Chemistry and Functions of Nucleotides

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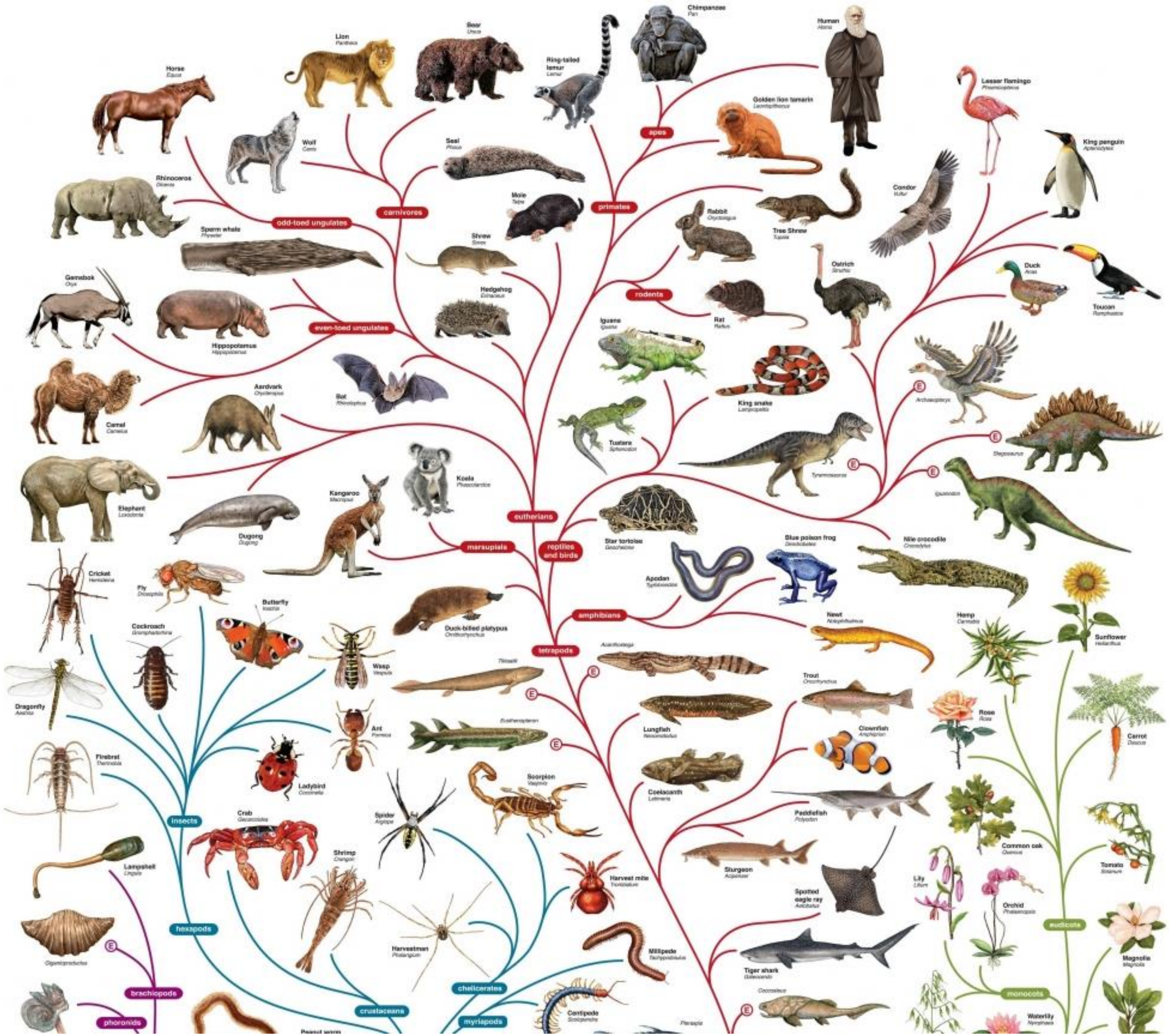
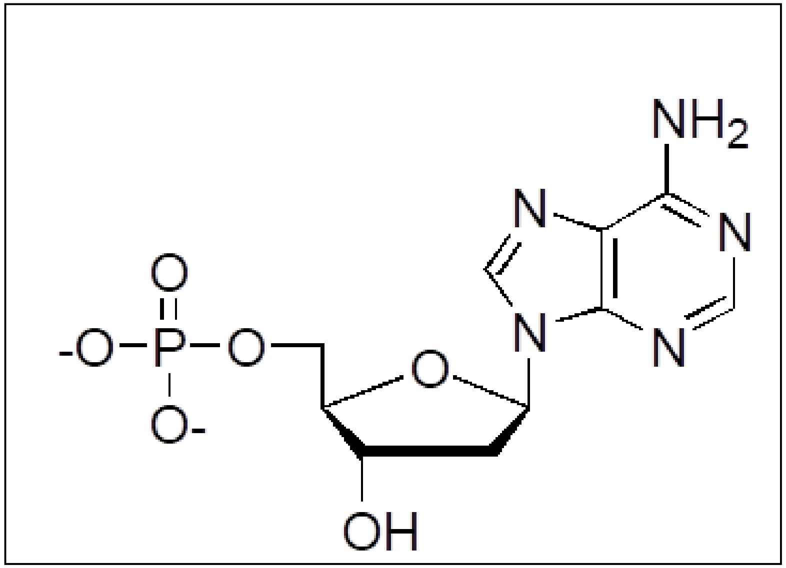

Chimpanzee
Human
Bear
Lion
Horse
Ring-tailed lemur
Golden lion tamarin
Lesser flamingo
King penguin
apes
Wolf
Seal
Rhinoceros
Mole
primates
carnivores
odd-toed ungulates
Sperm whale
Shrew
Rabbit
Tree Shrew
Condor
Duck
Toucan
Ostrich
Gemsbok
Hedgehog
rodents
Rat
Iguana
even-toed ungulates
Hippopotamus
Camel
Aardvark
Bat
King snake
Archaeopteryx
Tuatara
Elephant
Koala
Kangaroo
Dugong
Stegosaurus
Tyrannosaurus
Iguanodon
eutherians
marsupials
reptiles and birds
Star tortoise
Blue poison frog
Nile crocodile
Cricket
Fly
Apodan
Butterfly
Duck-billed platypus
amphibians
Newt
Hemp
Sunflower
Cockroach
Wasp
tetrapods
Acanthostega
Tiktaalik
Trout
Dragonfly
Ant
Eusthenopteron
Lungfish
Rose
Clownfish
Carrot
Firebrat
Ladybird
Scorpion
Coelacanth
Paddlefish
Crab
Spider
insects
Common oak
Shrimp
Harvest mite
Sturgeon
Tomato
Lampshell
Lily
Spotted eagle ray
Orchid
hexapods
Harvestman
Millipede
eudicots
Magnolia
Tiger shark
brachiopods
chelicerates
crustaceans
monocots
Centipede
Waterlily
phoronids
myriapods
Peanut worm

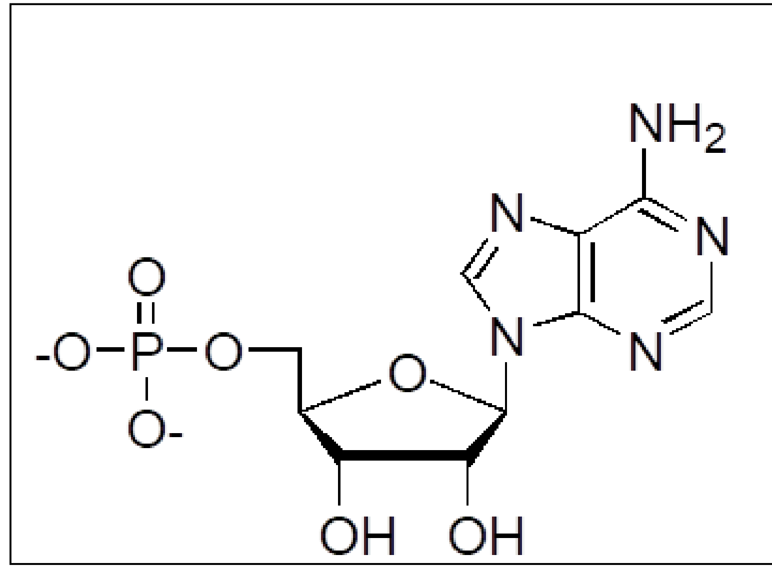
Objectives

After learning this topic, you will be able to:

- define the composition and derivatives of nucleotides.
- state functions of nucleotides.
- differentiate the basic unit of DNA and RNA
- define the properties and functions of DNA and RNA.

Building block of nucleic acids





A

B

Phosphoric acid

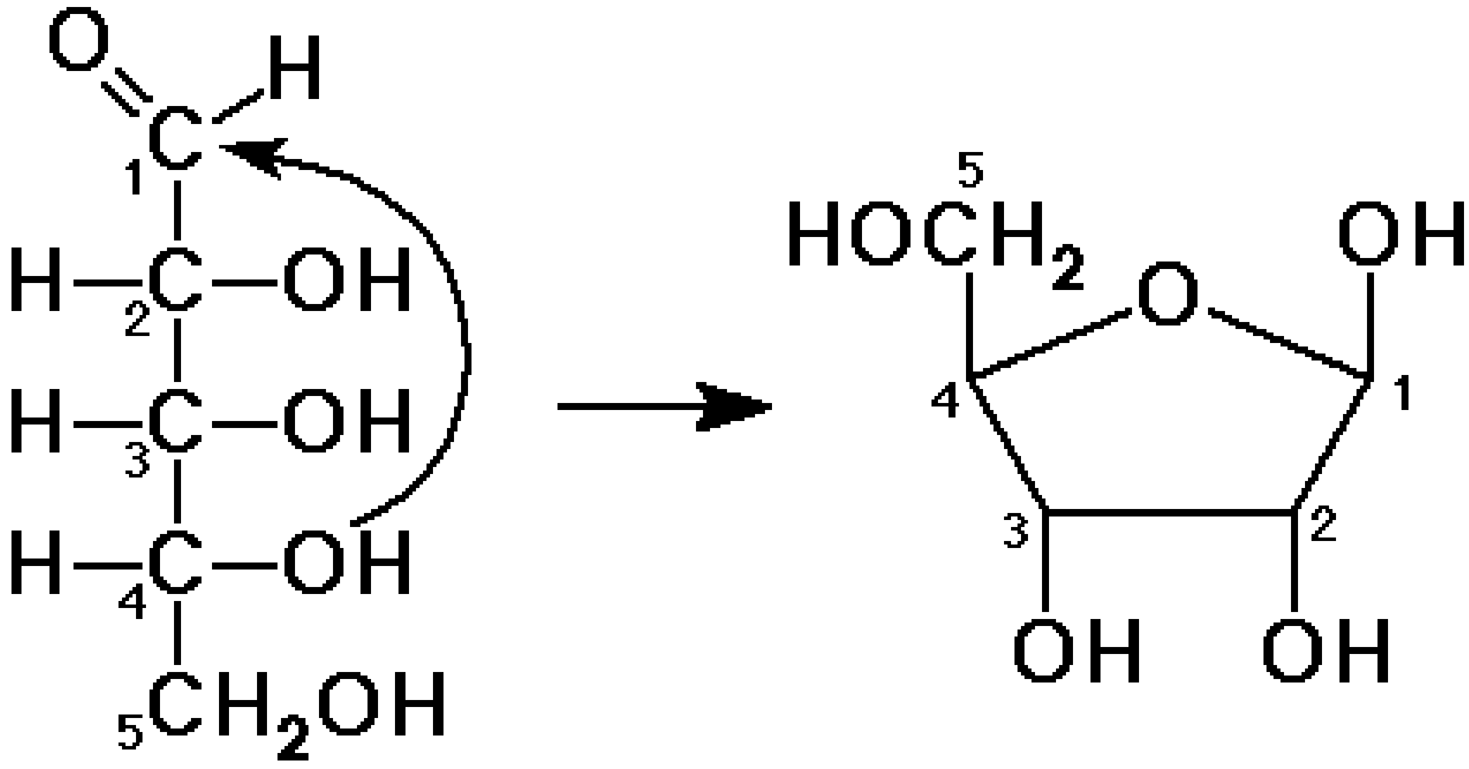
$H_3PO_4 \rightarrow H_2PO_4^{-} \rightarrow HPO_4^{2-} \rightarrow PO_4^{3-}$

$pK_{a1} = 1.9$

$pK_{a2} = 6.8$

$pK_{a3} = 12.4$

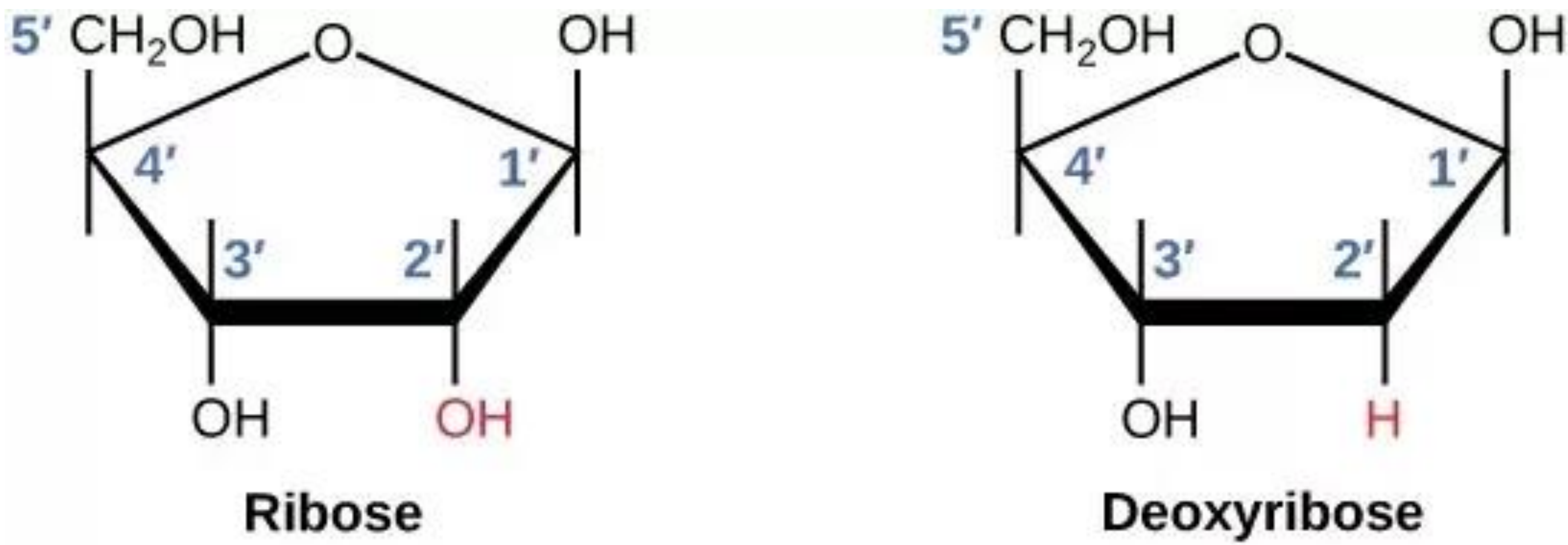
Pentose Sugar



D-ribose

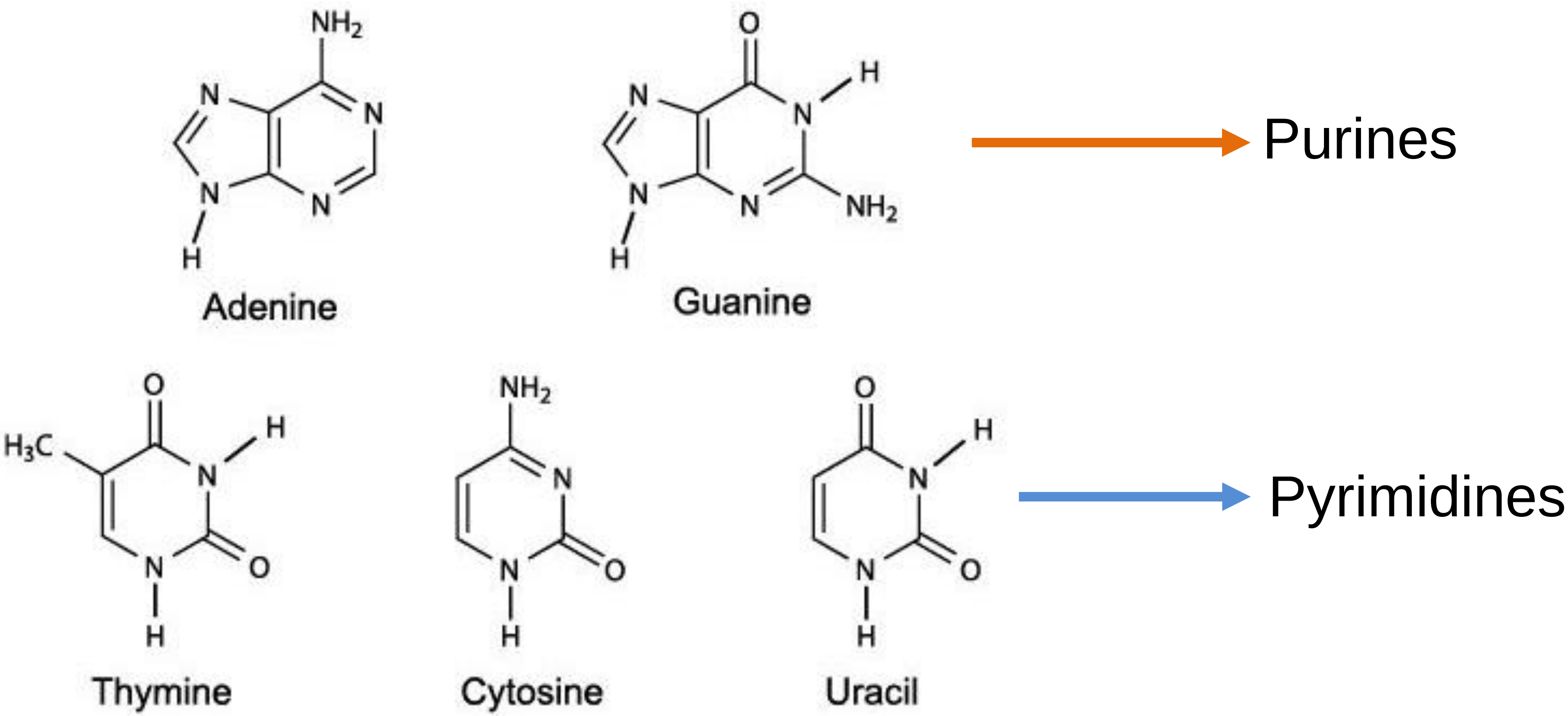
β-D-ribofuranose

Pentose Sugar



Type of pentose sugar defines the type of nucleic acid.

