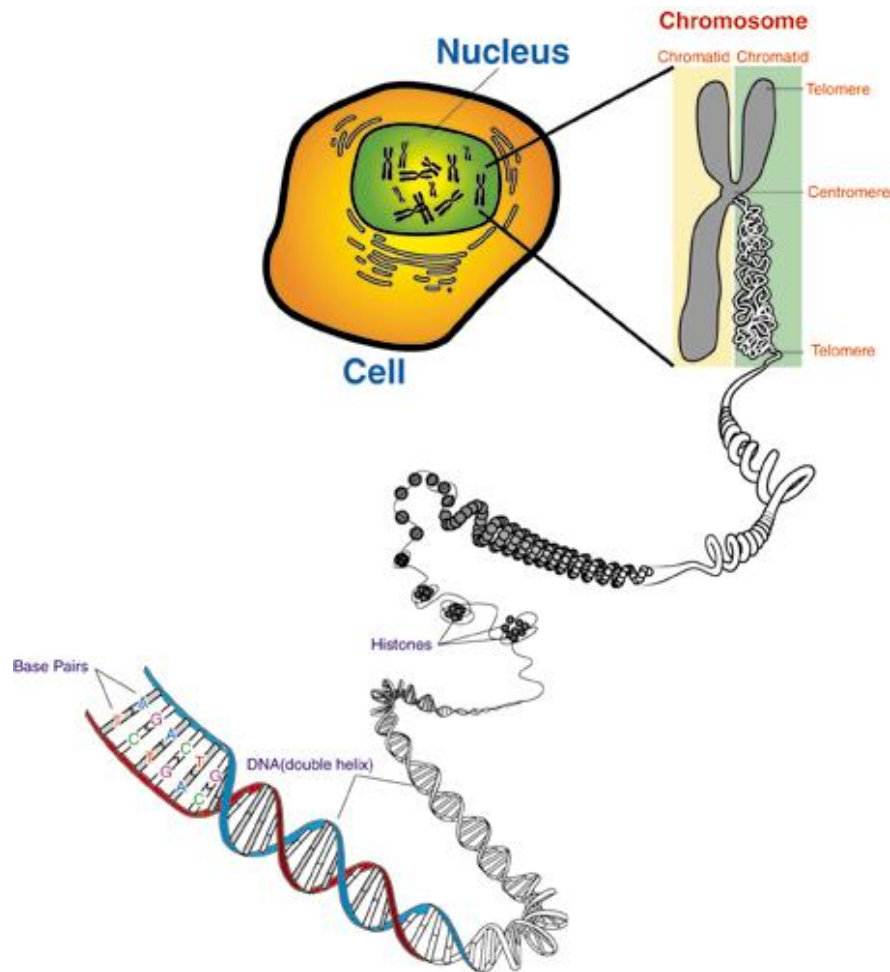


Chemistry of Nucleotides & Nucleic Acids



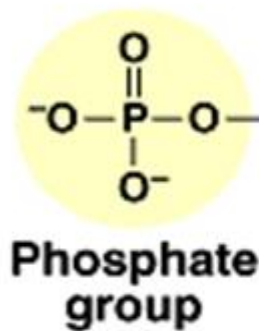
Sopit Wongkham
Department of Biochemistry
Faculty of Medicine
Khon Kaen University
Nov, 2014

- 
- บอกบทบาทความสำคัญทางชีวภาพของนิวคลีโอไทด์ พร้อมตัวอย่างได้
 - บอกโครงสร้าง องค์ประกอบ ชื่อพันธะเคมี และชนิดของนิวคลีโอไทด์และความสำคัญได้
 - บอกลักษณะที่สำคัญของแบบจำลองโครงสร้าง DNA ของ Watson-Crick ได้
 - บอกชนิดของ RNA และหน้าที่ทางชีวภาพของ mRNA, rRNA และ tRNA ได้

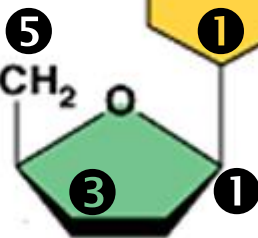
Nucleo.....

Nucleo.....

phosphoester

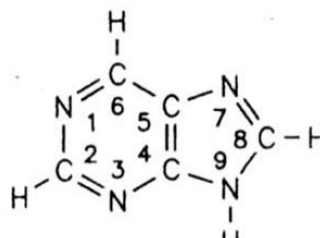


Nitrogenous base

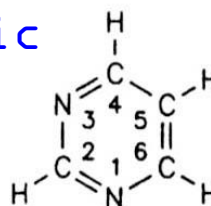
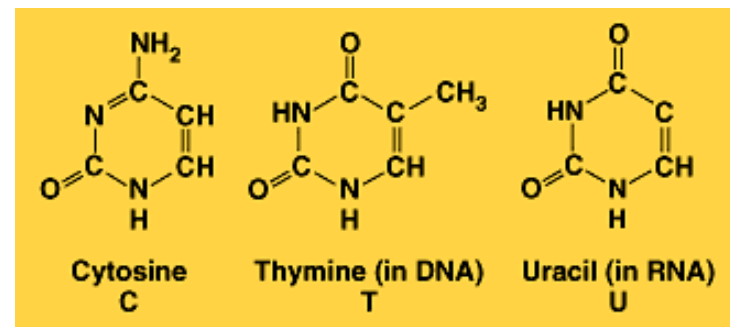
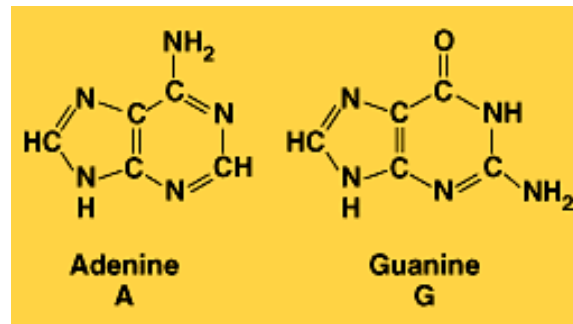


Pentose sugar

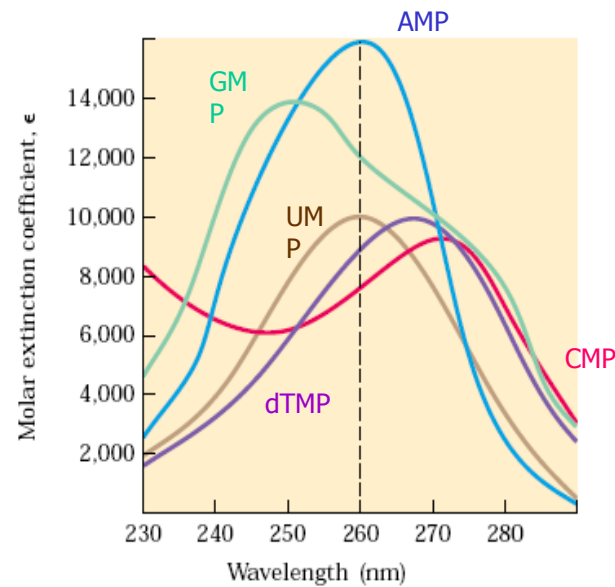
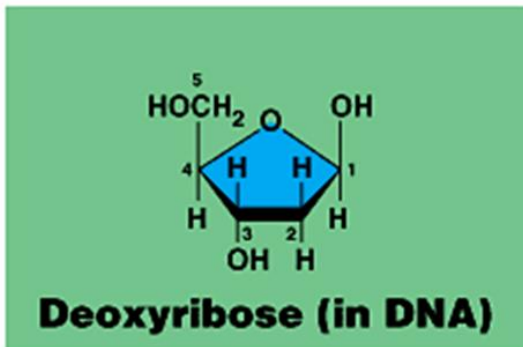
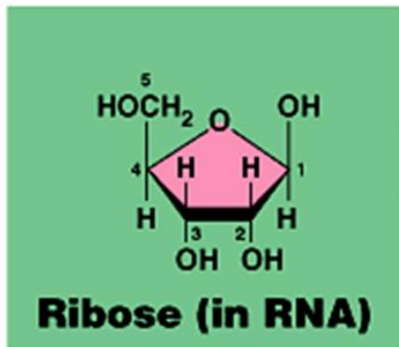
glycosidic



