The Cyprus International Institute for the Environment and Public Health
In collaboration with the Harvard School of Public Health

Lecture 1

Sherwood, Human Physiology

Cell Physiology (21-51)
Membrane Structure (53-60)]
Homeostasis (1-19)

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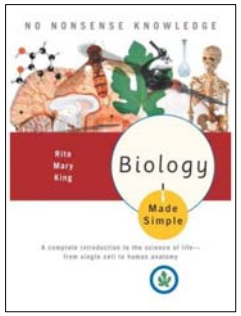
http://www.eng.ucy.ac.cy/cpitris/courses/ClIPhys/

Oh No!

- **What if I never had biology before?**



- Online Courses
  - Carnegie Mellon
    - http://www.cmu.edu/oli/courses/enter_biology.html
  - Palomar College
    - http://waynesword.palomar.edu/bio100.htm

- **Paperback: 208 pages**
- **Publisher: Made Simple Books (Aug 2003)**
- **Language English**
- **ISBN-10: 0767915429**
- **Price: 6 UKP form amazon.co.uk!**

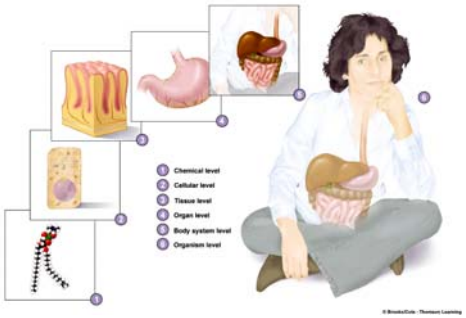
Lecture Objectives

- **Review of cell physiology**
  - Overview of cell structure
  - Major organelles
  - Energy production
  - Membrane structure and cell-to cell adhesions
  - Endocytosis, phagocytosis
- **Tissue/organ/system organization**
- **Homeostasis**

(see notes for more details)

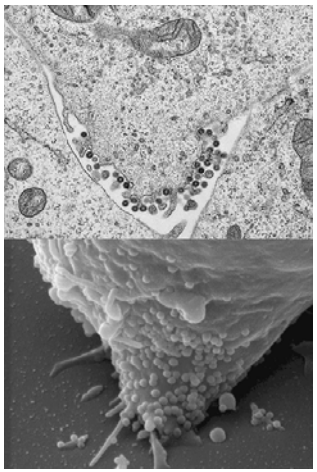
Physiology

- **What is physiology?**
  - Study of the functions of living things
  - Mechanistic approach (vs. teliologic approach)
    - Mechanisms of action instead of results
- **Levels of organization in the body**
  - Molecules
  - Cells (differentiation vs. single cell organisms)
  - Tissues
  - Organs
  - Systems
  - Organisms



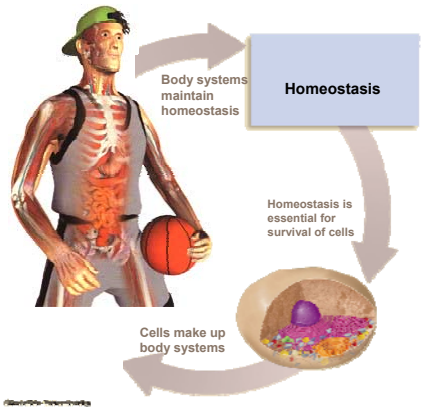
Cells

- **Most cells perform much the same functions**
  - Obtain nutrients and O_2
  - Provide energy from nutrients and O_2
  - Eliminate waste products
  - Synthesize proteins needed fro cell structure, growth and function
  - Control exchange of materials with the local environment
  - Respond to changes in the local environment
  - Reproduce (not all cells)
- **Specialization**
  - Use above functions to perform specific cells (kidney, liver, etc.)



Cell Physiology

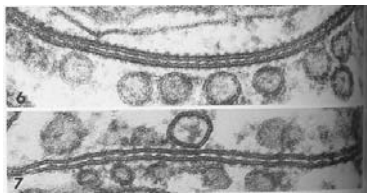
- **Cells are the smallest structural and functional units capable of carrying out life processes**
- **The functional activities of each cell depend on the specific structural properties of the cell**
- **An organisms structure and function depend on the individual and collective characteristics and organization of its cells**
  - Trillions of cells
  - More than 200 types
- **To understand function must study structural components of cells**

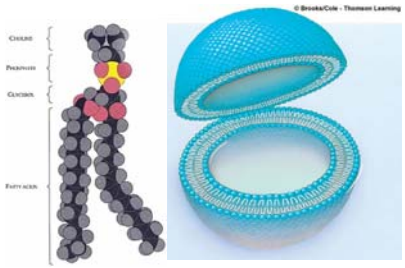


Background Material

Membrane Structure

- **Plasma membrane**
  - Fluid lipid bilayer embedded with proteins and cholesterol
- **Phospolipid bilayer**
  - Phospholipids
    - Polar (charged) hydrophilic head
    - Two nonpolar hydrophobic fatty acid chains
  - Assemble in a bilayer which separates two water-based volumes, the ICF and ECF
  - Barrier to passage of water-soluble substances
  - Not solid! "Fluid mosaic surface" → fluidity of membrane

