

# Contents

## Animals and Environments

Introduction . . . . .	3
Homeostasis . . . . .	4
Physiology and Time . . . . .	5

## Molecules and Cells in Animal Physiology

Cell Membrane Review . . . . .	6
Enzyme Fundamentals . . . . .	6

## Genomics

Genomics . . . . .	9
Transcriptomics . . . . .	9
Proteomics . . . . .	10
Metabolomics . . . . .	11

## Physiological Development

Epigenetics . . . . .	12
Mechanisms of Epigenetic Marking . . . . .	12
Epigenetic Inheritance. . . . .	12

## Transport of Solutes and Water

Passive Transport. . . . .	13
Concentration gradients . . . . .	13
Electrical gradients. . . . .	13
Biological Aspects of Diffusion . . . . .	14
Active Transport . . . . .	15
Diversity and Modulation of Channels and Transporters. . . . .	15
Colligative Properties of Aqueous Solutions . . . . .	16
Osmosis . . . . .	16
Osmoregulation . . . . .	18

## Nutrition, Feeding, and Digestion

Fundamentals of Animal Energetics . . . . .	19
Forms of Energy . . . . .	19
Major Functions of Physiological Work . . . . .	20
Metabolic Rate . . . . .	21
Principal Significance of Metabolic Rates. . . . .	22
Calorimetry . . . . .	22
Factors of Metabolic Rates. . . . .	23
Basal vs Standard Rates . . . . .	24
Metabolic Scaling . . . . .	24

## Aerobic and Anaerobic Metabolism

Mechanisms of ATP Production . . . . .	26
Aerobic Catabolism . . . . .	26
Anaerobic Catabolism. . . . .	29

Comparative Properties of the Mechanisms of ATP Production. . . . .	30
Themes in Exercise Physiology. . . . .	30
<b>Thermal Biology</b>	
Thermal Biology and Climate . . . . .	31
Poikilothermy (Ectothermy) . . . . .	31
Homeothermy and Endothermy . . . . .	31

# 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 of CO<sub>2</sub> as the pyruvate molecules are processed..
  - *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<sub>max</sub>**: the maximum velocity of a reaction and is determined by:
    - The **number** of active enzyme molecules of CO<sub>2</sub> as the pyruvate molecules are processed. 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
- **Sigmoidal**: approaches  $V_{\max}$  with a sigmoidal trajectory.
  - When multiple sites influence each other.
- **Turnover number ( $k_{\text{cat}}$ )**: 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.



## 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 microarrays:** 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

- ▷ **Epigenetics:** modifications in gene expression with **no change in DNA sequence** that are transmitted when genes replicate.
- ▷ **Marked:** aka tagged; when DNA is modified in way to alter expression.

#### Mechanisms of Epigenetic Marking

- **DNA methylation:** addition of methyl groups to cytosine residues in DNA.
  - Generally represses or silences the gene.
  - **DNA methyltransferase 1 (DNMT1):** an enzyme acts to perpetuate the pattern of methylation in daughter cells.
  - **Methylome:** the set of all methylated sites.
- **Histone modification:** modified histones that can make DNA more or less accessible for transcription.
  - Can be modified by methylation, acetylation, phosphorylation, or other covalent bonding of chemical groups at specific sites.
  - Also has mechanisms for perpetuation, e.g. small RNA molecules play a role.
- ▷ **Epigenome:** the global summary of marks or a set of epigenetic marks in a cell.

#### Epigenetic Inheritance

- **Mitotic inheritance:** aka somatic; perpetuation of marks during the process of cell division by mitosis within an **individual**.
- **Meiotic inheritance:** aka transgenerational; perpetuation of marks during meiosis that results in passing of marks to **offspring**.
- ▷ Research is continuing to provide strong evidence that epigenetics can radically alter physiology.
- ▷ Epigenetic marking may also play large roles in lifelong effects due early-life and prenatal environments.

## 5 Transport of Solutes and Water

### Passive Transport

- ▷ **Equilibrium:** the state at which a of minimum capacity to do work under locally prevailing conditions.
  - A change toward equilibrium is always in the direction of decreasing work potential.

