

HOMEOSTASIS & BASIC MECHANISMS

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LEARNING OBJECTIVES

1. Identify the tissues, organs, and organ systems that comprise the human body and name their functions.
2. Identify the fluid compartments of the body and their relative sizes.
3. Explain the terms homeostasis, steady state, and equilibrium.
4. Define components of a reflex loop.
5. Contrast reflex and local homeostatic control
6. Explain negative and positive feedbacks.
7. Explain tonic and antagonistic controls.
8. Explain circadian rhythms

DEFINITION OF PHYSIOLOGY

Physiology is an integrative science that studies the functions of complex living organisms at levels ranging from molecules and cells to organs and systems. Physiologists ask questions of how the specific organ or system works and of what advantage does this system provide. They use this information and that obtained from related fields of anatomy, biochemistry, genetics and immunology to develop a cohesive picture of how organ systems coordinate to maintain life in a constantly changing environment. It is this integrative approach and consideration of coordinated function among organs systems that is a special focus of physiology.

Because physiology deals with the integrated behavior of several organ systems in the maintenance of life, it is often considered to be one of the most challenging courses. The objective of this course is that you acquire the terms and concepts of specific areas in physiology but also develop a conceptual framework to analyze data and to predict how one or more organ systems respond to change. Towards this end it is helpful to recognize the recurrent themes or underlying principles (Table 1) as a means for approaching or understanding a new situation.

TABLE 1. GENERAL CONCEPTS

Cell-cell communications
Chemical mass action
Control systems
Elastic properties
Gradients and mass flow
Mass balance
Membrane transport

TISSUES, ORGANS, SYSTEMS & FLUID COMPARTMENTS

Differentiated cells are cells specialized for a specific function.

Tissues are groups of cells which carry out related functions. The four tissue types include: epithelium, muscle, nervous, and connective.

Organs are functional units formed by different tissues.

Organ systems include several organs that act in an integrated manner to perform a specific function. They provide a means for exchange of materials between the external environment surrounding the body and it's interior. The ten organ systems of the human body include cardiovascular, respiratory, digestive, endocrine, immune, integument, musculoskeletal, nervous, reproductive, and urinary.

The body can be divided into two fluid compartments (Fig 2): ICF and ECF.

Intracellular fluid (ICF) is the cytoplasm within cell.
Extracellular fluid (ECF) surrounds the cells and serves as a buffer.

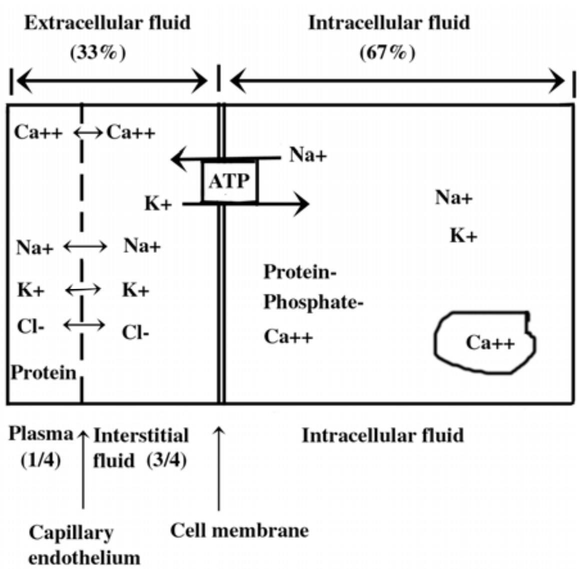

Figure 2. **Fluid compartments of the body.**

The ECF is divided into the **interstitial fluid (ISF)** that bathes the outside of the cells and the **intravascular fluid (IVF)** (i.e., plasma, lymph, and cerebral spinal fluid) (Fig. 2).
In the adult 70 kg male, approximately 60% of body weight is water. Under normal conditions, 2/3 of this is ICF and 1/3 is ECF of which ¾ is interstitial fluid and ¼ intravascular fluid.

Because most capillaries that separate the ISF and IVF are leaky, the composition of these two compartments is essentially identical. The main difference is that the IVF has higher protein content. However, the composition of the ICF and ECF differ (Table 2, Fig. 2) due to the hydrophobic nature of the cell membrane which prevents free exchange of ions and proteins.

ICF is a reducing environment that has a high concentration of K^+, but low concentrations of Na^+ and free Ca^{++}. Additionally, the concentrations of phosphates and proteins in the ICF are greater than in the ECF (Table 2).

ECF is an oxidizing environment that has low concentration of K^+ but high concentrations of Na^+ and free Ca^{++} (Table 2).