Purines



Pyrimidines





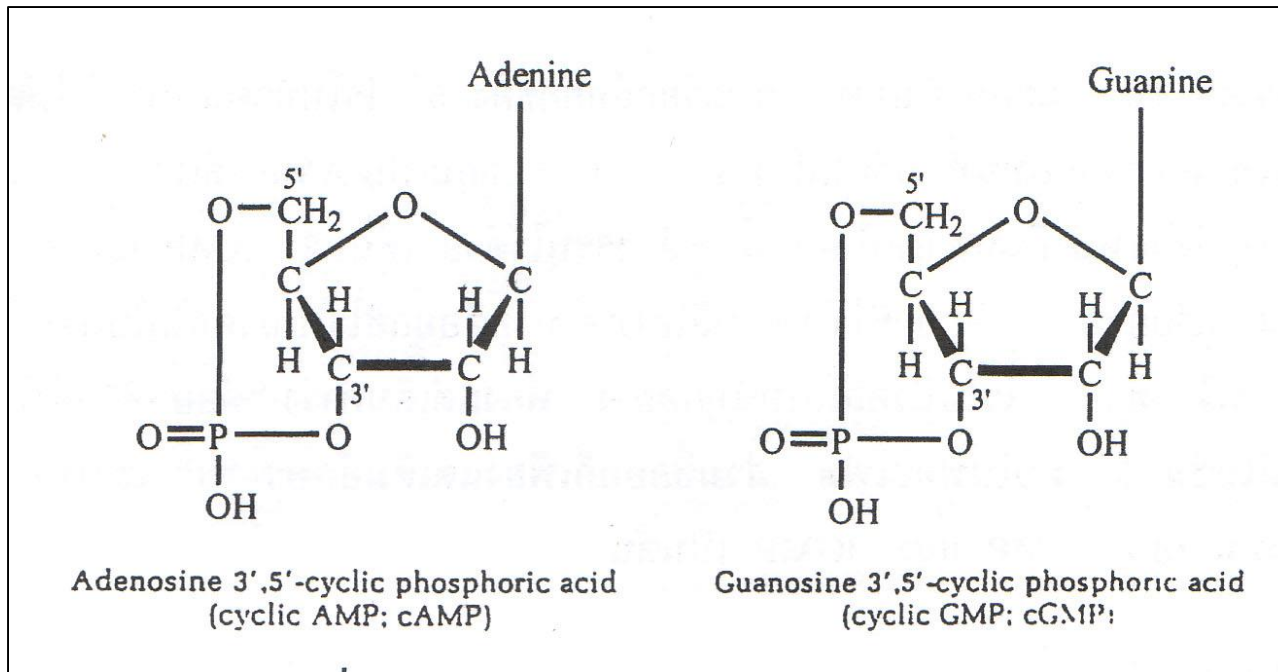
Base	Ribonucleoside	Deoxyribonucleoside
Adenine	Adenosine	Deoxyadenosine
Guanine	Guanosine	Deoxyguanosine
Cytosine	Cytidine	Deoxycytidine
Uracil	Uridine	-
Thymine	-	Thymidine
Hypoxanthine	Inosine	Deoxyinosine

Adenosine-5'-monophosphate (AMP)

Adenosine-5'-triphosphate (ATP)

Deoxyadenosine-5'-monophosphate (dAMP)

Cyclic nucleotides



cAMP

cGMP

ทำหน้าที่เป็น second messenger ในการส่งสัญญาณของ hormone บางชนิด



Biological roles of nucleotides

1. Building block :

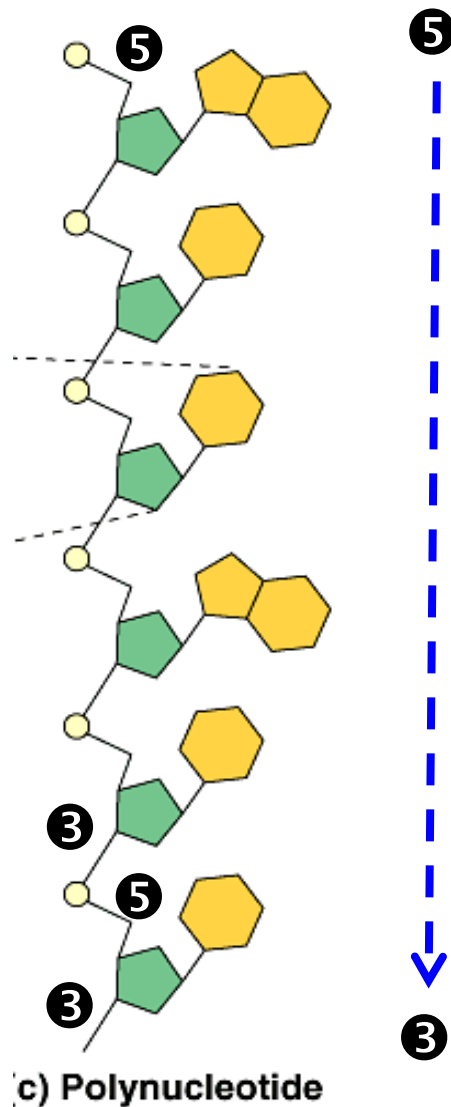
RNA (ribonucleotide: mRNA, tRNA, rRNA),

DNA (.....ribonucleotide)

2. Metabolic energy : **ATP**,

3. Second messenger: **cAMP, cGMP**

4. Coenzyme: **FAD⁺, NAD⁺, NADP⁺**



Phosphodiester Bonds (linkage)
link successive nucleotides in nucleic
Acids **5'→3'**

The **backbones** of both DNA & RNA are **hydrophilic (polar)**

- The hydroxyl groups of the sugar residues can form hydrogen bonds with water
- The phosphate groups are completely ionized and negatively charged at pH 7 (neutralized by ionic interactions with positive charges on proteins, metal ions, and polyamines)

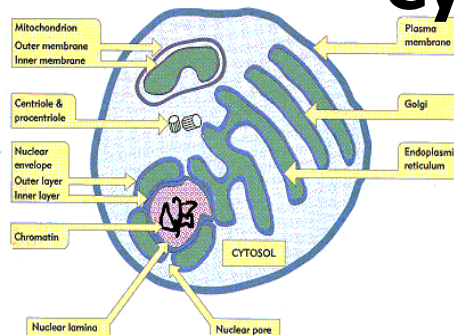


Nucleotides as the building blocks of polynucleotide (nucleic acids) that store genetic information

Deoxyribonucleic acid (**DNA**) contains specific set of genetic information called '.....' that composes of many basic units called '.....'

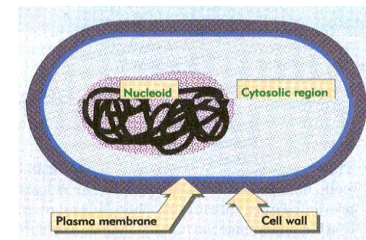
Eukaryote

- Genetic materials are in the nucleus = **genomic DNA**
- in mitochondria = **mitochondrial DNA**

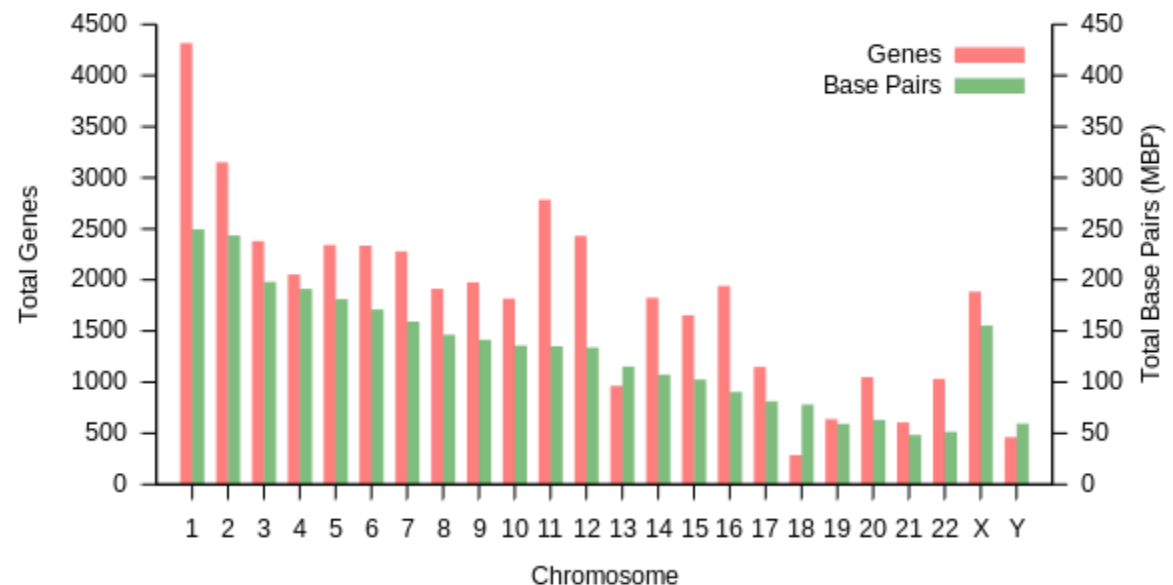
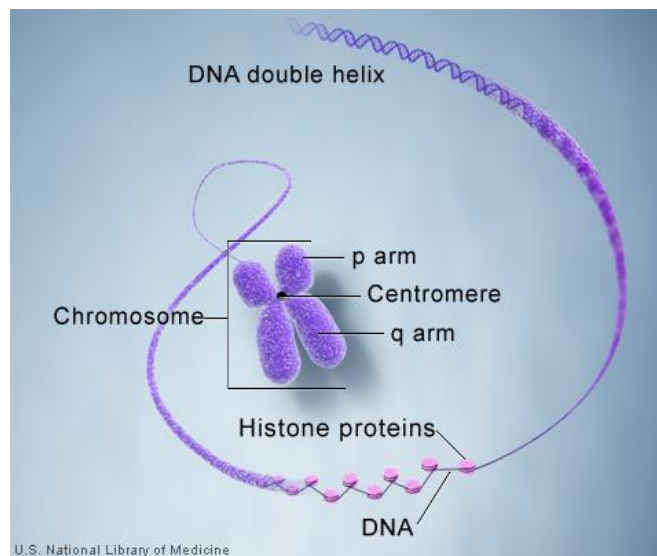


