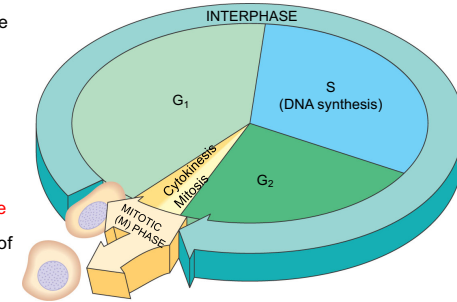


## Repetition

### Summary of last lecture

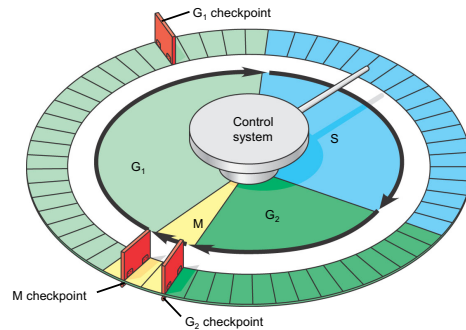
## Phases of the Cell Cycle

- The cell cycle consists of
  - the **Mitotic phase (M)**
  - **Interphase (G<sub>1</sub>, S, G<sub>2</sub>)**
- **Interphase** can be divided into sub-phases
  - **G<sub>1</sub> phase**
  - **S phase**
  - **G<sub>2</sub> phase**
- The **mitotic phase**
  - is made up of **mitosis and cytokinesis**



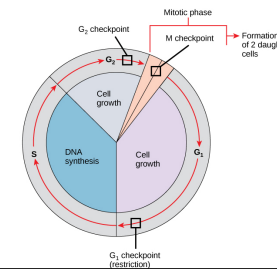
## The Cell Cycle Control System

- 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 G<sub>1</sub>, at the G<sub>2</sub>/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.

breakdown of nuclear membrane  
sister chromatids  
centromere  
lowly coiled replicated chromosomes

spindle fibers appear  
chromosomes condense  
spindle fibers attach to chromosomes  
chromosomes align

centromeres divide  
sister chromatids move to opposite poles  
chromosomes disperse

nuclear membrane reforms  
chromosomes decondense  
spindle fibers disappear

cytoplasm divides  
parent cell becomes 2 daughter cells with identical genetic information

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- 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

1 Synthesis of cyclin begins in late S phase and continues through G<sub>2</sub>. Because cyclin is protected from degradation during this stage, it accumulates.

2 Accumulated cyclin molecules combine with recycled Cdk molecules, producing enough molecules of MPF to pass the G<sub>2</sub> checkpoint and initiate the events of mitosis.

3 During anaphase, the cyclin component of MPF is degraded, terminating the M phase. The cell enters the G<sub>1</sub> phase.

4 MPF promotes mitosis by phosphorylating various proteins. MPF's activity peaks during metaphase.

### 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-G<sub>1</sub> cyclin-CDKs**  
Cyclin D-CDK4  
Cyclin D-CDK6

**Late-G<sub>1</sub> cyclin-CDK**  
Cyclin E-CDK2

**S-phase cyclin-CDK**  
Cyclin A-CDK2

Restriction point

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### A closer look to the Cyclins and Cdks

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

**Mid-G<sub>1</sub> cyclin-CDKs**  
Cyclin D-CDK4  
Cyclin D-CDK6

**Late-G<sub>1</sub> cyclin-CDK**  
Cyclin E-CDK2

**S-phase cyclin-CDK**  
Cyclin A-CDK2

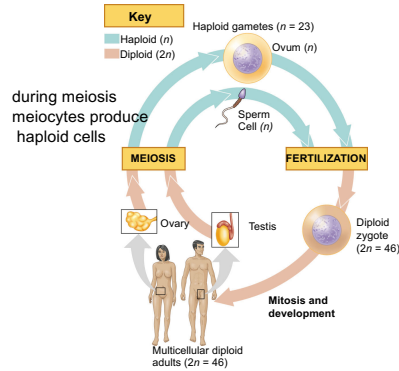
Restriction point

RB-E2F

-RB-p-E2F-complex  
---RB-ppp + E2F released

During G<sub>1</sub> 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.

