Lecture 04, 31 Aug 2006

Vertebrate Physiology
ECOL 437 (MCB/VetSci 437)
Univ. of Arizona, Fall 2006
Kevin Bonine & Kevin Oh

1. Biochem Blitz (Chap 2)
2. Osmosis and Water (Chap 3)
3. Nervous System (Chap 10)

Membranes, Molecules, Signaling, Pathways

http://eebweb.arizona.edu/eeb_course_websites.htm

Housekeeping, 31 August 2006

Lipid soluble hormones later in endocrine section.

Upcoming Readings

today: Textbook, chapter 2&3 (maybe 10)

Tues 05 Sept: Textbook, chapter 10&11
Wed 06 Sept: Tipsmark et al. 2002, bring problem set to do
Thurs 07 Sept: Textbook chapter 11

Lab oral presentations 06 Sept
9am – Nilam Patel
2pm – Nick Brown
Wed 06 Sept: Tipsmark et al. 2002

Kevin Oh will help with short glossary

Integrative

Good example of using multiple tools to address interesting physiological question

Filter the useful information from the unnecessary details

What other questions does this paper raise?

Hill et al. Chapter 2

Biochem Blitz

Membranes, Molecules, Signaling, Pathways
-highlights and review
(2) New model

(See Tipsmark et al 2002)
Membrane Selectivity (Channels)

Charge, ease of dehydration, size

Diffusion
- nonpolar/nonelectrolyte
- lipophilic
- few H bonds
- smaller size

Transport
- rates depend on
  1. electrochemical gradient
  2. # carriers/pores

Movement Across Membranes

(a) Passive diffusion through membrane

Rate of influx

(b) Passive transport through channels

Rate of influx

(c) Carrier-mediated transport (passive or active)

Rate of influx

All carrier molecules occupied

Extracellular substrate concentration
How would you describe this movement across membrane?

Cotransport with Na⁺ renders substrate transport against its concentration gradient energetically favorable.
Movement Across Membranes

How does glucose cross membranes?

Most tissues:
- Passive transport down [ ] gradient via carrier proteins

In gut:
- $2^o$ active to move Glu against [ ] gradient into blood from “food”
Leinhard et al. 1992
Enzymes and Energetics
(Hill et al. Ch 2, con’t)

Energetics (sun is origin)
- metabolism
- energy/ATP
- building blocks
- small, controlled oxidation steps

- 1st law - energy neither created or destroyed
- 2nd law - entropy will reign

- free energy $\Delta G$
  (energy available to do useful work)

- $\Delta G + \Delta G$
  - exergonic (~liberate heat)
  - endergonic (uphill)
Energetics

- exergonic (liberate heat) - $\delta G$
- endergonic (uphill) + $\delta G$

Coupled reactions

Ion Gradients as an Energy Source

**CET example:**
- Metabolism
- Electron Transport Chain
- ATP creation
  energy currency

1 Move molecules
2 Electrical Signalling
3 Chemiosmotic Energy Transduction
Energetics
- Activation Energy
- Enzymes (CATALYSTS)
- Temperature
- ↑ Reaction Rates

Figure 2.13 Enzymes speed reactions by lowering the needed activation energy
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>Ca²⁺</td>
<td>Phosphohexokinase</td>
</tr>
<tr>
<td></td>
<td>Protein kinase C</td>
</tr>
<tr>
<td>Cu²⁺ (Ca²⁺)</td>
<td>Cytosolene oxidase</td>
</tr>
<tr>
<td></td>
<td>Tyrosinase</td>
</tr>
<tr>
<td>Fe³⁺ or Fe²⁺</td>
<td>Catalase</td>
</tr>
<tr>
<td></td>
<td>Cytochrome c</td>
</tr>
<tr>
<td></td>
<td>Ferrodoxin</td>
</tr>
<tr>
<td></td>
<td>Peroxidase</td>
</tr>
<tr>
<td>K⁺</td>
<td>Pyruvate phosphokinase (also requires Mg²⁺)</td>
</tr>
<tr>
<td>Mg²⁺</td>
<td>Phosphohexokinase</td>
</tr>
<tr>
<td>Mg²⁺</td>
<td>Phosphofructokinase</td>
</tr>
<tr>
<td>Mn²⁺</td>
<td>Arginase</td>
</tr>
<tr>
<td>Na⁺</td>
<td>Phosphotransferase</td>
</tr>
<tr>
<td></td>
<td>Phosphocreatinase</td>
</tr>
<tr>
<td>Zn²⁺</td>
<td>Alcohol dehydrogenase</td>
</tr>
<tr>
<td></td>
<td>Carbonic anhydrase</td>
</tr>
<tr>
<td></td>
<td>Carbamoyl phosphate</td>
</tr>
</tbody>
</table>

Source: Adapted from Nelson and Cox, 2000.