Nitrogenous bases



A, T, C, G in DNA

A, U, C, G, in RNA.

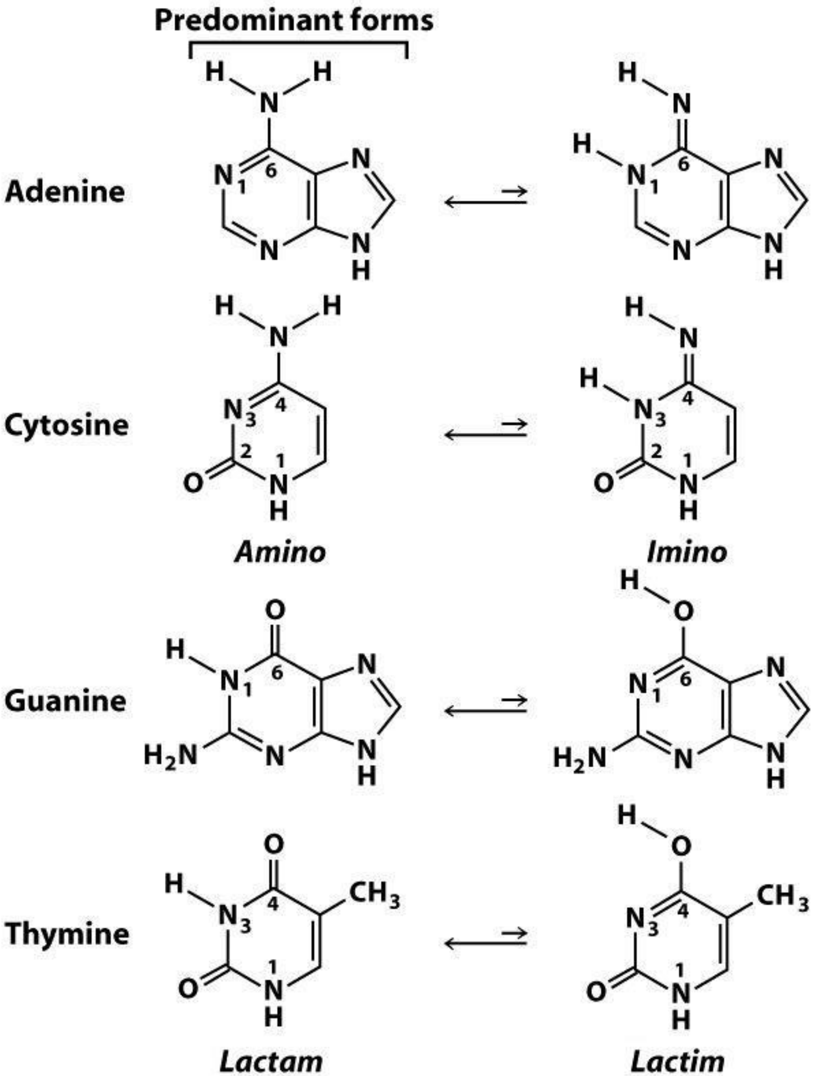
Nitrogenous bases and their properties

1. Tautomerization
2. Acid-base
3. Light absorption

Nitrogenous bases and their properties

1. Tautomerization

Tautomers are isomers of a compound which are **different** only in the position of the **protons** and **electrons**.

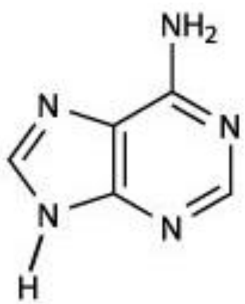


Nitrogenous bases and their properties

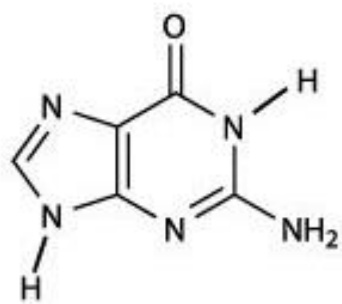
2. Acid-Base (weak)

Base: Nitrogen (N: in the ring) and Oxygen (:O:)

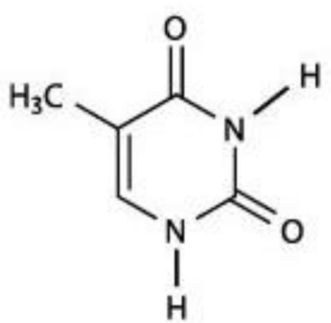
Acid: $-NH_2$, $=NH$,



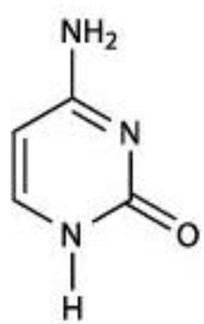
Adenine



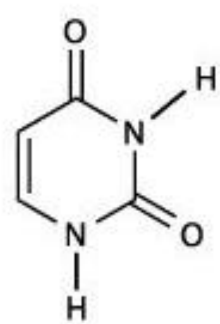
Guanine



Thymine



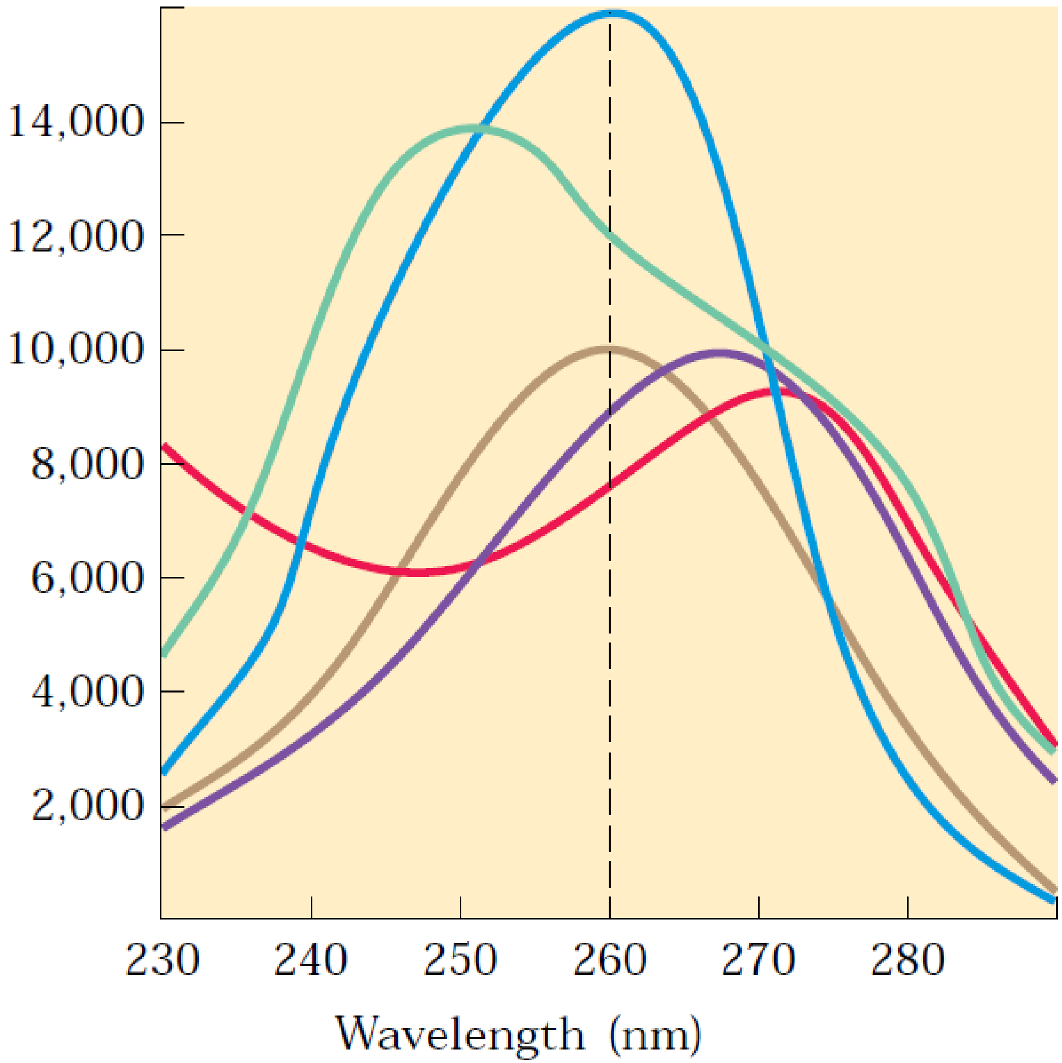
Cytosine



Uracil

Nitrogenous bases and their properties

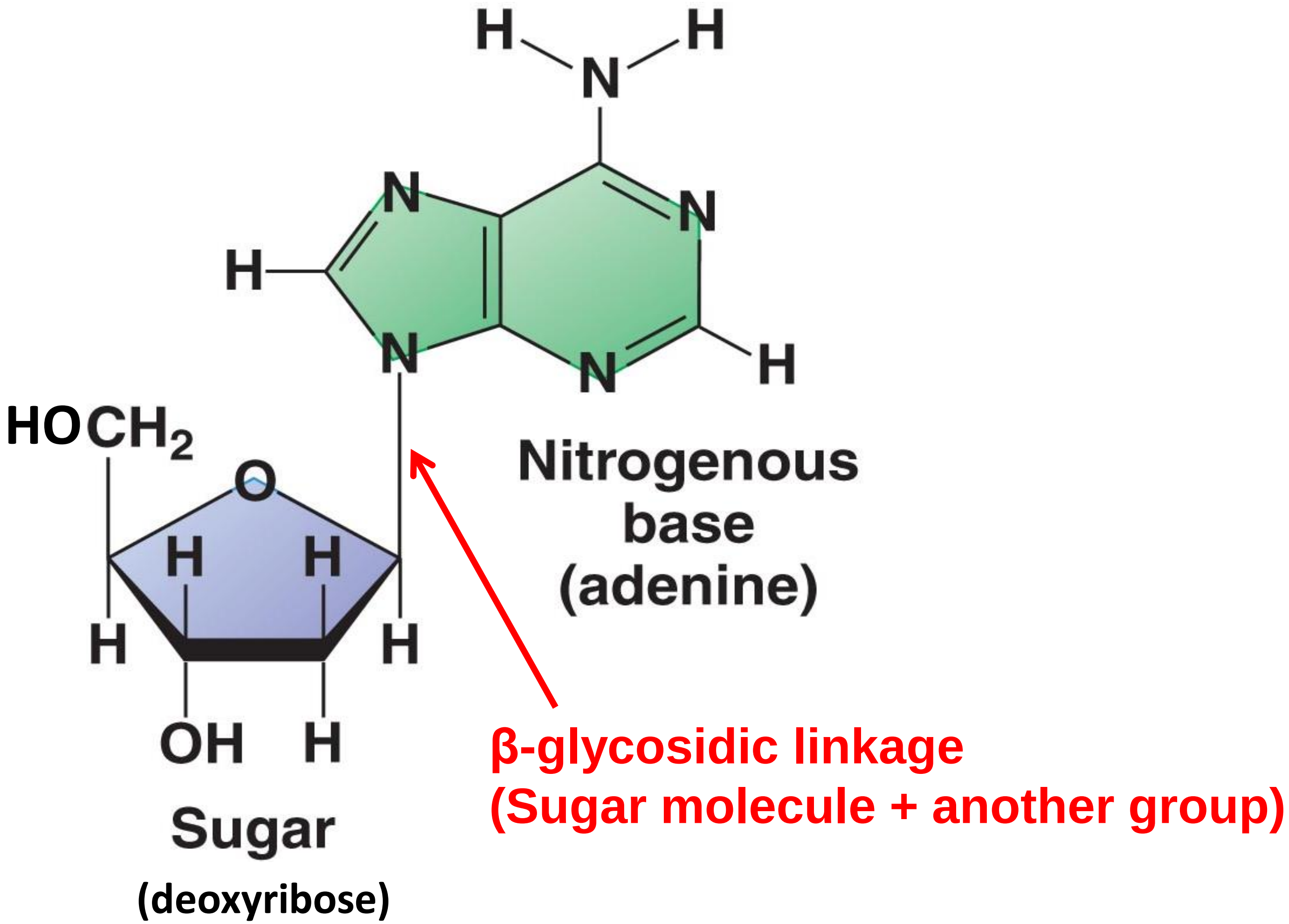
3. Light Absorption



Molar extinction coefficient at 260 nm, ϵ_{260} ($M^{-1}cm^{-1}$)	
AMP	15,400
GMP	11,700
UMP	9,900
dTMP	9,200
CMP	7,500

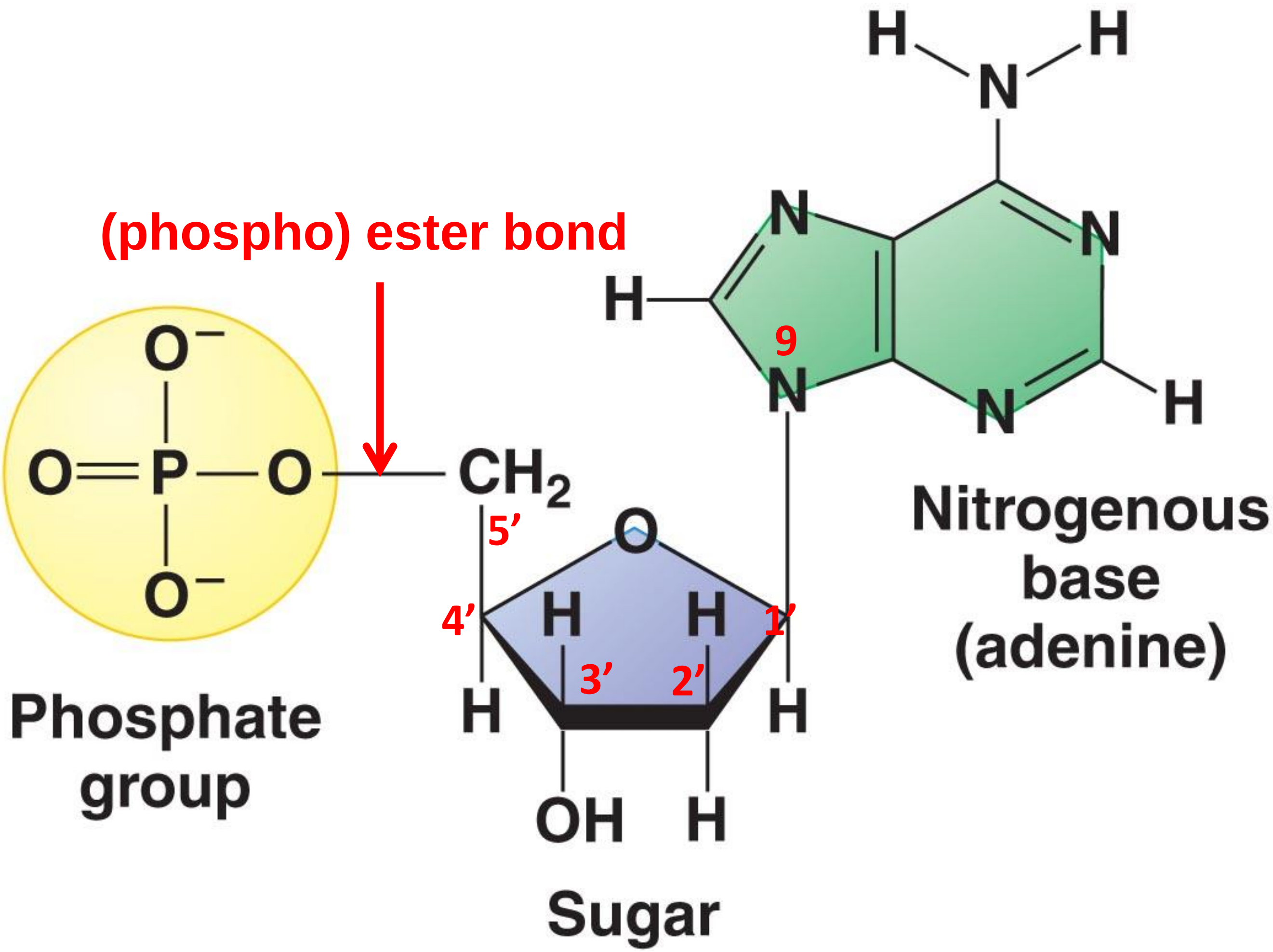
Source: Lehninger Principles of Biochemistry

