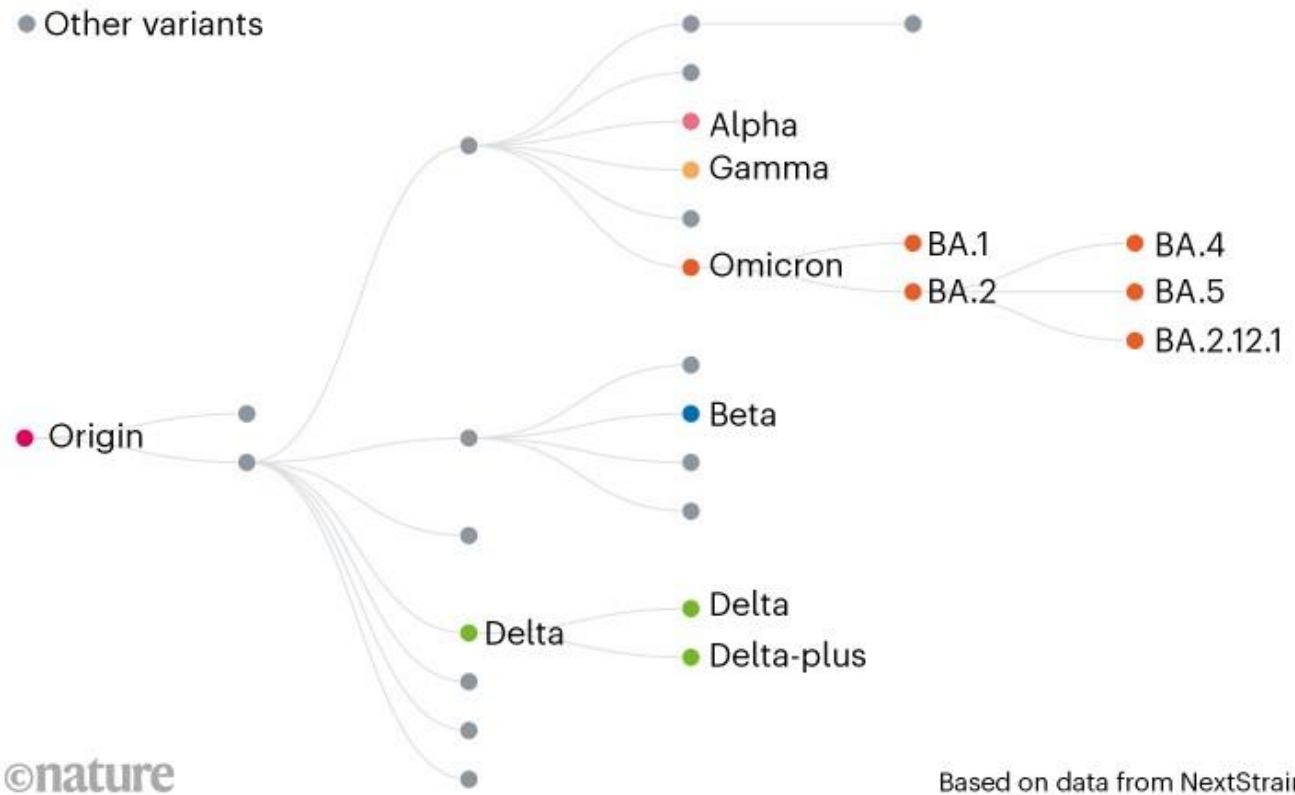
Scale drawings of some prokaryotic cells



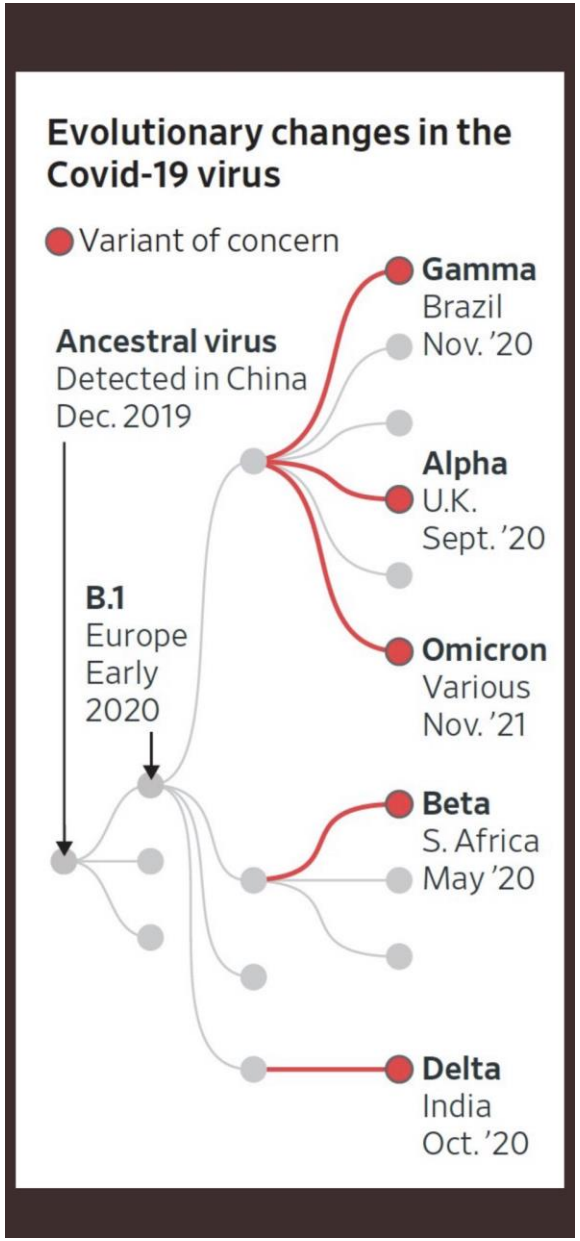
Three basic structures: spheroidal (cocci), rodlike (bacilli), and helically coiled (spirilla)

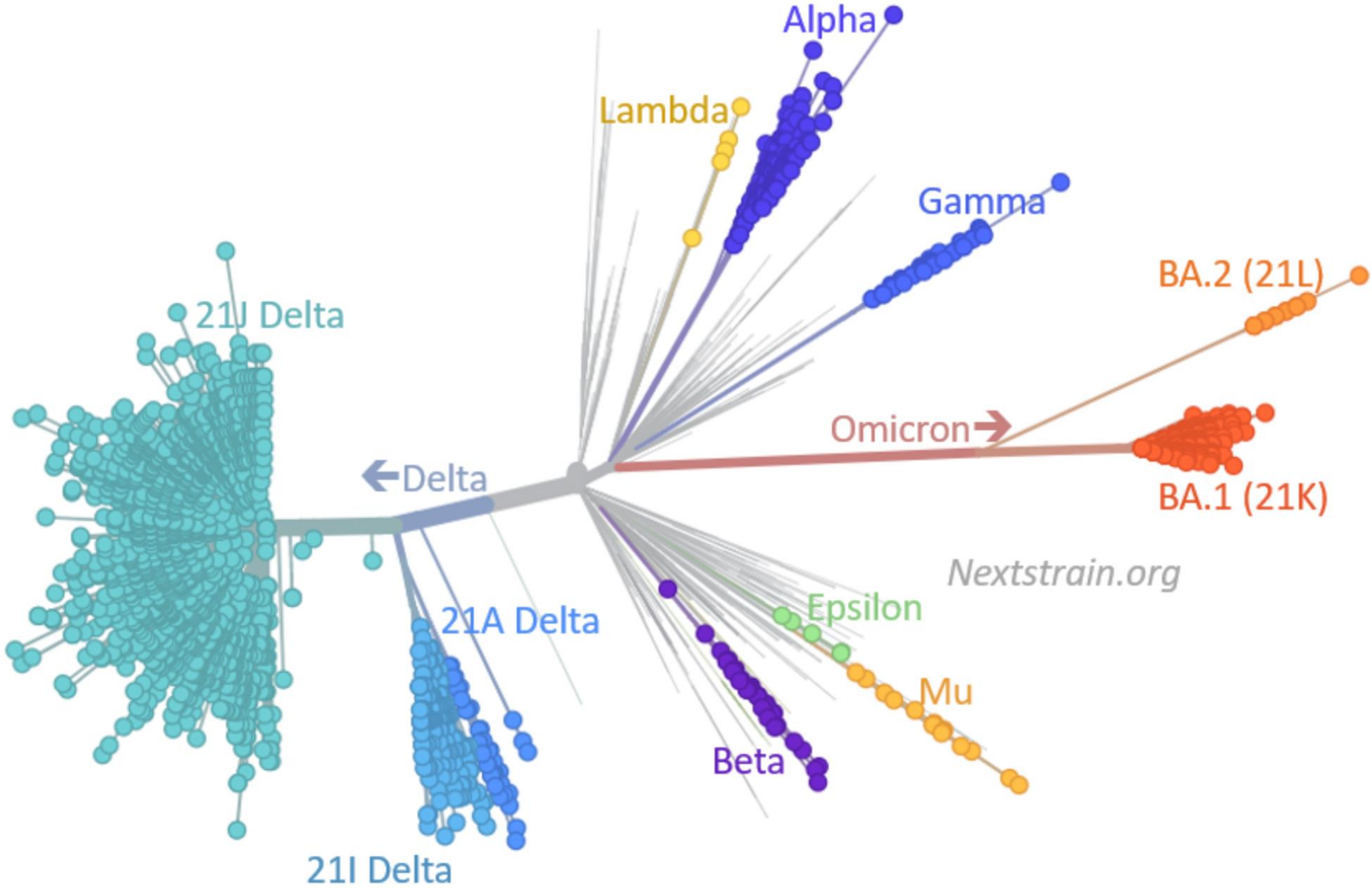
PATHOGEN PROGRESSION

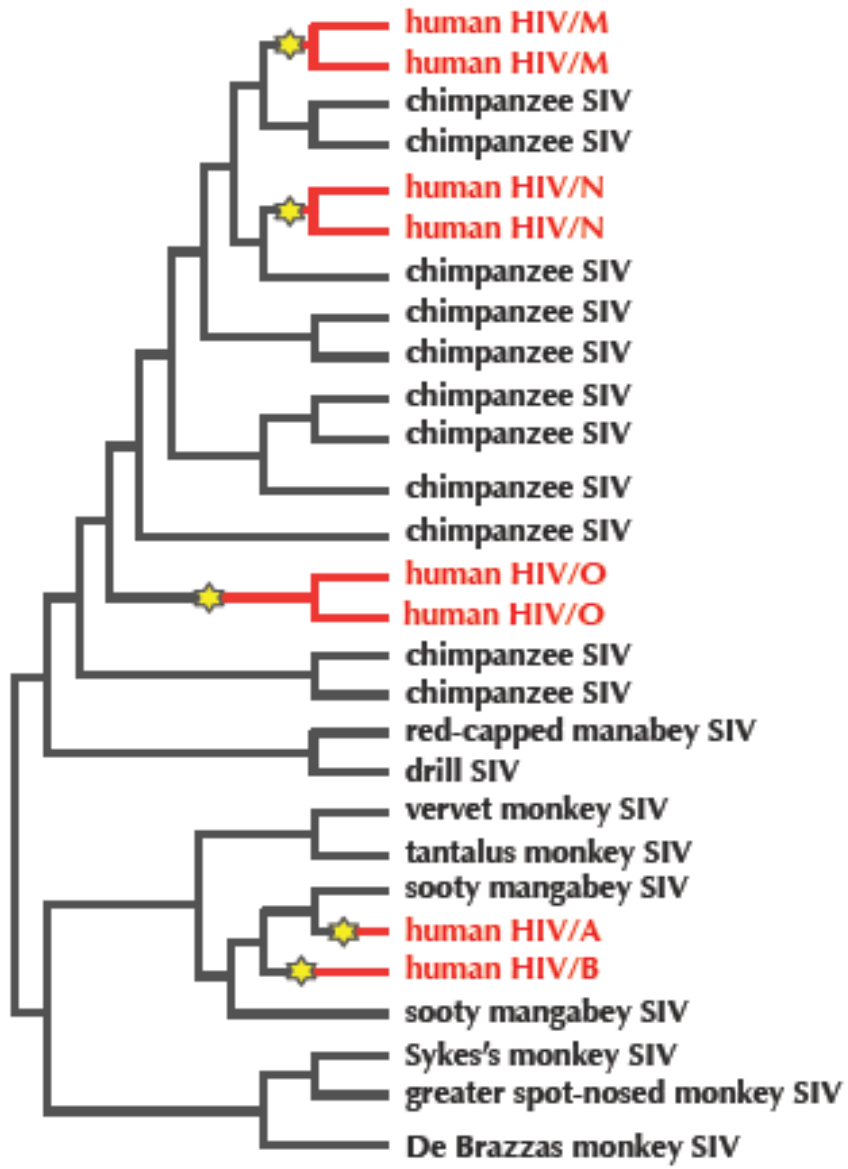
This diagram shows how the coronavirus SARS-CoV-2 has evolved to spawn several related variants. The latest are BA.4 and BA.5 along the Omicron lineage, which has dominated infections this year.

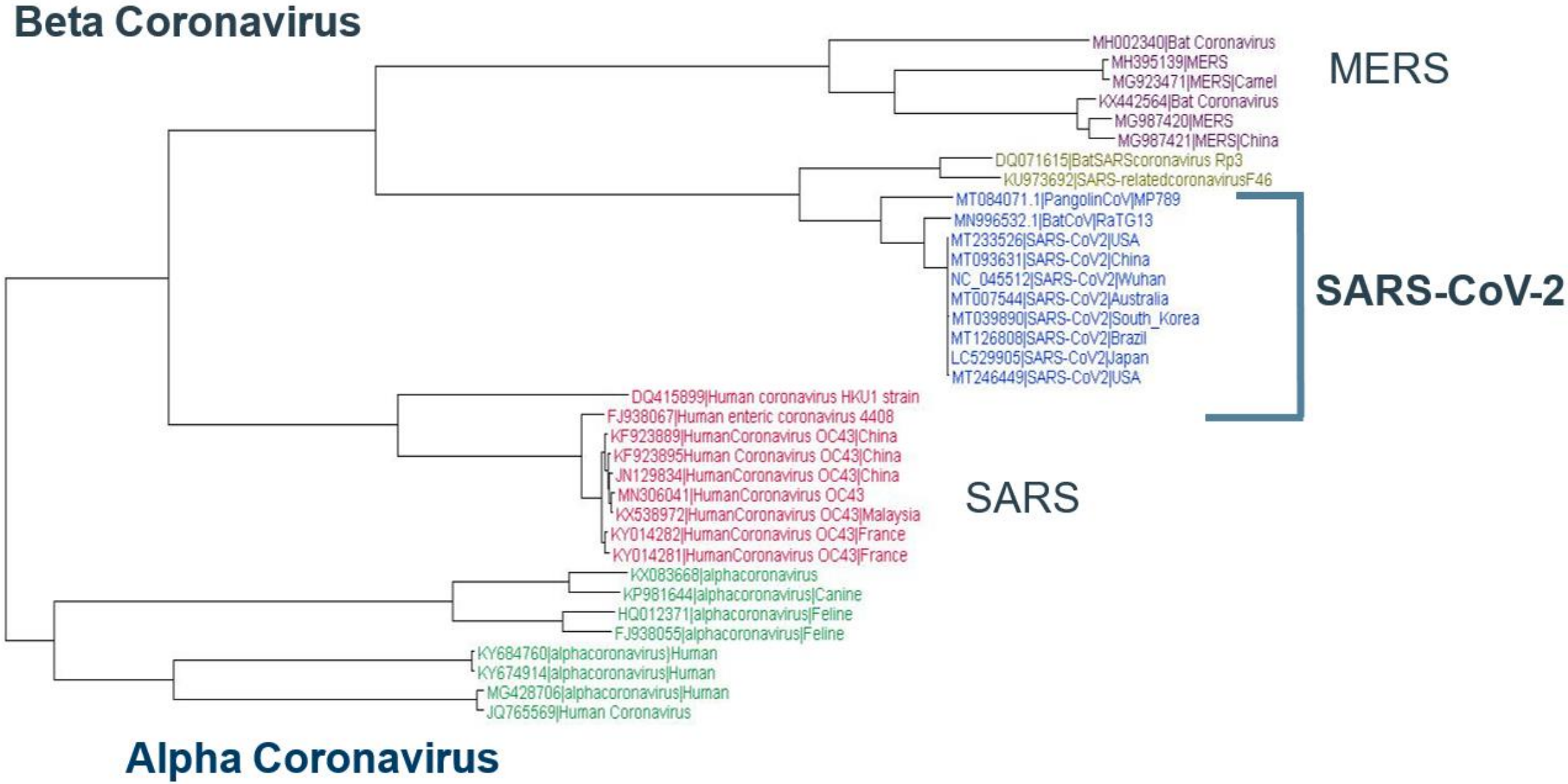


Based on data from NextStrain.




Alpha
Lambda
Gamma
BA.2 (21L)
21J Delta
Omicron
Delta
BA.1 (21K)
Nextstrain.org
Epsilon
21A Delta
Mu
Beta
21I Delta


human HIV/M
human HIV/M
chimpanzee SIV
chimpanzee SIV
human HIV/N
human HIV/N
chimpanzee SIV
chimpanzee SIV
chimpanzee SIV
chimpanzee SIV
chimpanzee SIV
chimpanzee SIV
chimpanzee SIV
human HIV/O
human HIV/O
chimpanzee SIV
chimpanzee SIV
red-capped manabey SIV
drill SIV
vervet monkey SIV
tantalus monkey SIV
sooty mangabey SIV
human HIV/A
human HIV/B
sooty mangabey SIV
Sykes's monkey SIV
greater spot-nosed monkey SIV
De Brazzas monkey SIV


Beta Coronavirus
MH002340|Bat Coronavirus
MH395139|MERS
MG923471|MERS|Camel
KX442564|Bat Coronavirus
MG987420|MERS
MG987421|MERS|China
MERS
DQ071615|BatSARScoronavirus Rp3
KU973692|SARS-relatedcoronavirusF46
MT084071.1|PangolinCoV|MP789
MN996532.1|BatCoV|RaTG13
MT233526|SARS-CoV2|USA
MT093631|SARS-CoV2|China
NC_045512|SARS-CoV2|Wuhan
MT007544|SARS-CoV2|Australia
MT039890|SARS-CoV2|South_Korea
MT126808|SARS-CoV2|Brazil
LC529905|SARS-CoV2|Japan
MT246449|SARS-CoV2|USA
SARS-CoV-2
DQ415899|Human coronavirus HKU1 strain
FJ938067|Human enteric coronavirus 4408
KF923889|HumanCoronavirus OC43|China
KF923895Human Coronavirus OC43|China
JN129834|HumanCoronavirus OC43|China
MN306041|HumanCoronavirus OC43
KX538972|HumanCoronavirus OC43|Malaysia
KY014282|HumanCoronavirus OC43|France
KY014281|HumanCoronavirus OC43|France
SARS
KX083668|alphacoronavirus
KP981644|alphacoronavirus|Canine
HQ012371|alphacoronavirus|Feline
FJ938055|alphacoronavirus|Feline
KY684760|alphacoronavirus}Human
KY674914|alphacoronavirus|Human
MG428706|alphacoronavirus|Human
JQ765569|Human Coronavirus
Alpha Coronavirus

Let us play the sequence alignment game!

Strings ATGCATGC and TGCATGCA !

```
ATGCATGC
TGCATGCA

ATGCATGC-
-TGCATGCA
```

We postulate a notion of a good alignment as one that matches as many symbols as possible.