Prokaryote

Genetic materials organize as nucleoid in Cytosol



- Human **body** contains app. 10^{14} cells
- total DNA = 2×10^{11} km
- Distance between the earth and the sun = 1.5×10^8 km
- Human genome = 23 chromosomes
- 1 somatic cell = 2×23 chromosomes
- 1 sex cell = chromosomes
- Every somatic cell in one organism contains **same** of DNA and **same set** of genes but has different expression

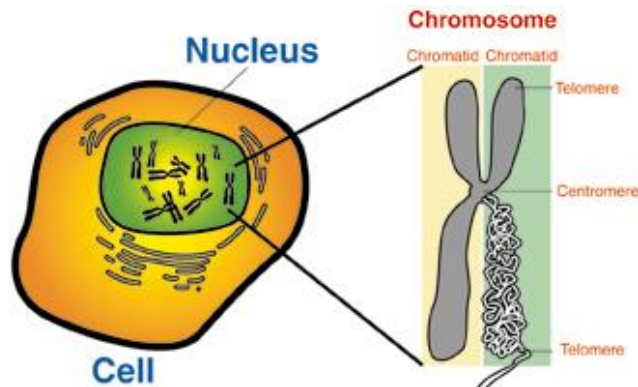




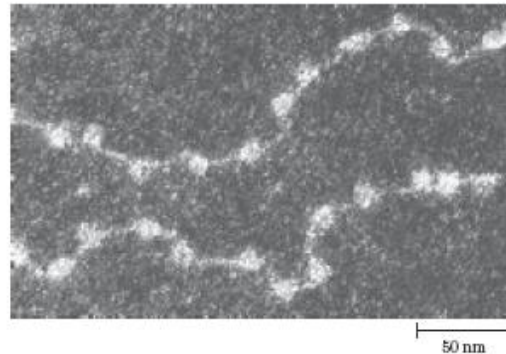
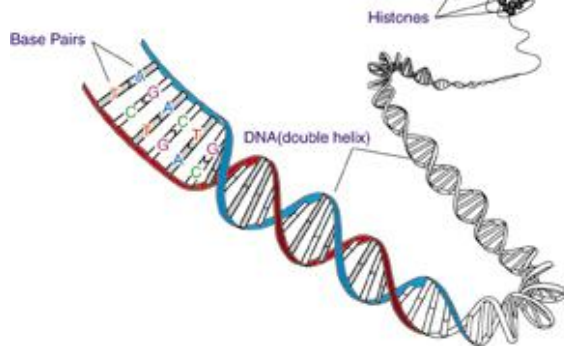
Chromosome numbers ($2n$) in some animals

Species	#		Species	#
Common fruit fly	8		Elephant	56
Earthworm	46		Donkey	62
Cat	36		Dog	78
mouse	40		Goldfish	100-104
Rabbit	44		Guinea pig	64
Gorillas, Chimpanzee	48		Hamster	44
Cow	60		Horse	64

In eukaryotic chromosome, DNA complexes with

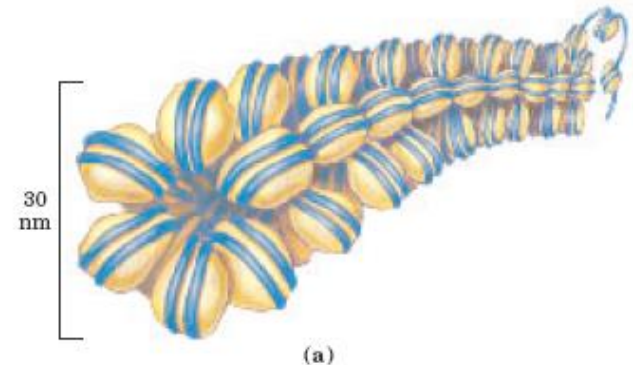
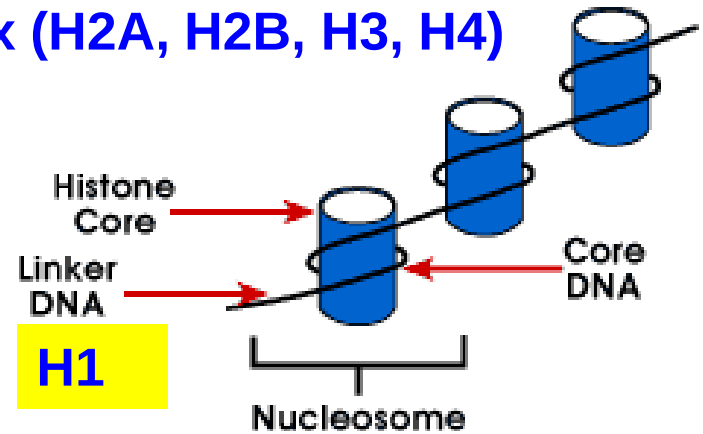


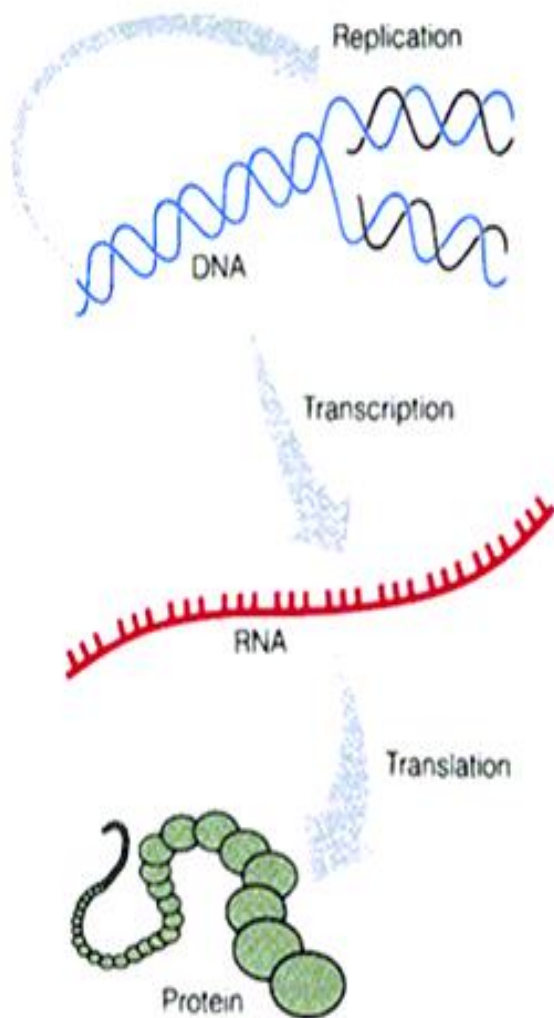
..... +
nonhistone
protein



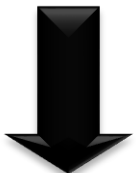
Histone

2x (H2A, H2B, H3, H4)

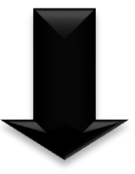




DNA  **Replication**
.....



