PHYS 4xx Cell division

Cell cycle

For most cells, the essence of life is to grow and replicate through division:

- **Growth** involves a doubling of a cell's size from its initial state just after division of its parent

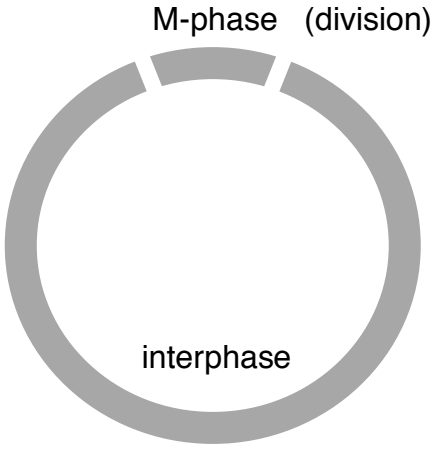
- The cell must also **duplicate** its DNA, a formidable task for eukaryotic cells with large amounts of DNA, even if large stretches of it are non-coding. The cell must also duplicate the number of cytoplasmic organelles in preparation for division.

- Lastly, there is the spectacular and complex operation of cell **division**, where the cell's DNA must be organized and separated, followed by the mechanical cleaving of the cell itself.

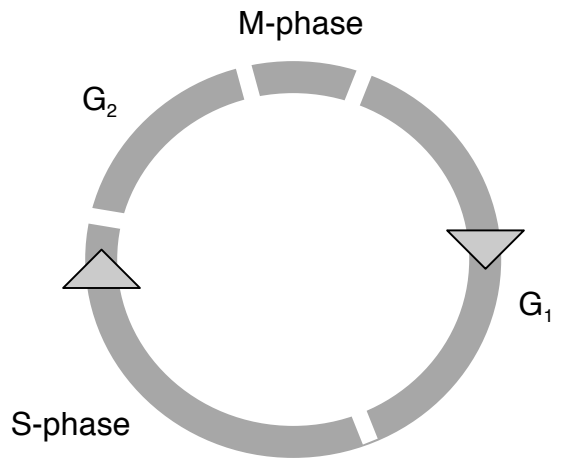
Exceptions to the above scenarios are early embryonic cells, which strongly curtail the growth stage - these cells just divide as rapidly as possible from one large egg cell, becoming smaller with each successive generation.

Cell **lifetimes** vary considerably, from 8 minutes in a fly embryo to more than a year in a mammalian liver cell.

At its simplest, the cell cycle is divided into interphase, where the cell grows continuously, and M-phase (**M** for mitosis) where it divides:



Interphase itself can be further divided in three as S-phase (**S** for synthesis, where DNA is replicated), which is separated from M-phase by G_1 and G_2 (**G** for gap):



Typical time scales for a cell with a 24-hour cycle:

G_1 - 10 hours
S - 9 hours
G_2 - 4 hours
M - 1 hour

Visually, the most spectacular part is M, the mechanical division of the cell. M phase is divided into mitosis (5 stages) and cytokinesis (1 stage)

1. *prophase* chromosomes (two chromatids each) are slowly condensing; centrosomes have duplicated and begun to form spindle poles; nuclear envelope intact

2. *prometaphase* nuclear envelope breaks up, allowing microtubules from the separated centrosomes (or spindle poles) to seek out the kinetochores on the chromosomes; polar microtubules extend towards midplane

3. *metaphase* opposing microtubules (once connected) exert tension on chromosomes, moving them to the midplane; polar microtubules extend from spindle poles

4. *anaphase* chromosomes break into pairs of chromatids, which are dragged by shortening kinetochore MTs to the spindle poles; pressure from polar MTs begins to push spindle poles apart

5. *telophase* kinetochore MTs disappear; chromatids decondense; nuclear envelope begins to reform; end of mitosis

