

Chapter 14 DNA: The Genetic Material

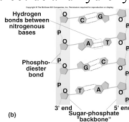


The Nature of Genetic Material

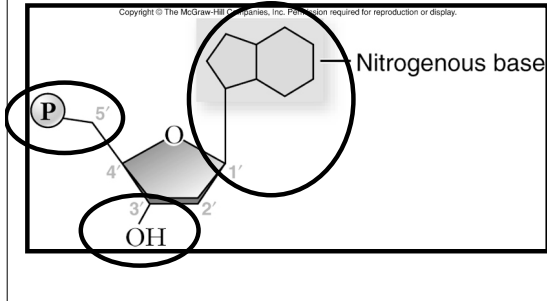
- Chromosomes - DNA and protein
 - Genes are subunits
 - DNA = 4 similar nucleotides
 - C(ytosine) A(denine) T(hymine) G(uanine)
 - Proteins = 20 different & diverse amino acids
 - Appears greater informational capacity in protein
 - BUT, evidence starts to point to DNA

Chemical Nature of Nucleic Acids

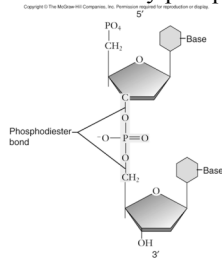
- DNA made up of nucleic acids
 - Each nucleotide is composed of a five carbon sugar, a phosphate group, and a nitrogenous (organic) base.
 - nucleotides distinguished by the bases
 - reaction between phosphate group of one nucleotide and hydroxyl group of another is dehydration synthesis
 - PHOSPHIDIESTER BONDS



- Carbon atoms are numbered 1'-5'
- "prime" - carbon belongs to sugar



5' phosphate & 3' hydroxyl group allow DNA and RNA to form long chains (polymer); nucleotides are linked by phosphodiester bond



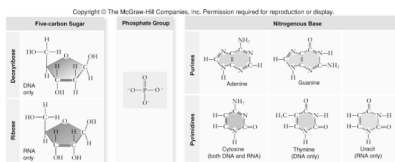
DNA and RNA strands written from 5' (free phosphate) to 3' (free hydroxyl)

DNA made of Nucleotides, which consist of:

1. 5 carbon sugar (deoxyribose) 1'2'3'4'5'
2. phosphate (PO₄) group
3. nitrogenous base

Can be a two ringed **Purine** (adenine, A, or guanine, G) or a single ringed **Pyrimidine** (thymine, T, or cytosine, C)

-RNA contains the pyrimidine uracil (U) in place of thymine



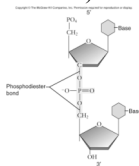
DNA



- Chargaff found DNA not simple structure; regularity in base ratios
 - Chargaff's rules:
 1. Proportion A = T, proportion G = C
 2. Always equal proportion of purines (A & G) and pyrimidines (C & T)
- Chargaff's rules mean:
 - adenine (A) pairs with thymine (T)
 - guanine (G) pairs with cytosine (C)
(purines pair with pyrimidines)

terms

- Nucleic acid – polymer, chain (DNA or RNA)
- Nucleotide – single unit (phosphate, sugar, base)
- Nucleoside – just base and sugar
- Bases – purine and pyrimidine
- Base pair – one of each (purine; pyrimidine)
 - Complementary



• 4 bases are in characteristic (NOT equal) ratios

why your cat is not a cauliflower

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Erwin Chargaff - DNA composition varies from species to species (1947)

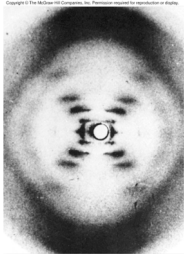
Organism	Base Composition (mole percent)			
	A	T	G	C
<i>Escherichia coli</i> (K12)	26.0	23.9	24.9	25.2
<i>Mycobacterium tuberculosis</i>	15.1	14.6	34.9	35.4
Yeast	31.3	32.9	18.7	17.1
Herring	27.8	27.5	22.2	22.6
Rat	28.6	28.4	21.4	21.5
Human	30.9	29.4	19.9	19.8

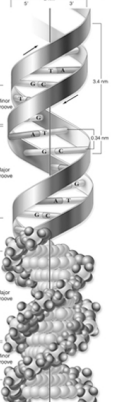
Source: Data from E. Chargaff and J. Davidson (editors), *The Nucleic Acids*, 1955, Academic Press, New York, NY.