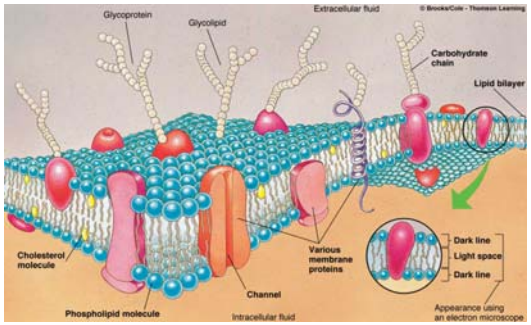




Background Material

Membrane Structure

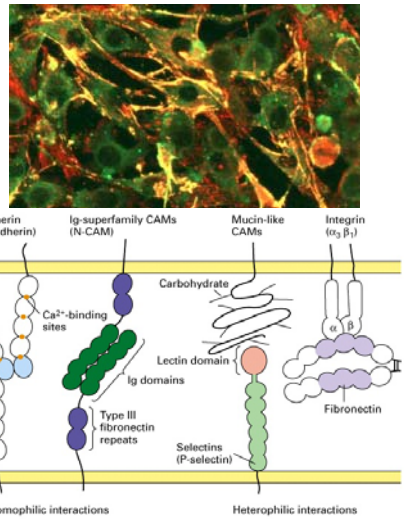
- **Other constituents**
  - Cholesterol stabilizes the membrane
  - Small amounts of carbohydrate "sugars" (glycoproteins or glycolipids)
  - Proteins are attached or inserted in the membrane
    - Channels
    - Carrier molecules
    - Receptors
    - Membrane bound enzymes
    - Cell adhesion molecules



Background Material

Cell-to-Cell Adhesions

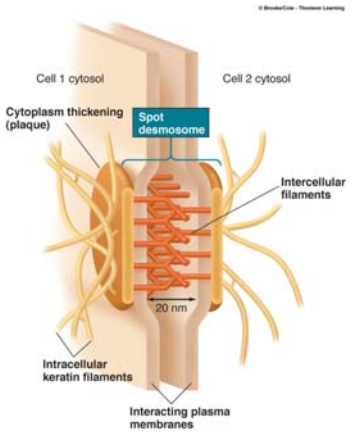
- **Organization of cells into appropriate groupings**
  - Extracellular matrix
  - Cell adhesion molecules
  - Specialized cell junctions
- **Extracellular matrix**
  - Secreted mostly by fibroblasts
  - Fibrous proteins (Collagen, Elastin, Fibronectin)
- **Cell adhesion molecules (CAMs)**
  - Glycoproteins and glycolipids



Background Material

Cell-to-Cell Adhesions

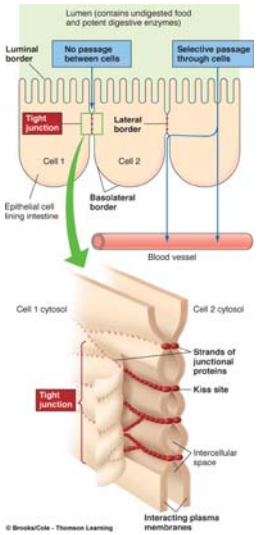
- **Cell Junctions**
  - Directly linking cells
    - Desmosomes
    - Tight Junctions
    - Gap Junctions
- **Desmosomes**
  - Connect adjacent but not touching cells
    - Plaques
    - Glycoproein filaments
  - Common in tissues that are subject to strain
    - Skin, heart, etc
  - Keratin connects them intracellularly forming continuous network



Background Material

Cell-to-Cell Adhesions

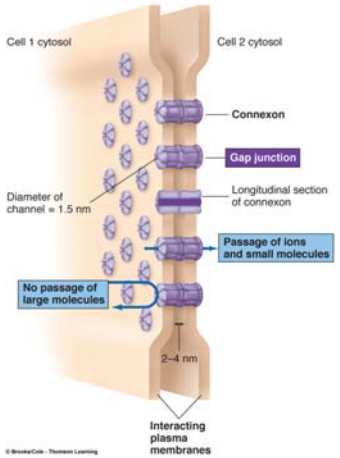
- **Tight Junctions**
  - Bind tightly in contact, blocking passageways
    - Junctional proteins form “kiss” sites
    - Impermeable
    - Materials must pass through cells ➔ well regulated
  - Common in epithelial layers → barriers between compartments



Background Material

Cell-to-Cell Adhesions

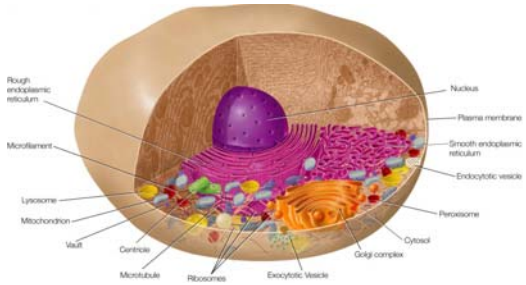
- **Gap Junctions**
  - Connects adjacent cells with small tunells
    - Connexon ➔six protein subunits in a tube-like stucture
    - Two join end-to-end between two cells
    - Small, water soluble, particles can pass, e.g. ions
  - Signaling
  - Abundant in cardiac and smooth muscle → transmit electrical activity