Nucleoside



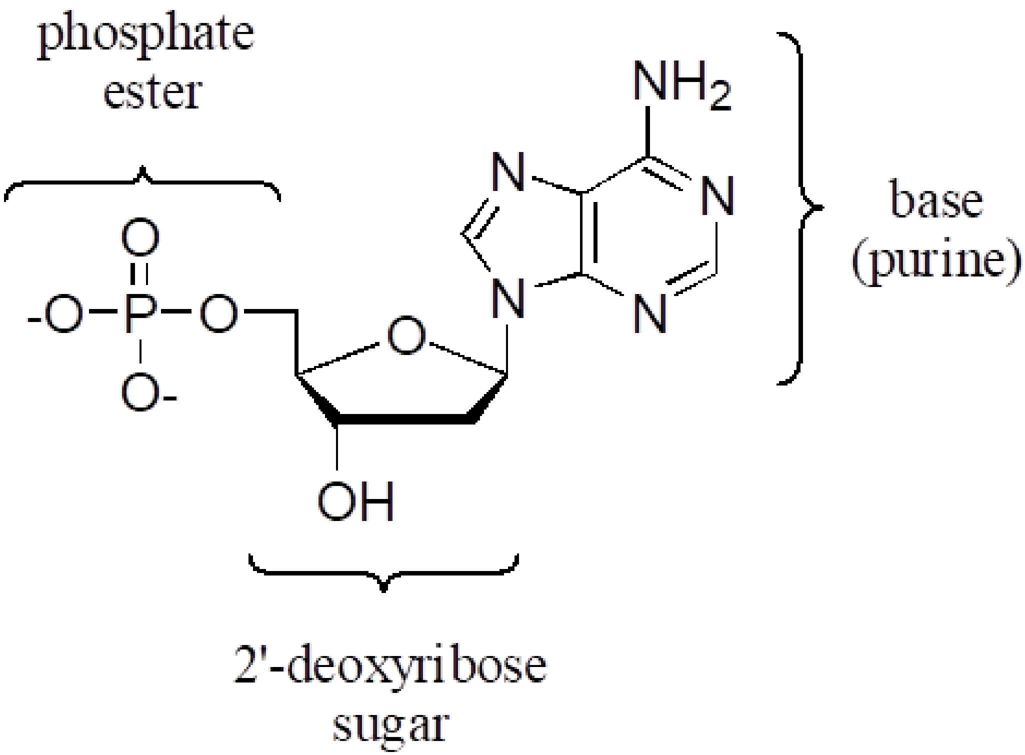
Nucleoside = Sugar + Nitrogenous Base

Nucleotide

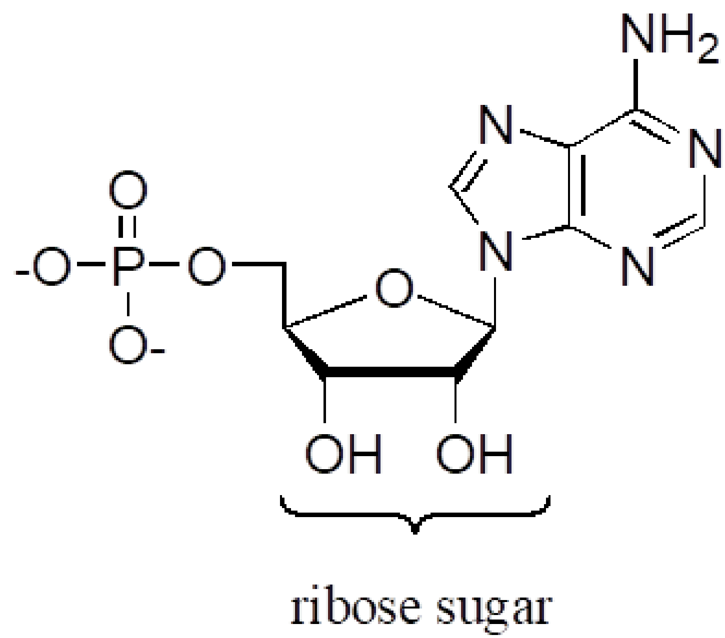


Nucleotide = Phosphate + Nucleoside

2'-deoxynucleotide 5'-phosphate (DNA form)

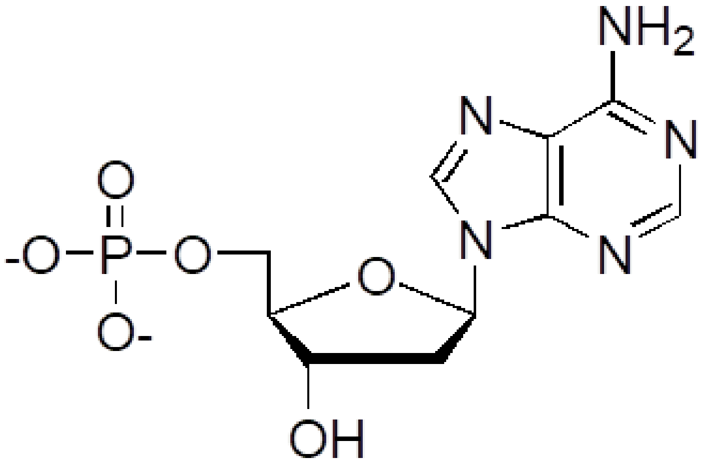


nucleotide 5'-phosphate (RNA form)

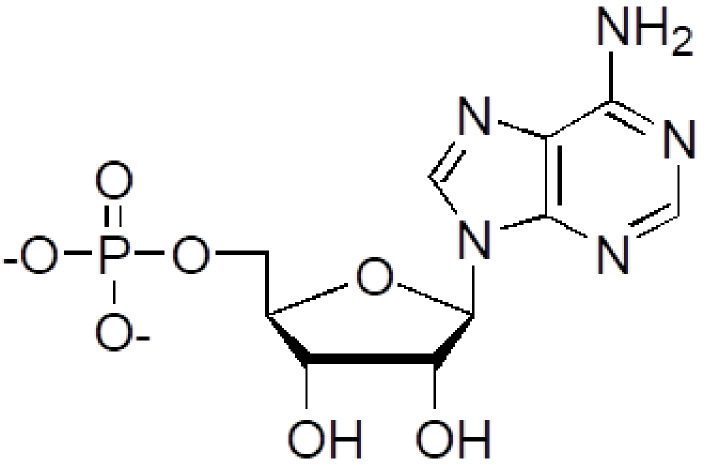


>> Continue in “Metabolism of Nucleotides”

DNA



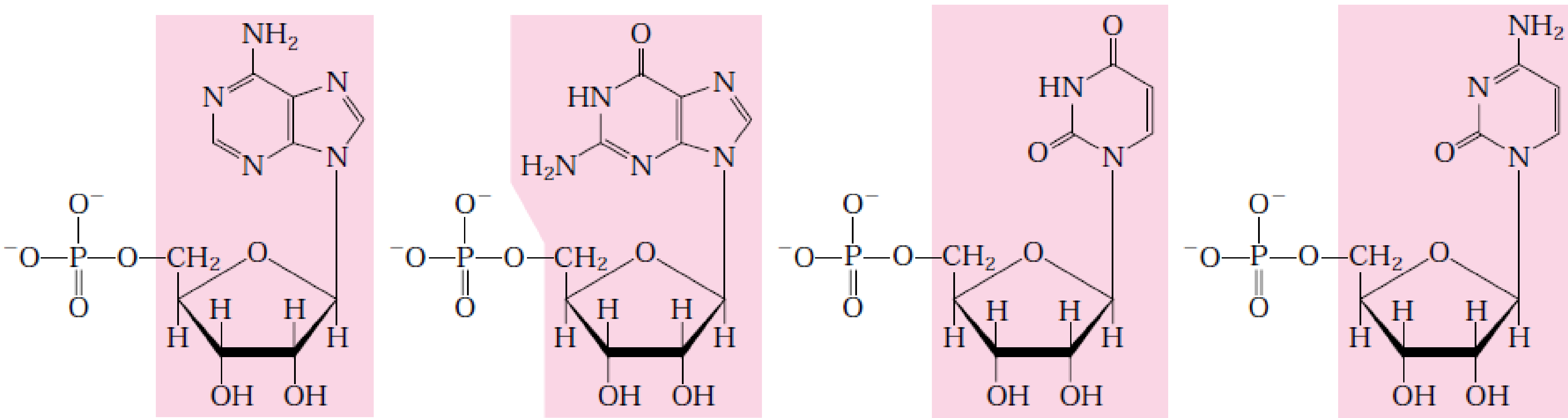
RNA



Phosphate (Phosphoric Acid)

DNA	RNA
deoxyribose	**ribose**
A, T, C, G	**A, U, C, G**

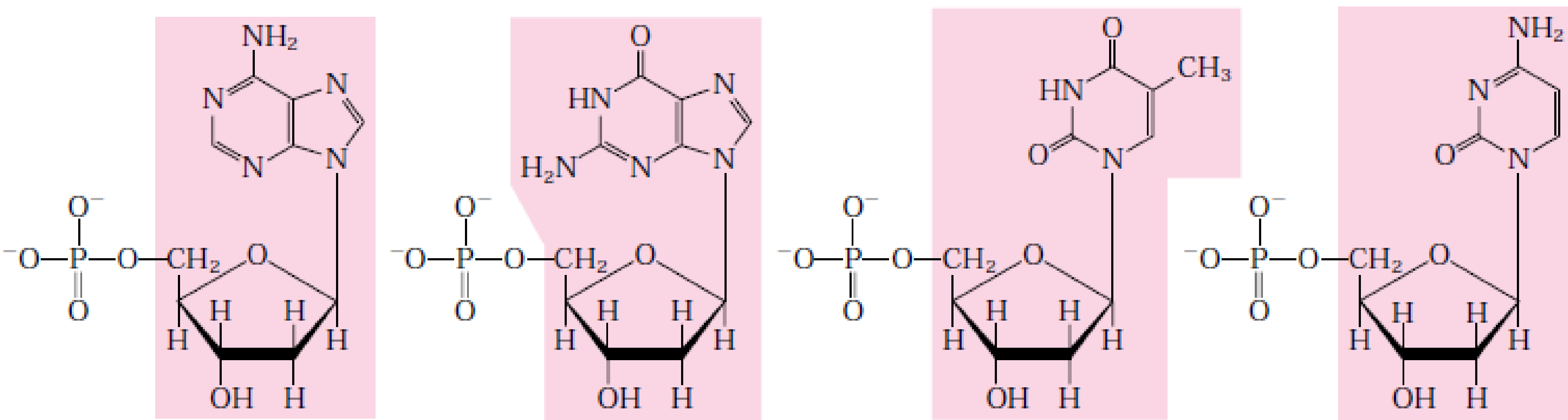
Ribonucleotides



Nucleotide:	Adenylate (adenosine 5′-monophosphate)	Guanylate (guanosine 5′-monophosphate)	Uridylate (uridine 5′-monophosphate)	Cytidylate (cytidine 5′-monophosphate)
Symbols:	A, AMP	G, GMP	U, UMP	C, CMP
Nucleoside:	Adenosine	Guanosine	Uridine	Cytidine

Source: Lehninger Principles of Biochemistry

Deoxyribonucleotide

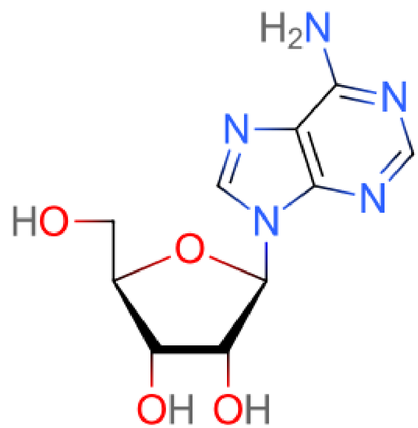


Nucleotide:	Deoxyadenylate (deoxyadenosine 5′-monophosphate)	Deoxyguanylate (deoxyguanosine 5′-monophosphate)	Deoxythymidylate (deoxythymidine 5′-monophosphate)	Deoxycytidylate (deoxycytidine 5′-monophosphate)
Symbols:	A, dA, dAMP	G, dG, dGMP	T, dT, dTMP	C, dC, dCMP
Nucleoside:	Deoxyadenosine	Deoxyguanosine	Deoxythymidine	Deoxycytidine

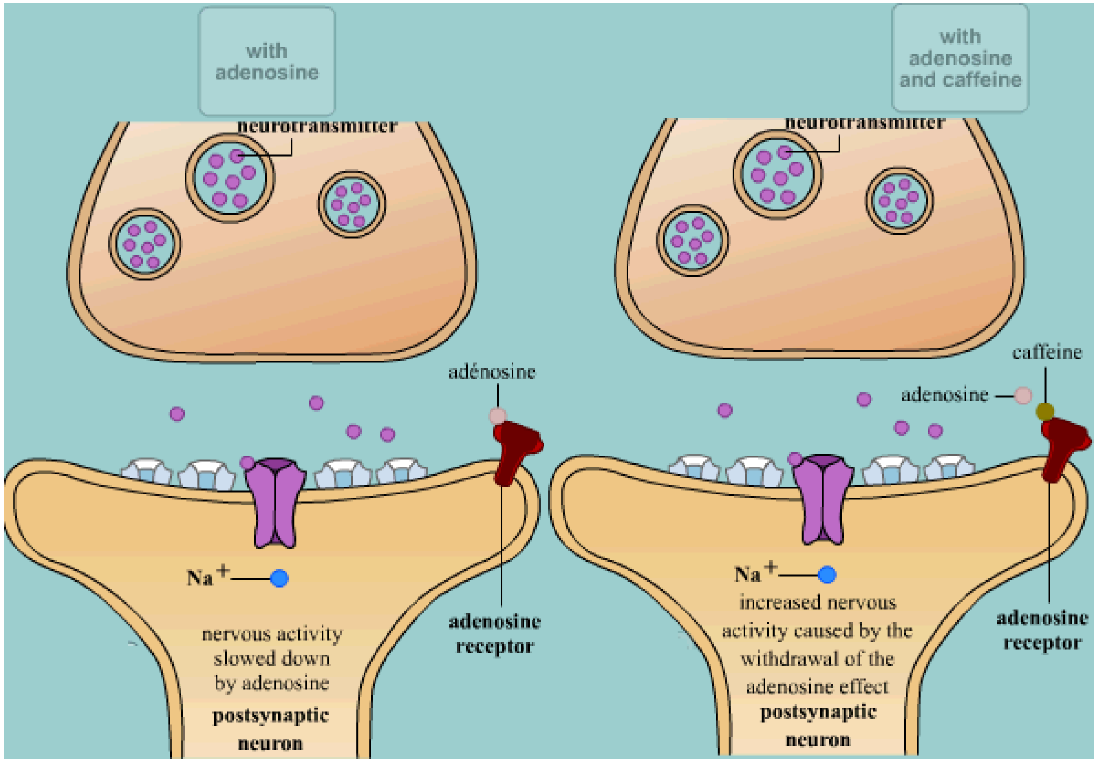
Source: Lehninger Principles of Biochemistry

