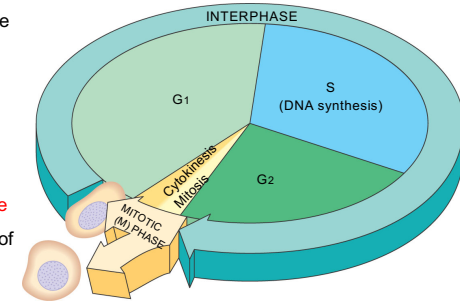


Repetition

Summary of last lecture

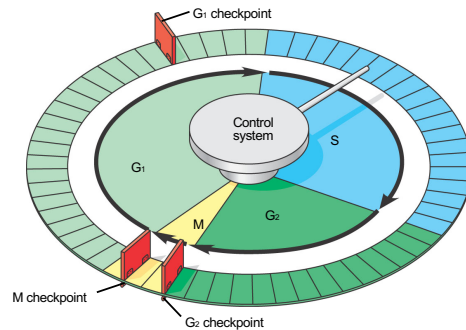
Phases of the Cell Cycle

- The cell cycle consists of
 - the **Mitotic phase (M)**
 - **Interphase (G1, S, G2)**
- **Interphase** can be divided into sub-phases
 - **G₁ phase**
 - **S phase**
 - **G₂ phase**
- The **mitotic phase**
 - is made up of **mitosis and cytokinesis**



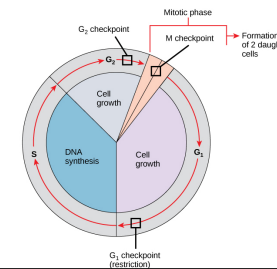
The Cell Cycle Control System

- The sequential events of the cell cycle
 - are directed by a distinct cell cycle control system, which is similar to a clock



Regulation of cell cycle

- Daughter cells have to be exact replicas of parent cells
- Mistakes in the duplication or distribution of the chromosomes lead to mutations that may be passed forward to every new cell produced from an abnormal cell.
- To prevent a compromised cell from continuing to divide, there are internal control mechanisms that operate at three main **cell cycle checkpoints**.
- A checkpoint is one of several points in the eukaryotic cell cycle at which the progression of a cell to the next stage in the cycle can be halted until conditions are favorable.
- These checkpoints occur near the end of G₁, at the G₂/M transition, and during metaphase



Cell cycle overview

The cell "double checks" the duplicated chromosomes for error, making any needed repairs.

Each of the 46 chromosomes is duplicated by the cell.

Cellular contents, excluding the chromosomes, are duplicated.

Cell cycle arrest.

- The cell cycle is an ordered set of events, culminating in cell growth and division into two daughter cells.
- Non-dividing cells not considered to be in the cell cycle. The stages, pictured to the left, are G1-S-G2-M.
- The G1 stage stands for "GAP 1". The S stage stands for "Synthesis". This is the stage when DNA replication occurs. The G2 stage stands for "GAP 2".
- G1-S-G2 stages are together known as interphase
- The M stage stands for "mitosis", and is when nuclear (chromosomes separate) and cytoplasmic (cytokinesis) division occurs. Mitosis is further divided into 5 phases, prophase, prometaphase, metaphase, anaphase and telophase

The Cell Cycle Clock: Cyclins and Cyclin-Dependent Kinases

two types of regulatory proteins are involved in cell cycle control: **cyclins and cyclin-dependent kinases (Cdks)**

the activity of cyclins and Cdks fluctuates during the cell cycle

(a) Fluctuation of MPF (Mitosis Promoting Factor, MPF) activity and cyclin concentration during the cell cycle

(b) Molecular mechanisms that help regulate the cell cycle

- During G₁, conditions in the cell favor degradation of cyclin, and the Cdk component of MPF is recycled.
- MPF promotes mitosis by phosphorylating various proteins. MPF's activity peaks during metaphase.
- Synthesis of cyclin begins in late S phase and continues through G₂. Because cyclin is protected from degradation during this stage, it accumulates.
- Accumulated cyclin molecules combine with recycled Cdk molecules, producing enough molecules of MPF to pass the G₂ checkpoint and initiate the events of mitosis.
- During anaphase, the cyclin component of MPF is degraded, terminating the M phase. The cell enters the G₁ phase.

Regulation of cell cycle

- The cell cycle is a highly regulated process
- Two types of regulatory proteins are involved in cell cycle control: cyclins and cyclin-dependent kinases (CDKs)
- The levels of the four cyclin proteins fluctuate throughout the cell cycle in a predictable pattern
- After the cell moves to the next stage of the cell cycle, the cyclins that were active in the previous stage are degraded.

Mitotic cyclin-CDKs
Cyclin A-CDK1
Cyclin B-CDK1

Mid-G₁ cyclin-CDKs
Cyclin D-CDK4
Cyclin D-CDK6

Late-G₁ cyclin-CDK
Cyclin E-CDK2

S-phase cyclin-CDK
Cyclin A-CDK2

Restriction point
RB-E2F complex
-RB-ppp + E2F released

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A closer look to the Cyclins and Cdks

Mitotic cyclin-CDKs
Cyclin A-CDK1
Cyclin B-CDK1

Mid-G₁ cyclin-CDKs
Cyclin D-CDK4
Cyclin D-CDK6

Late-G₁ cyclin-CDK
Cyclin E-CDK2

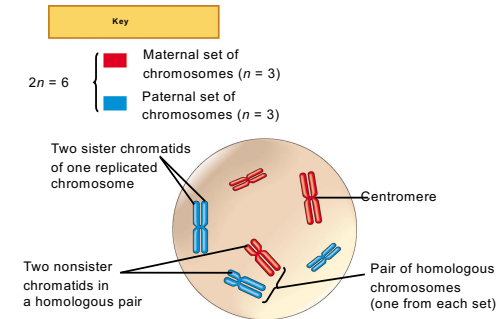
S-phase cyclin-CDK
Cyclin A-CDK2

During G₁ phase progression, activation of cyclin D/cdk4 and cyclin E/cdk2 complexes by cyclin activating kinase (CAK) leads to sequential phosphorylation of the transcription factor RB.