### Concentration gradients

- ▷ General definition: the difference in concentration between two solutions or regions.
- ▷ More accurately:  $\frac{C_1 - C_2}{X}$  where  $X$  is the distance separating (boundary layer) the regions of concentration of solute particles, making it a colligative property.
- ▷ **Fick diffusion equation:**  $J = D \frac{C_1 - C_2}{X}$ 
  - $J$  is the net number of solute molecules passing into the low-concentration region from the high-concentration of solute particles, making it a colligative property.
  - **Diffusion coefficient ( $D$ ):** proportionality factor determined by the permeability of the membrane or epithelium as well as the temperature.
- ▷ Each solute diffuses according to its own concentration of solute particles.
- ▷ **Simple diffusion:** aka diffusion; moves solute from an area of high solute concentration to an area of low solution concentration.
  - Does not use energy as it can only move material in the direction of the concentration gradient and towards equilibrium.

### Electrical gradients

- ▷ **Electrical gradient:** difference in charge across a membrane.
- ▷ Many solutes bear electrical charge that affects the diffusion of such solutes.
- ▷ **Bulk solution:** solution not in contact with with a membrane.
  - Has a net charge of zero, this regions do not differe in charge.
  - Lack of net charge does not affect diffusion in the bulk solution, though does affect diffusion across the cell membranes of epithelia.
  - *Bulk flow:* physical kinetic movement of fluid, typically due to pressure.
- ▷ **Electrochemical gradient:** gradient consisting of the chemical gradient (concentration gradient) and the electrical gradient.

### Biological Aspects of Diffusion

- ▷ **Ion channels:** integral membrane protein that permits the passive transport of inorganic ions by diffusion through the membrane.
  - Some can be selective for certain ions, such as  $\text{Na}^+$ ,  $\text{Cl}^-$ , and  $\text{K}^+$
  - Even the least selective discriminate between **anions** and **cations**
  - **Gated channels:** ion channels that can open and close due to the proteins allowing for conformational changes.
    - **Voltage-gated:** responds to voltage change.
    - **Stretch-gated:** aka tension gated: responds to physical tensions.
    - **Phosphorylation-gated:** responds due to changes in protein phosphorylation.
    - **Ligan-gated:** responds due to extracellular signaling.
- ▷ **Permeability:** the ease at which the solute can move through the membrane by diffusion.
  - Changed by use and quantity of ion channels
- ▷ **Facilitated diffusion:** the process of spontaneous passive transport of molecules of ions across a biological membrane via transmembrane integral proteins.
  - Always occurs in the direction of electrochemical equilibrium.
  - Solutes are transported faster than they are in simple diffusion.
  - Solutes must bind reversibly with binding sites on transporter proteins.
  - Temperature dependence is substantially different due to presence of an activated binding event.

## Active Transport

- ▷ **Active Transport:** the movement of molecules across a cell membrane that is **against** the concentration gradient.
- ▷ **Primary active transport:** uses protein pumps that normally use ATP.
  - Often transports metal ions such as  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Mg}^{2+}$ , and  $\text{Ca}^{2+}$
  - Most enzymes used are transmembrane ATPases, such as the sodium-potassium pump, which moves three  $\text{Na}^+$  ions out of the cell for every two  $\text{K}^+$  moved into the cell.
- ▷ **Secondary active transport:** uses potential energy derived through movement of ions (using transporter proteins and ATP) across the electrochemical gradient.
  - **Antiporter:** one substrate is transported across the membrane while the other is contransported in the opposite direction.
  - **Symporter:** two substrates are transported in the same direction across the membrane.
  - $\text{Na}^+$ ,  $\text{K}^+$ , or  $\text{H}^+$  ions are usually the ones moving down the gradient and used to transport the desired ion up the relative gradient.