RNA **mRNA**
rRNA
tRNA



Proteins

เป็นแหล่งเก็บข้อมูลทางพันธุกรรมและถ่ายทอดลักษณะของสิ่งมีชีวิต

Double helix DNA discovered in 1953

Cambridge University



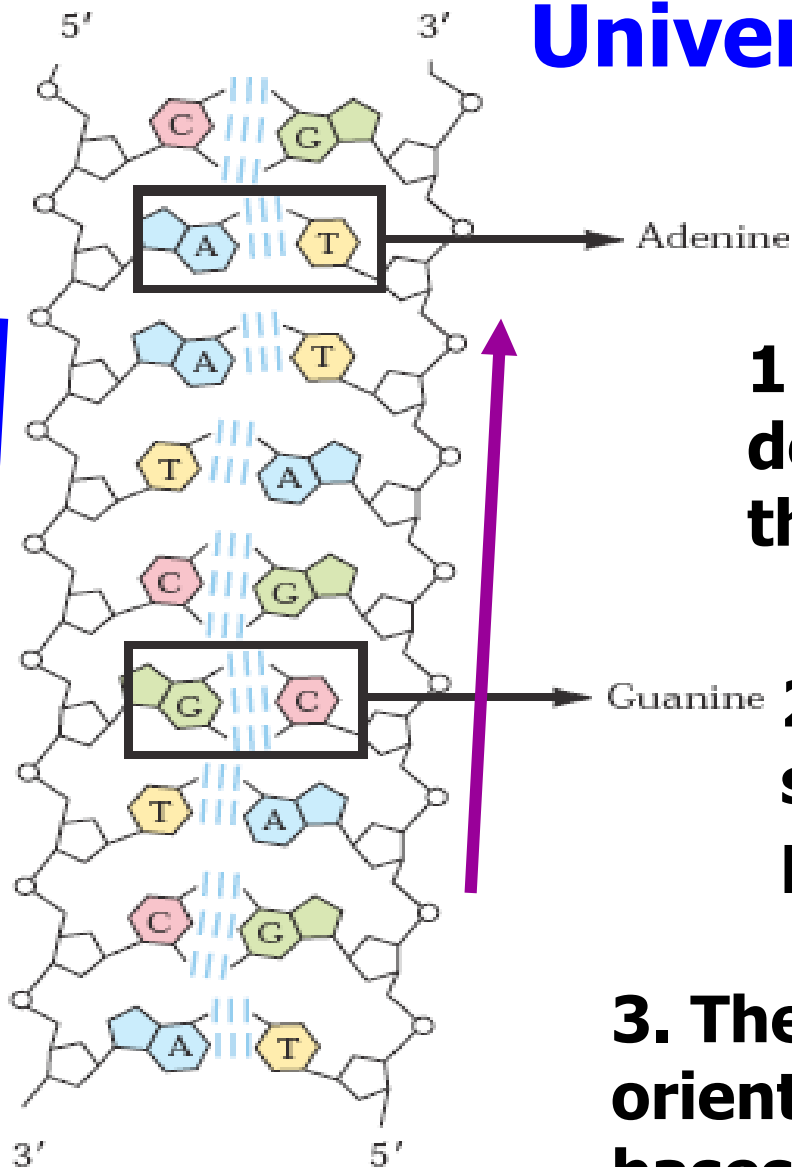
James Watson



Francis Crick

Nobel prize in 1962

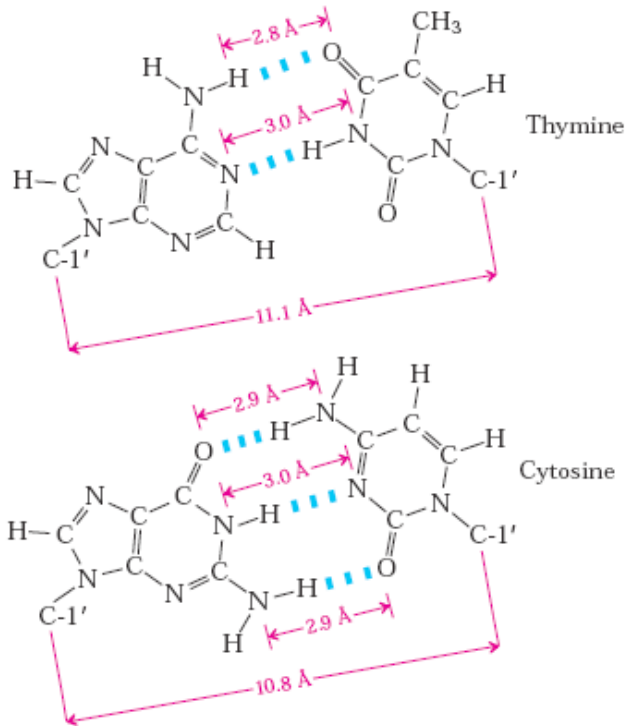
Universal Genetic language



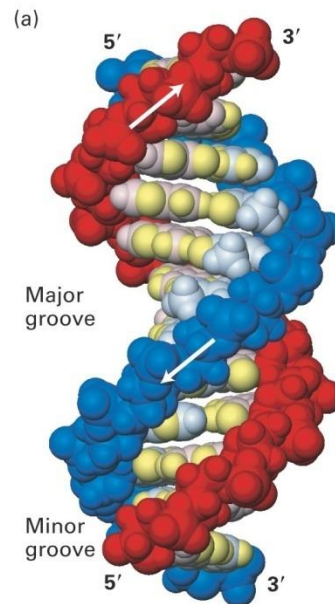
1. The hydrophobic backbone of deoxyribose and **P** are on the

2. Bases on both strands are stackedside and the bases perpendicular to the axis

3. The two stands are-parallel orientation with complementary bases



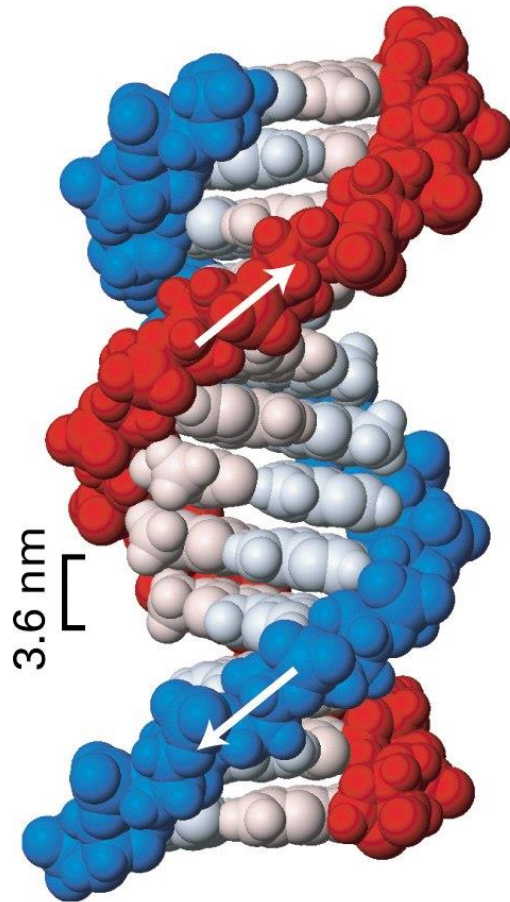
4. Base pairing by H bonds:
A=..... and **G≡.....**



5. Two helix DNA
wound around the
same axis to form
handed double helix

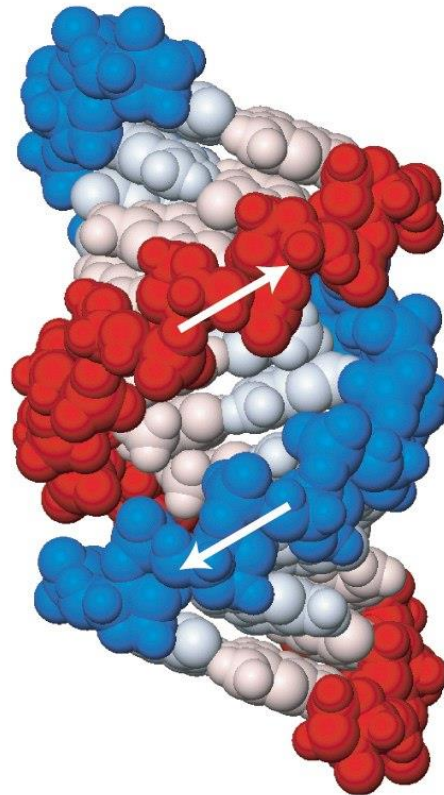
6. The pairing of two strands creates a major groove
and minor groove with 10 bases per turn (34°A)

(a) B DNA



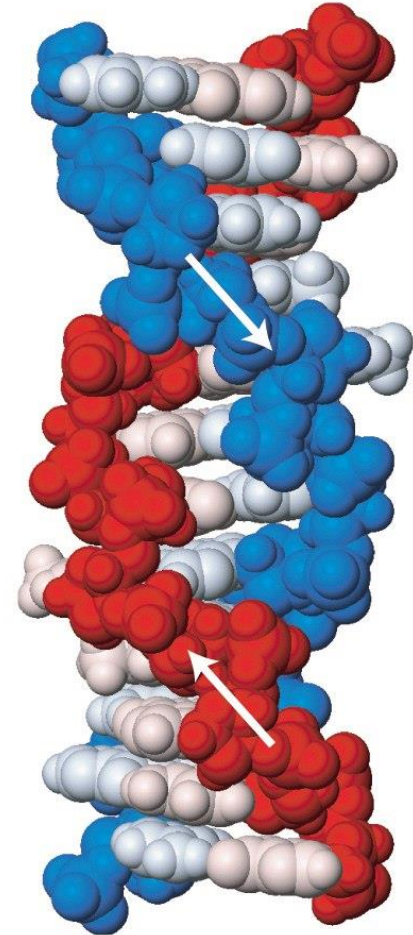
B-form (W/C model)
is the most stable
form

