Course Syllabus (Draft 1) This is based on the official requirements for a syllabus https://kb.wisc.edu/vesta/page.php?id=24561

Course # : Zoology, NTP, 616

Course Title: Lab Course in Neurophysiology and Behavior

Time Devoted to individual topics: Each semester of this laboratory course there will be three different laboratory exercises (modules), each lasting 5 weeks. The course will be taught on a 2 year cycle; each of the two years will comprise three independent modules. The course is 4 credits; there will be two four hour classes per week.

There will be eight hours of instruction each week. Thus about 40 hours will be devoted to each of three laboratory exercises. The topics of the individual exercises are a) neurophysiology of the crayfish muscle b) long term potentiation in the rodent hippocampal slice and c) behavioral tests opf hippocampal learning in the rodent. In the second year of the two year cycle the individual topics include d) Neurophysiology of snail central neurons e) recording of visual properties of the optic tectum in the frog and f) Behavioral tests of prefrontal cortex executive function. It is envisioned that new topics will be introduced in ensuing years when appropriate.

For the first one to two weeks of each module (8-16 hours) the students will learn the principles and basics of the techniques they will be using. For the next 1-2 weeks they will carry out experiments that have been reported in texts or in original papers. For the last 1-2 weeks the students will devise an original study based on their knowledge, their reading, and help from the faculty. The detailed apportionment of time between the three phases varies somewhat depending on the experimental technique.

There will generally be 6 set ups for each module and each set up will be run by 2-3 students. There will be one faculty and one teaching assistant in the laboratory all the time that students are there. Thus there will be potentially continual interaction between the faculty in charge of the module and the student groups. There will be ½ hour full group discussion at the end of each 4 hour laboratory period.

Learning Objectives: The two overriding objectives are described here: a) The course is Inquiry Based. Thus a major goal is to provide the means for students to develop an experimental question and to devise a way of answering that question. The times devoted to different aspects of the experiments as described above are set up to allow development of a question, and an effort to answer that question. b) A second objective is to help advanced undergraduate students become competent experimentalists. This will be done by providing a significant time with each of three different apparatuses and encouraging continual interaction between the student groups and the faculty, as well as discussion periods with all the students at the end of each session. There are other learning objectives. These include c) enhancing understanding of how research is incorporated into advances in neuroscience and d) enhancing students' understanding of important neuroscience issues by getting them into the experimental aspect of these issues.

Texts: Texts will be written by the faculty in charge of each module who will write a 3-4 page 'lab manual' that will guide students through the techniques they will be using. Further reading will include a very few carefully selected articles in the literature that cover a) review papers describing these techniques b) research articles that will describe what scientists are currently doing, or have done in the past, with the technique c) review articles containing ideas that could be investigated with the apparatus These will be read by the

students (with guidance) to help them devise their project and will be discussed during the last hour of each class. The particular texts have not been chosen yet.

Representative List of Readings and Content of Individual Modules*:*

Year 1 of 2 Yr Rotation

Module 1 (Stretton)

Background Reading: Pasztor V.M. (1989) Modulation of sensitivity of invertebrate sensory receptors. Sem in Neurosci. 1 5-14.

Techniques: Crawdad. A CD-ROM Lab Manual for Neurophysiology. Wyttenbach, Johnson and Hoy. Sinauer

Research Paper: Kennedy, D, and Takeda, K (1965) Reflex control of abdominal flexor muscles in the crayfish II. The tonic system. J. Exp. Biol. 43 229-246

Module description: In this module, students will learn basic electrophysiological techniques using sharp microelectrodes to record from crayfish in the abdominal muscle cells. The slow extensors and flexors are each innervated by 6 motoneurons, 5 excitatory and 5 inhibitory. Students will record neuronal extracellular action potentials and correlate each with its characteristic postsynaptic potential. The emphasis in this series of experiments is quantitative - students will determine values of several basic electrophysiological parameters of the muscles and synapses, including the membrane resistance and capacitance, and miniature end-plate potentials. Students will then do more investigative experiments such as examine the effect of bath-applied GABA and glutamate on input resistance, and measure the different facilitory behaviors of neuromuscular synapses from different motoneurons. They will also map the distribution of glutamate receptors by electrophoretic ejection from glutamate-filled microelectrodes.