## Diversity and Modulation of Channels and Transporters

- ▷ **Multiple molecular forms:** many forms of a channel and transporter proteins are common.
  - Different species have evolved different molecular forms, which can modulate function and efficiency.
  - Allows for opportunities for adaptation.
- ▷ **Modulation by gene expression:** common channels and transporters can be modulated throughout a lifetime via gene expression responses to environmental circumstances.
- ▷ **Noncovalent and covalent modulation:** both ligand (often noncovalent) binding and phosphorylation (covalent) allow for **rapid** regulation of channels and transporters.
- ▷ **Insertion-and-retrieval modulation:** the **location** of proteins in the membrane allow for another way of regulating activity.
  - Some proteins are held in reserve, and **inserted** into the membrane when necessary.
  - Inverse is also true, some proteins can be **retrieved** from the membrane in order to modulate usage.

- Often only takes minutes for modulation to occur.

## Colligative Properties of Aqueous Solutions

- ▷ **Colligative properties:** the properties of solutions that depend on the **ratio** between solute particles and solvent molecules.
  - Not dependent on the nature of the chemical species present.
  - Effects include: relative lowering of vapour pressure, elevation of boiling point, depression of freezing point, and *osmotic pressure*.
- ▷ **Vapour pressure:** the pressure of the vapour which is in equilibrium with that liquid.
  - Vapour pressure of a solvent is lowered when a non-volatile solute is dissolved in it to form a solution.
- ▷ **Boiling and freezing points:** additions of solute help stabilize the solvent in the liquid phase, lowering chemical potential, and thus a lower tendency to move to gas phase or solid.
  - **Freezing point depression:** lowering of freezing point of a solvent with the addition of a solute that is insoluble in the solid solvent.
  - **Boiling point elevation:** increased by the by the addition of a non-volatile solute.
  - Both are proportional to the lowering of vapour pressure in a dilute solution.

## Osmosis

- ▷ **Osmosis:** the spontaneous net movement of solvent molecules through a selectively permeable membrane into a region of higher solute concentration.
  - Can be made to do work.
  - The primary means by which **water** is transported into and out of cells.
  - **Turgor:** the force and which the cell pushes the plasma membrane against the cell wall.
  - Turgor is largely maintained by osmosis across the cell membrane between the interior and its relatively hypotonic environment.
- ▷ **Osmotic pressure:** the external pressure required to be applied so that there is no net movement of a solvent across the membrane.
  - The semipermeable membrane allows the passage of solvent molecules but not the solute particles.



- Also defined as the measure of tendency of a solution to take in pure solvent by osmosis. "Water wants to go where solutes are"
- **Osmotic gradient:** the difference in pressure between the solution and the pure liquid solvent when the two are in equilibrium across a semipermeable membrane.
  - Formula:  $K \frac{\Pi_1 - \Pi_2}{X}$
  - i.e., the **rate** at which water crosses the membrane by osmosis.
  - Similar to the Fick equation for concentration gradient, except  $\Pi_{1\&2}$  are the osmotic pressures of the solutions on each side of the membrane, and  $K$  is the osmotic permeability of the membrane + temperature.
- Proportional to the concentration of solute particles, making it a colligative property.
- **Isosmotic:** when two solutions have the same osmotic pressure.
- When solution  $A < B$  in terms of osmotic pressure then:
  - A is **hyposmotic** to B — A has less solutes than B
  - B is **hyperosmotic** to A — B has more solutes than A.
  - The direction of net water movement by osmosis is from hyposmotic solution into the hyperosmotic one, i.e.,  $A \rightarrow B$
- ▷ Water is still capable of diffusing directly through lipid membranes.
- ▷ **Aquaporins:** water-channel proteins that greatly increase water transport.
  - Water transport through aquaporins is strictly passive.
- ▷ Nonpermeating solutes often create persistent osmotic-gradient components across semipermeable membranes.
  - Plays an important role in blood, as blood pressure forces water out, but proteins create persistent tendency to take up water; termed **colloid osmotic pressure** of the blood.
- ▷ Passive solute transport and osmosis interact.
  - **Solvent drag:** when solute moves with water crossing the membrane.
  - Tends to alter electrochemical gradients which plays a continuous role in rates of passive transport of both water and solutes.
- ▷ Active solute transport provides a means to control passive water transport.
  - Water transport is strictly passive, though control of solutes indirectly allows for metabolic water transport.

