Vertebrate Physiology 437

1. Seminars and Legible Paper
2. Important molecules, physical and chemical properties (CH3)
4. Membranes (CH4)
5. We are a bit behind already!
Friday Physiology Seminars

See course website for link to schedule

PHYSIOLOGY

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Department of Anesthesiology
University of Arizona
College of Medicine

“Cannabinoids for the Treatment of Pain”

Friday, September 5, 2003 @ 11 a.m.
Room 5403, Arizona Health Sciences Center

Also available on-line at:
http://www.physio.arizona.edu/seminars
(Refreshments served @ 10:30 a.m.)
Biological Molecules

- **Lipids**

- **saturated -> cholesterol**
  No double bonds in side chains (saturated with hydrogens) ~solid at room temperature

- **high energy/ gram**

- **phospholipids**

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**Table 3-3** The energy content of the three major categories of foodstuffs

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Energy content (kcal·g⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbohydrates</td>
<td>4.0</td>
</tr>
<tr>
<td>Proteins</td>
<td>4.5</td>
</tr>
<tr>
<td>Fats</td>
<td>9.5</td>
</tr>
</tbody>
</table>

Randall et al. 2002
Biological Molecules

- **Carbohydrates**

- \((CH_2O)_n\)

- monosaccharides, (disaccharides)

- **glucose** is common metabolic currency from plants to animals

- **glycogen** (storage)
Biological Molecules

- **Proteins**
- linear chains of amino acids
- 20 common alpha-amino acids
- amphoteric
- peptide bonds
- polypeptide chains
- 1°, 2°, 3°, 4°

(a) General structure of alpha-amino acids

(b) Structure of a tetrapeptide

3-17 Randall et al. 2002
Biological Molecules

- **Proteins**
- Linear chains of amino acids
- $1^\circ, 2^\circ, 3^\circ, 4^\circ$

- H bonds
- Van der Waals
- Covalent

-HSPs
-Stress Proteins
Biological Molecules

- **Nucleic Acids**
  - pyrimidine (T,C) or
  - purine (A,G)

- Phosphodiester linkages between adjacent

- transcription (nucleus)
  DNA -> mRNA

- translation (ribosome)
  mRNA -> tRNA -> protein (genetic code)
Mid-Lecture Question (MLQ)

How is pH important to the biological activity of ionized groups such as amino acids (and their side chains) and proteins (including enzymes)?

Part Deux:

How do buffers and homeostasis play a role in the above topic?
Mid-Lecture Question (MLQ)

How is pH important to the biological activity of ionized groups such as amino acids (and their side chains) and proteins (including enzymes)?

- Amphoteric with acidic carboxyl groups and basic amino groups
- Enzyme binding involves electrostatic interactions
- pH can alter ionization state of molecules and side groups
- Biological activity relies on narrow pH range
Mid-Lecture Question (MLQ)

- Enzyme function has generally *evolved* within narrow pH range
- **Buffers** tolerate addition of acids and bases without changing pH much
- **Weak acids** (HA) and their dissociated **salts** (A⁻) work best
- Examples include **bicarbonates**, **phosphates**, **amino acids**, **peptides/proteins**
- Best buffering when **pH = pK'** (~dissociation constant)

How do **buffers** and **homeostasis** play a role in the above topic?
**Electrical Properties** (p. 49-51 in text)

- Important for many biological processes, especially **nerve** transmission and **muscle** contraction

- **Current** flows in direction of **cation** (+), by convention

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3-8 Randall et al. 2002
Electrical Properties (p. 49-51 in text)

I = current (amperes A)
V = electromotive force (voltage V or mV)
R = resistance (ohms)

V = electromotive force (voltage V or mV)
   potential difference (relative charge difference)

ohm’s law: I = V/R

All else being equal, how does size (x-sec area) of wire or neuron affect current?
Energetics (sun is origin)
- metabolism
- energy/ATP
- building blocks
- small, controlled oxidation steps

- 1\textsuperscript{st} law – energy neither created or destroyed
- 2\textsuperscript{nd} law – entropy will reign

- free energy $\Delta G$
  (energy available to do useful work)
  - $\Delta G$
  - exergonic (liberate heat)
  + $\Delta G$
  - endergonic (uphill)
Energetics

