New Section

Nucleic Acids - final group of macromolecules

Nucleotides - monomers

Central Dogma

Higher levels of cellular organization

Central dogma cannot explain how a cell works

Higher levels of organization - e. g. making a chloroplast - require complex interactions of hundreds (thousands) of genes and the context of an existing cell

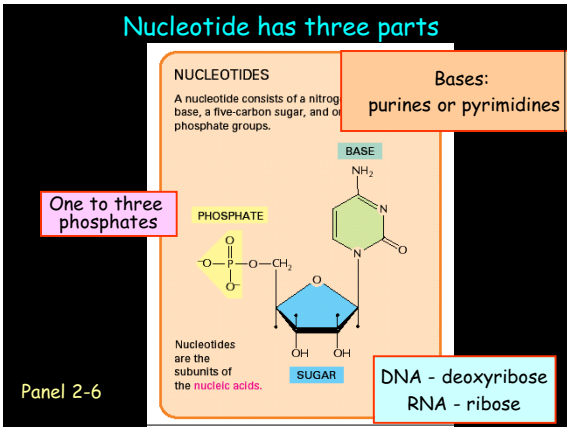
Lecture Outline

Nucleic acid structure

- *Nucleotide Monomer
- Linear DNA strand
- Double-stranded DNA
- Packaging of DNA into a chromosome

DNA replication

Nucleotide has three parts



Bases: purines or pyrimidines

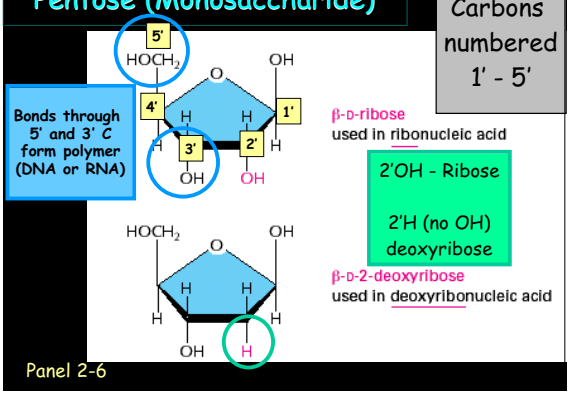
One to three phosphates

DNA - deoxyribose
RNA - ribose

Panel 2-6

Pentose (Monosaccharide)

Carbons numbered 1′ - 5′



Bonds through 5′ and 3′ C form polymer (DNA or RNA)

β-D-ribose
used in ribonucleic acid

2′OH - Ribose

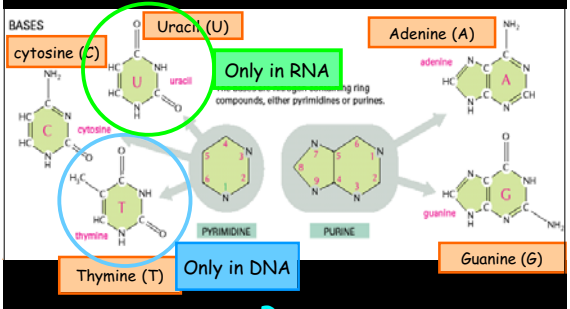
2′H (no OH) deoxyribose

β-D-2-deoxyribose
used in deoxyribonucleic acid

Panel 2-6

Pyrimidines (one N-containing ring)

Purines (two N-containing rings)



Thymine (T)

Only in DNA

Guanine (G)

Panel 2-6

Bases

Nucleotide nomenclature

Sugar + base = nucleoside
Sugar + base + phosphate = nucleotide

RNA

AMP, GMP, CMP, UMP	Monophosphates
ADP, GDP, CDP, UDP	Diphosphates
ATP, GTP, CTP, UTP	Triphosphates

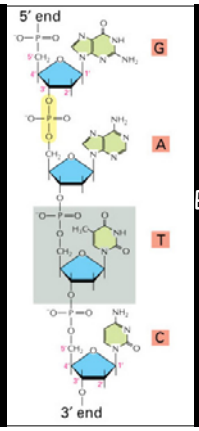
Energy metabolism

DNA

dAMP, dGMP, dCMP, dTMP	Monophosphates
dADP, dGDP, dCDP, dTDP	Diphosphates
dATP, dGTP, dCTP, dTTP	Triphosphates

Nucleotide to Nucleic Acid ...