## Osmoregulation

Excerpt from Chapter 27: Water and Salt in Physiology ⇨

- ▷ **Osmoregulation:** the active regulation of the osmotic pressure of an organism's body fluids.
  - Detected by osmoreceptors, primarily found in the hypothalamus.
  - Acts to maintain homeostasis of the water content and electrolyte concentration.
- ▷ **Osmoconformers:** match their body osmolarity to their environment actively or passively.
  - Most marine invertebrates are osmoconformers.
- ▷ **Osmoregulators:** tightly regulate their body osmolarity through internal conditions.
  - More common in animals.
- ▷ **Volume conformity:** passive changes in body-fluid volume.
- ▷ **Volume regulation:** regulation of the **total** amount of water in a body fluid.
- ▷ There is also ionic regulation and conformity that are subject to ion-specific physiological controls.
- ▷ Influx of H<sub>2</sub>O will tend to lower osmotic pressure, dilute ions, and increase volume.

## 7 Nutrition, Feeding, and Digestion

### Fundamentals of Animal Energetics

- ▷ **Energy metabolism:** the sum of the processes by which animals acquire energy, channel energy into useful functions, and dissipate energy.
  - Catabolic processes: breaking down of organic molecules to release energy.
  - Anabolic processes: use of energy to construct molecules.
- ▷ **Second law of thermodynamics:** the total entropy of an isolated system can never decrease over time.
  - **Isolate systems:** part of the material universe that does not exchange matter or energy with its surroundings.
  - Energy can be thought of both the capacity to do work, of the capacity to **increase order**.
  - **Thermodynamic equilibrium:** the state of maximum entropy; the state isolated systems spontaneously evolve towards.
- ▷ Animals require energy from the outside because energy is necessary to create and maintain their essential internal organization.

### Forms of Energy

- **Chemical Energy:** energy liberated or required when atoms are rearranged into new configurations.
- **Electrical Energy:** energy that a system possesses by virtue of separation of electrical charges.
- **Mechanical Energy:** energy of organized motion in which many molecules move simultaneously in the same direction.
- **Molecular kinetic energy (heat):** energy of random atomic-molecular motion.
- ▷ **Physiological work:** any process carried out by an animal that increases order.
  - All forms of energy are capable of doing work, though not equally capable of doing physiological work.
  - Chemical energy can be used by animals, directly or indirectly, to do **all forms** of physiological work (totipotent).
  - Electrical and mechanical energy are both heavily used in animals, though cannot be used for everything.

- E.g., electrical energy used to set ions in motion and mechanical energy to pump blood, but neither can synthesis proteins.
  - Animals **cannot use heat to do any form of physiological work.**
- ▷ **High-grade energy:** energy that can do physiological work; chemical, electrical, and mechanical.
- ▷ **Low-grade energy:** heat, which cannot do physiological work.
- ▷ **Degrade:** when the use energy to perform a function and downgrade it to form heat.
- ▷ Transformations of high-grade energy are **always inefficient.**
  - **Efficiency of energy transformation:** a ratio between output and input of high-grade energy.
    - Typically much less than a 1:1 ration.
    - ATP at most uses about 70% of the energy released from glucose into bonds of ATP.
    - Only a maximum of 25%-30% of energy is liberated and used for muscular motion.
- ▷ **Ingested chemical energy:** energy in the chemical bonds of food that animals use to do physiological work.
  - **Fecal chemical energy:** chemical-bond energy in compounds that are unable to be digested or absorbed.
  - **Absorbed energy:** portions of chemical-bonds that are able to assimilated and used

### Major Functions of Physiological Work

- **Biosynthesis:** the process that synthesizes body constituents, such as proteins and lipids, by the use of absorbed energy.
  - Some absorbed energy remains in chemical form since products are often organic molecules themselves.
  - During growth, chemical energy accumulates in the form of biosynthesized products.
  - Also produces organic compounds that are exported from the body during ht animals life.
  - All steps are inefficient, thus Biosynthesis produces heat and products.
- **Maintenance:** all the processes that maintain the integrity of the animal's system.