Applications: Caffeine

Caffeine



Adenosine



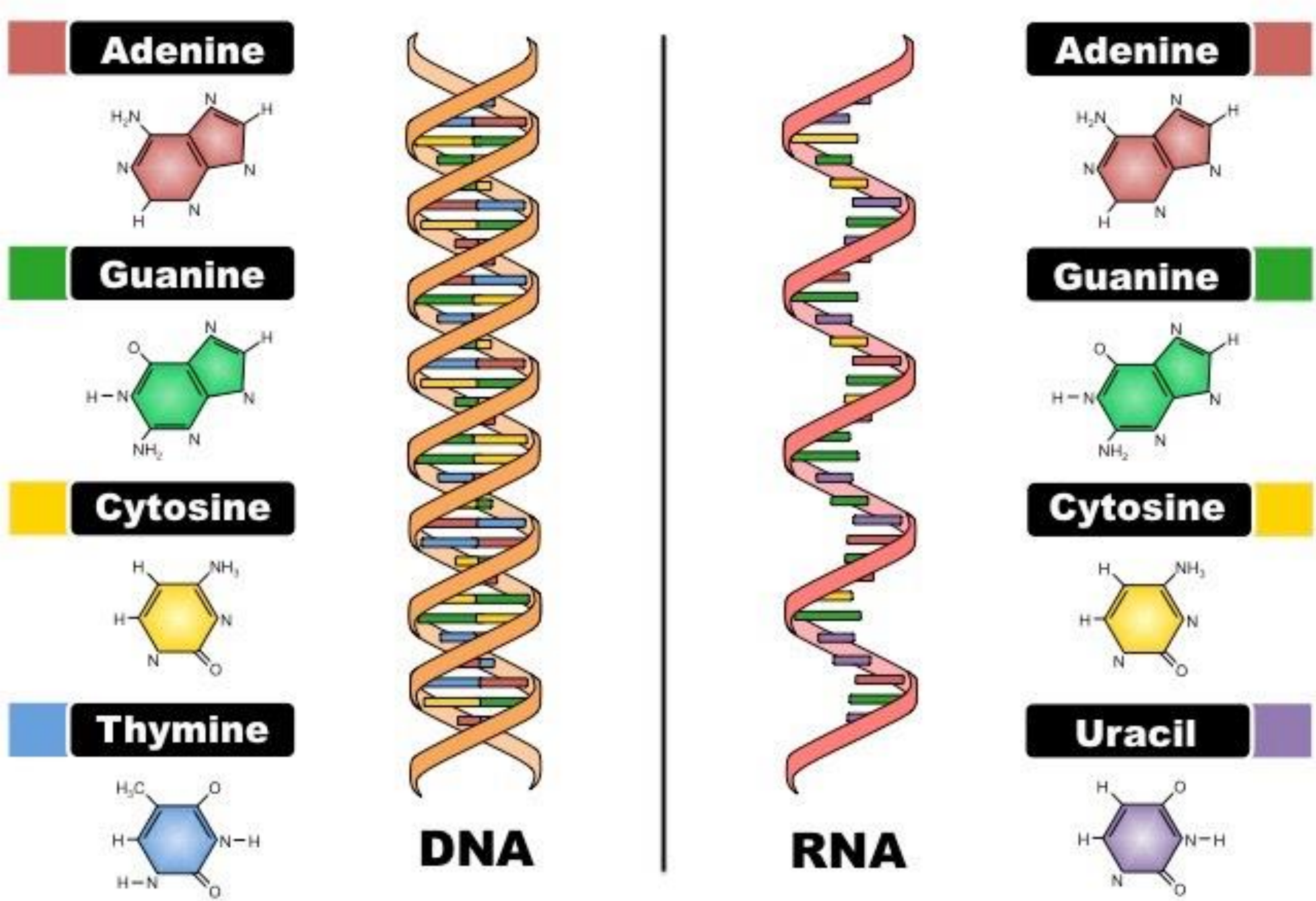
- Adenosine – slow down nerve cell activity, vasodilation
- Caffeine – speed up nerve cell activity, vasoconstriction, increase heart rate & blood pressure

Our best friend?

Product	Average caffeine content (mg/100 ml)
Red Bull®	32.0
Mountain Dew®	15.0
Coca Cola®	9.7*
Diet Coke®	9.7*
Coke Zero®	9.6*
Brewed black tea	22.5
Brewed green tea	12.1
Coffee, cappuccino	101.9
Coffee, flat white	86.9
Coffee, long black	74.7
Coffee, from ground coffee beans, espresso style	194.0
Chocolate, milk with added milk solids	20.0
Chocolate, dark, high cocoa solids	59.0

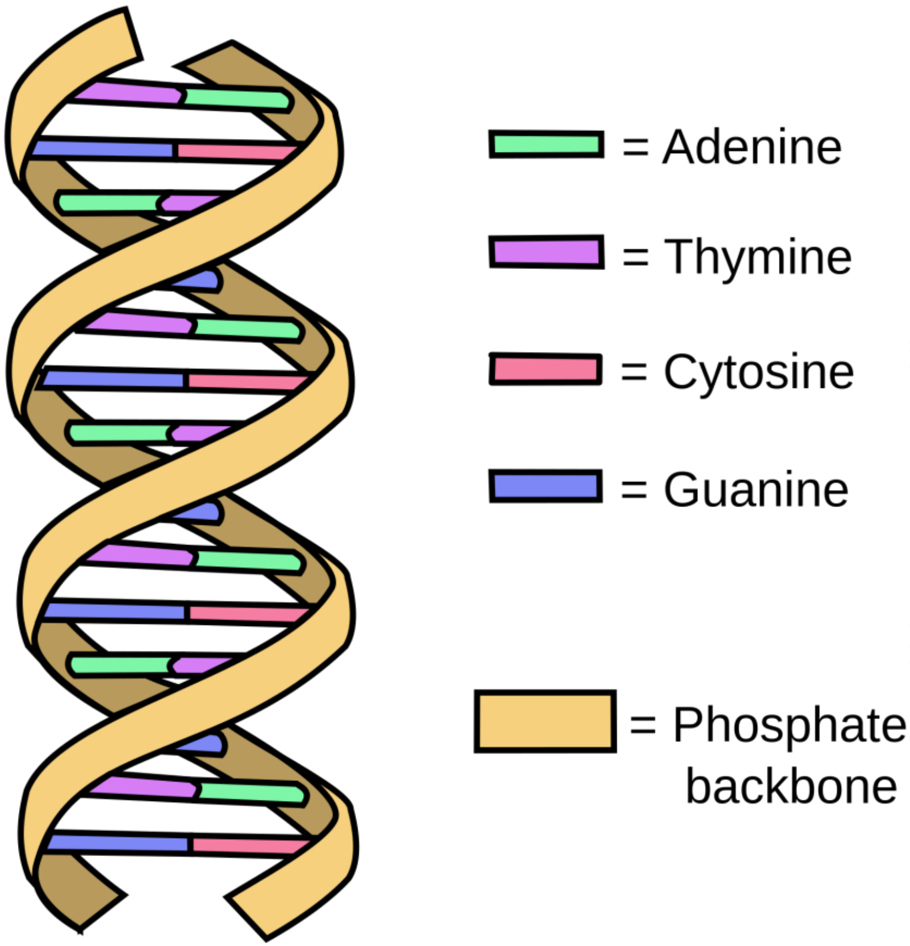
Alcohol and Drug Foundation of Australia, adf.org.au

Two types of nucleic acids

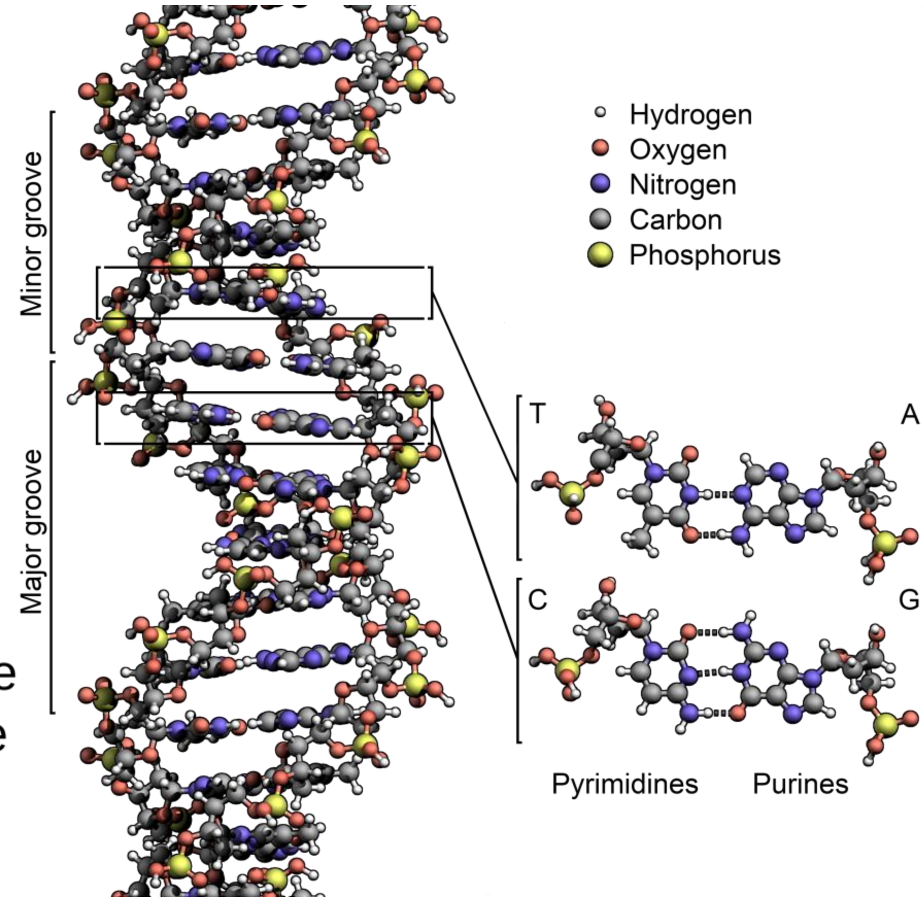


Source: http://ib.bioninja.com.au

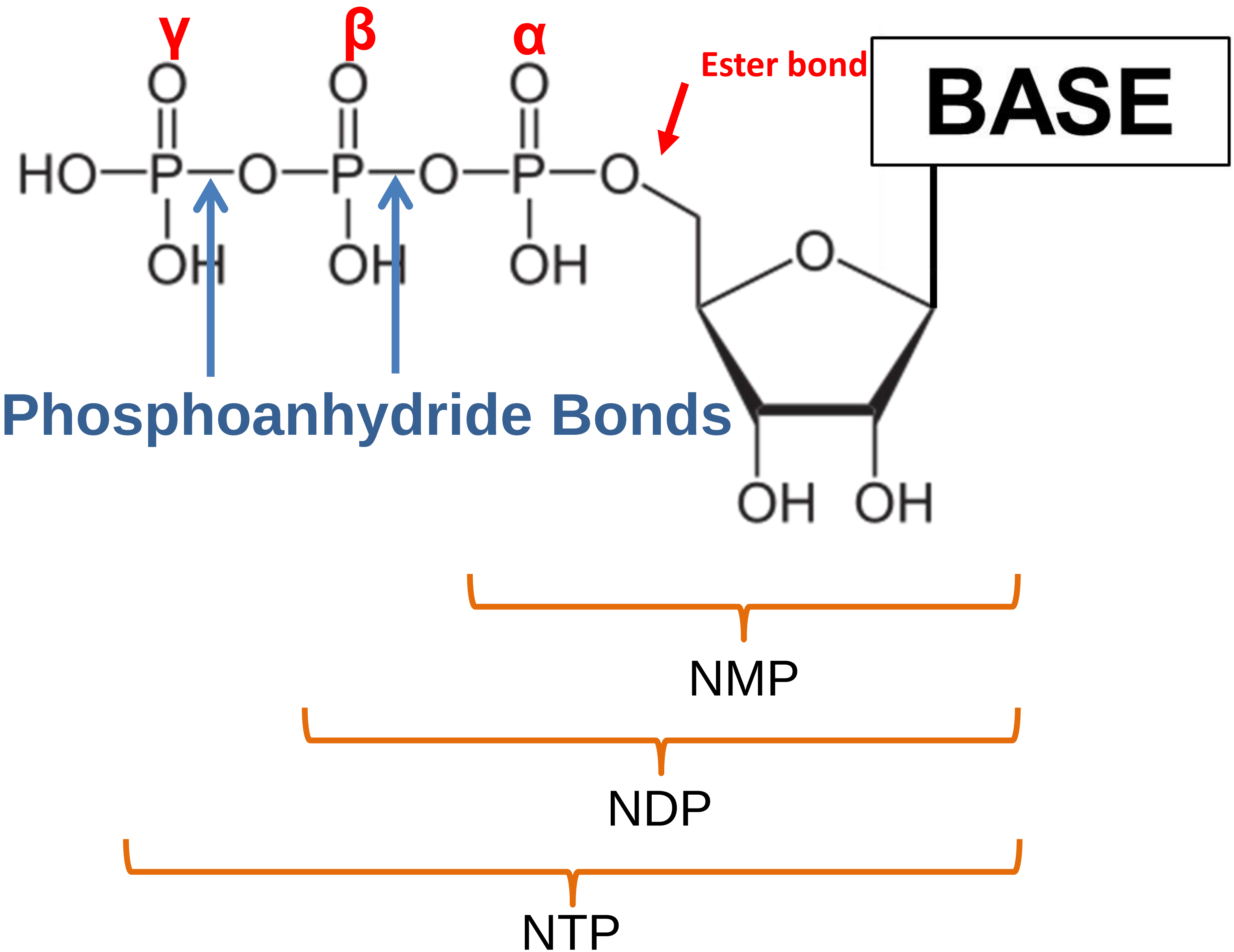
DNA is a polymer of deoxyribonucleotides.



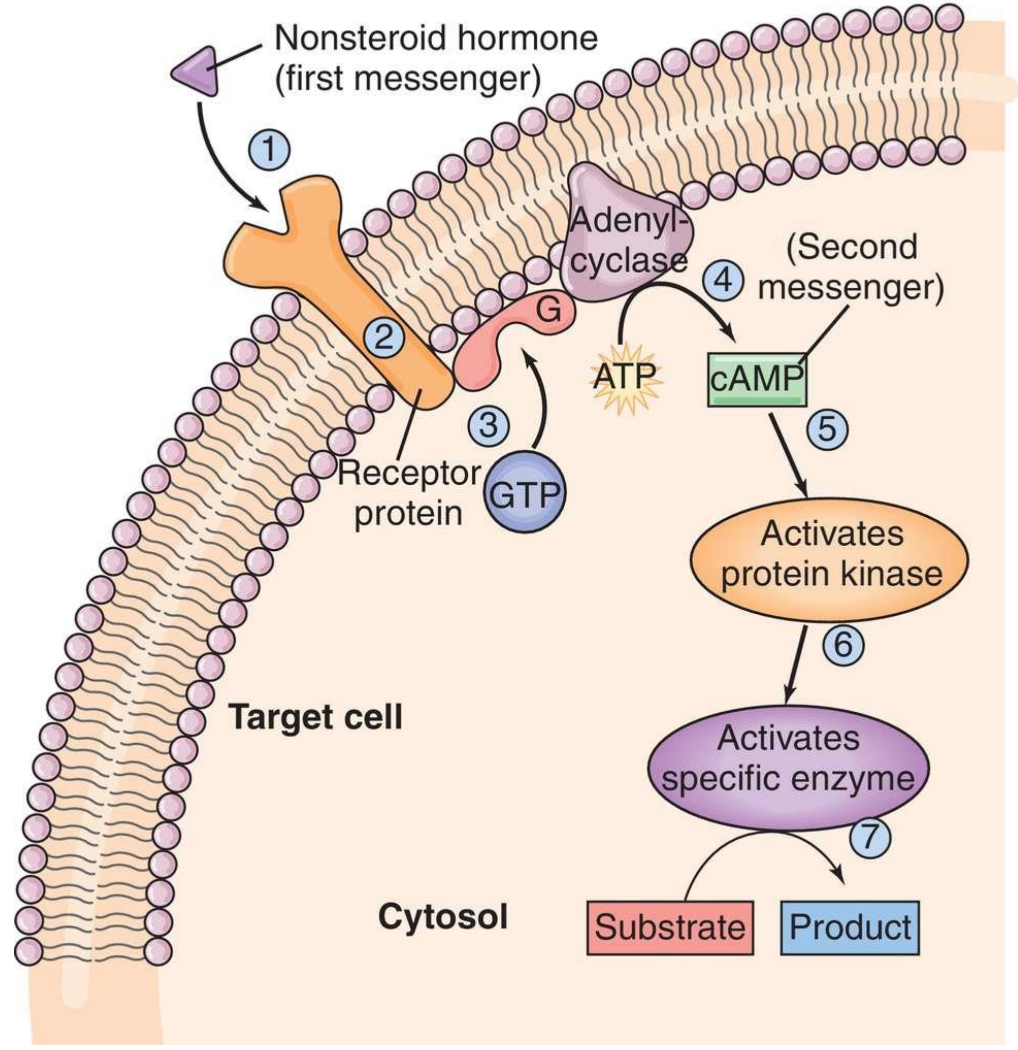
DNA



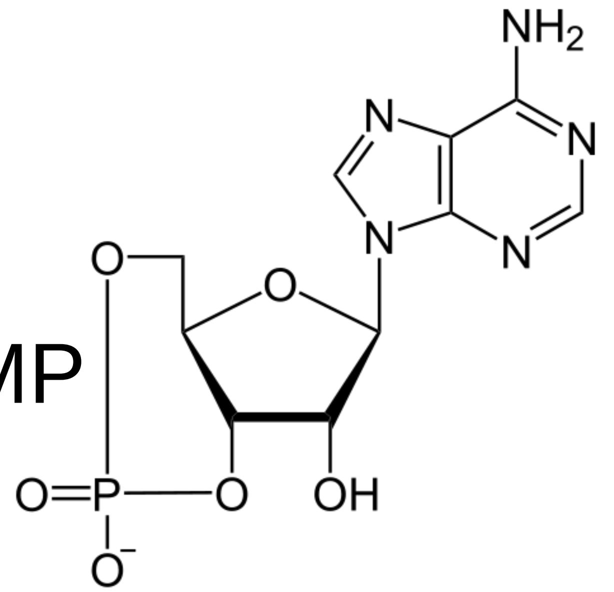
Nucleotide with more than 1 phosphate group