(b) A DNA



A-form (less water)
double stranded
RNA, DNA-RNA

(c) Z DNA



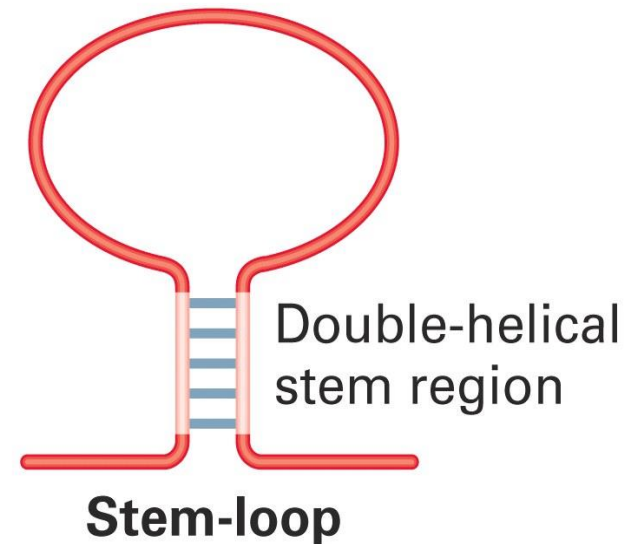
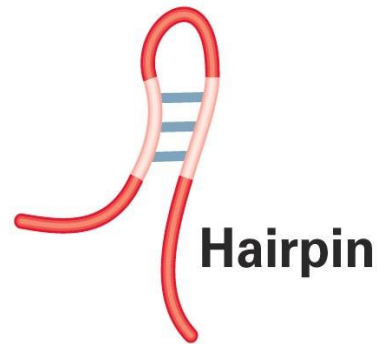
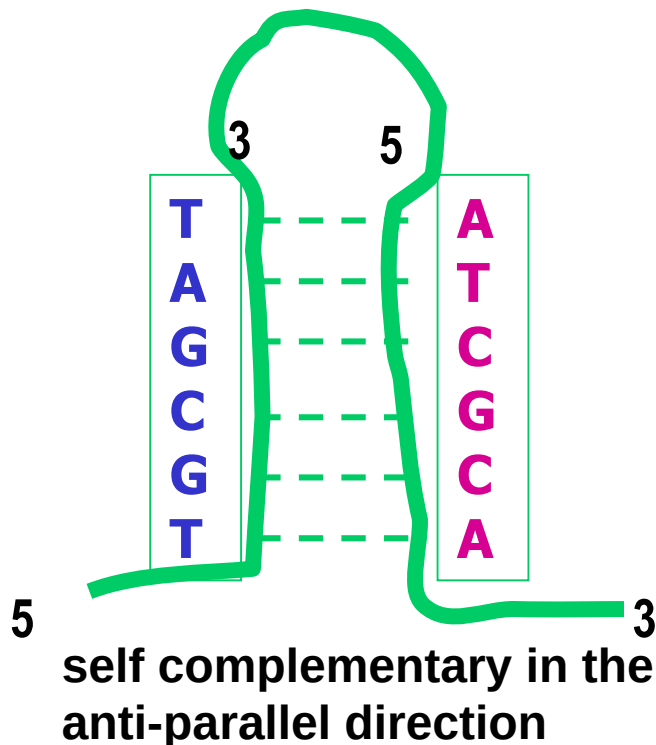
Z-form: left-handed
helix found in high
salt concentration

Unusual structures

Bends or loops form hairpin or cruciform

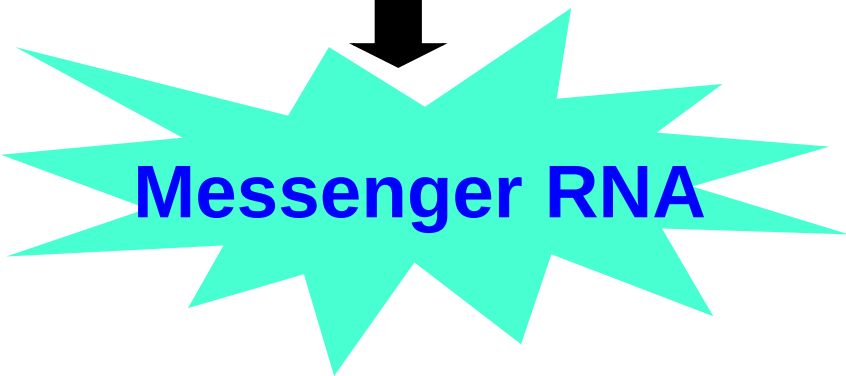
T G C G A T A C T C A T C G C A

(a) Secondary structure

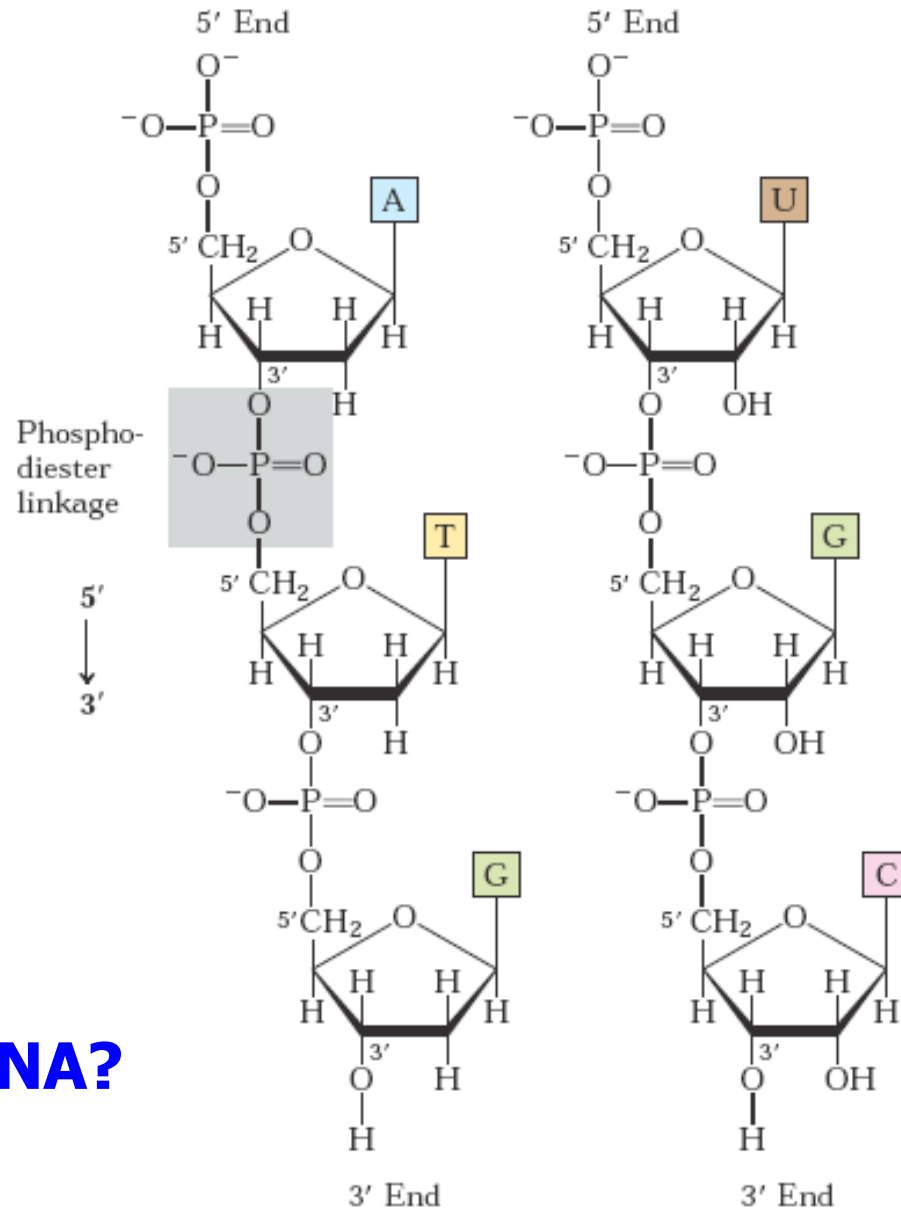


- 
- **DNA are in the nucleus whereas proteins synthesis occurs in the cytoplasm**
 - **Some molecules must carry the genetic message from the nucleus to the cytoplasm**

 - **RNA is found in both the nucleus and cytoplasm**
 - **Increase in protein synthesis is accompanied by an increase in the amount of cytoplasmic RNA and its turnover**

