Out-of-Class Questions

Article: P.E.M. Phillips, G.D. Stuber, M.L.A.V. Heien, R.M. Wightman, and R.M. Carelli, "Subsecond dopamine release promotes cocaine seeking," *Nature*, **2003**, *422*, 614-618.

1. What is the difference between tonic and phasic dopamine signaling?

2. Look up any other unfamiliar words in the abstract. Then summarize this study in one complete sentence.

Skip to the end and read the methods section to orient yourself to the study design.

3. How were the rats taught to self-administer cocaine? How was the cocaine delivered?

4. What stimulus accompanied cocaine delivery?

5. What were the working and reference electrodes in this study? Why wasn't a counter/auxiliary electrode necessary?

6. Sketch the potential applied to the working electrode as a function of time. Include as much detail in your plot as possible.

7. How many cyclic voltammograms (scans) were acquired per second?

8. How does the scan rate in these experiments compare to a typical CV scan rate? How does scan rate usually affect CV data?

9. How did the authors correct for current from interferents, movement of the animal, and pH changes in the extracellular space?

10. Complete the table below summarizing the means used to demonstrate that their signal came from dopamine release.

Experiment	How did this demonstrate the signal was from dopamine release?
anatomical	
physiological	
chemical	
pharmacological	

11. Draw the half-cell reaction for the oxidation of dopamine to dopamine quinone.

12. Consider the CV inset in Figure 1a. Label the oxidation and reduction half-waves. Was the oxidation of dopamine reversible? How can you tell?

13. Calculate the S/N ratio for the trace in Figure 3a.

14. Consider Figures 1-4. In the table, summarize the experimental design used for each experiment and the major results. In the column labeled stimulus/conditions, record what stimulus, if any, was used to elicit dopamine release or drug-seeking behavior. If no stimulus was used, note the conditions of the experiment. In the column labeled dopamine release, estimate the concentration of dopamine released in nM. In the column labeled timing, summarize any important findings about how the timing of the dopamine release related to the timing of the stimulus.

Figure	**Stimulus/Conditions**	**Dopamine Release (nM)**	**Timing of Response**
1			
2			
3			
4		n/a	

Note that the small bars labeled 500 nA or 50 nA should be used as a scale bar in evaluating peak height.

In-Class Questions

Reading Assignment 3: P.E.M. Phillips, G.D. Stuber, M.L.A.V. Heien, R.M. Wightman, and R.M. Carelli, "Subsecond dopamine release promotes cocaine seeking," *Nature*, **2003**, *422*, 614-618.

1. Suggest some advantages of electrochemical detection of dopamine for this application, compared to spectroscopic or mass spectrometric detection.

2. Why was the cyclic voltammetry data not sufficient to identify the signal as coming from dopamine? (Why do the additional experiments that you summarized in out-of-class question #10?)

3. In Figure 1, where do the values for the color scale in the bottom panel come from? What plot would you obtain if you took a slice horizontally through the color plot? What would you obtain for a vertical slice?

4. Suggest one software-based and one hardware-based method to improve the S/N or Figure 3a, and justify your choices.

5. Individuals recovering from drug addiction are often counseled to avoid "triggers", including locations and situations in which they previously used drugs. Do the findings in this study support this advice? Why or why not? Cite a specific figure or figures in your answer.