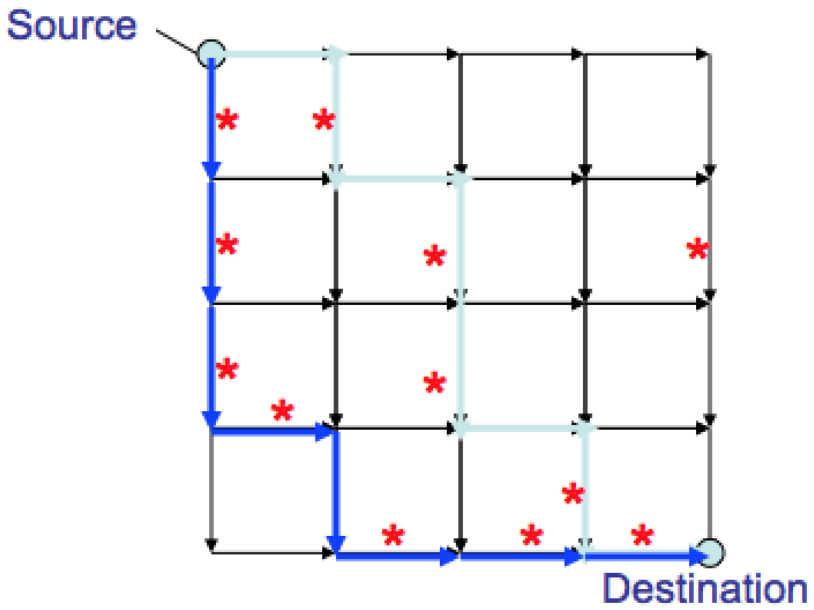
Strings ATGCTTA and TGCATTAA

```
ATGC-TTA-
-TGCATTAA
```

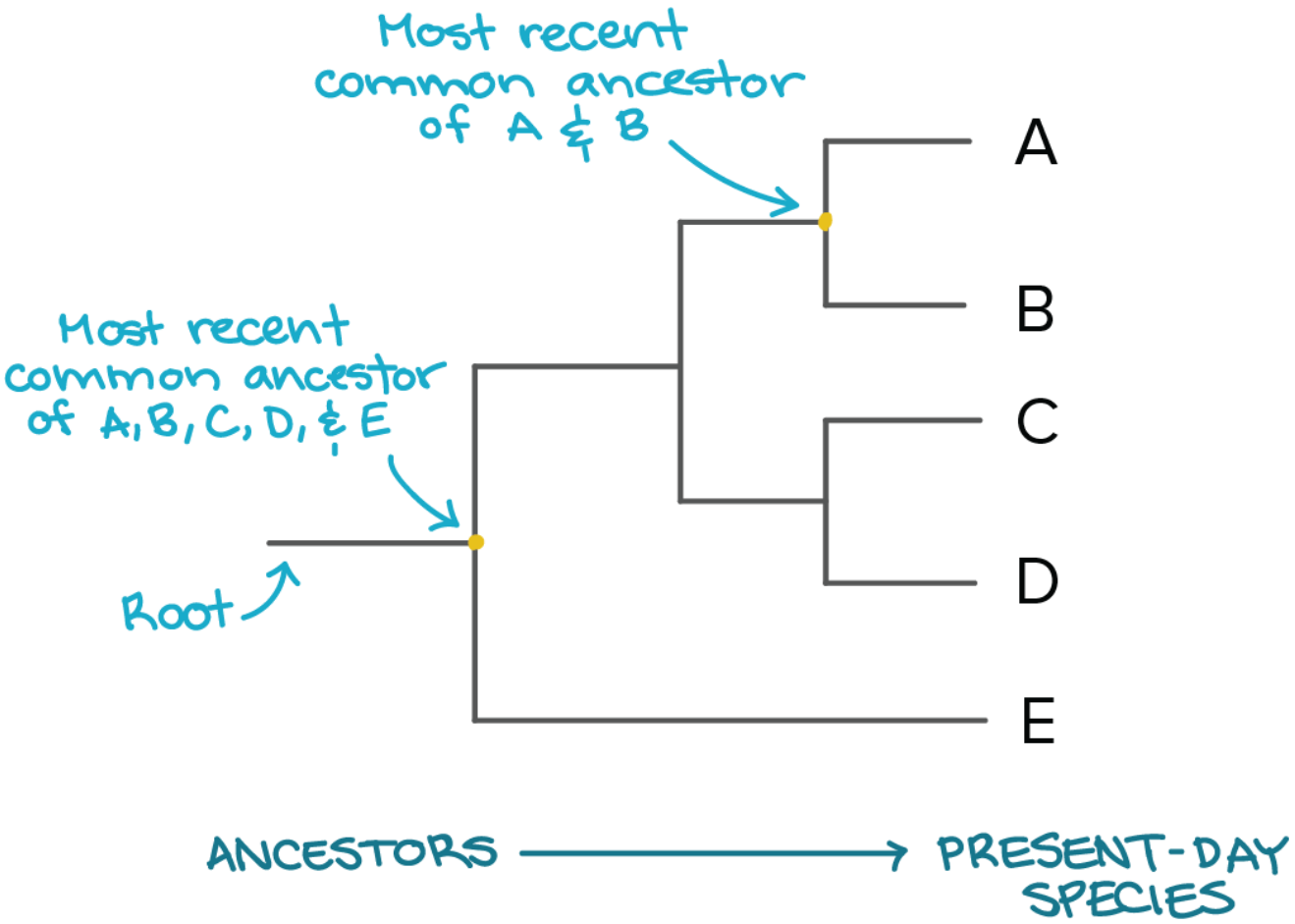
Longest Common Subsequence Problem:
Find a longest common subsequence of two strings.

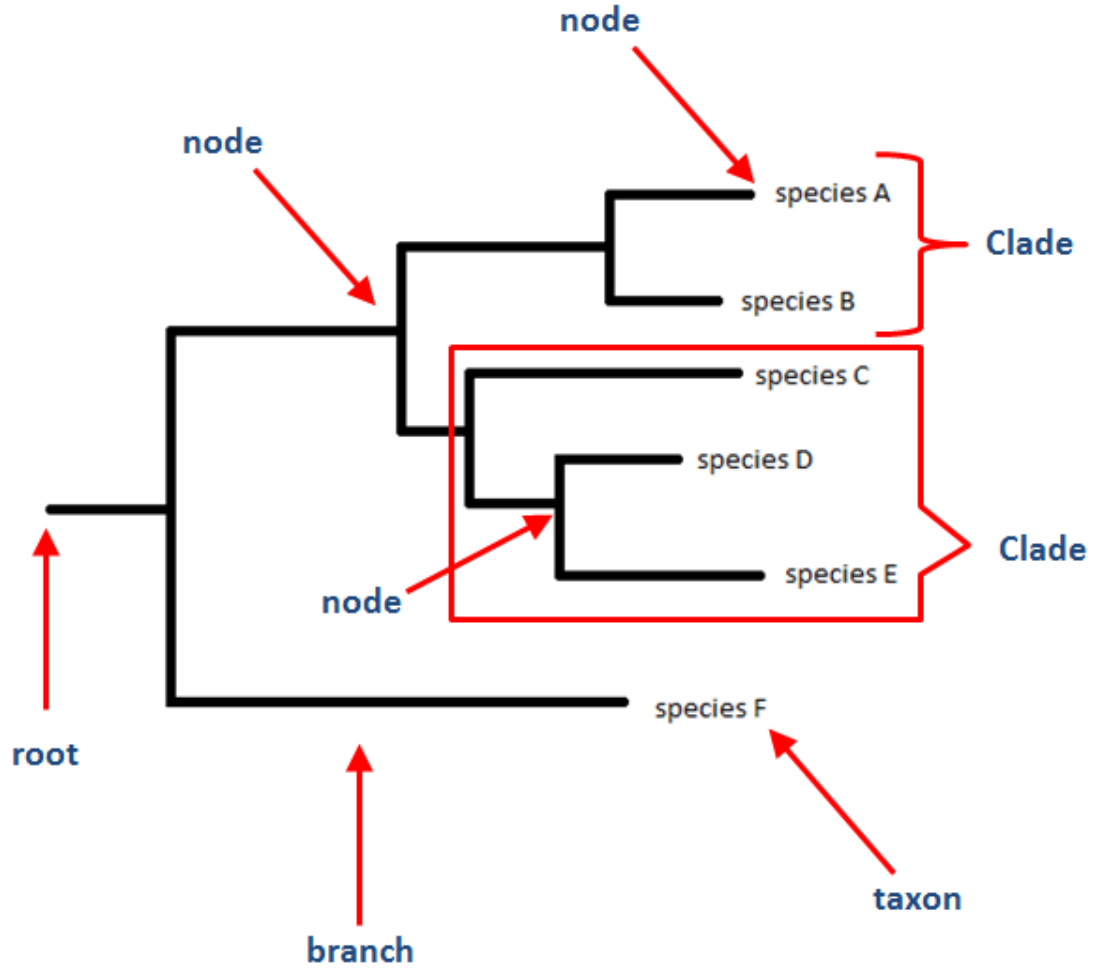
Input: Two strings.
Output: A longest common subsequence of these strings.

The Manhattan tourist problem!



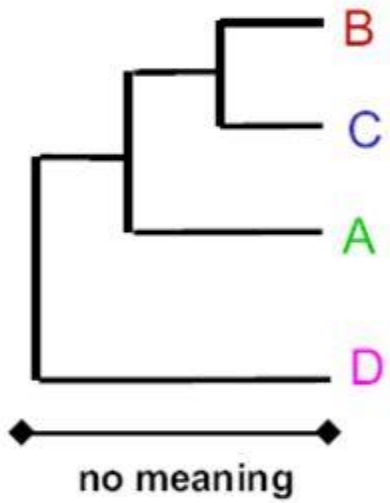
Parts of a phylogenetic tree





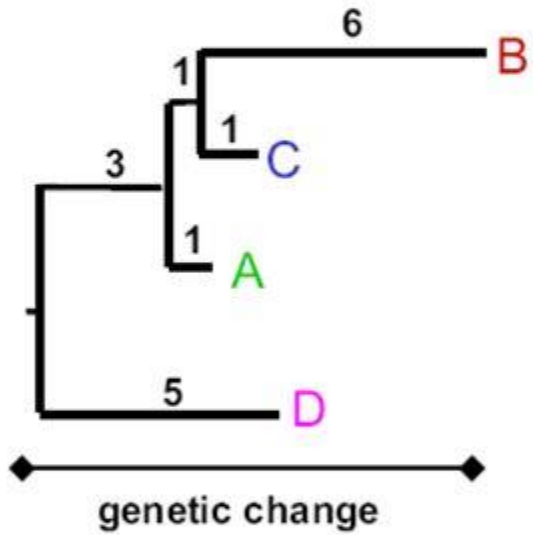
Types of trees

Cladogram



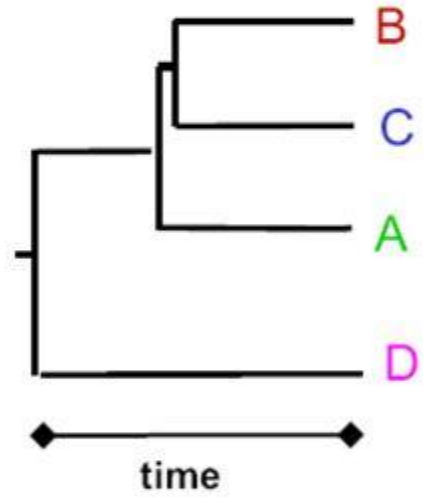
Simply shows relative recency of common ancestor

