Nucleic Acids

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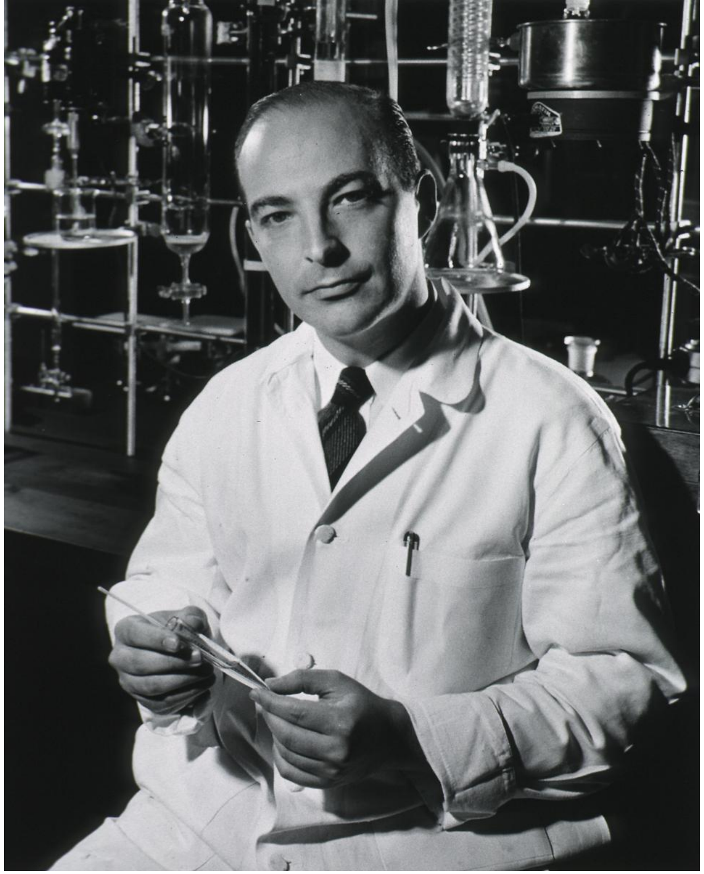
were isolated from the nucleus by F.Meicher in 1869

1953

J.Watson **F.Crick**

discovery of the structure of DNA

1958



Arthur Kornberg

and colleagues

purification and characterization of DNA polymerase from *E. Coli* cells, a enzyme now called

DNA polymerase I

1960

F.Jacob J.Monod

the operon model of gene regulation

1966

Marshall Nirenberg

Severo Ochoa

Gobind Khorana

Genetic Code

1972-1973

Herbert Boyer

Stanley N. Cohen

Paul Berg

DNA cloning

1990-2003

- **The Human Genome Project (HGP) international effort to discover all the estimated 20,000-25,000 human genes and make them accessible for further biological study.**

- **Another project goal was to determine the complete sequence of the 3 billion DNA subunits.**

- **As part of the HGP, parallel studies were carried out on selected model organisms such as the bacterium *E. coli* and the mouse to help develop the technology and interpret human gene function.**

Nucleic acids

are polymers of nucleotides,

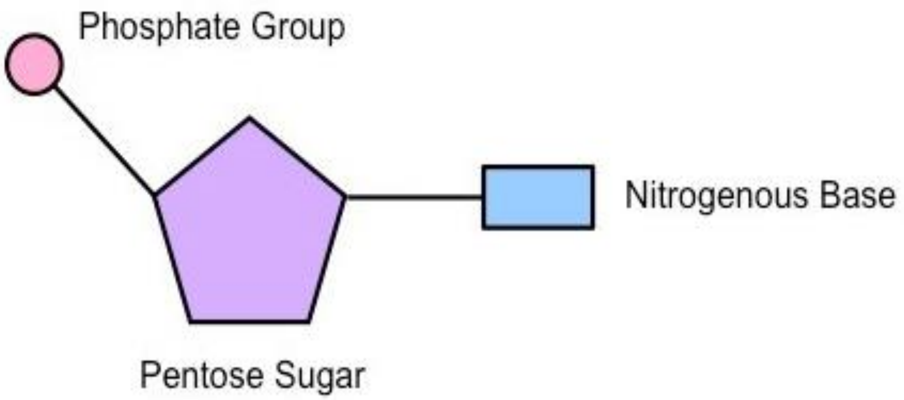
joined together by phosphodiester linkages between the

5-hydroxyl group of one pentose and the 3-hydroxyl group of the next

or

NA are a long polymers made from repeating units called nucleotides

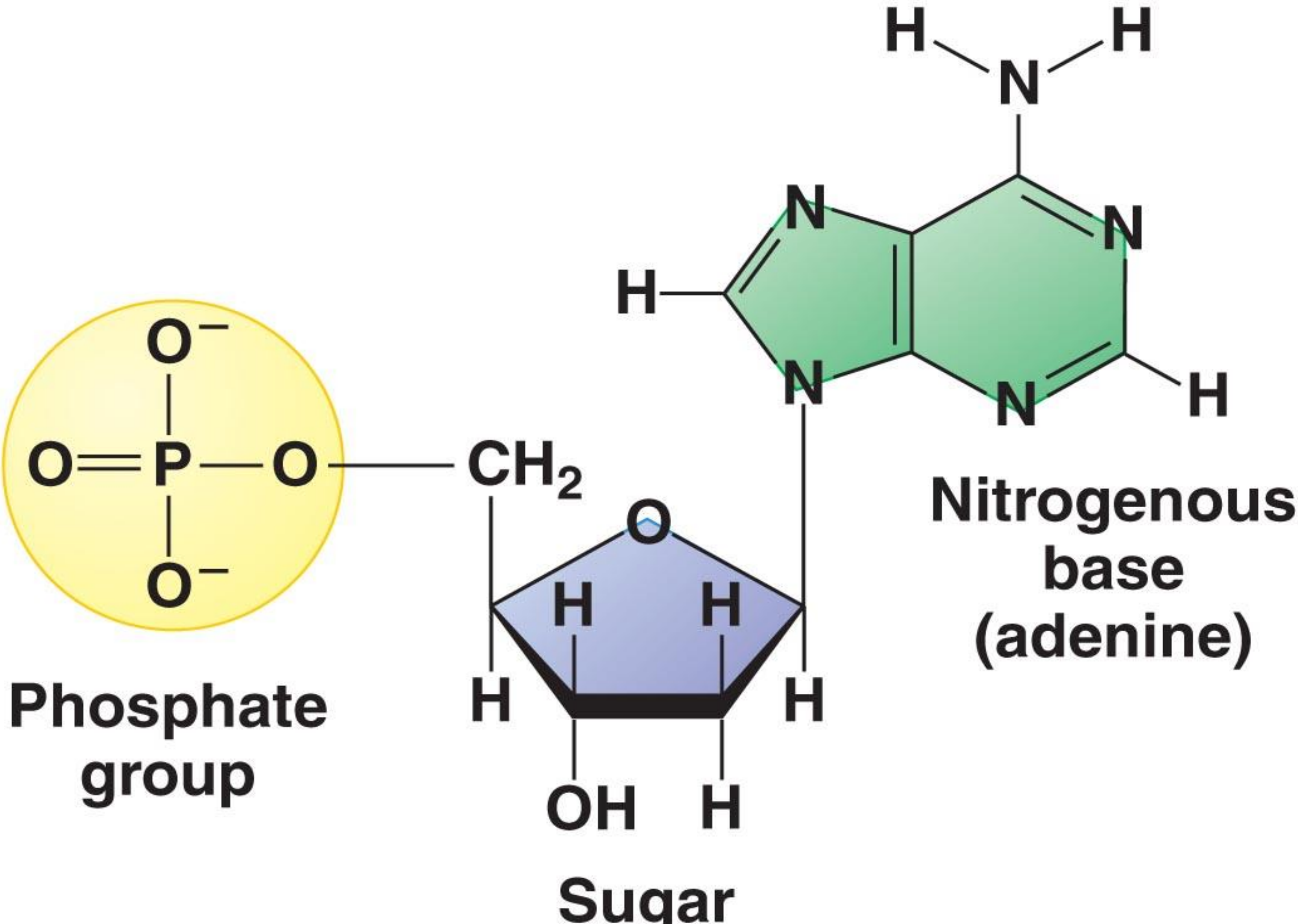
A nucleotide consists of



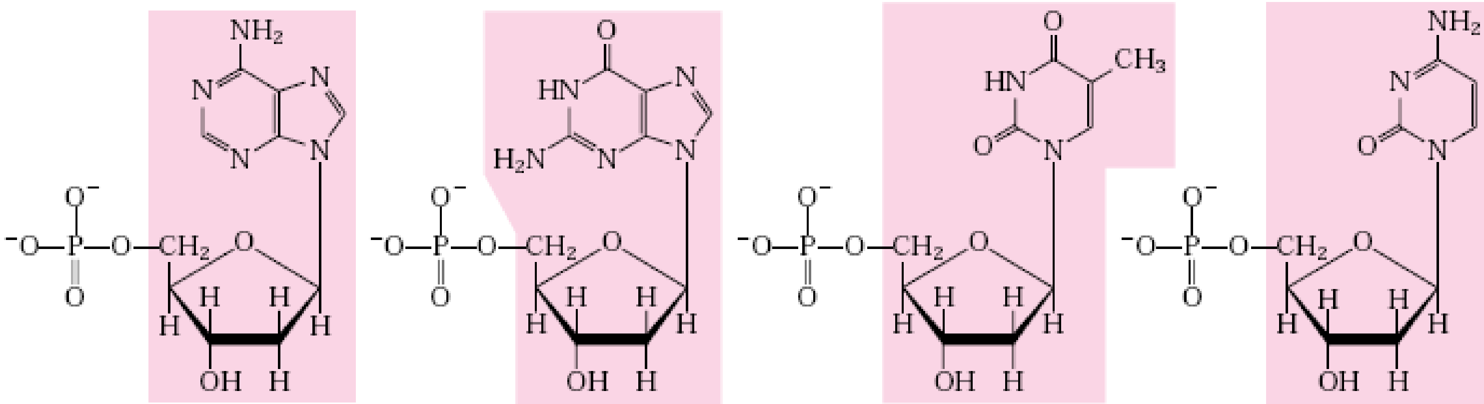
- **a nitrogenous base (purine or pyrimidine),**
- **a pentose sugar,**
- **and one or more phosphate groups.**

(nucleotide = base + pentose + phosphate)

(nucleoside = base + pentose)

