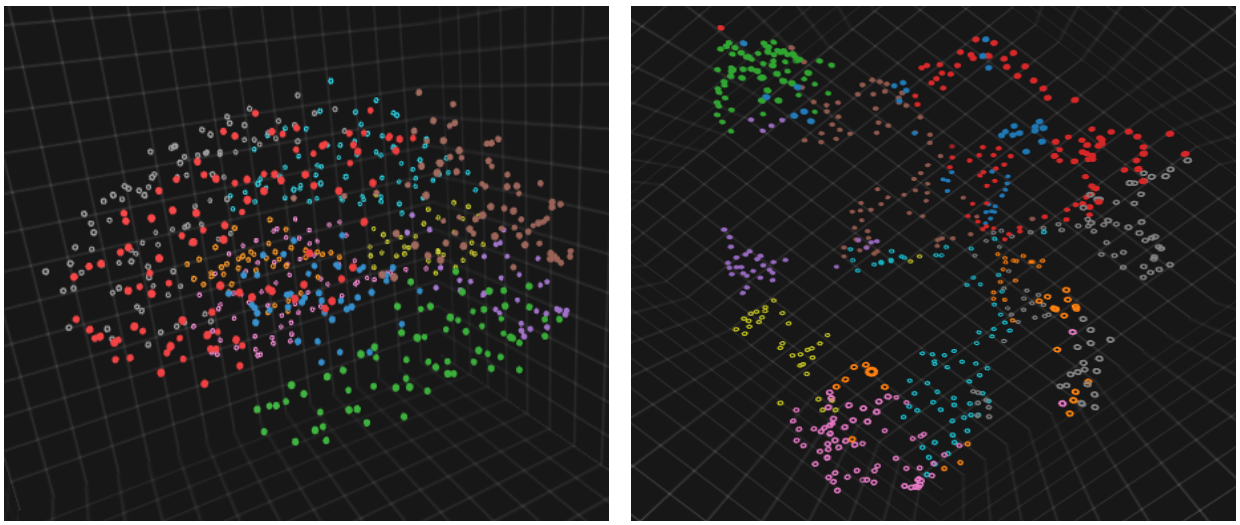
Visualizing the Intrinsic Geometry of the Human Brain Connectome

Author 1 and Author 2



(a) Anatomical Geometry (b) Intrinsic Geometry

Figure 1. The *BIGExplorer* visualization system enables researchers to better understand connectome datasets by providing representations of both the anatomical (left) and intrinsic (right) geometry of the data.

Abstract—Understanding how brain regions are interconnected is an important topic within the domain of neuroimaging. Thanks to the advances in non-invasive technologies such as functional Magnetic Resonance Imaging (fMRI) and Diffusion Tensor Imaging (DTI), larger and more detailed images can be collected more quickly. These data contribute to create what is usually referred to as a *connectome*, that is, the comprehensive map of neural connections. The availability of connectome data allows for more interesting questions to be asked and more complex analyses to be conducted. In this paper we present *BIGExplorer*, a novel web-based 3D visual analytics tool that allows user to interactively explore the *intrinsic geometry* of the connectome. That is, brain data that has been transformed through a dimensionality reduction step, such as multidimensional scaling (MDS), isomap, or t-distributed stochastic neighbor embedding (t-SNE) techniques. We evaluate the *BIGExplorer* visualization tool through a series of real-world case studies, demonstrating its effectiveness in aiding domain experts for a range of neuroimaging tasks.

Index Terms—Connectomics, connectome datasets, intrinsic geometry, neuroimaging.

1 Introduction

The problem of establishing a deeper understanding of the interconnectedness of the human brain is a primary focus in the neuroimaging community. Imaging techniques, such as *functional Magnetic Resonance Imaging* (fMRI), *diffusion tensor imaging* (DTI) and high angular resolution diffusion imaging (HARDI), enable neuroimagers to collect and derive data about how different brain regions connect from both a structural and a functional point of view [17]. Analagous to the *genome* for genetic data, the *connectome* is a map of neural connections [25].

Complex functional and structural interactions between different regions of the brain have necessitated the development and growth of the field of connectomics. The brain connectome at the macro-scale is typically mathematically represented using connectivity matrices that describe the interaction among different brain regions. Most current connectome study designs use brain connectivity matrices to compute summarizing statistics of either a global or a nodal level [26].

In the current work, we introduce the potential utility of deriving and analyzing the *intrinsic geometry* of brain data, that is, the topological space defined using derived connectomic metrics rather than anatomical features. The utility of this intrinsic geometry could lead to a greater distinction of differences not only in clinical cohorts, but possibly in the future to monitor longitudinal changes in individual brains in order to better deliver individualized precision medicine. To the best of the authors' knowledge, no such tool currently exists that effectively addresses these needs.

