Biol 436-01 – Spring, 2012 Instructor: Michael Chen, Ph.D.
Location: KH C4071 Office: Biol Sci 235
Mon, Wed, 9:50 – 11:30 am Office hrs: Tues, Thurs, 12:45 – 3:00 pm.
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BIOL 436: Neurobiology: Neurophysiology

This course provides an introduction to the cellular and molecular basis of the vertebrate nervous system.

PREREQUISITES: BIOL 380 (Cell Biology).

COURSE OBJECTIVES: The objectives of this course are to gain detailed knowledge of how the vertebrate nervous system functions at the cellular and molecular levels. In addition, students will successfully research and write a review paper germane to endocrinology.

COURSE TEXTBOOK: Hammond, C. *Cellular and Molecular Neurophysiology*. 3rd edition, Academic Press, 2008.

LECTURES: I will lecture using almost exclusively PowerPoint slides. I will make these lectures available to you on a weekly basis or every other week either by e-mailing them to you beforehand or by placing them on my faculty webpage.

GRADING: There will be 2 midterm exams each consisting of a mixture of multiple choice and short answer/short essay questions, worth 100 points each. There will also be 5 quizzes/assignments (10 points each), a final exam (100 points), attendance (2 points /day = 30 points), and a PowerPoint presentation (worth 100 points). Total points, therefore, will equal 500 (an approximate number, as each exam will be +/- 5-10 points). Grades will be assigned based on the following scale:

"A" = 91-100% of possible points
"B" = 81-90%
"C" = 71-80%
"D" = 61-70%
"F" < 60% of possible points

Within each grade range, the top 2% and the bottom 2% will receive "+" and "-" grades.

Exams, Quizzes, and Classroom Activities. In addition to the scheduled exams, I will be giving 5 (pop) quizzes (10 points each) throughout the quarter, at the end of a lecture. The purpose of these quizzes is 2-fold: (1) To get you to attend class regularly; and (2) To make sure that you are keeping up with the material and are paying attention. Don't worry --- If you were present in lecture, you are sure to do well on the quiz. If you miss an exam or classroom activity, I will consider a make-up, provided you can furnish me

with a valid reason for missing it. However, because one of the purposes of the quizzes is attendance, there will be no make-ups on the quizzes.

Oral Presentation:

You are to assemble into teams of 4-5, decide on any topic in neurophysiology that interests you all, and orally present the most cutting-edge research on that topic. You may choose from the following list or bring another topic to me for my approval. Your references should be current, no older than 10 years old, and should, therefore, cover cutting-edge research from journal articles. You should have no fewer than 10 such references. You may use books to clarify concepts in your mind, but not as a primary source. **Presentations should be 10-12 minutes long and will occur during Finals week, Wed, 6/13/12, 8:00 – 10:30 am.**

General Directions for Oral PowerPoint Presentations:

A. **Title** (Choose a short, descriptive title for your project.) and **Authors** (List full names of all authors.)

B. **Introduction** -

1. Use one to several paragraphs to introduce and familiarize the reader with your topic. Use this section to give your reader a ***general*** background to the topic. You may also want to comment on any questions that still remain to be answered about your topic.

2. Answer this question in your introduction - How does this subject fit into the broad context of neuroscience?

3. The last sentence of your introduction should explain to the reader what specific hypothesis about your topic you will examine in the body of your presentation.

C. **Description of Research** -

1. This section is the body of the presentation and so will constitute the majority of the presentation.

2. Use this section to summarize the data presented in the ten journal articles that you use to develop the presentation. To do this you need to:

a. Summarize the materials and methods used in the cited articles.

b. Show the data obtained in the cited articles.

- You ***do not*** need to include all of the data contained in the ten articles. Instead you can focus on part of the information.

- You can present the data as it appears in the original articles.

- Alternatively, you may summarize the findings in your own way. For example, you may want to combine data from several papers into a single table or graph.

- NOTE FOR SLIDE SHOW: Whenever possible use graphs and tables to present the data instead of verbal descriptions.

c. Generate short 1-2 sentence summaries for each figure and for discrete subsections within the body.