Module 2 (Lipton)

Background Reading: Luscher and Malenka (2012) NMDA receptor-dependent long term potentiation and long term depression. Cold Spring Harbor Perspectives in Biology 4: a005710

Techniques: Bortolotto,Amid,Anderson,Isaac,Collingridge (2011) Synaptic plasticity in the hippocampal slice preparation. Current Protocols in Neuroscience . January 2011. Chapter 6

Research Paper: Gelinas and Nguyen (2005) Beta adrenergic receptor activation facilitates induction of protein synthesis-dependent late phase of long term potentiation/ Journal of Neuroscience 25: 3294

Module description: Long term potentiation is the most robust and well-studied model for synaptic changes underlying memory formation in brain. In the first week of this module students will learn the incubation technique and basic extracellular electrophysiology of the in vitro rodent hippocampal slice - a widely used mammalian preparation. In the second and third weeks they will learn the methodology for producing short term, and long term long term potentiation of synaptic transmission at particular

synapses in this preparation. For the final two weeks they will devise a project using these techniques to study properties of long term potentiation that they will have read about in papers that were handed out and that will have been discussed in class. Originality will be encouraged, although re-testing of recent published studies will also be acceptable.

Module 3 (Burger)

Background Reading: Ramirez , Tonegawa, Liu, X (2014) Identification and optogenetic manipulation of memory engrams in the hippocampus. Front. Behav. Neurosci., 17 January 2014 | doi: 10.3389/fnbeh.2013.00226

Technique: Gerstein et al. (2013). A Behavioral Paradigm to Evaluate Hippocampal Performance in Aged Rodents for Pharmacological and Genetic Target Validation. PLoS One May 7;8(5) e62360.

Research Paper: Hawk Bookout, Poplawski, Bridi, Rao, Sulewski, Kroener, Manglesdorf, Abel (2012). NR4A nuclear receptors support memory enhancement by histone deacetylase inhibitors.J Clin Invest. 122(10):3593-602.

Module Description: In this module students will study learning and memory formation in rats or mice. The hippocampus is a principle brain region that is involved in episodic memory formation in humans and several animal models have been devised that apparently test hippocampal dependent memory in rodents. Three that will be used in this module include the Morris water maze, the fear conditioning response test and the object recognition task. For this module smaller groups will be combined so that there will be three total groups of 4-6 students. During the first week students will learn the basics of two of the three different apparatuses and will do control experiments to see the extent to which their technique can be made adequate to get reliable results. During the following four weeks the students will spend two weeks on each of the two apparatuses and for each apparatus firstly reproduce experiments that have been published and then test an hypothesis that they devise as a group. Some of the experiments will include assessing the roles of certain genes using different mouse models which are available. The students will learn to perform and will discuss statistical analysis of the behavioral data.

Year 2 of 2 Yr Rotation

Module 4 (Ziskind-Conhaim)

Background Reading: Ziskind-Conhaim (1988) Electrical properties of motoneurons in the spinal cord of rat embryos.Dev Biol. 128(1):21-9.

Technique: Altrup and Speckmann (1994) Identified neuronal individual cells in the buccal ganglia of Helix pomatia. Neurosci Behav Physiol.24(1):23-32.

Research Paper: Wu , Sonner ,Titus, Wiesner, Alvarez, Ziskind-Conhaim (2011) Properties of a distinct subpopulation of GABAergic commissural interneurons that are part of the locomotor circuitry in the neonatal spinal cord. J Neurosci.31(13):4821-33.

Module description: The primary objective of this section is to understand the electrophysiological properties of snail neurons and the characteristics of synaptic potentials generated by other cells that synapse onto them. The snail neurons are large, several hundred micrometers in diameter, and can be visualized using a low power dissecting microscope. Their size makes it relatively easy to impale them with microelectrodes to record stable electrical potentials that can last for several hours. In the first week of the module students will become familiar with the electronics and the data acquisition system. Students will fabricate microelectrodes for intracellular recordings of electrical signals. During the next two weeks they will learn the dissection of the subesophageal ganglia with the neurons of interest and will learn how to perform intracellular recordings of membrane potential and membrane resistance and capacitance. They will also record spontaneous synaptic potentials and generate and examine properties of action potentials. For the final two weeks of the module students will design a set of experiments using primarily pharmacological tools to manipulate action potential firing properties and/or alter the frequency and amplitude of spontaneous synaptic potentials with the goal of testing one or more hypothesis that they generate. This exercise will give the students a basic feel for how synaptic and action potentials are generated in central neurons and allow them to test a simple hypothesis.

