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Gene Expression

- Genes are DNA sequences that encode proteins (the gene product)
- Gene expression refers to the process whereby the information contained in genes begins to have effects in the cell.
- DNA encodes and transmits the genetic information passed down from parents to offspring.

Genetic code

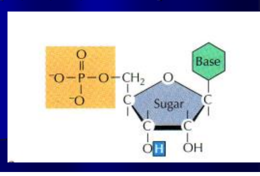
- The alphabet of the genetic code contains only four letters (A,T,G,C).
- A number of experiments confirmed that the genetic code is written in 3-letter words, each of which codes for particular amino acid.
- A nucleic acid word (3 nucleotide letters) is referred to as a *codon.*

Nucleic acids

- Principle information molecule in the cell.
- All the genetic codes are carried out on the nucleic acids.
- Nucleic acid is a linear polymer of nucleotides

Nucleotides

- Nucleotides are the unit structure of nucleic acids.
- Nucleotides composed of 3 components:
  - Nitrogenous base (A, C, G, T or U)
  - Pentose sugar
  - Phosphate

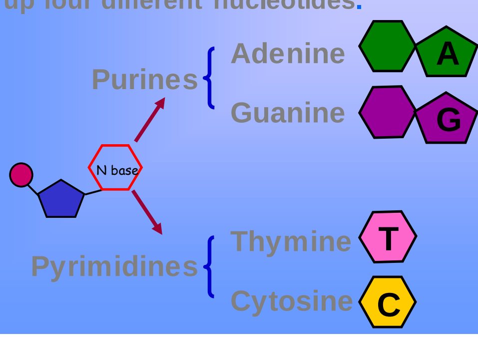


Nitrogenous bases

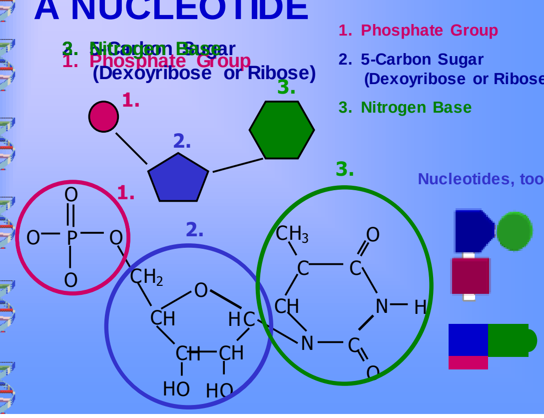
- There are 2 types:
  - Purines(pyoo r-een):
    - Two ring structure
    - Adenine (A) and Guanine (G)
  - Pyrimidines(pahy-rim-i-deen,):
    - Single ring structure
    - Cytosine (C) and Thymine (T) or Uracil (U).

Nucleotides

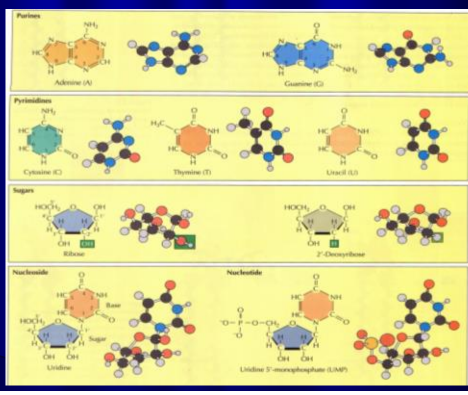
- There are four nitrogen bases making up four different nucleotides.



A NUCLEOTIDE



Nucleotide bases



Role of Nucleoside

- They carry packets of chemical energy—in the form of the nucleoside triphosphates
  ATP(Adenosine triphosphate)
  GTP(Guanosine triphosphate
  CTP(Cytidine triphosphate)

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Role of Nucleotides

- throughout the cell to the many cellular functions that demand energy
  - synthesizing amino acids
  - synthesizing proteins
  - cell membranes and parts
- Moving the cell and moving cell parts
  - internally and intercellularly
- Dividing the cell
- Participate in cell signaling
  - (cGMP and cAMP

Artificial Nucleotides

- In 2014, A team synthesized a stretch of circular DNA known as a plasmid containing natural T-A and C-G base pairs along with the best-performing UBP.