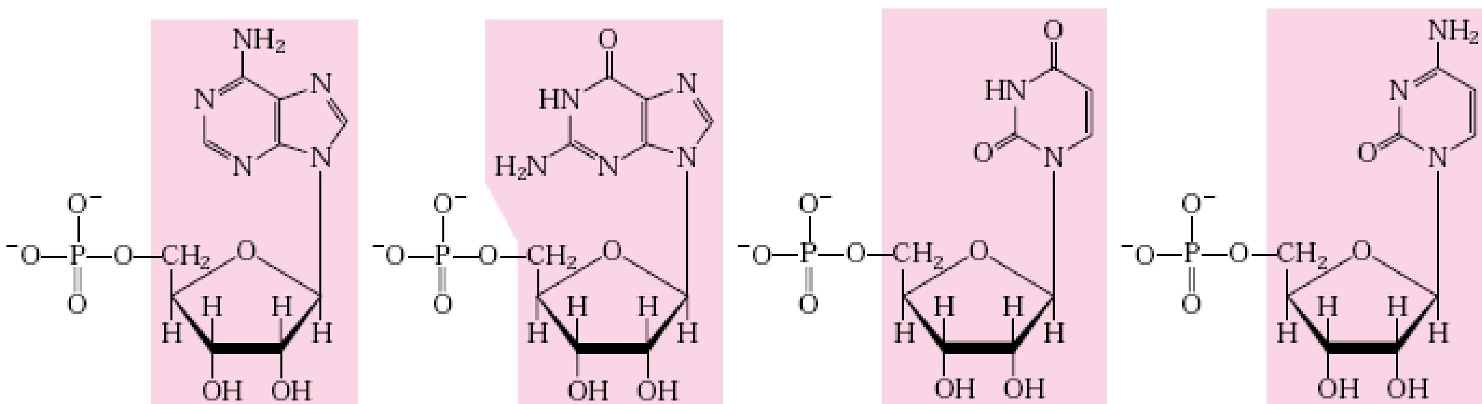


H
H
N
N
N
H
N
N
H
O⁻
O
P
O
CH2
O
O⁻
H
H
H
H
OH
H
Phosphate group
Sugar
Nitrogenous base (adenine)



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

(a) **Deoxyribonucleotides**



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

(b) **Ribonucleotides**

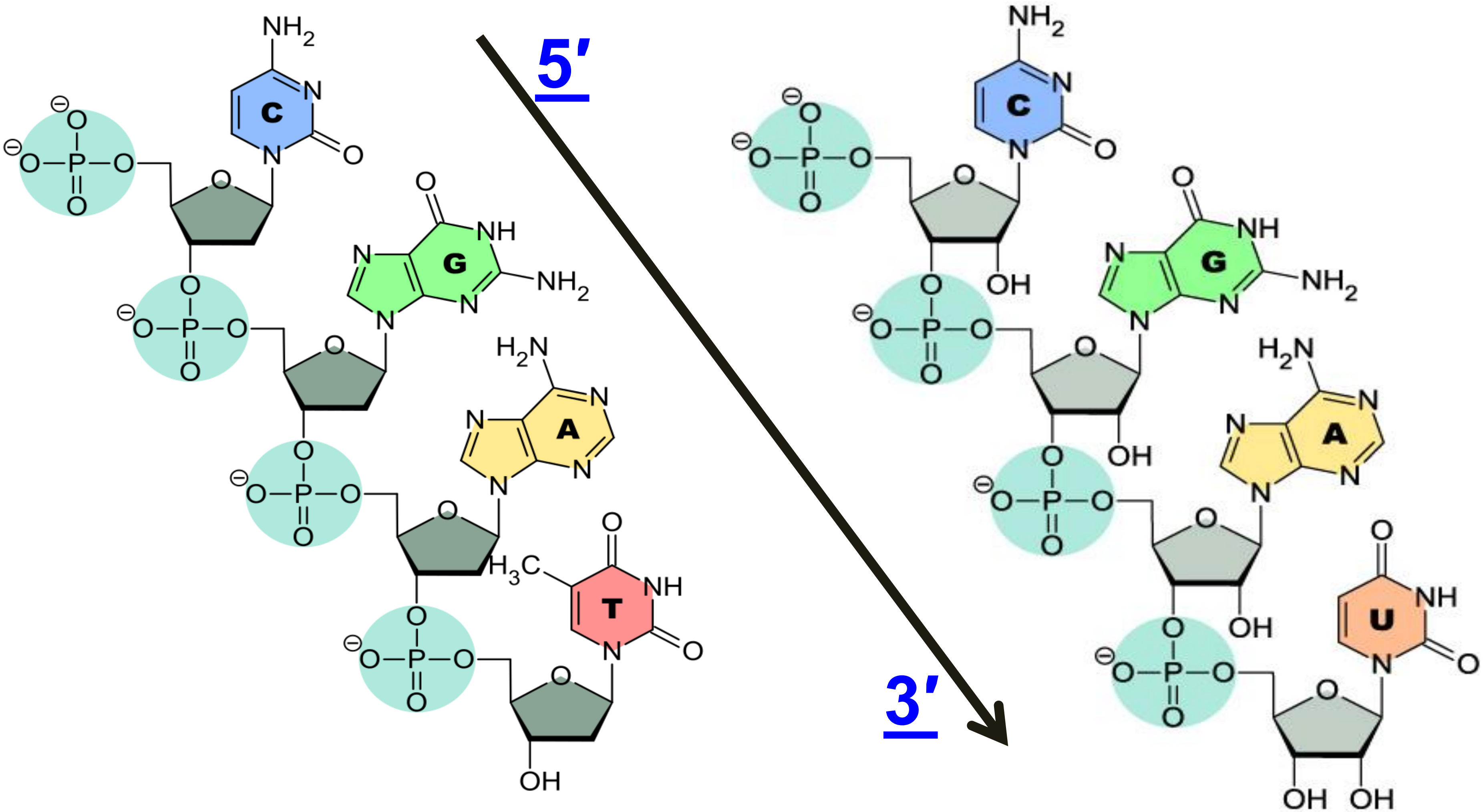
Chemical Composition of nucleic acids

DNA	RNA
Adenine, guanine, cytosine, thymine	Adenine, guanine, cytosine, uracil
Deoxyribose	Ribose
Phosphoric acid	Phosphoric acid

Differences between RNA and DNA

	RNA	DNA
Content	Ribose Adenine Gyanine Cytosine Uracil	Deoxyribose Adenine Gyanine Cytosine Thymine
Location	Cytoplasm	Nucleus
Structure	Irregular	Regular
Function	Transfer of information	Storage of information

Nucleotides of both DNA and RNA are covalently linked through phosphate-group “bridges,” in which the 5’-phosphate group of one nucleotide unit is joined to the 3’-hydroxyl group of the next nucleotide, creating a phosphodiester linkage



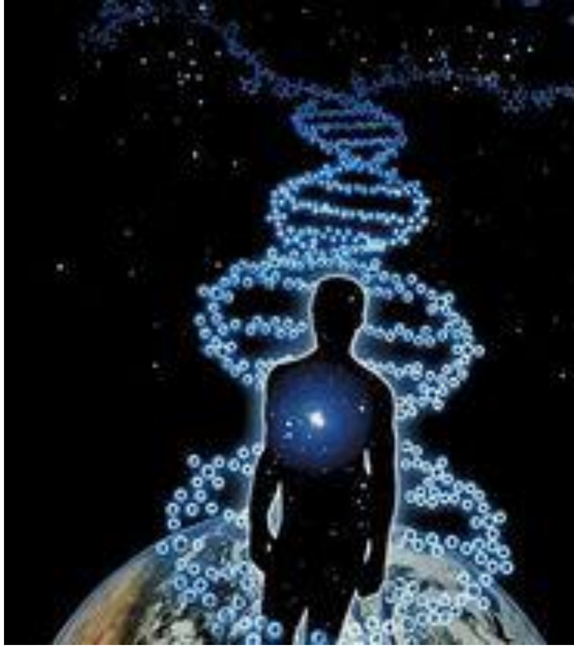
A strand of NA has a direction

<u>*5'*</u> ***(five prime)***

<u>*3'*</u>

(three prime)

DNA



contain and store
the genetic information

- **it is source of information for the synthesis of all proteins of the cell and organism**
- **provides the information inherited by daughter cell**

Erwin Chargaff and his colleagues found that the in *all* cellular DNAs, the number of adenosine residues is equal to the number of thymidine residues:

$$A = T$$

and the number of guanosine residues is equal to the number of cytidine residues:

$$G = C$$

The sum of the purine residues equals the sum of the pyrimidine residues:

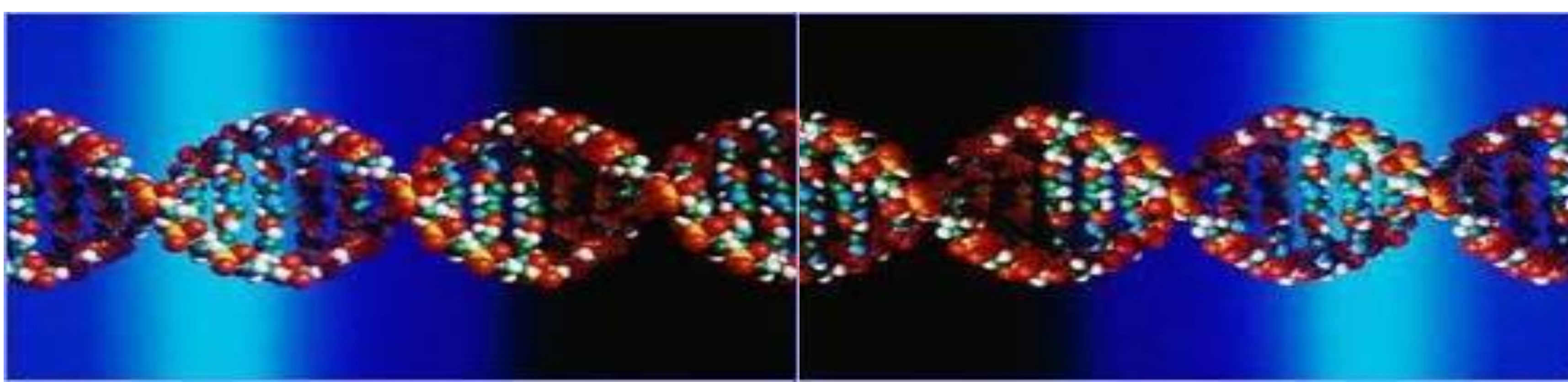
$$A + G = T + C.$$

These quantitative relationships, sometimes called "Chargaff's rules," were a key to establishing the 3D structure of DNA

In 1953 Watson and Crick postulated a 3D model of DNA structure.

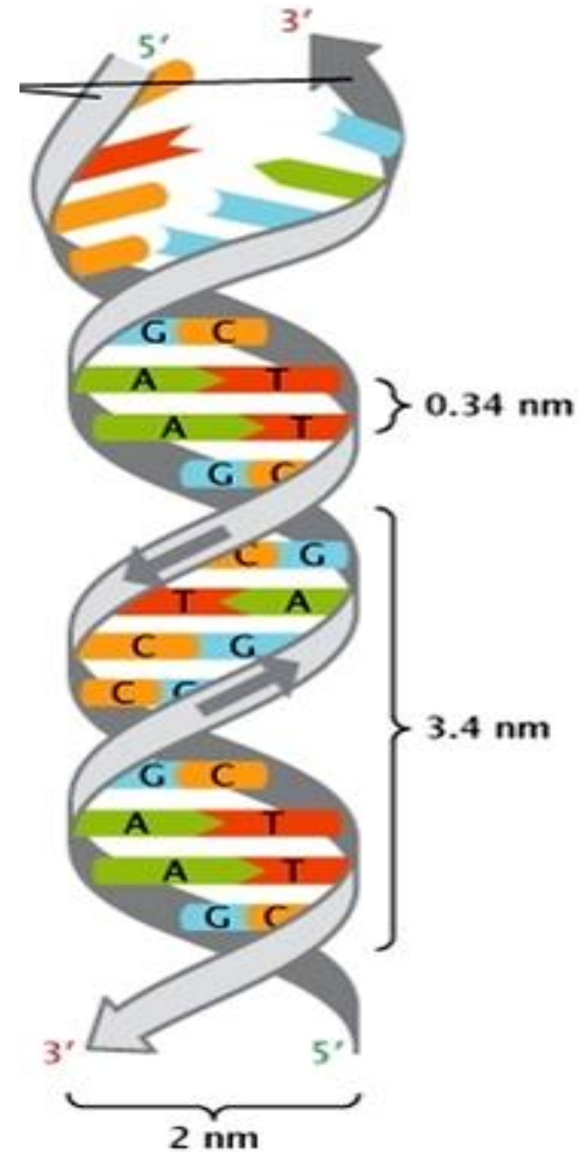
It consists of two antiparallel chains in a right-handed double-helical arrangement.