We propose *BIGExplorer* (Brain Intrinsic Geometry Explorer), a web-based 3D tool to visualize the intrinsic geometry of the brain. Its interactive approach to presenting detailed information about particular nodes and edges is effective at displaying highly interconnected networks such as the connectome. *BIGExplorer* provides researchers with the ability to perform visual analytics tasks related to the exploration of the intrinsic geometry of a dataset and the comparison of how the dataset looks when embedded within different topological spaces.

The paper is structured as follows. In Section 2 we provide more details about the construction of the *intrinsic geometry* of the brain. In Section 3 we discuss existing approaches to representing the human brain connectome. In Section 4 we identify domain-specific tasks that motivated the creation of the *BIGExplorer* tool. Section 5 gives a detailed description of the design decisions of *BIGExplorer* and de-

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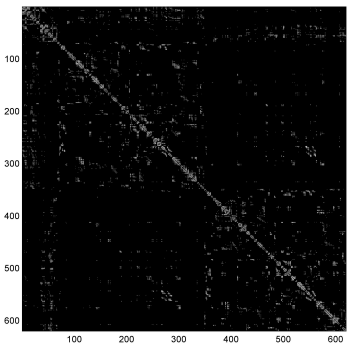
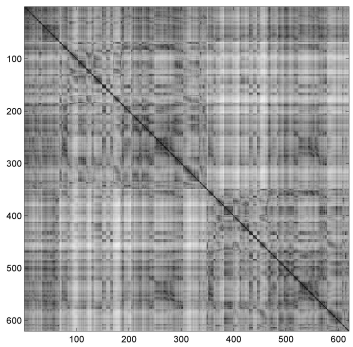
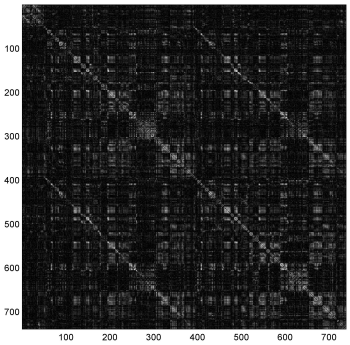


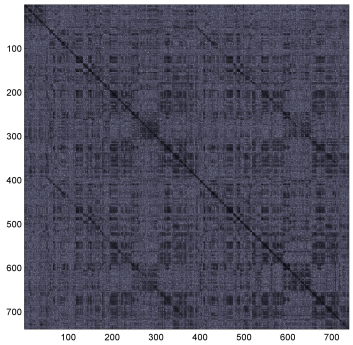
(a) Structural connectivity matrix.



(b) Graph Distance of matrix (a).



(c) Functional connectivity matrix.



(d) Resting-state fMRI log-transform using equation 1.

Figure 2. This figure shows all the adjacency matrices taken from the raw data and their transformed version when the shortest paths are computed.

scribes in detail the functionality it provides. In Section 6 we present real-world case studies in which new insights were obtained by using our tool. Finally, based on the use cases and the interviews with experts, we present some possible directions for future research in Section 7.