Background Material

Nucleus

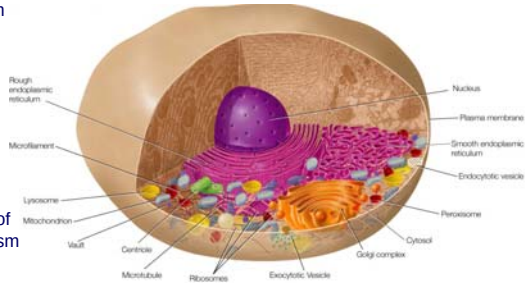
- **Basic Structure**
  - Nucleus
    - Surrounded by nuclear envelope with nuclear pores
    - Contains the genetic material of the cell → deoxyribonucleic acid (DNA)
  - DNA
    - Carries genetic information and serves as blueprint during cell replication
    - Directs protein synthesis



Background Material

Cytoplasm

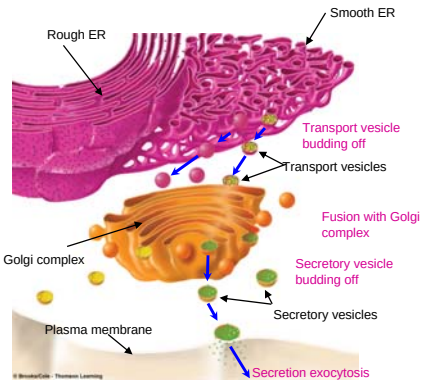
- **Basic Structure**
  - Cytoplasm
    - Various organelles
      - Endoplasmic reticulum
      - Golgi complex
      - Lysosomes
      - Peroxisomes
      - Mitochondria
      - Vaults
    - Cytosol (= cell, gel-like, liquid)
      - Enzymatic regulation of intermediary metabolism
      - Ribosomal protein synthesis
      - Storage of fat, carbohydrates
      - Includes the cytoskeleton



Background Material

Endoplasmic Reticulum (ER)

- **Endoplasmic Reticulum**
  - Protein and lipid synthesis
  - Elaborate fluid-filled membrane system
  - Rough ER
    - Rough appearance, flattened sacks
    - Proteins synthesized and released in the ER lumen
    - Lipids synthesized for cell walls
  - Smooth ER
    - Smooth appearance, small interconnected tubules
    - Packaging for molecules to be released
    - Transport vesicles bud off → Golgi apparatus for further processing
- **Golgi Complex**
  - Two major roles
    - Processing the raw proteins into their final form
    - Sorting and directing the destination
  - Stack of flattened membrane-enclosed sacs (a.k.a. cisternae)



Background Material

Lysosomes

- **Serve as the intracellular digestive system**
- **Small sacs full of powerful hydrolytic enzymes**
- **Vary in size**
- **Break down organic molecules from foreign materials (e.g. bacteria)**
- **Material internalized by endocytosis**

Background Material

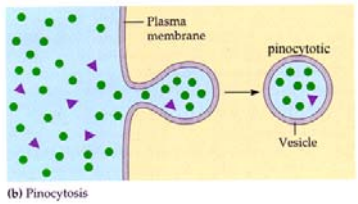
Peroxisomes

- **Detoxify waste products or foreign toxic compounds (e.g. alcohol)**
- **Similar in structure to lysosomes, only smaller**
- **Contain oxidative enzymes**
  - Use oxygen to strip hydrogen from organic molecules
- **Major product generated is hydrogen peroxide (H_2O_2)**
  - Powerful oxidant
  - Must not accumulate or escape
  - Enzyme ***catalase*** breaks into H_2O and O_2

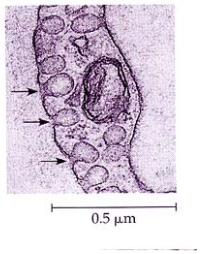
Background Material

Endocytosis

- **Endocytosis**
  - Pinocytosis
  - Receptor-mediated endocytosis
  - Phagocytosis
- **Pinocytosis**
  - Bring ECF into the cell or retrieve extra plasma membrane added by exocytotic vesicles
  - Procedure
    - Coat proteins bind to the ECF side
    - Membrane dips
    - Dynamin pinches the pouch off



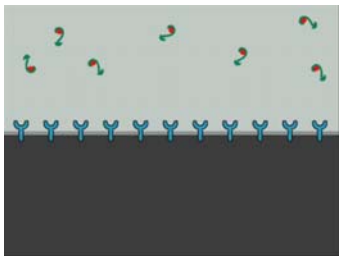
(b) Pinocytosis



Background Material

Endocytosis

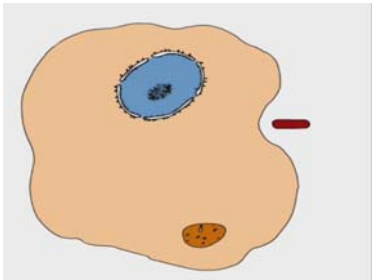
- **Receptor-Mediated Endocytosis**
  - Highly selective process to internalized needed molecules
  - Procedure
    - Molecule binds to receptor
    - Proteins coat ICF side
    - Membrane sinks in and seals at the surface
  - Important for cholesterol, vitamin B12, insulin, iron, etc, uptake
  - Used by viruses to enter the cell (e.g. Flu and HIV)