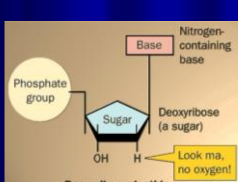
Artificial Nucleotides

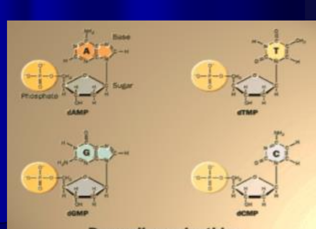
- inserted it into *E. coli*
- that successfully replicated the unnatural base pairs through multiple generations.
- This is the first known example of a living organism passing along an expanded genetic code to

Types of Nucleic acids

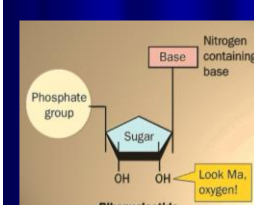
There are 2 types of nucleic acids:

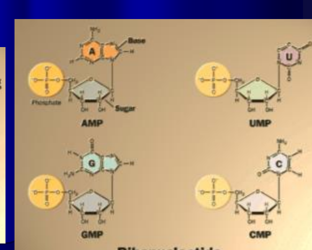
1. Deoxy-ribonucleic acid (DNA)
   - Pentose Sugar is deoxyribose (no OH at 2' position)
   - Bases are Purines (A, G) and Pyrimidine (C, T).





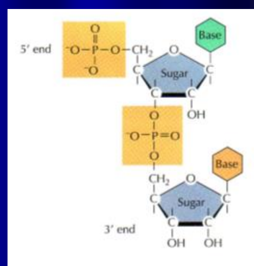
2. Ribonucleic acid (RNA)
   - Pentose Sugar is Ribose.
   - Bases are Purines (A, G) and Pyrimidines (C, U).





Polymerization of Nucleotides

- The formed polynucleotide chain is formed of:
  - Negative (-ve) charged Sugar-Phosphate backbone.
    - Free 5' phosphate on one end (5' end)
    - Free 3' hydroxyl on other end (3' end)
  - Nitrogenous bases are not in the backbone
    - Attached to the backbone
    - Free to pair with nitrogenous bases of other polynucleotide chain



Polymerization of Nucleotides

- Nucleic acids are polymers of nucleotides.
- The nucleotides formed of purine or pyrimedine bases linked to ***phosphorylated sugars*** (nucleotide back bone).
- The bases are linked to the pentose sugar to form ***Nucleoside***.
- The nucleotides contain one phosphate group linked to the 5' carbon of the nucleoside.

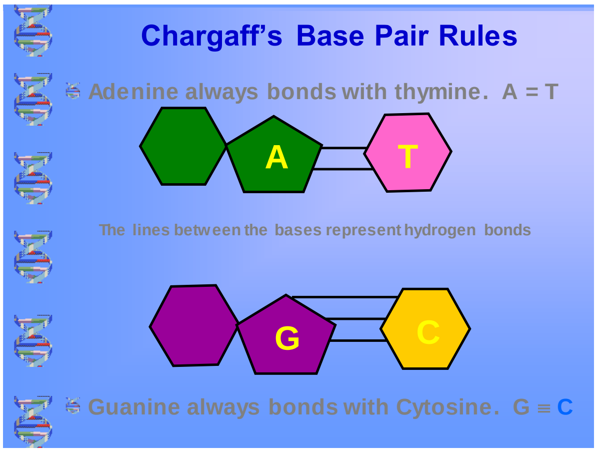
Nucleotide = Nucleoside + Phosphate group

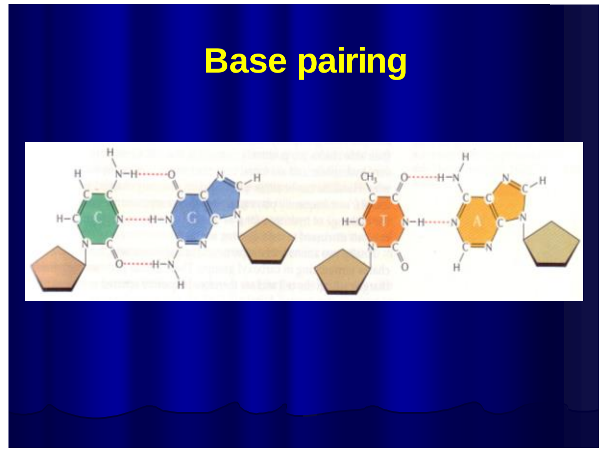
N.B.

