**Assembly of Neural Circuits Final Examination**

**Due: Friday May 13th at 5:00PM**

**PLEASE ANSWER ALL OF THE FOLLOWING QUESTIONS. This is a take home examination. Students are expected to work independently and to use the full resources provided by their lectures and the literature to answer these questions. Each question will be weighted equally in the overall mark. Concise answers (less than 2 pages, single spaced) with references to the literature (and compiled references at the end of each question) as appropriate (more for factual than theoretical questions). This examine will comprise 50% of your final course grade.**

**Please email answers as Word document, with separate pages for each answer to** [**Alexandra.Wesnousky@nyumc.org**](mailto:Alexandra.Wesnousky@nyumc.org)**. Questions about question? Contact the Lecturer.**

**Q1. (Dasen)** In a microarray screen you have identified a novel transcription factor that is expressed in the ventral spinal cord which you think might be involved in establishing the central pattern generator (CPG) circuits required for locomotion. You wish to characterize this gene in detail using both mouse and chick. Describe experiments that will allow you to 1) define whether it is expressed in progenitor or postmitotic neurons 2) the identity of the cell populations it is expressed in 3) whether it is regulated (directly or indirectly) by Shh, and what class of Shh-responsive gene it is. 4) What kinds of experiments and assays could you perform to assess its synaptic partners and function+? 5) Suggest a simple experiment that would implicate an evolutionary conserved role in CPG function. In answering provide details of how you perform these experiments and how you interpret the resulting data.

**Q2. (Treisman)**. In a genetic screen in Drosophila, you have identified a new mutation, no commissures (nocs), in which the axons of commissural neurons fail to cross the midline. Describe two possible models for the mechanism of Nocs action and explain how you would test your models experimentally. Please include experiments that you could do before you have molecularly identified the nocs gene as well as experiments that would require knowledge of the nocs sequence.

**Q3. (Michael Long)** Newly born neurons are constantly added to specific brain regions throughout life.

1)  Historically speaking, three cell markers were pivotal to increasing our understanding of the role of adult-born neurons: [3H]thymidine, Bromodeoxyuridine (BrdU), and retroviral genetic marking.  What new insights were enabled by each of these methodologies?

2)  Describe two observations that suggest that adult-born neurons become functionally integrated into neural networks.

3)  What two manipulations were discussed in class to gauge the impact of adult neurogenesis on pattern separation? What did the Danielson paper demonstrate concerning the activity and spatial tuning of adult born granule cells relative to mature granule cells?

**Q4. (Salzer).**

1. Describe how axons regulate the myelination program of Schwann cells and oligodendrocytes – in what ways does this regulation by axons differ between these cell types?

2. What is the evidence that experience and motor activity functionally impact the amount of myelin that forms in the CNS? What mechanisms might be involved?

3. How would you design an experiment in mice to directly test the importance of axonal conduction as a signal that regulates myelination in the CNS?

**Q5. (Ziff).** Imagine that you have discovered a new pair of cell adhesion proteins, Neuropresin and Neuropostin, that are expressed respectively pre- and post-synaptically in neurons at mature synapses. Both are single pass transmembrane proteins, each with an N-terminal extracellular domain, a membrane spanning region and a C-terminal, intracellular domain. The extracellular domain of Neuropresin interacts across the synaptic cleft with the extracellular domain of Neuropostin.

Describe an experiment that tests whether the Neuropresin/Neuropostin interaction is: a) sufficient to induce the formation of a functional synapse; b) necessary for the formation of a functional synapse.

Illustrate your answer with a diagram explaining your experimental approach.

**Q6: (Lin)** Many if not all brain regions contain cells with diverse morphology, electrophysiology property, projection patterns and gene expression profile. If you are an electrophysiologist who wish to link the cell activity to its other properties, how would you like to achieved that? Please give one solutions for an in vitro slice preparation, one solution for recording in anesthetized animal and one for free moving animal.

**Q7 (Desplan).** The Drosophila mushroom body (MB) is involved in memory formation and retrieval. Each MB is made of 2,000 neurons that emerge from only 4 neuroblasts.The MB is composed of four cell types:

- gamma neurons

- alpha'-beta'

- pioneer alpha-beta

- alpha-beta

These cells types are produced by all four (equivalent) neuroblasts. The MB NBs are the longest active NBs, which divide many times starting in the embryo, continue in the larva and end in pupae. As a note, flies take 10 days to emerge as adults and a NB divides every 1-3hours

- Imagine a molecular process by which these four cell types are produced.

- Larger insects like grasshoppers have much larger MBs with more than 50,000 cells, presumably also belonging to four cell types.

Suggest a way by which these many cells are produced.

**Q8. (Fishell).**

An intrepid neurobiologist takes a chicken embryo and at the beginning of neurogenesis (Stage 8) takes out the developing neurotube and does two forms of tissue graft 1) An anterior-posterior (A-P) reversal graft where Cervical level 2 of the spinal cord is grafted to Cervical level 7 and vice versa Cervical level 6 is apposed to cervical level 1. 2) the same graft is done but the tube is now inverted so dorsal becomes ventral and ventral becomes dorsal (i.e. D-V inversion graft).

A) Predict what the polarity of the grafted tissue in the graft in 1 versus 2.In describing the polarity of the tissue, explain the effects on cell type identity, projections of neurons, and circuit organization.

B) How might the result of the experiment be different if the graft were done at an earlier stage (stage 4) or a later age (stage 17)?

C) Explain what extrinsic and intrinsic signals are utilized for A-P and D-V signaling.

**Q9: (Ringstad)**

Your laboratory is studying the gene YFG1, which encodes an actin-binding protein. You have generated a knockout mouse that lacks this gene and it is viable. Your graduate student notices that YFG1 is expressed in the brain and that the YFG1 promoter contains several CREs (cyclic AMP-responsive elements), and is interested in testing the hypothesis that YFG1 functions in synaptic plasticity.

(1) Propose at least two experiments to test whether YFG1 functions in synaptic plasticity. Describe the methods you will use and what controls will be required to interpret your data. For each experiment, imagine what the results will be and interpret them. In order to answer part 2, at least one of your experiments must confirm a role for YFG1 in synaptic plasticity.

(2) The experiments you have described in your answer to part 1 confirm a function for YFG1 in synaptic plasticity. Describe at least three molecular mechanisms that are involved in synaptic plasticity. Design experiments to determine whether YFG1 is required for any of these known mechanisms. Again, give detailed descriptions of experimental design and controls.