Background Material

Endocytosis

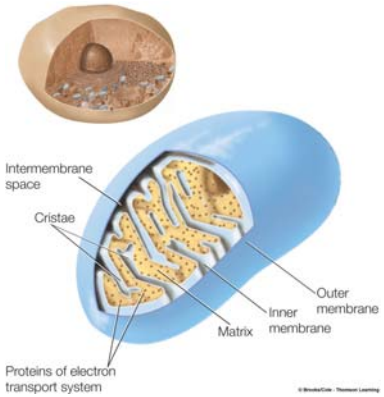
- **Phagocytosis**
  - Internalization of large multimolecular particles
  - Performed by phagocytes (mainly white blood cells)
  - Procedure
    - Encounter of particle
    - Extension of pseudopods
    - Internalized into vesicle
    - Fusion with lysosome
    - Break down of engulfed material
    - Useful byproducts



Background Material

Mitochondria

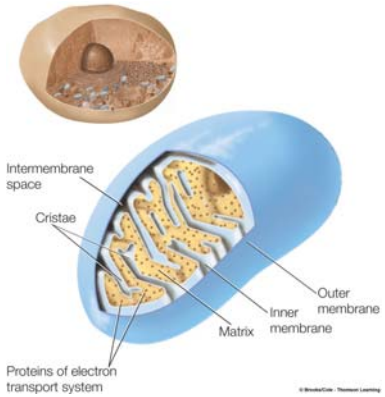
- **Generate 90% of the cells's energy**
- **Number varies (100s-1000s) depending on the cell type's energy needs**
- **About the size of bacteria → descendants of engulfed bacteria**
- **Possess their own DNA**
  - Produce products needed to generate energy
  - Flaws
    - Can be passed from mother to children
    - Accumulate over time (implicated in aging and degenerative diseases)



Background Material

Mitochondria

- **Structure**
  - Double membrane
  - Smooth outer membrane
  - Inner membrane with cristae (infoldings)
    - Increased surface area
    - Contains enzymes of the electron transport chain
  - Matrix
    - Contains enzymes of the cytric cycle



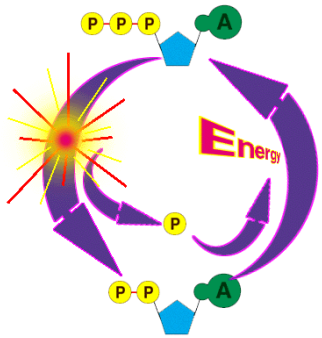
Background Material

Energy Production

- **Energy derived from carbon bonds of ingested food**
  - Food broken up into smaller absorbable units
  - E.g. carbohydrates → glucose
  - Absorbed into blood
  - Delivered to tissues
  - Uptake of molecules into cells
- **Processed and stored into a usable form**
  - High energy phosphate bonds of adenosine triphospate (ATP)
  - Split of one P yields ADP and energy

$$ATP \xrightarrow{splitting} ADP + P_i + energy$$

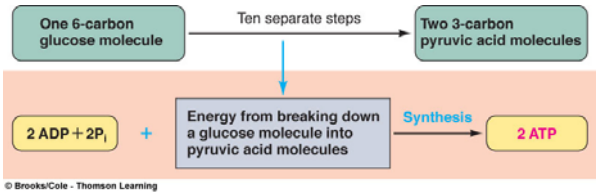
  - Three steps (for glucose)
    - Glycolysis
    - Citric acid cycle
    - Electron transport chain



Background Material

Energy Production

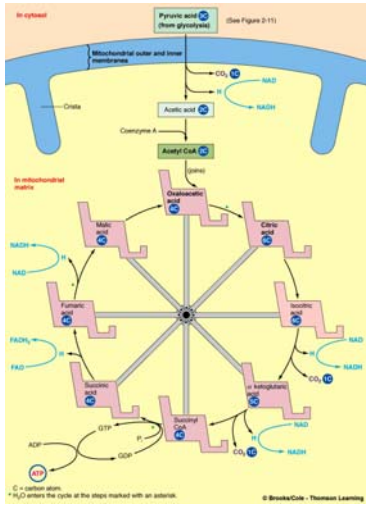
- **Glycolysis**
  - Occurs in the cytosol
  - 10 sequential reactions
  - Break glucose into 3 pyruvic acid molecules
  - Release 2 ATP molecules
  - Not efficient
    - Most of the energy still in the pyruvic acid
  - Mitochondria come into play