- e.g., circulation, respiration, nervous coordination, gut motility, and tissue repair.
- Energy used for Maintenance is degraded entirely to heat within the body in majority of cases.
- **Internal work:** mechanical work that takes place inside an animal's body.
  - Many forms of maintenance, such as blood circulation and gut motility, are types of internal work.
- **External work:** application of mechanical forces on objects outside of an animal's body.
  - Much of absorbed chemical energy is used to fuel external work.
  - Some energy leaves the body as mechanical energy transmitted to the environment.
  - Energy of external work is stored if it is converted into increased potential energy of position.

## Metabolic Rate

- ▷ **Metabolic rate:** the rate at which an animal consumes energy.
  - Heat is always the dominant component of the metabolic rate.
  - Knowing average metabolic rates of animals allows for calculations of chemical energy usage.
- ▷ calorie (cal): the amount of heat needed to raise the temperature of 1g of water by 1 °C.
  - kilocalorie (kcal): 1000 cal, often written as Calorie.
  - One calorie is equivalent to 4.186 J (joule).
  - Watts: joules/second.
  - Metabolic rates are often expressed as calories per unit of time or watts.

### Principal Significance of Metabolic Rates

- The metabolic rate is one of the most important determinants of how much food it needs.
  - Adults' food needs depend almost entirely on metabolic rates.
- The total rate of heat production provides a quantitative measure of the total activity of all its physiological mechanisms.
  - Metabolic rate typically correlates with the intensity of living.
- Ecologically the metabolic rate measures the drain the animal places on the physiologically useful supplies of the ecosystem.

### Calorimetry

- **Direct calorimeter:** a device that measures the rate at which heat leaves the animal's body.
  - Not all work energy is converted to heat; some energy converted to mechanical or potential energy can be measured inaccurately.
- **Indirect calorimetry:** measures of an animal's metabolic rate by means other than quantifying heat and work.
  - Indirect methods are often cheaper and easier.
- **Respirometry:** metabolic rate measured indirectly through respiratory gas exchange with the environment.
  - Rate of oxygen consumption provides a convenient and readily measured estimate of metabolic rate.
    - $C_6H_{12}O_6 + 6 O_2 \rightarrow 6 CO_2 + 6 H_2O + 2820 \text{ kJ/mol}$
    - Glucose + Oxygen → Carbon Dioxide + Water + Energy
  - Oxidization of an unknown quantity of glucose, but with known measurements of  $O_2$  used or  $CO_2$  produced, then you can calculate exact heat produced.
  - Different food sources require different amounts of  $O_2$  and produce different amounts of  $CO_2$  during catabolism, which causes issues with identifying correct conversion factor
  - **Respiratory quotient (RQ):** the metabolic signature that reveals particular food sources being oxidized.
    - $$\frac{\text{moles of } CO_2 \text{ produced per unit of time}}{\text{moles of } O_2 \text{ consumed per unit of time}}$$
    - $RQ \approx 0.7 = \text{lipids.}$
    - $RQ \approx 0.83 = \text{proteins.}$

- $RQ \approx 1$  = carbohydrate.
- The most common approach used today is measuring rate of  $O_2$  and accepting relatively small potential errors ( $\pm 5\%$ - $8\%$ ).
  - External work does not have to be measured in most cases.
  - Excludes anaerobic metabolism of the gut microbiome.
  - Does not work well for measurement of metabolic rate during anaerobically fueled exercise.
- **Material Balance:** the measurement of the chemical-energy content of organic materials entering and leaving the animal's body.
  - Assumes that any energy that an animal ingests as chemical energy, but does not void as chemical energy, must be consumed.
  - If animal is currently gaining or losing biomass, then calculations will be off.
  - Animals can lose chemical energy in other ways than food, feces, or urine.
  - Best suited for **long term** measurements of average metabolic rates.

### Factors of Metabolic Rates

- **Physical activity** and **temperature of the environment** are often the most influential factors.
- Other factors include: ingestion of food, age, gender, time, body size, reproductive condition, hormonal states, psychological stress, and salinity of ambient water.
- **Specific dynamic action (SDA):** the increase in the metabolic rate caused by ingestion of food.
  - Not the greatest factor, but almost always must be taken into account.
  - Under many circumstances, if an animal has not eaten for a while, then consumes food, then metabolic rates will rise despite all other factors kept constant.
  - The **magnitude** of SDA represents the total excess metabolic heat production induced by the meal.
    - Roughly proportional to the amount of food eaten.
    - Protein foods exhibit relatively much higher SDA than other macromolecules.