Diploid vs. Haploid

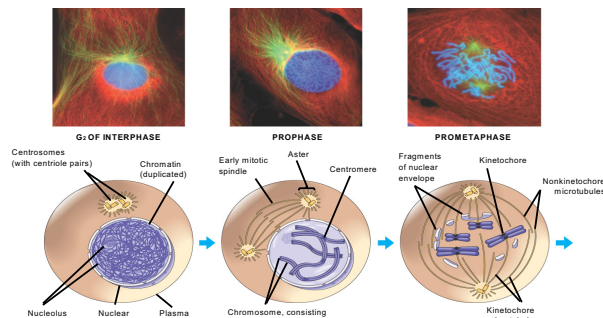
- Most human **somatic (body) cells** have **46 chromosomes**
 - This is called the **diploid condition**
 - $2n = 46$ ($2 \times 22 + X, Y$)
- **Gametes (sperms and eggs)** are an exception: they only have **23 chromosomes**
 - This is the **haploid condition**
 - $n = 23$

- In a cell in which DNA synthesis has occurred
 - all the chromosomes are duplicated and thus each consists of two identical sister chromatids

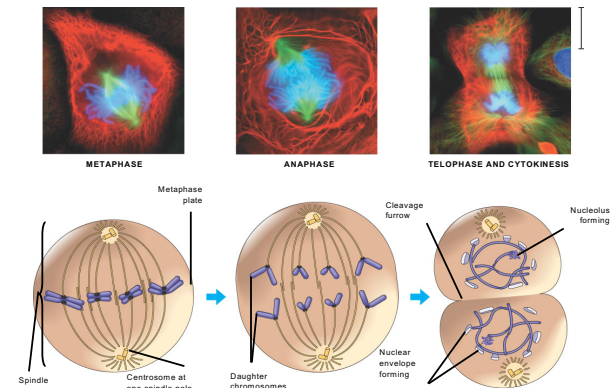


- **Mitosis** consists of five distinct phases

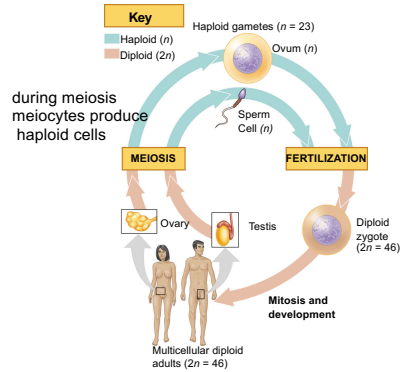
- Prophase Prometaphase



- Metaphase, - Anaphase, - Telophase



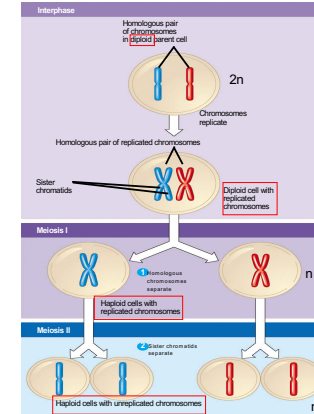
• The human life cycle



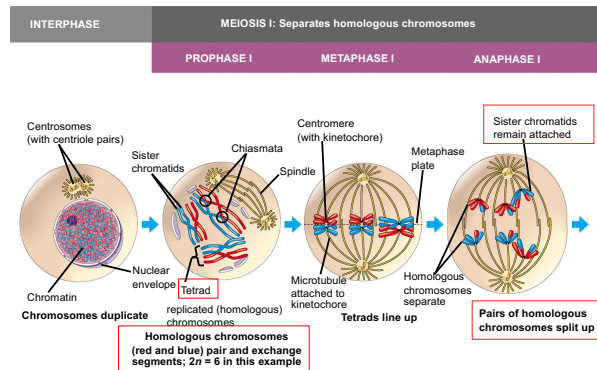
- Meiosis reduces the number of chromosome sets from diploid to haploid
- Meiosis takes place in two sets of divisions, meiosis I and meiosis II

The Stages of Meiosis

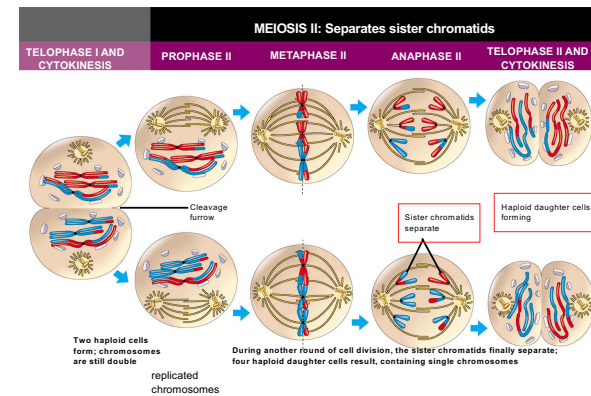
- An overview of meiosis
- Meiosis I reduces the number of chromosomes from diploid to haploid
- Meiosis II produces four haploid daughter cells



• Interphase and meiosis I



• Telophase I, cytokinesis, and meiosis II



• A comparison of mitosis and meiosis