Linear strand has polarity: 5′ to 3′

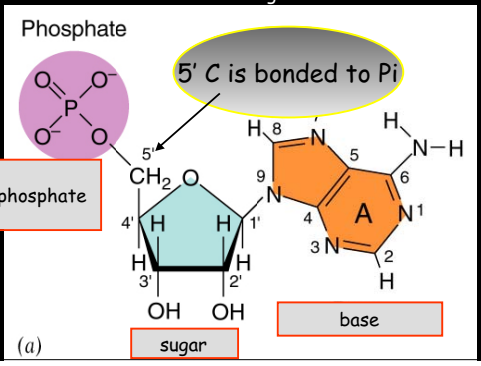


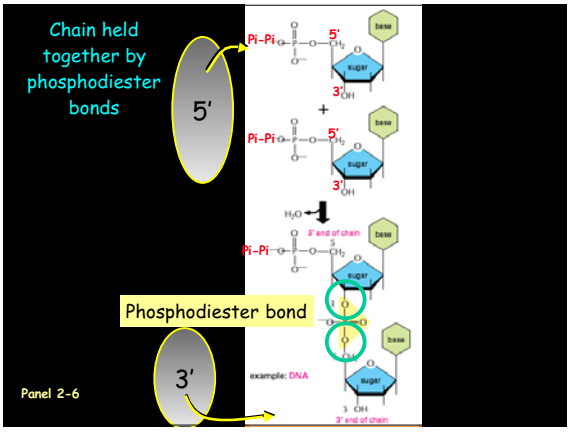
Bases

ECB 2-25

Bonding of nucleotides into strand:

Ester bonds through 5′C and 3′C...



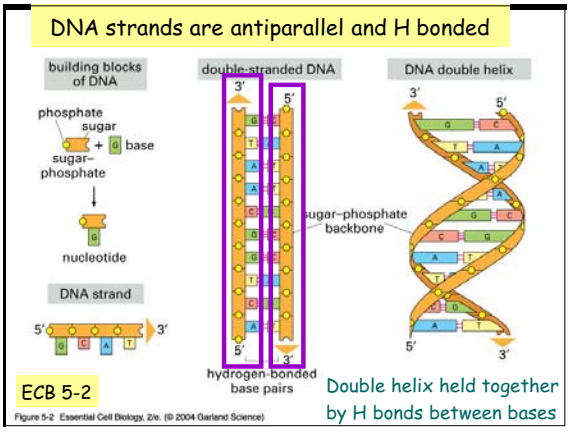


Nucleic Acids

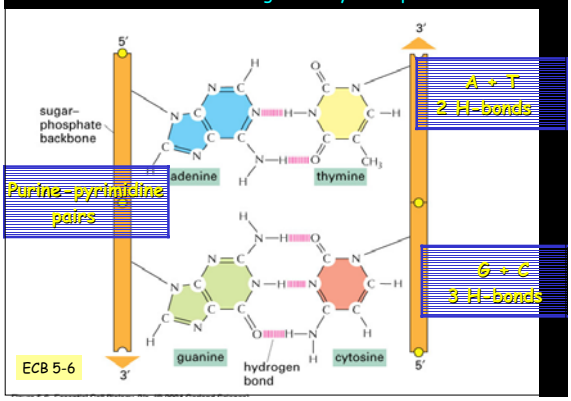
Nucleic acid structure
- Nucleotide Monomer
- Linear DNA strand
- *Double-stranded DNA
- Packaging of DNA into chromosome

DNA replication

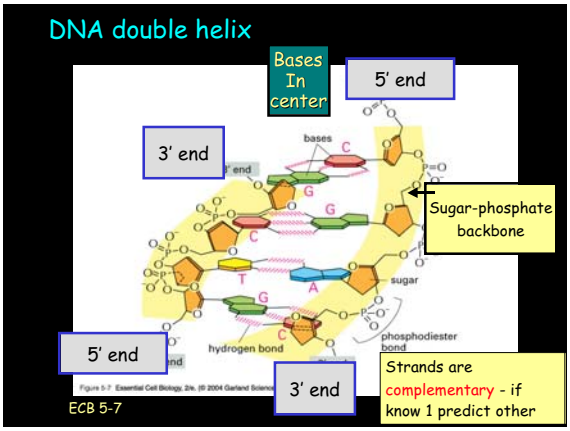
Where in the cell do we find DNA?