2 Intrinsic Geometry

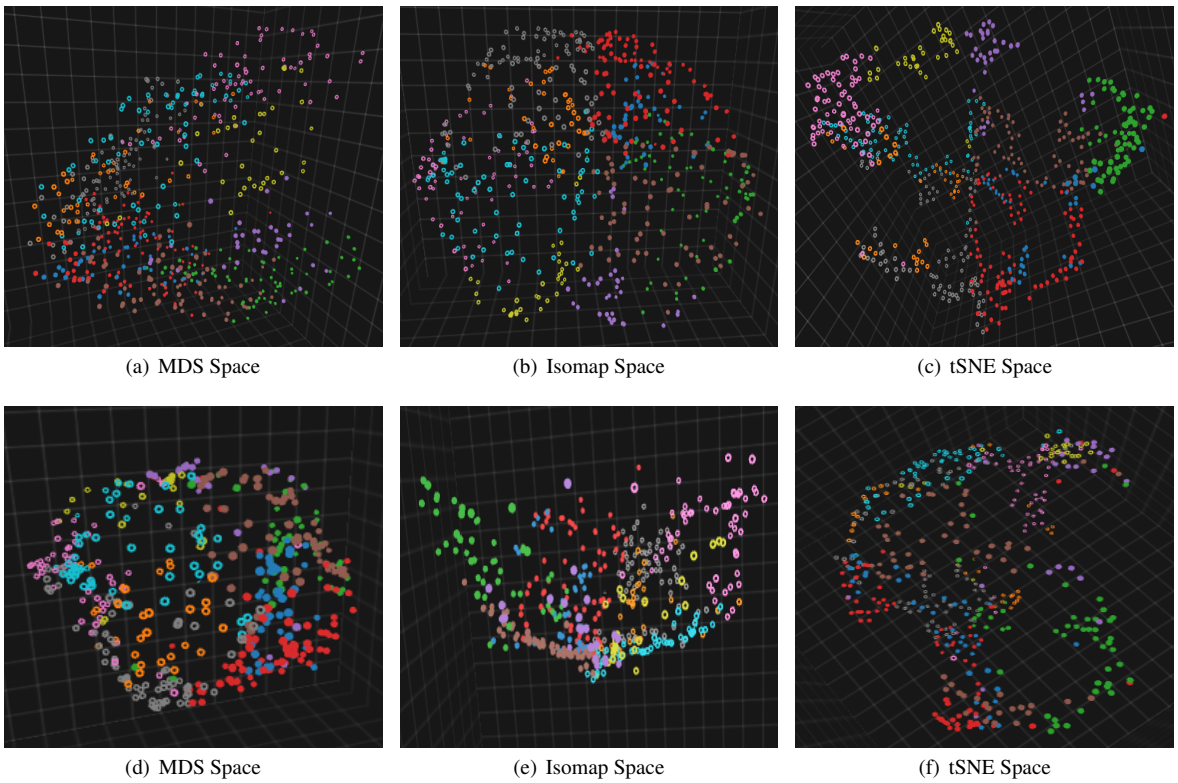
The *intrinsic geometry* represents the brain connectome after nonlinear multidimensional data reduction techniques are applied. This means that the position of each node does not correspond to its anatomical location, as it does in the original brain geometry. Instead, its position is based on the strength of the interaction that each region has with the others, whether structural or functional. The stronger the connectivity between two regions, the closer they are in the intrinsic geometry. To put into context why intrinsic geometry may be a better space to understand brain connectivity data, for decades cartographers have mapped quantitative data onto world maps to create unique, informative visualizations. For example, by resizing countries according the Gross Domestic Product (GDP), the viewer can easily appreciate that the United States has the largest GDP. Similarly, dimensionality reduction techniques remap the brain according to network properties. In the intrinsic geometry we are more interested in the shape the brain connectome assumes independent of the anatomical distances between nodes. Thus, the space in which the intrinsic geometry is plotted in is called *topological space* [4].

Through using a variety of dimensionality reduction techniques such as isomap [27] and t-distributed stochastic neighbor embedding (t-SNE) [28], a brain's connectivity matrix can be directly embedded into topographical spaces. Linear dimensionality reduction techniques such as multidimensional scaling (MDS) [2] and principal component analysis (PCA) [16] have been previously used in unrelated fields of medicine as a way to distinguish clinical cohorts through biomarkers, although it can be argued that they are not suitable for complex high-dimensional connectome data [14, 31]. To our knowledge our approach represents the first comprehensive application of dimensionality reduction techniques in the ever-expanding field of brain connectomics.

This intrinsic geometry concept provides an underlying connectomic visualization that is not obscured by the standard anatomical structure. That is, visualizing connectivity information within an anatomical representation of the brain can potentially limit one's ability to clearly understand the complexity of a human brain connectome; some meaningful structural patterns may be much easier to see in topological space. The intrinsic geometry approach relies on the intuition that the brain's intrinsic geometry should reflect graph properties of the corresponding brain connectivity matrix, rather than the inter-regional Euclidean distances in the brain's physical space.

2.1 Data Acquisition and Intrinsic Geometry Reconstruction

We gathered the data we used for the development of *BIGExplorer* from 46 healthy control subjects (HC, mean age: 59.7 ± 14.6, 20 males). The study was approved by the Institutional Review Board and conducted in accordance with the Declaration of Helsinki. Resting-state functional MRI data were also acquired on 15 patients diagnosed with bipolar depression and 10 healthy controls. To obtain the intrinsic geometry of the brain, we generated individual structural brain networks for each subject using a pipeline reported previously by GadElkarim et al. [10]. First, diffusion weighted (DW) images were eddy current corrected using the automatic image registration (AIR)



(a) MDS Space (b) Isomap Space (c) tSNE Space

(d) MDS Space (e) Isomap Space (f) tSNE Space

Figure 3. In these figures we present the different shapes the structural connectome assumes in topological space when different dimensionality reduction techniques are applied. With any reduction of data from a higher dimension to a lower one some information is lost, and so *BIGExplorer* enables users to investigate intrinsic geometries resulting from different techniques in order to explore the different topological spaces that may shed light on a particular connectome dataset. The screenshots are taken from different points of views and the colors represent different lobes of the brain.

tool embedded in DtiStudio software.[1] This was followed by computation of diffusion tensors and deterministic tractography using fiber assignment by a continuous tracking algorithm [21].