Phylogram

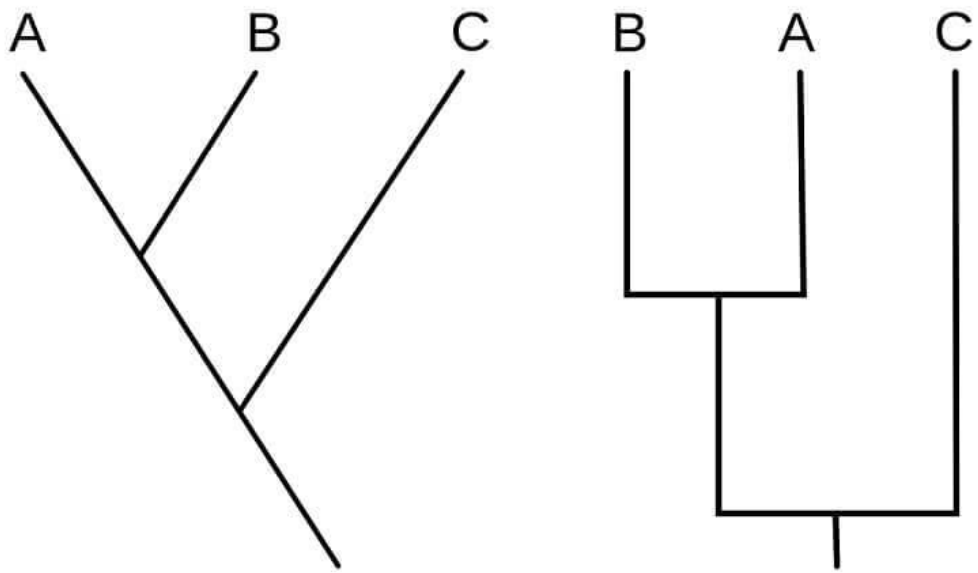


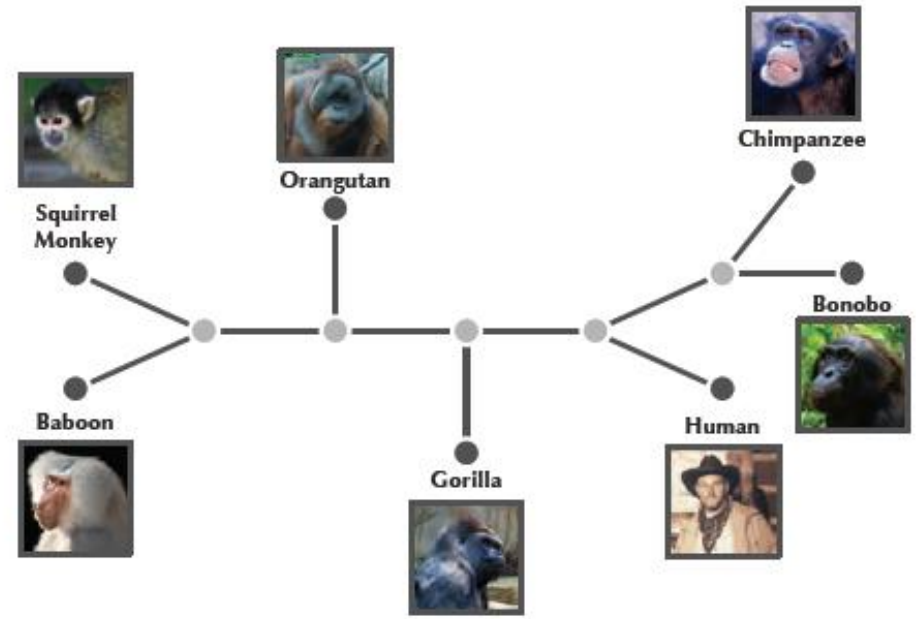
A cladogram with branch lengths

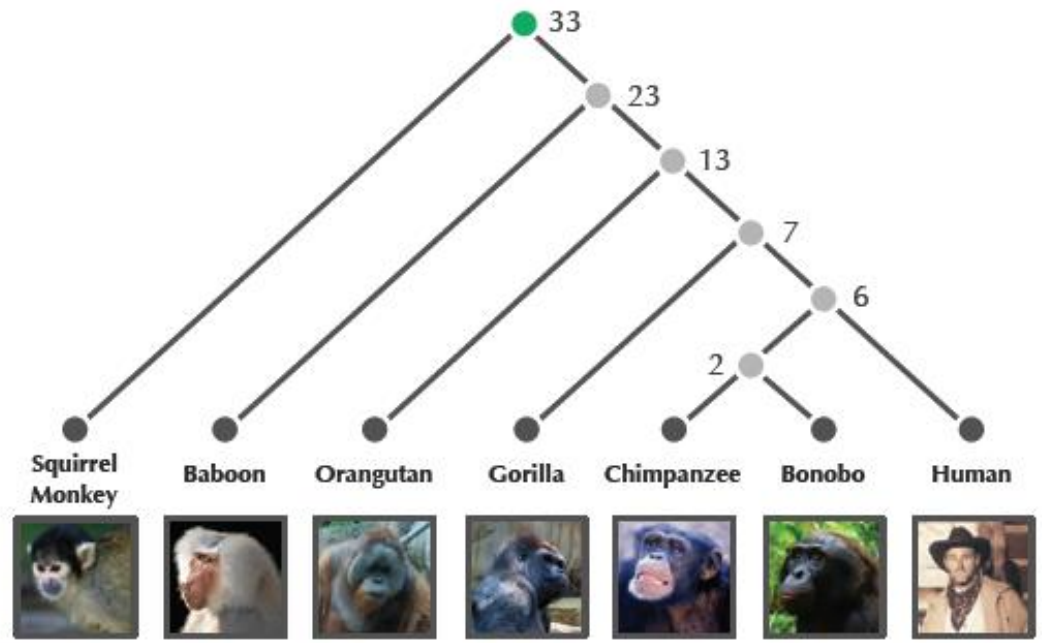
Ultrametric tree



A dendogram having all tips equidistant from root


A
B
C
B
A
C

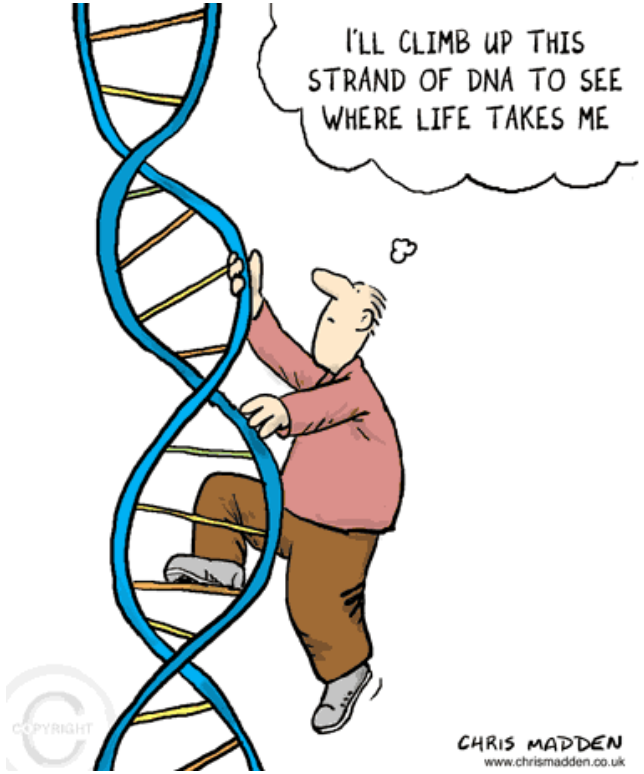

Squirrel Monkey
Orangutan
Chimpanzee
Bonobo
Baboon
Human
Gorilla


33
23
13
7
6
2
Squirrel Monkey
Baboon
Orangutan
Gorilla
Chimpanzee
Bonobo
Human

Some definitions

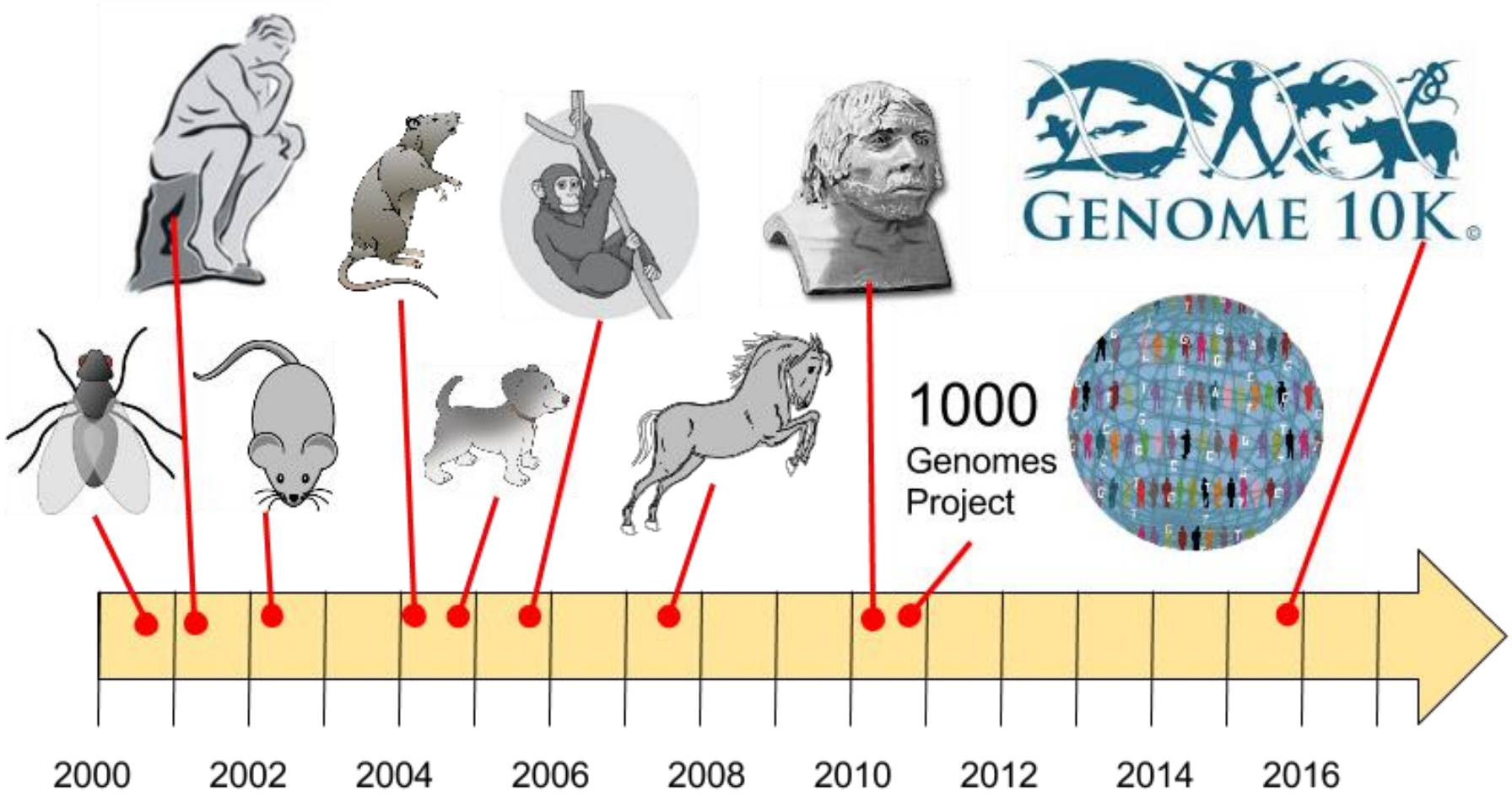
- Classification - Grouping of things into classes.
  - e.g. Kingdom, phylum, class, order, family, genus, species.
- Taxonomy - Giving names to things.
  - e.g. Taxons -Mammalia, *Homo sapiens*, *Felis*
- Systematics- Understanding the relationships between things.
  - e.g. The daughter of my aunt is my cousin. The sister of my grandmother is my great-aunt.
- Phylogeny - The evolutionary history of a species.
  - If you don't know your history, you don't know anything!
- Cladistics - Phylogenetic systematics. Using the evolutionary history of species to understand their relationships, classify them, and give them names!

Universal feature-Chemical code



Organism	Genome size* (nucleotide pairs)	Approximate number of genes
Escherichia coli (bacterium)	4.6×10^6	4300
Saccharomyces cerevisiae (yeast)	13×10^6	6600
Caenorhabditis elegans (roundworm)	130×10^6	21,000
Arabidopsis thaliana (plant)	220×10^6	29,000
Drosophila melanogaster (fruit fly)	200×10^6	15,000
Danio rerio (zebrafish)	1400×10^6	32,000
Mus musculus (mouse)	2800×10^6	30,000
Homo sapiens (human)	3200×10^6	30,000

*Genome size includes an estimate for the amount of highly repeated DNA sequence not in genome databases.


GENOME 10K
1000
Genomes
Project
2000
2002
2004
2006
2008
2010
2012
2014
2016

TGCCAAGCAGCAAAGTTTTGCTGCTGTTTATTTTTGTAGCTCTTACTATATTCTACTTTTAC
CATTGAAAATATTGAGGAAGTTATTTATATTTCTATTTTTTATATATTATATATTTTATGTATTT
TAATATTACTATTACACATAATTATTTTTTATATATATGAAGTACCAATGACTTCCTTTTCCAG
AGCAATAATGAAATTTCACAGTATGAAAATGGAAGAAATCAATAAAATTATACGTGACCT
GTGGCGAAGTACCTATCGTGGACAAGGTGAGTACCATGGTGTATCACAAATGCTCTTTCC
AAAGCCCTCTCCGCAGCTCTTCCCCTTATGACCTCTCATCATGCCAGCATTACCTCCCTGG
ACCCCTTTCTAAGCATGTCTTTGAGATTTTCTAAGAATTCTTATCTTGGCAACATCTTGTAG
CAAGAAAATGTAAAGTTTTCTGTTCCAGAGCCTAACAGGACTTACATATTTGACTGCAGT
AGGCATTATATTTAGCTGATGACATAATAGGTTCTGTCATAGTGTAGATAGGGATAAGCCA
AAATGCAATAAGAAAAACCATCCAGAGGAAACTCTTTTTTTTTTCTTTTTCTTTTTTTTTT
TTCCAGATGGAGTCTCGCACTTCTCTGTCACCCGGGCTGGAGCGCAGTGGTGCAATCTT
GGCTCACTGCAACCTCCACCTCCTGGGTTCAGGTGATTCTCCCACCTCAGCCTCCCGAGT
AGTAGCTGGAATTACAGGTGCGCGCTCCCACACCTGGCTAATTTTTTGTATTCTTAGTAG
AGATGGGGTTTCACCATGTTGGCCAGGCTGGTCTCAAACTCCTGCCCTCAGGTGATCTG
CCCACCTTGGCCTCCCAGTGTTGGGTTTACAGGCGTGAGCCACCGCGCCTGGCCTGGA
GGAAACTCTTAACAGGGAAACTAAGAAAGAGTTGAGGCTGAGGAACTGGGGCATCTG
GGTTGCTTCTGGCCAGACCACCAGGCTCTTGAATCCTCCCAGCCAGAGAAAGAGTTTCC
ACACCAGCCATTGTTTTCCTCTGGTAATGTCAGCCTCATCTGTTGTTCCTAGGCTTACTTG
ATATGTTTGTAAATGACAAAAGGCTACAGAGCATAGGTTCCTCTAAAATATTCTTCTTCCT
GTGTCAGATATTGAATACATAGAAATACGGTCTGATGCCGATGAAAATGTATCAGCTTCTG
ATAAAAGGCGGAATTATAACTACCGAGTGGTGATGCTGAAGGGAGACACAGCCTTGGA
TATGCGAGGACGATGCAGTGCTGGACAAAAGGCAGGTATCTCAAAAGCCTGGGGAGCC
AACTCACCCAAGTAACTGAAAGAGAGAAACAAACATCAGTGCAGTGGAAGCACCCAAG
GCTACACCTGAATGGTGGGAAGCTCTTTGCTGCTATATAAAATGAATCAGGCTCAGCTAC
TATTATT .....

The Human Genome

2003

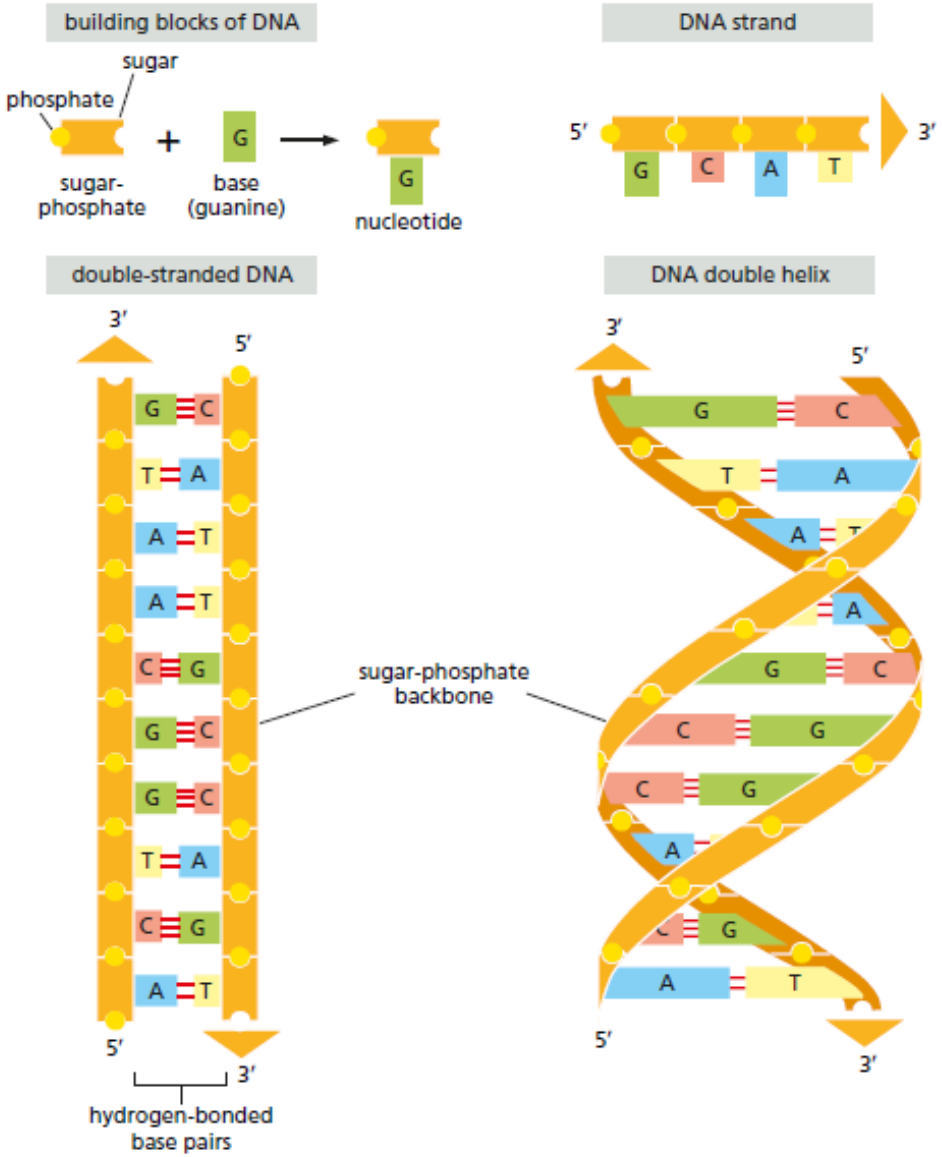
"*Fifteen years, six countries, twenty centers. Three billion dollars, three billion letters. One dollar per letter – such a deal*!"

Eric Lander's seven-word " Nano Lecture"

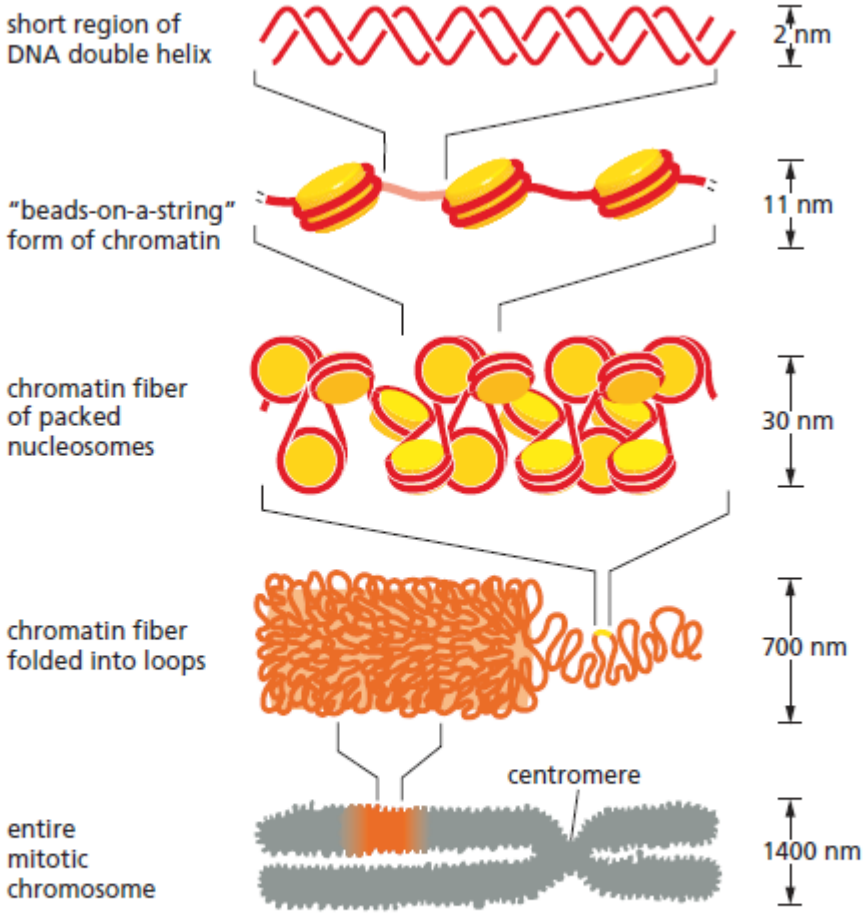
"Genome: bought the book; hard to read"

TGCCAAGCAGCAAAGTTTTGCTGCTGTTTATTTTTGTAGCTCTTACTATATTCTACTTTTACCATTGAAAATATTGAGGAAGTTATTTATATTTCTATTTTTTATA
TATTATATATTTTATGTATTTTAATATTACTATTACACATAATTATTTTTTATATATATGAAGTACCAATGACTTCCTTTTCCAGAGCAATAATGAAATTTCACAGTA
TGAAAATGGAAGAAATCAATAAAATTATACGTGACCTGTGGCGAAGTACCTATCGTGGACAAGGTGAGTACCATGGTGTATCACAAATGCTCTTTCCAAAG
CCCTCTCCGCAGCTCTTCCCCTTATGACCTCTCATCATGCCAGCATTACCTCCCTGGACCCCTTTCTAAGCATGTCTTTGAGATTTTCTAAGAATTCTTATCTTG
GCAACATCTTGTAGCAAGAAAATGTAAAGTTTTCTGTTCCAGAGCCTAACAGGACTTACATATTTGACTGCAGTAGGCATTATATTTAGCTGATGACATAATA
GGTTCTGTCATAGTGTAGATAGGGATAAGCCAAAATGCAATAAGAAAAACCATCCAGAGGAAACTCTTTTTTTTTTCTTTTTCTTTTTTTTTTTTTCCAGATG
GAGTCTCGCACTTCTCTGTCACCCGGGCTGGAGCGCAGTGGTGCAATCTTGGCTCACTGCAACCTCCACCTCCTGGGTTCAGGTGATTCTCCCACCTCAG
CCTCCCGAGTAGTAGCTGGAATTACAGGTGCGCGCTCCCACACCTGGCTAATTTTTTGTATTCTTAGTAGAGATGGGGTTTCACCATGTTGGCCAGGCTGG
TCTCAAACTCCTGCCCTCAGGTGATCTGCCCACCTTGGCCTCCCAGTGTTGGGTTTACAGGCGTGAGCCACCGCGCCTGGCCTGGAGGAAACTCTTAACA
GGGAAACTAAGAAAGAGTTGAGGCTGAGGAACTGGGGCATCTGGGTTGCTTCTGGCCAGACCACCAGGCTCTTGAATCCTCCCAGCCAGAGAAAGAG
TTTCCACACCAGCCATTGTTTTCCTCTGGTAATGTCAGCCTCATCTGTTGTTCCTAGGCTTACTTGATATGTTTGTAAATGACAAAAGGCTACAGAGCATAGG
TTCCTCTAAAATATTCTTCTTCCTGTGTCAGATATTGAATACATAGAAATACGGTCTGATGCCGATGAAAATGTATCAGCTTCTGATAAAAGGCGGAATTATAA
CTACCGAGTGGTGATGCTGAAGGGAGACACAGCCTTGGATATGCGAGGACGATGCAGTGCTGGACAAAA

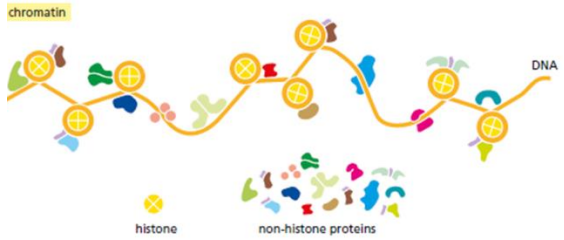
DNA and its building blocks



The organization of Chromosomes

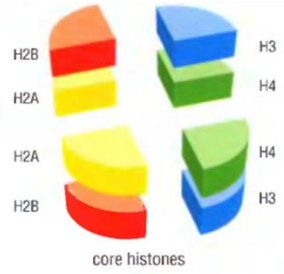


NET RESULT: EACH DNA MOLECULE HAS BEEN PACKAGED INTO A MITOTIC CHROMOSOME THAT IS 10,000-FOLD SHORTER THAN ITS FULLY EXTENDED LENGTH