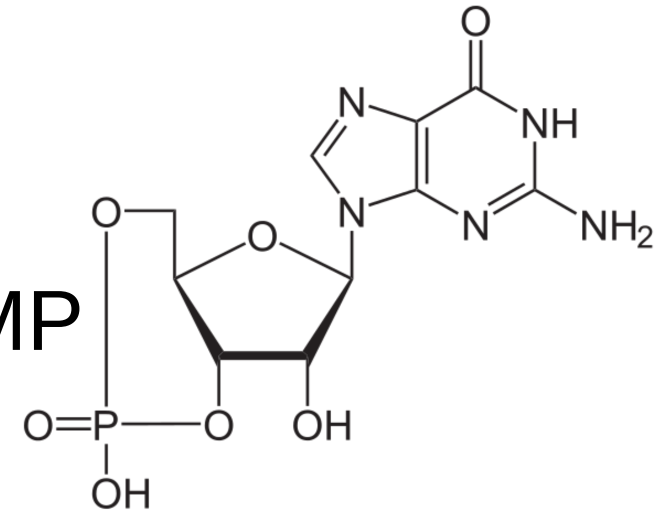
Cyclic Nucleotide



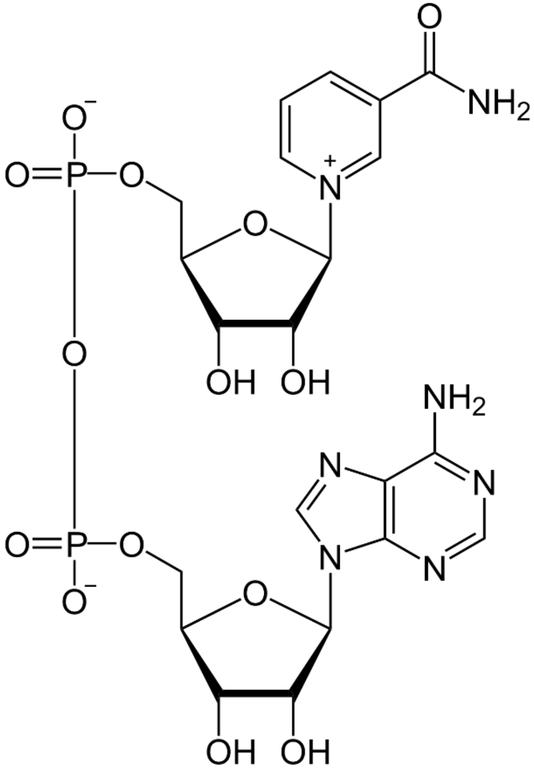
cAMP



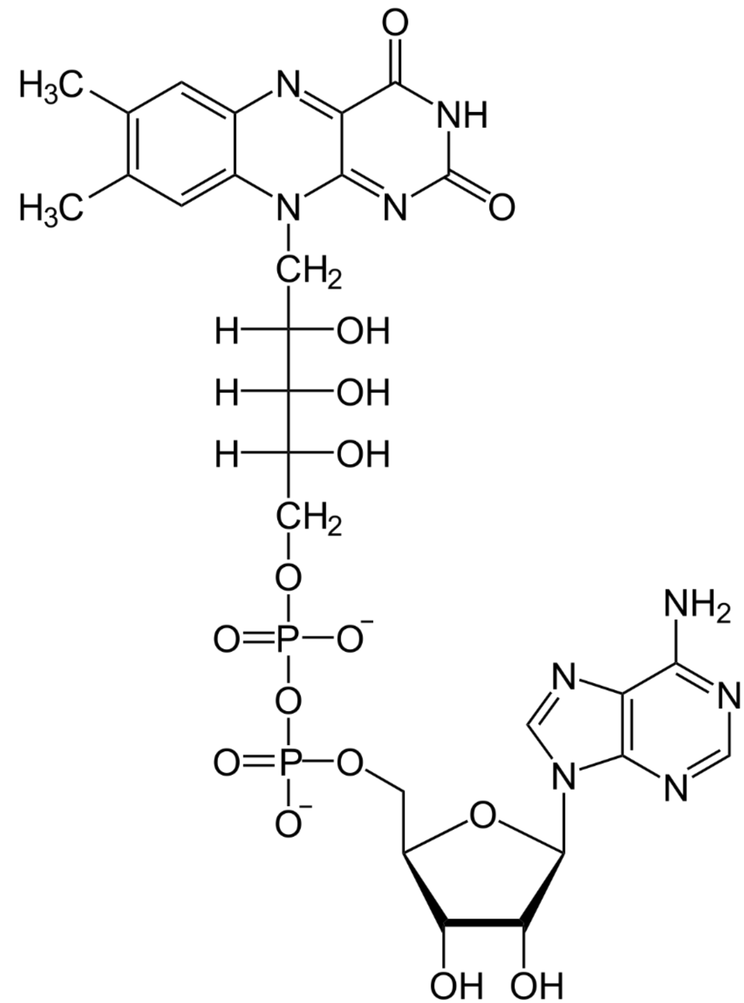
cGMP



Coenzymes



Nicotinamide adenine dinucleotide (NAD)



Flavin adenine dinucleotide (FAD)

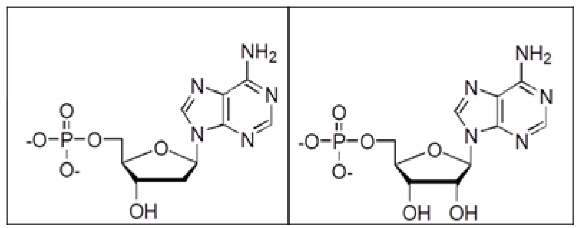
Conclusions

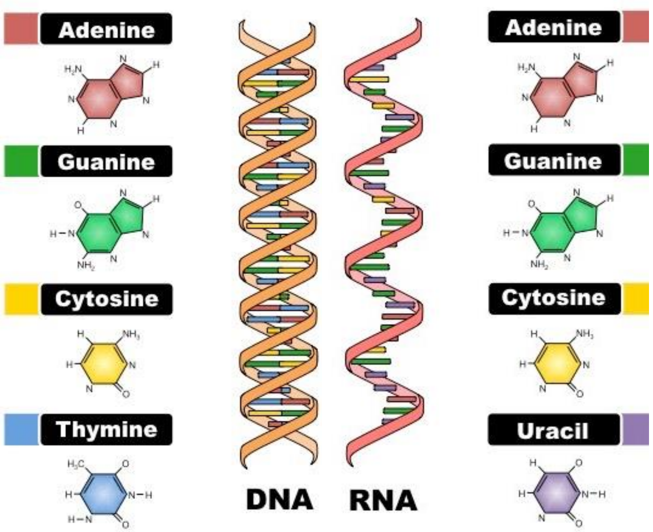
Phosphate
Acidic properties

Pentose sugar
- D-ribose
- 2’-deoxyribose

Nitrogenous bases
- Tautomerization (keto-enol, amino-imino)
- Acid-base
- Light absorption (260 nm)

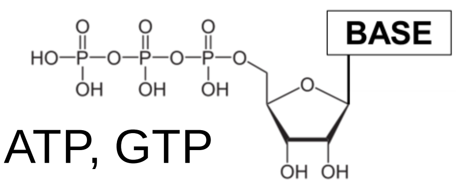
Nucleotide



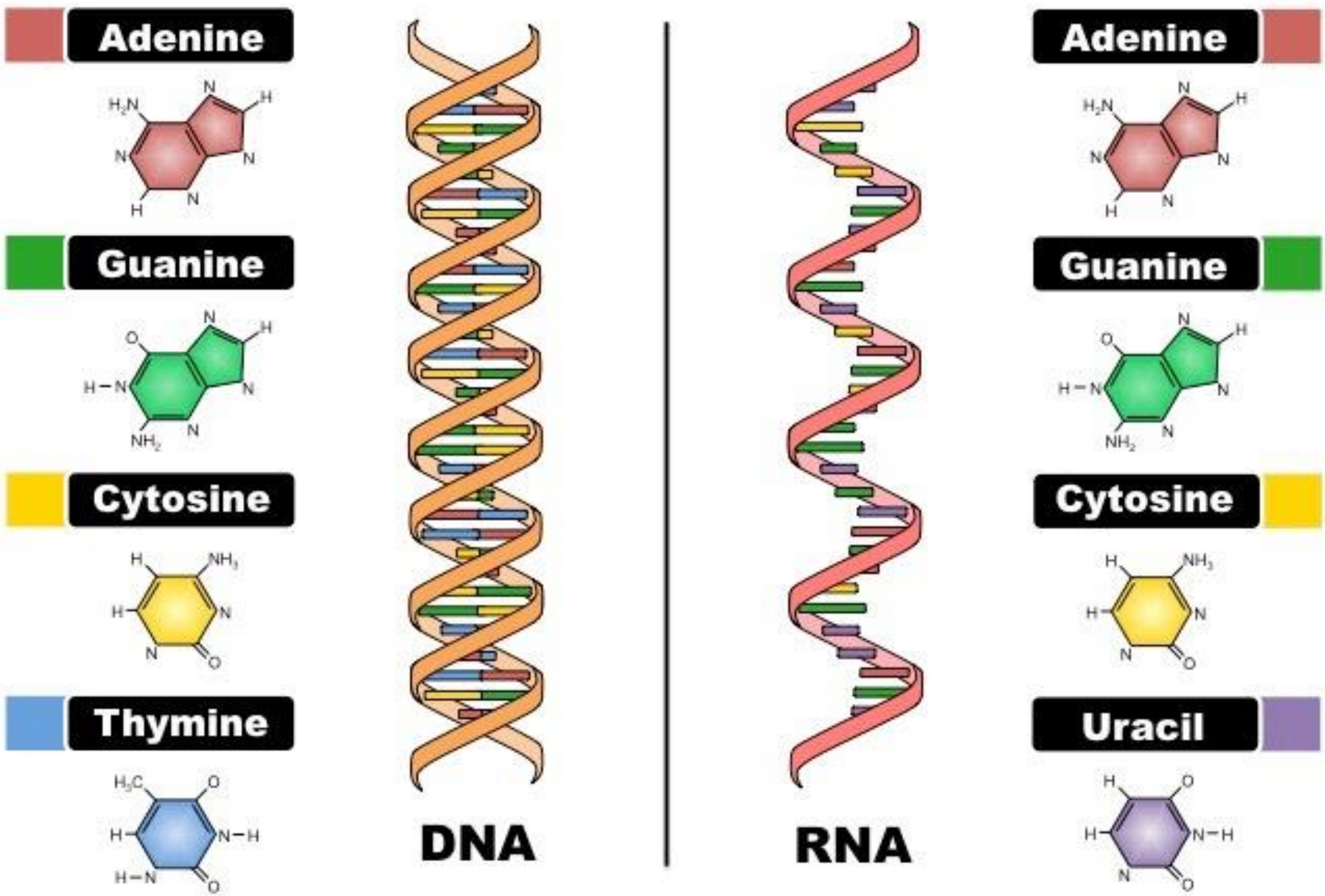


Function
- The building blocks of nucleic acids

Other
- Metabolic energy → ATP, GTP
- Secondary messenger → cAMP, cGMP
- Coenzymes → FAD, FMN, NAD^+, $NADP^+$



Nucleic acids are the polymer of nucleotides.



Source: http://ib.bioninja.com.au

1953

MOLECULAR STRUCTURE OF NUCLEIC ACIDS

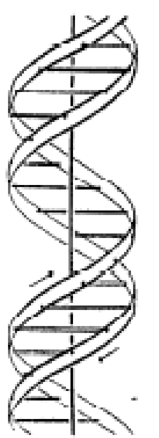
A Structure for Deoxyribose Nucleic Acid

WE wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

A structure for nucleic acid has already been proposed by Pauling and Corey[1]. They kindly made their manuscript available to us in advance of publication. Their model consists of three intertwined chains, with the phosphates near the fibre axis, and the bases on the outside. In our opinion, this structure is unsatisfactory for two reasons: (1) We believe that the material which gives the X-ray diagrams is the salt, not the free acid. Without the acidic hydrogen atoms it is not clear what forces would hold the structure together, especially as the negatively charged phosphates near the axis will repel each other. (2) Some of the van der Waals distances appear to be too small.

Another three-chain structure has also been suggested by Fraser (in the press). In his model the phosphates are on the outside and the bases on the inside, linked together by hydrogen bonds. This structure as described is rather ill-defined, and for this reason we shall not comment on it.

We wish to put forward a radically different structure for the salt of deoxyribose nucleic acid. This structure has two helical chains each coiled round the same axis (see diagram). We have made the usual chemical assumptions, namely, that each chain consists of phosphate diester groups joining β-D-deoxyribofuranose residues with 3',5' linkages. The two chains (but not their bases) are related by a dyad perpendicular to the fibre axis. Both chains follow right-handed helices, but owing to the dyad the sequences of the atoms in the two chains run in opposite directions. Each chain loosely resembles Furberg's[2] model No. 1; that is, the bases are on the inside of the helix and the phosphates on the outside. The configuration of the sugar and the atoms near it is close to Furberg's 'standard configuration', the sugar being roughly perpendicular to the attached base. There is a residue on each chain every 3·4 A. in the z-direction. We have assumed an angle of 36° between adjacent residues in the same chain, so that the structure repeats after 10 residues on each chain, that is, after 34 A. The distance of a phosphorus atom from the fibre axis is 10 A. As the phosphates are on the outside, cations have easy access to them.



This figure is purely diagrammatic. The two ribbons symbolize the two phosphate—sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis

The structure is an open one, and its water content is rather high. At lower water contents we would expect the bases to tilt so that the structure could become more compact.

The novel feature of the structure is the manner in which the two chains are held together by the purine and pyrimidine bases. The planes of the bases are perpendicular to the fibre axis. They are joined together in pairs, a single base from one chain being hydrogen-bonded to a single base from the other chain, so that the two lie side by side with identical z-co-ordinates. One of the pair must be a purine and the other a pyrimidine for bonding to occur. The hydrogen bonds are made as follows: purine position 1 to pyrimidine position 1; purine position 6 to pyrimidine position 6.

If it is assumed that the bases only occur in the structure in the most plausible tautomeric forms (that is, with the keto rather than the enol configurations) it is found that only specific pairs of bases can bond together. These pairs are: adenine (purine) with thymine (pyrimidine), and guanine (purine) with cytosine (pyrimidine).

In other words, if an adenine forms one member of a pair, on either chain, then on these assumptions the other member must be thymine; similarly for guanine and cytosine. The sequence of bases on a single chain does not appear to be restricted in any way. However, if only specific pairs of bases can be formed, it follows that if the sequence of bases on one chain is given, then the sequence on the other chain is automatically determined.

It has been found experimentally[3,4] that the ratio of the amounts of adenine to thymine, and the ratio of guanine to cytosine, are always very close to unity for deoxyribose nucleic acid.

It is probably impossible to build this structure with a ribose sugar in place of the deoxyribose, as the extra oxygen atom would make too close a van der Waals contact.

