Defining cell types by their electrophysiology

Table of contents

Background

In this project, we'll look at open-source data from mouse and human recordings in order to compare cell types across species. We'll examine how different structural properties of dendrites might relate to the shape of their action potentials, and ultimately their role in neural computation.

Learning objectives:

- Understand the metrics that we can use to compare cell types
- Practice Python code skills and access the Allen Software Development Kit (SDK)
- Compare electrophysiological characteristics of neurons between humans and mice

Resources

Review these before you start the project and/or refer to them as you work with the sources of data if you have questions

Documentation on the Allen Cell Types dataset:

1. Cell Types Documentation
    i. Overview (of Methods for Cell Types database)
    ii. Electrophysiology Overview
    iii. Case Qualification and Donor Profiles
2. Electrophysiology and Morphology

Sample publications with the Allen Cell Types dataset:

Kalmbach et al. (2018) "h-Channels Contribute to Divergent Intrinsic Membrane Properties of Supragranular Pyramidal Neurons in Human versus Mouse Cerebral Cortex" Cell

Gouwens et al. (2019) "Classification of electrophysiological and morphological types in mouse visual cortex" Nature

Most recent (October 2023) collection of (21!) papers published in Science journals

Part I. Accessing the Allen Cell Types Dataset Website

Before we go behind the scenes and practice our coding skills, we'll look at a few cells on the Allen online interface to better understand what the data looks like.

1. Go to http://celltypes.brain-map.org/

    a. Read through “About Electrophysiology” and “About Morphology”
    b. **Task:** Answer questions 1 and 2 in the Data Sheet

Scroll down to “Download Single Cell Data and Models” and the section “Morphology and Electrophysiology” and click on **Electrophysiology Page**. This page shows us all of the electrophysiology data for one sample cell (identified with the ID number at the top).

2. On the top, in the ‘Electrophysiology Summary’ (blue box) you’ll see a **Mouse Line, Brain Area**, and **Layer** where this cell comes from

    a. **Task:** Note them in **Table 1** of the Data Sheet

3. The Mouse Line tells us the Cre-driver line that was used — in other words, the cells that they targeted had that gene, and therefore they also expressed Cre-recombinase.

    a. Go to https://www.ncbi.nlm.nih.gov/gene/ and search for the name of this gene (without -Cre)

    b. **Task:** Answer question 3.

4. This page also gives us some key details about the cell

    a. **Task:** Note the **resting membrane potential** in **Table 1.**

5. Click through the stimulus sweeps (the colored boxes) to find the first one that elicited an action potential.

    a. **Task:** Record the **minimum stimulus amplitude** required to elicit an action potential in this cell in **Table 1** of the Data Sheet

    b. **Note**: This value is either very close or identical to the **rheobase** of the cell, as reported on the table on the top. As a reminder, the rheobase is defined as the minimum current needed to elicit an action potential. When the current is below the rheobase, an action potential will never occur regardless of how long the stimulation is.

6. Click through to a stimulus sweep with a higher current injection (click on other colors beyond the one from Question 5).

    a. **Task:** Does the cell adapt to the stimulus? In other words, does the space between spikes increase? Is there a metric here that would help quantify this? Record that **metric** in **Table 1.**

7. Under the lower blue box labeled ‘Browse Electrophysiology Data’ (blue box), use the dropdown menu on the left to change the stimulus type to “Short square.”

    a. **Task:** Record the minimum current needed to elicit an action potential at this stimulus

    b. **Task:** Answer question 4

What is a 'square' pulse? Square simply describes the shape of the stimulus, and it's a common way to inject current into cells. There are more details on the stimuli used (**page 7- Figure 3**) online here.

8. Use the dropdown menu on the left to change the stimulus type to “Noise.” Take a look at the current injection trace to get an idea of what this stimulus looks like. Note the differences between the cell’s response to this stimulus versus the square wave pulses.

    a. **Task:** Answer question 5

9. Click on **View Morphology** on the right, to check out the morphology of this cell. Take note of the distribution of the axon and the dendrites. Close this window or Click on the ‘View Electrophysiology’ back up in the blue box at the top.