Functional connectomes were generated using the resting state fMRI toolbox, CONN.[2] In brief, raw EPI images were realigned, co-registered, normalized, and smoothed before analyses. Confound effects from motion artifact, white matter, and CSF were regressed out of the signal. Using the same 82 labels as the structural brain networks [9], functional brain networks were derived using pairwise fMRI signal correlations.

These 82 anatomical regions were then further subdivided using an algorithm that continuously bisected each region across all subjects at an identical angle until the average region size reached a certain threshold. Previous studies using similar algorithms have shown that up-sampling regions into higher-resolution voxels maintains network connectivity [13]. The resulting data converted 82 regions into 620 sub-regions for structural data and 739 sub-regions for functional data. Brain networks formed by either the structural fiber connections or the functional correlations between up-sampled cortical/subcortical gray matter regions were generated using an in-house program in Matlab. These up-sampled regions were also re-registered to original cortical regions in preparation for nonlinear dimensionality reduction. All networks were examined to ensure that all regions were directly connected to at least one other region preventing the formation of any isolated "islands". To compensate for inter-subject variations, we averaged individual subjects' networks together to obtain a group average network.

Computing Shortest Paths. To construct graph distances, we performed different actions according to the kind of connectome we were dealing with. For the **structural** connectome, edge lengths are assumed to be the numerical inverse of fiber counts. To compute the shortest paths, we use Dijkstra's algorithm [8]. By iterating the algorithm over the entirety of the network, this produces a new network based on effective cost of travelling from any node i to any other node j. It should be emphasized again that at this key step, instead of inter-regional Euclidean distances (i.e., the Cartesian coordinates) in the brain's physical space, the graph distances are used as the input for the dimensionality reduction algorithms. For the **functional** connectome, after we obtained the functional correlation between regions [7], edge lengths are assumed to be as follows:

$$distance_{i,j} = log(\frac{1}{|r_{i,j}|}) \quad (1)$$

where $r_{i,j}$ represents the correlation coefficient between region i and j. Note that Equation 1 dictates that nodes that show completely coupled fMRI activities (i.e., a correlation of -1 or 1) have a graph distance of 0, consistent with intuition. We compute this value for each node pair to obtain the adjacency matrix. Figure 2 shows the adjacency matrices before and after these transformations are applied.

Constructing D-Dimensional Embedding. To promote uniformity throughout the analyses, we used the dimensionality reduction toolbox introduced by van der Maaten for all reductions [29]. Values were increased iteratively for Isomap in order to make sure that all points were included in the manifold building. This created the coordinates for all the up-sampled regions of interest so that they could be visualized using the tool described in Section 5. Figure 3 shows the shape of the intrinsic geometry for our group average structural connectome using isomap, MDS, and t-SNE reduction techniques.

[1] `http://www.mristudio.org`

[2] http://www.nitrc.org/projects/conn

3 Approaches to Connectome Visualization

Many approaches to visualizing the connectome have been presented and, broadly speaking, three main types have emerged: node-link diagrams, matrix representations, and circular layouts. The *Connectome Visualization Utility* [19], the *Brain Net Viewer* [33], and the *Connectome Viewer Toolkit* [11] each provide a 3D node-link representation. In these tools, the dimension of the nodes is bound to a graph-based metrics, like nodal strength or nodal degree, while the weight of the edges is displayed using different colors or by changing diameter of the cylindrical link. Less recent studies on functional brain connectivity instead utilize 2D node-link diagrams [24]. The main advantage of using node-link diagrams is that they provide an overview of the entire graph that makes it easy to understand which nodes are indirectly connected. The 3D versions additionally provide meaningful spatial information, and the tools that utilize 3D node-link diagrams locate the nodes relative to the real anatomical position. However, when the graph and the number of edges increase, the cleanliness of the visualization is affected and the view becomes less clear and less understandable.

