• A sea urchin begins life as a single cell that (a) divides to form two cells, visible by scanning electron microscopy. After four rounds of cell division, (b) there are 16 cells, as seen in this SEM image. After many rounds of cell division, the individual develops into a complex, multicellular organism, as seen in this (c) mature sea urchin. (credit a: modification of work by Evelyn Spiegel, Louisa Howard; credit b: modification of work by Evelyn Spiegel, Louisa Howard; credit c: modification of work by Marco Busdraghi; scale-bar data from Matt Russell)
Cell Division & Reproduction
I. Cell Division Plays Many Important Roles In Living Organisms
   A. can lead to the production of genetically identical offspring – asexual reproduction
      1. gametes are not involved
      2. daughter cell/clone is genetically identical to parent
         a. yeast cell has duplicated its chromosomes & is dividing
         b. sea star is regenerating from fragmented pieces
         c. African violet is producing another individual plant from a cutting
B. can lead to offspring that are genetically distinct from either parent – sexual reproduction (uses meiosis & cytokinesis)
1. human zygote is the result of fusion of gametes from 2 different individuals
   a. mixture of parental genes
2. zygote divides (mitosis & cytokinesis) into embryo which during early stages consists of like cells
3. cells continue to divide (mitosis & cytokinesis) & differentiate even though they contain like DNA
   a. eventually a human consisting of trillions of cells (via mitosis & cytokinesis)
C. sexually reproducing organisms use cell division (mitosis & cytokinesis) for tissue renewal, replacement, growth
1. millions of cells must divide every second to replace lost/damaged cells
   a. via mitosis & cytokinesis
Prokaryotes Reproduce By Binary Fission

I. As singular circular DNA is copied – copies migrate poleward
   A. cell is elongating during this time

II. Upon completion of chromosome duplication, the plasma membrane grows inward & a cell wall develops
   A. parent cell divides into 2 daughter cells
      1. asexual reproduction
The Eukaryotic Cell Cycle & Mitosis

I. The large, complex chromosomes of eukaryotes duplicate w/ each cell division

A. most human somatic cells carry 46 chromosomes, dogs - 78, mosquitoes - 6
   1. just under 21,000 genes
   2. ~ 2 meters length

B. chromosome consists of DNA molecule + attached proteins
   1. chromatin in thin, diffuse state
   2. DNA molecule consists of 2 complementary strands of DNA

*PRIOR TO DNA DUPLICATION*

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<td>46</td>
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<tr>
<td>how many DNA molecules</td>
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<tr>
<td>how many DNA strands in nucleus</td>
<td>12</td>
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Sister Chromatids

Chromosome

Duplicated chromosomes consist of 2 sister chromatids

Sister chromatids separate into different cells & become 2 separate chromosomes
C. prior to dividing, a cell will duplicate its chromatin

1. this produces duplicated chromosomes (condensed chromatin)
   a. each duplicated chromosome consists of 2 sister chromatids
      1) genetically identical
      2) held together via cohesin proteins
      3) centromere is constricted region
   b. each chromosome consists of 2 DNA molecules
   c. each chromosome consists of 4 DNA strands

*AFTER DNA DUPLICATION*

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2. chromatids will separate during cell division
   a. individual, non-duplicated chromosomes
II. The cell cycle includes growing & division phases
* this is the process that enabled each of us to grow from a single-celled zygote to some 10 trillion celled person

A. Interphase (~90%)
   1. **G\textsubscript{1}**: cell begins doubling most everything in its cytoplasm
   2. **S**: cell duplicates the chromosomes
      a. DNA synthesis/replication
      b. each chromosome consists of 2 sister chromatids
   3. **G\textsubscript{2}**: cell completes preparation for cell division

A cell moves through a series of phases in an orderly manner. During interphase, **G\textsubscript{1}** involves cell growth and protein synthesis, the **S** phase involves DNA replication and the replication of the centrosome, and **G\textsubscript{2}** involves further growth and protein synthesis. The mitotic phase follows interphase. Mitosis is nuclear division during which duplicated chromosomes are segregated and distributed into daughter nuclei. Usually the cell will divide after mitosis in a process called cytokinesis in which the cytoplasm is divided and two daughter cells are formed.
B. Mitotic phase (M phase - ~10%)
*divided into mitosis & cytokinesis

1. prophase
   a. chromatin fibers condense into discrete chromosomes
   b. mitotic spindle begins to form out of centrosomes
      1) microtubules + proteins
   c. centrosomes/centrioles begin moving poleward

Animal cell mitosis is divided into five stages—prophase, prometaphase, metaphase, anaphase, and telophase—visualized here by light microscopy with fluorescence. Mitosis is usually accompanied by cytokinesis, shown here by a transmission electron microscope. (credit “diagrams”: modification of work by Mariana Ruiz Villareal; credit “mitosis micrographs”: modification of work by Roy van Heesbeen; credit “cytokinesis micrograph”: modification of work by the Wadsworth Center, NY State Department of Health; donated to the Wikimedia foundation; scale-bar data from Matt Russell)
2. prometaphase
   a. nuclear envelope begins to fragment
   b. some microtubules begin attaching to kinetochores of sister chromatids
      1) kinetochore microtubules
   c. opposite pole microtubules will attach to 2 sister chromatids of a duplicated chromosome
      1) get into a “tug of war”
         a) chromosomes are jerked back & forth
3. metaphase
   a. “tug of war” stalemate results in chromosomes aligned along metaphase plate
      1) centromeres are along metaphase plate
      2) chromosomal arms may be dangling above/below plate
4. **anaphase**
   
a. motor protein inside a kinetochore begins “walking” its sister chromatid towards the pole it faces
   1) south facing kinetochores walk south
   2) north facing kinetochores walk north
      a. this separates sister chromatids of duplicated chromosomes
   b. cell elongates as non-kinetochore microtubules lengthen
5. telophase
   a. nuclear envelope forms around each set of nonduplicated chromosomes
      1) each daughter cell has its own nucleus
         a) daughter cells are genetically identical to one another
      b. chromosomes uncoil into chromatin form
c. cytokinesis divides the cytoplasm of the 2 newly forming cells

