BrainViewer: interacting with spatial connectome data at the mesoscale

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Abstract
Scientists construct connectomes, comprehensive descriptions of neuronal connections across a brain, in order to better understand and model brain function. Interactive visualizations of these pathways would enable exploratory analysis of such information flows. Current tools can be used to see individual tracing experiments which are used to build mesoscale connectomes of the mouse brain, but not the brain network itself. We present a connectivity visualization program called BrainViewer, which we use with a high-resolution mouse cortical connectome. This has the ability to display connectomes from other datasets when they become available and compare spatial connectivity across multiple brain structures. Our tool, optimized for speed and portability, presents a GUI visualization in 2-D top view and flatmap projections, allowing users to select and explore the connections of every source voxel to everywhere else in the cortex. Anatomists and other neuroscientists will find BrainViewer useful for building understanding beyond the known topography of cortical connectivity.

Index Terms: Computing methodologies—Modeling and simulation; Human-centered computing—Interactive systems and tools; Human-centered computing—Visualization systems and tools; Human-centered computing—Visualization application domains; Software and its engineering—Software creation and management;

1 Introduction
Connectivity patterns in the brain reveal important information about brain function. Differences in brain-wide connectivity patterns, or connectomes, are at the root of some functional and behavioral differences across animals. Improved connectomic knowledge could lead to new treatments for disease, improved brain-machine interfaces, and influence the development of brain-inspired computing and artificial intelligence.

Topography refers to the functional spatial maps across the brain. For instance, it is known that many sensory systems maintain maps of sensory space which are transformed between brain regions. Retinotopy—the mapping of visual space onto visual regions of cortex—is one example of this and was the original inspiration for deep convolutional neural networks which have revolutionized computer vision [2][11]. It is now evident that retinotopy arises from topographic patterning of connections between brain areas [22], however such data have been difficult to visualize.

Modern neuronal tracing methods allow researchers to trace the major pathways in the brain. Such tracing experiments have been conducted on the mouse [3][9][14][23], fly [15], marmosets [6][12][20][21], rat [1] and macaque [13]. Results of these experiments have then been used to build brain models at the mesoscale, i.e. showing the connections between areas containing the order of thousands of neurons. Oh et al. used the anterograde tracer adeno-associated virus expressing green fluorescent protein to track connections in the mouse brain [14]. After injecting mice with the virus, each brain is then sliced, imaged and processed to reveal a volumetric image of fluorescence. In the dataset we use from the Allen Institute for Brain Science, areas are defined using a common coordinate framework and individual experiments are mapped into this common voxel space [19]. Many of these experiments can be combined into a weighted connectivity matrix which stores projection strength between source and target regions [8][14], and individual tracing experiments can be visualized in 3D using the BrainExplorer tool [10]. Most connectome work has focused on measuring brain connectivity at the level of regions and various tools exist to display such regional connectivity. New methods have been developed to estimate spatially-resolved connectivity at the resolution of voxels—discrete locations within the brain volume [5][8].

The closest work to our own is the web-based BrainModules from R. Hira [8] that displays functional and structural connectivity patterns from marmoset and mouse in the browser. However, these are only available at low display resolution and the code is undocumented and unmaintained.

We present a tool BrainViewer to display and interact with high resolution spatial brain connectivity. We have built it to work with the mouse voxel connectome from [8], but it is portable and can be used across datasets with a number of capabilities described in Section 2. The user may click on any location in right hemisphere of the mouse cortex and see the outgoing projections of neurons from that location. Our tool provides a 2-D visualization of the connectivity in two projections, flatmap and top view; the relative advantages of each are discussed in the methods, Section 3. Switching between the two projections allows for easy comparison, and the user may also navigate the source voxel using their keyboard. This interactive visualization of a spatial connectome enhances the understanding of the brain’s information processing patterns and allow researchers to generate new and interesting topographic anatomical hypotheses.

2 BrainViewer: a connectome visualizer tool
Our tool allows users to navigate and explore the estimated mouse cortical connectivity from Knox et al. [8] in a GUI environment (see Fig. 1). The code is available at https://github.com/glomerulus-lab/brainviewer We include the following features:

- A colormap annotating the strength of connectivity from the source voxel to any given voxel in the plot.
- Click-to-plot allows users to select any voxel on the right hemisphere of either the flatmap or top view, visualizing the connectivity from that source voxel.
- Arrow key navigation which enables users to carefully move the source voxel across the cortex.

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within primary visual cortex (VISp), an area known to be important
voxel when switching between flatmap and top view. This allows
voxels in addition to context for each region. For instance, when
a given injection.

Moving slowly. The real-time plotting method preserves the source
cursor quickly can result in lag, but the tool still performs well when
moving about the brain, adjusting the source to an adjacent voxel.

Once a

move about the brain, adjusting the source to an adjacent voxel.

source voxel is chosen, the arrow keys on the keyboard can precisely
of the cortex to select a source voxel for plotting Fig. 1. Once a

data. Here we show the mouse voxel connectome from [8]. The

voxxel (cyan) is seen in the VISa region and projection strength
from that voxel is shown by the hot colors. Cortical region boundaries
and labels are overlaid in magenta. The user may switch to a flatmap
view with the button, navigate by keyboard, and save resulting figures.