Other approaches to visualizing the connectome are included in tools such as the Connectome Visualization Utility [19] and the Connectome Viewer Toolkit [11]. Both of these use adjacency matrices to represent connections. Additionally, the former also includes a circle layout view. This view, also known as a *connectogram* was first introduced by Irimia et al. [15]. A connectogram displays brain regions around a circle, and the interconnections between them are represented as edges that connect regions together inside the circle. Transparency is used to represent the weight of the edges, which reduces the visual clutter and highlights only on strong links, while weak edges fade into the background. By using connectograms it is possible to incorporate additional information adding more than one nested circles; the outermost circle can be used to represent the cortical parcelations, while the inner circles could use heat maps to display different structural measures associated with the corresponding regions. This approach mitigates the clutter that can occur in other approaches when the number of edges and nodes increases.

Each of these tools and the approaches they take to representing the connectome have their own strengths and weaknesses. A main drawback of each of them is their static nature. To the best of our knowledge, there are no effective tools that enable a user to interactively investigate the intrinsic geometry of connectome data, and none that allow a user to apply and visualize complex transformations to connectome datasets. To address these issues, *BIGExplorer* uses an interactive 3D node-link diagram to visualize connectome data.

4 Tasks

Visual analysis tasks are an important component of research in scientific and medical domains that make use of neuroimaging. A cardinal rule amongst neuroimaging researchers is to "always inspect your data visually" [22]. Tasks relevant to the visualization of connectome data can be said to fall into three main areas: exploration, comparison, and identification.

Due to the high complexity of the human connectome, simply being able to *explore* the data to support sense making is a fundamental task. However, a researcher typically has a well defined assumption about the contents of their data and a clear idea about which aspects of the data he or she wants to explore. Effective exploration involves being able to find relevant information quickly, filtering the data in order to identify patterns, to assist in the generation of new hypotheses, or to confirm or invalidate expected results.

Researchers often need to examine multiple datasets in order to *compare* the structure or activity of one region of a brain with another, or to compare different populations or experimental conditions. For example, a psychiatric researcher could be interested in understanding the differences between the functional connectivity of healthy controls versus depressed participants. Individuals with depression show a higher functional connectivity between the regions within the default mode network than in healthy controls [12]. Being able to visually distinguish details about the different activity levels within specific brain regions is necessary to support a deeper understanding of these pathologies, as well as to verify experimental results and enable the generation of new hypotheses.

To this end, neuroimagers may also need to *identify* the importance of regions that can be directly or indirectly affected by damage to the brain, such as in the case of traumatic brain injury [18]. It is also important to understand the structural and functional implications of neurosurgical interventions such as temporal lobotomy [1], or as a predictive measure towards behavioral therapy outcomes for use in aphasia treatment [20, 30]. Lastly, experts are interested in identifying culpable regions when investigating neuro-degenerative disease and neuropsychological disorders such as Alzheimer's [6, 35] and schizophrenia [5] among several others. We argue that having both neuroanatomical and intrinsic structure /function topological representations allows researchers to more comprehensively address these complex issues.

5 The *BIGExplorer* Application

In this section we describe the *BIGExplorer* application for exploring the intrinsic geometry of the human brain connectome, both in terms of our design choices and the main functionality.

5.1 Design Decisions

Each of the main design decisions are influenced by the need to effectively enable the domain tasks delineated in the previous section. The primary layout for the application is a 3D node-link diagram, motivated by researchers interest have in understanding the brain's *intrinsic geometry*. The position of each region in the *topological space* is highly relevant in this context. Although many visualization researchers have noted some potential pitfalls in making use of 3D representations for visual analysis tasks, the importance of being able to compare the anatomical geometry with the different intrinsic geometries necessitates this layout. When viewing the intrinsic geometry, the individual nodes represent different brain regions and are represented with circular glyphs, while edges representing a functional or a structural connection between these regions are displayed using lines.

A main concern with the use of node-link diagrams is the potential for visual clutter when displaying a highly interconnected graph, such as the human brain connectome. Instead of showing all the connections simultaneously, by default *BIGExplorer* only shows nodes, hiding all links unless explicitly required. Through interaction, users are able to display or hide connections according to their preferences and current needs. We also allow the user to choose to view the connections only within a particular sub-graph that is relevant for a particular task. This edges-on-demand technique allows exploration tasks to be performed by showing only the connections starting from a specific region that is currently being interrogated. The user can pin the connections in the scene just by clicking on the node itself. We use varying degrees of transparency to visually encode the strength of edge weights. Stronger connections are then represented using opaque lines, while weaker edges are more transparent. Transparency is scaled relative to only the currently displayed edges.

Information about which hemisphere particular nodes belong to can be meaningful for particular tasks. Being able to understand quickly whether or not global right/left symmetric patterns are still recognizable in the intrinsic geometry also helps the domain experts by providing an anatomical reference during the exploration of the intrinsic geometry. We represent nodes from hemispheres using two different glyphs, circular and toroidal.