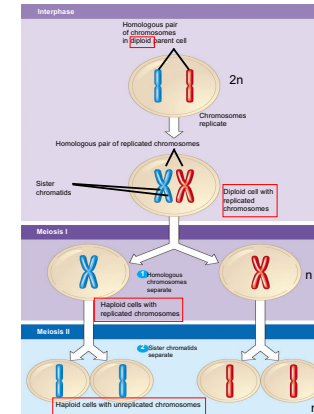
• The human life cycle



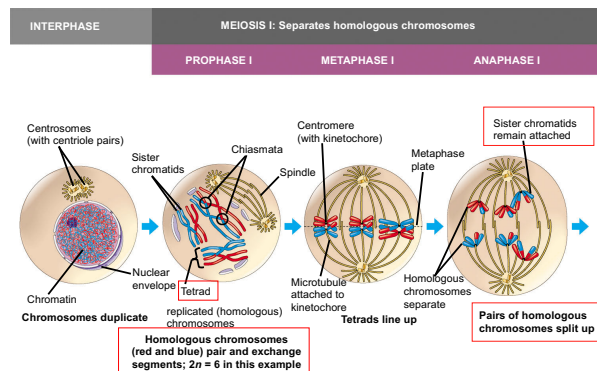
- Meiosis reduces the number of chromosome sets from diploid to haploid
- Meiosis takes place in two sets of divisions, meiosis I and meiosis II

The Stages of Meiosis

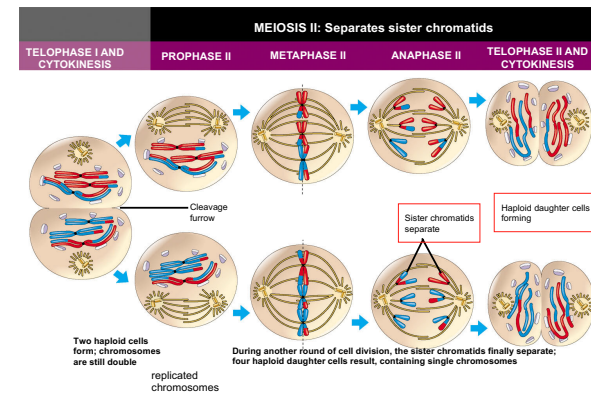
- An overview of meiosis
- Meiosis I reduces the number of chromosomes from diploid to haploid
- Meiosis II produces four haploid daughter cells



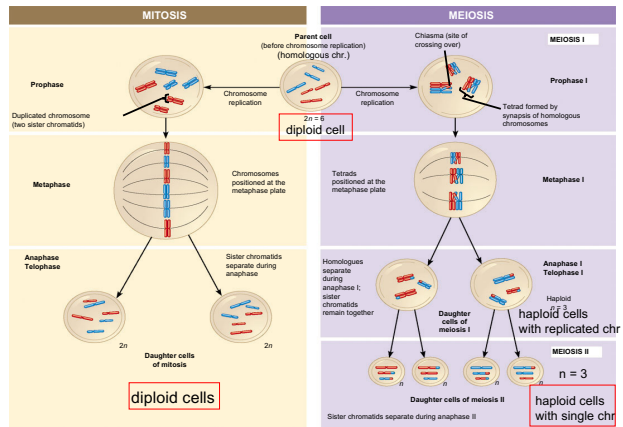
• Interphase and meiosis I



• Telophase I, cytokinesis, and meiosis II



• A comparison of mitosis and meiosis



Row	Mitosis	Meiosis
	In somatic cells	In cells in the sexual cycle
1	One cell division, resulting in two daughter cells	Two cell divisions, resulting in four products of meiosis
2	Chromosome number per nucleus maintained (e.g., for a diploid cell)	Chromosome number halved in the products of meiosis
3	One premeiotic S phase per cell division	One premeiotic S phase for both cell divisions
4	Normally, no pairing of homologous chromosomes in prophase	Full synapsis of homologous chromosomes in prophase
5	Normally, no recombination in prophase	At least one recombination between nonsister chromatids
6	Bi-oriented sister kinetochores	Co-orientation of sister kinetochores
7	Loss of cohesion between sister chromatid arms during metaphase	Maintenance of cohesion between sister chromatid arms during metaphase of meiosis I
8	Centromeres divide at anaphase	Centromeres do not divide at anaphase I but do at anaphase II
	Conservative process: daughter cells' genotypes identical with parental genotype	Promotes variation among the products of meiosis
	Cell undergoing mitosis can be diploid or haploid	Cell undergoing meiosis is diploid