The previously published X-ray data[5,6] on deoxyribose nucleic acid are insufficient for a rigorous test of our structure. So far as we can tell, it is roughly compatible with the experimental data, but it must be regarded as unproved until it has been checked against more exact results. Some of these are given in the following communications. We were not aware of the details of the results presented there when we devised our structure, which rests mainly though not entirely on published experimental data and stereochemical arguments.

It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material.

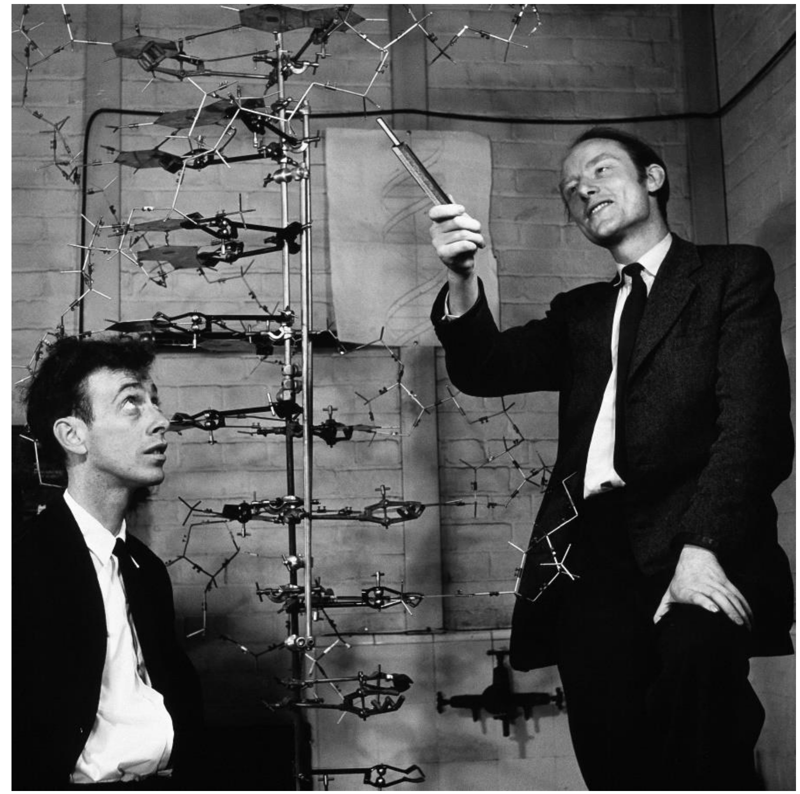
Full details of the structure, including the conditions assumed in building it, together with a set of co-ordinates for the atoms, will be published elsewhere.

We are much indebted to Dr. Jerry Donohue for constant advice and criticism, especially on interatomic distances. We have also been stimulated by a knowledge of the general nature of the unpublished experimental results and ideas of Dr. M. H. F. Wilkins, Dr. R. E. Franklin and their co-workers at King's College, London. One of us (J. D. W.) has been aided by a fellowship from the National Foundation for Infantile Paralysis.

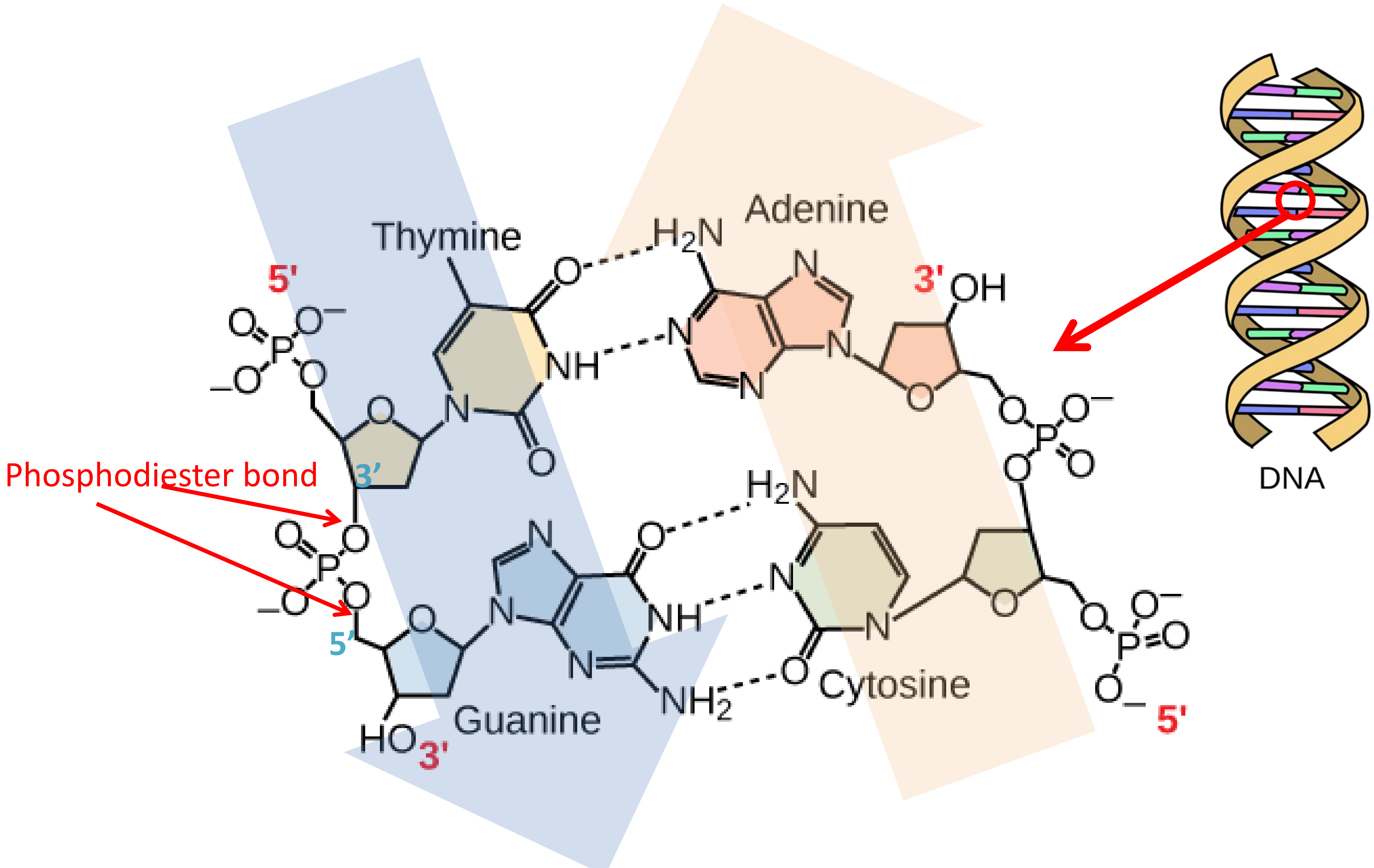
J. D. WATSON
F. H. C. CRICK

Medical Research Council Unit for the Study of the Molecular Structure of Biological Systems,
Cavendish Laboratory, Cambridge.
April 2.

[1] Pauling, L., and Corey, R. B., *Nature*, 171, 346 (1953); *Proc. U.S. Nat. Acad. Sci.*, 39, 84 (1953).
[2] Furberg, S., *Acta Chem. Scand.*, 6, 634 (1952).
[3] Chargaff, E., for references see Zamenhof, S., Brawerman, G., and Chargaff, E., *Biochim. et Biophys. Acta*, 9, 402 (1952).
[4] Wyatt, G. R., *J. Gen. Physiol.*, 36, 201 (1952).
[5] Astbury, W. T., Symp. Soc. Exp. Biol. 1, Nucleic Acid, 66 (Camb. Univ. Press, 1947).
[6] Wilkins, M. H. F., and Randall, J. T., *Biochim. et Biophys. Acta*, 10, 192 (1953).

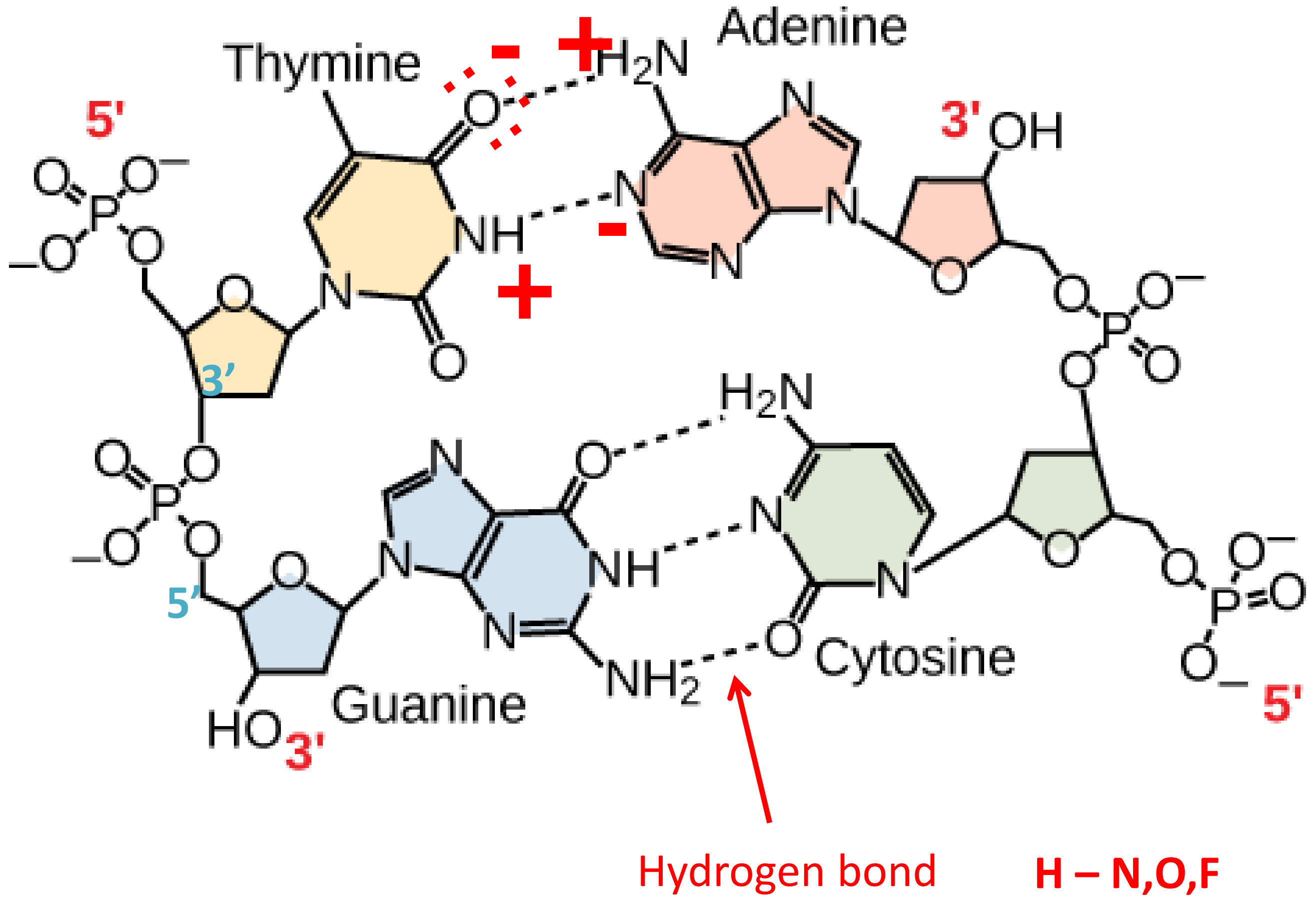


DNA



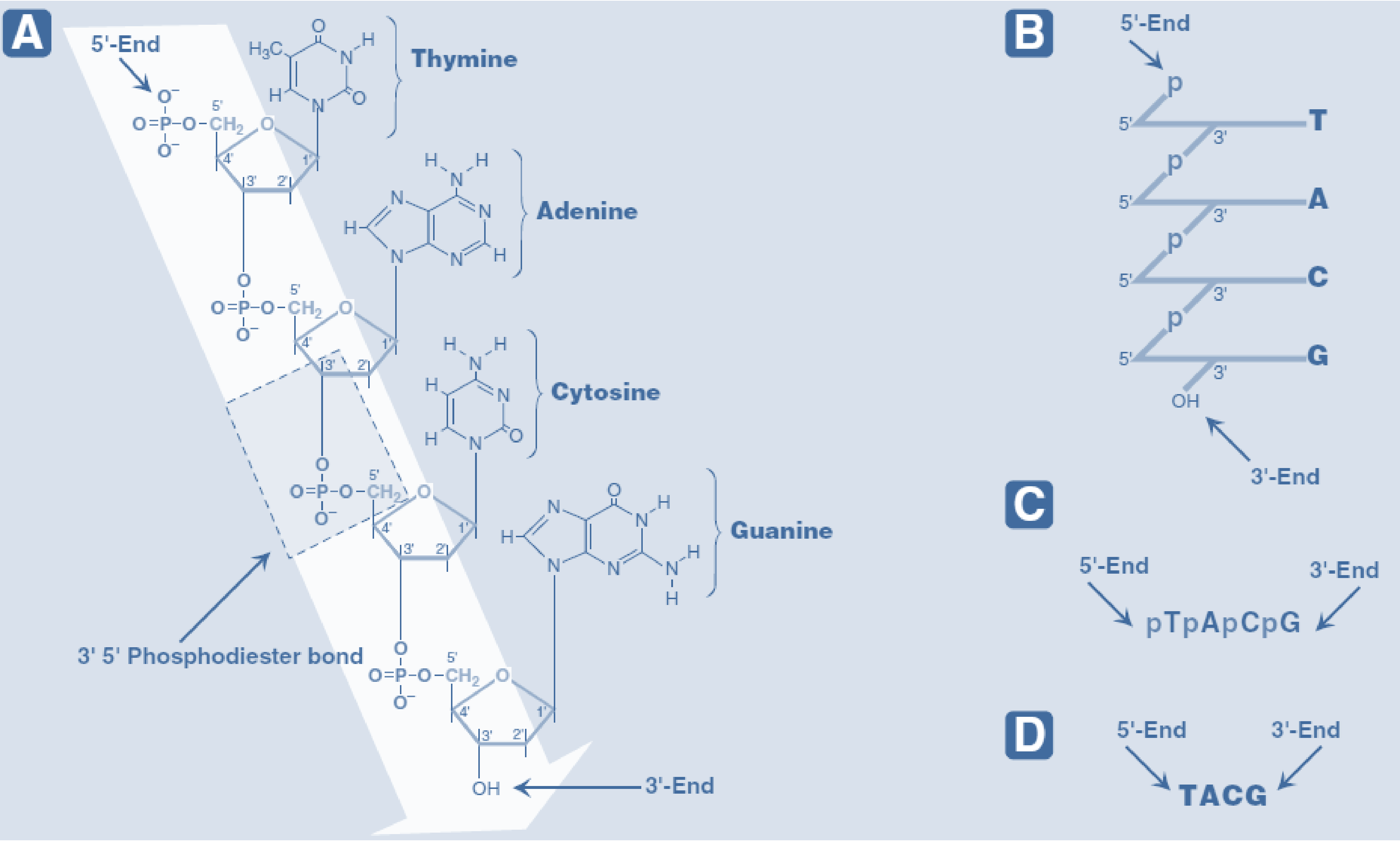
Thymine
Adenine
Guanine
Cytosine
5'
3'
3' OH
HO 3'
5'
3'
5'
3'
Phosphodiester bond
DNA

Base Pairing



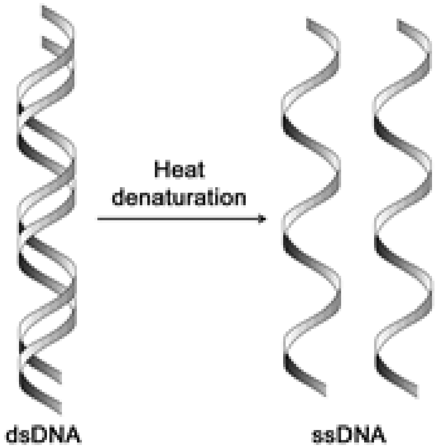
Base - "complementary base"
DNA strand – "complementary strand"