Colors are used to highlight the neuroanatomical membership of each node in the brain. In our application, each glyph belongs to one of the 82 neuroanatomical regions as defined by Freesurfer [9]. However, the data structure is flexible enough to accept any membership or affiliation structure. Currently, these affiliations are hard-coded by default, but *BIGExplore* has the ability to compute affiliations on the fly according to specific graph metrics.

5.2 Analytics Features

BIGExplorer enables a range of user interactions to support visual analysis, including the ability to:

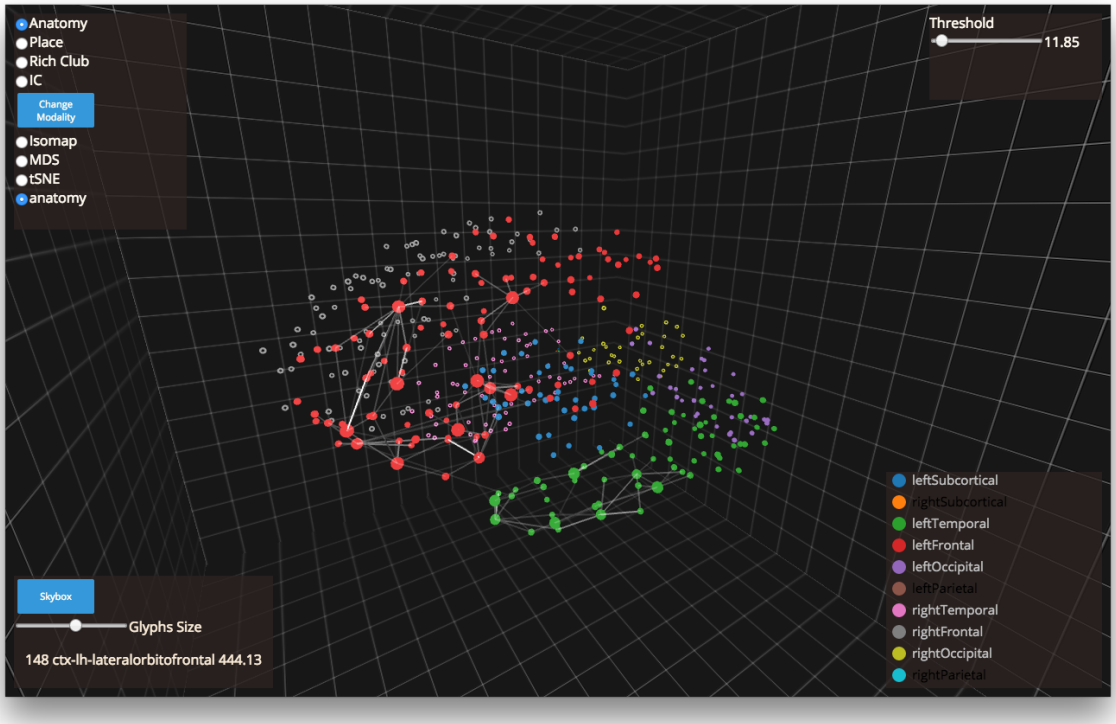


Figure 4. This figure shows the main view of *BIGExplorer*. On the upper left a simple menu allows users to choose the way nodes are grouped (color encodings) and the topological space in which we visualize connectome data. On the upper right a slider sets the minimum edge weights for an edge to be visible. On the bottom left the name of the node selected and its nodal strength are showed. We also allow users to change the size of the glyphs and to hide/show the 3D grid in the background. On the lower right, a figure legend mapping each color to its neuroanatomical label is shown. The connectome visualization is displayed at the center of the scene.

- create the shortest path tree rooted in the node selected by the user;
- visualize the shortest path between the two nodes;
- let the user turn on and off particular regions;
- let the user quickly switch between different geometries;
- compute the nodal strength for each node of the graph.

We use Dijkstra's algorithm [8] to create the **shortest path tree**. In structural connectomes, since the adjacency matrix defines the number of reconstructed white matter tracts connecting two regions, the edge length is set to the inverse of the fiber count (the higher the number of tracts, the more coupled two nodes are and thus the shorter their distance is). From a mathematical point of view:

$$d(i,j) = \frac{1}{w_{ij}} \tag{2}$$

where $d(i,y)$ is the distance between node i and node j and w_{ij} is the weight of the edge which links i and j contained in the adjacency matrix. This is a novel feature for a connectome viewer tool; at the time of this writing, no tools provide this functionality. The user can filter the shortest path tree according to two different measures: graph distance and number of intermediate nodes or "hops." In the first case the user can filter the tree according to the relative distance with respect to its farthest node. Given a threshold t, all the nodes that satisfy the following inequality are drawn:

$$\begin{cases} d(r,i) \leq maxDistance(r) \cdot t \\ 0 \leq t \leq 1 \end{cases} \tag{3}$$

where r is the root node, i is the node considered, $maxDistance(r)$ is the distance between the root node and the farthest node, and t is the threshold chosen by the user. If $t = 0$ then only the root node is displayed, while if $t = 1$ the entire shortest path tree is drawn. In the latter case, the user is able to filter out nodes that are not reachable within a certain number of nodes from the root.

