
Toward a Visual Interface for Brain Connectivity Analysis

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Abstract

In this paper, we report on the needs for, the design of, and feedback about a web-based platform that supports flexible exploration of existing brain connectivity knowledge. We analyze the needs in brain connectivity research for an integrated visual knowledge base and discuss the design of the platform and the design rationales. Preliminary user feedback suggests diverse analytical patterns and additional needs in brain connectivity analysis, which distinguish it from generic network analysis. Finally, we describe open issues motivated by preliminary feedback and observation in designing more advanced features to support additional needs and characterizing user analysis patterns.

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Author Keywords

Visual analysis; Brain connectivity analysis; Design study

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Introduction

Complex communications happen all the time among ensembles of neurons and form the basis of cognitive

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functions such as memory, language and motor control. The study of brain connectivity, i.e., how brain regions are connected and influence each other, is central to understanding brain functions. Numerous experiments have been conducted and results published on brain connectivity. As of 2010, Pubmed has indexed over 7,000 publications on topics related to brain connectivity [6]. As of 2012, Neuroscience Information Framework, a website that centralizes neuroscience resources, has indexed over 60,000 connectivity records from nine connectivity databases [3].

Given the large amount of brain connectivity information and heterogeneity in techniques, species and ontologies used in connectivity experiments, reasoning with the existing knowledge to generate new hypotheses about brain connectivity is a challenging task. Based on initial interviews with our collaborators in neuroscience, we identified basic needs such as the ability to trace multi-hop paths between two brain regions. We then iteratively designed two prototypes, collected anecdotal feedback on the prototypes, and identified more advanced analytical needs and open research problems such as data source integration based on user feedback and observation.

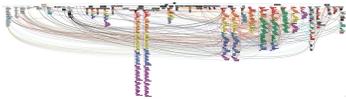


Figure 1: Mind map created by Schnitzer's group

Challenges and Needs in Brain Connectivity Research

An important step in research is to synthesize relevant research results to generate hypotheses. Currently, to collect existing connectivity information, our collaborators in neuroscience either use conventional document search engines such as Pubmed and Google Scholar to find relevant publications or perform query searches in brain connectivity databases to find curated records. Initial interviews with two senior neuroscience researchers have revealed two disadvantages of the current practice.

First, it is reported to be very difficult to formulate as traditional search queries questions about indirect connections, that is, if and how the interactions between two brain regions are mediated by some other brain regions. This essentially requires the scientist to enumerate all the possible intermediate regions as search terms, which is impractical given the large number of brain regions, especially if the researcher is interested in more than one level of indirection.

Another disadvantage of the traditional search paradigm stems from the fact that there is no widely agreed-upon brain ontology. Brain regions can be organized based on either their cognitive functions or the brain's anatomical structure, and there are many variations for each of these two organizing principles. While searching for connectivity information about a particular brain region, it is easy to miss publications or records that are relevant but have used different naming conventions or are on a different level of granularity than the researcher has in mind.

To start addressing these challenges, one of the authors, with help from other neuroscientists in his lab, created a mind map (Fig. 1) while curating brain connectivity publications. The vertical organization of the nodes reflects the anatomical hierarchy of the brain and the horizontal links represent known connections. While the mind map allows the user to trace indirect connections, it must be reproduced impractically large to be legible, which signifies the challenge of managing and displaying the connectivity information.

Design and User Feedback

Motivated by the challenges and needs outlined in the previous section, we iteratively designed and implemented two prototypes of the brain connectivity analysis tool. In

this section, we detail the design iterations and use cases.

Data The two prototypes use connectivity data from Brain Architecture Management System (BAMS) [2], which was generated through curation of hundreds of Pubmed publications on neuron projections in rat brains. We have processed the dataset to remove brain regions that are not associated with any known connection and connections that are reported to be non-existent. The final dataset contains 555 brain regions and 7771 connections. Each connection is associated with one or more publications. The data has been transformed into a compound graph with nodes, tree edges and network edges; the nodes represent the brain regions, the tree edges indicate the anatomical containment relationships among brain regions, and the network edges represent connections among brain regions.

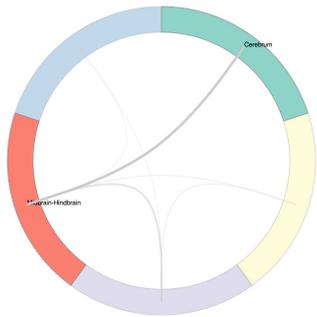


Figure 2: The link between cerebrum and midbrain-hindbrain is selected.

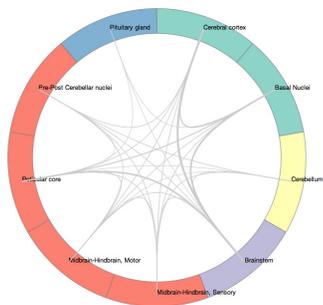


Figure 3: The interface after expanding the link selected in Fig. 2.

pairs of a and b where a is a descendent of A and b is a descendent of B as well as the exact matches.