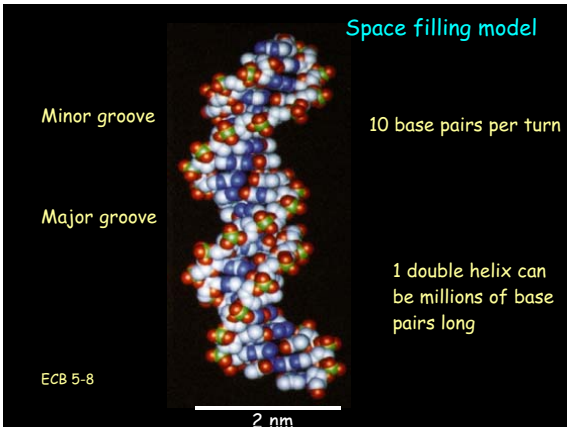
Strands held together by base pairs



DNA double helix



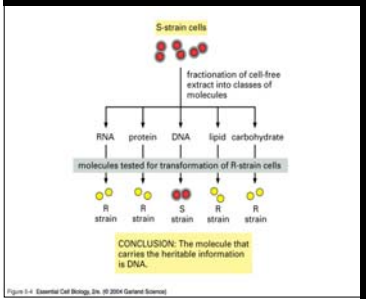
Space filling model



DNA is the genetic material

Debate raged in 1920s to 1940s; protein or nucleic acid or..

Mid 1940s; Avery MacLeod and McCarthy



DNA sequencing

The linear sequence of nucleotides can be determined by DNA sequencing technologies - facility on campus

β globin
ECB 5-11

Genome Projects

Complete sequence of all nuclear DNA from an organism (prokaryotes, yeast, plant, man etc)

Human genome (3,000,000,000 nucleotides)

Arabidopsis genome: 5,000,000 nucleotides

Last lecture in this section - Biotechnology

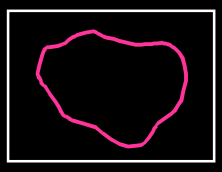
Introduction to nucleic acids

DNA structure

- Nucleotide Monomer
- Linear DNA strand
- Double-stranded DNA
- *Packaging of DNA into chromosomes

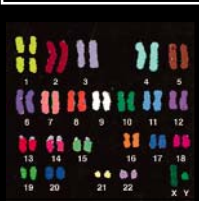
DNA Replication

Prokaryotes versus eukaryotes



Prokaryotes-
Circle of ds DNA
Few million base pairs

DNA packaging not a big issue

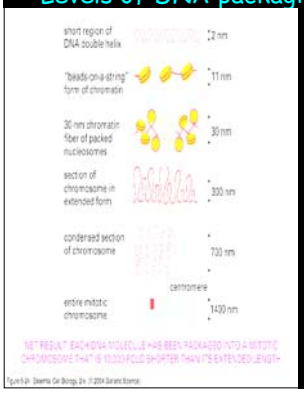


Eukaryotes-
Multiple chromosomes
Few billion base pairs total

DNA packaging a big issue

ECB 5-12

Levels of DNA packaging in a eukaryotic cell

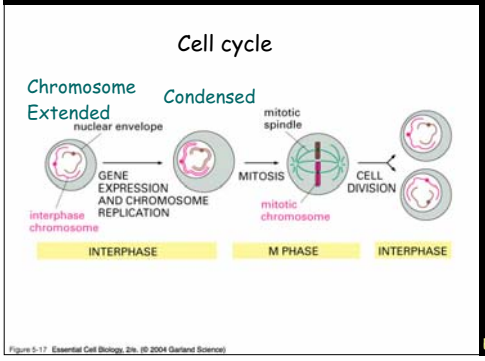


Typical human cell contains about 2 meters of DNA in nucleus

Yet the nucleus is only ~10 μm in diameter

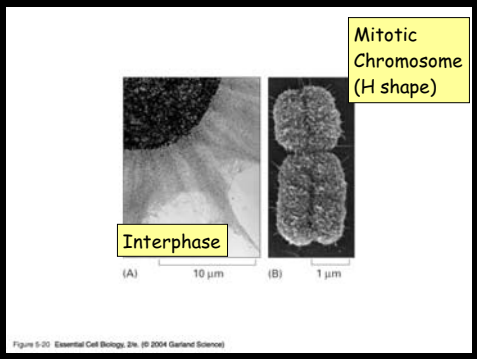
ECB 5-24

DNA condenses in preparation for mitosis and cell division



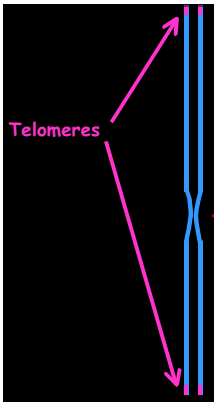
ECB 5-17

Transmission EM view of a chromosome



ECB 5-20

CHROMOSOME STRUCTURE



Condensed chromosome has two copies of each double helix held together

Centromere - region where two chromatids are held together

Duplicated chromosome drawn as an 'H'

Each line is double-stranded DNA

1 strand is a chromatid

Extent of chromatin condensation varies at different locations on chromosome

Heterochromatin Condensed chromatin

Stays condensed throughout cell cycle

Common around centromeres and telomeres

Does not code for protein

Euchromatin "true chromatin"

Condenses prior to division

Transcription occurs from euchromatin that is not highly condensed

Most chromatin in humans does not code for RNA or protein

X-chromosome Inactivation (heterochromatin)

Female mammals - 2 X chromosomes

Early embryos, random selection of X chromosome for inactivation (condensed into inactive heterochromatin)

Calico Cat. Black coat color gene is on one X chromosome, yellow coat color is on the other X chromosome. Random inactivation (condensation) during early embryogenesis results in patches of different coat colors.