- **exergonic** (liberate heat)  \(- \Delta G\)
- **endergonic** (uphill)  \(+ \Delta G\)

\[
\begin{align*}
\text{Phosphoenolpyruvate} & : \Delta G^\circ = -14.8 \text{ kcal} \cdot \text{mol}^{-1} \\
1,3-\text{Diphosphoglycerate} & : \Delta G^\circ = -11.8 \text{ kcal} \cdot \text{mol}^{-1} \\
\text{Phosphocreatine} & : \Delta G^\circ = -10.3 \text{ kcal} \cdot \text{mol}^{-1}
\end{align*}
\]
Metabolic Production of ATP

- Oxidation (lose e-) / Reduction (gain e-)

- Phosphorylation
  steps for harnessing energy

- Energy Transfer
  electron transport chain

O₂ is ultimate electron acceptor

3-39 Randall et al. 2002

3-40 Randall et al. 2002
Metabolism

IN:

fat, CHO, protein, (O₂)

OUT:

CO₂, H₂₀, urea

Food oxidized to CO₂ and H₂₀ in presence of O₂
Metabolism

\[ \text{C}_6\text{H}_{12}\text{O}_6 + 6\text{O}_2 \rightarrow 6\text{CO}_2 + 6\text{H}_2\text{O} \]
\[ \Delta G = -686 \text{ kcal/mol} \text{ (e.g., bomb calorimeter)} \]

\[ \text{C}_6\text{H}_{12}\text{O}_6 + 6\text{O}_2 + 38\text{Pi} + 38\text{ADP} \rightarrow 6\text{CO}_2 + 6\text{H}_2\text{O} + 38\text{ATP} \]
\[ \Delta G = -420 \text{ kcal/mol} \text{ (lost as heat), therefore } 266 \text{ kcal stored in 38 ATP (40-60% efficient)} \]

anaerobic 2% (20x less efficient)
Energetics

- Activation Energy
- Enzymes
- CATALYSTS
- Temperature
- \( \uparrow \) Reaction Rates

(a) Enzyme activity versus temperature

3-30 Randall et al. 2002

3-27 Randall et al. 2002

3-26 Randall et al. 2002
Enzymes

- pH, temperature
- Cofactors (often vitamins)

Randall et al. 2002

<table>
<thead>
<tr>
<th>Metal ion</th>
<th>Some enzymes requiring this cofactor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca$^{2+}$</td>
<td>Phosphodiesterase</td>
</tr>
<tr>
<td></td>
<td>Protein kinase C</td>
</tr>
<tr>
<td>Cu$^{2+}$ (Cu$^+$)</td>
<td>Cytochrome oxidase</td>
</tr>
<tr>
<td></td>
<td>Tyrosinase</td>
</tr>
<tr>
<td>Fe$^{2+}$ or Fe$^{3+}$</td>
<td>Catalase</td>
</tr>
<tr>
<td></td>
<td>Cytochromes</td>
</tr>
<tr>
<td></td>
<td>Ferredoxin</td>
</tr>
<tr>
<td></td>
<td>Peroxidase</td>
</tr>
<tr>
<td>K$^+$</td>
<td>Pyruvate phosphokinase (also requires Mg$^{2+}$)</td>
</tr>
<tr>
<td>Mg$^{2+}$</td>
<td>Phosphohydrolases</td>
</tr>
<tr>
<td>Mn$^{2+}$</td>
<td>Arginase</td>
</tr>
<tr>
<td></td>
<td>Phosphotransferases</td>
</tr>
<tr>
<td>Na$^+$</td>
<td>Plasma membrane ATPase (also requires K$^+$ and Mg$^{2+}$)</td>
</tr>
<tr>
<td>Zn$^{2+}$</td>
<td>Alcohol dehydrogenase</td>
</tr>
<tr>
<td></td>
<td>Carbonic anhydrase</td>
</tr>
<tr>
<td></td>
<td>Carboxypeptidase</td>
</tr>
</tbody>
</table>

Source: Adapted from Nelson and Cox, 2000.
Enzymes

- Regulation
  1 - Competitive
  2 - Allosteric
Enzymes

- Rates of Rxn \((V)\)