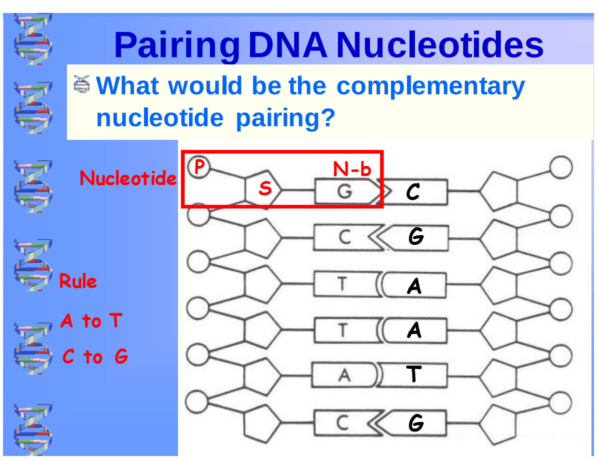
- The polymerization of nucleotides to form nucleic acids occur by condensation reaction by making phospho-diester bond between 5' phosphate group of one nucleotide and 3' hydroxyl group of another nucleotide.
- Polynucleotide chains are always synthesized in the 5' to 3' direction, with a free nucleotide being added to the 3' OH group of a growing chain.

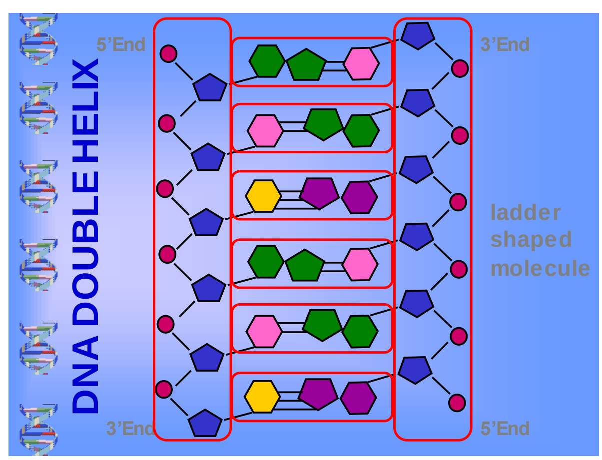
Complementary base pairing

- It is the most important structural feature of nucleic acids
- It connects bases of one polynucleotide chain (nucleotide polymer) with complementary bases of other chain
- Complementary bases are bonded together via:
  - Double hydrogen bond between A and T (DNA), A and U (RNA) **(A═T or A═U)**
  - Triple H-bond between G and C in both DNA or RNA **(G≡C)**


Chargaff's Base Pair Rules
Adenine always bonds with thymine. A = T
A
T
The lines between the bases represent hydrogen bonds
G
C
Guanine always bonds with Cytosine. G ≡ C


Base pairing


Pairing DNA Nucleotides
What would be the complementary nucleotide pairing?
Nucleotide
P
S
N-b
Rule
A to T
C to G
G C
C G
T A
T A
A T
C G


DNA DOUBLE HELIX
5'End
3'End
3'End
5'End
ladder shaped molecule

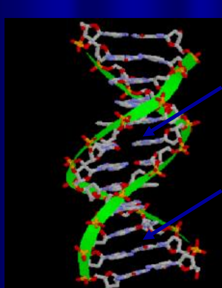
Significance of complementary base pairing

- The importance of such complementary base pairing is that each strand of DNA can act as template to direct the synthesis of other strand similar to its complementary one.
- Thus *nucleic acids are uniquely capable of directing their own self replication*.
- The information carried by DNA and RNA direct the synthesis of specific proteins which control most cellular activities.

DNA structure

- DNA is a double stranded molecule consists of 2 polynucleotide chains running in opposite directions.
- Both strands are complementary to each other.
- The bases are on the inside of the molecules and the 2 chains are joined together by double H-bond between A and T and triple H-bond between C and G.
- The base pairing is very specific which make the 2 strands complementary to each other.
- So each strand contain all the required information for synthesis (replication) of a new copy to its complementary.

Forms of DNA



Minor groove

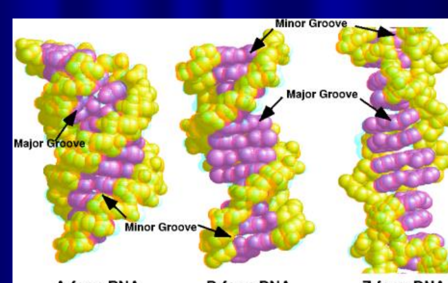
The minor groove is generated by the smaller angular distance between sugars.