TABLE 2. ELECTROLYTES (mM) IN HUMAN CELLS

Ion	ECF (Plasma)	ICF (Cytosol)
Na^+	140.0	15.0
K^+	4.4	140.0
Ca^{++}	1.2*	0.0005
Cl^-	105.0	7.0

* Plasma contains bound as well as free Ca^{++}

In most cells, there is a passive leak of K^+ across the plasma membrane allowing K^+ ions to move from the inside of cells to the outside. This leak is matched by pumping K^+ back into the cell via the Na^+ -K^+ ATPase, an integral membrane protein. The movement (pumping) of K^+ back into the cells requires energy (ATP). During each cycle of the ATPase, two K^+ are exchanged for 3 Na^+ and one molecule of ATP is hydrolyzed to ADP.

When K+ is pumped into cells, Na+ is pumped out. This generates an unequal distribution of Na^+ and K^+ across the plasma membrane which is called a **chemical gradient**. The unequal distribution of ions also establishes a **charge** (electro) **gradient** with the **inside** of the cell more **negative** relative to the outside of the cell. The "electrochemical" gradient represents a storehouse of energy (called the **electrochemical potential**). Sodium ions can enter cells through special protein channels. When Na+ enters, it moves passively down its electrochemical gradient. Its entry is matched by the rate of its removal via the Na^+ -K^+ ATPase so that the intracellular concentration of Na remains low and constant. The actions of the Na^+-K^+ ATPase pump balance the amounts of Na^+ and K^+ entering and leaving the cell per unit time; however, their intracellular and extracellular concentrations are **NOT** equal. This is called a **steady state**. Metabolic energy (ATP) is expended to maintain a steady state.

EQUILIBRIUM, STEADY STATE & HOMEOSTASIS

The keys to maintaining stability of the ECF are self-regulatory mechanisms which allow us to adapt to a changing environment. To understand these adaptations, we need to consider the concepts of equilibrium and steady state.

Equilibrium is a condition in which the opposing forces are balanced. There is no net transfer of a substance (or of energy) from one compartment to another. An equilibrium state will occur if there is sufficient time for exchange and if there is no barrier to movement from one compartment to the other. **No energy expenditure is required to maintain an equilibrium state.**

Steady state, is a condition in which the amount (or concentration) of a substance is constant within a compartment and does not change with time. There is no net gain or net loss of a substance in a compartment because the input and output are equal. A steady state is not necessarily an equilibrium state. **Energy expenditure may be needed to maintain a steady state.**

Homeostasis is the maintenance of the ECF as a steady state. When conditions outside of the body change (e.g., temperature), these changes are reflected in the composition of the ECF which surrounds the individual cells of the body. The ECF is the site of exchange where nutrients are delivered and cellular wastes removed. Therefore the composition of the ECF dynamically changes with time, but certain factors must be kept within a narrow range for optimal functioning of cells, tissues, and organs. These specific factors include oxygen (O_2) and carbon dioxide (CO_2), glucose and other metabolites, osmotic pressure, concentrations of H^+, Ca^{++}, K^+, Mg^{++}, and temperature. Uncorrected deviations can lead to disease and/or death.

HOMEOSTATIC REGULATION

To maintain homeostasis, the functions of various organ systems must be integrated. Both homeostasis and integration require that the cells of the body (~ 75 trillion!) communicate with each other in a rapid and efficient manner. There are two basic types of extrinsic physiological control paths: local and reflex.

Local control involves paracrine (between neighbors) and/or autocrine (self-to-self) responses. Proteins called cytokines mediate local control.

Reflex control involves the nervous and endocrine systems. Reflex control responds to changes that are more widespread or systemic in nature. In a reflex control pathway (or loop), the decision to respond is made at a distance from the target cell or tissue. Reflex control has three basic components (Fig 3): an input stimulus, integrator of the stimulus, and a response (effector).

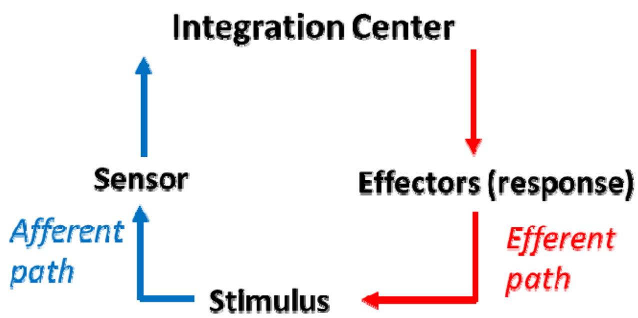

Figure 3. Components of a reflex loop.

The integrating center evaluates the incoming signal, compares it with a set point (desired value), and decides on an appropriate response. The effector carries out the appropriate response to bring the situation back to within normal limits. Reflex pathways are closed loops.

Mass balance in the body refers to a steady state in which the total amount of a substance equals its intake plus its production minus its output.

