Quiz
Class Business

• All extra credit is due by Friday 5PM

• PS 13 no longer exists
Structure and Function of Biomolecules
What is the point?
What have we covered in this class?

• Structure and Function
  – Nucleic acids
  – Proteins
  – Carbohydrates
  – Lipids

The molecular forces that stabilize the structure and facilitate the function.
Reversal of Lectures

• Examples of cell functions and the structure and function of the molecules involved – signal transduction

• The “big” picture
  – What will you learn next semester?
  – How is it connected to this course?
Demonstration by example

• Visual transduction – how we sense light

• Action potential – mechanism of cell – cell communication to pass on information
Path to Vision

- Eye
- Optic nerve
- Optic chiasm
- Optic tract
- Large geniculate nucleus
- Optic radiations
- Primary visual cortex
Where does photoreception (detection of light) occur?
The Rod Cell
Rod outer segment discs

Fig. 6. Drawing of rod outer segment discs.
Rod Cells

Before light

After light

Absorbance

Wavelength, nm

pA

Time (s)
G-protein signal transduction cascade: The molecular players
Rhodopsin

Cytoplasm

Disk Membrane

Intradisk space

C-terminus

Retinal Chromophore

N-terminus

COOH-terminal

NH2-terminal
Light activation of rhodopsin

http://www.blackwellpublishing.com/matthews/rhodopsin.html
Freaky!
Lowered cGMP levels
Lowered Na+ and Ca++ conductance
Hyperpolarization of rod cell
Transducin and Arrestin interactions with Rhodopsin
Rhodopsin Mutations linked to Disease

Mutations in the gene for rhodopsin are known to cause retinitis pigmentosa (RP) and congenital stationary night blindness (CSNB)

G90D, T94I, A292E
Protein misfolding in RP
The Nerve Impulse
The synapse

(a) Excitatory synapse

Exocytosis of neurotransmitter

Fibers of basal lamina

Direction of signaling

Postsynaptic cell

Receptors for neurotransmitter

Axon terminal

Axon of presynaptic cell

Synaptic vesicles

Synaptic cleft

(b) Inhibitory synapse

Acetylcholine added

Resting potential

Acetylcholine

CH₃-C-O-CH₂-CH₂-N⁺-(CH₃)₃

mV

Time (ms)

10 20 30 40

-70

-80

-90

-60

Time (s)

1 2 3 4

-70

-72

Resting potential
Action Potential

http://www.blackwellpublishing.com/matthews/channel.html
Threshold potential

[Diagram of a neuron with labels for presynaptic cell, postsynaptic cell, axon, dendrite, synapse, cell body, axon terminal, and axon hillock. Diagram also shows the membrane potential in the postsynaptic cell with threshold potential and action potential highlighted.]

Electrode to measure electric potential

Membrane potential in the postsynaptic cell

-40 mV

-60 mV

Time (ms)

10 ms
Ion channels are the major players in generating the action potential
Ion channels are the major players in generating the action potential.
Different ion channels have similar architecture

(a) Voltage-gated K⁺ channel protein (tetramer)

(b) Cyclic nucleotide-gated channel protein (tetramer)

(c) Voltage-gated Na⁺ channel protein (monomer)

(d) Voltage-gated Ca²⁺ channel protein (monomer)

Binding site for cAMP or cGMP
Shaker isoforms exhibit different voltage dependencies and K+ conductivities. Thus differential expression of Shaker isoforms can affect the timing of repolarization during an action potential, accounting for differences in the electrical activity of different types of neurons.
K+ Selectivity

Diagram A: Illustration of molecular structure with labeled positions.

Diagram B: Comparative molecular structure highlighting specific regions labeled D80 and E71.

Diagram C: Detail of molecular interaction at positions 1 and 4, showing K+ and Ti+.

Diagram D: Graph plotting filter position (Å) against p values for K+ and Ti+.

Diagram (b): Molecular models of K+ in water and Na+ in water, with additional models of K+ in a pore and Na+ in a pore.
K+ channel Voltage Sensor
Highly contested structure
Propagation of action potential
Structure and Function of Myelin

http://www.blackwellpublishing.com/matthews/actionp.html
<table>
<thead>
<tr>
<th>Substance $^a$</th>
<th>Human</th>
<th>Bovine</th>
<th>Rat</th>
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<tbody>
<tr>
<td>Protein</td>
<td>30.0</td>
<td>24.7</td>
<td>29.5</td>
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<tr>
<td>Lipid</td>
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<tr>
<td>Cholesterol</td>
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<td>28.1</td>
<td>27.3</td>
</tr>
<tr>
<td>Cerebroside</td>
<td>22.7</td>
<td>24.0</td>
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<tr>
<td>Sulfatide</td>
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<td>3.6</td>
<td>7.1</td>
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<tr>
<td>Total galactolipid</td>
<td>27.5</td>
<td>29.3</td>
<td>31.5</td>
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<tr>
<td>Ethanolamine phosphatides</td>
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<td>17.4</td>
<td>16.7</td>
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<tr>
<td>Lecithin</td>
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<td>10.9</td>
<td>11.3</td>
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<tr>
<td>Sphingomyelin</td>
<td>7.9</td>
<td>7.1</td>
<td>3.2</td>
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<tr>
<td>Phosphatidylserine</td>
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<td>6.5</td>
<td>7.0</td>
</tr>
<tr>
<td>Phosphatidylinositol</td>
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<td>0.8</td>
<td>1.2</td>
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<tr>
<td>Plasmalogens $^b$</td>
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<td>14.1</td>
<td>14.1</td>
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<tr>
<td>Total phospholipid</td>
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<td>43.0</td>
<td>44.0</td>
</tr>
</tbody>
</table>

$^a$ Protein and lipid figures in percent dry weight; all others in percent total lipid weight.

$^b$ Plasmalogens are primarily ethanolamine phosphatides.