Background Material

Energy Production

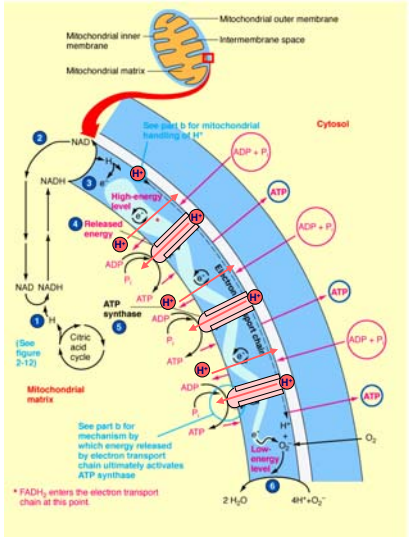
- **Citric Acid or Kerbs Cycle**
  - Occurs in the mitochondria
  - Requires O_2 (derived from molecules involved)
  - 2 ATP molecules from each pyruvic acid
- **Important points**
  - Carbon atoms released
    - Form CO_2
  - Hydrogen released
    - Binds to hydrogen carrier molecules
    - To be subsequently used in the electron transport chain
  - Hydrogen carrier molecules
    - Nicotinamide Adenine Dinucleotide (NAD) from B vitamin niacin
    - Flavine Adenine Dinucleotide (FAD) from B vitamin riboflavin



Background Material

Energy Production

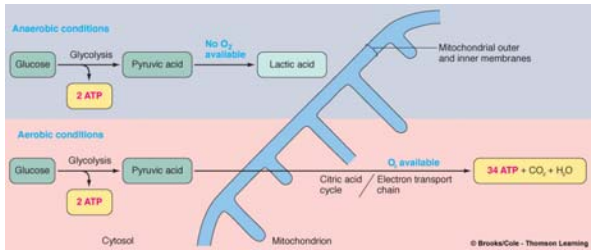
- **Electron transport chain**
  - Oxidative phosphorilation
  - Electron carriers arranged in specific ordered structure within the cristae membrane
  - Carrier molecules deliver hydrogen and high energy electrons to the chain
  - Electrons move down the chain using their energy to transport hydrogen (against its concentration gradient) in the intermembrane space
  - After 3 successive transports the weakened electrons are passed to O_2 (from breathing) → form H_2O
  - The hydrogen returns back to the matrix through channels which activate ATP synthase



Background Material

Energy Production

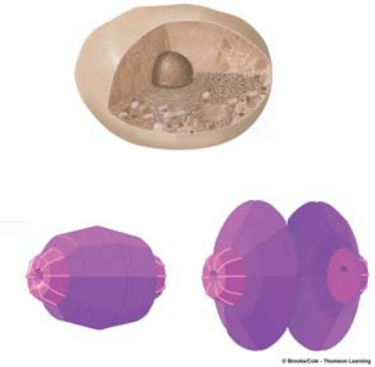
- **Burn vs. Oxidative phosphorylation**
  - Controlled storage of energy
- **Aerobic vs. Anaerobic Conditions**
  - Glycolysis alone not sufficient to sustain body
  - Exception
    - Muscle→ energy during short bursts of strenuous exercise
    - RBCs → no mitochondria but also not many metabolic needs



Background Material

Vaults

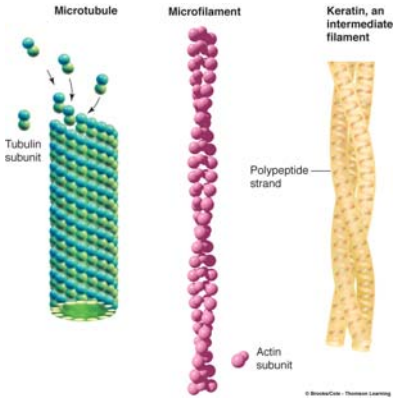
- **Newly discovered organelles (1990s)**
- **Octagonal shaped, barrel like, structures**
- **Sometimes can be seen open**
- **Function not well understood**
  - Transport of molecules from nucleus to cytoplasm (nuclear pores are also octagonals of the same size)
    - Ribosomal units
    - mRNA



Background Material

Cytoskeleton

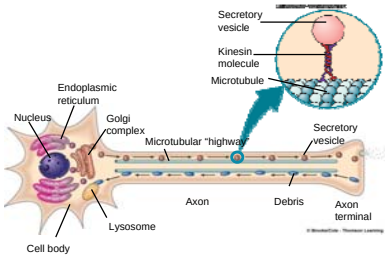
- **Structural proteins in the cells responsible for**
  - Maintaining structure and shape
  - Movement of parts or the whole cell
  - Signaling (?)
- **Three major components**
  - Microtubules
    - Tubulin forming tubes, 22 nm diameter
  - Microfilaments
    - Actin and myosin forming twisted strands, 6 nm diameter
  - Intermediate filaments
    - Various proteins forming irregular thread-like strands, 7-11 nm diameter

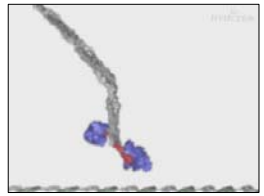


Background Material

Cytoskeleton

- **Microtubules**
  - Function
    - Maintain asymmetric shapes
    - Facilitate complex movements
  - Maintain structure
    - Stabilize long axons of neurons
  - Transport of secretory vesicles
    - Secretory vesicles leave the Golgi apparatus
    - Transported along microtubules to the axon terminal – kinesin (globular protein with "feet") → expenditure of ATP
    - Debris transported back – dynein → expenditure of ATP
    - Some viruses, like herpis, use the same transport mechanism