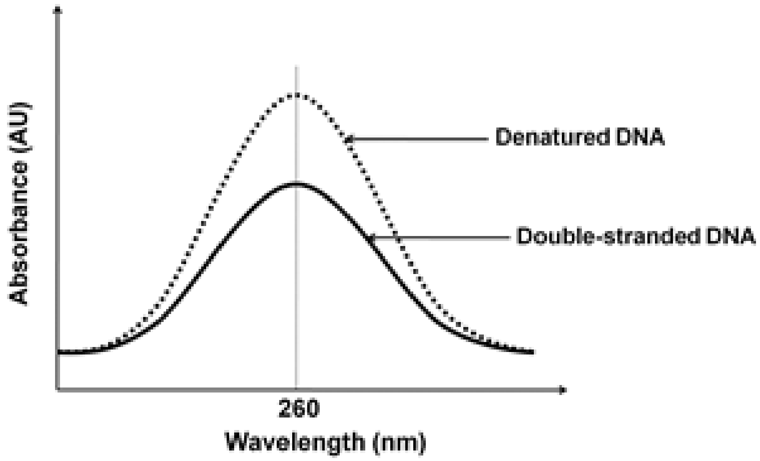
Polynucleotide Illustrations

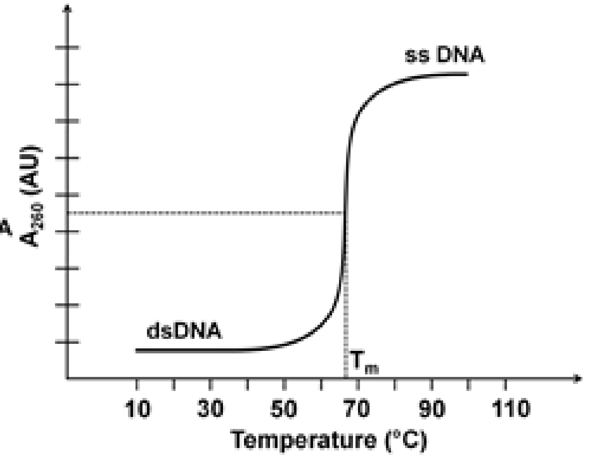


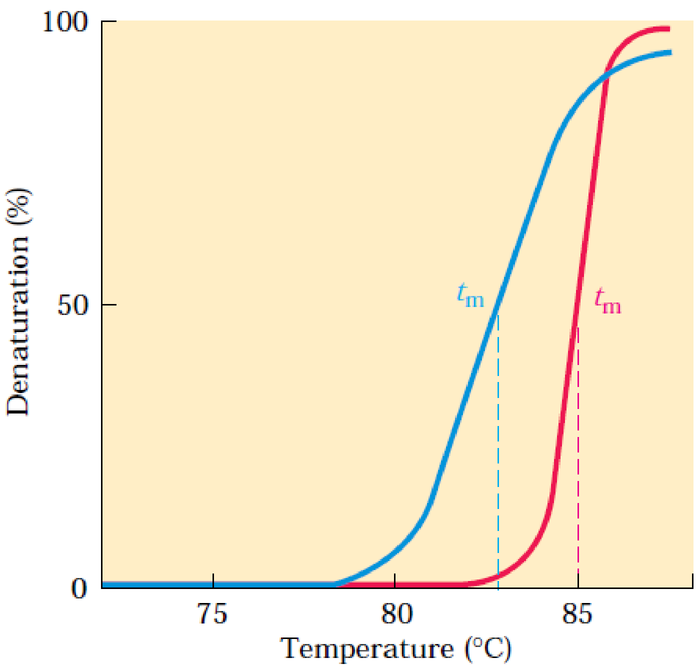
Source: Lippincotts Illustrated Reviews Biochemistry

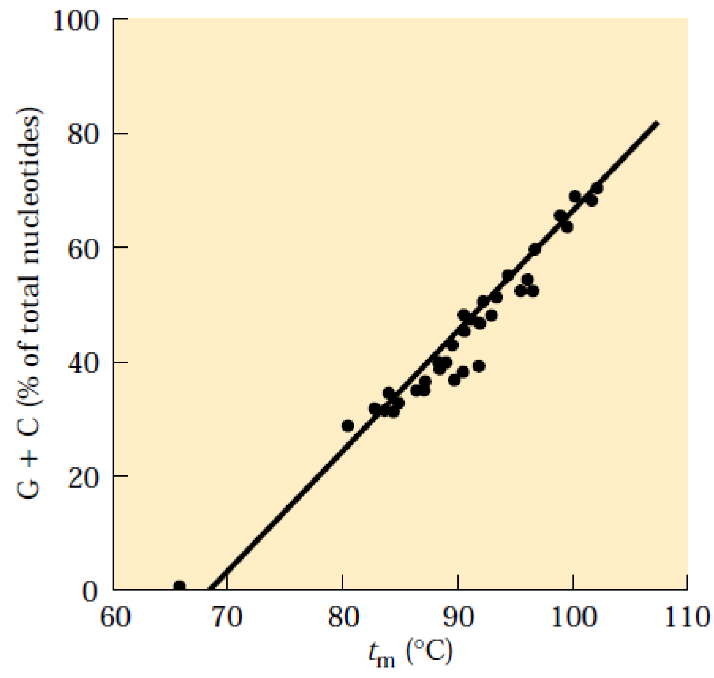
Denaturation and Renaturation







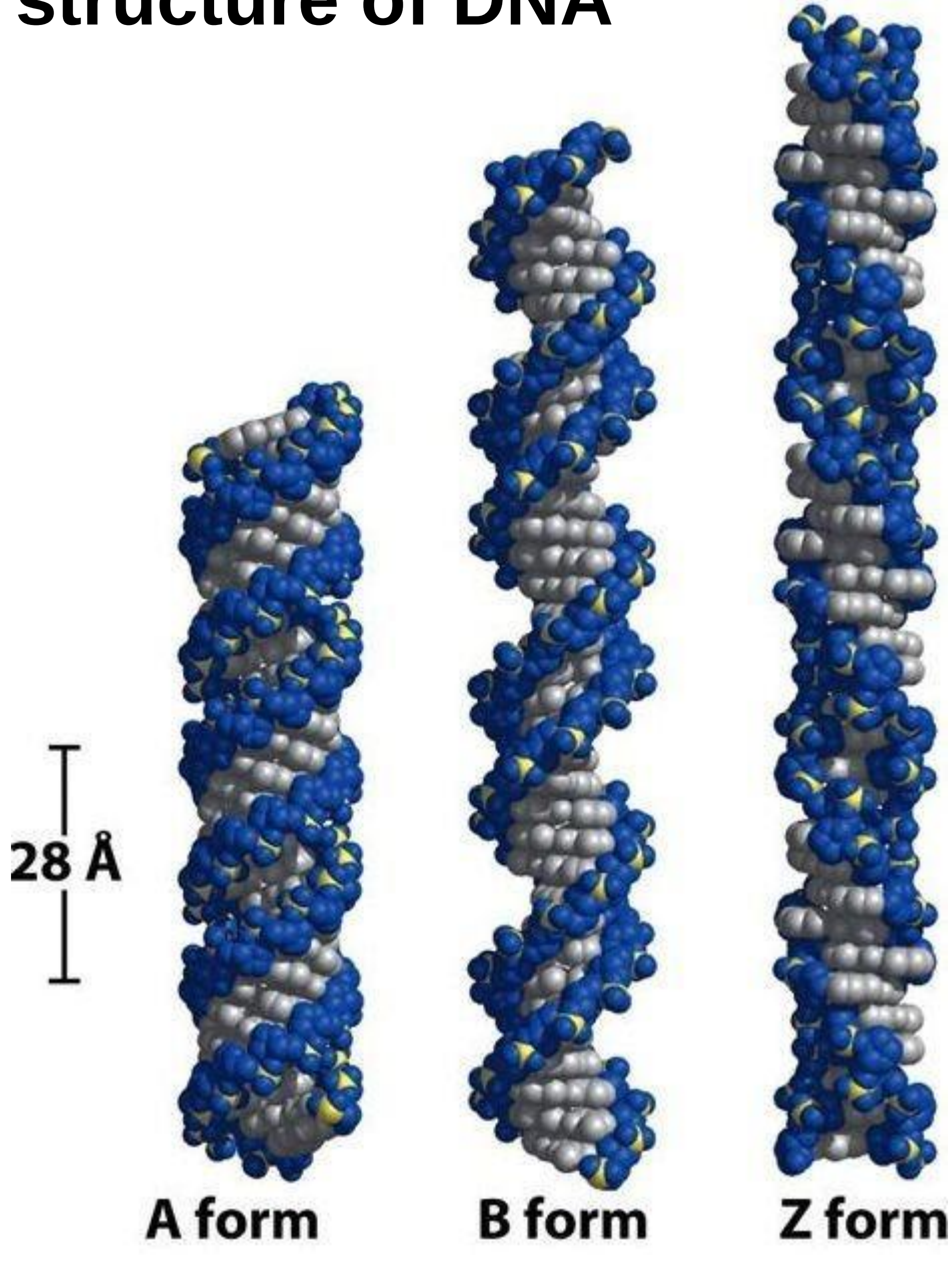




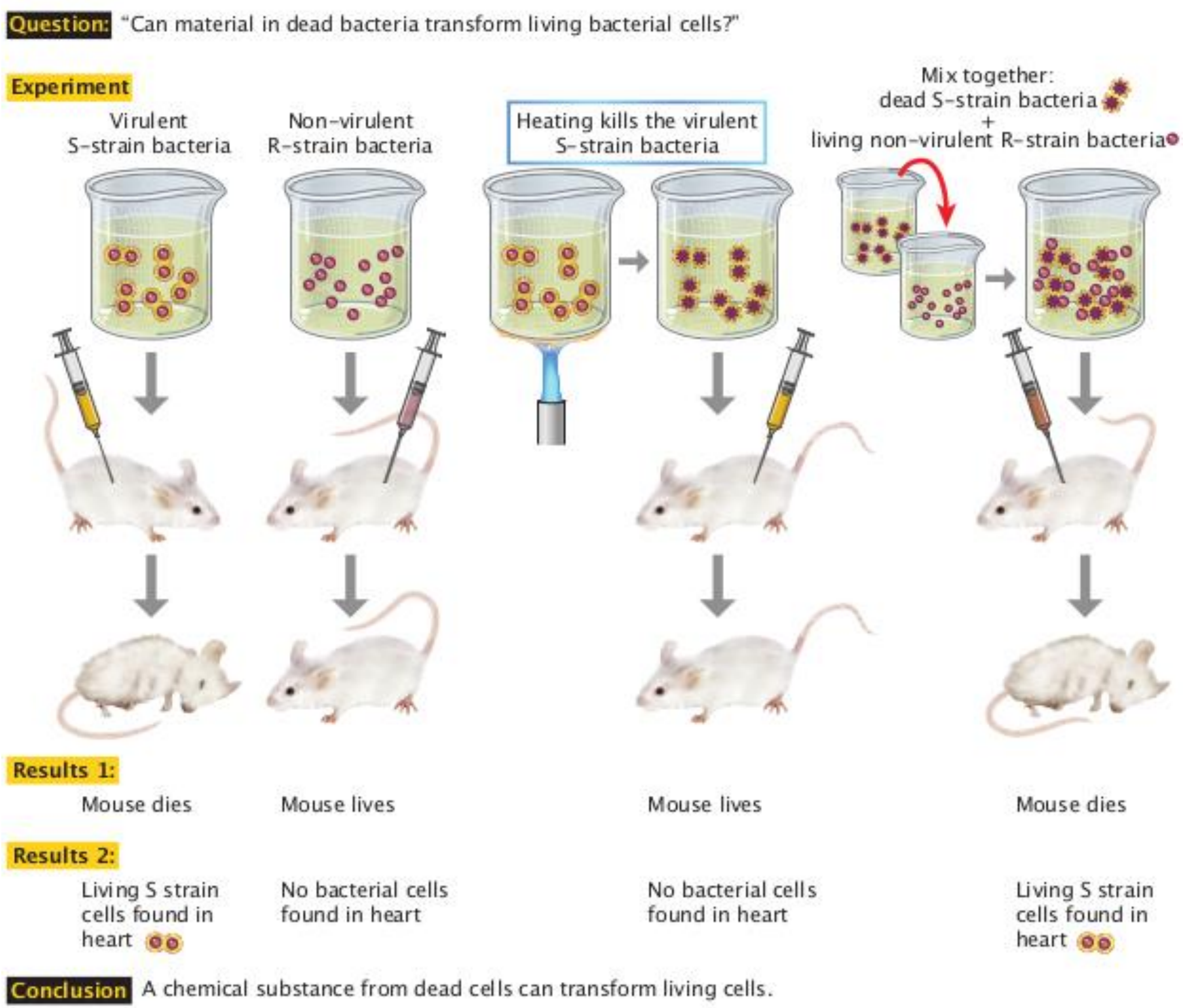
Hypochromism - a decrease in the absorption of UV.

Hyperchromism - the UV absorption is increased when the two single DNA strands are being separated.

Double helix structure of DNA

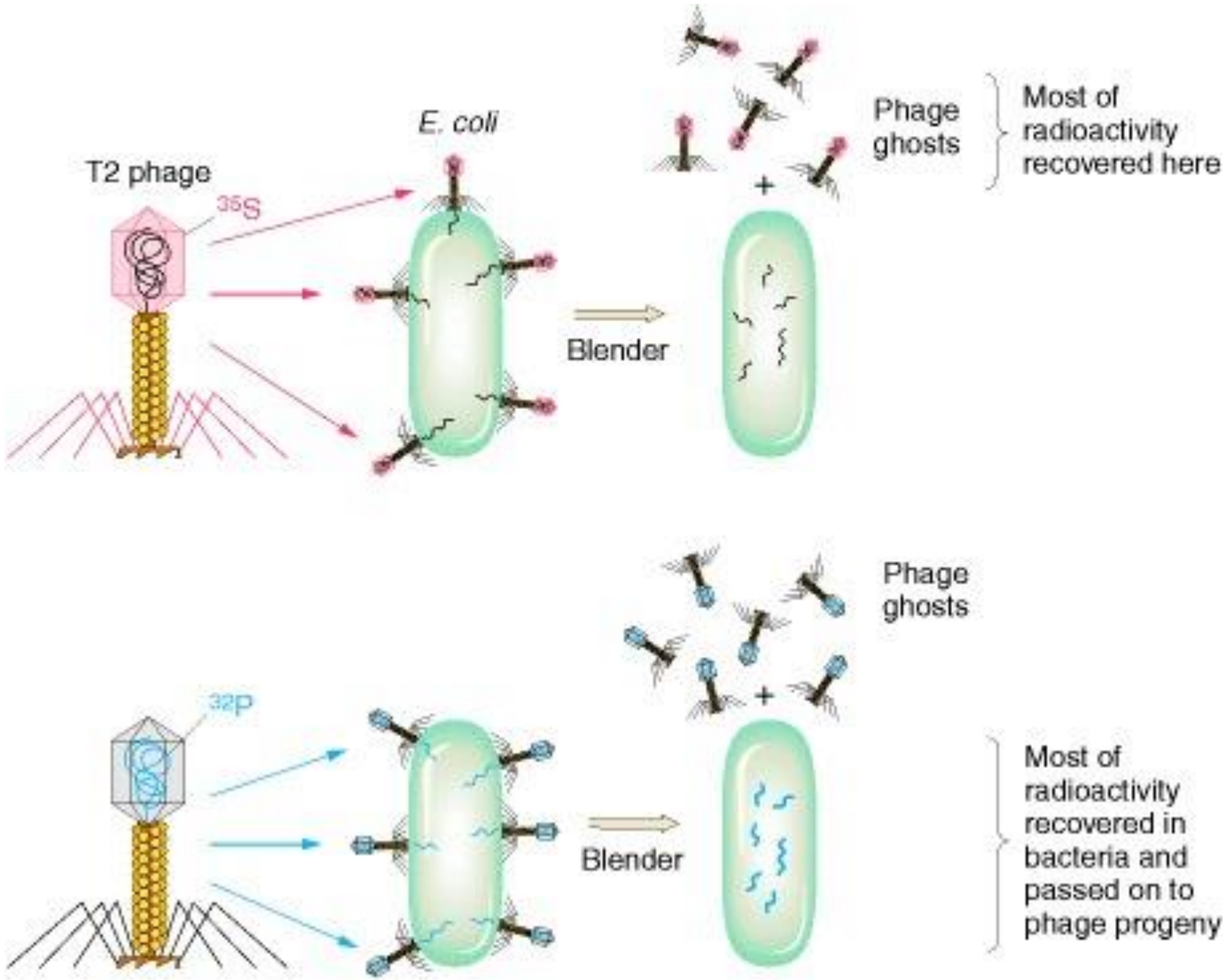


DNA as the Hereditary Material using *Streptococcus pneumoniae* (Frederick Griffith Experiment)