D. **Summary or Conclusions** -

End the presentation with a final summary or conclusion section that allows the reader to quickly understand the "take home" message from your presentation.

E. **References** - The 10 journal articles from the primary literature used to generate your presentations should be turned in to me just before your presentation. Remember that you can use review articles and book chapters to help prepare your presentation, but they cannot be counted as part of the 10 required references. However, they should be cited if used. References should be cited in alphabetical order as follows:

Altar, C.A., Whitehead, R.E., Chen, R., Wortwein G., Madsen, T.M. Effects of electroconvulsive seizures and antidepressant drugs on brain-derived neurotrophic factor protein in rat brain. *Biological Psychiatry*, 54, 703-709, 2003.
[Authors, Article title, Journal, volume, pages, year]

As a general rule of thumb for oral research presentations, you should not spend more than 1 minute, on average, per slide. Because the presentation is to be about 10-12 minutes, there should be 10-12 slides. If a group reaches the 12-min mark and has not yet finished, I will stop the presentation and everyone in that group lose 5 points from their presentation grade.

Intra-Group Evaluation: Each member of a group will be required to evaluate each other member of that group in terms of contribution and participation to the presentation. These evaluations will be anonymous and only I will know the results. This will count towards 30% of the presentation grade (30/100 points).

My powerpoint lectures can be found at www.calstatela.edu/faculty/mchen/. Please be sure you have downloaded them before each lecture:

Biol Sci 436 Lecture Schedule:

Date	**Topic**	**Reading Assignment**
M, 4/2	Introduction to the course; Presentation and Peer Evaluation	None
W, 4/4	Microanatomy of Neurons	Ch. 1
M, 4/9	Microanatomy of glia and glia functions	Ch. 2
W, 4/11	Neuron-glial interactions. **Topics and Teams Due**	Ch. 2
M, 4/16	Resting membrane potentials	Ch. 3
W, 4/18	Membrane potentials; membrane channels	Ch. 4, 5
M, 4/23	Chemical and electrical synapses	Ch. 6
W, 4/25	**Midterm Exam 1 (100 pts)**	None
M, 4/30	Action potential	Ch. 4, 5
W, 5/2	Action potential	Ch. 4, 5
M, 5/7	Propagated action potential	Ch. 4, 5
W, 5/9	Types of Neurotransmitters and their Release **Presentation titles/1st 2 references due.**	Ch. 7
M, 5/14	Types of Neurotransmitters and their Release	Ch. 7
W, 5/16	Synaptic Transmission	Ch. 7
M, 5/21	**Midterm Exam 2 (100 pts)**	None
W, 5/23	Types of receptors: Inotropic, metabotropic. **Presentation outlines and full bibliography of references due. Groups should start meeting with me for approval of presentation.**	Ch. 8-12, Will be more specific when the time comes
M, 5/28	No Class – Memorial Day	
W, 5/30	Firing patterns of neurons: synaptic plasticity	Ch. 16
M, 6/4	Firing patterns of neurons; synaptic plasticity	Ch. 16
W, 6/6	**Final Exam (100 pts)**	
M, 6/13	**Oral Research presentation; 8:00 – 10:30 am** Attendance for ALL presentations is mandatory or no credit for the final presentations will be awarded to the absent team member.	

Cross-Course Contamination: For those of you who have also been enrolled in my Biol 448 course (Molecular Biology of the Brain) or are currently enrolled in my Biol 449 course (Neurobiology of Development): Despite the fact that the potential for topic overlap between this course and Biol 448 and 449 is great, I cannot allow students, per University policy, to do the same presentation, assignment, *etc*. for both courses. The 2 presentations must differ significantly. If you have any doubt, please consult with me before proceeding any further. In addition, please do not assume that policies for one

course are the same as those in my other courses. Administratively, the courses have nothing to do with each other.

COURSE OBJECTIVES:

Lecture Objectives -

Learning Objectives for *Microanatomy of Neurons* and *Microanatomy and Functions of Glia*

1) The student will demonstrate a knowledge of neuron microanatomy by:
    a. identifying and defining or giving functions for the various parts of a neuron.
    b. identifying the three basic types of neurons, unipolar, bipolar and multipolar.