4. Support for tracing indirect connections. The user needs be able to retrieve paths connecting a pair of brain regions by specifying a limit on the number of hops.

Iterative design Both prototypes are written in Javascript using D3 library [1]. The initial prototype is shown in Fig. 4. Arcs around the circumference represent the nodes, and are arranged in layers to encode the anatomical hierarchy of the brain regions. The links represent the connectivity edges. An edge bundling algorithm [5] is applied to reduce visual clutter as well as to show the connectivity trend among large-scale brain regions. The arcs and links are arranged into a radial layout to enhance space utilization. The user can interactively filter the nodes by selecting a link or filter the links by selecting a node. The user can also search for paths by specifying source, target and number of hops.

Design requirements Based on challenges and needs outlined in the previous section, we list basic criteria that guided the design of the prototype:

- 1. Visual encoding of brain hierarchy.** In the study of the brain, it is conventional to organize the brain regions hierarchically based on the brain's anatomical structure. Therefore, showing the brain hierarchy could help users orient themselves when exploring brain connectivity.
- 2. Availability of detailed information for individual connections.** Since the brain scientists care about the individual connections as well as the global connectivity trend, the interface needs to allow single connection selection and connection information retrieval.
- 3. Connection propagation.** Given the hierarchical organization of the brain, the tool needs to be able to propagate connection queries down the brain hierarchy. Given a request for all connections between brain regions A and B , the tool should return connections between all

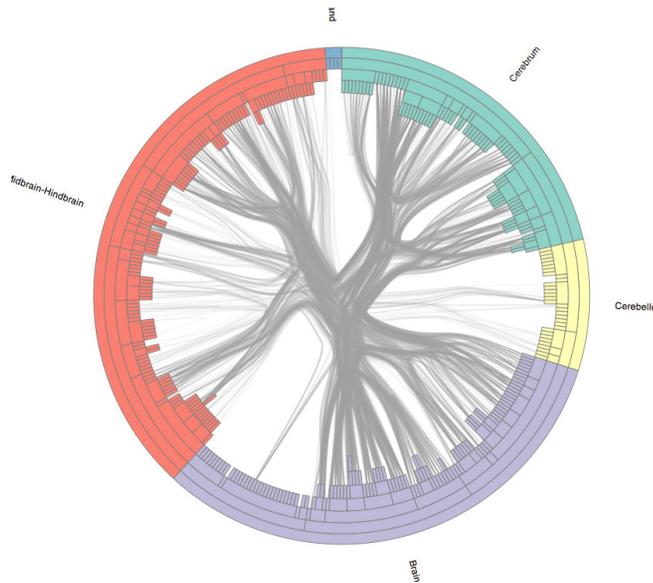


Figure 4: The first prototype

We interviewed six neuroscience experts after building the first prototype. The interviewed users have varying degrees of expertise, ranging from undergrads and graduate students to postdoctoral and senior researchers. Users showed enthusiasm about the tool's potential, but also suggested that there existed ample room for improvement. A user pointed out that given the large number of visible links and regions, it is difficult to locate a particular brain region or select a link. Also, search for indirect connections could be slow, largely due to the naive implementation of connection propagation which involved the costly operation of propagating search queries down the tree hierarchy.

Based on the user feedback, we developed the second prototype, which implicitly encodes the hierarchy of the

brain using the zoom level. Only the coarse division of the brain regions is shown initially, and the user can click and expand a brain region to see its finer division. We also changed the underlying data structure to propagate the connectivity information along the node hierarchy. For each edge e that connects two nodes a and b , a corresponding "meta" edge is added between a 's parent A and b 's parent B . This data structure brings a bonus in performance since it eliminates the need to propagate connection search queries down the nodes hierarchy during runtime. Informally, it is estimated that this new data structure speeds the search up at least 100 times.

The visual design of the second prototype is similar to TreeNetViz [4], but it differs from TreeNetViz in three aspects given the unique properties of brain connectivity:

1. TreeNetViz explicitly encodes depths of the nodes by their radii and colors. However, we have chosen to not visually encode node depths since, unlike social networks, node depths in a brain anatomy tree might lack semantics. The tree levels do not necessarily correspond to anatomical levels given the many factors to be considered (e.g., functional division, consistency with conventions) when building brain ontology. Instead, we use uniform node radii and assign colors to nodes based on their coarse anatomical locations. We made this design decision to help the user maintain an anatomy-based mental map when drilling deep into the brain hierarchy.
2. Since a user might be interested in several particular brain regions, we allow the user to activate a brain region using a dropdown list. The nodes in the visualization will be automatically expanded or collapsed so that the activated brain region will become visible.
3. We provide link-centric operations in addition to the

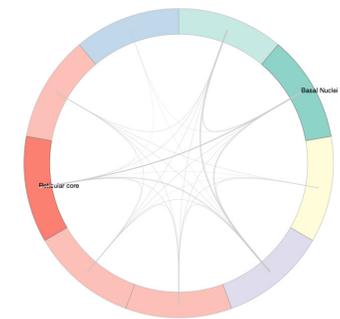
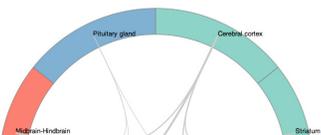


Figure 5: By collapsing the selected link, the interface will return to the state shown in Fig.9



node-centric operations available in TreeNetViz considering the rich information carried by each connection in the network. The user can expand a link, which will trigger simultaneous expansion of the source and the target of the expanded link. Similarly, links can also be collapsed which will result in collapse of the corresponding sources and targets. The operations are illustrated in Fig. 2, 3 and 5. The user can also click on a link to retrieve the associated publications.