1) cleavage furrowing in animal cells
   a) contracting ring of actin & myosin

2) cell plate formation in plant cells
   a) Golgi vesicles coalesce along midline & form a cell plate
   *matures into a cell wall

• In part (a), a cleavage furrow forms at the former metaphase plate in the animal cell. The plasma membrane is drawn in by a ring of actin fibers contracting just inside the membrane. The cleavage furrow deepens until the cells are pinched in two. In part (b), Golgi vesicles coalesce at the former metaphase plate in a plant cell. The vesicles fuse and form the cell plate. The cell plate grows from the center toward the cell walls. New cell walls are made from the vesicle contents.
III. Anchorage, cell density & growth factors affect cell division
   A. most cells exhibit anchorage dependence
      1. cell-surface proteins must be in contact w/ a solid surface for most cells to be able to run through a life cycle
         a. cancerous cells are an exception to this
   B. most cells exhibit density-dependent inhibition
      1. crowded cells stop dividing
         a. cell-surface proteins sense crowded conditions
         b. cancerous cells continue to divide
C. protein growth factors stimulate cells to divide
   1. researchers have discovered ~ 50 different growth factors that stimulate cell division
   2. different cell types respond to certain growth factors or a combination of growth factors
      a. PDGF – platelet derived growth factor
         1) platelets arriving at injury site to skin will secrete PDGF
             a) binds to receptors on fibroblasts
                *common member of connective tissue
                *stimulates fibroblasts to divide to heal wound
      b. VEGF – vascular endothelial growth factor
         1) stimulates growth of new blood vessels
            a) during fetal development & after injury
            b) overproduction is a hallmark of many dangerous cancers
IV. Growth factors signal the cell cycle control system
   A. most cells do not divide unless they are signaled by other cells to do so
      1. growth factors are the main signals
   B. intracellular signals detected by the control system tell the system whether key cellular processes up to each point have been completed & whether the cell cycle should proceed past that point
   C. the control system also receives messages from outside the cell indicating general environmental conditions & the presence of specific signal molecules from other cells
D. 3 major checkpoints in the cell cycle

1. $G_1$: seems to be the most important for many cells
   a. if a cell receives a go ahead signal, growth factor, it will usually enter S phase
      1) binding leads to a signal transduction pathway
         a) protein-protein interactions that lead to override of checkpoint
      2) cell goes on to divide
   b. mature nerve & muscle cells never receive a $G_1$ go ahead signal
      1) they go into a $G_0$ phase
         a) permanently non-dividing state
2. G₂: involves activation of cyclin-dependent kinases (CDK) via cyclin
   a. leads to a complex: maturation promoting factor (MPF)
      1) MPF phosphorylates many different proteins which seem to be involved in:
         a) condensing chromatin into chromosomes
         b) building the mitotic spindle
         c) fragmenting the nuclear envelope

3. M: all kinetochores must be attached to spindle microtubules at metaphase plate
   1) only then will the appropriate regulatory protein complex (not a Cdk)
      become activated
      *the activated protein complex will then set off a chain of molecular
       events that results in the activation of separase which will cleave cohesion proteins between the sister chromatids

* Cyclin-dependent kinases (Cdks) are protein kinases that, when fully activated, can phosphorylate and thus
  activate other proteins that advance the cell cycle past a checkpoint. To become fully activated, a Cdk must bind to a cyclin protein and then be phosphorylated by another kinase.
V. Growing out of control, cancer cells produce malignant tumors
   A. cancer claims 1 out of every 5 lives in the U.S.
   B. a cancer cell is a once normal cell that has undergone transformation
      1. this follows a mutation in 1 or more genes that encode proteins for the cell cycle
         control system
      2. cancer cell is not a productive contributor
      3. usually recognized by the immune system & is destroyed
   C. if a transformed cell evades detection by the immune system it may multiply to form
      a tumor
1. mass of abnormally growing cells w/in otherwise normal tissue
2. benign tumor: abnormal cells remain at original site
   a. can cause problems if the growth disrupts some organs like the brain
3. malignant tumor: tumor that has spread to neighboring tissues & other parts of the body
   a. can displace normal tissue & disrupt organ function
   b. a person w/ a malignant tumor is said to have cancer
4. cancer cells may break loose from original site
5. cancer cells may signal angiogenesis
   a. blood vessels proliferate in area of cancer
      1) cancer may metastasize via blood or lymphatic system
E. normal cells can divide 20-50 times
F. cancer cells are immortal in the lab
G. tumors may be treated w/ radiation
   1. does more damage to cancer DNA than to normal cells
      a. may be because cancer cells have lost the ability to repair their DNA
H. tumors may be surgically removed
I. metastatic tumors are treated w/ chemotherapy
   1. drugs that disrupt the cell cycle
      a. Taxol: from the bark of the Pacific Yew tree
         1) freezes the mitotic spindle after it forms so cells can’t go past metaphase
         2) lung, ovarian & breast cancers
b. Vinblastin: from periwinkle
   1) prevents mitotic spindle from forming
   2) Hodgkin’s lymphoma, lung, breast, testicular

c. ER+ cancer cells can be treated w/ tamoxifen
   1) blocks estrogen receptor active sites

2. side effects of chemotherapy are due to the drugs’ effects on rapidly dividing normal cells
   a. nausea: intestinal cells
   b. hair loss: follicle cells
   c. increased risk of infection: immune cells