

Lab 13: Allen Brain Atlas project

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You will spend the rest of the semester working on your final group project using the Allen Brain Atlas (ABA). It is up to your group to figure out what you want to research and your plan might change as you look through the data. Instructors and this lab manual will help you understand the resources available to you and can help guide you in a direction that yields interesting results. There have been research articles published using only data from the ABA, so there is a lot of interesting data here for you to work with.

I. Introduction to resources

Go to the overview of the ABA available on their website: <http://www.brain-map.org/overview/index.html>

Some of these resources will be more useful to you than others. You can use any of the databases, but the ones listed below will probably be the easiest and most interesting for you to use. Look at the tutorial videos and online help available for each resource you plan on using.

Allen Mouse Brain Connectivity Atlas

This is the database we used to trace the Papez circuit in Lab 12. A virus expressing GFP was injected into different regions of the mouse brain to trace where neurons in a particular region project to. Is there a particular region of the brain that you're interested in studying more? Find all the different areas it connects to. What is the function of each one of these connections? Try to go in-depth and look at connections, which are not the common ones you have learned about in class.

Allen Human Brain Atlas

This database integrates human brain imaging (MRI and diffusion tensor imaging of white matter) with genetic expression data (microarray and in situ hybridization (ISH) to look at RNA expression). Search by gene and use MRI data to correlate with anatomy, or ISH data in controls and disease states like autism and schizophrenia. Look up these genes to determine their significance, where you expect to see expression, and expression of what other genes they might be associated with.

Allen Mouse Brain Atlas

This was the first atlas published and is also the most detailed, with resolution to the single cell level. The atlas provides a genome-wide, three dimensional map of gene expression. Look up your favorite brain region to see which genes are expressed there, or search by gene to see where it is expressed. Are there other genes expressed in the same pattern?

Allen Developing Mouse Brain Atlas

How does gene expression change throughout development and aging? Search data from ISH by gene, location or developmental time. You can also look for other genes that have similar developmental expression patterns.

Brainspan Atlas of the Developing Human Brain

Similar to the developing mouse brain atlas, but also includes microarray data and RNA sequencing.

Available at brainspan.org.

NIH Blueprint Non-Human Primate Atlas

Gene expression atlas in rhesus macaque brain. It could be interesting to compare with the human and mouse data.

Allen Spinal Cord Atlas

Gene expression atlas in mouse spinal cord. You can see where genes are expressed along the spinal cord from rostral to caudal. This resource doesn't seem to be as complete as the mouse brain atlases. But if you are looking at expression of a particular gene, it might be worth looking to see if it is expressed in the spinal cord too.

Allen Cell Types Database

Individual cells in the mouse visual cortex were characterized based on cortical location, morphology, and electrophysiological parameters using patch-clamp recordings. Are there any patterns in terms of location in the cortex or correlations between morphology and firing rate? This would likely be a difficult database to use, because these are not topics we discussed much in class, but if you are really interested in electrophysiology, then maybe this is the database for you. Read online help to get an idea about how to conduct searches in this database.

II. Schedule for Lab 13

As you can see below, you have a number of lab periods to work on this project. Your group presentation will be on the last day of class and your lab 13 reports are due the following Friday.

Lab notebook before Lab 13.1

Watch the tutorial videos for a couple of the databases you are most interested in using. Take notes on the videos in your lab notebook.

Write down a couple of ideas for your project before you go to Lab 13.1.

Need help coming up with ideas? Check out the data highlights in the ABA website: <http://www.brain-map.org/highlights/index.html>

Nov 5	M	Lec 10: Allen Brain atlas project (RB)	
Nov 6/7	Tu/W	Lab 13.1: Develop Allen brain project	
Nov 8/9	Th/F	Oral exam in lab section	Oral exam
Nov 12	M	No class - Veteran's Day	
Nov 13/14	Tu/W	Lab 13.2: Allen brain project	
Nov 15/16	Th/F	Lab 13.3: Allen brain project	Exam 2 - Thursday Nov 15 evening
Nov 20-23	T-F	NO LAB	
Nov 27/28	Tu/W	Lab 13.4: Prepare presentation	
Nov 29/30	Th/F	Lab 13 group presentations	Lab 13 presentations
Dec 7	F	Lab 13 reports due	Lab 13 report due

Lab 13.1

Use Lab 13.1 to start exploring the resources for the most interesting ideas in your group. During Lab 13.1, consult with the GSI to make sure your idea is feasible. You may need to refine your experimental questions or add more details to expand the project.

By the end of Lab 13.1, you should have two specific research aims, which are defined research outcomes or intentions. For example, “To determine the relative expression levels of Ntng2 throughout the adult mouse brain.” Within each aim, create a brief outline of how you plan on using the databases to accomplish the goal. You may also want to think about who will do each task in your group since three people crowded around a computer may not work well. It is okay if you do not end up following this outline exactly; be willing to change your focus if your data takes you in a different direction.