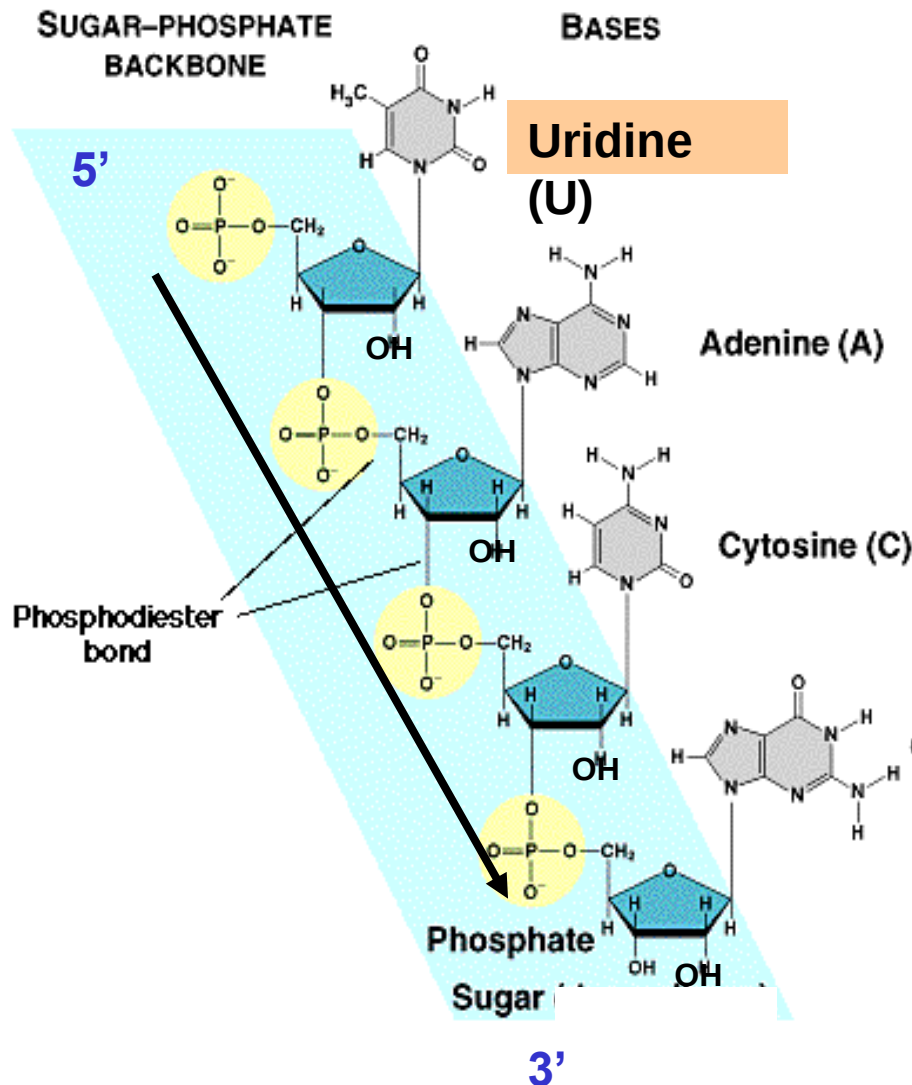


Messenger RNA

A**B**

A or B is RNA?

Ribonucleic acid (RNA)



Primary structure

- base sequence

Secondary structure

- right handed helix
- hair-pin loop
- base stacking interaction

Tertiary structure

- self complementary in the anti-parallel direction



Biological roles of RNA

- Acts as **material** in RNA viruses
- Acts as an enzyme called
- Regulates protein synthesis by **small interference RNA (.....), microRNA (miRNA)**
- Ribonucleic acids are synthesized by using specific region of DNA as the template
- 3 types of cytoplasmic RNAs involve in protein synthesis
 - **mRNA** (messenger RNA)
 - **tRNA** (transfer RNA)
 - **rRNA** (ribosomal RNA)

Components of nucleic acids in *E. coli*

Component	Proportion of dry cell mass	Molecule per cell	Different type	Copies of each type
DNA	1.5%	1	1	1
mRNA	1%	1,500	600	2-3
tRNA	3%	200,000	60	>3000
rRNA	16%	38,000	2	19,000

5'CAP

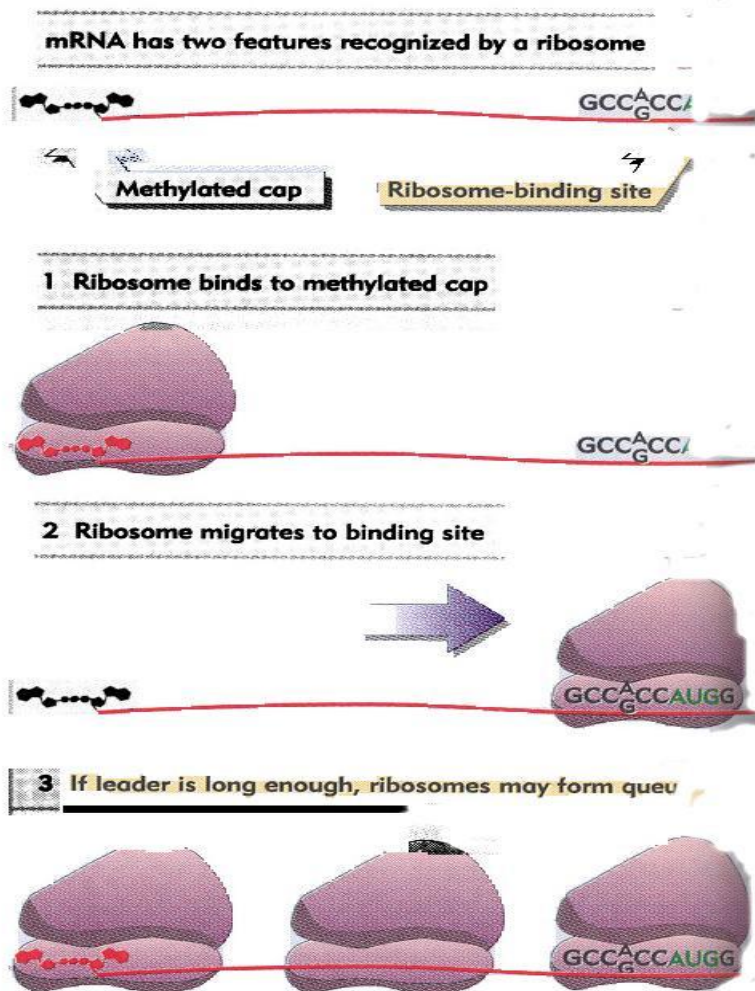


mRNA

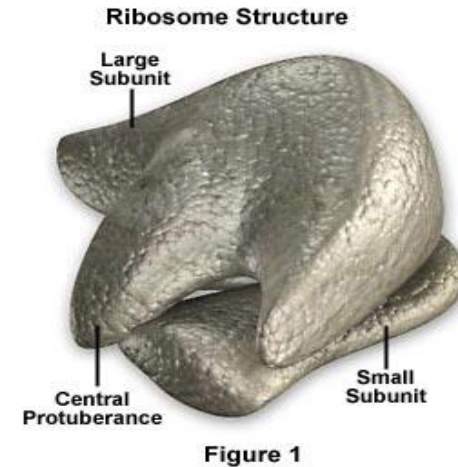
3'polyA



mRNA



Ribosomal RNA



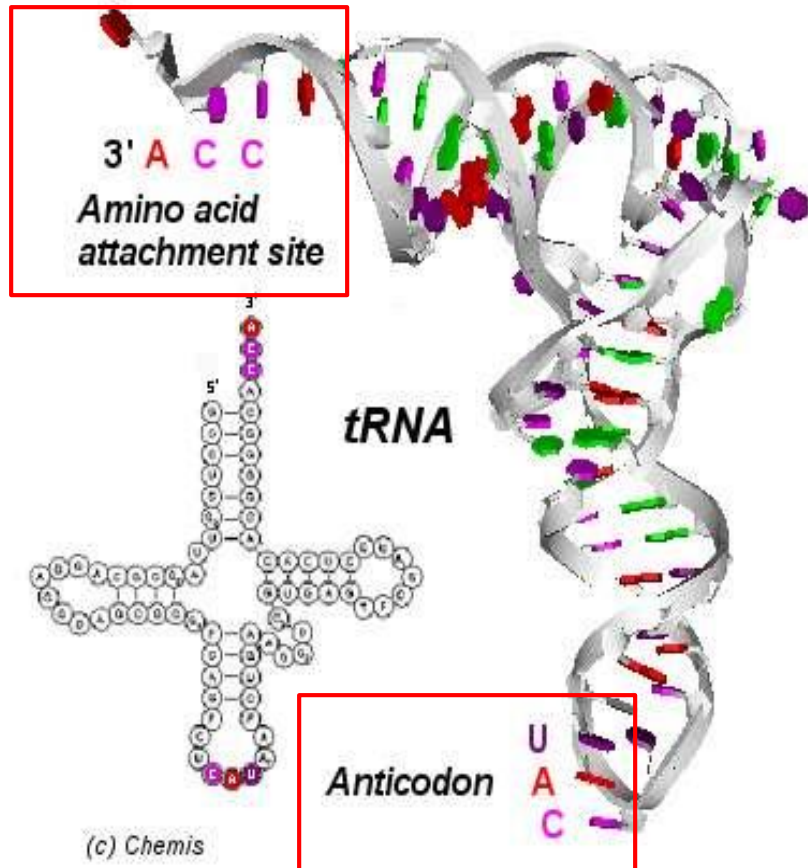
Bacteria

70S, (50S + 30S)