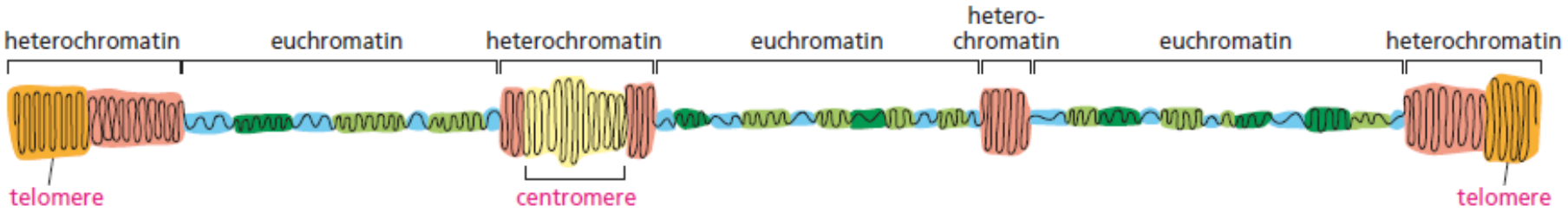


beads on a string - Nucleosome

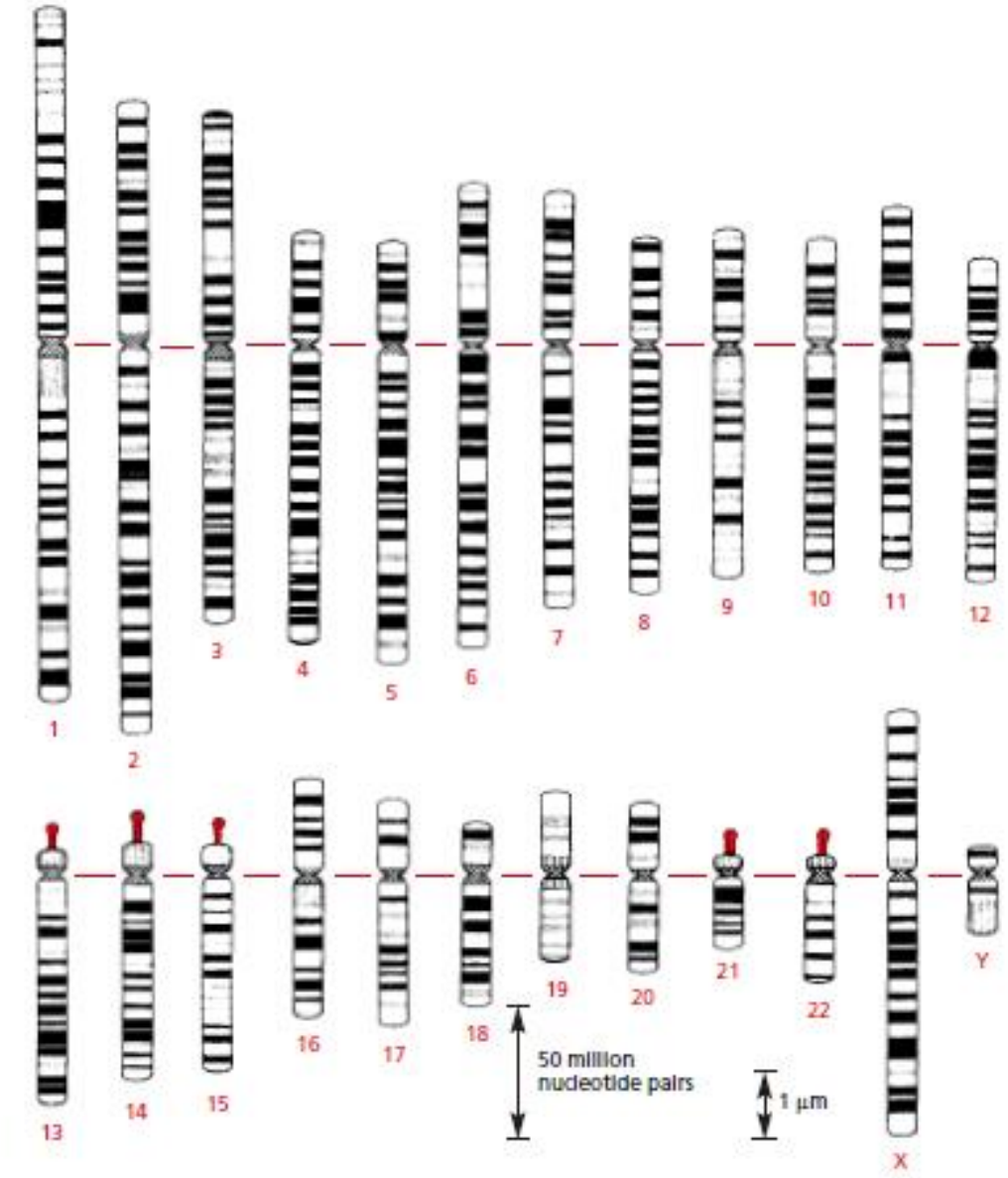
147 nucleotide pairs long makes 1.7 turns around each protein core



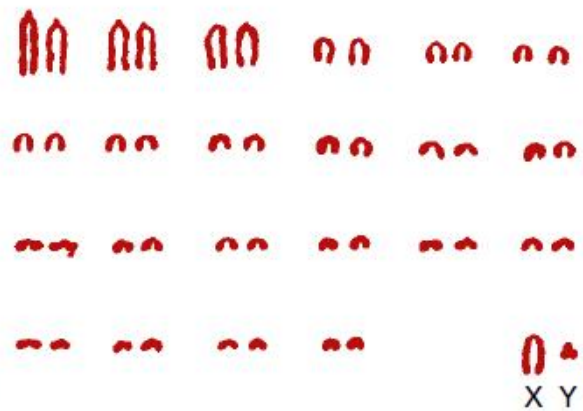
The structure of chromatin varies



The banding patterns of human chromosomes



Giemsa Staining



Chinese muntjac

Indian muntjac

Interesting observations from Beatrice !

- In some insects like grasshoppers, crickets, and roaches, there is only one kind of sex chromosome, X. If you get 2 of them, you're female, and if you just get one, you're a male.

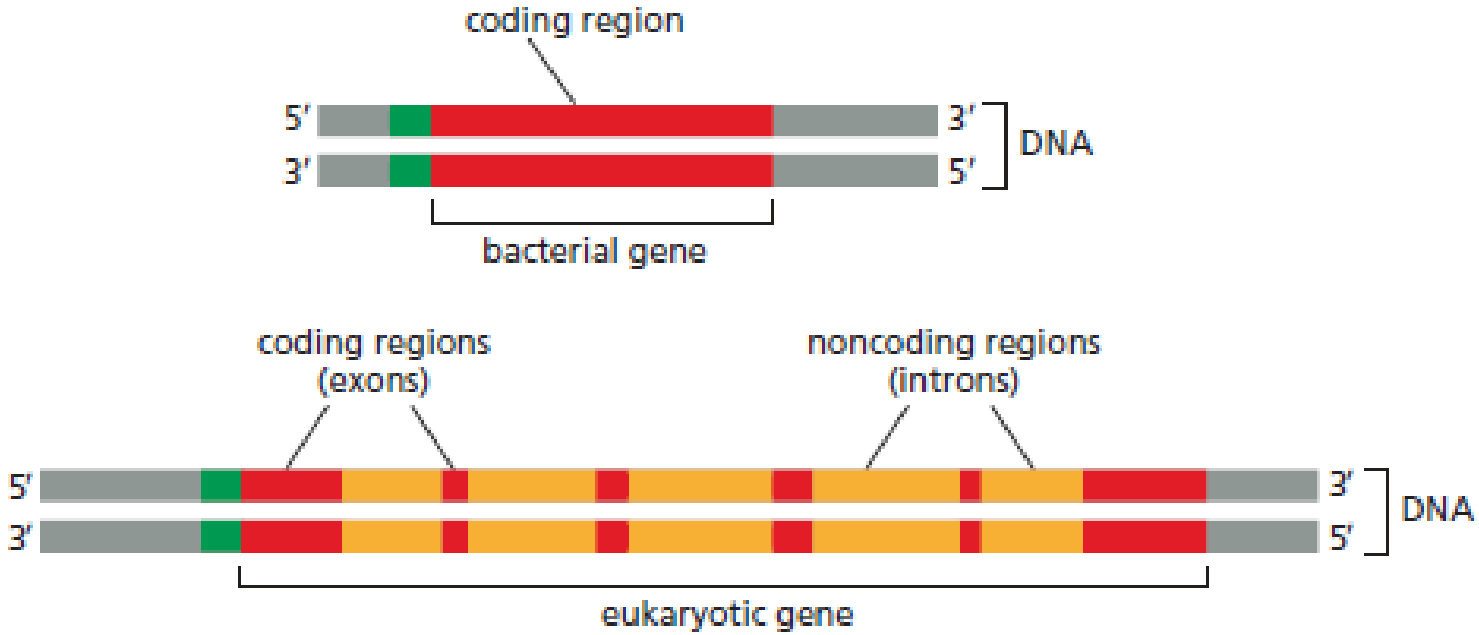
- In birds (and even some insects and fishes) it's the females that have different sex chromosomes. Females are ZW and males are ZZ. Scientists changed the letters to differentiate between the XX-female, XY-male scenario.

- In ants and bees, there are no sex chromosomes. Instead, sex is determined by whether or not an egg was fertilized. If the egg isn't fertilized, the offspring is male. If the egg is fertilized, it's female. So male ants have no fathers, and they have half as many chromosomes as females. Poor little things!

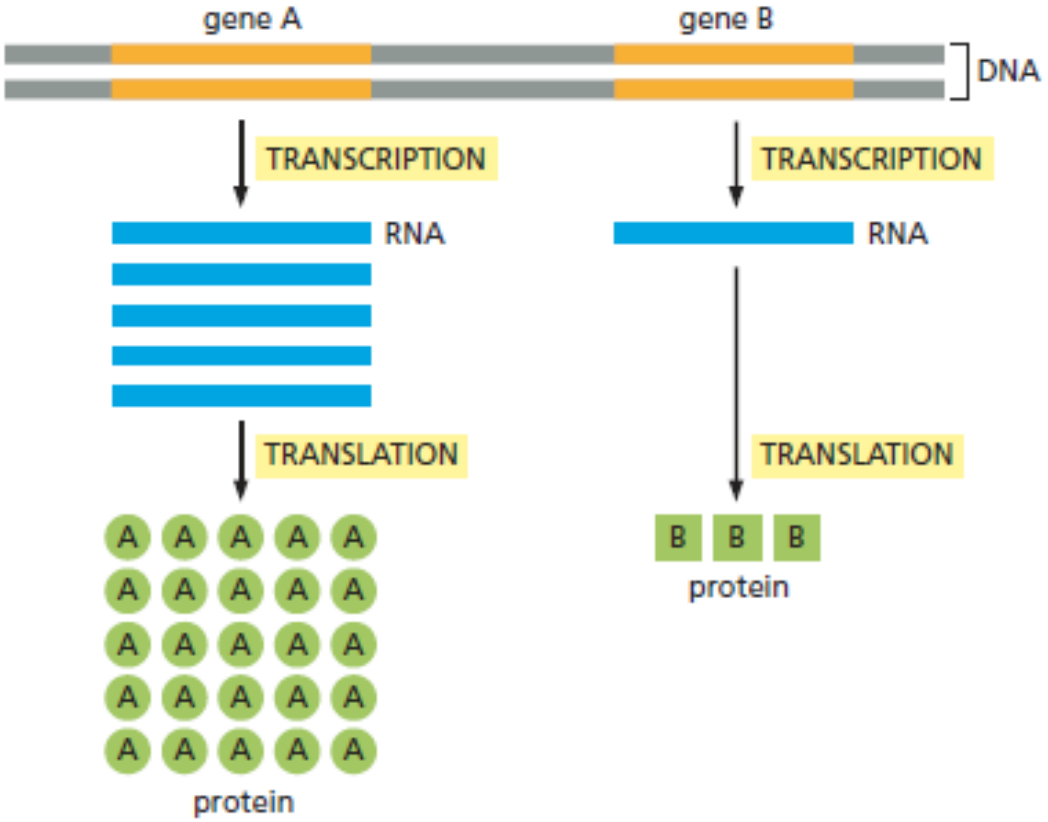
- A species of deer called the Indian muntjac (as opposed to the Chinese muntjac) has three different kinds of sex chromosomes–X and two versions of Y, called Y1 and Y2. Females are XX, and males are XY1Y2. Ha, those crazy muntjacs.

- May we never forget that biology is a complicated, messy, random process that has found several ways for dealing with sex and reproduction (and just about every other bit of life business). There is really no rhyme or reason for any of it. If it works, it works. If it doesn't, you die. That's pretty much the only rule in nature that applies all the time.

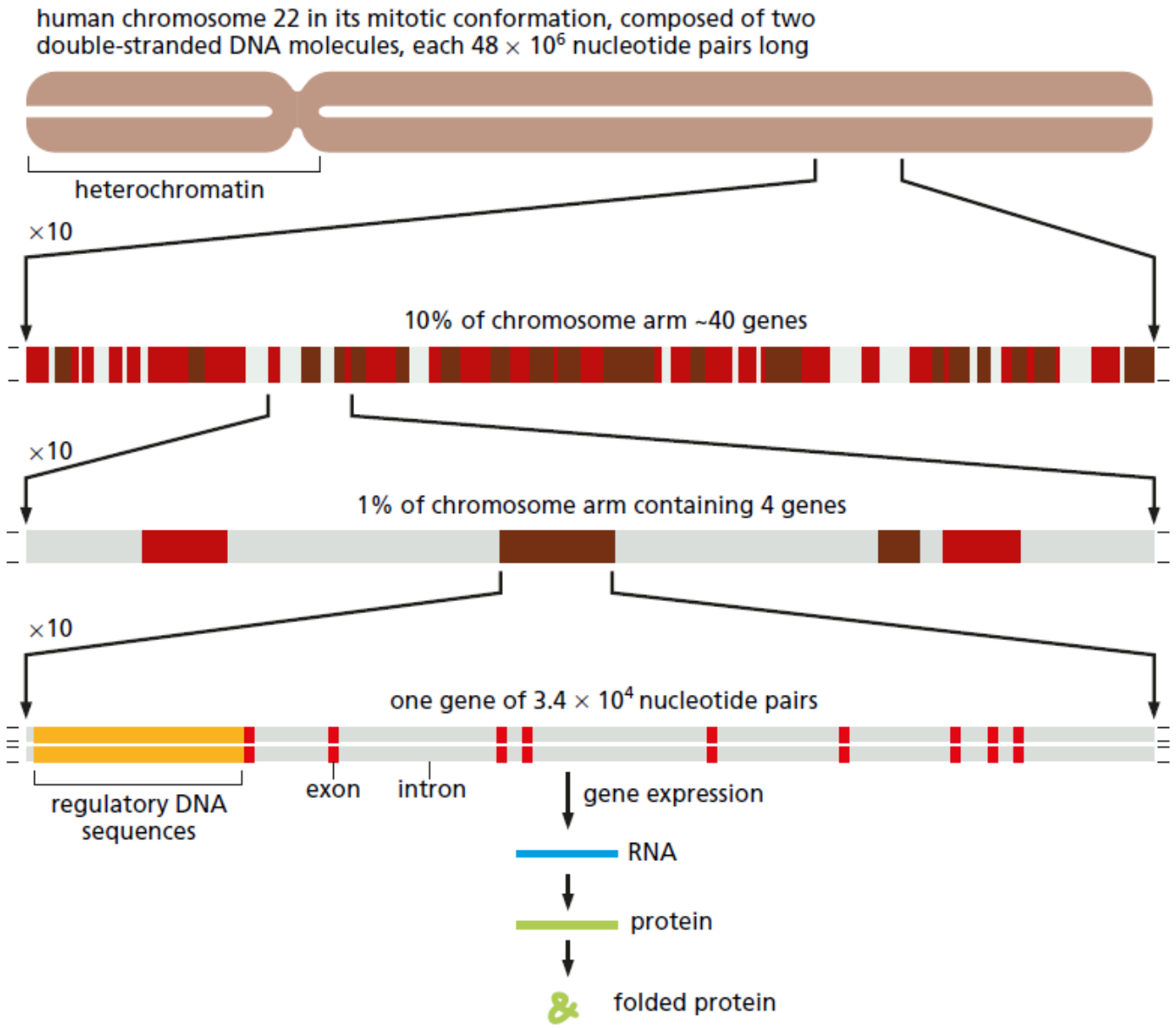
Eukaryotic and bacterial genes are organized differently



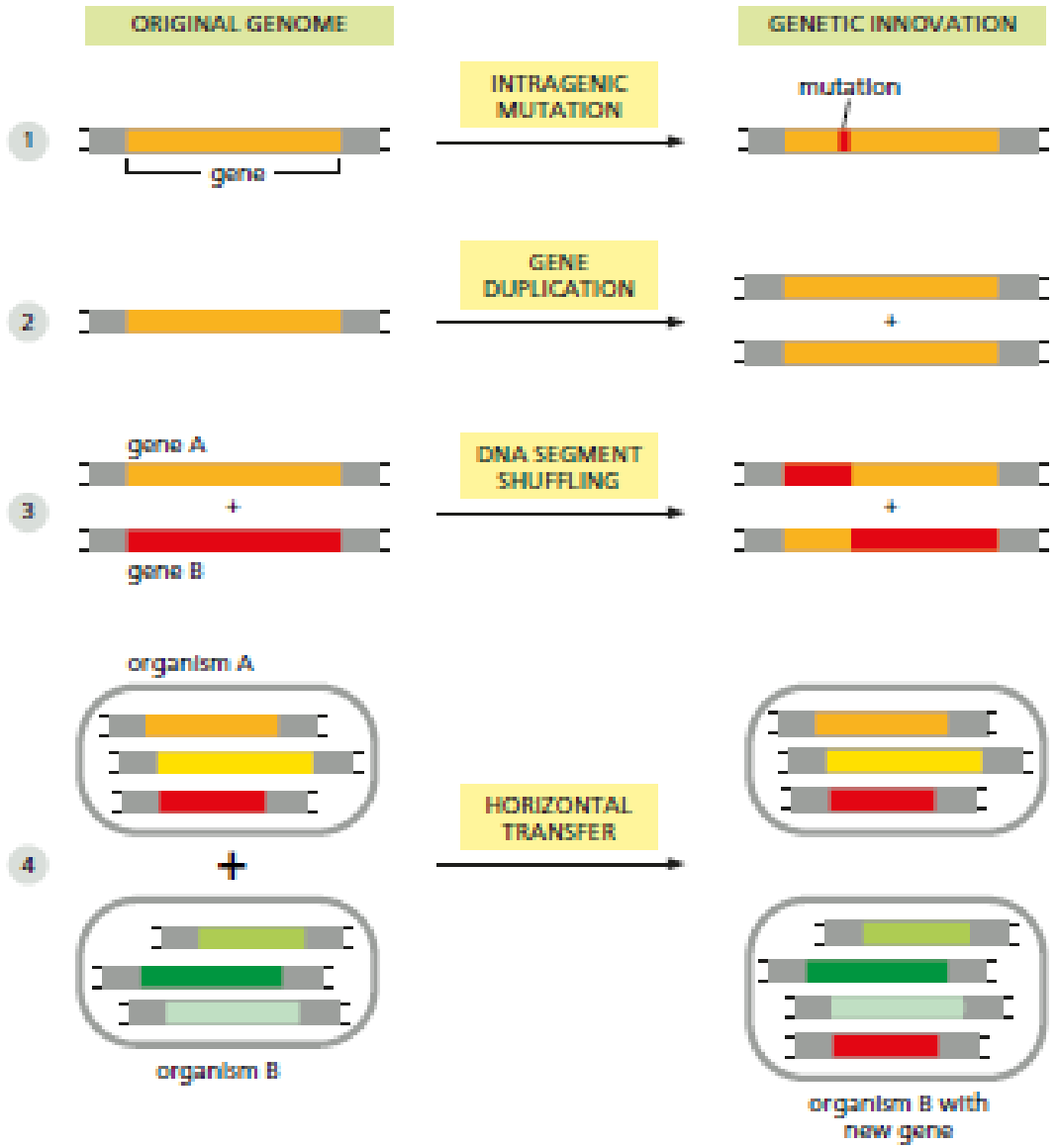
How Cells Read the Genome



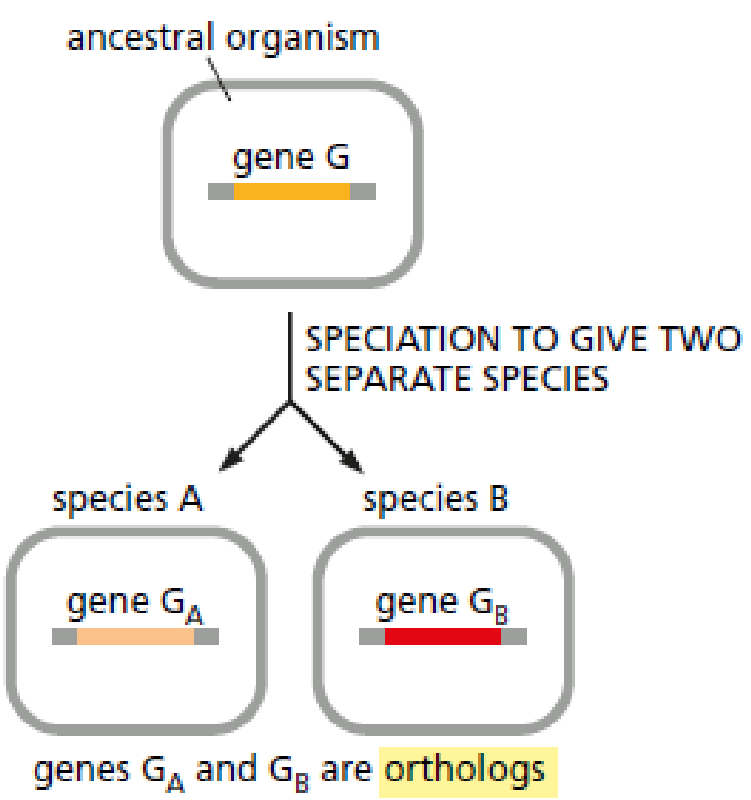
The organization of genes on a human chromosome