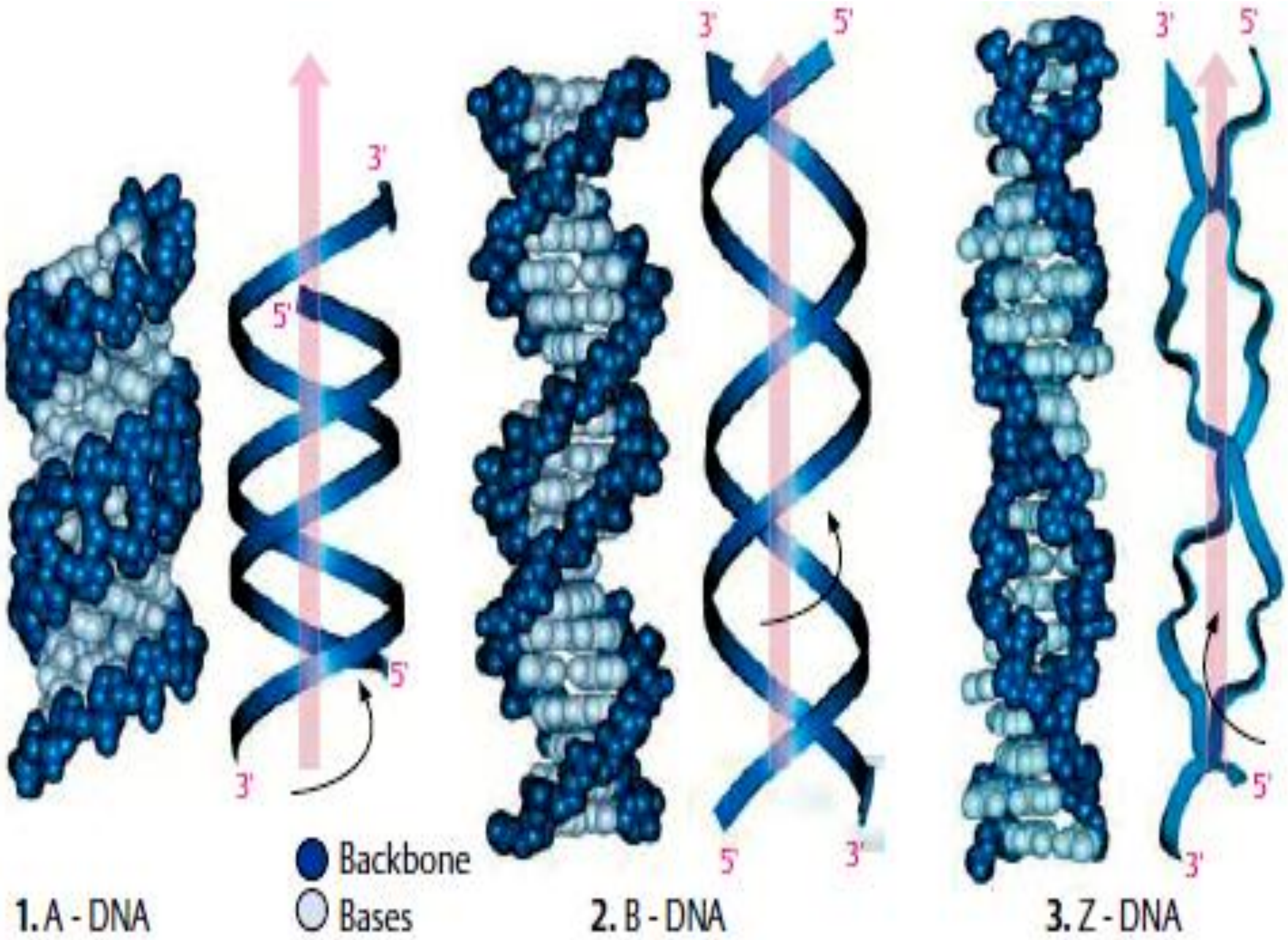
Complementary base pairs (A-T and G-C) are formed by hydrogen bonding within the helix



The base pairs are stacked perpendicular to the long axis of the double helix,

- **with a radius of 1 nm,**
- **distance spanned by one complete turn - 3.4 nm**
- **1 turn of the double helix include 10 base pairs**

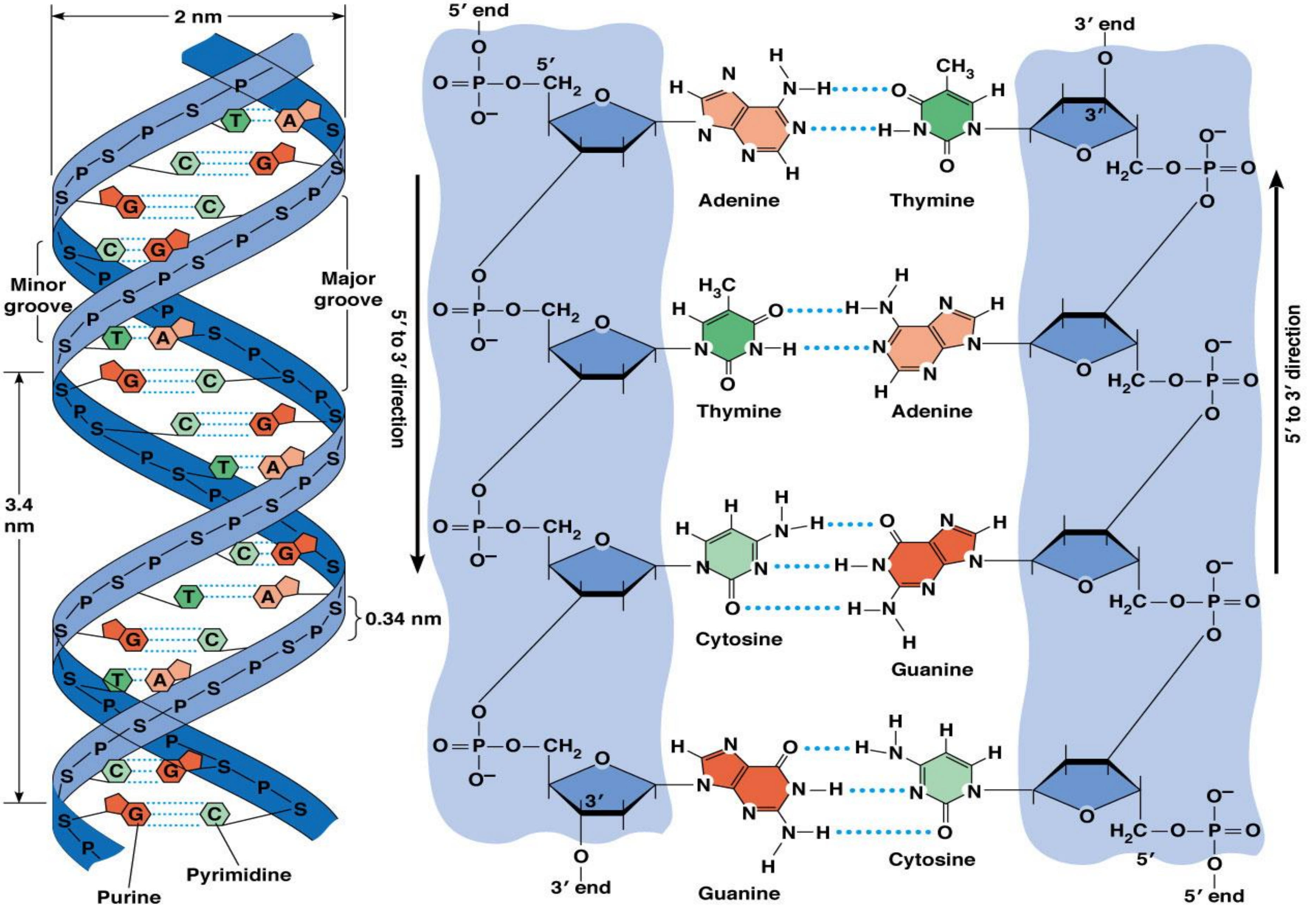



3'
5'
3'
5'
3'
3'
5'
5'
3'
3'
5'
5'
3'
Backbone
Bases
1. A - DNA
2. B - DNA
3. Z - DNA

The DNA double helix is stabilized primarily by two forces:

1. **hydrogen bonds between nucleotides**

2. **base-stacking interactions among the aromatic nucleobases**



(a) Double helix

(b) Antiparallel orientation of strands

Chromatin is the combination of DNA and proteins that make up the contents of the nucleus of a cell.

The functions of chromatin are:

- **to package DNA into a smaller volume to fit in the cell,**
- **to strengthen the DNA to allow mitosis,**
- **to prevent DNA damage,**
- **to control gene expression and DNA replication.**

The primary protein components of chromatin are

histones

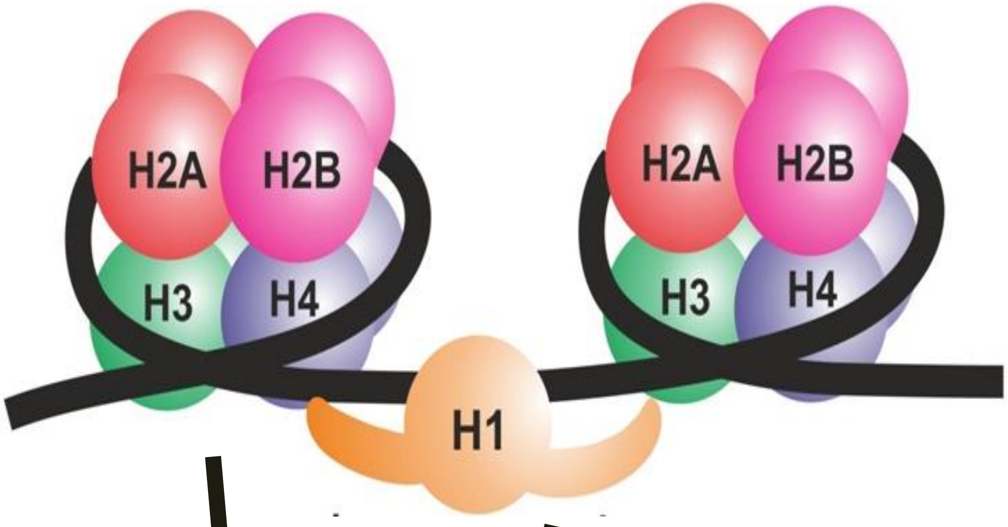
that compact the DNA.