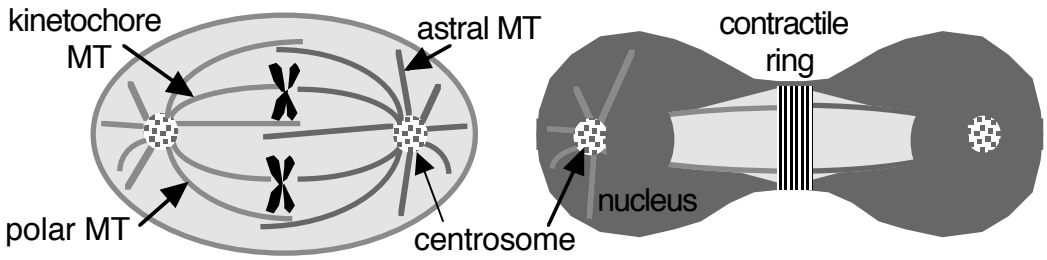
6. *cytokinesis* nuclear envelopes complete; contractile ring (which may have begun forming in anaphase) causes cleavage furrow and leads to cell division

Role of microtubules

kinetochore microtubules seek out the kinetochore on a chromosome

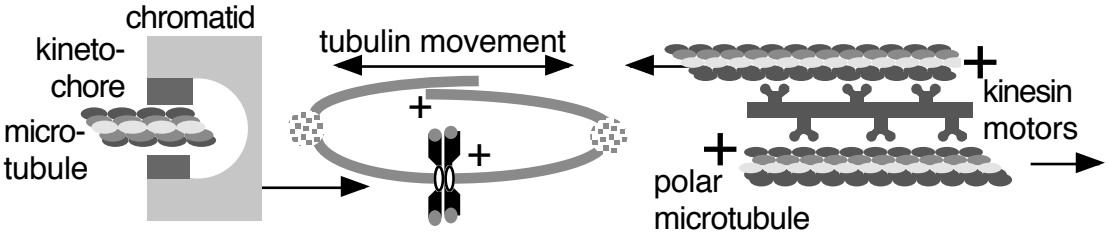
polar microtubules run between the spindle poles defined by the centrosomes, meeting plus end to plus; they may be linked by motor proteins to form a dynamic bond

astral microtubules just end at the plasma membrane



Kinetochore microtubules

- one kinetochore is present on each of the two sister chromatids of a chromosome, each capable of attaching more than one microtubule
- attachment may be like an open collar, rather than a cap, permitting tubulin dimers to be added to, or lost from, the plus end
- minus end is buried in the centrosome, and loses tubulin with time, such that a tubulin dimer moves along a microtubule from plus to minus
- kinetochore microtubule can drag a chromatid towards a centrosome at a rate of about 2 μm per minute (or 13 dimers/second)
- ~60-80% of the loss is at the plus end, remainder at minus (treadmilling rates are of the order microns per hour, far slower than the migration of tubulin during mitosis)



- the collar at the kinetochore must pull itself along the filament as the plus end of the MT depolymerizes
- combination of collar movement and tubulin loss at the centrosome results in a tensile force of several hundred piconewtons applied to the attached chromatid

- with tens of microtubules attached to a given kinetochore, the force per filament is closer to 50 pN, requiring a collection of molecular motors, at ~5 pN per motor
- viscous drag on a chromatid is estimated at 10^{-1} pN
- typical motor protein speed is microns per second, not the microns per minute of a chromatid
- drag force and speed are less than what a dynein can deliver

Polar microtubules

- pairs of opposing polar microtubules are thought to overlap at a junction complex containing the molecular motor kinesin
- a candidate structure is displayed above, like the actin-myosin complex in muscles
- Walking towards the plus end of the filament, kinesin motors generate compression on the microtubule, driving the spindle poles to move apart
- if the junction contains several kinesin motors, then the compressive force on the pair of microtubules will lie in the 10-20 pN range, which is not far from the threshold force that will cause buckling in a microtubule 5-10 microns long

Actin

- in division of animal cells, the contractile ring comprises some 20 actin filaments
- myosin-II is thought to provide the driving force to shorten the ring (as in muscle cells)
- ring operates like a belt, cinching down the middle region of the dividing cell; surplus actin is released as the neck narrows, and the ring disappears before the daughter cells separate