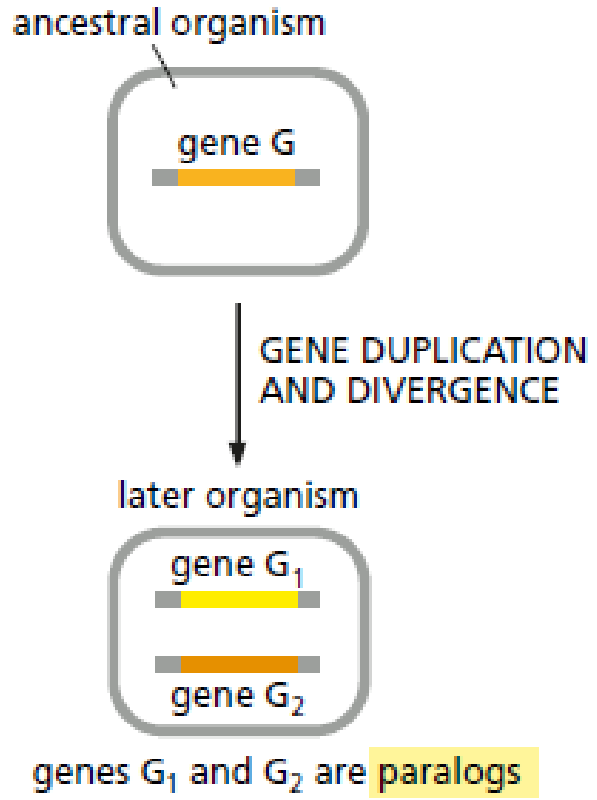


New genes are generated from existing genes

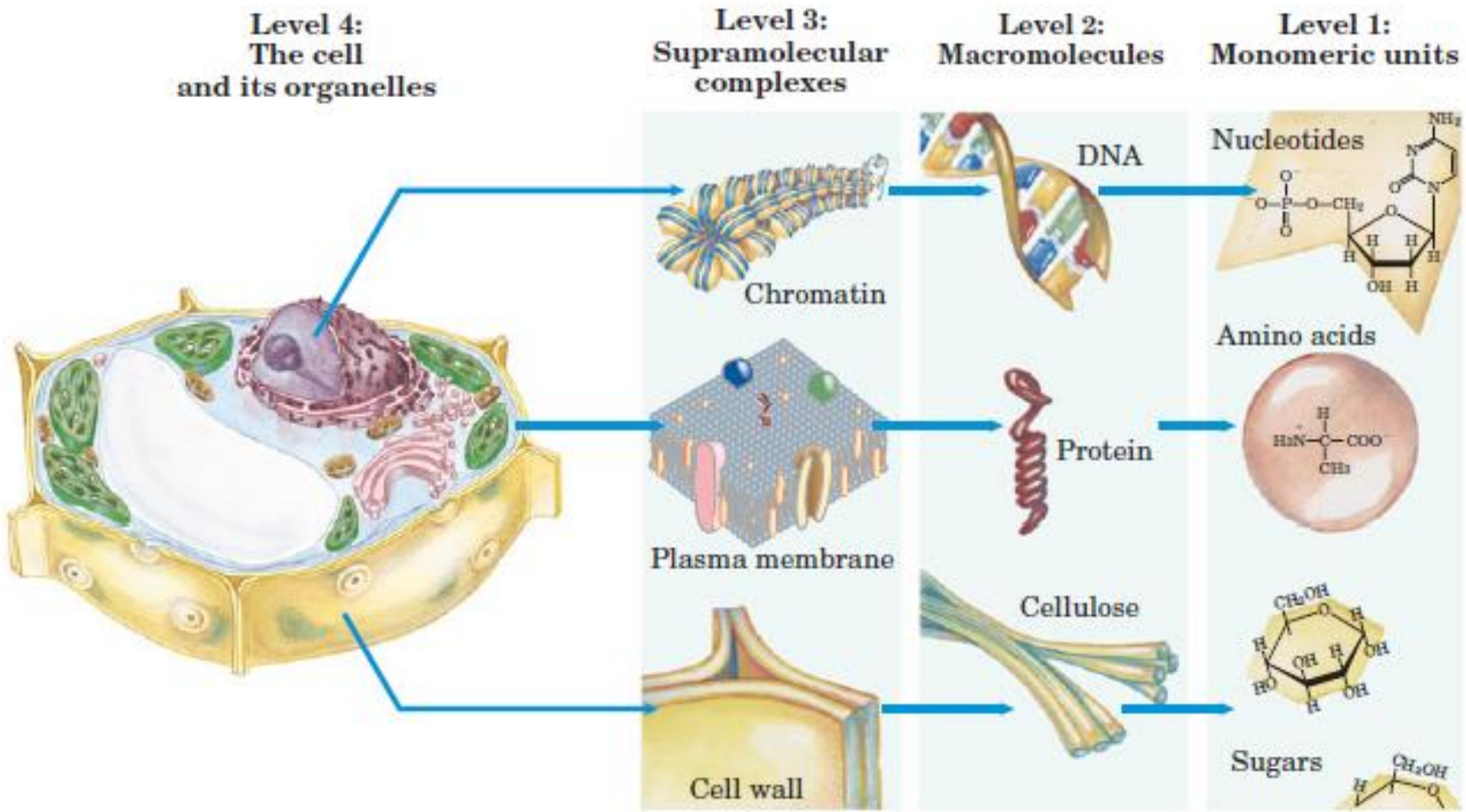


Gene duplications give rise to families of genes

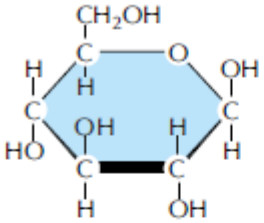




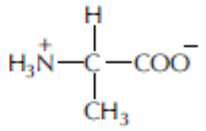
Structural hierarchy in the molecular organization of cells



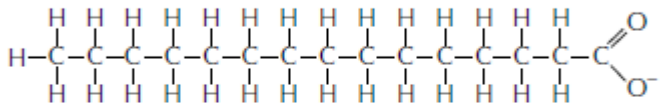
Cells function as biochemical factories



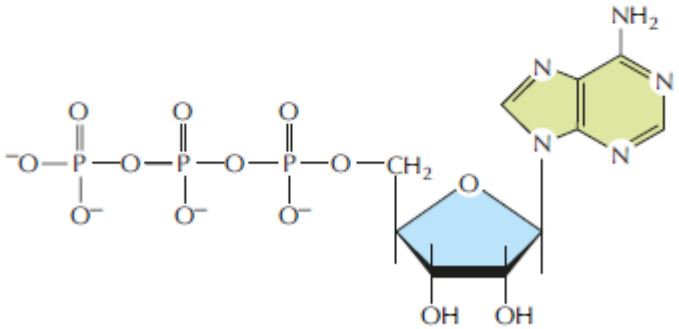
A SUGAR



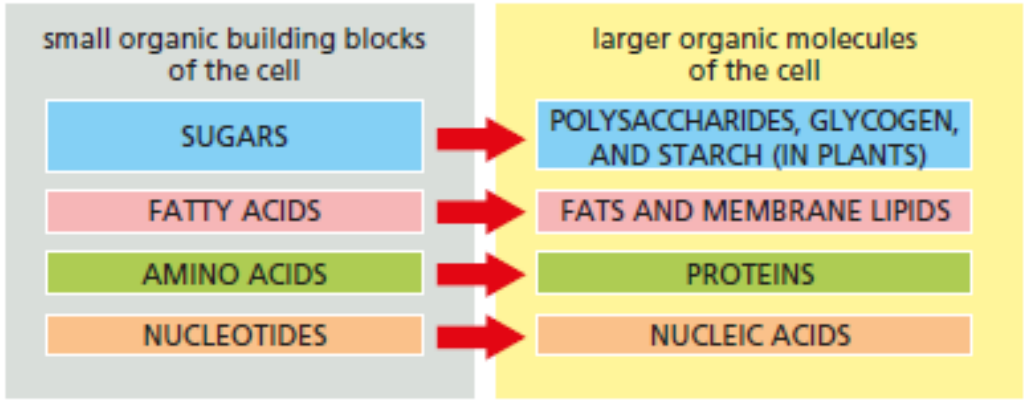
AN AMINO ACID

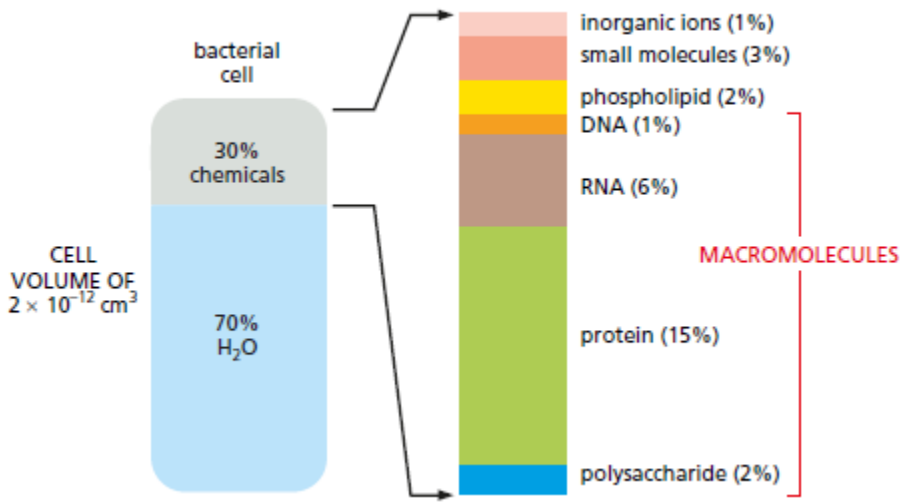


A FATTY ACID

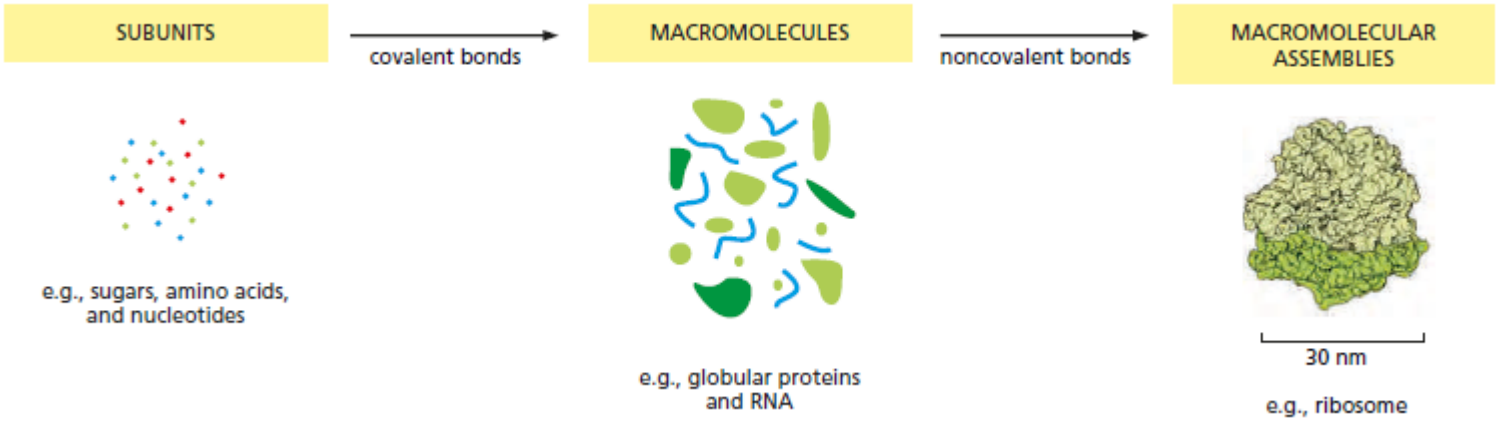


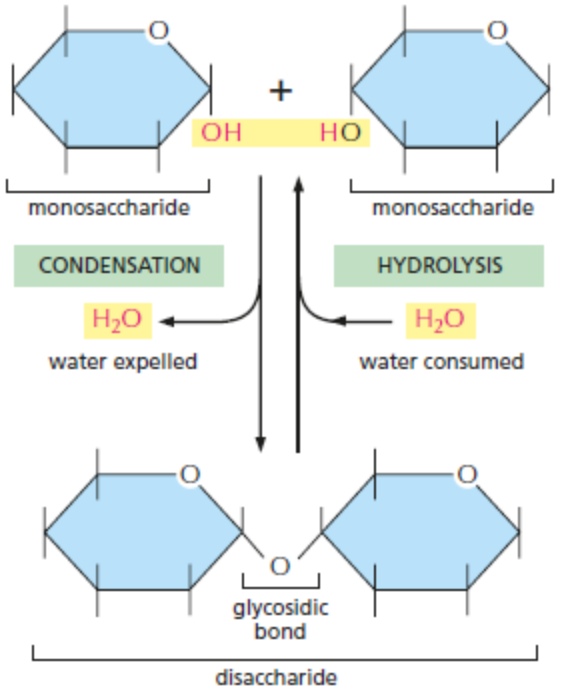
A NUCLEOTIDE



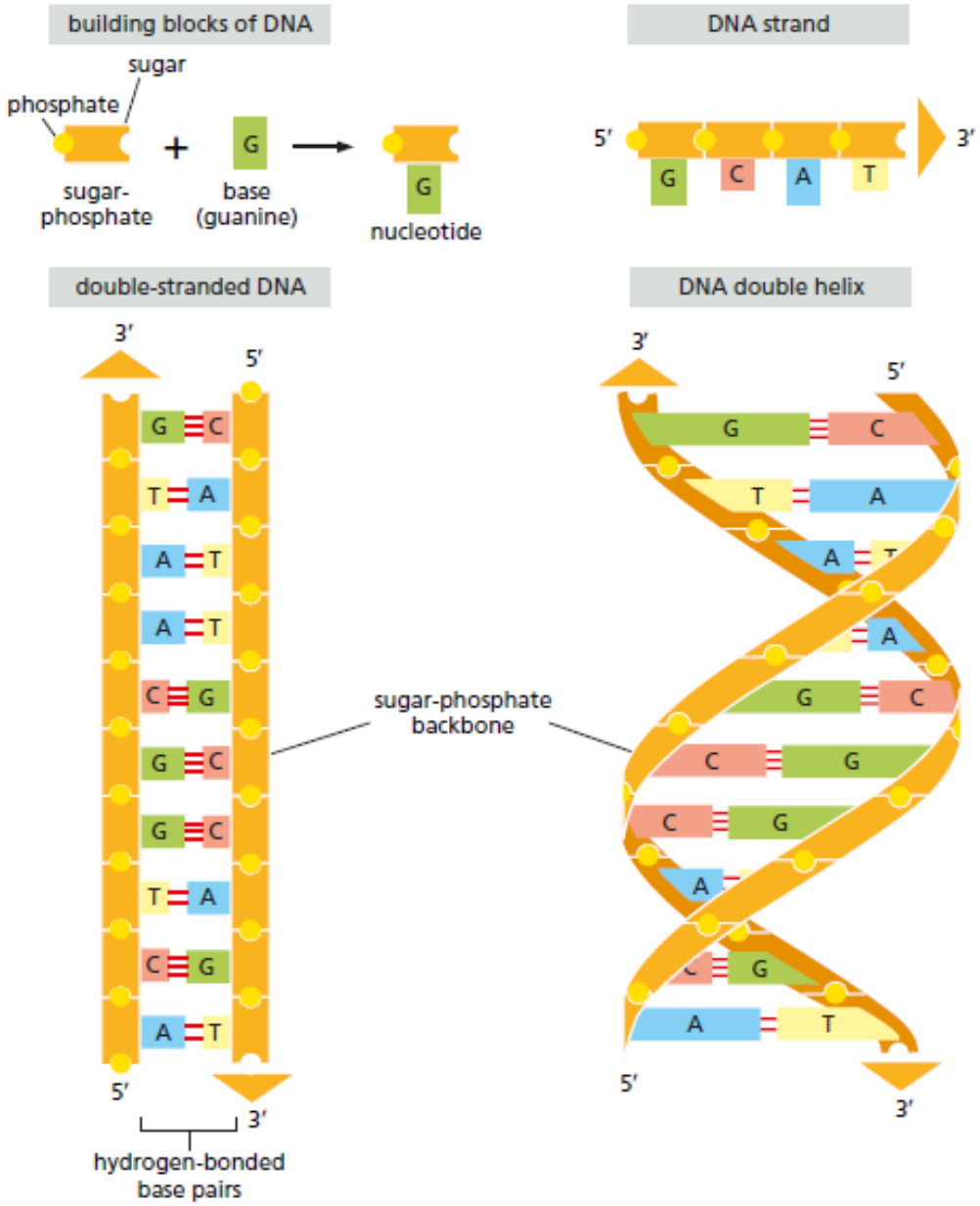


Biochemical bond formation



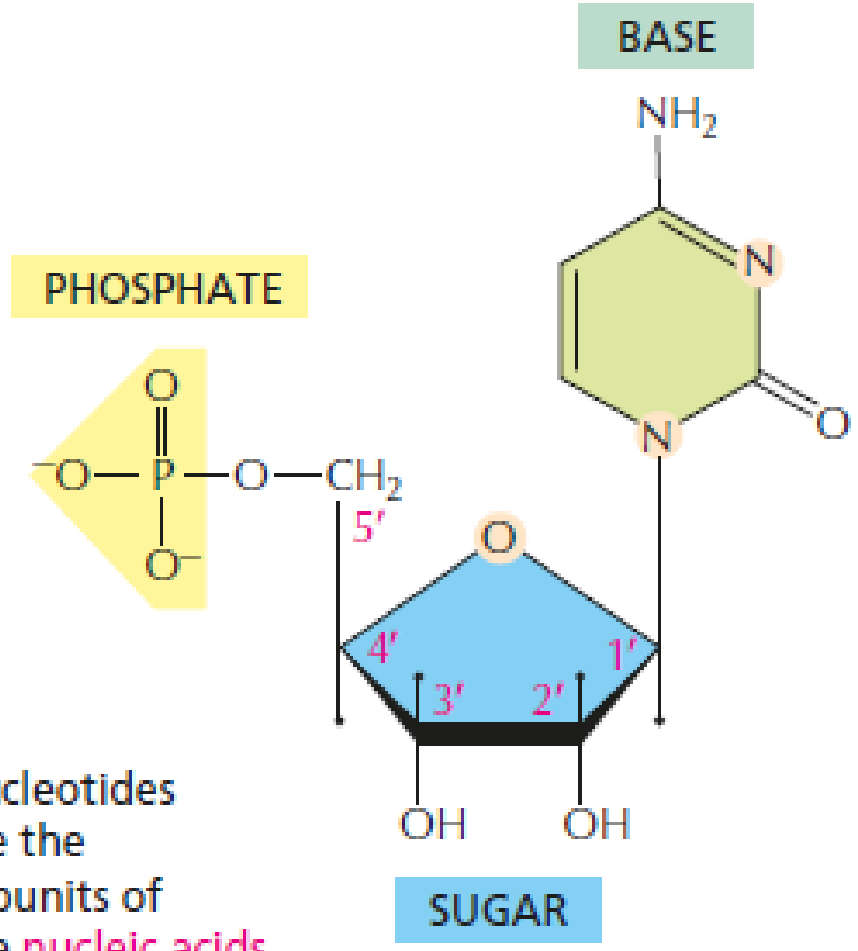


DNA and its building blocks



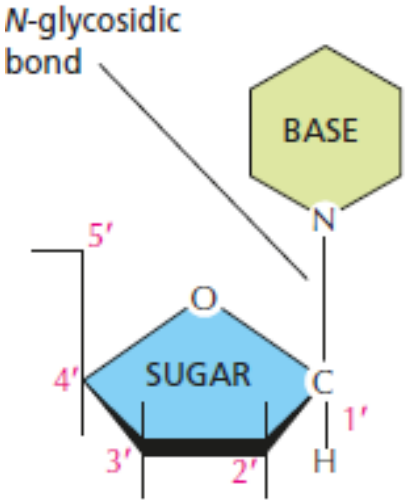
Nucleotides

A nucleotide consists of a nitrogen-containing base, a five-carbon sugar, and one or more phosphate groups.