- **Diet-induced thermogenesis (DIT):** long-term increase in metabolic rate induced by persistent overeating.

### Basal vs Standard Rates

- **Basal metabolic rate (BMR):** a standardized measure of metabolic rate that applies to **homeotherms**.
  - **Thermoneutral zone:** the range of environmental temperatures which the basal metabolic rate is minimal.
  - **Fasting:** when SDA effects of meal have ended.
  - Represents an animal that is in the thermoneutral zone, fasting, and resting.
- **Standard metabolic rate (SMR):** a standardized measure of metabolic rate that applies to **poikilotherms (ectotherms)**.
  - Represents metabolic rate of an animal is at rest and fasting.
  - A single animal may have many SMRs due to conformity of body temperatures.
- **Routine metabolic rate:** refer to metabolic rates of animals exhibiting regular, typically minimal, movements or behaviors.

### Metabolic Scaling

- ▷ **Metabolic scaling:** the relation between metabolic rate and body size.
  - Energy needs of the species are not proportional to their respective body sizes.
  - Increases as a whole, but less significantly.
- ▷ **Weight-specific metabolic rate:** metabolic rate calculated per unit of body weight.
  - Decreases as weight increases, though it's not indirectly proportional.
- ▷ **Kleiber's law:**  $M = aW^b$  ( $B = B_o M^{3/4}$ )
  - M (B): whole-body metabolic rates, unit of power—watts typically.
  - W (M): body weight, unit of mass—kg typically.
  - a ( $B_o$ ): mass-independent-normalization constant, unit of power/unit of mass.
  - b ( $3/4$ ): mean observed allometric scaling factor.
    - **Allometric equation:** when b is not equal to 1, meaning a lack of proportionality.



- Weight specific:  $M/W = aW^{b-1}$
- Logarithmic:  $\log M = \log a + b \log W$ , useful for comparing a wide range of species in a linear representation.
- ▷ Resting heart rate varies in functionally similar way as weight-specific BMR.
  - Small species tend to have higher heart rate than large ones.
  - However, heart weight per unit of body weight shows little relation to body size.
- ▷ Physiologists are not in consensus for the explanation to why we see consistent observed allometric relations.
  - Runer's law is based on heat loss on animal, but it predicts a lower rate ( $b = 2/3$ ) and does not account for poikilotherms.
  - Fractal geometry of scaled circulatory systems may give rise to more concrete answer.

## 8 Aerobic and Anaerobic Metabolism

### Mechanisms of ATP Production

- ▷ **Burst exercise:** sudden intense exercise, generally leading to quick exhaustion.
- ▷ **Sustained exercise:** exercise that can be sustained at a steady rate for long periods of time.
- ▷ ATP is not transported from one cell to another.
  - Each cell must make its own ATP.
  - ATP is not stored by cells to any substantial extent.
- ▷ The rate at which a cell can do muscular work depends on the rate the cell can produce ATP at the given moment.
  - $\text{ADP} + \text{P}_i + \text{energy from foodstuff molecules} \rightarrow \text{ATP}$
  - $\text{ATP} \rightarrow \text{ADP} + \text{P}_i + \text{usable energy by cell processes}$
  - $\text{P}_i$ : inorganic phosphate ions,  $\text{HPO}_4^{2-}$
  - Energy-demanding processes are dependent on the cellular mechanisms that drive this equation and can only happen as fast as such mechanisms.

### Aerobic Catabolism

- **Aerobic catabolic pathways:** pathways that use  $\text{O}_2$  to completely oxidize foodstuff molecules to  $\text{CO}_2$  and  $\text{H}_2\text{O}$  in order to capture released energy into ATP bonds.
- Subdivided into four major reactions:
  - Glycolysis (in cytoplasm)
  - Krebs cycle (in mitochondrial matrix)
  - Electron transport chain (inner mitochondrial membrane)
  - Oxidative Phosphorylation (inner mitochondrial membrane)
- **Glycolysis:** the series of enzymatically catalyzed reactions in which glucose (or glycogen) is converted to pyruvic acid.
  - Occurs in the cytosol and is an oxygen-independent metabolic pathway.
  - Each molecule of glucose is converted into 2 pyruvate ( $\text{C}_3\text{H}_3\text{O}_3^-$ ) molecules.