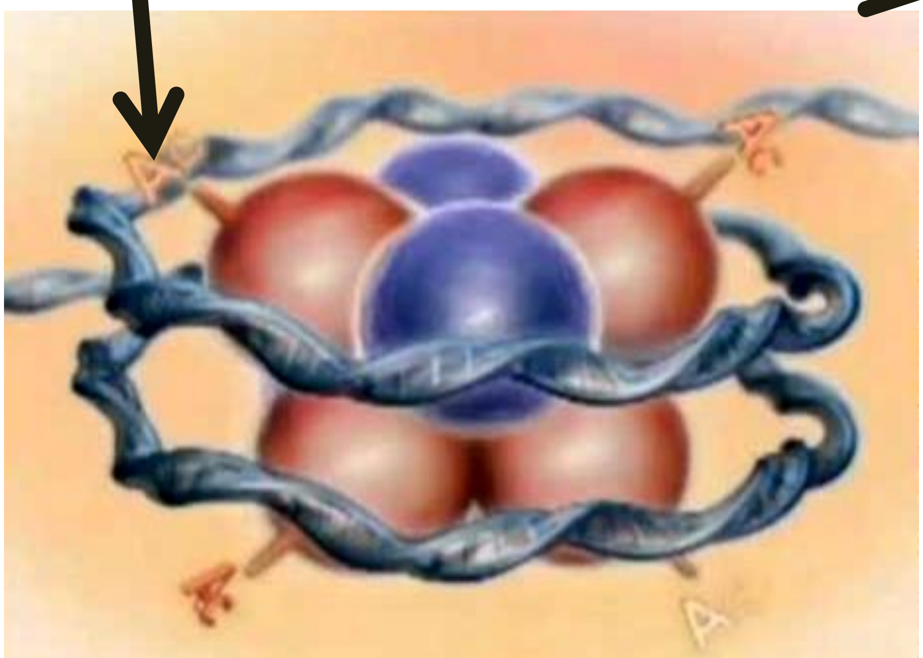
Chromatin is only found in eukaryotic cells.

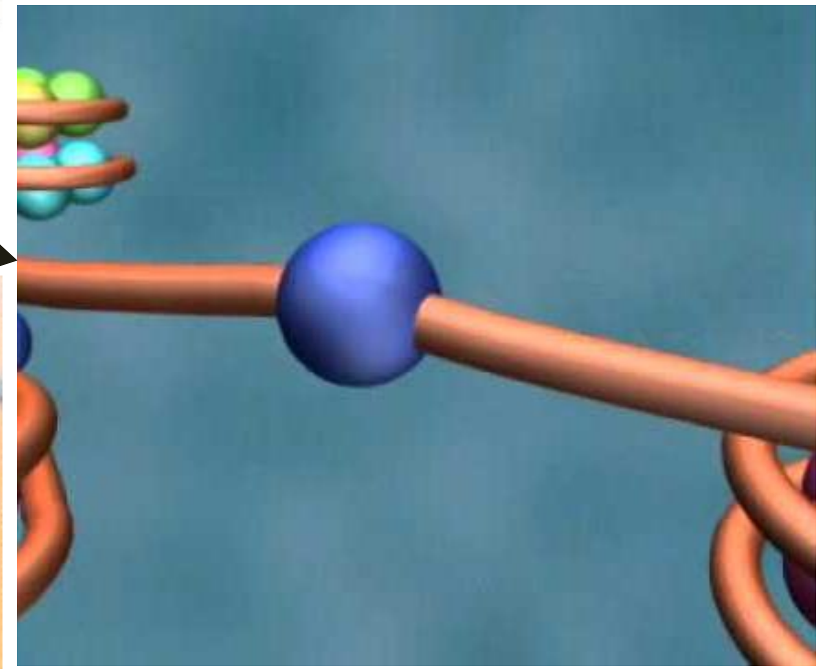
There are four levels of chromatin organization:

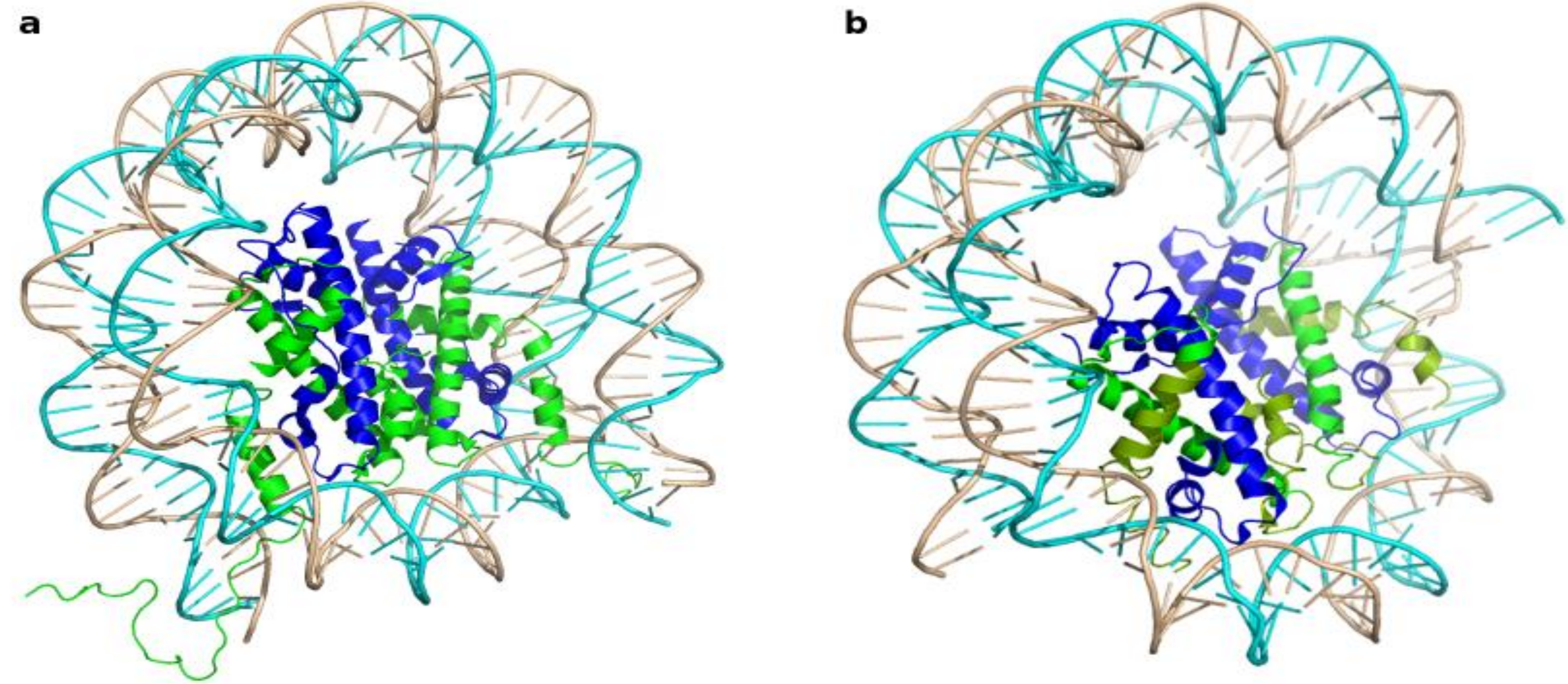
DNA wraps around histone proteins forming nucleosomes
(the "beads on a string“)

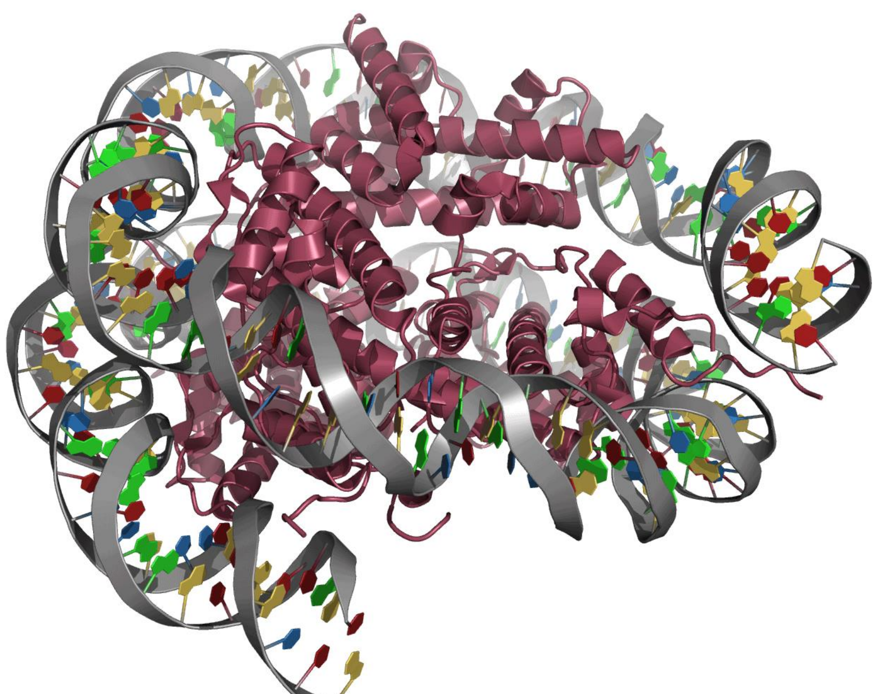
Chromatine (1)