- Switching between the top view and flatmap while maintaining
the source voxel, allowing for visualization of connectivity in
regions of the cortex obscured when viewed from above.

2.1 Exploratory interaction capabilities

BrainViewer can display estimated projections between a source
and target voxels using either the top view or flatmap. The top view
projection is shown in Fig. 2 including an overlay of the cortical
regions. With this view the user sees projection strength between
voxels in addition to context for each region. For instance, when
navigating the visual cortex, projections vary from source voxels
within primary visual cortex (VISp), an area known to be important
for retinotopy [22].

The flatmap is projection flattens the curved cortex by
introducing less distortion than top view for the most
medial areas [3, 16, 17]. This provides information about voxels not
directly seen from the top view projection as implied by Fig. 2.

The user may click on any pixel within the right hemisphere
of the cortex to select a source voxel for plotting Fig. 1. Once a
source voxel is chosen, the arrow keys on the keyboard can precisely
move about the brain, adjusting the source to an adjacent voxel.

The other projection BrainViewer uses is a cortical flatmap, shown
in Fig. 2B. The flatmap is a truer representation of the curved surface
of the cortex, introducing less distortion than top view for the most
anterior-posterior (AP) axes. We
lie underneath. We

we use their mouse coordinates to get \((x_p, y_p)\) in the projection, then the
lookup table tells us which voxels \(\{(x_i, y_i, z_i)\}\) lie underneath. We
plot the connectivity from the voxel in the middle of this path, corre-

Fig. 2B shows how the
top view is reflective of a top-down view of a three-dimensional
model, giving a 114 × 132 bird’s eye view of the brain directly
corresponding to medial-lateral (ML) × anterior-posterior (AP) axes.
An example of such data for a source voxel in SSp-bfd (primary
somatosensory barrel field, the whisker sensory region) is shown in
Fig. 2C. The top view helps users contextualize the plotted connec-
tivity for a given source voxel with a cortical region overlay.

Our tool also includes a flatmap of the connectome, seen in
Fig. 2C. The flatmap is projection flattens the curved cortex by
following paths which actually trace cortical depth, rather than just
using the dorsal-ventral axis. The flatmap’s 272 × 136 coordinates
roughly correspond to a curved set of ML-AP axes. This reveals
the complete cortical surface, including areas which are curled
underneath and inaccessible in the top view. For the example shown in
Fig. 2D, projections from the same voxel in SSp-bfd that extend
more deeply into adjacent lateral areas are more evident than in the
top view (compare Fig. 2D).

Because all top view points are visible in the flatmap, there is
no issue switching from top view to the flat map projection while
preserving the source voxel. However, switching from flatmap to
top view has the problem that some points shown in flatmap are
not visible in the top view perspective. In this case, our method
computes the closest source voxel in the top view projection.
3.3 Optimizations for speed and portability

We have developed two versions of BrainViewer which function similarly but use different methods under-the-hood to generate the images. The first method implements real-time plot generation from a $(x_p, y_p)$ coordinate pair after a mouse click event. Using these coordinates and the mapper, the corresponding column vector in the projection matrix $W$ is computed and plotted. The entire low-rank decomposition of $W$ must be loaded at runtime along with the mapper utilities. These steps are not particularly efficient, leading to a nearly two minute preprocessing before any data can be displayed and a noticeable delay between image refreshes after the user clicks.

To speed up this process and also enable greater portability across datasets, we built a version of BrainViewer which can work directly with image stacks in the projected coordinate system. We preprocess the projection plots as images that are named by the $(x_p, y_p)$ coordinates of the source voxel being displayed. Because we do not need to load the $W$ matrix or compute any 2-D projections, this version of BrainViewer starts quickly and has a much faster refresh latency. There are only two requirements for formatting images from a new dataset: images are named based on the source voxel coordinates, and the coordinate space of the connectome must be easily mapped to the coordinate space of the image that the user is viewing and interacting with. For us, this is simply a scaling factor between the voxel coordinate space and the resolution of the saved images.

4 Conclusions

BrainViewer is a point-and-click software for viewing the projections from any voxel in a flattened view of the brain to any other voxel with high resolution and fast response. The comprehensive spatial mouse cortical connectome is presented at the voxel level, which allows for more in depth analysis. While we show results here for mouse, the framework is flexible and other datasets can be incorporated easily. Our code is freely available and documented online.

Using a GUI interface in Python allows us to overcome earlier limitations encountered by BrainModules [6], which displays connectivity in a small window, making it challenging to view specific sections of the brain. However, BrainModules does incorporate other datasets using a correlation-based method to estimate the connectome, which is different than the smoothing method of [8]. BrainModules also provides multiple volumetric projections simultaneously.

In the future, we hope that BrainViewer will be used to visualize the connectomes of other species where tracing data are being collected such as marmoset, rat, etc. These data are not as easily accessible as the Allen Institute’s mouse dataset, and voxel-based connectomes in those species have not been published. We would like to incorporate multiple projections as well as overlays in the flatmap projection. Other desirable features include display of the projection data in a native 3-D interface and a web-based version. Visualization software like BrainViewer will continue to be an important way to understand connectomic data in the future.
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