DNA

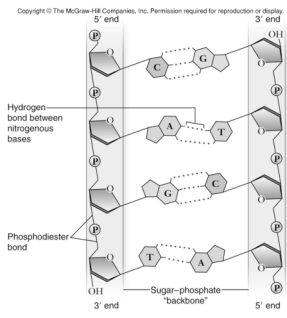
- Human DNA
- BASES
- 30.9% adenine
- 29.4% thymine
- 19.9% guanine
- 19.8% cytosine


Rosalind Franklin
Died 1958
Xray diffraction


b.



The ladder forms a twist every ten bases.



- handrails are phosphate groups
- sugars (deoxyribose) are backbone
- bases are steps

Model for DNA

James Watson

Francis Crick

Nobel prize 1962

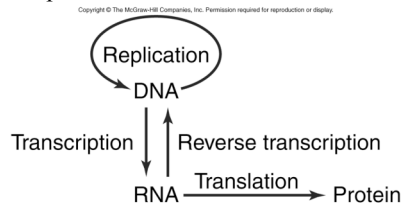


DNA STRUCTURE

Two important concepts!!!!

- 1) How does it initiate protein synthesis?
(Gene expression)
- 2) How does it replicate?

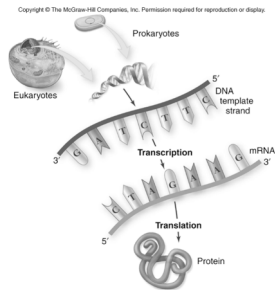
- Gene expression
- conversion genotype to phenotype
 - (DNA to RNA) = **transcription**
- RNA to protein = **translation**



- Oversimplification
 - Retroviruses can convert RNA into DNA using reverse transcriptase enzyme

Central Dogma

- Information passes in 1 direction
- DNA (gene) → RNA → protein



Antiparallel

Typically read bases from 5' to 3' ←

DNA model

- Base pairing = Complementary
 - 1 strand ATGC, other strand must be ?
 - Critical for DNA replication

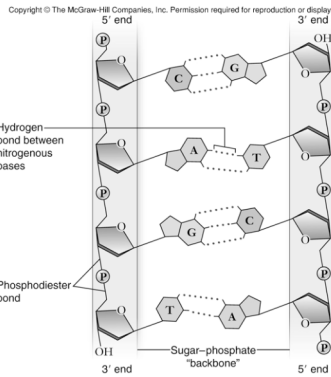
More on RNA later.....

NOW for DNA replication

Note the
Hydrogen
bonds &
antiparallel
configuration

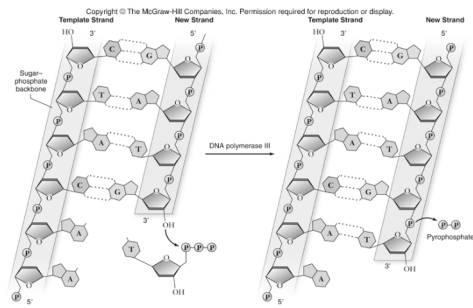
purines pair
with
pyrimidines

- phosphate groups and sugars (deoxyribose) like hand rails on a staircase
- bases are steps



Replication Process: an overview

- each strand is complementary to each other
- each can form a template when separated.



Replication Process: an overview

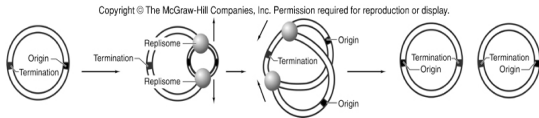
- Parental DNA = template
- Enzymes copy template
- nucleotide triphosphates = building blocks

Initiation

- begins at specific site (origin of replication)
- initiator proteins recognize and bind to origin
- opens helix to expose strands

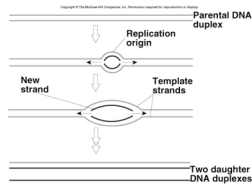
Prokaryotic Replication

- After initiation, replication proceeds bidirectionally from its unique origin to the unique terminus.
- The complete chromosome plus origin called Replicon.



*strand separation creates replication “bubble”

*replication proceeds from each end of bubble at the replication forks



eukaryotes - hundreds even thousands origin sites!!