Module 5 (Yin)

Background Reading: Lettvin, Maturana, McCulloch,W.S. Pitts, W.H. (1959) What the frog's eye tells the frog's brain. Proceedings of the IRE. 1959: 1940

Techniques and Research Paper: Hubel and Wiesel (1959) Receptive fields of singe neurons in the cat's striate cortex J. Physiol. 148: 574-591

Module Description: In amphibians the optic tectum serves as the principal brain center for sensory processing and sensorimotor integration. During the first two weeks of this *in vivo* electrophysiology module students will first learn basic technique that will enable them to record from the amphibian brain in vivo so they can record from single neurons and small groups of neurons in the optic tectum of frogs. In the final three weeks students will take on two basic questions about the visual cortex in mammals by examining the optic tectum in the frogs. They will learn to examine receptive field properties of single visual neurons of the tectum in much the same way that Hubel and Wiesel examined single neurons in the cat visual cortex. They will also determine whether the optic tectum, like the visual cortex, contains a topographic map of visual space, and some properties of this map. Testing these basic questions in an experimental situation will provide students with a hands-on science experience that illustrates a fundamental concept they will have learned within a traditional classroom/lecture setting.

Module 6 (Bakshi/Baldo)

Background Reading: Berridge (2004) Motivation concepts in behavioral neuroscience. Physiol Behav 81: 179-202

Technique: Perry et al. (2010) Intra-accumbens infusion of a muscarinic antagonist reduces food intake without altering the incentive properties of food-associated cues. Behavioral Neuroscience 124: 44-54

Research Paper: Barbano and Cador (2006) Differential regulation of the consummatory,

motivational, and anticipatory aspects of feeding behavior by dopaminergic and opiatergic drugs. Neuropsychopharmacology 31: 1371-81.

Module description: Appetitive motivation causes pursuit of positive goal objects in the environment. Several ongoing societal problems (drug abuse, obesity) are related to the dysregulation of appetitive motivation. Drugs of abuse are currently thought to 'usurp' the function of normal appetitive brain systems. This module will show students how to test for appetitive behavior in mammals and will allow them to examine hypotheses about control of these behaviors. Prior to start of this module, rats will be prepared with chronically indwelling cannulae aimed to allow for direct infusions of drugs into the nucleus accumbens, a brain region that is key to appetitive motivation. The behavioral testing will be done using a classic test to evaluate food motivation, the food- screen test. Hungry rats are placed behind a mesh screen; the screen separates the animals from palatable food pellets. While the screen is in place, animals can see and smell the food. This engenders a considerable degree of hyperactivity and screen approaches in the rats. Fifteen minutes later, the screen is removed, and the rats are allowed to eat for 30 min. Thus, both anticipatory and consumptive behaviors can be monitored. During the first week of the module students will learn the basics of this test and do statistics on control studies of the population. During the next two weeks of the module students will carry out studies of previously tested effects one or both of these aspects of behavior. For example, dopamine receptor blockade only reduces anticipatory hyperactivity behind the screen, while opioid receptor blockade has more specific effects on food intake. During the 4th and 5th weeks of the module students will devise and test hypotheses about control of one or both these aspects of the behavior.

Evaluation of students:
The major evaluation will be based on a written description of the work carried out in each module. The data from each group of students will be pooled and completely shared, but each student will be expected to write up their own Module Report for each of the three modules. This will include the i) background, ii) a description of the experimental techniques c) rationale and the results of the experiments that were assigned to the group and d) the rationale, results, and conclusions from the group's original project for the experiments they chose to do e) an overall discussion/interpretation of their results in context. Approximately 60% of the grade will be based on these write ups and it is assumed they will be finalized in the time between the final experimental session and the beginning of the next module, or in the last week of the semester for the third module.

At the end of each module there will be a two hour group session where each group presents their results to the students and faculty. Students will be evaluated on how well they contribute to these discussions and how good their original project was. Approximately 20% of the grade will be based on these discussions, And finally at the end of the course, during exam week, each student will have a discussion with the course faculty that will last about half an hour. The faculty will ask questions based on the write ups by the students of each of their original projects. About 20% of the grade will be awarded on the basis of this conversation. This will primarily examine the students' understanding of the techniques they used.

We are not certain yet of the grading scale but on the basis of past gradings for non lab courses (in %'s) A= 92-100; AB = 87-91; B = 83-86; BC=80-82; C= 70-79; D=60-69; F= 0-59 will be very close to the grade levels. In all the work we will generally be looking for good experimental technique, understanding of the experiment the student is doing, student's ability to interpret results, originality of thought. We will always encourage creativity, during experimental work or in write up or in verbal reports and that will be rewarded greatly.