MCB 160, Fall 2003 -- Midterm #1 Review Questions

NOTE: This is just a brief outline of some of the major concepts covered in lecture. Please study your notes/book for additional comprehensive details.

1. The electrical properties of membranes
    a. What are the properties of biological membranes, and how are they essential to the function of neurons?
    b. What are charge, conductance, resistance, voltage, current, and capacitance? How do they relate to one another? ($V = IR$ and $V = Q/C$)
    c. How does a neuron maintain a resting potential? Know the Nernst equation and how to use it to determine the driving force on an ion for a given resting potential. Know how to solve the Nernst in simple cases (without a calculator) –> $\log_{10} 10 = 1$. Be able to predict which direction an ion will move if a channel is opened at a given resting potential, and what will happen to the membrane potential. Know the Goldman-Hodgkin-Katz equation, and how the membrane potential depends on relative permeabilities of many/different ions.
    d. What are the time and space constants of membranes, and what do they do mean for the propagation of signals? What happens to the time and space constants if channels are opened or closed?
    e. What is the equivalent circuit diagram for a patch of membrane?

2. Ion channels
    a. What are the different types of ion channels, and what are their structures and functions? How do they differ from other membrane proteins?
    b. What is the basis of ion selectivity?
    c. How are ion channels gated? (What causes them to open and close?)
    d. What is the basis of fast inactivation (Shaker or v-gated Na^+ channel)?

3. Action Potentials
    a. How do voltage-gated sodium and potassium channels generate and propagate action potentials?
    b. Be able to draw an action potential over time, and explain how different relative ion permeabilities affect the different voltage changes.
    c. What is an absolute and relative refractory period and what's responsible for each?
    d. What are the currents underlying the leading and trailing edge of an action potential?
    e. What role does myelin play in propagating the action potential?

4. Synaptic transmission
    a. What are the major neurotransmitters (small molecules and bigger peptides)? What are their similarities/differences? Know the major enzymes involved in their synthesis pathways.
    b. What are the differences/similarities between chemical and electrical synapses (include structural and functional differences)?
    c. What defines a neurotransmitter?

c. What ion is necessary for synaptic transmission? What occurs when an action potential arrives at an active zone?
e. What is quantal transmission? What are some other experiments that led to the hypothesis that neurotransmitter release is vesicle-mediated?
f. What proteins are involved in docking and fusion? Know synaptotagmin (Ca+2 binding), synaptobrevin (v-snare) SNAP-25 and syntaxin (t-snares), and synapsin (cytoskeletal bound).
g. Starting with the presynaptic action potential, list the events that occur during fast synaptic transmission (ionotropic channels).
h. What is slow synaptic transmission? Does it play a mediating or a modulatory role? What kind of receptors is it mediated by?
i. What are the structural differences between ionotropic and metabotropic receptors?
j. How do second-messenger systems work? Why is their effect delayed, sustained, and capable of acting at a distance? How do receptors that use the same second messenger have distinct effects on the cell?

5. Synaptic integration
    a. How do a cell's space/length constant and time constant contribute to a cell's ability to fire an action potential (be able to explain in terms of spatial and temporal summation)?
    b. Know the differences between pre- and post-synaptic inhibitions.

6. Learning and Memory
    a. Describe the aplysia circuits involved in habituation and sensitization. What are the synaptic changes involved in each of these behaviors?
    b. What is the definition of long-term potentiation? What is the role of the NMDA receptor in LTP?
    c. What are the three properties of LTP (i.e. associativity…)?
    d. Be able to devise/understand experiments that distinguish whether the synaptic changes are pre- or post-synaptic.
    e. Be able to compare/contrast the molecular events underlying the facilitation in aplysia and that of the hippocampal LTP (CA3 → CA1), i.e. which is more dominated by changes in pre-synaptic terminal and which one is more dominated by changes in the post-synaptic terminal?
    f. What are the cellular events necessary to consolidate short-term to long-term memory?

Sample Questions

1) A cell has a resting potential of -70mV, E of K+ = -100mV, E of Cl- = -70mV, E of Na+ = +60mV, E of Ca+2 = +120mV, and three classes of ligand-gated channels: NMDARs, AMPARs, and GABARs. EXPLAIN what happens to the membrane potential and intracellular Ca+2 under the following conditions:

a) You wash on GABA:
ANS: No impact on voltage, even though Cl- channels open, since Vm=E of Cl-.

b) You wash on a ligand specific for NMDARs:
ANS: No impact on voltage, since although NMDARs open their gates they remain blocked at the negative resting Vm by external Mg+2.

c) You wash on glutamate:
ANS: nice depolarization due to opening of AMPARs and NMDARs, now unblocked due to the AMPAR-dependent depolarization kicking the Mg+2 block out.

2) Axons from three presynaptic neurons synapse onto the same dendrite, close to the cell body ("near input"), far out on the dendrite ("far input"), and in the middle ("middle input"). The three have an equal probability of fusion of vesicles. "Far input" and "near input" release glutamate, while "middle input" releases GABA. Respond to the following questions and explain your answers.

a) Compare the size of the voltage response recorded in the postsynaptic cell body in response to a single action potential in the "near" versus the "far" glutamate input? Explain and illustrate.
ANS: EPSP from near input will be larger because there is less decrement (decay) with shorter distance of passive conduction down dendrite. The degree of decay is described as the space constant (the distance over which the EPSP decays to 1/e of its amplitude at the site of initiation = square root of (Rm/Ra), where Rm is the membrane resistance and Ra (Ri) is the axial (internal) resistance). The less leaky the cell membrane (higher Rm) or wider (larger diameter) the dendrite (lower Ra), the smaller the degree of decay over a given distance.