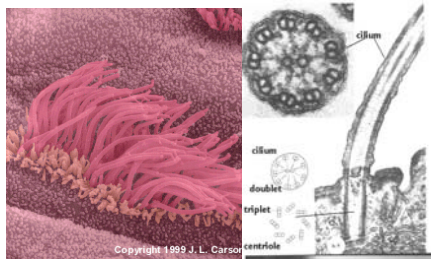


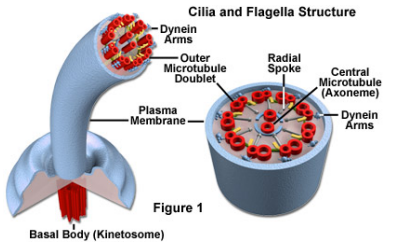


Background Material

Cytoskeleton

- Movement of cilia and flagella
  - Cilia
    - Numerous tiny hair-like protrusions
    - Beat in unison, e.g.
    - respiratory tract → move foreign bodies out
    - oviducts → move ovum to the uterus
  - Flagellum: single, whip-like appendage
    - Sperm → movement and alignment with ovum
  - Structure
    - Nine double (fused microtubules) arranged around two single microtubules
    - Accessory proteins including "arms" of dynein
    - Sliding of tubes along each other causes the motion
  - Control mechanisms of cilia not well understood

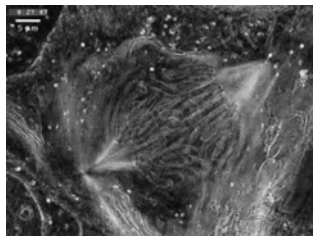


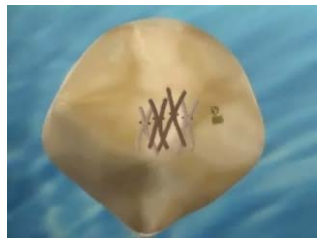


Background Material

Cytoskeleton

- Formation of the mitotic spindle
  - During mitosis the DNA-containing chromosomes are duplicated
  - Must be divided equally between the two daughter cells
  - Pulled apart by mitotic spindle → transiently assembled microtubules starting from tube-like structures, the centrioles

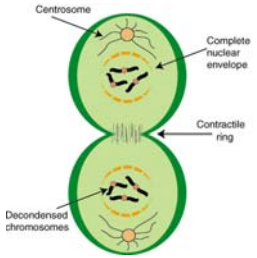


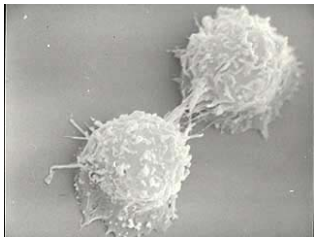


Background Material

Cytoskeleton

- **Microfilaments**
  - Function
    - Cell contractile systems
    - Mechanical stiffeners for specific cell projections
  - Contraction of muscle
    - Chapter 8
  - Separation of cells during division
    - Contractile ring

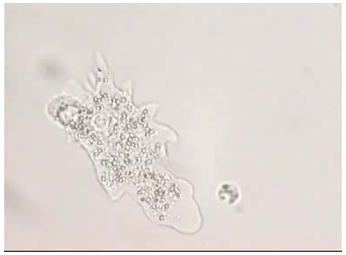


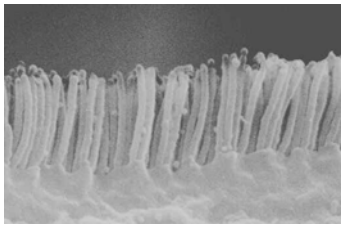


Background Material

Cytoskeleton

- Cell locomotion
  - White blood cells and fibroblasts
  - Amoeboid movement
  - Pseudopods extend and contract to move the cell → actin networks which grow at the leading edge and simultaneously disassembled at the rear
- Mechanical stiffeners
  - Microvilli → Non-motile projections of epithelial cells (increased surface area for absorption)

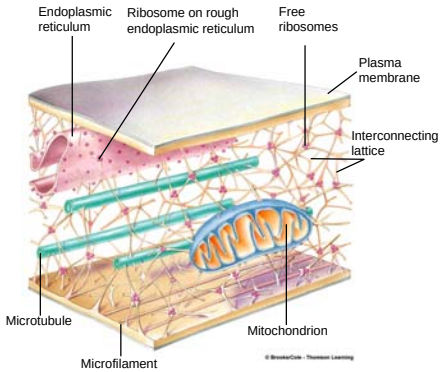




Background Material

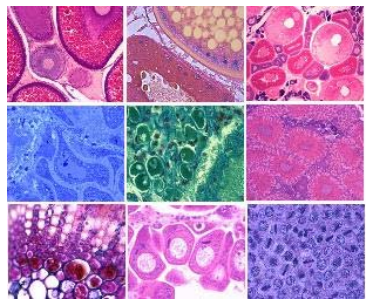
Cytoskeleton

- **Intermediate filaments**
  - Function
    - Maintain the structural integrity of the cell
    - Resist externally applied stress
  - Varying compositions to suit the cell type's needs
    - E.g. keratin network in skin cells



Tissues

- **Combination of**
  - Cells of similar structure and function
  - Varying amounts of extracellular material
- **Basic tissue types**
  - Muscle tissue
  - Nerve tissue
  - Epithelial tissue
  - Connective tissue