The **shortest route between nodes** is relevant as well. This feature enables the user to select two specific nodes in order to show the shortest path between them. In this case, we display all the nodes in the network to provide the overall context of this sub-graph.

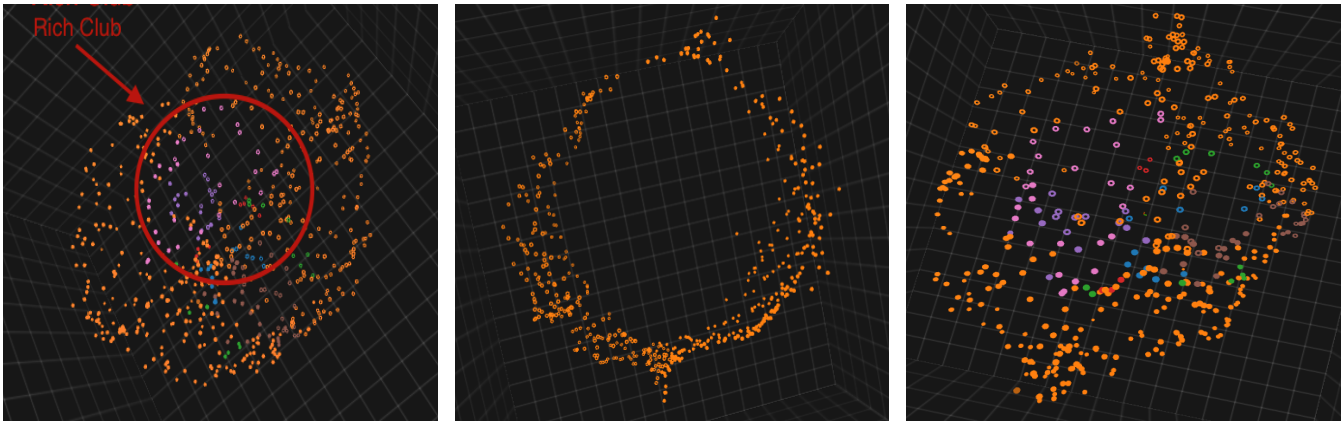
Being able to **select regions** is also important. The number of nodes displayed could affect the visual clutter of the display. We let the user choose whether to display or not groups of nodes depending on their affiliations. Thus, neuroimagers can explore only the regions that are strictly relevant to their research goals.

A main feature of *BIGExplorer* is the ability to **switch between geometries**. We provide a menu to select the space they want to explore. Switching geometries can be done with just one click, allowing the users to see how the connectome data appears embedded in different topological spaces.

Nodal strength is a graph-based metric which defines the *centrality* of a node. The nodal strength is defined as follows:

$$nodalstrength_i = \sum_{j=0}^{N} w_{ij} \tag{4}$$

where N is the number of nodes in the graph and w_{ij} is the weight of the link between i and j [23]. This graph-based metric helps experts to understand the relevance of a node in the network. This value is presented in a numerical label that appears when a node is interacted with; the user can filter out nodes below a particular threshold according to this measure.



(a) Complete Structural Connectome (b) Structural Connectome Without Rich Club (c) Random Regions Removed

Figure 5. This figure compares the complete structural connectome, Figure (a), and the structural connectome when nodes with the colored *Rich Club* property are removed, Figure (b). By comparing (a) and (b), it is very clear that without the rich club nodes, the intrinsic geometry of the brain becomes diffuse and nodes are less coupled to each other. Rich club regions form the core of the brain's structural connectome. These results are put in context when we consider Figure (c). Figure (c) shows a connectome after an equivalent number of nodes to *Rich Club* nodes were randomly selected and removed. It is clear there are subtle differences between the (a) and (c) but no gross changes to the structure as with targeted *Rich Club* removal (b). Put together, these simulated region removal analyses confirm the importance of *Rich Club* nodes.