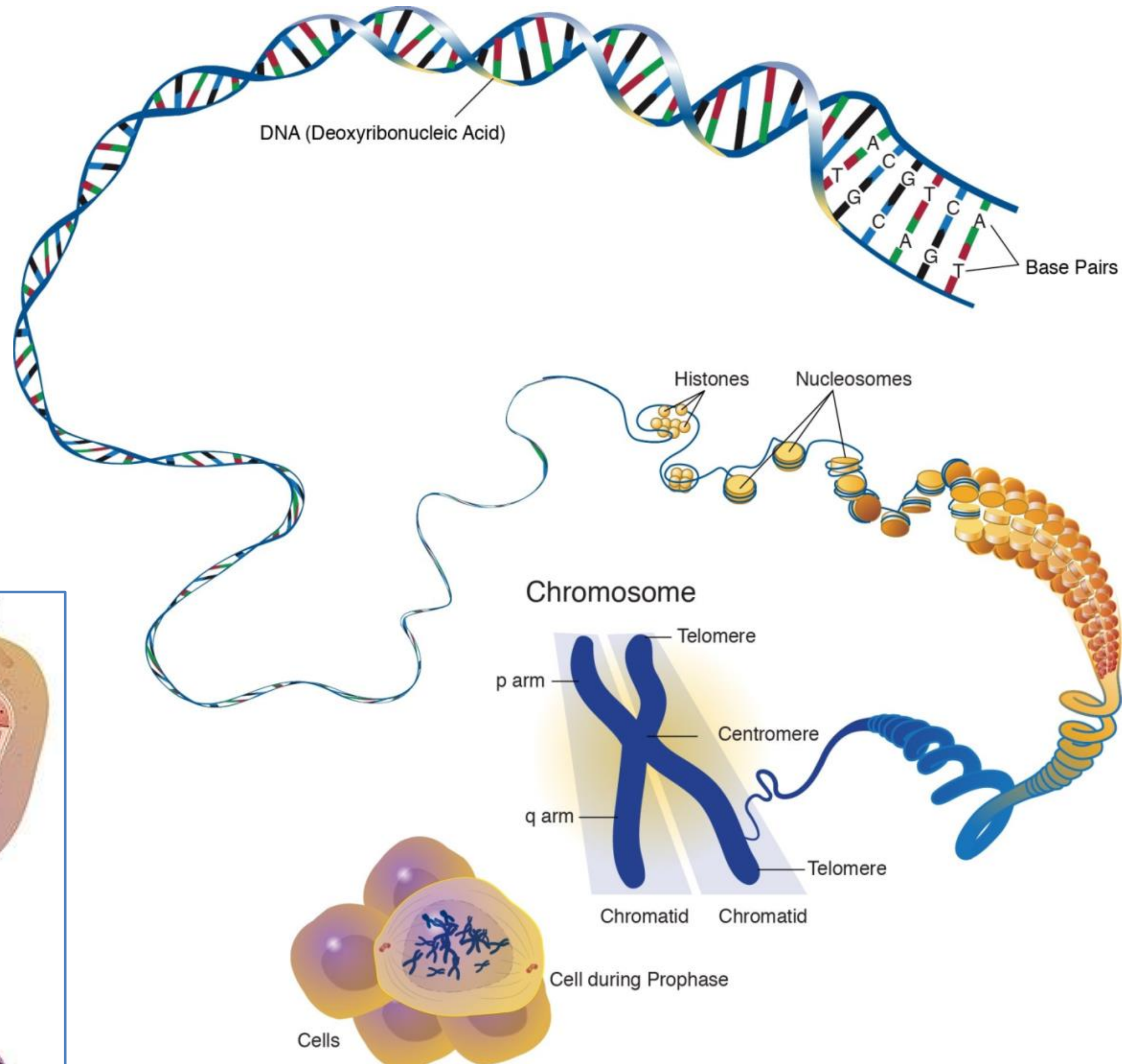


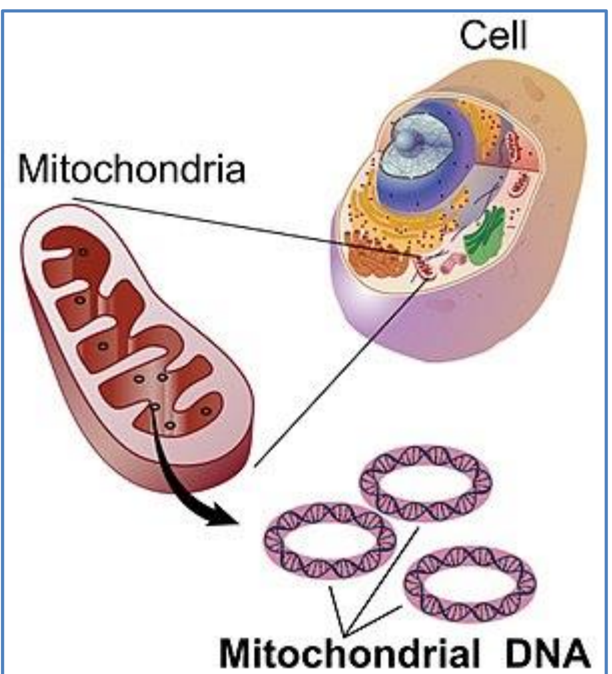
Source: nature.com/ scitable

The Hershey-Chase experiment



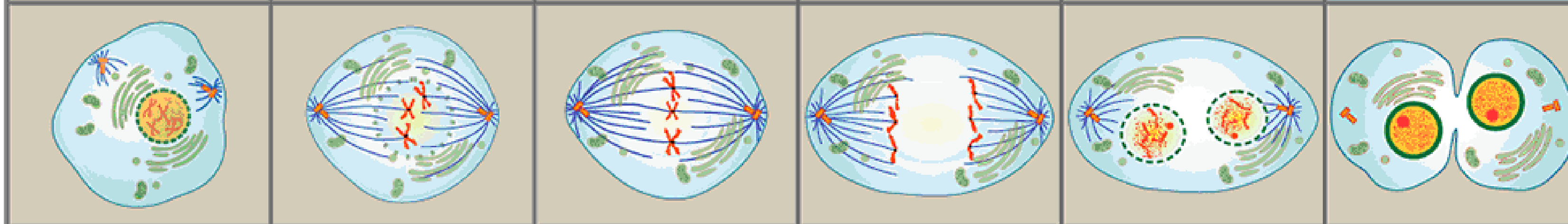
Source: nature.com/scitable



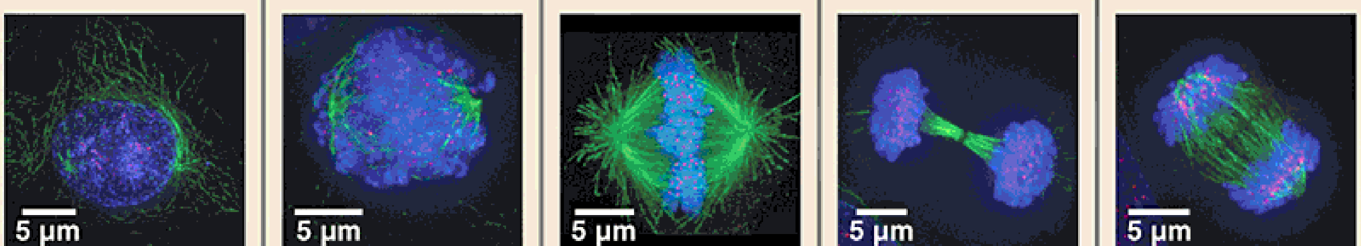


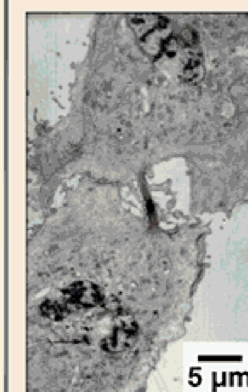
Source: kintalk.org

Cell Division



Prophase	Prometaphase	Metaphase	Anaphase	Telophase	Cytokinesis
• Chromosomes condense and become visible • Spindle fibers emerge from the centrosomes • Nuclear envelope breaks down • Centrosomes move toward opposite poles	• Chromosomes continue to condense • Kinetochores appear at the centromeres • Mitotic spindle microtubules attach to kinetochores	• Chromosomes are lined up at the metaphase plate • Each sister chromatid is attached to a spindle fiber originating from opposite poles	• Centromeres split in two • Sister chromatids (now called chromosomes) are pulled toward opposite poles • Certain spindle fibers begin to elongate the cell	• Chromosomes arrive at opposite poles and begin to decondense • Nuclear envelope material surrounds each set of chromosomes • The mitotic spindle breaks down • Spindle fibers continue to push poles apart	• Animal cells: a cleavage furrow separates the daughter cells • Plant cells: a cell plate, the precursor to a new cell wall, separates the daughter cells

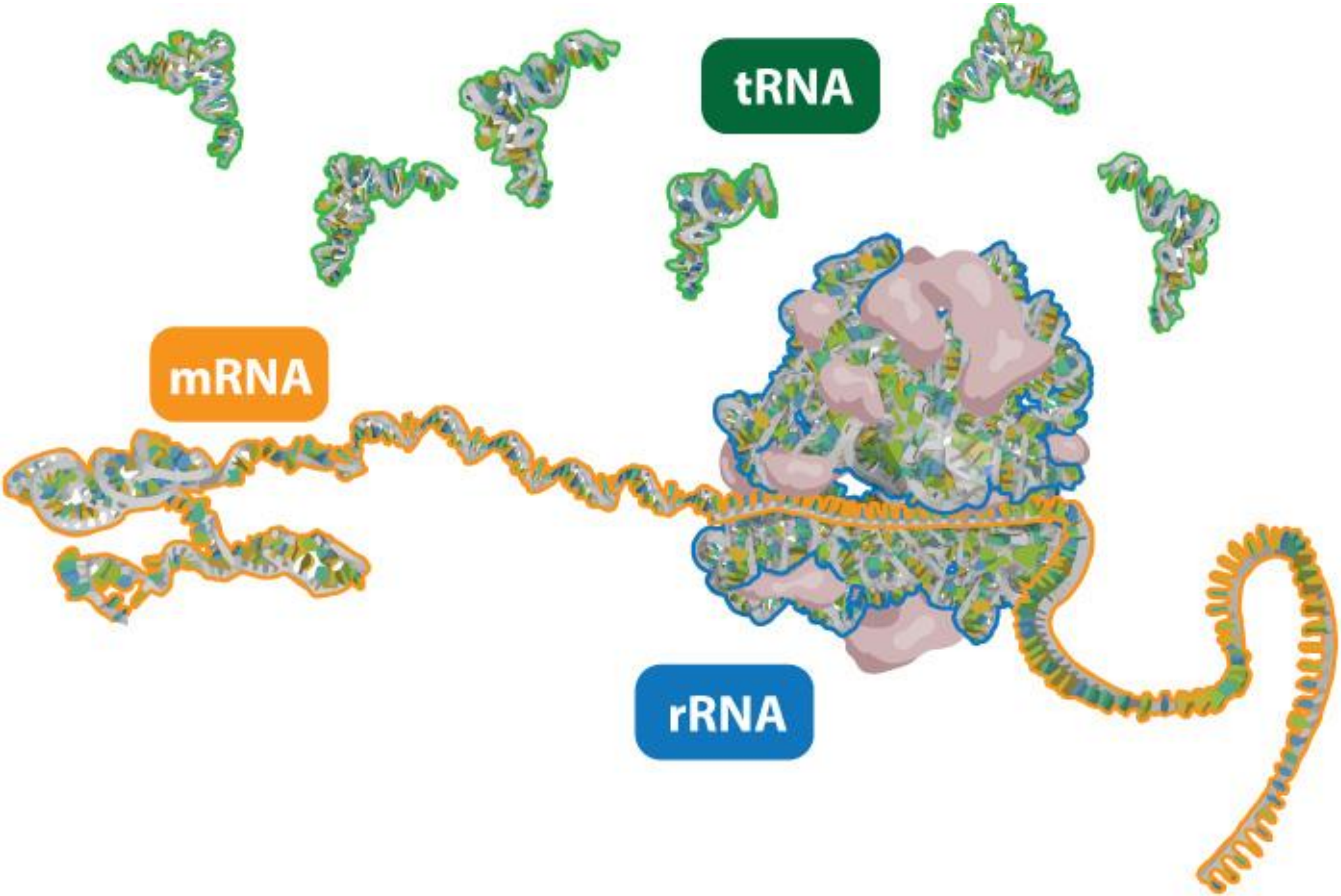




MITOSIS

https://askabiologist.asu.edu/cell-division

RNA



http://learn.genetics.utah.edu/content/basics/beyond/

Deoxyribonucleic Acid (DNA)

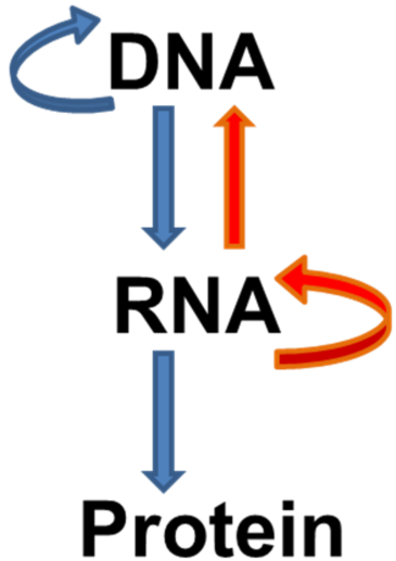
- Polymer of deoxyribonucleotide
- Nuclear DNA + Mitochondrial DNA (human)
- A,T, C, G
- 5’ to 3’ direction, anti-parallel
- Double helical with major groove and minor groove
- Acidic due to phosphate groups
- Light absorption (260 nm) due to nitrogenous bases
- Denaturation and renaturation
- G+C content affects melting temperature (T_m)

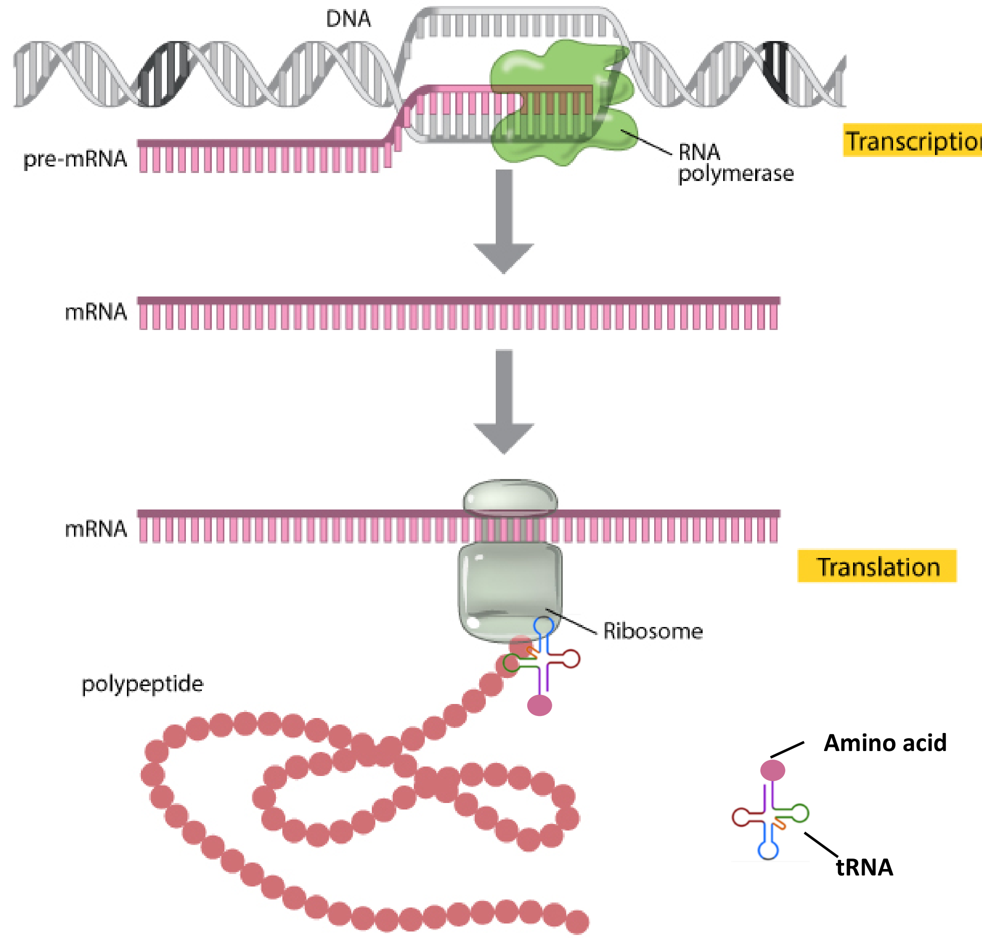
Ribonucleic Acid (RNA)

- Polymer of ribonucleotide
- Single strand, exceptional case in virus
- A,U,C,G
- Ribosomal RNA, Transfer RNA, Messenger RNA
- Secondary structure
- Found in nucleus, cytoplasm and mitochondria

Central Dogma of Molecular Biology

General





Source: nature.com/scitable

Suggested Readings