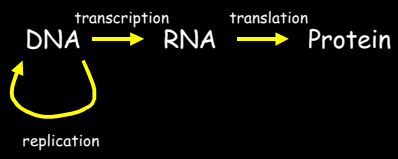
Introduction to nucleic acids

DNA structure

- Nucleotide Monomer
- Linear DNA strand
- Double-stranded DNA
- Packaging of DNA into chromosomes

*DNA Replication

Central Dogma



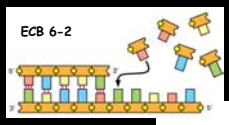
Begin with DNA replication
(Nucleus of eukaryote, cytoplasm of prokaryote)

Outline

- Replication is semi-conservative and bidirectional
- Biochemistry of replication
- Problem of replicating chromosome ends (telomeres)

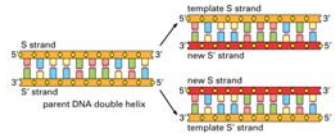
Replication is semi-conservative

ECB 6-2



Parental DNA strand = template

ECB 6-3



Semiconservative- both new DNA helices contain 1 old and 1 new strand

1. Selection of sites for initiation of DNA synthesis
2. Separate DNA strands (form open complex)
3. Directionality of DNA synthesis
4. Assemble molecules for DNA synthesis

Origin of replication

specific sequence

Double-stranded DNA

5' 3'

3' 5'

Double helix opened with aid of initiator proteins

Single-stranded DNA ready for DNA synthesis

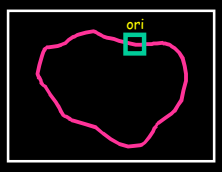
2 Replication forks

5' 3'

3' 5'

Parental DNA = template

Prokaryotes versus eukaryotes

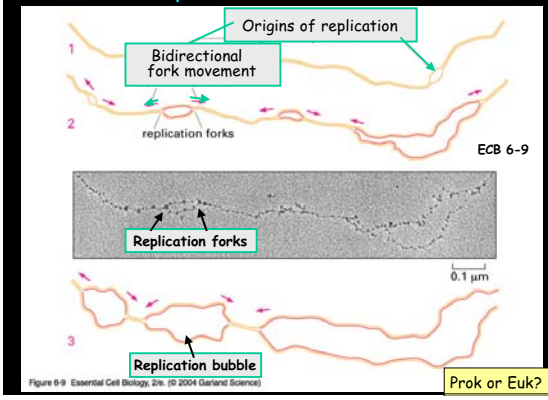


Prokaryotes-
1 origin of replication
~100 base pairs

Eukaryotes-
Multiple origins on each chromosome

Human-~10,000 origins total

Replication is bidirectional



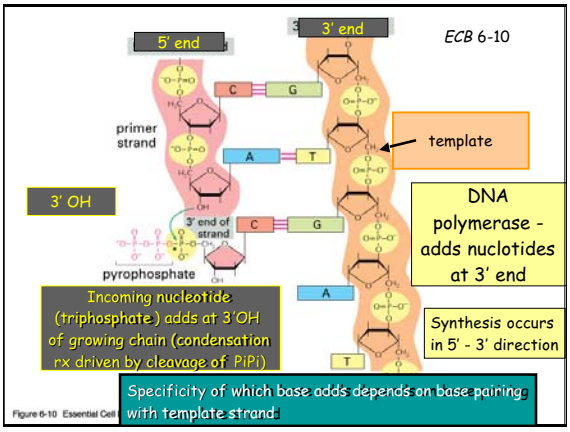
Prok or Euk?

1. Selection of sites for initiation of DNA synthesis

2. Separate DNA strands (form open complex)

3. Directionality of DNA synthesis

4. Assemble molecules for DNA synthesis


5' end
3' end
ECB 6-10
primer strand
template
3' OH
DNA polymerase - adds nuclotides at 3' end
3' end of strand
pyrophosphate
Incoming nucleotide (triphosphate) adds at 3'OH of growing chain (condensation rx driven by cleavage of PiPi)
Synthesis occurs in 5' - 3' direction
Specificity of which base adds depends on base pairing with template strand
Figure 6-10 Essential Cell