Total body content of X = intake of X + production of X – output of X.

Mass flow is mass balance over time, such that:

Mass flow (amt/min) = [concentration (amt/vol)] X [volume flow (vol/min)]

For example, infusion of 4g of glucose in 10 ml at a rate of 2 ml/min gives a mass flow of:

(4g /10 ml) X (2ml/min) = 0.8 g/min

There are several different types of reflex pathways within the body. These include negative feedback, positive feedback, feed forward, tonic control, antagonistic control and circadian rhythms.

In **Negative feedback** loops, the response removes the stimulus (Fig 4). A critical consequence of negative feedback control is that it allows the system to resist deviation of a given parameter from a preset range (or set point). Negative feedback is the most common form of homeostatic control in biological systems.

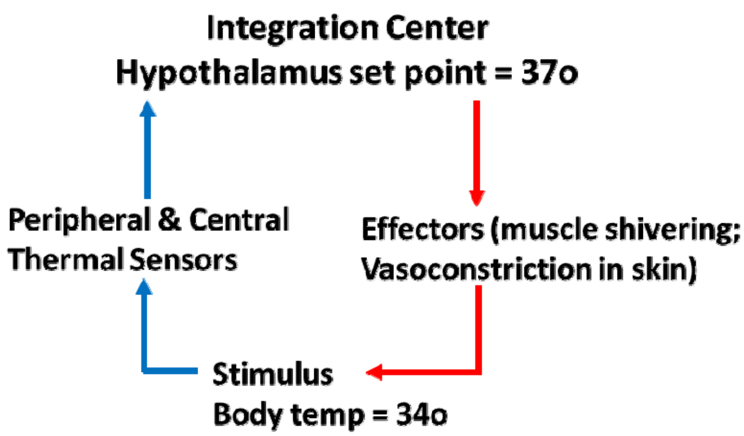

Figure 4. Negative feedback control systems responds to external change that lowers body temperature.

In physiological systems, we encounter two types of negative feedback systems (Fig.5): simple (A) and complex (B). The complex negative feedback system permits finer control.

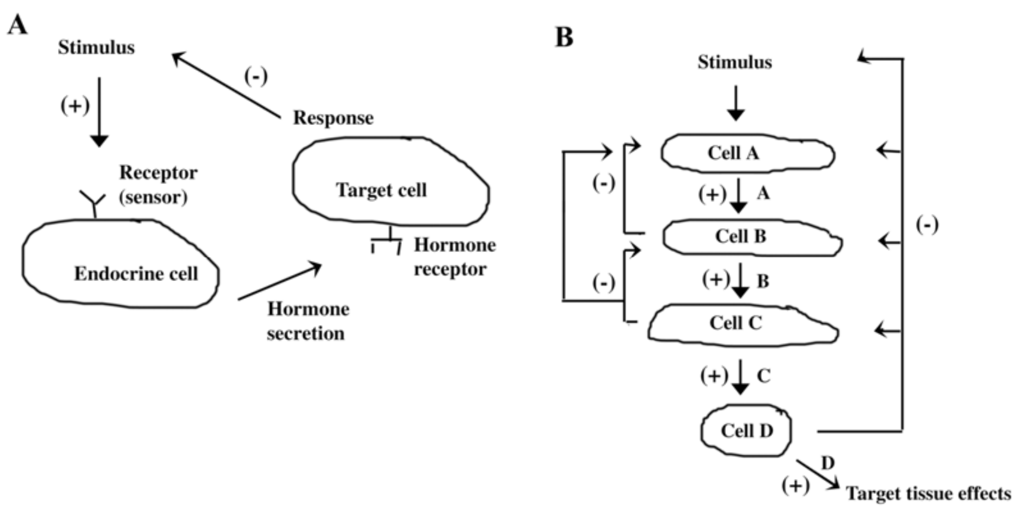

Figure 5. Simple and complex negative feedback loops. (A) Simple negative feedback involves two cellular compartments. (B) Complex negative feedback involves more than two cellular components. Typically the feed back signal inhibits secretion at all previous levels.

In **positive feedback** loops, the response reinforces the stimulus rather than decreasing or removing it (Fig. 6) and is therefore an unstable condition. The consequence of positive feedback is not to maintain homeostasis but to elicit a change. Positive feedback loops are found during development or maturation. They are finite loops; often negative feedback will reduce or terminate these responses.