- **NAD**: small non-protein molecule that undergoes reversible oxidation and reduction; synthesized from niacin.
- 2 NADs are reduced into 2  $\text{NADH}_2$  per molecule of glucose catabolized.
- 2 ATPs are used and 4 are formed from each glucose processed, providing net yield of 2 APT per glucose.
- **Krebs (citric acid) cycle**: when pyruvic acid is oxidized in the mitochondria by cyclic series of enzymatic reactions.
  - The 2 pyruvate molecules from glycolysis enter the mitochondria matrix by facilitated diffusion to start the cycle.
  - Each pyruvate is oxidatively decarboxylated, forming  $\text{CO}_2$  and a two-carbon acetyl group that is combined with coenzyme A to form acetyl coenzyme A (acetyl-CoA).
  - Acetyl-CoA is the starting point for the citric acid cycle; can be obtained from oxidation of fatty acids too.
  - Overall outcomes:
    - 6 carbons of each glucose molecule catabolized emerge in the form of 6 molecules of  $\text{CO}_2$  as the pyruvate molecules are processed.
    - 8 molecules of  $\text{NADH}_2$  and 2 molecules of  $\text{FADH}_2$  are produced for each glucose molecule. (4/1 per pyruvate)
    - 2 molecules of ATP are produced for each glucose catabolized.
    - $\text{C}_6\text{H}_{12}\text{O}_6 + 6 \text{O}_2 \longrightarrow 6 \text{CO}_2 + 6 \text{H}_2\text{O} + 2820 \text{ kJ/mol}$ .
- $\text{O}_2$  is not a direct participant of glycolysis or the Krebs cycle, though it is essential.
  - $\text{NADH}_2$  and  $\text{FADH}_2$  are intermediate electron acceptors, but cannot serve as the final resting places for electrons due to limited quantity in cell.
  - $\text{O}_2$  is required for the continuation of aerobic catabolism by acting as the final electron acceptor in the remaining steps, which generates the majority of ATP produced.
- **Electron Transport (respiratory) chain**: a series of complexes that transfer electrons via redox (reduction+oxidation) across a membrane that drives synthesis of ATP.
  - The chain takes electrons from  $\text{NADH}_2$  (complex I) and  $\text{FADH}_2$  (complex II) and passes them through redox reactions by the use of accompanying  $\text{H}^+$  ions, via ubiquinone/cytochrome ( $b - c_1$  and  $c$ ).

- The electrons are passed along to cytochrome oxidase, which reduces the  $O_2$  to  $H_2O$ , acting as the **final electron acceptor**.
- An adult human produces about 0.8 L of metabolic water per day in the process of voiding electrons from cells.
- Pumps **10  $H^+$**  for **1 oxygen** (pair of electrons) reduced.
- **Oxidative phosphorylation:** the process of forming ATP from ADP via the energy released in the transport of electrons through the electron-transport chain.
  - **Chemiosmotic hypothesis:** the indirect two-step process that pumps protons across the inner mitochondrial membrane, creating an electrochemical gradient far from equilibrium.
  - The proton motive energy (back-diffusion) is used by ATP-synthase to generate ATP from ADP.
  - **P/O ratio:** ratio between phosphate and oxygen; defined as the number of ATP formed per atom of oxygen reduced to water.
    - Current estimates in mammalian mitochondria: 1 ATP : 4.3  $H^+$ .
    - Results in 2.3 ATP per oxygen, i.e., a **P/O ratio of 2.3**.
    - 2.3 represents the current maximum P/O ratio observed.
  - **Coupling:** the linkage of electron transport with oxidative phosphorylation.
    - Capable of being graded in its efficiency, ranging from 0 to 2.3.
    - Tightly coupled = P/O of 2.3
    - Uncoupled = P/O of 0.
  - **Uncoupling protein 1 (UCP1):** can use back-diffusion protons to generate much greater degree of heat rather than ATP.
- **Net yield of ATP from aerobic catabolism:**
  - **Substrate level phosphorylation:** phosphorylations that occur in glycolysis and the Krebs cycle:
    - Altogether, 6 ATP molecules are formed.
  - Together, the electron transport chain and oxidative phosphorylation produce per molecular of glucose:
    - 2.3 ATP/ $NADH_2$  and 1.4 ATP/ $FADH_2$
    - With a max of 25 ATP.
  - 31 total generated, with 2 used at start of glycolysis.
  - Actual **net yield: 29 ATP per glucose**.