2) The student will demonstrate a knowledge of glial cell microanatomy and function by:
    a. giving a general definition of glia.
    b. identifying microglia and the 4 types of macroglia (ependymal cells, astrocytes, oligodendrocytes and Schwann cells).
    c. defining or giving functions for the 5 types of glial cells.
    d. explaining how astrocytes regulate blood flow in the brain.
    e. diagramming the currently accepted model of extracellular potassium buffering by astrocytes and evaluating this model.
    f. demonstrating how astrocytes' regulation of cytosolic calcium levels in neurons could be important to information processing in the brain.
    g. explaining how astrocytes modify synaptic function.
    h. comparing and contrasting myelination in the central and peripheral nervous systems.

Learning Objectives for *Membrane Potentials*

1) The student will demonstrate knowledge of overall signal generation in the nervous system by explaining how action potentials and neurotransmitters convey information within and between pre- and postsynaptic neurons.

2) The student will demonstrate an understanding of membrane potentials by:

    a. Defining membrane potentials.
    b. Explaining how membrane potentials are measured.
    c. Explaining how the membrane potential is related to differential distribution of charges and ions across the plasma membrane.
    d. Making generalizations about trends in ionic concentrations in the intracellular and extracellular fluids.
    e. Showing why long-term maintenance of ionic concentration gradients argues against the concept of a freely permeable plasma membrane.
    f. Showing why long-term maintenance of ionic concentration gradients and

negative membrane potentials argues for a plasma membrane that is selectively permeable to potassium.
g. Using the Nernst equation to calculate the theoretical membrane potential needed to prevent potassium from equilibrating across the plasma membrane.
h. Using theoretical and observed membrane potentials to argue for a plasma membrane that is selectively permeable to potassium.
i. Using the Nernst equation to make predictions about how membrane potential will change if intracellular or extracellular potassium concentrations change.

Learning Objectives for *Neuron Function: Resting Membrane Potentials*

1) The student will demonstrate a knowledge of resting neuron membrane permeability by:
    a. defining and giving evidence for resting permeability.
    b. giving examples of relative permeability for K^+, Na^+ and Cl^-.
    c. drawing a model of the resting neuron membrane with leak channels for all appropriate ions.
    d. giving examples of why permeability to some ions may be greater than others.

2) The student will demonstrate a knowledge of how resting membrane potential is achieved in a neuron by:
    a. explaining how the addition of sodium leak channels alters the equilibrium established between chemical and electrical forces acting on potassium across a typical cell membrane.
    b. explaining why resting membrane potential equilibrates between the Nernst equilibrium potentials for sodium and potassium ions.
    c. explaining what is in equilibrium (i.e. remains constant) in a resting neuron.
    d. explaining how the passive ionic leaks across a resting membrane are countered to insure that ion concentrations also remain constant through time.
    e. predicting how resting membrane potential would theoretically change if permeability or ionic concentrations were changed.
    f. explaining how to predict the intracellular and extracellular chloride concentrations using V_R.
    g. using the Goldman equation to predict membrane potential.

Learning Objectives for *Neuron Function: Channels*

1) The student will demonstrate knowledge of membrane channels by:
    a. explaining why channels are required in order to move hydrophilic substances, specifically ions, across the membrane.
    b. comparing and contrasting the effects of enzymes on rates of chemical reactions with those of channels on movement of ions across membranes.
    c. describing current models of channel selectivity including ionic charge, ionic size and selectivity filters.
    d. giving evidence for the presence of a selectivity filter in some channels.
    e. using the concept of a selectivity filter to rationalize the selectivity of the

