Contents

1 Animals and Environments

Introduction

- What is physiology?
  - Form and function of organisms; the study of how organisms work.
- Central questions of physiology: mechanism and origin.
  - Mechanism:
    - Refers to the components of living organisms and understanding how components interact to enable the organism to function.
  - Origin:
    - Asks why a mechanism exists, or what is the mechanistic adaptive significance of the mechanism.
  - Mechanism and adaptive significance are distinct concepts; knowing about one doesn't necessarily mean you know anything about the other.
- Krogh's principle:

  > "For such a large number of problems there will be some animal of choice or a few such animals on which it can be most conveniently studied."

  - This idea is central to disciplines that rely on the *comparative method*.
  - Other key concepts:
    - There is unity in diversity; many organisms are very much alike at the most fundamental levels.
    - The differences are subject to particular niches and often highly specialized that allow for biologist to study more complex systems.
    - The similarities allow us overcome technical limitations via animals that are easier to study.
- Physiology subdisciplines:
  - Mechanistic: emphasizes the mechanisms by which organisms perform their life functions.
  - Evolutionary: emphasizes evolutionary origins and the adaptive significance of traits.
  - Comparative: emphasizes the way in which diverse phylogenetic groups resemble and differ from each other.

- Environmental: emphasizes the ways in which physiology and ecology interact.
- Integrative: emphasizes the importance of all levels of organization, from genes to proteins and tissues to organs in order to better understand whole physiological systems.

Homeostasis

- Important ideas to remember:
  - Organisms are structurally dynamic; form stays relatively static while individual cells recycle frequently.
  - Most cells are exposed to the internal environment, not external.
  - Internal cells may vary or kept constant with the environment.
- Temperature regulation:
  - **Conformity**: organism's internal temperature correlates with external temperature in a particular range of temperatures.
  - **Regulation**: internal environment is held mostly constant using celluar mechanisms.
- **Homeostasis**: the coordinated physiological processes that maintain a relatively constant state in the organism.
  - Positive feedback: less common in homeostasis due difficulty in regulation; leads to runaway effect easily.
  - Negative feedback: more common in homeostasis due to self correcting nature.
  - **Effector**: executes the change in action that produces an effect, e.g. signals to increase temperature.
  - **Sensor**: sense changes in environment and sends information to the effector.

Physiology and Time

- Timeframes of physiological change:
  - **Acute**: short-term, reversible, and quick to adapt to changes in environment. Usually minutes to hours.
  - **Chronic**: long-term after prolonged exposure to new environments. Changes are usually reversible, but often slower.

- Chronic can be termed acclimation, or phenotypic plasticity/flexibility.
- Repetitive acute responses usually lead to chronic responses.

- **Evolutionary**: changes due to alteration in gene frequencies in populations exposed to new environments.

▷ Acclimation is not the same as adaption.

- *Adaption* is an evolutionary trait presnet at high frequency in a population due to survival/reproductive advantages.
- Not all traits are adaptations.
- The amount of natural variation in a trait must be considered across populations, species etc.

2 Molecules and Cells in Animal Physiology

Cell Membrane Review

- Major cell memberane structures:
  - **Glycoproteins**: carbohydrate chain attached to a protein.
  - **Glycolipids**: similar to glycoproteins, but attached to lipid molecues.
  - *Glycocalyx*: combination of glycoproteins and glycolipids on the surface of cell.
  - **Integral proteins**: embedded in phospholipid bilayer.
  - **Peripheral proteins**: associated with one side of the bilayer.
- **Unsaturated phospholipid**: whey hydrocarbon tails contain double bonds (less hydrogen).
  - Increase membrane fluidity due to extra space created.
- The fluidity of the cell membrane allows proteins to from complexes and dynamically change shape.

Enzyme Fundamentals

- **Enzymes**: a protein catalyst that plays two primary roles: accelerating and regulating chemical reactions.
- *Substrates*: the initial reactants of the reaction that an enzyme catalyzes.
- **Enzyme-substrate-complex (E-S)**: a combination of enzyme (E) with a molecule of substrate (S) that starts a reaction.
  - Usually stabalized by non-covalent bonds.
  - The substrate is converted to a product by first becomeing an *enzyme-product complex (E-P)*, then dissociates to yield free product and free enzyme.
  - $E + S \rightleftharpoons \text{E-S} \rightleftharpoons \text{E-P} \rightleftharpoons E + P$
- **Saturation kinetics**:
  - $\mathbf{V_{max}}$: the maximum velocity of a reaction and is determined by:
    - The number of active enzyme molecues present relative to substrate.
    - The catalytic effectiveness of each enzyme molecule.
    - These properties usually undergo heavy selection pressure.