Lab 13.2 and 13.3

Use Labs 13.2 and 13.3 to collect data from the databases. We know exam 2 is coming up or happening on the same day as these labs. We expect you to be working on Lab 13 during lab section and not studying for your exam.

- Take notes in your lab notebook of what you are doing and ideas you have.
- Write down the searches you do and save the resulting images and expression data.
- Confused about what the data means? Do a Pubmed search for that gene or anatomical region. You are trying to create a story with the data you are getting. What is the functional consequence of that gene being expressed or that axonal connection?
- Feel free to branch off into more than one atlas.

Think you have collected all your data after just a few hours? Great, that means you can expand your project. Let's say your project started by looking at expression of Ntng2 (a type of Netrin) in the parasubthalamic nucleus and you got some nice ISH images from the mouse atlas. Here are some follow-up questions you could ask:

- Why is Ntng2 expressed in the parasubthalamic nucleus (literature search)?
- Is it expressed anywhere else in the mouse brain (mouse brain atlas)?
- How does its expression change over development (developing mouse brain atlas)?
- Why would it be expressed at some time points and not others (literature search)?
- Is it expressed in a similar manner in the human or monkey brain atlas?
- Are there other genes that have similar expression patterns (this is a type of search you can do)?
- Are these other genes involved in the same cellular processes (literature search)?
- Is this gene associated with any diseases (look in the OMIM database)?
- Or maybe you want to focus on the parasubthalamic nucleus. Netrin is an axon guidance protein, so what axons is it guiding to the parasubthalamic nucleus? Use the mouse connectivity atlas.
- What is the function of the parasubthalamic nucleus (literature search)? How does it develop over time?

You wouldn't need to address all of these questions, but you can see that there are many avenues to follow after your initial data search. If you need help coming up with ideas, ask your GSI or talk to other groups to see what kind of searches they are doing.

Three hours straight of staring at a computer and doing intense research might get tedious, so feel free to take a few breaks during each lab period, but do plan on staying for the entire three hours on

both days.

Lab 13.4

Use this last lab period to prepare your group presentation. Your presentation should be about 15 minutes long (plus time for questions), so you may not be able to present all of your findings. Focus on the most interesting results. Include images from the ABA and figures from related journal articles.

Try to tell a biological story with your data, but also let the audience know what still needs to be studied and what experiments could be done next. Get your audience excited about your project and your findings.

Your GSI will provide you with a more detailed rubric for your presentation.

III. Lab report guidelines

This lab report is going to be structured more like a journal article. Although you may not have discovered something new (or maybe you did!), you still did independent work and followed a similar process as a researcher.

1. Abstract (300 word limit)

Abstracts are succinct one paragraph summaries of the entire research article. Your abstract should include:

- 1-2 sentences about the motivation for the work and previous findings.
- A brief description of the methods.
- A few sentences describing your two aims and the main findings
- A few sentences about the significance of the findings.

2. Introduction

Introduce us to the anatomical regions or genes you investigated. Most of the information about the structures or genes you researched will be in the next section, so this is just a short introduction to the topic of your project and what you previously knew about the topic. You could also mention why you were interested in these structures or genes.

3. Results/discussion

Write about each aim separately with clear headings for each aim. For each aim include the following:

- At least two images or figures, one of which must be from the ABA (like from the connectivity atlas or ISH images). You can also include figures from published articles, but make sure you include the citation in the legend. You might want to make tables with gene expression data or other numbers you obtained from the atlas.
- Discuss what you did to get the data (what did you search for)
- What the results were (“gene X is expressed in more cells in the CA1 region of the hippocampus than in the entorhinal cortex”)
- What is the biological explanation or significance of each result? This is where you can discuss the function of these genes and/or anatomical structures based on published literature. Incorporate the discussion with your results.

4. Future experiments (1-2 paragraphs)

What experiments would you want to do next? This could be things you want to search in ABA, but you ran out of time to do. Or it could be other experiments that get more at the functional consequences of your findings (like maybe you want to do some biochemistry experiments to investigate protein interactions, or you want to do behavioral studies in mice, or you want to look more at disease models, or do some functional test in humans (like fMRI/EEG)). Be creative and thoughtful.

5. References

Include a reference list of literature you cite in your lab report, using the Neuron format you have been following in your other lab reports.

General grading rubric (60 pts total)

1 pt: Title

5 pts: Abstract

5 pts: Introduction

36 pts: Results/Discussion

18 pts for each aim (x2 aims)

5 pts Figures and legends

5 pts How you got the results and description of the results

8 pts Biological explanation

5 pts: Future experiments

3 pts: Reference list and appropriate citation in text

5 pts: Style (clear writing, easy to follow, well organized)