CHAPTER 4 OUTLINE

DNA replication is semi-conservative (Meselson and Stahl)

DNA polymerase
1. requires a 3’OH
2. adds dNTPs to the 3’ end
3. template is anti-parallel

DNA replication is semi-discontinuous
Leading strand is continuous
Lagging strand is discontinuous.

The lagging strand is synthesized as Okazaki fragments. RNA primers (primase) required for initiation of DNA fragments.

POL III is the DNA polymerase in prokaryotes involved in elongation. POL I removes the RNA primers and replaces them with deoxy-nucleotides. LIGASE used to join Okazaki fragments.

Other key DNA replication proteins include:
- Helicase (unwinds DNA)
- Single-stranded binding proteins (maintains single-stranded regions during replication)
- Gyrase (relieves tension in front of replication fork)

Replication is bi-directional. Prokaryotic genomes often associated with a single origin of replication (one replicon). In eukaryotes, the chromosomes have multiple origins of replication.

The termination problem. For linear genomes the ends are not completely replicated due to the nature of replication (3’ ends will lose bases at each round of replication, as primers cannot be replaced). Solution is the presence of a telomerase activity that can restore telomere ends by adding 6 base repeats.

Cell Division
Mitosis: asexual cell division that ensures that same genetic material is passed on to progeny cells.
Meiosis: sexual cell division that halves genetic material during generation of gametes. Allows for genetic variation.

MITOSIS

Cell cycle: G1 → S (genetic material duplicated) → G2 → M (mitosis)

One parent diploid cell gives rise to two progeny diploid cells that are genetically identical to parent.

Phases of Mitosis
Prophase: condensation of genetic material, break down of nuclear envelope, disappearance of nucleoli, and formation of spindle fiber apparatus. Chromosomes
interact with spindle. Replicated chromosome made up of two chromatids joined at centromere. Kinetochores form at centromere and interact with microtubules. Metaphase: The kinetochore-microtubule interaction allows chromosomes to line up at the metaphase plate, half way between the poles of the spindle. Anaphase: centromeric separation. Chromatids separate from each other and migrate to poles. Once separated, they can be referred to as chromosomes. Telophase: chromosomes reach the two poles and nuclear envelope forms around the daughter nuclei. Cytokinesis (separation of cytoplasm) occurs.

Meiosis (DNA replicated once, followed by two divisions)  
Division I is reductive (i.e. chromosome number is halved). Based on separation of homologous chromosomes which occurs after they have paired up.  
Division II is equational (centromeric)  
Meiosis I  
Prophase I: chromosomes condense, homologues synapse (synaptonemal complex) and exchange genetic material. Spindle fiber apparatus forms.  
Metaphase I: The paired homologues (tetrads) line up at metaphase plate  
Anaphase I: Homologues separate from each other and migrate to poles. Replicated chromosomes remain associated at centromere (i.e. separation is between the centromeres of the homologues.)  
Telophase I: Replicated haploid chromosome sets reach poles. Nuclear envelopes may or may not form depending on organism.  
Interkinesis is the variable intervening period between Meiosis I and Meiosis II.  
Meiosis II is very similar mechanically to mitosis.  
Prophase II: Chromosomes condense and spindles form.  
Metaphase II: Replicated chromosomes line up on metaphase plate.  
Anaphase II: centromeric separation. Chromatids separate and migrate to poles.  
Telophase II: Chromosomes reach poles and the final haploid products are separated into precursor sex cells.  
Four equivalent haploid products are generated during spermatogenesis.  
In oogenesis, cell divisions are uneven, and only one of the four products may become a functional egg cell.