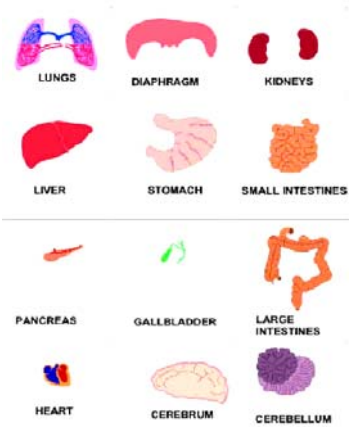


Tissues

- **Muscle tissue**
  - Contracting and generating force
  - Skeletal muscle → movement
  - Cardiac muscle → heart
  - Smooth muscle → GI, blood vessels
- **Nerve tissue**
  - Information transport and processing
  - Initiate and transmit electrical and chemical signals
- **Epithelial tissue**
  - Serve as boundaries and specialize in the exchange of materials
  - Epithelial sheets and secretory glands (endocrine and exocrine)
- **Connective tissue**
  - Connect, support and anchor other tissues
    - Loose connective tissue, tendons, bone, blood, etc
  - Few cells with abundant extracellular material
  - Produce specific structural proteins (e.g. collagen, elastin)

Organs and Systems

- **Organ**
  - Collection of two or more tissues
  - Combine to perform specific task
  - e.g stomach (epithelial sheets and glands, smooth muscle connective tissue) → food digestion
- **System**
  - A collection of organs which perform a specific task
  - e.g. digestive system (mouth, larynx, esophagus, stomach, small and large intestine, pancreas) → absorption of food



Systems

Circulatory system heart, blood, blood vessels

Digestive system mouth, pharynx, esophagus, stomach, small intestine, large intestine, salivary glands, exocrine pancreas, liver, gallbladder

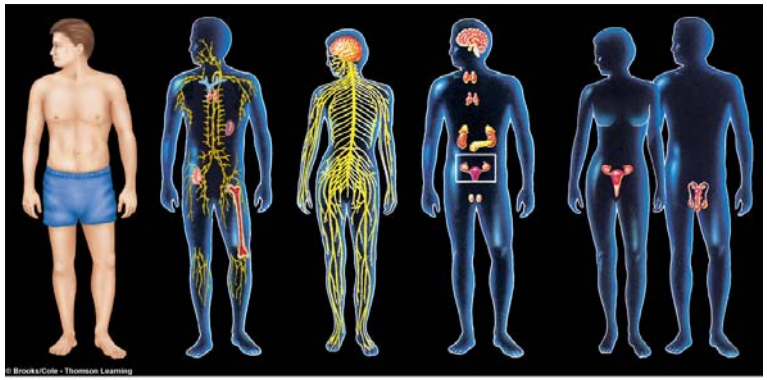
Respiratory system Nose, pharynx, larynx, trachea, bronchi, lungs

Urinary system kidneys, ureters, urinary bladder, urethra

Skeletal system bones, cartilage, joints

Muscular system skeletal muscles

Systems



Integumentary system skin, hair, nails

Immune system lymph nodes, thymus, bone marrow, tonsils, adenoids, spleen, appendix, and, not shown, white blood cells, gut-associated lymphoid tissue, and skin-associated lymphoid tissue

Nervous system brain, spinal cord, peripheral nerves, and, not shown, special sense organs

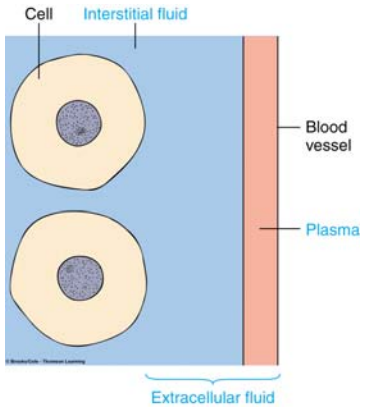
Endocrine system all hormone-secreting tissues, including hypothalamus, pituitary, thyroid, adrenals, endocrine pancreas, gonads, kidneys, pineal, thymus, and, not shown, parathyroids, intestine, heart, and skin

Reproductive system Male: testes, penis, prostate gland, seminal vesicles, bulbourethral glands, and associated ducts

Female: ovaries, oviducts, uterus, vagina, breasts

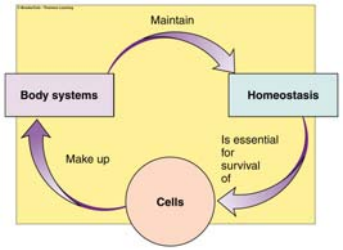
Internal Environment

- **Cells in multicellular organisms**
  - Contribute to organism survival
  - Most are not in contact with the external environment
- **Watery internal environment**
  - Appropriately maintained to support life and functioning
  - Intracellular fluid (ICF)
    - The fluid in all the cells
  - Extracellular fluid (ECF)
    - The fluid outside the cells
    - Interstitial fluid (in between cells)
    - Plasma (in blood vessels)