- MM constant \((K_m)\)

- Michaelis-Menten equation

\[
V_0 = \frac{V_{max}[S]}{K_m + [S]}
\]
Enzymes
- Lineweaver-Burk Plot

\[
\frac{1}{V_0} = \frac{K_m}{V_{max}[S]} + \frac{1}{V_{max}}
\]

Lineweaver-Burk plot

- Intercept \( = - \frac{1}{K_m} \)
- Slope \( = - \frac{K_m}{V_{max}} \)

3-33 Randall et al. 2002

3-34 Randall et al. 2002
Membrane Structure and Composition

1. Phospholipids
   - bilayer, fluidity

2. Cholesterol
   - stabilizer

3. Proteins
   - integral
   - peripheral

4-2 Randall et al. 2002
Membrane Structure and Composition

**Protein Structure**

**Fluid Mosaic Model**
- Type of lipids
- Length of tails
- Amount of cholesterol
- Amount and type of protein
- "Sided"
Mid-Lecture Question (MLQ)

How do scientists come up with the protein conformations such as pictured here:

4-5 Randall et al. 2002

5-25 nm thick
Movement Across Membranes - Background

Diffusion (net movement)

(a) Semipermeable membrane

I  II

Individual fluxes

- $J_{I \rightarrow II}$
- $J_{II \rightarrow I}$

(b) Net flux

- $J_{I \rightarrow II}$ minus $J_{II \rightarrow I}$

Movement of solutes

-Diffusion coefficient, Partition coefficient, Thickness

Viscosity, size, dissolved components

4-8 Randall et al. 2002
Movement Across Membranes - Background

**Osmosis**

Initially, there is net movement of water from I to II.

At equilibrium, there is no net movement of water.

-Osmotic Pressure; Hydrostatic Pressure

4-9 Randall et al. 2002
# Movement Across Membranes - Background

## Osmosis

<table>
<thead>
<tr>
<th>Sucrose (%)</th>
<th>Osmotic pressure (atm)</th>
<th>Ratio of osmotic pressure to percentage of sucrose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.70</td>
<td>0.70</td>
</tr>
<tr>
<td>2</td>
<td>1.34</td>
<td>0.67</td>
</tr>
<tr>
<td>4</td>
<td>2.74</td>
<td>0.68</td>
</tr>
<tr>
<td>6</td>
<td>4.10</td>
<td>0.68</td>
</tr>
</tbody>
</table>

* Results were obtained by Pfeffer (1877) in experimental measurements.

-Osmotic Pressure; Hydrostatic Pressure
Movement Across Membranes

Iso  
Hypo  osmotic  
Hyper  

In specific tissues and cells:

Iso  
Hypo  tonic  
Hyper  

4-14 Randall et al. 2002
Movement Across Membranes

**Electrochemical Gradient**

**Electrical gradient**

**Concentration gradient**

Electrochemical equilibrium

**Equilibrium potential** \( (E_x \text{ in mV}) \)

when \([X]\) gradient = electrical gradient
Osmotic Properties of Cells and Relative Ion Concentrations

[Diagram showing ion concentrations inside and outside the cell.]

- Exterior: [Na⁺] = 120 mM, [K⁺] = 2.5, [Ca²⁺] = 2.0, [Cl⁻] = 120

[Note: A⁻ = molar equivalent of negative charges carried by other molecules and ions.]

Normally, Na⁺ levels are maintained at equilibrium as ion passively enters the cell and is pumped back out.

When inhibitor blocks active transport of Na⁺ outward, the intracellular concentration of Na⁺ rises, and water enters osmotically, increasing cell volume.

Eventually, increasing cell volume causes cell to burst.

4-12 Randall et al. 2002

4-16 Randall et al. 2002
Movement Across Membranes

1. Passive Diffusion (= simple diffusion)
2. Passive Transport (= facilitated diffusion)
3. Active Transport

Transport (pore or carrier) may be **highly selective**
End
3x5 card

Discussion section: 9 (=morning) or 2 (=afternoon) on Wed.

Name (and what you prefer to be called)
- distinguishing characteristics

Email address

Year in school

Major

Relevant courses taken, or research projects, etc.

Why are you taking this course?

Hold onto card til photo