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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 cellular 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 present 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 membrane structures:
 - **Glycoproteins:** carbohydrate chain attached to a protein.
 - **Glycolipids:** similar to glycoproteins, but attached to lipid molecules.
 - *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:** when hydrocarbon tails contain double bonds (less hydrogen).
 - Increase membrane fluidity due to extra space created.
- ▷ The fluidity of the cell membrane allows proteins to form 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 stabilized by **non-covalent** bonds.
 - The substrate is converted to a product by first becoming an *enzyme-product complex (E-P)*, then dissociates to yield free product and free enzyme.
 - $E + S \rightleftharpoons E-S \rightleftharpoons E-P \rightleftharpoons E + P$
- ▷ **Saturation kinetics:**
 - **V_{max}:** the maximum velocity of a reaction and is determined by:
 - The **number** of active enzyme molecules 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 converted 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.

- Stabilized 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 four proteins are called *dimeric*, *trimeric*, or *tetrameric* respectively.
- ▷ Enzymes catalyze reversible reactions in both directions.
 - This is because they accelerate 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 gene 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

Genomics

- ▷ **Genomics:** study of the genomes—the full set of genetic material—of organisms.
- ▷ Methods of genomics:
 - Computational biology and bioinformatics use various computational methods to process large amount of genomic data.
 - **High-throughput:** methods of analyzing large data with out much human attention and mostly computation.
 - **Annotation:** laborious direct human interpretation.
- ▷ The **overarching goals** of genomics is to elucidate the **evolution** and the **current functioning** of genes and genomes.
- ▷ **Gene families:** genes that share distinctive DNA base sequences and *tend to* code for functionally similar proteins.
- ▷ **Postgenomic era:** the study of species after genome is sequenced.

Transcriptomics

- ▷ **Transcriptomics:** the study of which genes are transcribed to make mRNA and the rates at which they are transcribed.
 - aka transcription profiling.
 - Implies the study of great numbers of mRNAs.
- ▷ **Transcriptome:** a species full set set of mRNA molecules. It represents the full complement of genes being transcribed at any given time.
 - Time is emphasized; it's a snapshot transcription activity during the observed period.
 - Very useful in comparative methods.
- ▷ Methods of transcriptomics:
 - **DNA midroarrays:** aka gene chips; a high throughput method tht allows simultaneous analysis of large number of mRNAs.
 - **mRNA sequencing:** aka RNA-Seq; similar to microarrays, but can identify both known and **novel** transcripts.
 - More sensitive than microarrays.
 - Readily applicable across wide range of species.

- **Gene manipulation:** studies that permit the direct assessment of gene function by directly altering its expression.
 - **Gene deletion:** aka gene knockout; breaking or disturbing function of an animal's gene to interfere with proteins, creating deficient or inferior phenotypic traits.
 - **Forced overexpression:** inverse of gene deletion; experimentally increasing synthesis of the mRNA.
 - **Compensation:** phenotypic alterations of that tend to make up for the manipulation done by forced expression or gene deletion.
 - **RNA interference (RNAi):** allows specific mRNA targets to be silenced in animals with *normal* genomes.
 - **Normal genomes:** wild type that is not artificially manipulated.
 - RNAi is reversible.
 - **CRISPR/Cas:** used to edit nuclear DNA in eukaryotic cells.
 - Can be used to insert sequences that then can be transcribed and translated, providing insights on protein function.

Proteomics

- ▷ **Proteomics:** the study of proteins being synthesized by cells and tissues.
 - Implies simultaneous study of large numbers of proteins.
 - Predicting proteins from gene transcription is still very difficult; transcription, translation, and post-translational processing are all regulated dynamically and independently.
- ▷ **Two-dimensional gel electrophoresis:** the primary proteomics method that separates complex mixtures of samples using two different protein properties.
 - Separated by **isoelectric points** and then **molecular weights**.

Metabolomics

- ▷ **Metabolomics:** study of organic compounds in the cells and tissues other than macromolecules coded by the genome.
 - **Metabolites:** compounds currently being processed by metabolism and the majority of metabolomics focus of study.
 - e.g. sugars, amino acids, and fatty acids.

- ▷ **Nuclear magnetic resonance (NMR)**: primary method of metabolomics that is capable of detecting and quantifying a large variety of compounds through identification of unique signatures in the NMR spectrum.

4 Physiological Development

Epigenetics



5 Transport of Solutes and Water



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7 Nutrition, Feeding, and Digestion