Homeostasis

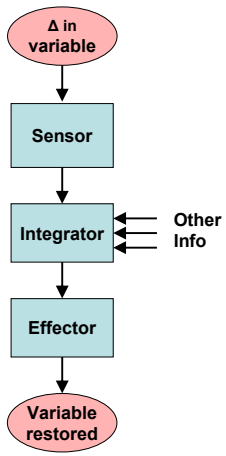
- **Homeostasis**
  - A state of the internal environment which is compatible with life
  - Maintained at approximately stable levels
    - All cells, tissues and systems contribute
    - Many aspects are maintained
  - Dynamic state
    - External perturbations
    - Short term transient responses or long term adaptation
    - Return to steady state



- Factors regulated
  - Concentration of nutrient molecules
  - Concentration of O_2 and CO_2
  - Concentration of waste products
  - pH
  - Concentration of water, salt and other electrolytes
  - Volume and pressure
  - Temperature

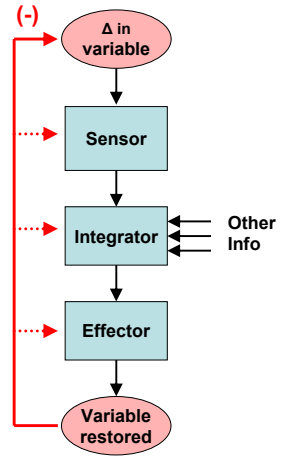
Homeostasis

- **Homeostatic control systems**
  1. Detect deviation from normal
  2. Integrate relevant information
  3. Make appropriate adjustments
- **Intrinsic control**
  - Local to the organ
  - E.g. chemical changes in exercising muscle → vasodilation → more O_2
- **Extrinsic control**
  - Actions in response to changes outside the organ
  - Coordinated action of organs and systems
  - Mediated by the nervous and endocrine systems
  - E.g. overall response to exercise (short term and long term)



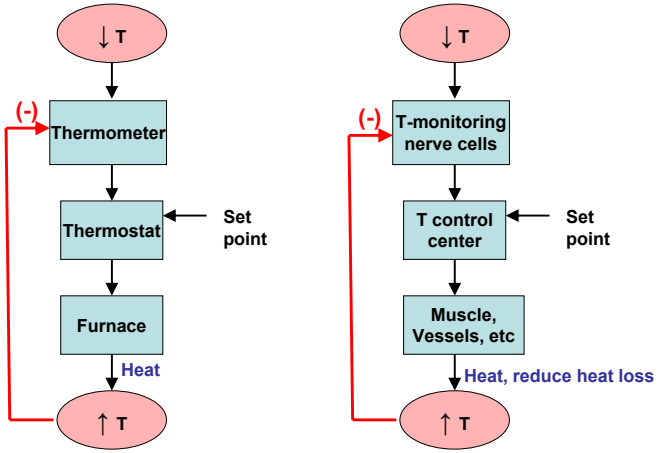
Homeostasis

- **Feedback**
  - Mechanism that tends to stabilize the physiological factor being regulated
- **Negative feedback**
  - Change in a variable initiates response to the opposite direction
  - Tends to correct the change and return the system to its steady state



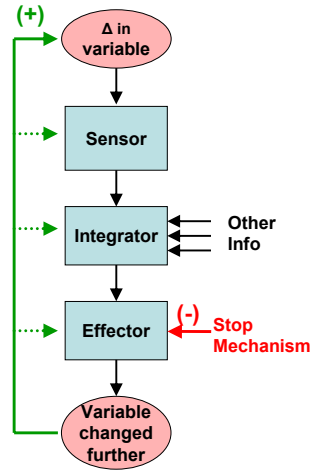
Homeostasis

- **Example of negative feedback**
  - Temperature control – Home and Body



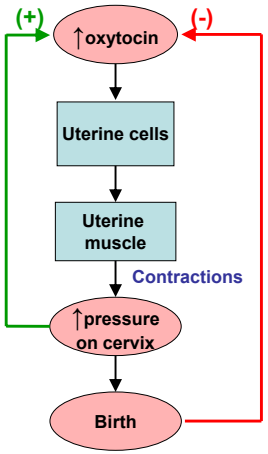
Homeostasis

- **Positive feedback**
  - Change in a variable initiates response to the further amplify the change
  - Tends to amplify the change initiated from the external perturbation
  - Not as common as negative feedback
  - Always a stop mechanism required
  - Appears when abnormal circumstances disable negative feedback



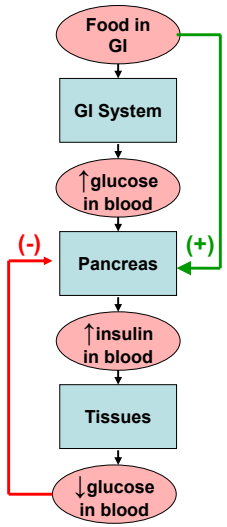
Homeostasis

- **Example of positive feedback**
  - Birth



Homeostasis

- **Feedforward Mechanisms**
  - Initiate responses in anticipation of change
  - E.g. food in the gastrointestinal → insulin secretion in anticipation of glucose arrival
- **Disruption in homeostasis**
  →pathophysiology



Next Lecture …

Sherwood, Human Physiology

Membrane Transport, Membrane Potential and Neural Communication (60-113)