voltage-gated sodium channel.
f. describing the basic structure of a typical membrane channel.
g. explaining how information on primary structures has been used to propose three dimensional structures of and functions for parts of the proteins (i.e. describing the use of sequence homologies and hydrophobicity plots).
h. interpreting sequence homology data and hydrophobicity plots as they relate to structure and function of membrane channels.
i. describing how immunocytochemistry, site-directed mutagenesis and chimaeric channel construction can be used to test proposed models of channel structure and function.
j. interpreting the results of immunocytochemistry, site-directed mutagenesis and chimaeric channel construction experiments designed to test proposed models of channel structure and function.
k. designing experiments to test proposed models of channel structure and function using immunocytochemistry, site-directed mutagenesis and chimaeric channel construction.
l. describing the three types of conformational changes that are thought to lead to channel gating (i.e. change in discrete region of the protein, generalized change in protein configuration, blocking portion of protein changes position)
m. describing the three main mechanisms for induction of conformational changes in channels (i.e. binding of chemicals = ligand-gating, changes in membrane potential = voltage-gating, membrane deformation = mechanical-gating).
n. describing the types of chemicals that influence a ligand-gated channel (i.e. neurotransmitters and hormones on the extracellular surface, second messengers and protein kinases on the intracellular surface).

Learning Objectives for *Neuron Function: Cellular Basis of Action Potentials*

1) The student will demonstrate knowledge of action potentials by:

a. diagramming the changes in membrane potential that accompany a typical action potential.
b. describing the changes in membrane permeability that lead to the production of action potentials.
c. explaining how changes in membrane permeability are accomplished.
d. using the Goldman and Nernst equations to predict the membrane potential at the peak of an action potential and comparing these theoretical values to observed values.
e. diagramming and explaining how the voltage clamp is used to study action potentials.
f. interpreting data and drawing conclusions from voltage clamp experiments that document that sodium and potassium move through two different sets of channels during an action potential.
g. diagramming and explaining how the patch-clamp technique is used to study individual channel activity.

h. interpreting data and drawing conclusions from patch-clamp studies that document that channels open in an all-or-none fashion and usually behave according to Ohm's Law.
i. using patch-clamp data to develop a model of voltage-gated sodium channel function.
j. describing experiments, interpreting data and drawing conclusions from experiments that use site-directed mutagenesis and chimeric channel construction to test models of channel function.

Learning Objectives for *Neuron Function: Propagated Action Potentials*

1) The student will demonstrate knowledge of propagated action potentials by:

a. diagramming the changes in membrane potential that accompany an action potential and explaining the following at each point along the curve -
    1. the magnitude and direction of the sodium current through both leak and voltage-gated channels.
    2. the magnitude and the direction of the potassium current through both leak and voltage-gated channels.
    3. the state (open versus closed) of the voltage-gated sodium and potassium channels.
    4. the positions of the activation gate and the inactivation particle for the voltage-gated sodium channels.
b. defining, in terms of changes in V_m and activity of the voltage-gated sodium channels, and identifying threshold potential for generation of a propagated action potential.
c. defining, in terms of changes in V_m and activity of the voltage-gated sodium channels, and identifying the absolute refractory period for a propagated action potential.
d. defining, in terms of changes in V_m and activity of the voltage-gated sodium channels, and identifying the relative refractory period.
e. diagramming and explaining how electrotonic current flow carries charge from one local region of the membrane to the next, depolarizing adjacent sites to threshold and regenerating the original signal, during a propagated action potential.
f. explaining how the refractory period and leak channels prevent backward conduction of a propagated action potential.
g. explaining that a propagated action potential leads to neurotransmitter release at the presynaptic terminals.
h. diagramming and explaining how electrotonic current spread from node to node leads to saltatory conduction in myelinated axons.
    1. explaining why the differential expression of voltage-gated channels between the nodes and internodes aids in saltatory conduction.
    2. explaining why the presence of myelin (insulation) at internodes and none at nodes aids in saltatory conduction.
    3. explaining the advantages on saltatory conduction, including rate of action

potential transmission and cost associated with successive signals.