Eukaryote

80S, (60S + 40S)

Transfer RNA



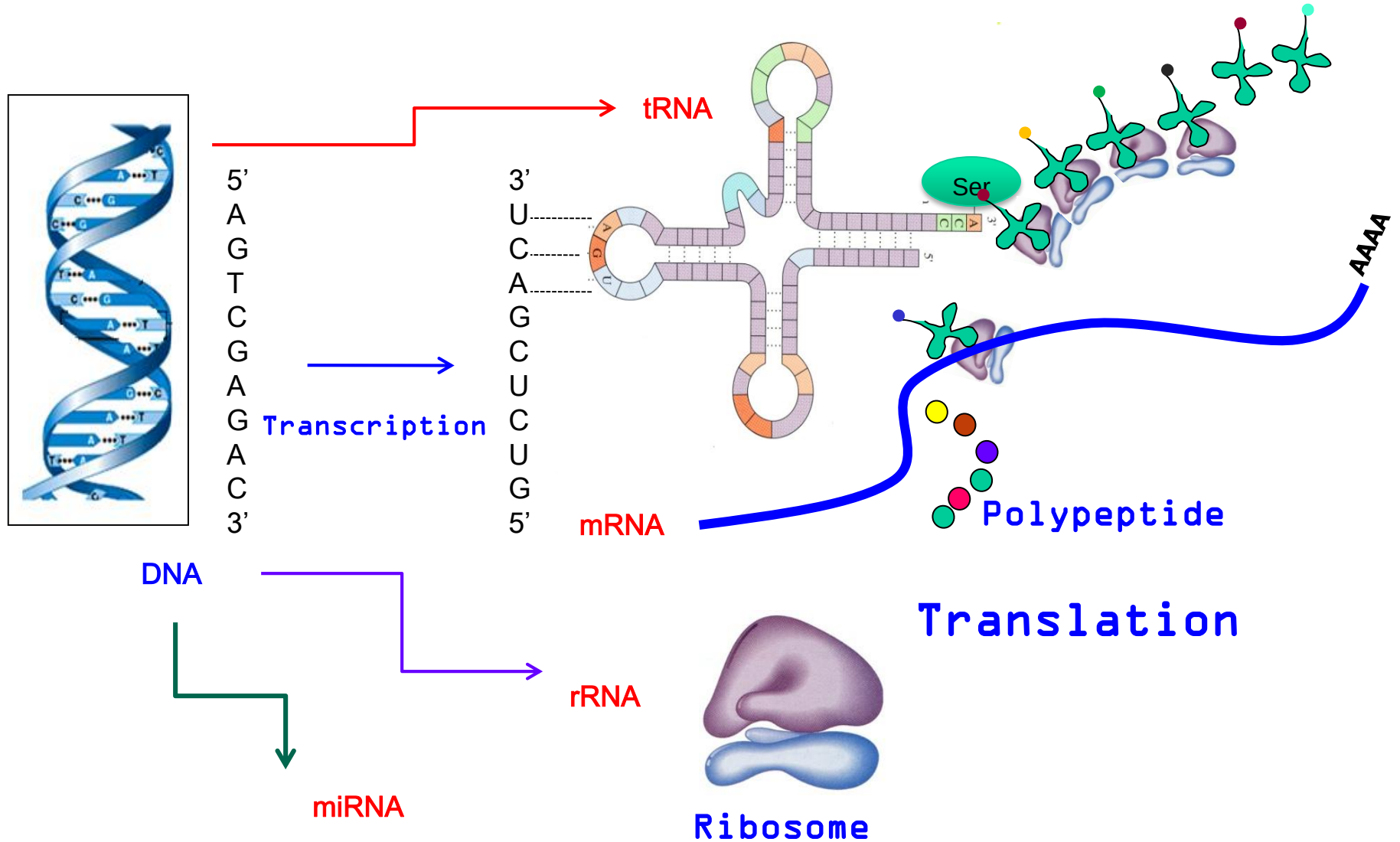
- small RNA about 75-85 bases
- Each type of tRNA links with a specific amino acid



aminoacyl tRNA

- 
- **rRNA มีปริมาณมากที่สุด**
 - ✓ เข้าร่วมกับโปรตีนเกิดเป็นไรโบโซม
 - ✓ ทำหน้าที่เป็นแหล่งผลิตโปรตีน
 - **tRNA เป็น RNA ที่อ่าน triplet code บนสาย mRNA**
 - ✓ โดยทำหน้าที่ในการพากรดอะมิโนมาที่ไรโบโซมเพื่อประกอบกันเป็นสาย polypeptide ที่ถูกต้อง
 - **mRNA พบทั้งใน nucleus และ cytoplasm**
 - ✓ ทำหน้าที่ถ่ายทอดข้อมูลทางพันธุกรรมจาก DNA เพื่อสร้างโปรตีน
 - ✓ กำหนดลำดับของโปรตีนผ่าน triplet code

mRNA, tRNA และ rRNA ในการสร้างโปรตีน





Slow accumulating-irreversible alterations of DNA



Diseases : cancer, aging

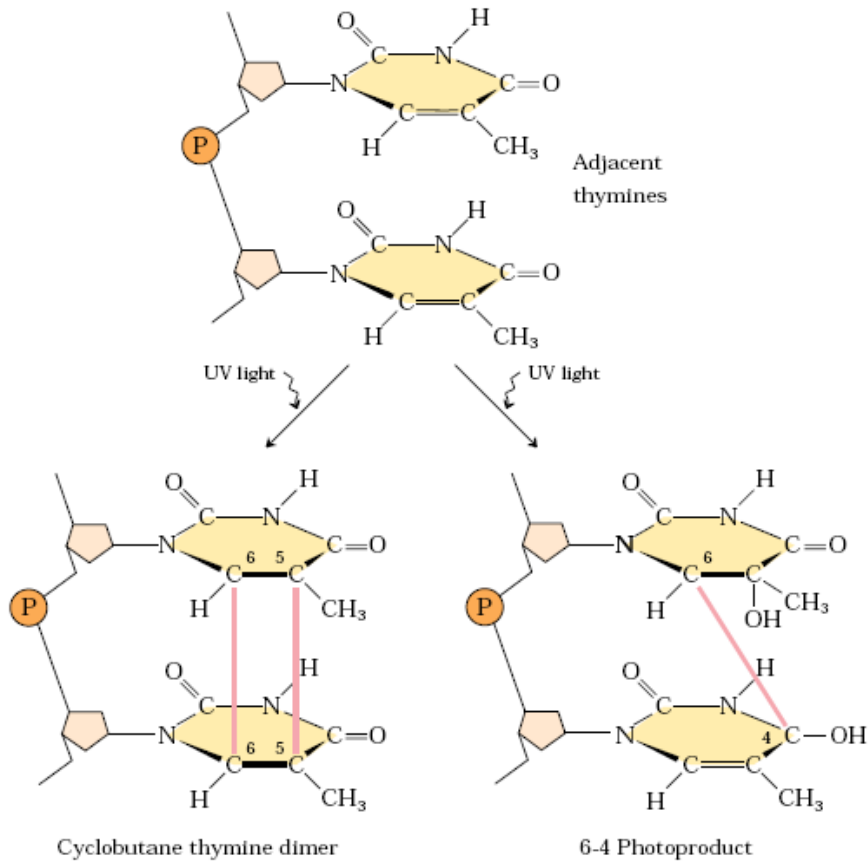
NA has acid/base property

They contain PO_4 which carries charge

- **NA has globular/rod like structure**
- **High/low viscosity**
- **Reacts with water good/poor**