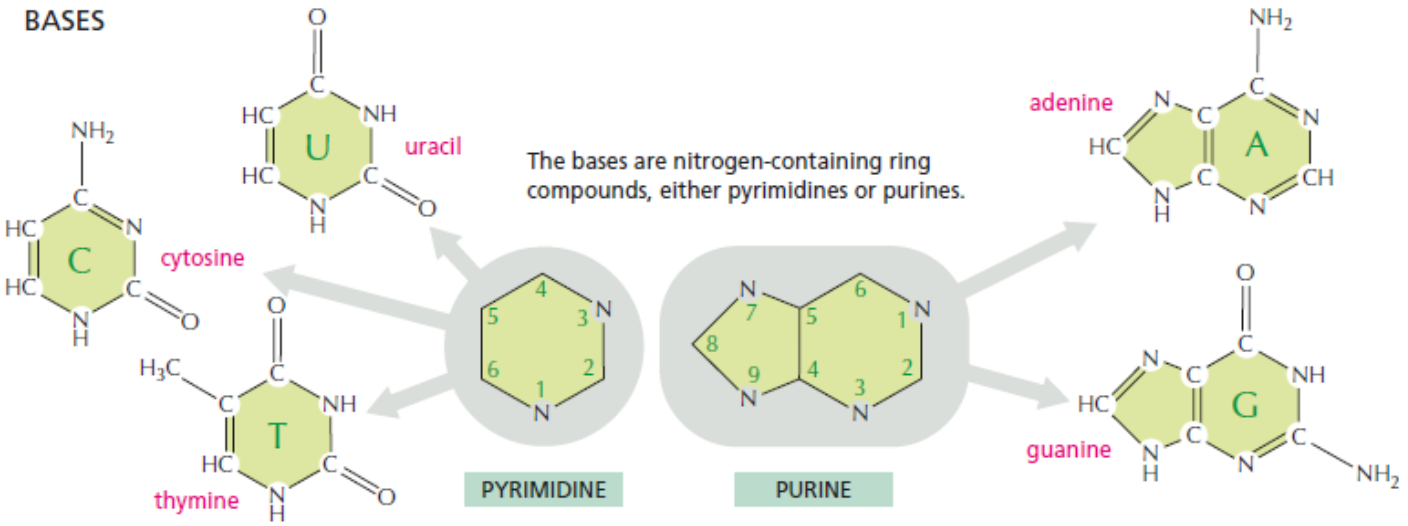
Nucleotides are the subunits of the nucleic acids.

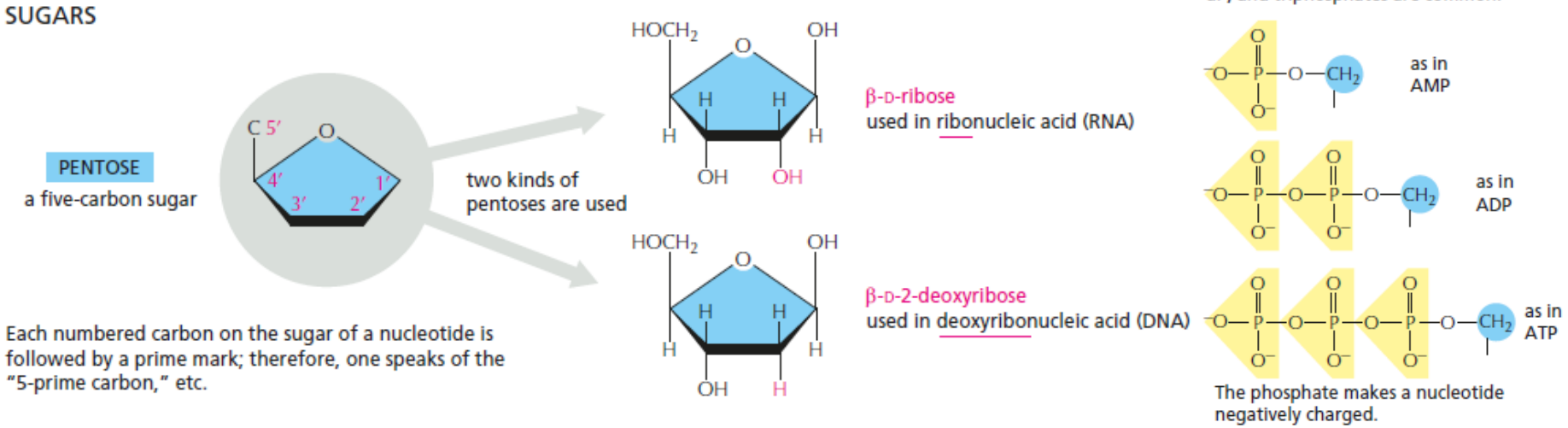
BASE–SUGAR LINKAGE



The base is linked to the same carbon (C1) used in sugar–sugar bonds.

Nucleotides





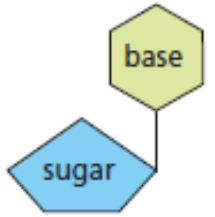
Nucleotides vs Nucleoside

NOMENCLATURE The names can be confusing, but the abbreviations are clear.

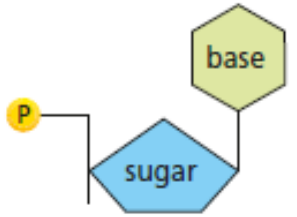
BASE	NUCLEOSIDE	ABBR.
adenine	adenosine	A
guanine	guanosine	G
cytosine	cytidine	C
uracil	uridine	U
thymine	thymidine	T

Nucleotides are abbreviated by three capital letters. Some examples follow:

AMP = adenosine monophosphate
dAMP = deoxyadenosine monophosphate
UDP = uridine diphosphate
ATP = adenosine triphosphate

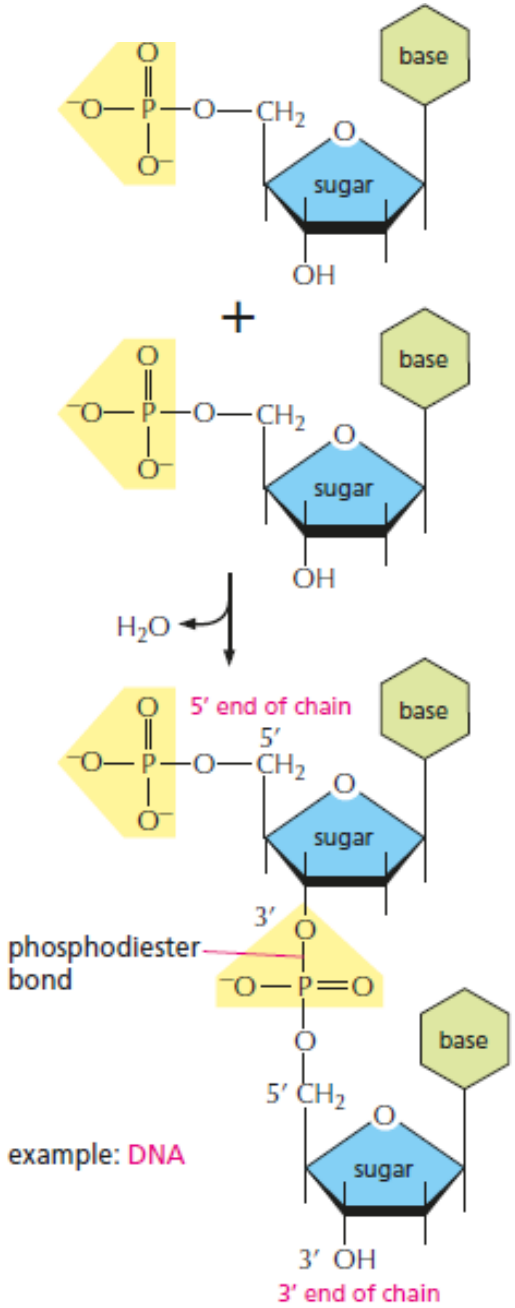


BASE + SUGAR = NUCLEOSIDE



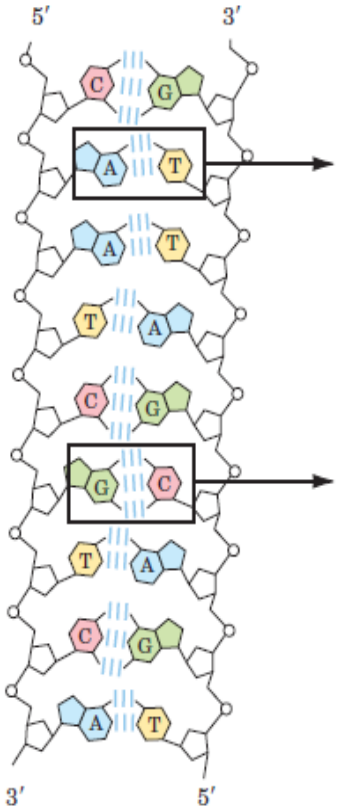
BASE + SUGAR + PHOSPHATE = NUCLEOTIDE

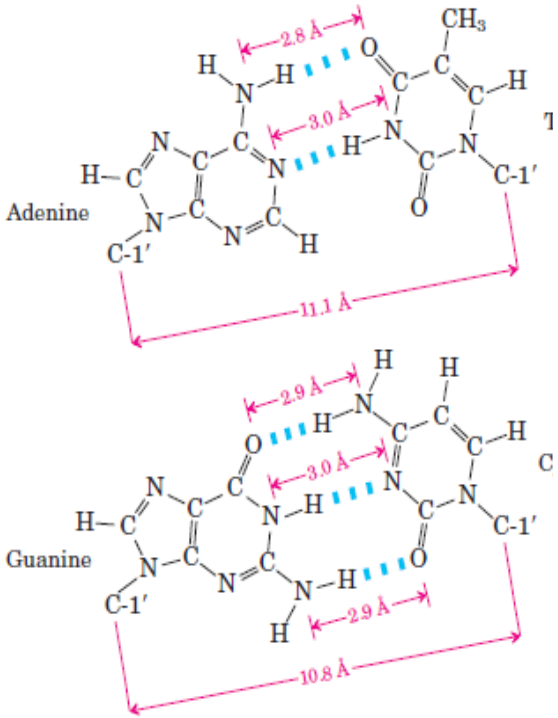
Nucleic Acids

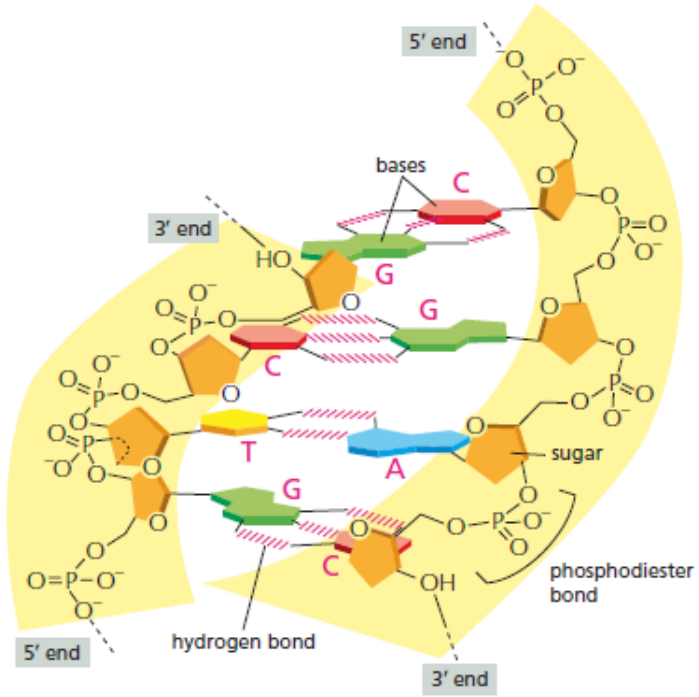


Nucleotides are joined together by phosphodiester bonds between 5’ and 3’ carbon atoms of the sugar ring, via a phosphate group, to form nucleic acids. The linear sequence of nucleotides in a nucleic acid chain is commonly abbreviated by a one-letter code, such as AGCTTACA, with the 5’ end of the chain at the left.

Hydrogen-Bonding Patterns



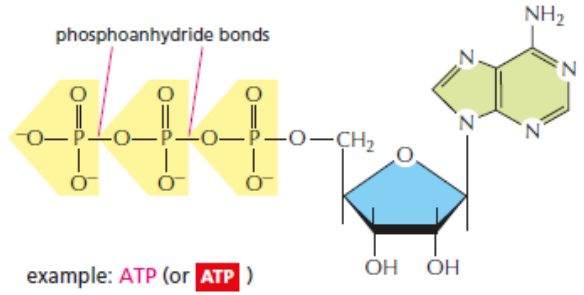




Nucleotides

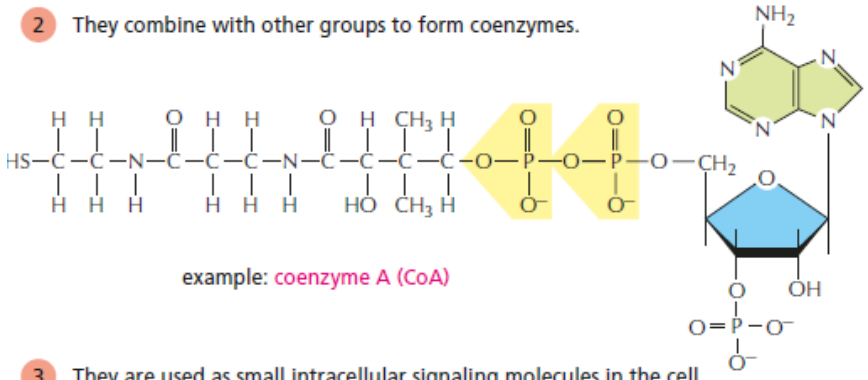
NUCLEOTIDES HAVE MANY OTHER FUNCTIONS

1 They carry chemical energy in their easily hydrolyzed phosphoanhydride bonds.



example: ATP (or ATP)

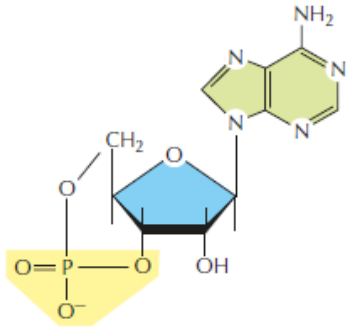
2 They combine with other groups to form coenzymes.



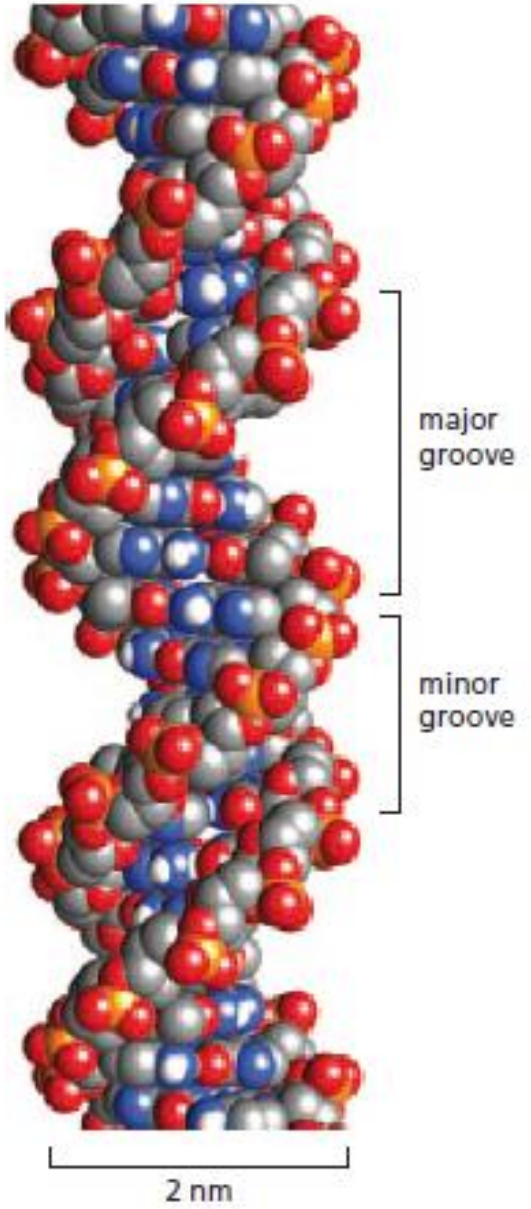
example: coenzyme A (CoA)

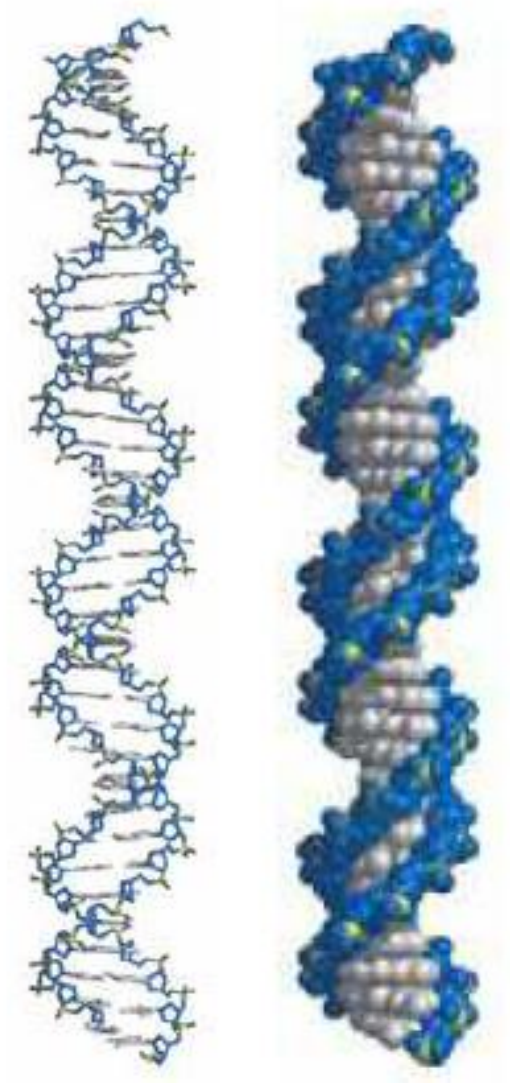
3 They are used as small intracellular signaling molecules in the cell.

