Atlas Fitting for CLARITY Brains

Albert Lee, Tony Sun, Luke Zhu

September 12, 2016

Introduction

Atlases are an overlayed set of labeled points on brain images that neuroscientists can use to locate a specific lobe or area. Originating from when computing power was sparse, brain atlases were originally developed by a team of trained individuals whom manually outlined specific regions using their relative locations and relative histological compositions. Recent advancements in computing technology allow autonomous processes to estimate and generate atlases using image processing techniques. Here we've outlined some preliminary approaches we can take to fit atlases to our CLARITY brains.

Scaling by AC-PC, Applying Talairach/MN Coordinates, Then Fitting the Allen Brain Institute Mouse Mapping

In order to overlay the axis, we would first have to find the Talairach/MN coordinate systems' axes. To do so, we would have to visually locate the position of the anterior commisure to posterior commisure axis in each CLARITY brain dataset. After doing so, we would have to scale the axes of the CLARITY brain to match each axis as defined on the Allen Brain Institute Mouse Mapping, such that the size and overall shape matches the atlas copy. From there, we could immediately determine the relative position of each point in the CLARITY brain dataset by comparing it to the exact same point on the Allen Brain Institute Mouse Mapping. This technique seems simple, in the sense that as long as we can somewhat accurately define the AC-PC axis in the CLARITY data set, we should be able to obtain an atlas.

Talairach Coordinates Approach

Talairach coordinates set the origin location as the anterior commissure. From there, the y axis is defined as the line cutting from the anterior commissure to the posterior commissure (think a line from the nose to the occipital lobe). The x axis is defined as the line that perpendicularly cuts from the left ear to the right ear. The z axis runs dorsal to ventral (from the apex of the head down through the chin). The Talairach atlas and coordinate system uses 2D approximations of

Brodmann regions drawn by Talairach, and so are somewhat imprecise for specific regions. Time estimates for each step are as follows.

1. Given the sparse nature of some of the data sets (eg, Fear199), it might be difficult to locate the exact location of the anterior commisure/posterior commisure. Estimated time: 2 day to determine which CLARITY brains have the appropriate densities (by manually opening each file and determining. 3 days to locate the AC-PC axis on 12 brains.

2. After applying the axes to each brain, we'll need to scale each image to match the size of the Talairach coordinate axes. We'll need to download a copy of the Allen Brain Atlas and then figure out the exact dimensions used. Estimated time: 2 day to download the atlas, 4 days to apply scaling values to each data point in data set.

3. After scaling, we need to find a way to have a script automatically label each XYZ coordinate with the name of the atlas location. Estimated time: 7 days to figure out how to get the atlas position given the XYZ coordinates.

MNI (Montreal Neurological Institute and Hospital) Coordinates

An alternative update to the Talairach coordinates would be the MNI coordinate system. The MNI coordinate system was more recently introduced, and is the industry standard for statistical parameter mapping (which is often used to highlight the differences in brain activity recorded during fMRI scans) for human brains. The MNI coordinates were designed by collecting MRI images from a large set (241) of healthy subjects and then labeling key landmark points on the MRI images. From there, these MRIs were scaled to fit the Talairach coordinates and then mapped to more-accurately represent brain regions. Time estimates are similar to the previous ones given for the Talairach coordinate system, since this is just a variation on a theme.

Utilizing 2D Cross-Sections of Known Depth

This approach is very similar to the previously defined scaling approach. In this approach, we would have to still have to define an AC-PC axis on the pre-existing CLARITY data. We would also have to download 2D cross-sections of the mouse atlas from the Allen Brain Institute. Then, given the 2D cross-sections at known coordinate locations on the atlas, we could apply the atlas to specific points

at each height. This might be simpler given the download types available from the Allen Brain Institute (https://scalablebrainatlas.incf.org/mouse/ABA12).