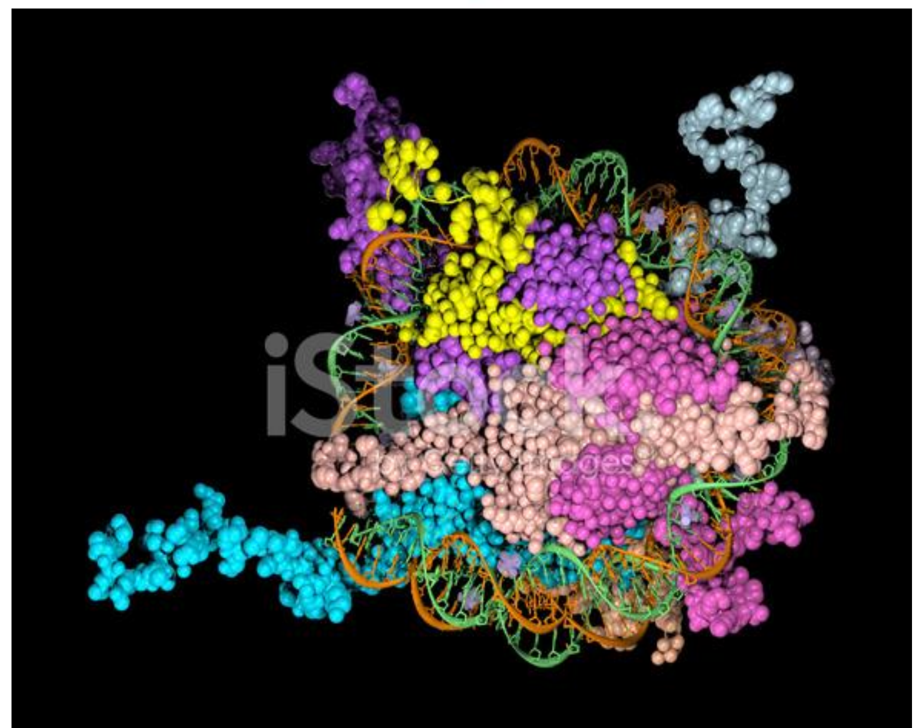




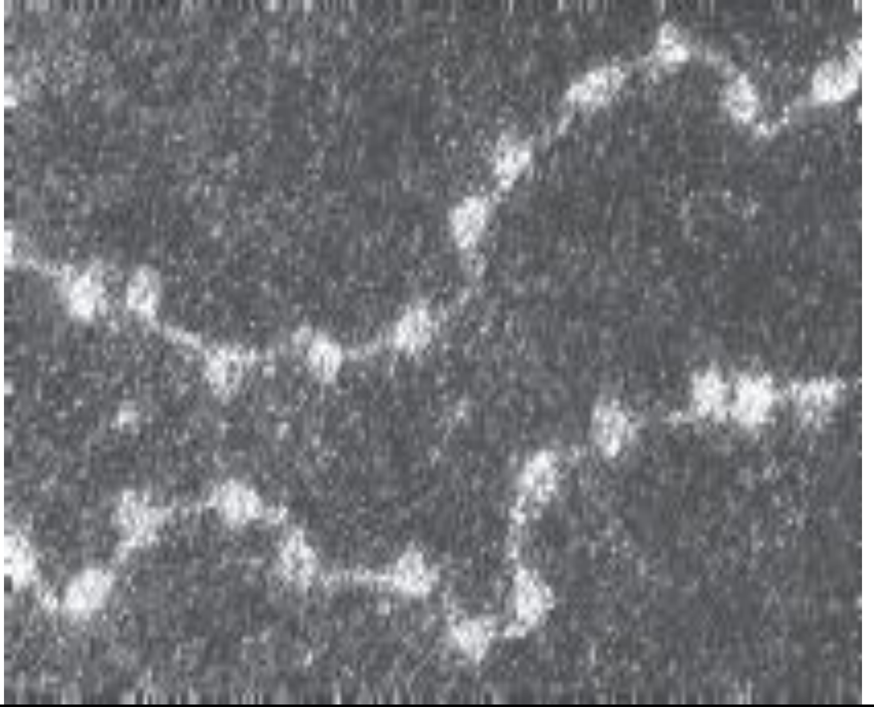


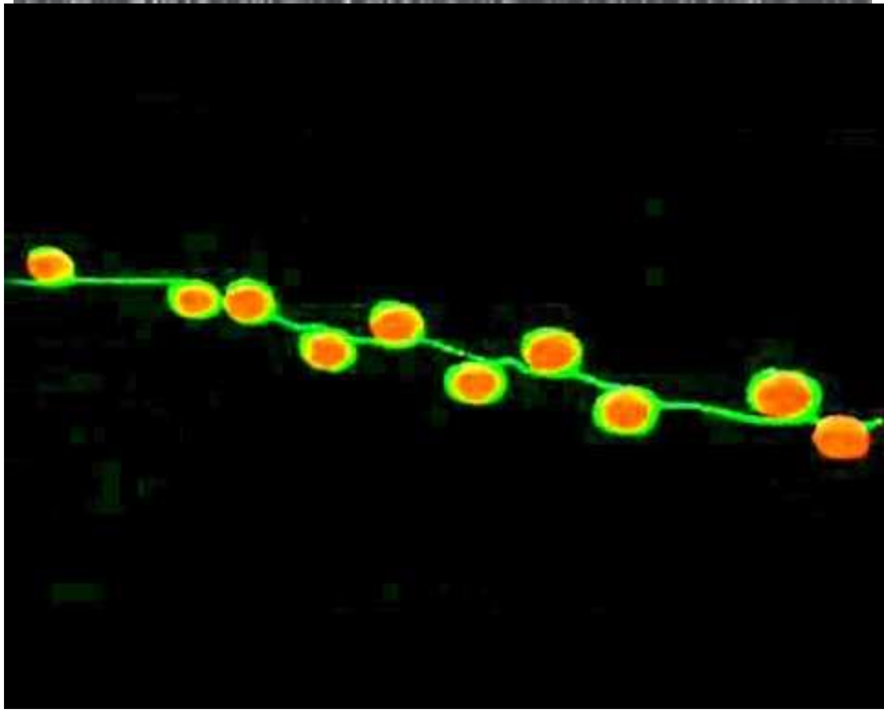

a
b



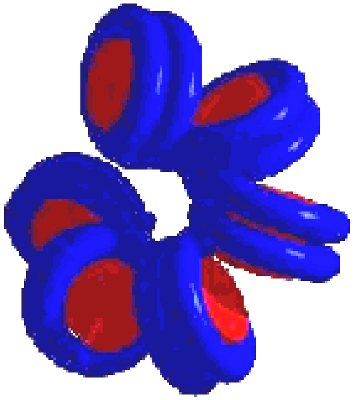


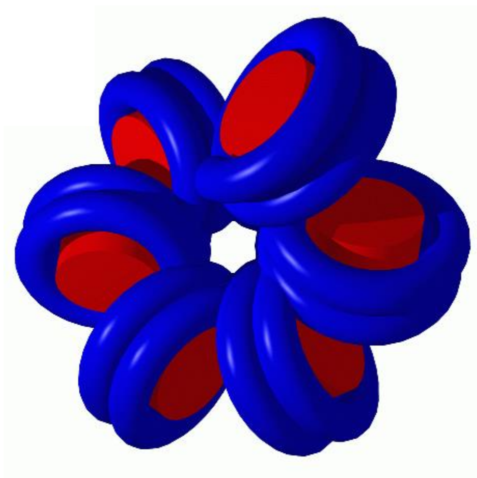
Chromatine (1)

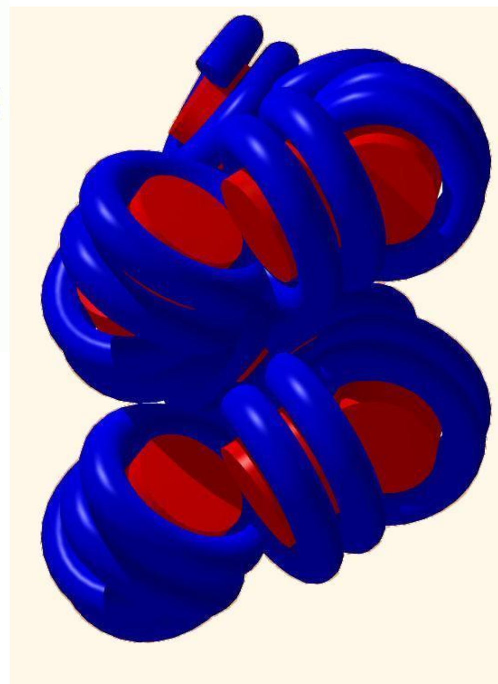


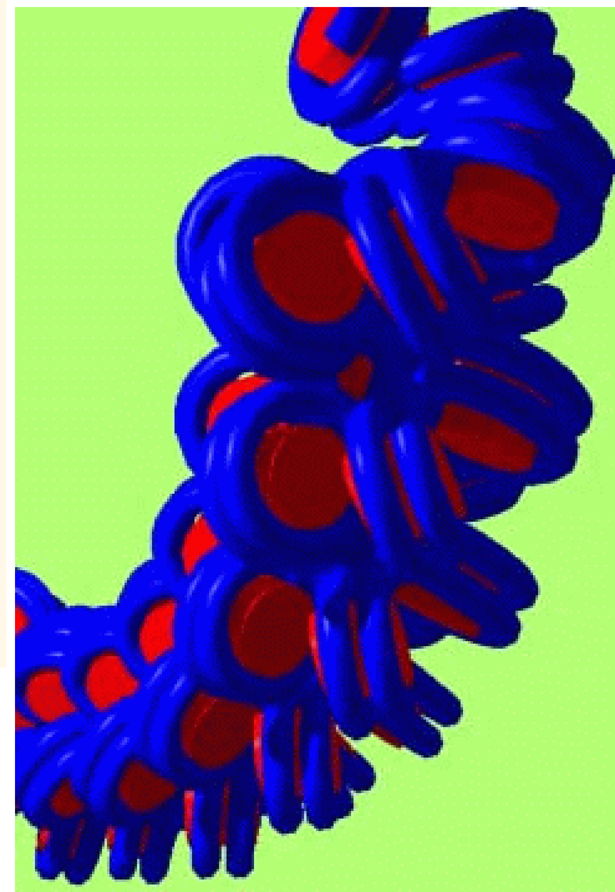


This fibril is supercoiled and form 30-nm chromatine fiber



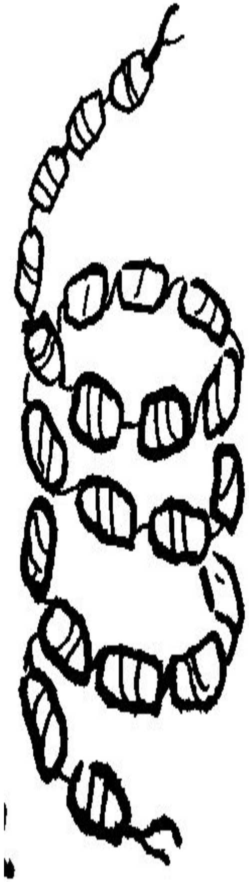






Chromatine (2)

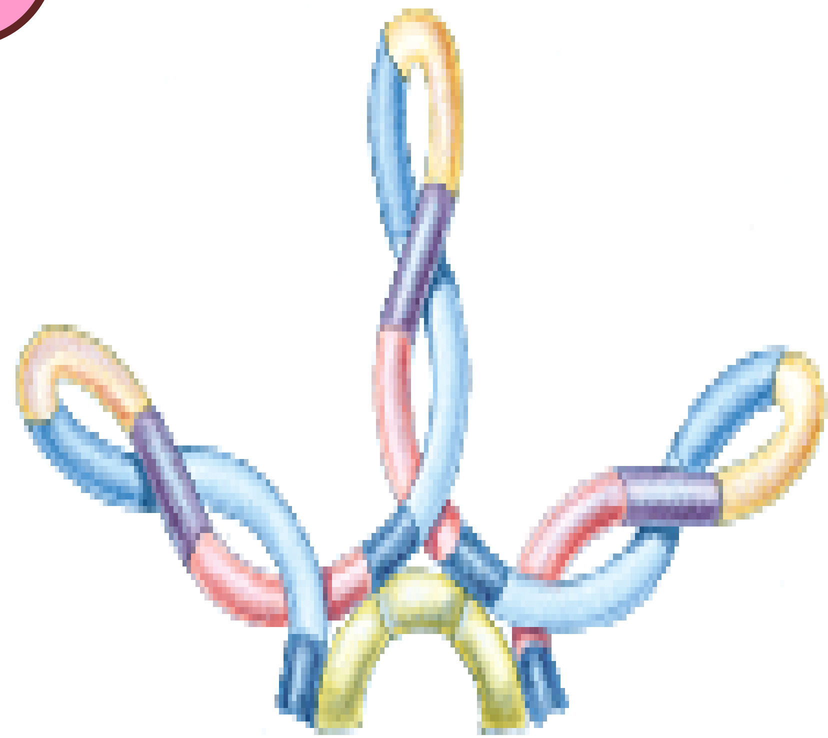
Chromatine (2)