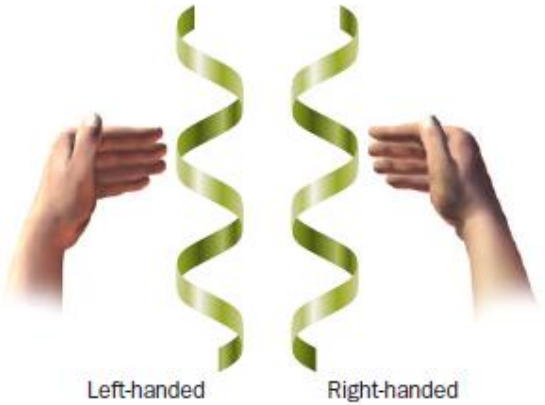
example: cyclic AMP



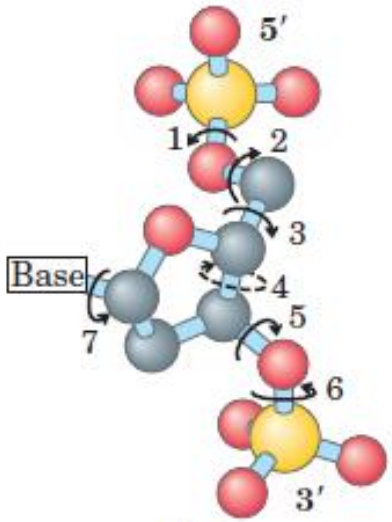
Structure of DNA

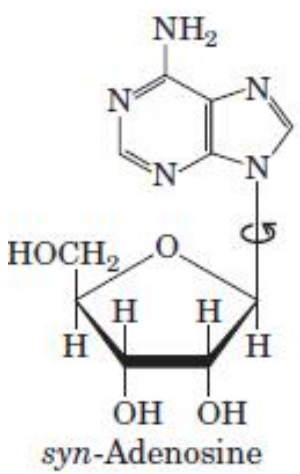




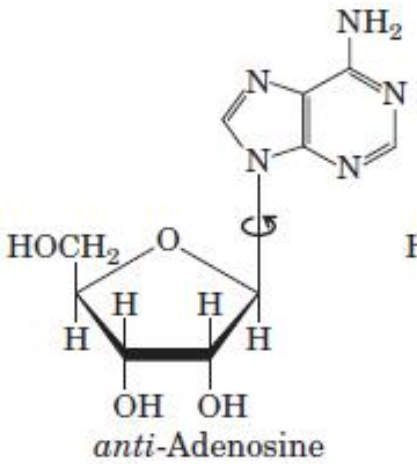


Structural variation in DNA

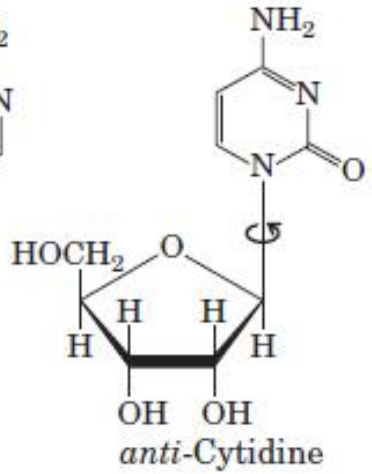




syn-Adenosine

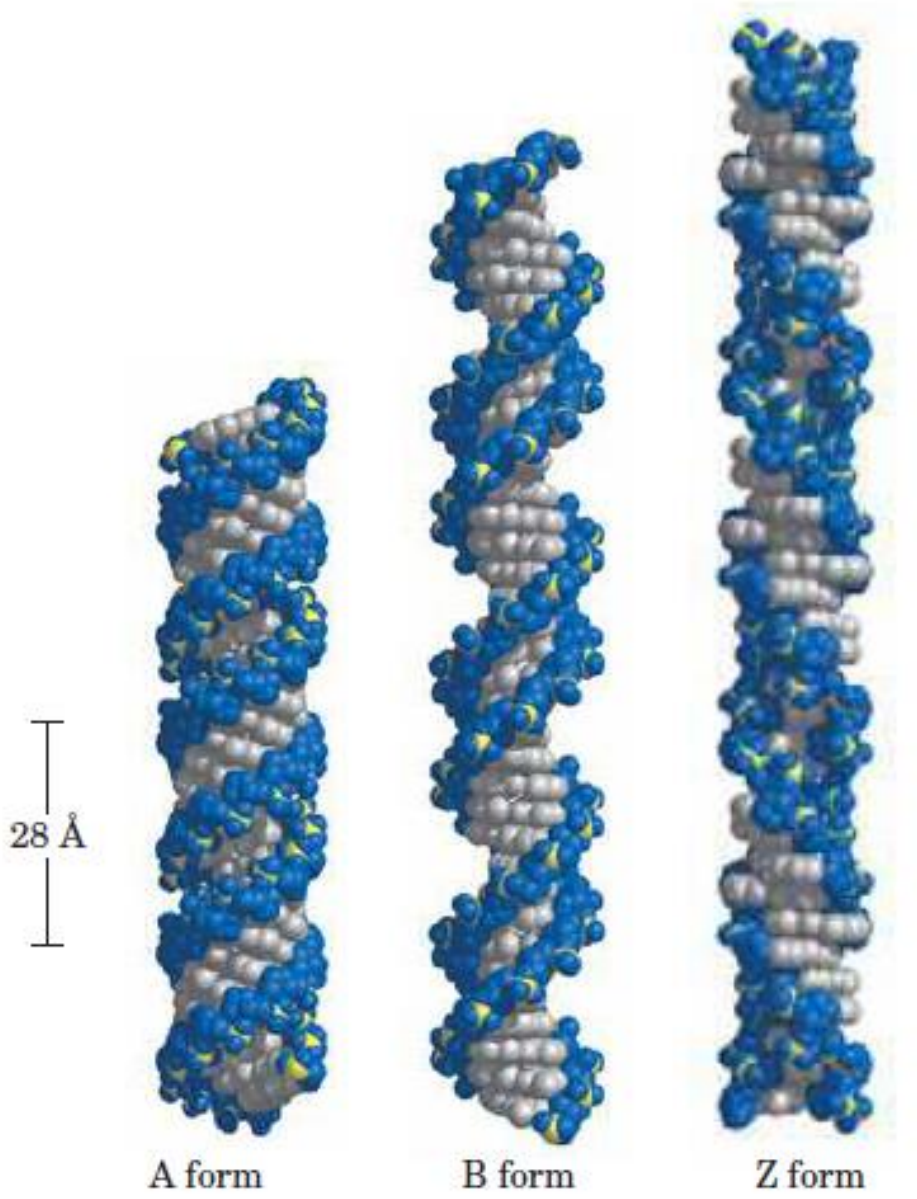


anti-Adenosine



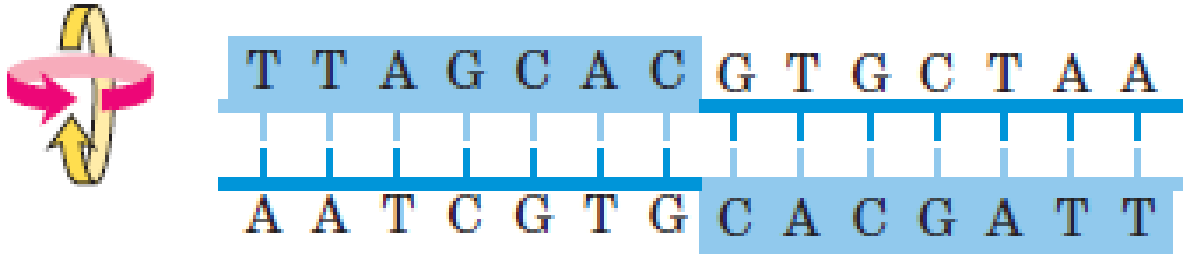
anti-Cytidine

Structural variation in DNA

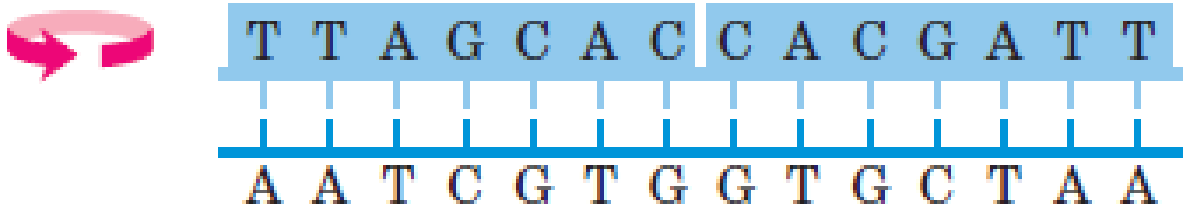


Certain DNA Sequences Adopt Unusual Structures

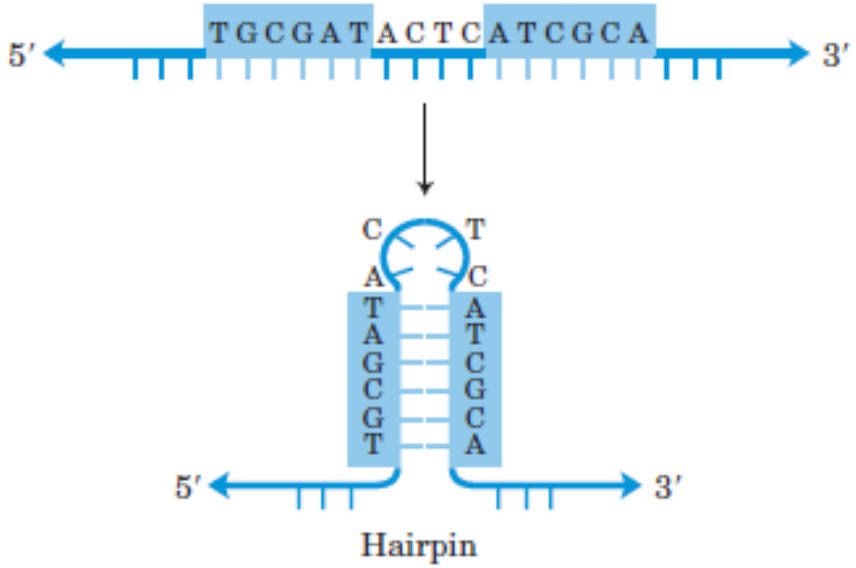
Palindrome



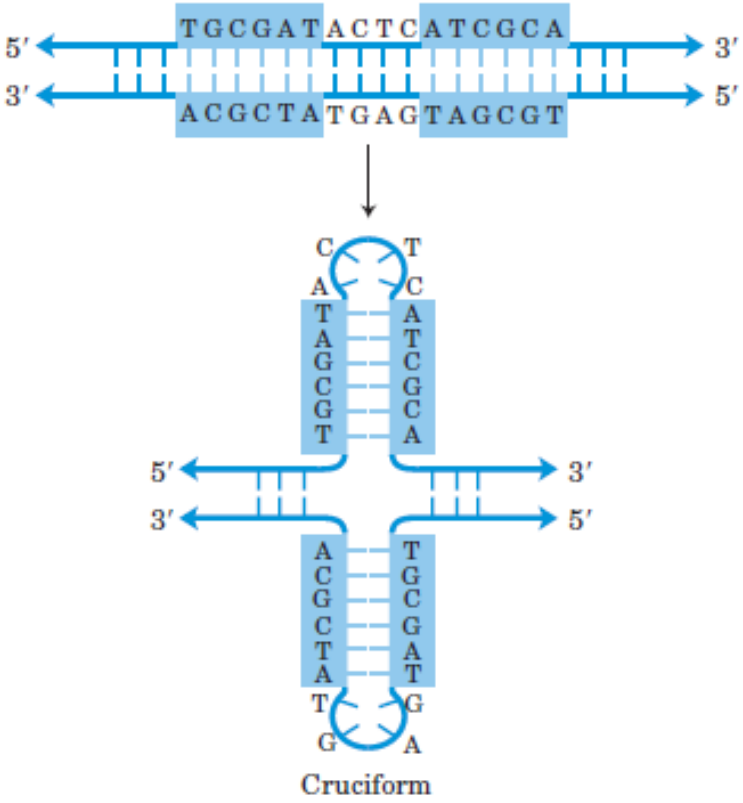
Mirror repeat



Hairpins and cruciforms

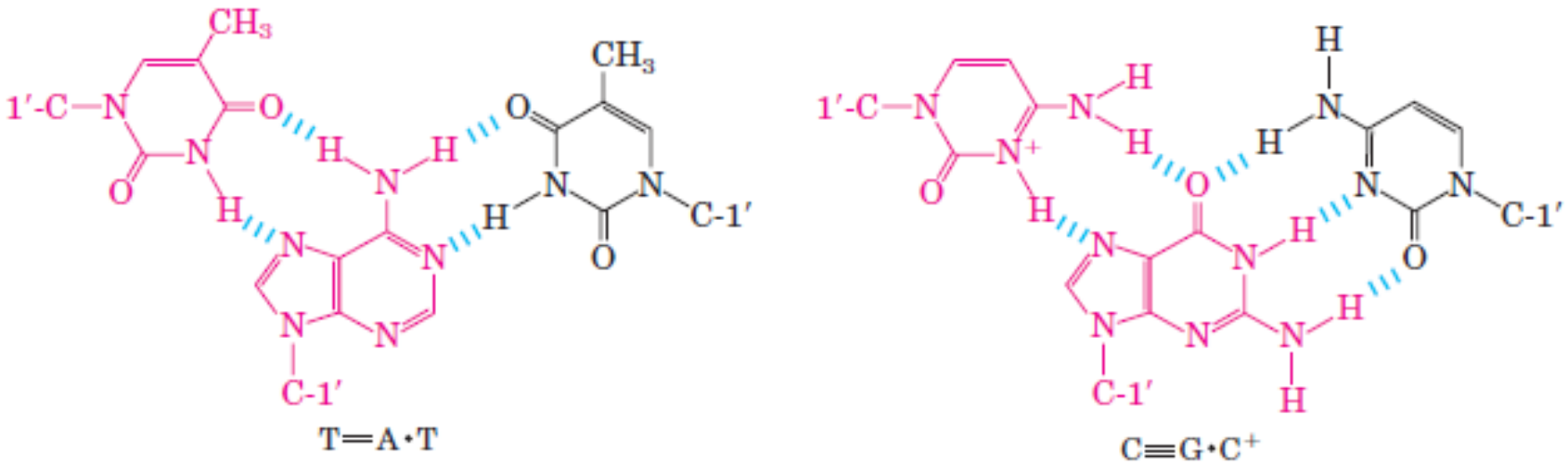


Hairpin

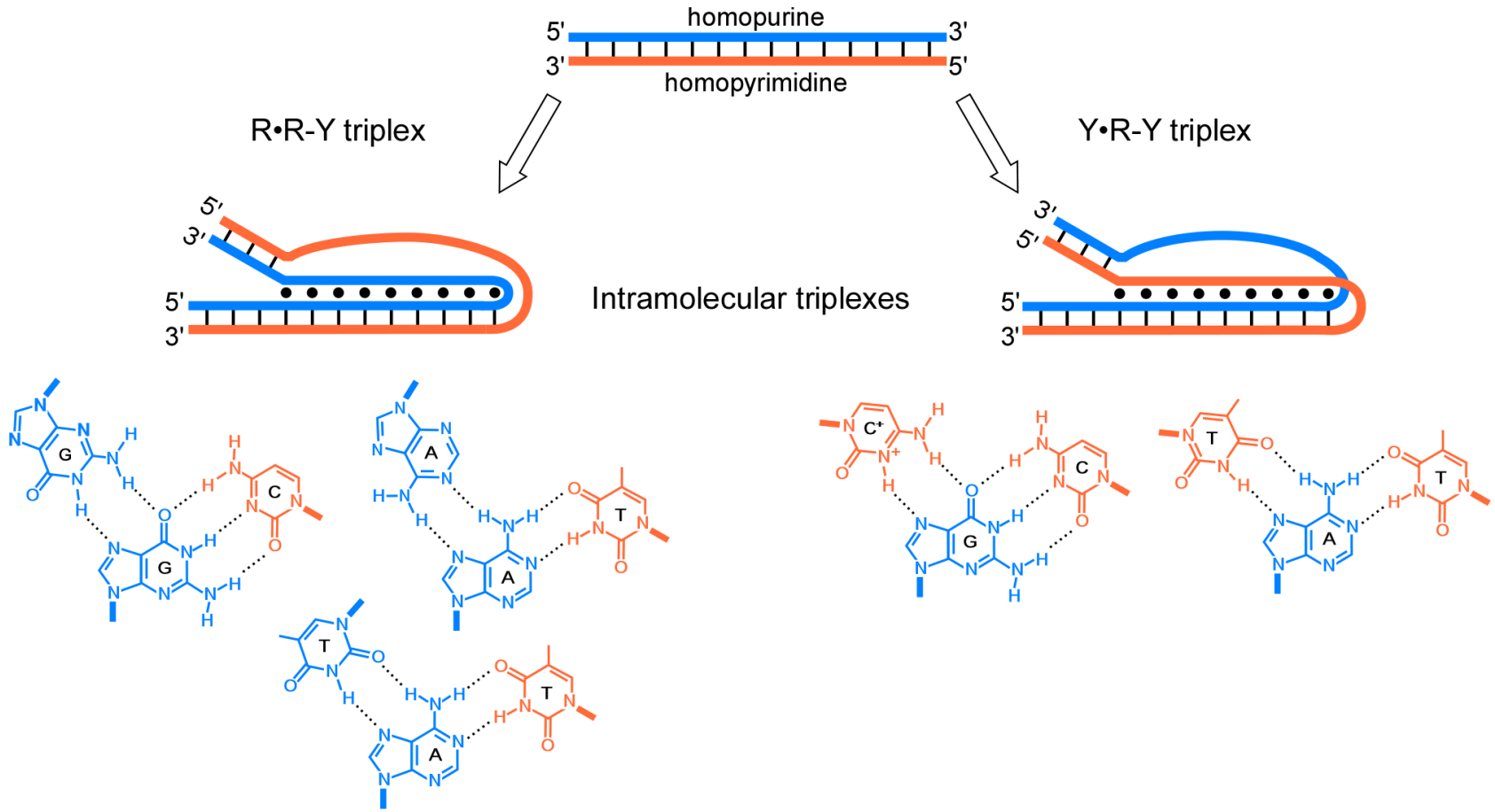


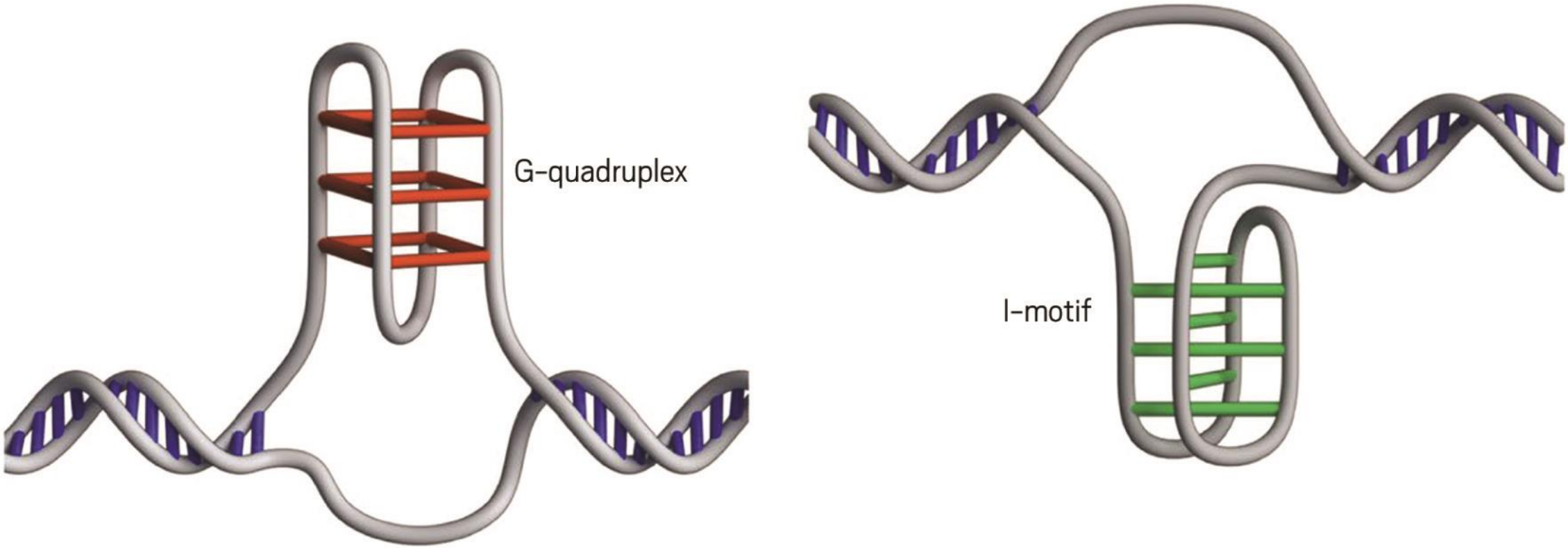
Cruciform

Several unusual DNA structures involve three or even four DNA strands

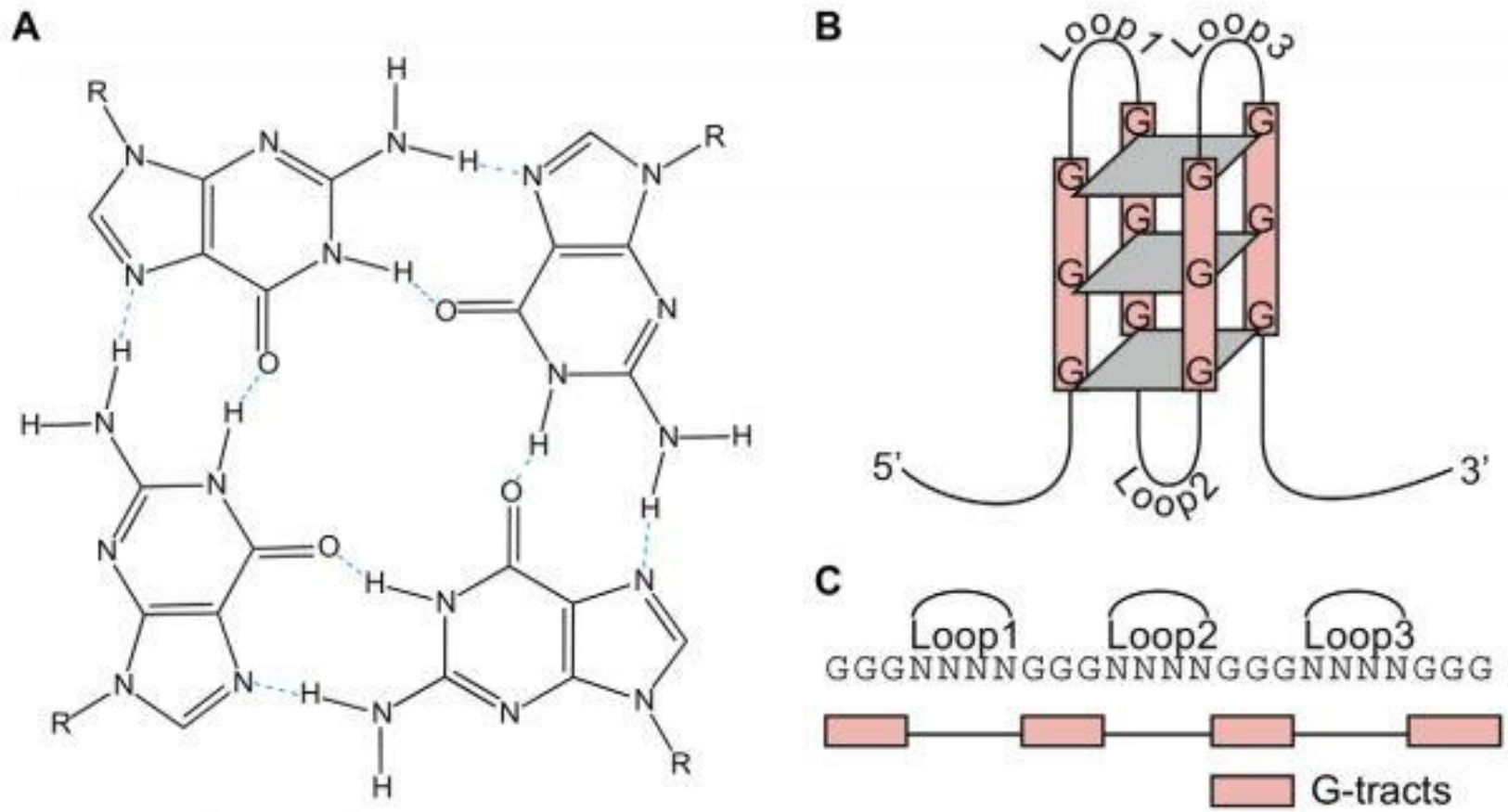