Use Cases We now describe two use cases observed during interviews which, we believe, represent common usages of the tool. In the first case, the user wanted to know which brain regions are connected to striatum. The process is illustrated in Fig. 6, 7 and 8. At the end, the user exported a list of publications on connections between striatum and hypothalamus, including sub-connections between areas within these two regions respectively. The user commented that he could have missed these sub-connections if he had been using a traditional search engine. In the second case, the user was interested in how striatum and dorsal thalamus are connected through some intermediate regions. The operations performed by the user are illustrated in Fig. 10 and 11.

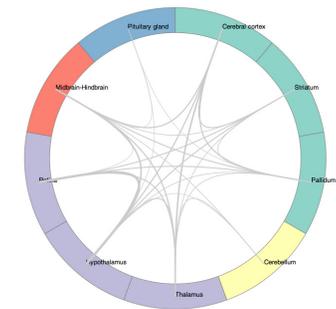


Figure 7: Use case 1(b): The user noticed that there were a relatively large number of reported connections between striatum and brainstem, represented by a relatively thick link, so he decided to expand brainstem.

Home Publications BAMF records Sub-connections

Current link: Striatum-Hypothalamus
This is a main link. Open the central connections for more information.

Children links:

Source	Target	Publication
Anterior amygdala area	Lateral hypothalamic area	Patenaude D.D., Carmona N.S., Swanson L.W. Combinatorial amygdalar inputs to hypothalamic domains and hypothalamic behavior systems. In: <i>Brain Res Brain Res Rev</i>
Anterior amygdala area	Posterior hypothalamic nucleus	Patenaude D.D., Carmona N.S., Swanson L.W. Combinatorial amygdalar inputs to hypothalamic domains and hypothalamic behavior systems. In: <i>Brain Res Brain Res Rev</i>
Nucleus accumbens	Lateral hypothalamic area	Risold P.Y., Thompson R.H., Swanson L.W. The structural organization of connections between hypothalamus and cerebral cortex. In: <i>Brain Res Brain Res Rev</i>
Nucleus accumbens	Lateral hypothalamic area	Migerson D.J., Swanson L.H., Ho M. Neural projections from nucleus accumbens to globus pallidus, substantia nigra, and dorsal preoptohypothalamic area: an anatomical and electrophysiological investigation in the rat. In: <i>J Neurosci</i>

Figure 8: Use case 1(c): After the expansion, the user became

and are usually not suitable for node-based analyses.

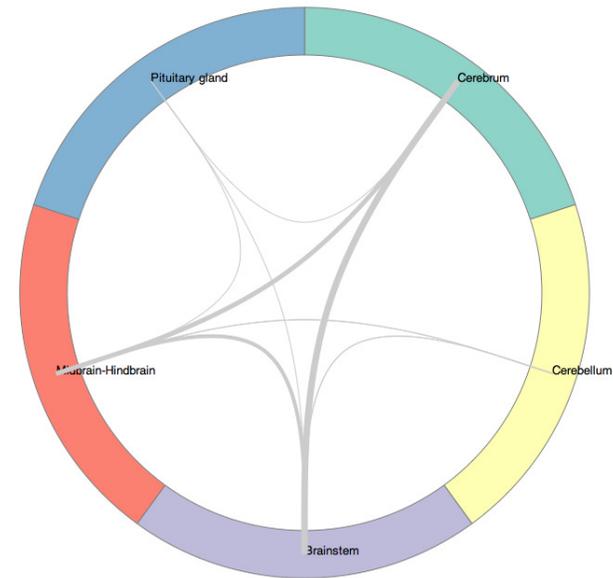


Figure 9: The initial view in the second prototype.

One hypothesis is that different brain connectivity analysis workflows can be characterized on a spectrum: on one end, the scientist focuses on the connectivity and properties of a single brain region, while on the other end, the scientist studies the brain connectivity network as a whole. One reason for the diversity might be that brain analyses happen on different scales. For a researcher who studies a major brain region, the publications and records associated with the corresponding node might be the most valuable information. When the basic units in the analysis are neurons or voxels, studying the whole brain or regions of interest as networks might lead to more

Brain Connectivity Analysis Patterns Users exhibited different analysis focuses when trying out the prototype. Some users valued most the ability to retrieve publications associated with a brain connection and wished for more information about individual brain regions such as slice images, while others were more interested in seeing the connectivity network structure. Based on the varying analysis focuses, we see a need for domain-specific analysis tools that diverge from commonly used network analysis systems such as Cytoscape [7], which are designed to support analyses of the network as a whole

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