10. Click on **Cell Feature Search** in the top left corner.

11. Here, you can look through other cells in this dataset.

    a. **Task:** Find a cell from human tissue that is in the same **Layer** and has the same **Dendrite Type** as the first cell you looked at.

    b. **Task:** Use the data on that cell and repeat the steps above to fill out **Table 1**.

    c. You can view some characteristics of human cells by filtering here or scrolling to the bottom and seeing what is available: https://celltypes.brain-map.org/data

Submission on WebCampus

Once you’ve completed these steps along with recording your answers on the Data Sheet, save the file as: Project2_DataSheet_YourName.docx and upload it to WebCampus for your checkpoint submission.

Part II. Accessing the Allen SDK in Colab Notebook

As you’ve seen, there are many variables you can look at for each cell and across cells. You could spend all day going through them on the website to find some interesting comparisons! But, as you’ve noticed this can be tedious, and it’s much quicker to do these comparisons by accessing the entire database directly, through the AllenSDK.

Now you will use the Project 2 Colab Notebook on WebCampus to complete the remainder of the project exercises.

Complete the notebook code questions and submit your notebook file (.ipynb) to the submission slot in Webcampus.

Filename: Project2_DataSheet.docx

Name:
https://celltypes.brain-map.org/overview

Data Sheet

1. **Which method are the Allen researchers using to record from cells? (3pts)**

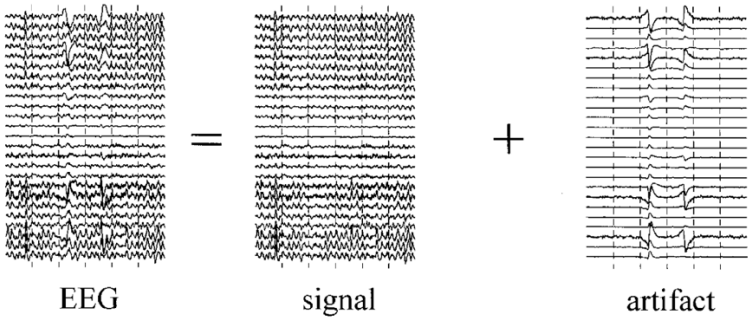
2. **What are the cells filled with to visualize their morphology? (3pts)**

3. **Which neurotransmitter receptor does this gene code for? (3pts)**

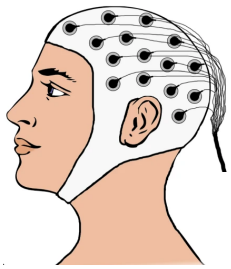
4. Why would a longer stimulus require less current to elicit an action potential? (3pts)

5. Why would you want to inject a noisy current into the cell? (3pts)
("Noisy" current here is random, fluctuating around a certain value but not a perfect sine wave. To answer this question, consider what happens in a real neural circuit. Is the input as simple as a square wave?)

It might be helpful to look at an example of human Electroencephalography (EEG). With this method we are measuring electrical activity from neurons in the brain from electrodes placed on the scalp. Remember we are recording the signal far away from the actual source in the neurons themselves. The signal we record must pass through meninges, skull (bone), and scalp (skin/tissue/hair)!



Ille, Berg, & Scherg, 2002



Nagel & Spüler (2019)

Table 1. (10 pts)

	Mouse	Human
Cell ID		
Cre Line		N/A
Area		
Layer		
Dendrite type		
Resting potential		
Minimum current to elicit an AP with the long square wave		
Minimum current to elicit an AP with a short square wave		
Adaptation Index		

https://celltypes.brain-map.org/experiment/electrophysiology/474626527

https://celltypes.brain-map.org/data

Credit, Resources, and Acknowledgements

These exercises and documents were adapted from Ashley Juavinett, PhD at UCSD. The results from this lesson plan for teaching have also been published and are available online: Juavinett A. Learning How to Code While Analyzing an Open Access Electrophysiology Dataset. J Undergrad Neurosci Educ. 2020 Dec 31;19(1):A94-A104.