Learning Objectives for *Synaptic Transmission*

1) The student will demonstrate knowledge of synaptic transmission by:

a. Comparing (how are they similar?) and contrasting (how do they differ?) electrical and chemical synapses.
b. Describing the anatomy of an electrical synapse (bridged or gap junction) including-
    1. The size of the extracellular space separating the pre- and post-synaptic cells.
    2. The structure of the channels including connexons or hemi-channels and connexin molecules.
    3. Cytoplasmic continuity between pre- and post-synaptic cells.
c. Providing evidence that signal transmission across an electrical synapse is by electrotonic current spread.
d. Interpreting data from experiments that demonstrate that current transmission across an electrical synapse is by electrotonic current spread.
e. Providing evidence that rectifying electrical synapses exist, i.e. that some electrical synapses only allow unidirectional current transmission.
f. Interpreting data from experiments that demonstrate that rectifying electrical synapses exist.
g. Designing experiments to demonstrate that current transmission across an electrical synapse is by electrotonic current spread and that rectifying electrical synapses exist.
h. Describing the anatomy of a chemical synapse including -
    1. The size and shape of the extracellular space (synaptic cleft).
    2. The branching of the presynaptic cell terminating in the terminal knobs or boutons.
    3. The microanatomy of the boutons (synaptic or neurotransmitter vesicles, mitochondria and active zones).
    4. The microanatomy of the postsynaptic membrane (invaginations and neurotransmitter receptors).
i. Providing evidence that signal transmission across a chemical synapse is by neurotransmitter release and NOT electrotonic current spread.
j. Interpreting data from experiments that demonstrate that signal transmission across a chemical synapse is by neurotransmitter release and NOT electrotonic current spread.
k. Designing experiments to demonstrate that signal transmission across a chemical synapse is by neurotransmitter release and NOT electrotonic current spread.
l. Describing and diagramming the calcium dependent mechanism for neurotransmitter release, including the role of the synaptic proteins, synapsin, synaptotagmin, synaptophysin, and physophilin.
m. Providing evidence that neurotransmission across a chemical synapse requires

a calcium current, but not sodium or potassium currents.

n. Interpreting data from experiments that demonstrate that neurotransmission across a chemical synapse requires a calcium current, but not sodium or potassium currents.
o. Designing experiments to demonstrate that neurotransmission across a chemical synapse requires a calcium current, but not sodium or potassium currents.
p. Discussing the sources of the synaptic delay in chemical neurotransmission including slow opening of calcium channels, time for exocytosis of vesicles, neurotransmitter diffusion across the synaptic cleft and molecular events of action potential production at the postsynaptic membrane.

Learning Objectives for *Postsynaptic Responses: Neuromuscular Junction*

The student will demonstrate knowledge of postsynaptic events in a muscle fiber by:

1. Providing evidence that the end-plate potential (epp) –

    a. Is confined to the region of the motor end plate.
    b. Is a result of a net inward current flow carried by sodium in response to neurotransmitter release, but also involves outward movement of potassium.
    c. Is proportional to the amount of neurotransmitter (acetylcholine) released by the motor neuron, i.e. is a graded response.
    d. Spreads by electrotonic transmission from the end plate.
    e. Causes an action potential in the membrane adjacent to the end plate that propagates down the muscle fiber if the epp is large enough to cause opening of voltage-gated channels.

2. Interpreting data from experiments that demonstrate that the end-plate potential (epp)

    a. Is confined to the region of the motor end plate.
    b. Is a result of a net inward current flow carried by sodium in response to neurotransmitter release, but also involves outward movement of potassium.
    c. Is proportional to the amount of neurotransmitter (acetylcholine) released by the motor neuron, i.e. is a graded response.
    d. Spreads by electrotonic transmission from the end plate.
    e. Causes an action potential in the membrane adjacent to the end plate that propagates down the muscle fiber if the epp is large enough to cause opening of voltage-gated channels.

3. Designing experiments that demonstrate that the end-plate potential (epp) –

    a. Is confined to the region of the motor end plate.
    b. Is a result of a net inward current flow carried by sodium in response to neurotransmitter release, but also involves outward movement of potassium.
    c. Is proportional to the amount of neurotransmitter (acetylcholine) released by the

motor neuron, i.e. is a graded response.
   d. Spreads by electrotonic transmission from the end plate.
   e. Causes an action potential in the membrane adjacent to the end plate that propagates down the muscle fiber if the epp is large enough to cause opening of voltage-gated channels.

4. Diagramming the postsynaptic events in a muscle fiber following acetylcholine release from a motor neuron.

5. Defining and predicting reversal potentials for synaptic currents.
6. Describing and diagramming the acetylcholine receptor's structure and function.
7. Comparing the pharmacology and permeability of the acetylcholine channel to the voltage-gated sodium and potassium channels.

