i. Fundamentals of human physiology and cellular function

Introduction to Human Physiology

1. **Definition and Scope**
   - **Physiology** studies the mechanical, physical, and biochemical functions of living organisms.
   - **Human physiology** focuses on how cells, tissues, and organs coordinate to maintain health and respond to internal and external challenges.
2. **Homeostasis**
   - Coined by Walter Cannon, **homeostasis** refers to the body's ability to maintain stable internal conditions (e.g., temperature, pH, ion concentrations) despite external fluctuations.
   - Involves **feedback loops**—negative feedback (common; opposes change) and positive feedback (less common; amplifies an initial stimulus, e.g., in blood clotting or labor contractions).
3. **Levels of Organization**
   - **Cellular → Tissues → Organs → Organ Systems**
   - Specialized cell types form tissues with distinct structures and functions, which integrate into larger organ systems (e.g., nervous, cardiovascular, respiratory).

Cellular Architecture and Function

1. **Cell Membrane and Fluid Compartments**
   - **Phospholipid Bilayer**: Embedded with proteins (channels, transporters, receptors) and cholesterol (stabilizes fluidity).
   - **Intracellular Fluid (ICF)**: High K^+, low Na^+, abundant proteins and organelles.
   - **Extracellular Fluid (ECF)**: Composed of interstitial fluid and plasma, higher Na^+, lower K^+, crucial for nutrient delivery and waste removal.
2. **Organelles**
   - **Nucleus**: Houses genetic material (DNA), site of transcription, cell cycle control.
   - **Mitochondria**: Powerhouse for ATP production via oxidative phosphorylation, also key in apoptosis and calcium buffering.
   - **Endoplasmic Reticulum (ER)**:
     - **Rough ER**: Synthesizes membrane-bound and secretory proteins.
     - **Smooth ER**: Lipid metabolism, detoxification, calcium storage.
   - **Golgi Apparatus**: Modifies, sorts, and packages proteins/lipids for secretion or organelle targeting.
   - **Lysosomes/Peroxisomes**: Degradation and recycling of cellular waste; detoxification of reactive oxygen species.
3. **Cytoskeleton**
   - **Microfilaments (Actin)**: Cell shape, motility, muscle contraction (in concert with myosin).
   - **Intermediate Filaments**: Structural integrity (e.g., keratins, neurofilaments).
   - **Microtubules**: Intracellular transport, mitotic spindle, ciliary/flagellar motility (with dynein, kinesin).

Membrane Transport and Electrochemical Gradients

1. **Passive Transport**
   - **Simple Diffusion**: Movement of small or lipid-soluble molecules down their concentration gradient.
   - **Facilitated Diffusion**: Movement down a gradient via carrier proteins or ion channels (e.g., glucose transporter, ion-specific channels).
2. **Active Transport**
   - **Primary Active Transport**: Directly uses ATP (e.g., Na^+/K^+ ATPase pumping Na^+ out, K^+ in).
   - **Secondary Active Transport**: Coupled transport (e.g., Na^+-glucose symport) uses the gradient established by a primary pump.
3. **Vesicular Transport**
   - **Endocytosis** (phagocytosis, pinocytosis, receptor-mediated) and **Exocytosis** (secretion of hormones, neurotransmitters) require membrane remodeling and ATP.

4. **Membrane Potential**
    - **Resting Membrane Potential (RMP)**: Cells maintain an electrical potential difference (usually −70 mV in neurons) due to ion gradients and selective permeability.
    - **Excitable Cells**: Neurons and muscle cells can rapidly alter membrane potential (action potentials, signaling).

Intercellular Communication

1. **Chemical Messengers**
    - **Hormones (Endocrine Signaling)**: Released into the bloodstream by glands, act on distant targets (e.g., insulin, cortisol).
    - **Paracrine Factors**: Local signaling molecules (e.g., nitric oxide, growth factors).
    - **Neurotransmitters**: Released by neurons into synaptic clefts for rapid, localized signaling (e.g., acetylcholine, dopamine).
2. **Receptors**
    - **Cell-Surface Receptors**: G protein-coupled receptors (GPCRs), ion channels, enzyme-linked receptors.
    - **Intracellular Receptors**: For lipophilic molecules (e.g., steroid hormones); alter gene transcription directly in the nucleus.
3. **Signal Transduction Cascades**
    - **Second Messengers** (cAMP, Ca^2+, IP_3, DAG) amplify signals.
    - **Protein Kinase Cascades** (e.g., MAPK, PKA, PKC) modulate cellular processes—gene expression, metabolism, cell division.

Tissue Organization and Function

1. **Epithelial Tissue**
    - Covers body surfaces and lines cavities (e.g., intestines, kidney tubules).
    - Functions in protection, absorption, secretion.
    - Tight junctions form selectively permeable barriers.
2. **Connective Tissue**
    - Provides structural support (extracellular matrix, collagen, elastin).
    - Includes bone, cartilage, blood, adipose tissues.
    - Fibroblasts, osteoblasts, chondrocytes produce and maintain ECM.
3. **Muscle Tissue**
    - **Skeletal Muscle**: Voluntary control, striated fibers, multinucleated.
    - **Cardiac Muscle**: Involuntary, striated, intercalated discs for synchronized contraction.
    - **Smooth Muscle**: Involuntary, non-striated, present in walls of hollow organs (e.g., intestines, blood vessels).
4. **Nervous Tissue**
    - **Neurons**: Excitable cells that transmit electrical impulses.
    - **Glial Cells**: Support and protect neurons (astrocytes, oligodendrocytes/Schwann cells for myelin formation).

Integration into Organ Systems

1. **Neural Control**
    - Central (brain and spinal cord) and peripheral nervous systems coordinate rapid communication.
    - **Reflex arcs** integrate sensory inputs with motor outputs for immediate responses.
2. **Endocrine Regulation**
    - Hormone-secreting glands (pituitary, thyroid, adrenals, pancreas) orchestrate slower, long-term regulation (e.g., growth, metabolism, reproduction).
3. **Cardiovascular and Respiratory Systems**
    - Work together to supply oxygen, remove CO_2, circulate nutrients, and maintain tissue perfusion.
    - **Homeostatic Mechanisms**: Blood pressure control (baroreceptor reflex), regulation of blood gases (chemoreceptors).
4. **Renal and Digestive Systems**

- **Kidneys** filter blood, maintain electrolyte balance and pH, excrete waste (urea).
- **Gastrointestinal Tract** breaks down nutrients, absorbs them into circulation, eliminates undigested residues.

5. **Immune and Lymphatic Systems**
   - Defend against pathogens, clear damaged cells, involve both innate (macrophages, neutrophils) and adaptive immunity (T/B lymphocytes).

Concluding Perspectives

Human physiology is fundamentally anchored in **cellular function**—how cells harness chemical gradients, respond to signals, generate electrical impulses, and coordinate their activities to sustain life. The human body relies on a delicate **equilibrium** maintained by feedback mechanisms across organ systems. Advances in molecular and cellular biology continue to deepen our knowledge, informing disciplines from **medicine** and **pharmacology** to **bioengineering** and **systems biology**. Understanding these foundational principles is essential for exploring disease pathology (when regulation fails) and designing novel therapeutic interventions.

Key Takeaways

- **Cellular organization** underpins tissue and organ function.
- **Membrane physiology** (transport, potentials) drives excitability, communication, and metabolism.
- **Tissue specialization** (epithelial, connective, muscle, nervous) enables the diverse roles of organ systems.

Homeostatic feedback loops and **signal transduction** unify processes across systems, ensuring adaptability and stability in a changing environment.