Utilizing Centroid Clustering, Block-wise Analysis, Boundary Analysis

Previous approaches focused primarily on scaling the 3D CLARITY brains and then fitting the Atlas directly over the points. A more data-oriented approach would be centroid clustering, block-wise analysis, or boundary analysis.

Centroid Clustering

In centroid clustering, the main goal would be to define a certain number of 'k-clusters', aka centers of interest. Having defined these centers of interest, where every nearby point falls in some specific cluster, we could then just assign the centroid clusters to their corresponding points on the Allen Brain Institute Atlas. For choosing the centroid clusters, We could do so by examining particularly dense voxels (eg: those that have a significant number of neighbors within a certain radii). The main concern is that some individual points may not be covered (centroids too sparse), or that the conditions (eg: fear) disproportionately affects certain areas of certain lobes (eg: hypothetically, the lower amygdala showing significantly more response than upper amygdala) causing the mis-labeling of certain regions. The main thing that is difficult to this approach would be defining the exact size/location of the clusters of interest, since defining the clusters requires a complex method to find out which nodes belong to which clusters. Time estimates are as follows:

1. Determine a good sample data set to use as the backbone. This process means just looking through our 12 CLARITY plots and finding an image with reasonably high densities in all given areas (no large areas that are extremely sparse). Estimated time: 1 day to choose a reasonable data set.
2. Determine method on how to find clusters of interest. Read up and investigate a way to write an objective function that can attempt to minimize error (distance) about 'k' interest clusters of our choosing, or use the spheroid approach (whereby we choose some number of clusters and then manually link nearby values to their closest cluster). Estimated time: 1.5 to 2 weeks for the objective function, 1 to 1.5 weeks for the manual approach.
3. Import cluster coordinates into axis, then overlay all points in cluster with the designations from atlas. Estimated time: 7 days to

figure out automated way to get atlas designations from XYZ coordinates and apply this designation to all the previously clustered points.

Block-wise Analysis

In block-wise analysis, we would segment the existing CLARITY brain data-sets into equally-dense blocks, and then assign the centers of the blocks to their corresponding atlas values. This technique seems less accurate when compared to the centroid clustering technique by cursory inspection, but is only different by a small amount. Time estimates are as follows:

1. Determine a good sample data set to use as the backbone. In this case, we'd like the entire data set to have around the same density, so that our blocks aren't significantly different in size. Estimated time: 1 day to choose a reasonable data set.
2. Define a method on how to make variable-sized 'blocks' with equal size densities, or manually draw boxes over regions. Estimated time: 1.5 to 2 weeks for the objective function, 1.5 weeks for manual drawing over a small area.
3. Overlay center of block onto axis. Estimated time: 7 days to get automated atlas designations from XYZ coordinates.

Boundary Analysis

In boundary analysis, we would somehow try to match the CLARITY brain edge list to the edges highlighted on the existing atlas. The difficulties in this are apparent just by inspection; our edge-list was created by assuming an arbitrary distance linked the 'nearest' neighbors, while the real edges of the atlas my differ greatly. Implementing this technique seems particularly difficult, as we'd need to figure out way to do 2D image overlays to get similar edges to the given Atlas, and then apply that in 3D.

1. Determine a good sample data set to use, one with no significant number of outlier points. Estimated time: 2 days to choose a reasonable data set.
2. Downsample the data, and remove any extraneous data points. Estimated time: 7 days to write code to remove all outliers (some preset maximum distance away from other points) and also downsample the data.

3. Make model edge list from Atlas results (eg: hippocampus edge list that defines XYZ coordinates of edges of the hippocampus). Estimated time: 14 days
4. Find closest points in CLARITY plots to each point in the model edge list. Estimated time: 7 days
5. Define CLARITY edges that most closely match the hippocampus model edge list. Estimated time: 7 days
6. Define everything equal to and inside the edge list as the particular lobe in question. Estimated time: 3 days
7. Repeat process for other lobes. Estimated time: n x 1 month, where n is the number of lobes.