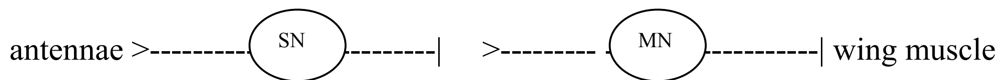
b) How will the size and shape (rise and decay rates) of the postsynaptic voltage response differ if "near" and "far" inputs fire at roughly the same time instead of at different times as in part (a)? How about if "far" and "middle" fire together? Draw the responses and explain your logic.
ANS: -- If near and far axons fire at the same time, they will generate EPSPs at the same time and these will summate and make a larger EPSP.
-- If far and middle fire together, then the EPSP will be smaller than far alone, since inward current through GluRs will be opposed by outward current through Cl- channels.
-- The decay of the smaller EPSP will be faster because opening of the Cl- channels will reduce Rm and Tau=R*C.

3) Compare and contrast the molecular mechanisms underlying LTP in the hippocampal CA3→CA1 synapse and the synaptic facilitation in the aplysia.

Serotonin-induced SYNAPTIC FACILITATION (Aplysia)	LTP (CA3→CA1)
Induced by an outside influence (serotonin); also known as Heterosynaptic facilitation	Homosynaptic (plasticity simply involves the pre- and post-synaptic neurons)
Glutamatergic synapse modulated by 5HT (serotonin)	NMDAR-dependent
Presynaptic mostly	Postsynaptic mostly
Molecular events: shock acts on the serotenergic pathway→ release of 5-HT→ 5-HT binds to the serotenergic receptors in the sensory neurons → G-protein cascade where activates PKA and PKC.	Molecular events: presynaptic train → release of glutamate → opens AMPAR → depolarization of the postsynaptic terminal → release Mg+2 block from the NMDAR → with glutamate still present, current flow through NMDAR → Ca+2 enters → Ca+2 binds to calmodulin → Ca+2/calmodulin binds and activates CamKinaseII (autophosphorylates and becomes constitutively active)
Short term: closure of K+ channels (through phosphorylation); increase in Ca+2 influx through opened v-gated Ca+2 channels; increase in vesicle fusion and NT release.	Early LTP: involves CamKII phosphorylating AMPAR and can make recruit more AMPAR to postsynaptic membrane. Perhaps also retrograde messenger.
Long term: PKA goes to nucleus → phosphorylation of CREB → gene expression of ubiquitin hydroxylase and other genes → 1) ubiquitin degrades regulatory subunit of PKA, so PKA constitutively active; 2) and morphological changes due to formation of new synapses.	Late LTP: PKA is activated and goes to nucleus → phosphorylation of CREB → gene expression → morphological changes due to formation of new synapses.
No putative retrograde signals known thus far.	May involve retrograde signaling (NO?).

4) You are studying a locust that shows the following behavior: when you touch one of its antennae, it retracts its wings. As you repeat the stimulation, the retraction of the wing becomes smaller and smaller until no response can be seen. This is a clear example of _(ANS: habituation)_.

The following diagram corresponds to the circuit underlying this behavior (all of the following are excitatory synapses, with the synapse between the SN and MN being glutamatergic):



a) What experiment could you perform to determine the location of the synaptic change underlying this behavior? At which synapse would you expect to see the change?
ANS: You could record from both the sensory and motor neurons while you stimulate the antennae and see whether there is a decrement in EPSP size in either the sensory or the motor neuron. In theory, you could see it at any or at more than one synapse. If this system were similar to the aplysia case, you'd see a depression (underlying the habituation) at the sensory synapse on the motor neuron.

b) You have performed one of the above experiments and discovered that the synaptic change takes place in the motor neuron and the wing muscle (different from what we've studied in the case of aplysia). You also performed some recordings which show that as you stimulate the motor neuron, the EPSP in the muscle gets smaller and smaller. Devise one experiment to determine whether the change is presynaptic (more vesicle release) or postsynaptic (greater number of receptors being activated) or both?
ANS: One thing would be to do a quantal analysis, where you reduce the extracellular concentration of Calcium at the neuromuscular junction and then record the spontaneous/background activity in the motor neuron, where you record the amplitude of the EPPs and count how many you observe. Then you stimulate a small number of times in the motor neuron and do the same type of recording as for the spontaneous case. Then you can plot a histogram of the amplitude of EPPs, where the y-axis would tell you the count/number of events observed (or presynaptic events) and the x-axis would tell you the amplitude of the EPPs (or postsynaptic events). This way, you can compare the histogram that was obtained from the evoked case versus the background/spontaneous case. If it were a presynaptic change, you would not see a change in the size of the EPP, but you would see an increase in the number of failed events but a decrease in the number of EPPs. If it were a postsynaptic change, you'd see a decrease in the mean size of the EPPs.