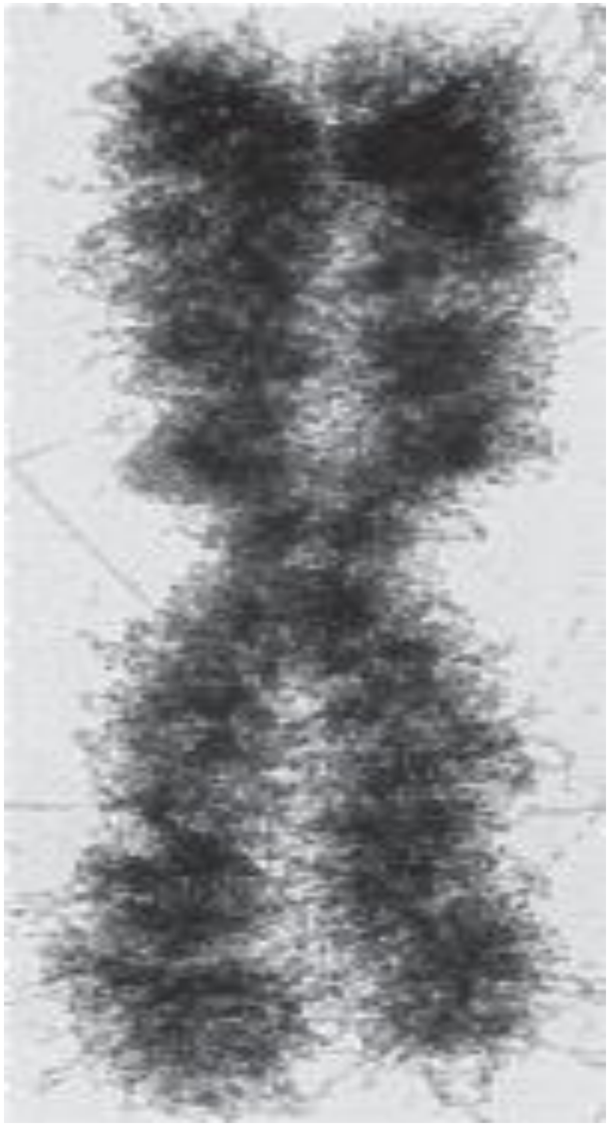
The 30-nm fiber must be compacted in length another 100-fold

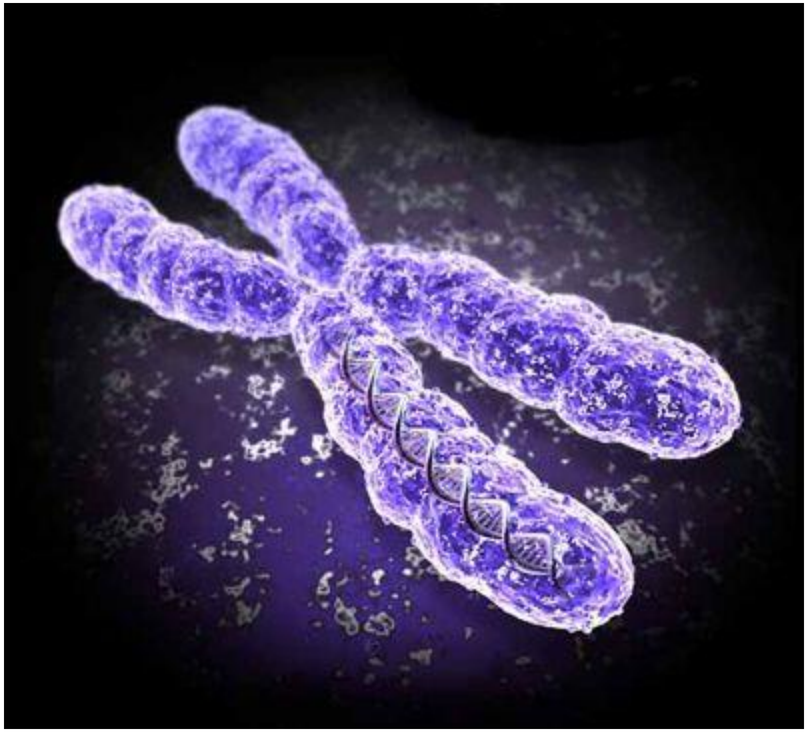
It forms condensed and non-condensed loops anchored in supporting matrix

Chromatine (3)

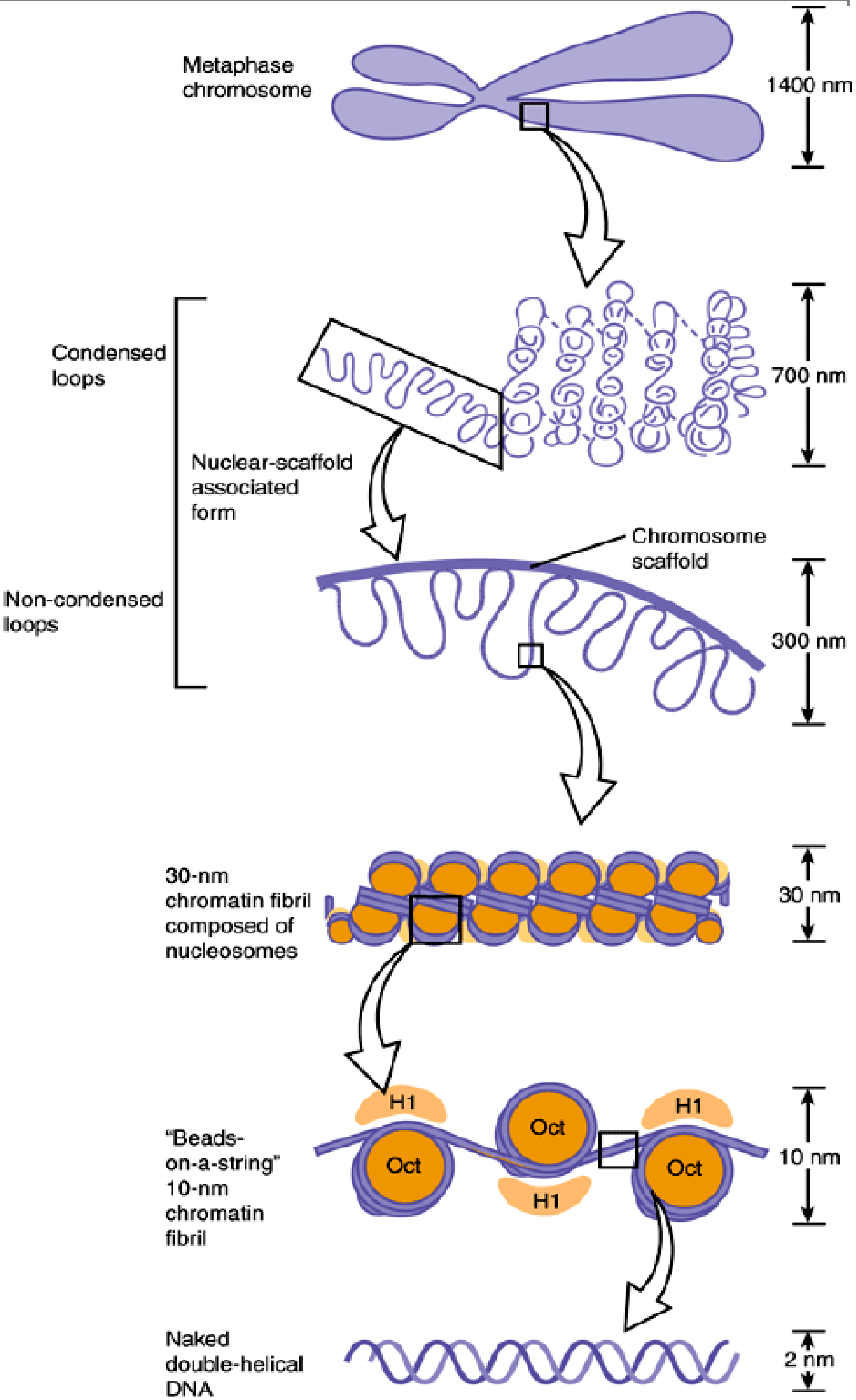


Chromatine (4)



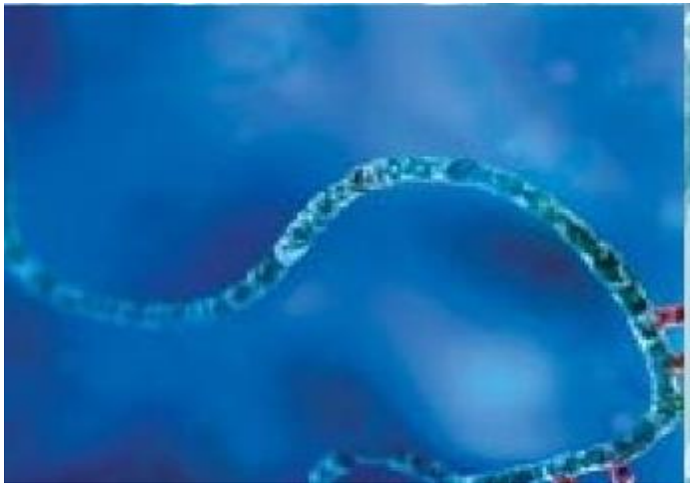


Metaphase chromosome



Metaphase chromosome
1400 nm
Condensed loops
700 nm
Nuclear-scaffold associated form
Chromosome scaffold
Non-condensed loops
300 nm
30-nm chromatin fibril composed of nucleosomes
30 nm
H1
Oct
H1
"Beads-on-a-string" 10-nm chromatin fibril
10 nm
Naked double-helical DNA
2 nm

Messenger RNA (mRNA)



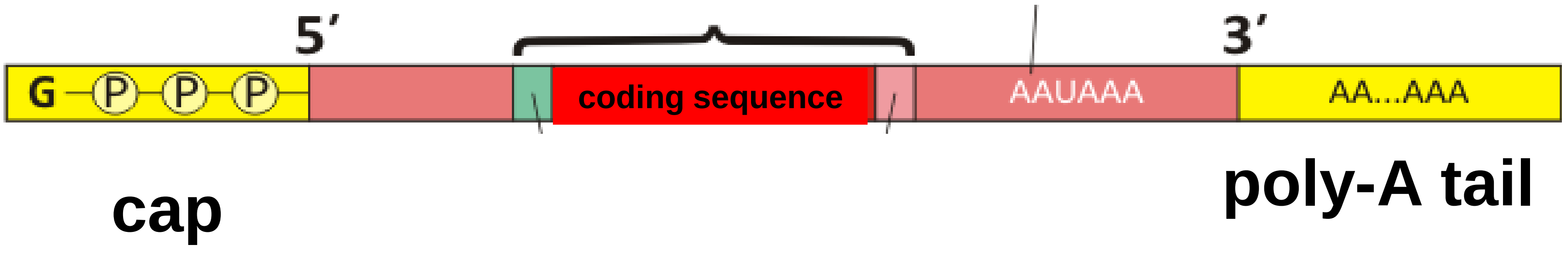
- **messenger conveying the informatiom from the gene to the protein synthesizing machinery**