Learning Objectives for *Postsynaptic Responses: CNS*

The student will demonstrate knowledge of postsynaptic responses in the central nervous system by:

1. Defining and diagramming the types of synapses found in the central nervous system, axosomatic, axodendritic and axoaxonic synapses.
2. Comparing (How are they similar?) and contrasting (How do they differ?) the neuromuscular junction and central nervous system synapses.
3. Defining excitatory postsynaptic potential (epsp) and inhibitory postsynaptic potential (ipsp).
4. Comparing and contrasting epsps and ipsps.
5. Defining and giving examples of temporal and spatial summation.
6. Comparing and contrasting temporal and spatial summation.
7. Giving evidence that the synaptic current is non-regenerative and spreads from the initial site of neurotransmitter binding on the dendrites by electrotonic transmission.
8. Defining the grand postsynaptic potential and explaining that it is transmitted to the axon hillock by electrotonic transmission which causes a propagated action potential if the trigger zone reaches threshold for opening of voltage-gated channels.
9. Explaining why axosomatic and axoaxonic synapses have more influence on the production of a propagated action potential than do axodendritic synapses.
10. Explaining why distal axodendritic synapses have less influence on production of propagated action potentials than do proximal axodendritic synapses.
11. Using information about reversal potentials to predict which ions carry synaptic currents.
12. Explaining how chloride and potassium currents produced during ipsps can reduce the probability of action potential production.

Team Project Objectives -

1. The student demonstrates an understanding of the group process by:
   a. working with his/her team to create a set of Peer Evaluation Criteria. (lecture #1, Peer Evaluation Criteria)

b. evaluating his/her peers' performances on the team project. (lecture #1, Peer Evaluations)
c. successfully completing all parts of the team project. (lecture #1, Peer Evaluation Criteria, Project Topic, Project Outline, Oral Project Presentation, Written Slide Presentation, and Peer Evaluations)

2. The student demonstrates knowledge of the use of on-line bibliographic databases to locate appropriate primary scientific references for use in scientific research. To demonstrate this knowledge the student successfully completes the Project Outline and the Oral Power Point presentations.

3. The student demonstrates the knowledge of accepted conventions of and the ability to construct scientific communications by: (Project Outline, Oral Presentation, Written Slide Presentation)

a. selecting articles that relate to an approved topic in neuroscience.
b. summarizing these articles.
c. grouping articles that show similar or related results.
d. integrating both similar and conflicting results.
e. organizing information into the appropriate format.
f. evaluating whether the results support or refute current scientific models or hypotheses.

ADA: Reasonable accommodation will be provided to any student who is registered with the Office of Students with Disabilities and requests needed accommodation.

ACADEMIC HONESTY: Students are expected to read and abide by the University's Academic Honesty Policy, which can be found at http://www.calstatela.edu/academic/senate/handbook/ch5a.htm. Students who violate this policy will be subject to disciplinary action and may receive a failing grade in the course for a single violation.

Possible project topics for your consideration or you are welcome to come up with your own topic. This is not a comprehensive list of possibilities and may include other topics. NOTE: I will only accept a limited number of topics that examine disease states so that there will be an appropriate balance between basic and clinical topics.

1. The roles of glia cells -
    a. buffering of extracellular potassium
    b. regulation of cerebral blood flow
    c. modification of synaptic functioning
    d. microglia involvement in immune function
    e. neuronal involvement in glia cell proliferation

2. Molecular mechanism of ion channel action

3. Why do the dendrites of some mammalian central nervous system neurons have voltage-gated channels?

4. The role of calcium in neurotransmitter release -

    a. role in fusion of vesicles with the presynaptic membrane
    b. role in movement of vesicles from their cytoskeleton attachment sites

5. Nitric Oxide's role as a neurotransmitter

6. Neurotransmitters that act via second messenger systems

7. Cellular mechanism of action of any of the general receptors

8. How is recovery to the "dark state" accomplished in the vertebrate eye?

9. Mechanism of vertebrate color vision

10. Molecular basis of learning

11. Molecular basis of drug abuse

12. Neurotrophins