Major groove

major groove:
The larger of the two grooves that spiral around the surface of the B-form of DNA.

DNA structure:
Secondary Structure: alternative conformations

Lecture 7, 2
10/4/2006



Forms of DNA

1- ***B-form helix***:

- It is the most common form of DNA in cells.
  - Right-handed helix
  - Turn every 3.4 nm.
  - Each turn contain 10 base pairs (the distance between each 2 successive bases is 0.34 nm)
  - Contain 2 grooves;
    - Major groove (wide): provide easy access to bases
    - Minor groove (narrow): provide poor access.

2- ***A-form DNA***:

- Less common form of DNA , more common in RNA
  - Right handed helix
  - Each turn contain 11 b.p/turn
  - Contain 2 different grooves:
    - Major groove: very deep and narrow
    - Minor groove: very shallow and wide (binding site for RNA)

3- ***Z-form DNA***:

- Radical change of B-form
  - Left handed helix, very extended
  - It is GC rich DNA regions.
  - The sugar base backbone form Zig-Zag shape
  - The B to Z transition of DNA molecule may play a role in gene regulation.

Denaturing and Annealing of DNA

- The DNA double strands can denatured if heated (95ºC) or treated with chemicals.
  - AT regions denature first (2 H bonds)
  - GC regions denature last (3 H bonds)
- DNA denaturation is a reversible process, as denatured strands can re-annealed again if cooled.
- This process can be monitored using the hyperchromicity (melting profile).

Hyperchromicity (melting profile)

- It is used to monitor the DNA denaturation and annealing.
- It is based on the fact that single stranded (SS) DNA gives higher absorbtion reading than double stranded (DS) at wavelength 260º.
- Using melting profile we can differentiate between single stranded and double stranded DNA.

RNA structure

- It is formed of linear polynucleotide
- It is generally single stranded
- The pentose sugar is Ribose
- Uracile (U) replace Thymine (T) in the pyrimidine bases.

Although RNA is generally single stranded, intra-molecular H-bond base pairing occur between complementary bases on the same molecule (secondary structure)

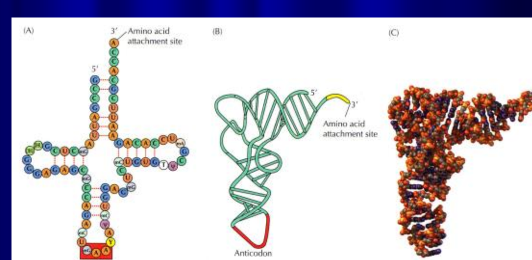
Types of RNA

- Messenger RNA (mRNA):
  - Carries genetic information copied from DNA in the form of a series of 3-base code, each of which specifies a particular amino acid.
- Transfer RNA (tRNA):
  - It is the key that read the code on the mRNA.
  - Each amino acid has its own tRNA, which binds to it and carries it to the growing end of a polypeptide chain.
- Ribosomal RNA (rRNA):
  - Associated with a set of proteins to form the ribosomes.
  - These complex structures, which physically move along the mRNA molecule, catalyze the assembly of amino acids into protein chain.
  - They also bind tRNAs that have the specific amino acids according to the code.

RNA structure

- RNA is a single stranded polynucleotide molecule.
- It can take 3 levels of structure;
  - Primary: sequence of nucleotides
  - Secondary: hairpin loops (base pairing)
  - Tertiary: motifs and 3D foldings

RNA structure



Transfer RNA (tRNA) structure

DNA Replication

- Replication of the DNA molecule is semi-conservative, which means that each parent strand serves as a template for a new strand and that the two (2) new DNA molecules each have one old and one new strand.
- DNA replication requires:
  - A strand of DNA to serve as a *template*
  - *Substrates* - deoxyribonucleoside triphosphates (dATP, dGTP, dCTP, dTTP).
  - *DNA polymerase* - an enzyme that brings the substrates to the DNA strand template
  - A source of *chemical energy* to drive this synthesis reaction.

DNA Replication

- Nucleotides are always added to the growing strand at the 3' end (end with free -OH group).
- The hydroxyl group reacts with the phosphate group on the 5' C of the deoxyribose so the chain grows
- Energy is released when the bound linking 2 of the 3 phosphate groups to the deoxyribonucleoside triphosphate breaks
- Remaining phosphate group becomes part of the sugar-phosphate backbone