- **Energetic efficiency:** assuming tight coupling, is estimated to be  $\approx 60\%$ -70%.
  - I.e., 60%-70% of chemical energy released by oxidizing glucose to  $\text{CO}_2$  and  $\text{H}_2\text{O}$  is captured into chemical-bond energy of ATP.

### Anaerobic Catabolism

- **Redox balance:** the inability of the electron transport chain to regenerate NAD and FAD from  $\text{NADH}_2$  and  $\text{FADH}_2$  in the absence of  $\text{O}_2$ .
  - Describes the cell's ability to remove electrons from a given compound as fast as electrons are added to it.
  - Without a balance, the cell will not be able to generate any ATP due to substrate level phosphorylation breakdown.
- Some tissues can produce ATP at a substantial rate without  $\text{O}_2$ , however, the mammalian brain lacks such ability.
- **Anaerobic glycolysis:** the sequence of reactions that converts glucose to lactic acid.
  - **Lactate dehydrogenase (LDH):** the enzyme that catalyzes the reduction of pyruvic acid and produces lactic acid.
    - The rate limiter of anaerobic glycolysis.
  - Lactic acid is used as the final electron acceptor.
  - Only about 7% of free energy is released by the conversion of glucose to lactic acid; yielding vastly lower amounts of ATP compared to aerobic catabolism.
  - A cell must synthesize significant amounts of LDH for the intracellular process that must prevail during  $\text{O}_2$  deprivation.
- Anaerobic glycolysis is not the only mechanism of anaerobic catabolism.
- When vertebrates use anaerobic glycolysis they must deal with the lactic acid once  $\text{O}_2$  becomes available.
  - **Gluconeogenesis:** the conversion of lactic or pyruvic acid to glucose or glycogen; represents one path of lactic acid metabolism.
  - The second path is for the carbon chains to be fully oxidized by the way of Krebs cycle and electron-transport chain, which makes 27 (requires already functioning electron transport chain).
- Often tissues that generate lactic acid export it to tissues that are better supplied with  $\text{O}_2$ .
- **Phosphagens:** Compounds that serve as temporary stores of high-energy phosphate bonds.

- Occurs in skeletal muscles of vertebrates and muscles of many invertebrates.
- Creatine phosphate is the phosphagen of vertebrate muscle, and some invertebrates.
- Arginine phosphate is most common for invertebrates.
- Synthesized by use of ATP to store energy, allowing for donate bonds back to ADP later.

## Comparative Properties of the Mechanisms of ATP Production

- ▷ **Steady state:** a state at which a reaction can go on indefinitely, free of intrinsic limitations. In terms of ATP production:
  - Can produce ATP as fast as it is used.
  - Uses raw materials (foodstuff molecules) no faster than they are replenished.
  - Chemical by-products (not ATP) are voided or destroyed as fast as they are made.
  - Does not cause other changes in cell function that progress to the point of disruption.
  - Nonsteady-state mechanisms violate one or more of the above, resulting in short lived processes.
    - Anaerobic glycolysis, phosphagen use, and aerobic catabolism using preexisting O<sub>2</sub> are examples of nonsteady-state mechanisms.
  - Aerobic catabolism using O<sub>2</sub> from environment is a steady state mechanism, but it does use nonsteady-state mechanisms as intermediate parts of the reaction.

▷

## Themes in Exercise Physiology

▷

## 9 Thermal Biology

### Thermal Biology and Climate



### Poikilothermy (Ectothermy)



### Homeothermy and Endothermy