- **serves as a template for protein synthesis**

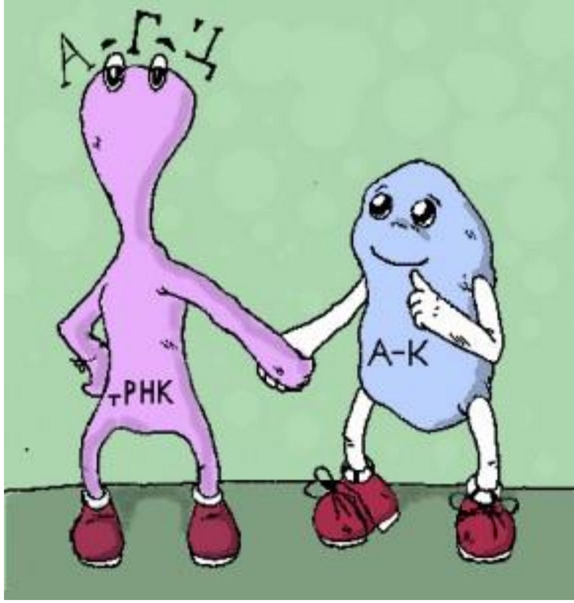
mRNA

- **5' terminal is "capped" by a 7-methilguanosine triphosphate**

- **3'-hydroxil terminal has an attached polymer of 20-250 adenilate residues**



tRNA



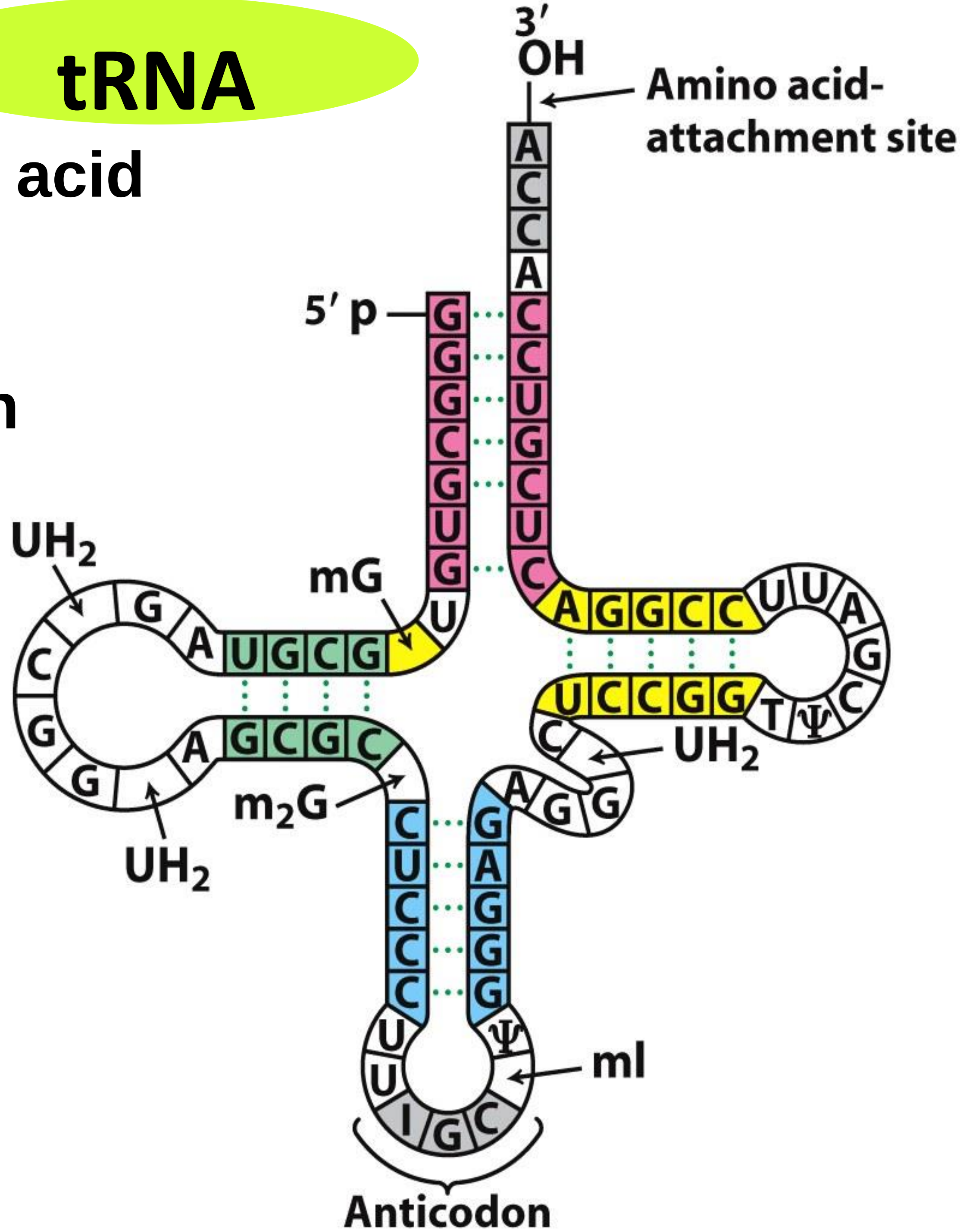
- **transfers a specific amino acid to a growing polypeptide chain at the ribosomal site of protein synthesis during translation.**
- **serve as adapter for the translation of the information in the sequence of nucleotides of the mRNA into specific aminoacids**

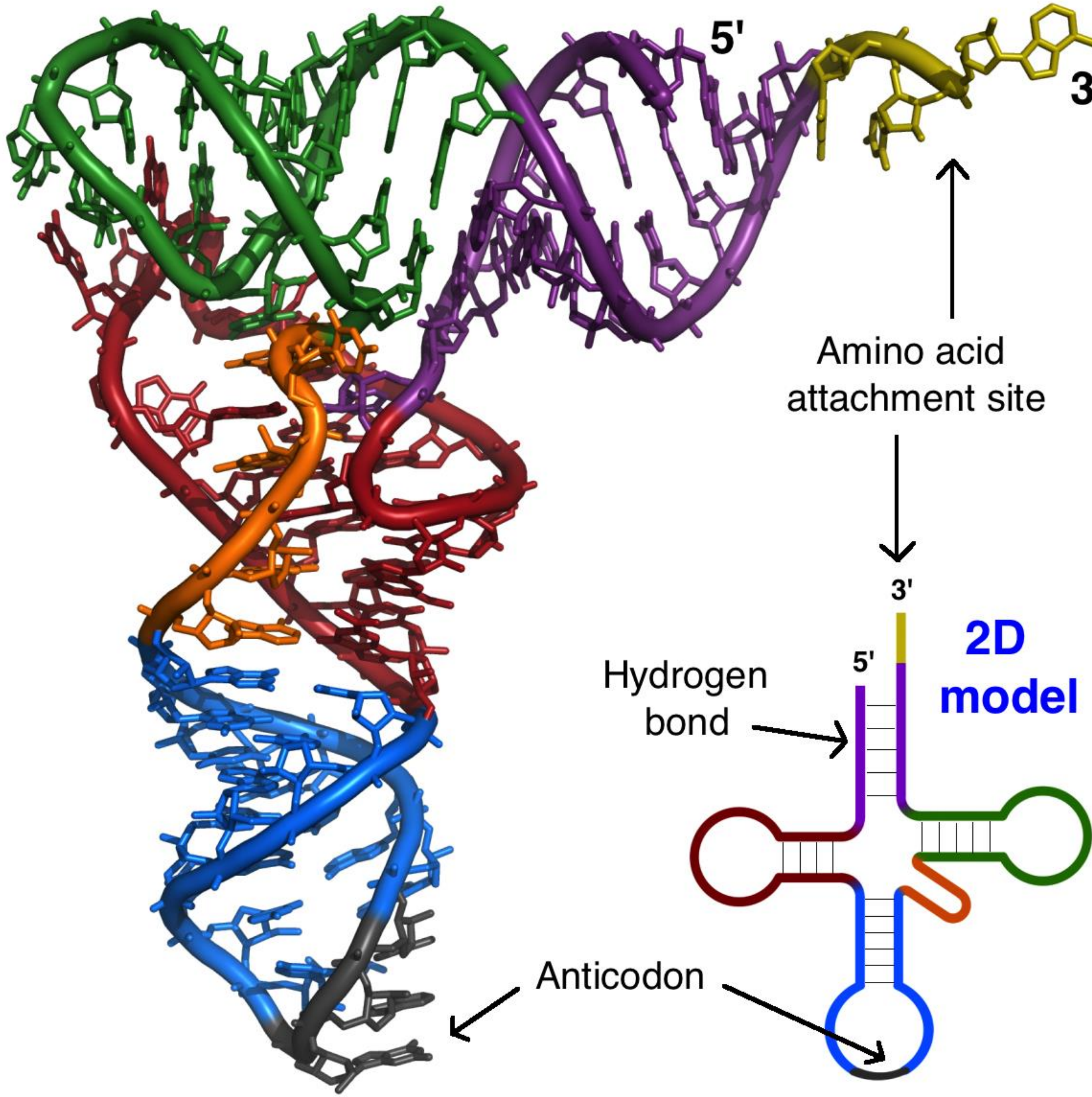
tRNA

- **length from 74 to 95 nucleotides**
- **the primary structure of all tRNA allows extensive folding and intrastrand complementarity to generate a secondary structure like a clover leaf**

tRNA

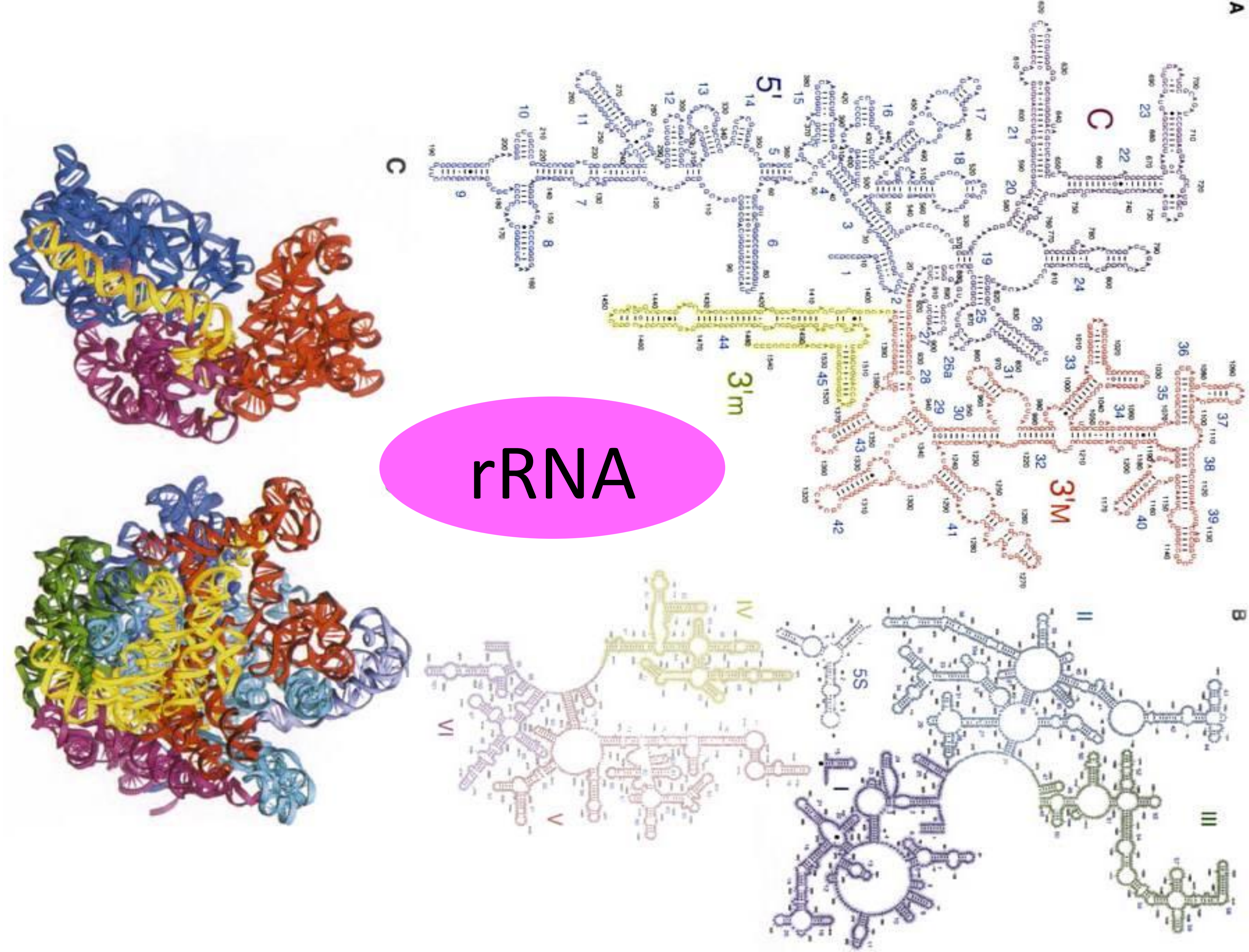
It has sites for amino acid attachment and
an anticodon region
for codon recognition
that binds
to a specific
sequence
on the mRNA