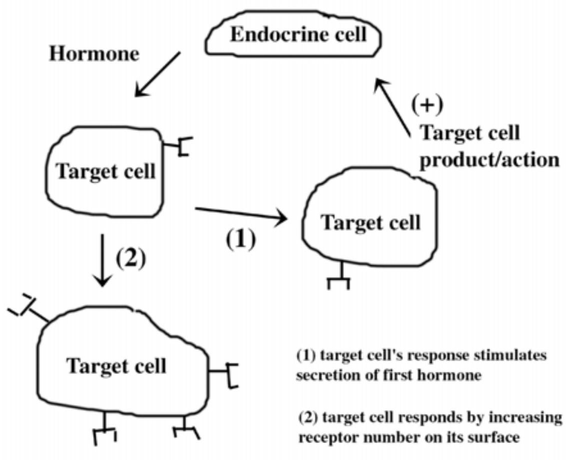

Figure 6. Positive feedback loops. A positive feedback occurs when a hormone signal increases its stimulation rather than decreasing it.

Feed-forward Control enables the body to anticipate a change and start a reflex loop. For example, the sight, smell, or even the thought of food starts our mouths to water. The saliva lubricates the food particles during chewing.

Tonic Control permits the activity of the organ system to be modulated (either up or down). This is like the volume control on a radio which enables you to make the sound louder or softer by turning a single knob. For example, the diameter of a blood vessel is set by the activity of the sympathetic nervous system (Fig. 7). A moderate rate of signaling from the nerve results in a blood vessel of intermediate diameter. An increase in the rate of signaling by the nerve results in constriction of the vessel; a decrease in signaling leads to dilation.

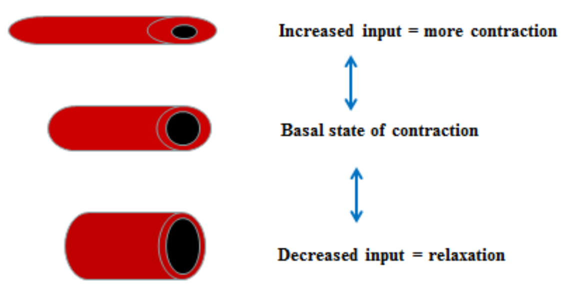

Figure 7. Tonic control. Physiological parameters that are under tonic control are regulated by modulation (up-down) rather than by on-off switches. Tonic control is an important regulator of blood flow to the organs.

Antagonistic Control modulates the activity of an organ system by two separate regulators which act in opposition. For example (Fig. 8), chemical signals (neurotransmitter) from a sympathetic neuron increase heart rate, whereas neurotransmitters from a parasympathetic neuron decrease it.

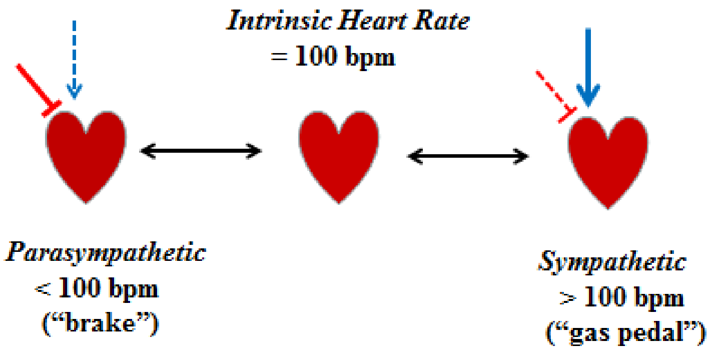

Figure 8. Antagonistic control of heart rate.

Circadian Rhythms allow control systems to fluctuate in a predictable, timed manner over a 24 hour cycle as their set points change. Circadian rhythms govern many biological functions, including blood pressure, body temperature, and metabolic processes. Circadian rhythms arise from special group of cells in the brain (hypothalamus) which are programmed by either the light-dark, day-night cycle by input from the retina or our sleep (rest) -activity periods. When the circadian clock is altered (e.g., jet lag), temperature rhythms and the secretion of various hormones are also altered.

KEY CONCEPT

The human body is an inter-dependent set of self-regulating systems whose primary function is to maintain an internal environment compatible with living cells and tissues (homeostasis).

Important Generalizations of Homeostatic Control Systems

- Stability of internal variables is achieved by balancing inputs and outputs to the body and among organ systems.

- In negative feedback systems, a change in a variable is corrected by bringing the body back to the initial set point. Note that set points can be "reset" at a higher or lower physiological value.

- Not always possible to maintain everything relatively constant by homeostatic control mechanisms in response to change. There is a hierarchy of importance in the maintenance of life.

Problem:
Identify the components of the reflex loop in the following scenario.
You have finished the marathon in just under three hours. You are tired, sweating profusely, and start to drink Gatorade. After a few minutes you are still tired but no longer sweating or thirsty.

Answer:
Sweating = loss of ECF water (**stimulus**); the stimulus is recognized by the hypothalamus (**integrator**); the thirst **response** (effector) is triggered; the individual drinks Gatorade; this removes the stimulus; i.e., no longer thirsty; this is classic negative feedback