The atoms that participate in the hydrogen bonding of **triplex DNA**, are often referred to as **Hoogsteen positions**, and the non-Watson-Crick pairing is called **Hoogsteen pairing**, after Karst Hoogsteen, who in 1963 first recognized the potential for these unusual pairings

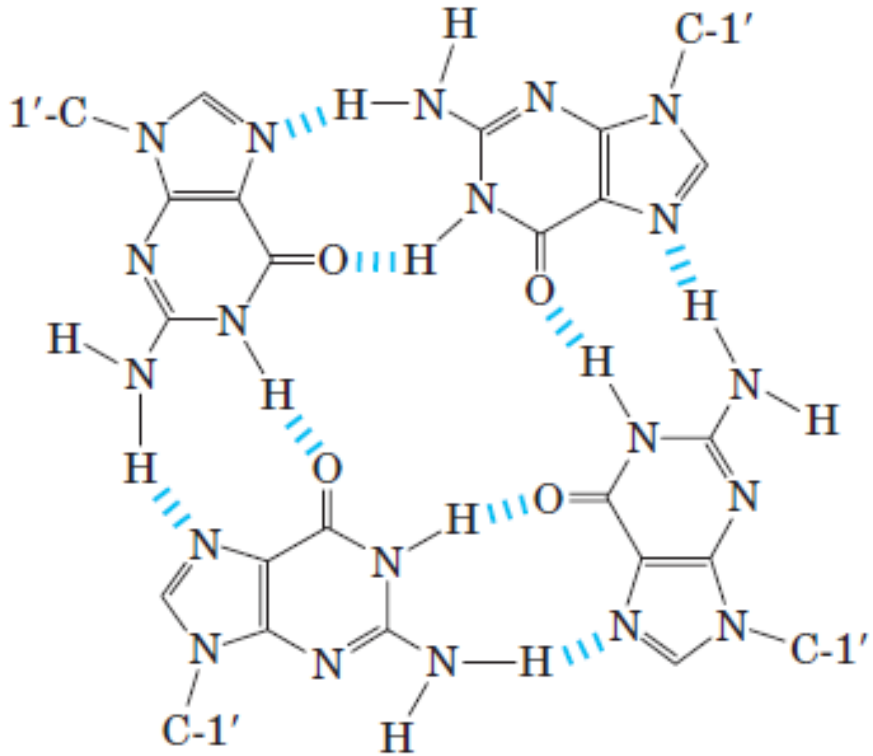

homopurine
5'
3'
3'
5'
homopyrimidine
R•R-Y triplex
Y•R-Y triplex
5'
3'
5'
3'
Intramolecular triplexes
3'
5'
5'
3'
G
C
G
A
T
A
T
C+
G
C
T
A
T

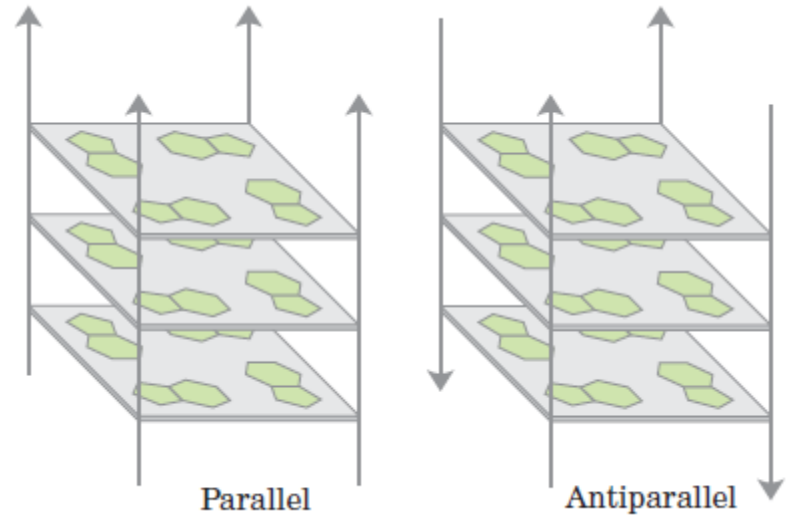

G-quadruplex
I-motif

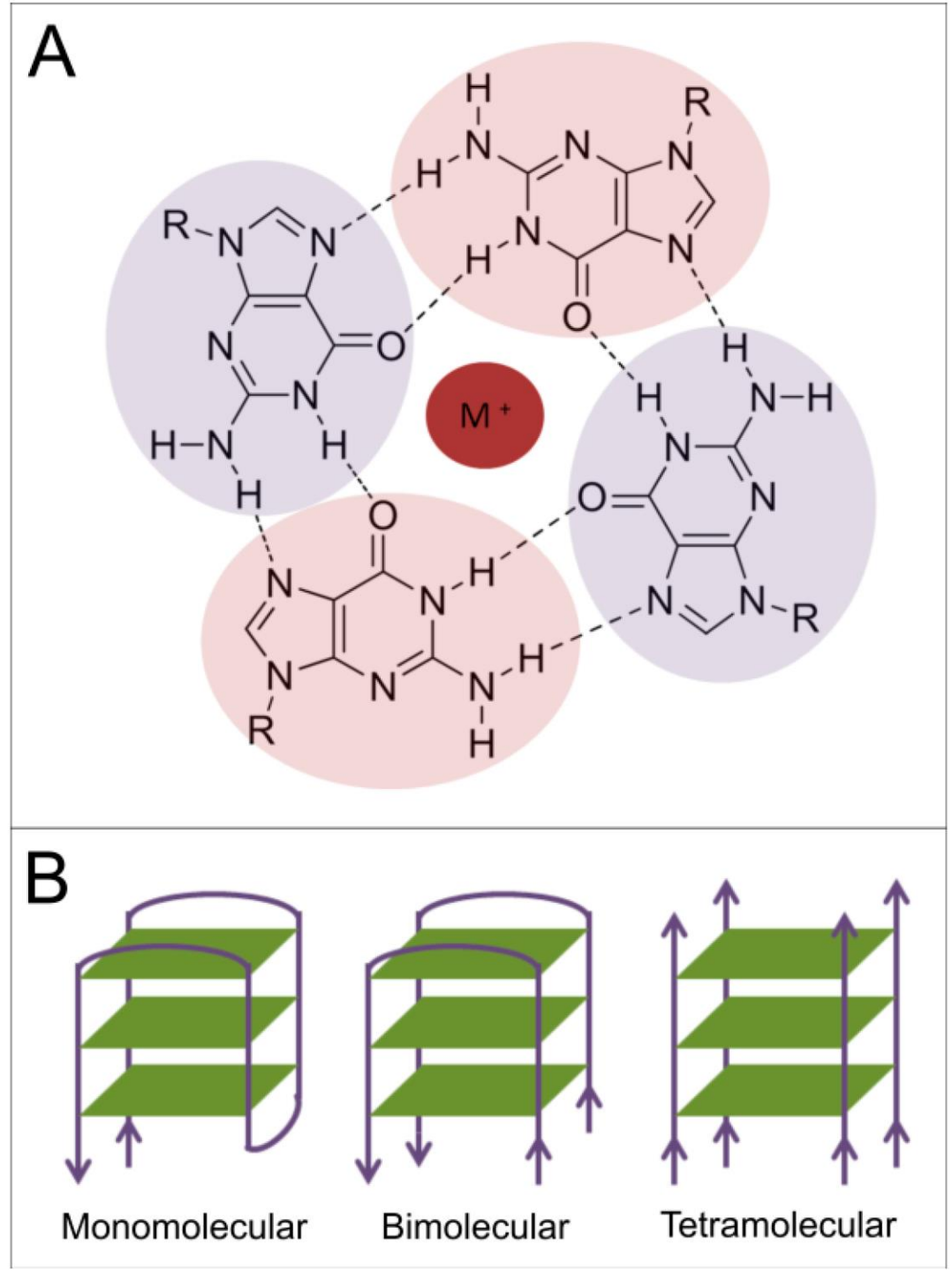
G-quadruplexes

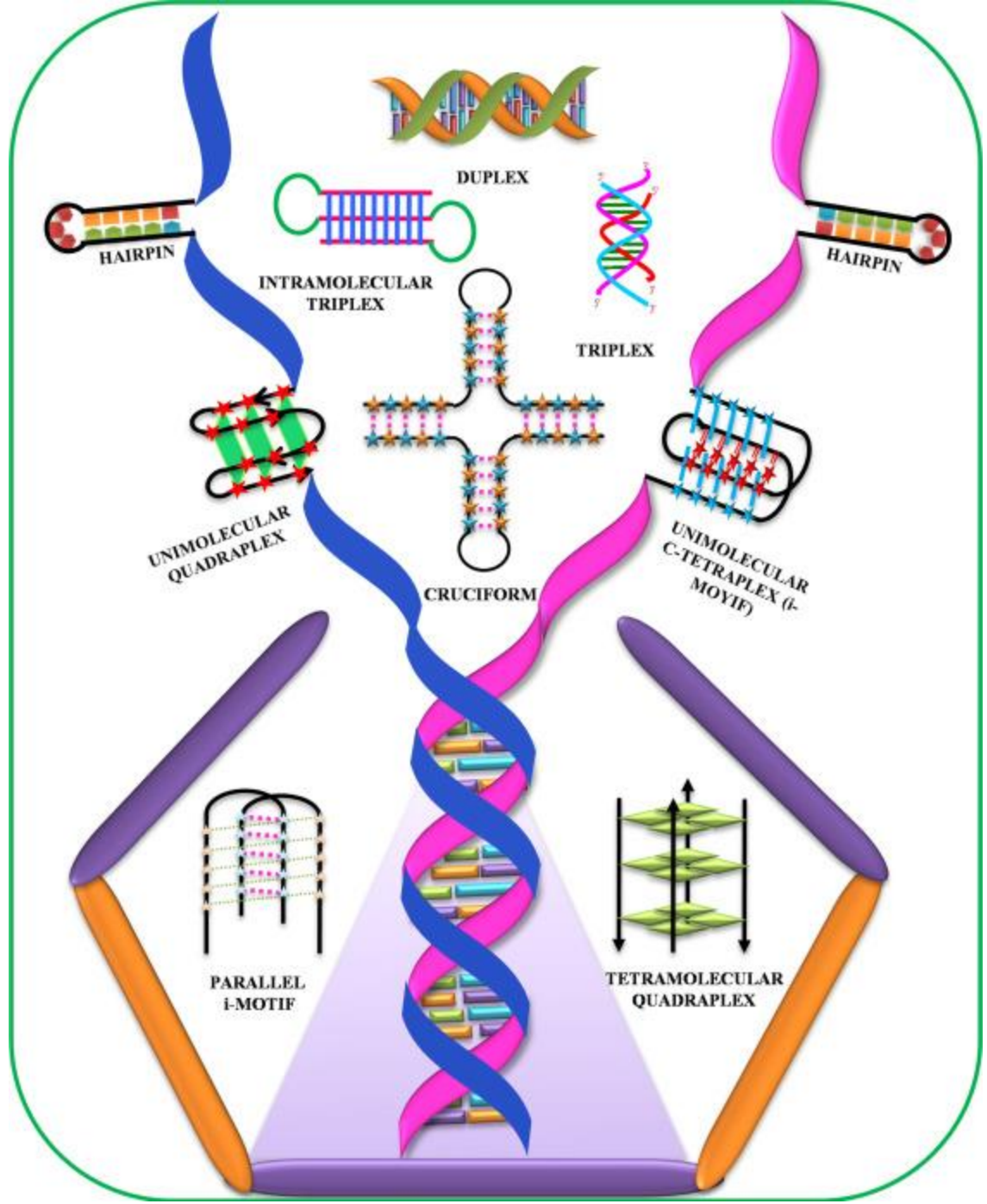


G-quadruplexes






A
B
M+
Monomolecular
Bimolecular
Tetramolecular

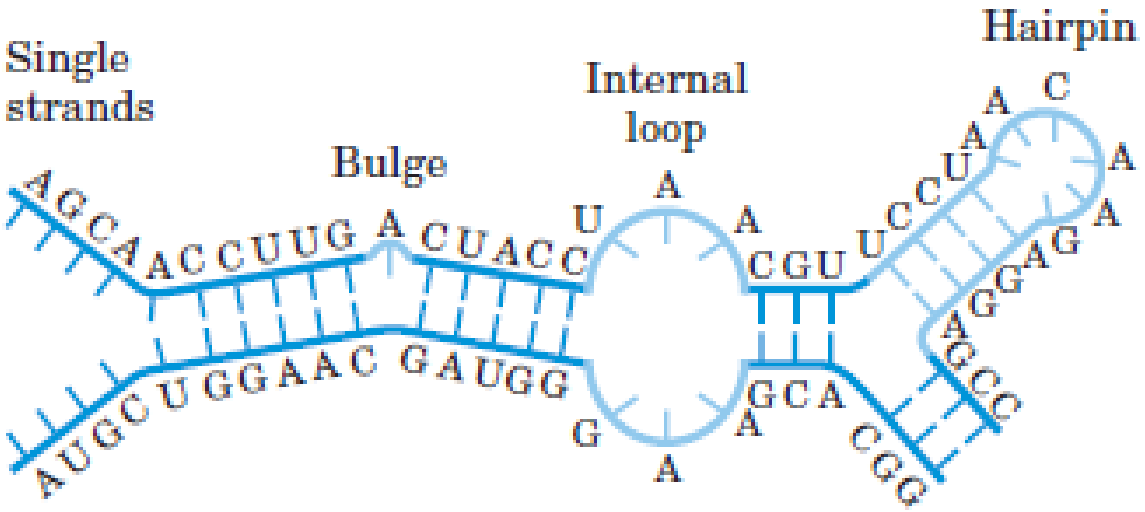


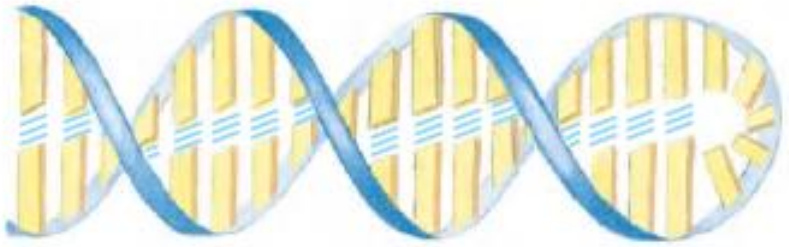
Intramolecular

Vs

Intermolecular

Structure of RNA





Hairpin double helix

The paired regions generally have an A-form right-handed helix, as shown for a hairpin