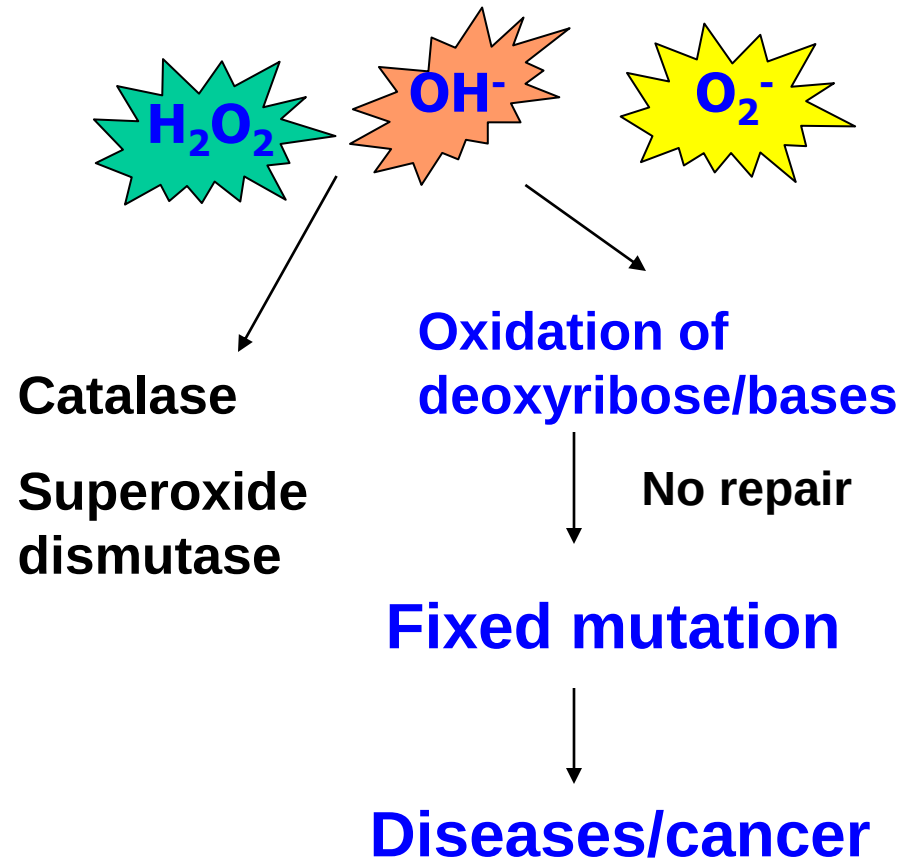
DNA mutation

UV, ionizing radiation

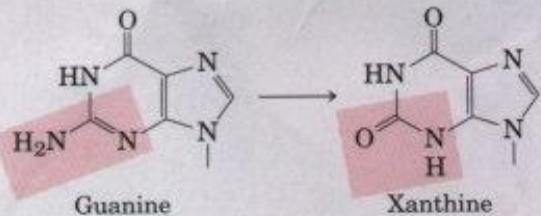
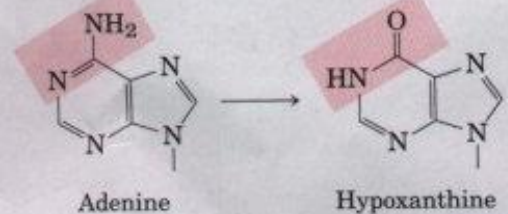
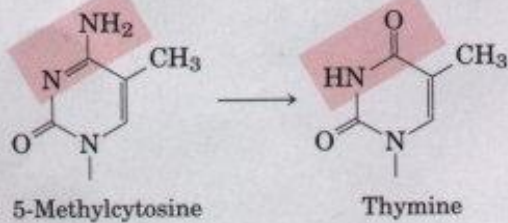
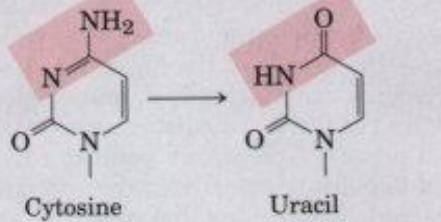


(a)

Reactive oxygen species



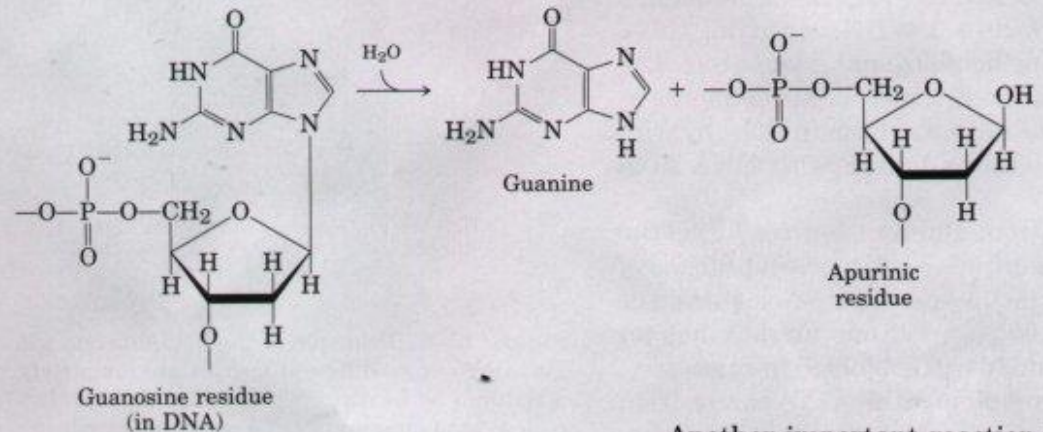
Deamination



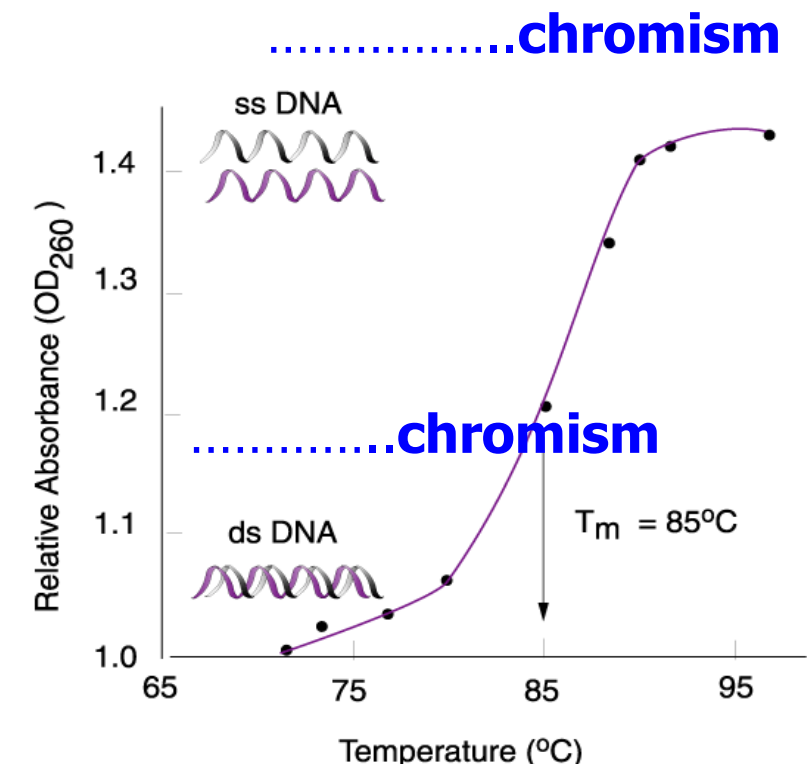
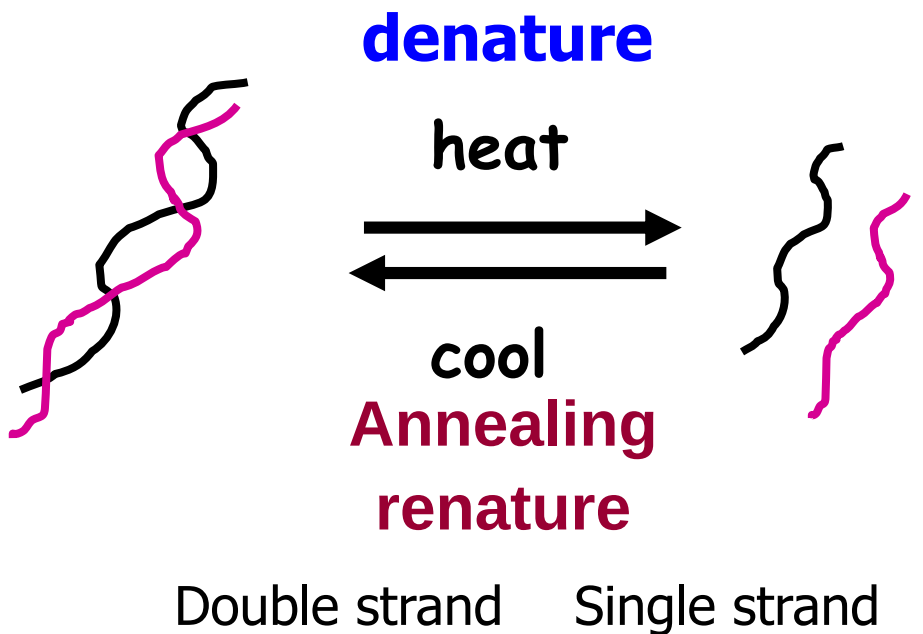
(a)

Nucleotides and nucleic acids undergo nonenzymatic transformation

Depurination



Another important reaction in



Viscosity

OD 260

T_m or t_m = melting temperature