Enzymes

- **Regulation**
  1 - Competitive
  2 - Allosteric

Randall et al. 2002
(b) An example of an α-conotoxin

Disulfide bond

Glutamine-Asparagine-Proline-Asparagine-Proline-Alanine-Cysteine-Cysteine-Cysteine-Cysteine

Disulfide bond

(c) Block of receptor action by α-conotoxin

Extra-cellular fluid

End of nerve cell

Acetylcholin

Muscle cell membrane

Closed acetylcholine receptor

Open

NORMAL

POISONED

Hill et al. 2004

Journal of Physiology Figure 2.10 (Part B) © 2004 Blackwell Publishing, Ltd.

Allosteric activation/inhibition

Glucose

ATP

Hexokinase

ADP

Glucose-6-phosphate

Hexose phosphate isomerase

Fructose-6-phosphate

ATP

Phosphofructokinase

ADP

Fructose-1,6-diphosphate

Citrate

AMP

Pyruvic acid

Hill et al. 2004

Journal of Physiology Figure 2.10 (Part B) © 2004 Blackwell Publishing, Ltd.
Enzymes

- Rates of Rxn (V)
- MM constant (Km)

- Michaelis-Menten equation

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

Figure 2.14 The approach to saturation depends on enzyme-substrate affinity

(b) Determination of $K_m$ for two of the enzymes from (a)
Lactate dehydrogenase
2 alleles

Enzymes
- Lineweaver-Burk Plot

\[\frac{1}{V_0} = \frac{K_m}{V_{max}[S]} + \frac{1}{V_{max}}\]
Figure 2.12  Reaction velocity as a function of substrate concentration

Enzyme Kinetics
- hyperbolic
- sigmoidal

Osmotic Properties of Cells and Relative Ion Concentrations

Permeabilities
K+ >> Na+ ; Cl-

A⁻ (includes proteins, phosphate groups, etc.)
Electrogenic vs. Electroneutral

Just add water...

How does water move across membranes?

aquaporins
Movement Across Membranes

Iso
Hypo osmotic
Hyper

In specific tissues and cells:
Iso
Hypo tonic
Hyper

Osmotic Properties of Cells and Relative Ion Concentrations

K+ Na+ K+ Na+
Ca+ Cl-
Cl-

[Na+] = molar equivalent of negative charges carried by other molecules and ions.

[H2O]

Na+ pumped out

Ca2+, Na+/K+ ATPase pump

Metabolic inhibitor added

H2O

Na+ influx

Eventually, increasing cell volume causes cell to burst.

4-14 Randall et al. 2002

4-12 Randall et al. 2002

4-16 Randall et al. 2002
Colligative Properties

- Osmotic Pressure
- Freezing Point
- Water Vapor Pressure (boiling point; evaporation)
1 osmolar solution (Osm)
has 1 Avogadro’s number of dissolved particles/liter solvent

1 milliosmolar solution (mOsm)
has 0.001 Avogadro’s number of dissolved particles/liter solvent

What osmolarity do you get if you add $6 \times 10^{23}$ molecules of glucose to a liter of water?

What osmolarity do you get if you add $6 \times 10^{23}$ molecules of table salt to a liter of water?

NaCl (strong electrolyte)
Osmotic Pressure Vs. Hydrostatic Pressure
Rate of Osmosis = \[ \frac{K}{X} (\Pi_1 - \Pi_2) \]

Proportionality Coefficient (\sim permeability and temp)

Distance between solutions

Difference in osmotic potential

Electrochemical equilibrium

\( (a) \) Reinforcing concentration and electrical effects

\( (b) \) Opposing concentration and electrical effects

Fig 3.6, Hill et al 2004
Movement Across Membranes

Electrochemical Gradient

Electrical gradient
Concentration gradient

Electrochemical equilibrium

Equilibrium potential ($E_x$ in mV)
when [X] gradient = electrical gradient

Equilibrium potential ($E_x$ in mV)

“Every ion’s goal in life is to make the membrane potential equal its own equilibrium potential ($E_x$ in mV)”
Nervous System
Comprises
- Neurons / Nerve Cells
- Glial Cells (support)
- Signalling via combination of Electrical and Chemical
- Integrate information
  AFFERENT
- Coordinate Response
  EFFERENT