Replication Process: an overview

Termination

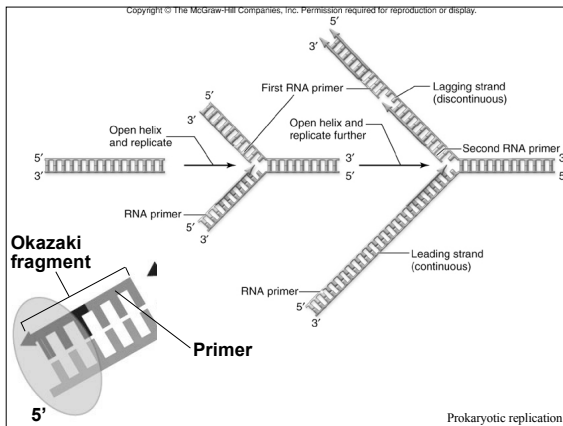
- In prokaryotes (circular DNA) replication ends when reach origin again

- In eukaryotes, endpoint for each chromosome indicated by Telomeres, specified regions of repeating bases

Linear Chromosomes Require Different Termination

- Telomeres = special structures found on ends of eukaryotic chromosomes (TTAGGG)
 - Functions: protect ends of chromosomes from nucleases
 - Keeps one chromosome from linking to another
- Replication of leading strand (5' to 3') easy
- On lagging strand (3' to 5') when reach end, removal of last primer leaves gap; polymerase cannot fix
 - Means gradual shortening of chromosomes with each round of cell division!

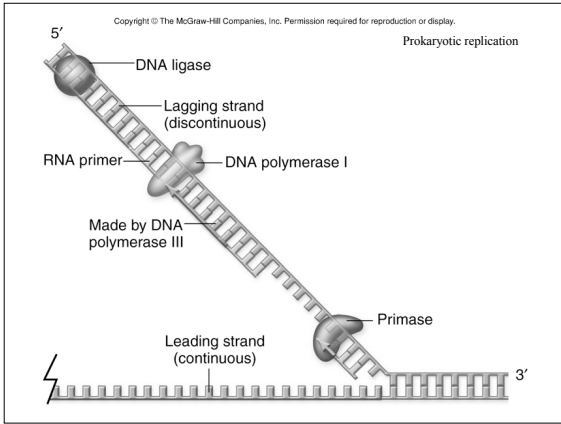
Eukaryotic replication



Prokaryotic replication

Lagging Strand Synthesis

- Discontinuous = more work required
- Primase synthesizes primers for each Okazaki fragment
- These RNA primers have to be replaced with DNA, and then stitched together
- DNA pol III synthesizes Okazaki fragments
- DNA pol I removes and replaces primer segments
- DNA ligase seals nick



PCR polymerase chain reaction!!!

- Kary Mullis

- Primers start replication sequences
- 20 sequences = 1 million

- Nobel prize 1993

Telomerase makes telomeres

- Telomeres are short repeating DNA sequences made by

- Telomerase
 - Uses internal RNA as template

The diagram shows the mechanism of telomerase. It consists of a protein subunit and an internal RNA subunit. The RNA subunit acts as a template to synthesize a DNA strand. The process is shown in three stages: 1. Synthesis by telomerase, where the RNA template is used to create a DNA-RNA hybrid. 2. Telomere extended by telomerase, where the DNA strand is released and the RNA remains base-paired with the end. 3. Telomerase moves and continues to extend telomere, where the enzyme translocates and repeats the process. The final state is labeled 'Now ready to synthesize next repeat'. The 5' and 3' ends are indicated.

Eukaryotic replication

Telomerase

- Relationship aging (senescence) and telomere length
- # cell divisions a cell can undergo determined by telomere length
- Cancer cells divide indefinitely; not possible if chromosomes continually shortened
 - Telomerase allows them to maintain telomere length

Eukaryotic replication

DNA

- DNA polymerase proofread during replication
- Many specific and non-specific pathways to repair damage – including excision of damaged area

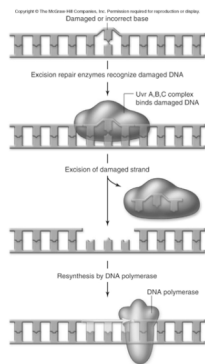
Excision repair: (nonspecific)

- Damaged region removed (excised) and replaced by DNA synthesis

– 3 steps:

1. Recognition of damage
2. Removal of damaged region
3. Resynthesis using the information on the undamaged strand as a template

-DNA pol I or III replaces damaged DNA



DNA Damage

Errors in replication; most fixed by DNA polymerase

*enzyme errors

*chemicals

*UV light

*X rays

*radiation

*can occur as
frequently as
10,000
errors/cell/day

Mutagen = any agent that increases
mutations above background levels

mutations –RANDOM

in somatic cells - tumors (colon cancer takes several)

in GERM CELLS (will become eggs or sperm)- inherited