- *Saturated*: all enzymes are occupied by a substrate molecule nearly all the time and now unable to increase reaction velocity.
- **Hyperbolic**: asymptotically approaches V_{max}
  - Tends to happen when enzymes have just one substrate binding site.
  - Or when substrate sites behave independently
- **Sigmodal**: approaches V_{max} with a sigmodal trajectory.
  - When multiple sites influence each other.
- **Turnover number (k_{cat})**: the total effectiveness, expressed as the number of substrate molecules coverted to product per second by each enzyme molecule when saturated.
  - Depends partly on the *activation energy* of the enzyme-catalyzed reaction.
  - **Activation energy**: the energy required for the substrate to enter the *transition state*.
  - **Transition state**: the intermediate chemical state between substrate and product.
  - Enzymes lower the activation energy required to enter transition state.

▷ **Enzyme-substrate affinity**: The proclivity of the enzyme to form a complex with the substrate when they meet.

- Likely complex formation results in high-affinity.
- Unlikely complex formation results in low-affinity.
- Affinity affects the shape of the reaction velocity.
  - Higher affinity produces a steeper velocity, and a lower affinity produces a more linear result.
  - Enzyme concentration is not changed.
- **Half-saturation constant, K_m**: the substrate concentration required to attain one-half maximum reaction velocity.
  - K_m and enzyme-substrate affinity are inversely related.
  - i.e. low-affinity enzyme has a greater K_m.

▷ **Molecular Flexibility**:

- **Conformation**: the three-dimensional shape of a protein.

    - Stabalized mostly by weak, noncovalent bonds—hydrogen, van der Waals, hydrophobic, electrostatic, etc.
    - Weak interactions allow for easy yet stable conformational changes.
  - Enzyme molecules composed of two, three or our proteins are called *dimeric, trimeric*, or *tetrameric* respectively.
- Enzymes catalyze reversible reactions in both directions.
  - This is because they accelrate the approach towards equilibrium (principles of mass action).
- **Ligand**: any molecule that selectively binds by noncovalent bonds to structurally and complementary sites on a specific protein.
- **Cooperativity**: the interactions between multiple binding sites that may facilitate or inhibit the binding of other sites.
  - Can either positive or negative; facilitating or inhibiting binding on the same molecule.
  - *Homotropic cooperativity*: facilitation or inhibition of the same ligand.
  - *Heterotropic cooperativity*: influences on the binding of other ligands.
  - Interactions occur at a distance, resulting in delayed, or rippling responses.
  - **Allosteric modulation**: the modulation of the catalytic properties.
    - **Allosteric sites**: nonsubstrate-binding regulatory sites for nonsubstrate ligands that modulate the catalytic properties.
    - *Allosteric modulators*: the nonsubstrate ligands.
    - Allosteric **activation**:increases and **inhibition**:impairs affinity, thus the catalytic activity.
- **Isozymes**: enzymes that catalyze the same chemical reaction but differ in amino acid sequence.
- **Interspecific enzyme homologs**: different molecular forms of an enzyme coded by homologous gen loci in different species.
  - Isozymes and interspecific enzyme homologs often differ in their catalytic and regulatory properties.
  - Functional differences often prove to be adaptive in different environments.

Post-Lecture Questions

- ▷ What are the two central questions of physiology?
- ▷ Describe the different sub-disciplines of physiology.
- ▷ What is the Krogh principle? Explain what it means to physiology.
- ▷ Define the terms conformity and regulation and understand how they relate to physiological processes. Discuss examples.
- ▷ Define the term homeostasis. Understand the process of negative and positive feedback regulation.
- ▷ Describe how physiology changes with time in response to the external environment. Define the terms acclimation, adaptation, natural selection, and evolution.
- ▷ Describe the structure and chemical components of lipid membranes.
- ▷ What are the effects of low and high temperatures on membranes? How are membrane properties altered to offset these effects?
- ▷ Describe the five functional types of membrane proteins and their basic functions.
- ▷ What are the two primary roles of enzymes?
- ▷ Define the terms V_{max} and K_m. Explain the factors that affect these reaction properties.
- ▷ Define activation energy. Understand the effect of enzyme catalysis on a reaction's energy of activation.
- ▷ What are the effects of substrate concentration on the rate of an enzymatic reaction? How does enzyme-substrate affinity affect the reaction rate?
- ▷ Why are enzymatic rates unresponsive to increases in substrate concentration above a physiologically relevant range?
- ▷ Understand why conformational change is a critical part of enzyme function.
- ▷ Define the term isozyme and understand how they can contribute to natural selection.
- ▷ Define and understand the process of allosteric modulation.

3 Genomics

Genetics in Physiology

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Genomics

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Transcriptomics

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Proteomics

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Metabolomics

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4 Physiological Development

Epigenetics

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5 Transport of Solutes and Water

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27 Water and Salt Physiology: Mechanisms

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7 Nutrition, Feeding, and Digestion

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