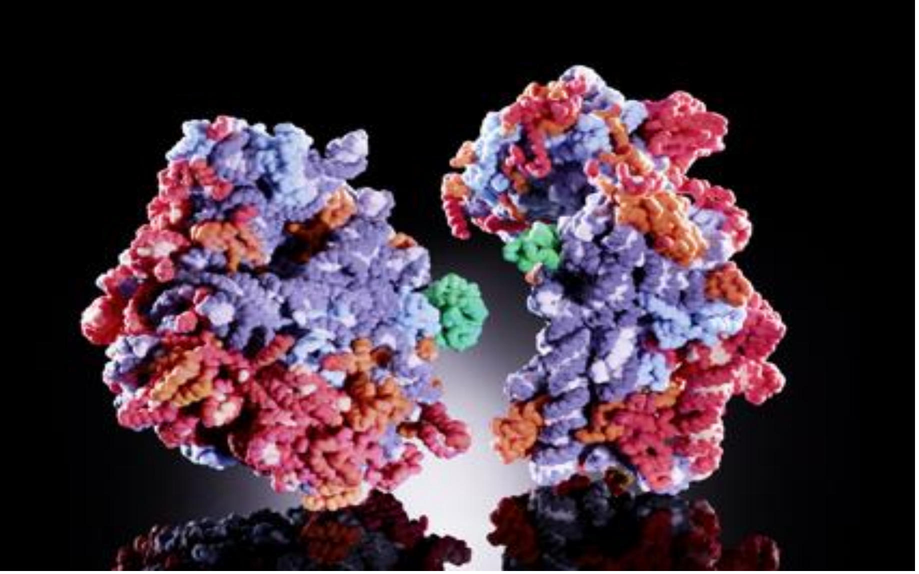

5'
3'
Amino acid attachment site
3'
5'
2D model
Hydrogen bond
Anticodon

rRNA

- **is the structural and catalytic component of the ribosomes**.



rRNA



Structure of ribosomes

Ribosome 80S

60 S subunits 40 S

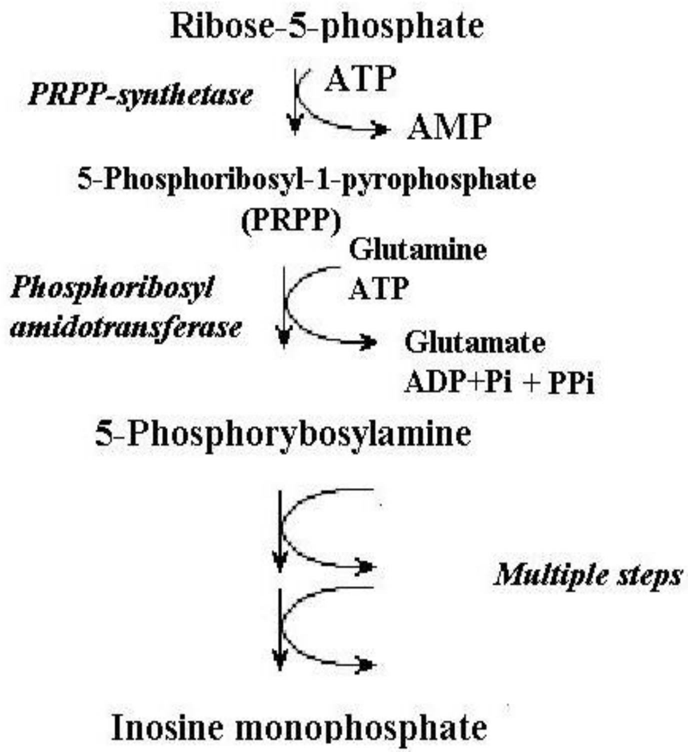
5.8 S, 5 S, 28 S rRNA

+ 50 proteins

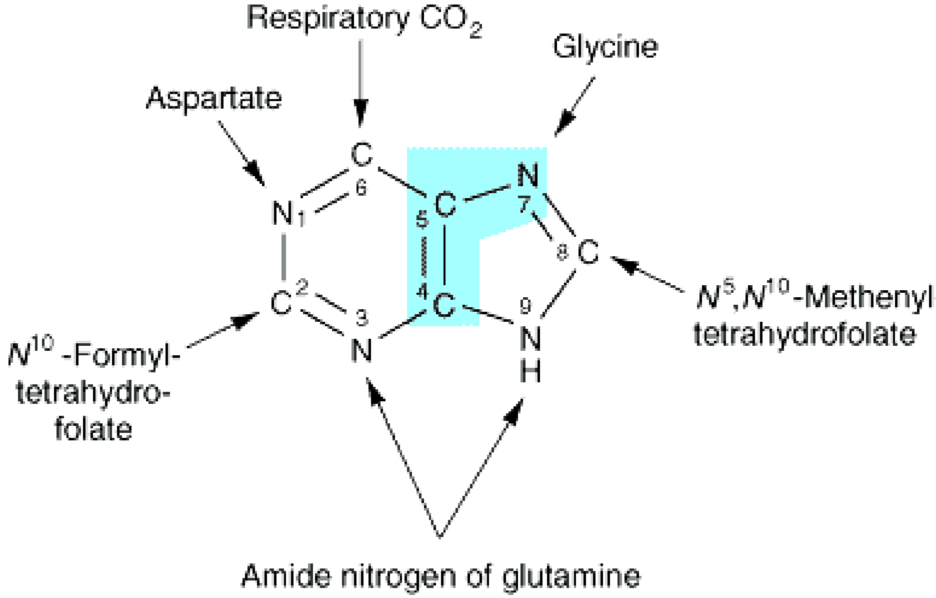
18 S rRNA

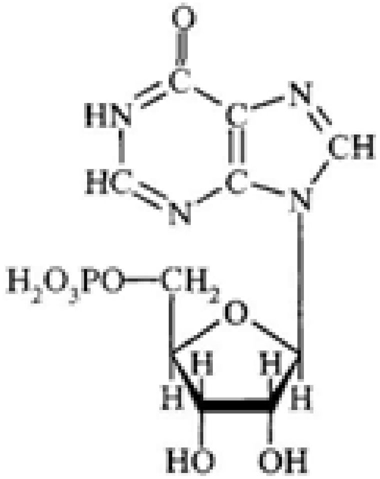
+ 33 proteins

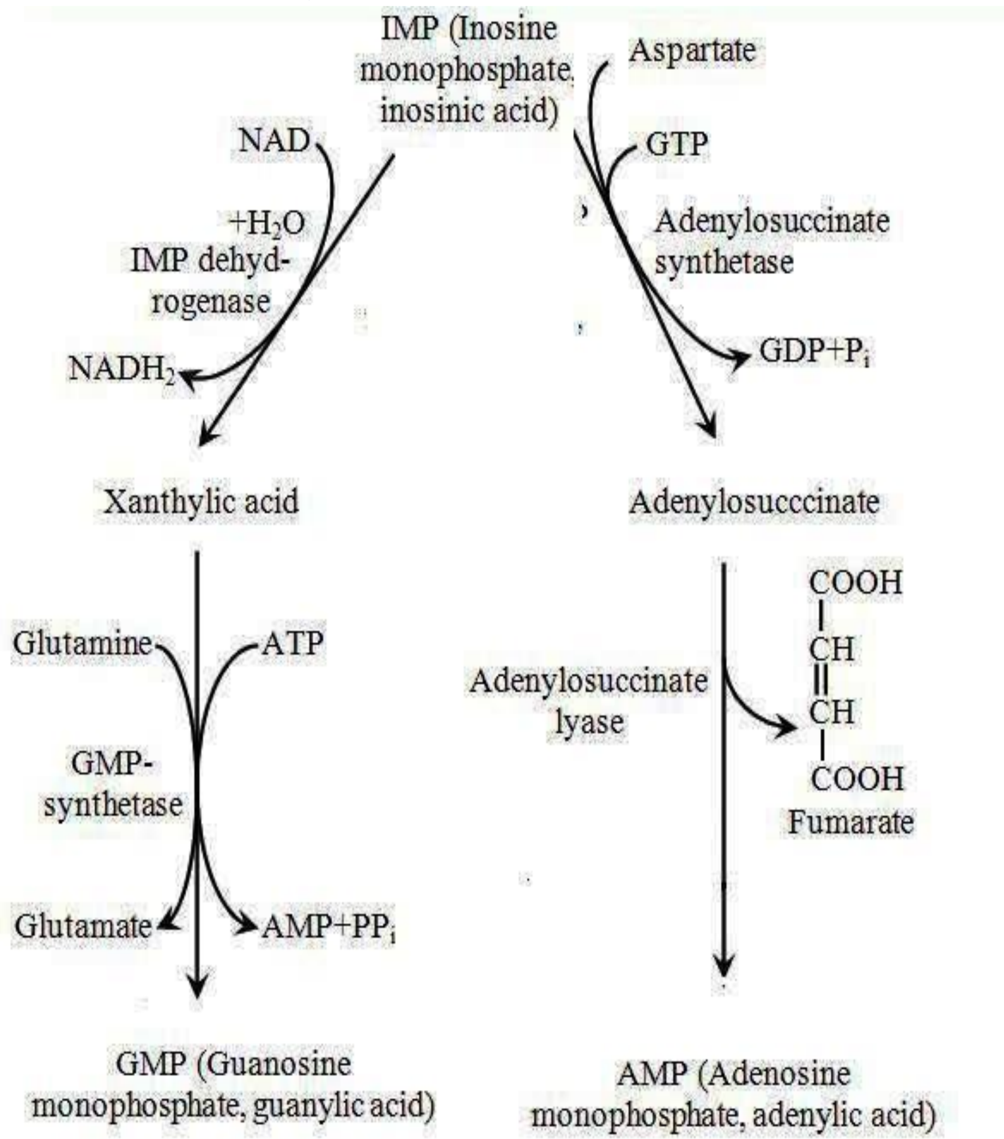
Biosynthesis of purine nucleotides



Origin of atoms in purine ring






IMP (Inosine monophosphate, inosinic acid)
NAD
$+H_2O$
IMP dehyd-rogenase
$NADH_2$
Aspartate
GTP
Adenylosuccinate synthetase
$GDP+P_i$
Xanthylic acid
Adenylosucccinate
Glutamine
ATP
GMP-synthetase
Glutamate
$AMP+PP_i$
Adenylosuccinate lyase
COOH
CH
CH
COOH
Fumarate
GMP (Guanosine monophosphate, guanylic acid)
AMP (Adenosine monophosphate, adenylic acid)

Regulation of purine synthesis