5.3 System Details

BIGExplorer is written in *Javascript* using the *threejs* library,[3] an open source wrapper for the hardware accelerated graphics functionality provided by *WebGL*.[4] BIGExplorer was designed to be fully compatible within a virtual reality environment. Although outside the scope of this paper, our initial investigations lead us to believe that a more interactive and engaging immersive environment could help experts to understand connectome datasets more deeply. Presently, BIGExplorer can be also used with the Oculus Rift device.[5] The code is open source and publicly available at the authors' code repository.

6 Case Studies

In the following section, we present real-world case studies for both the functional connectome and the human connectome.

6.1 Case Study 1

We wanted to understand how the structure of the brain changes when specific regions of the brain are removed. In particular, we wanted the see the differences between a complete structural connectome and a connectome in which nodes belonging to the *rich club* were removed. The basic concept behind the rich club property is the tendency for nodes with high nodal strengths to form tightly interconnected groups [34]. Mathematically speaking, given a graph N and the parameter k which defines a nodal strength cut off, the rich club property is defined as

$$\phi(k) = \frac{2E_{>k}}{N_{>k}(N_{>k}-1)} \tag{5}$$

where $E_{>k}$ is the number of edges in N between the nodes of nodal strength greater or equal to k and $N_{>k}$ is the number of nodes in N with nodal strength greater or equal then k. This metric could also be seen as follows:

$$\phi(k) = \frac{E_{>k}}{\binom{N_{>k}}{2}} \tag{6}$$

Given that, $\phi(k)$ is the number of realized edges ($E_{>k}$) normalized with respect all the possible edges there could be between these nodes in a complete graph.

[3] http://threejs.org
[4] http://webgl.com
[5] http://oculus.com

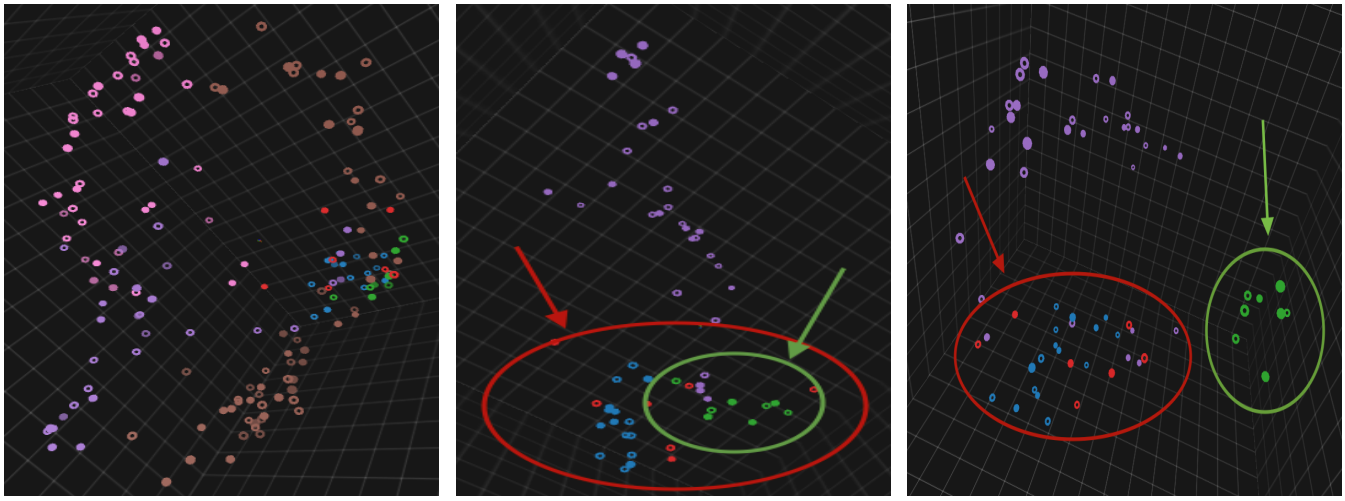
From Figure 5 it is possible to see that the complete structural connectome forms a shape similar to a "bowl", while the connectome without rich club nodes shows a big "hole" in the middle. It is clear that those rich club nodes keep the entire network tightly interconnected. When they are missing, the remaining brain regions are more distant from each other, becoming less correlated and less coupled together.

Those differences gain particular relevance as we consider a different simulation. Instead of removing the nodes that were shown to have a particular characteristic (i.e. the rich club property), we also performed a random nodes removal using a uniform probability distribution and removing an equivalent number of nodes. As we can see from Figures 5(a) and 5(c), the differences between the complete structural connectome and the one with random removal are not significant. Thus, this result validates the importance of rich club nodes.

6.2 Case Study 2

Functional MRI has been widely used to study neural tasks, but a growing subset of fMRI is being dedicated to the *default mode network* (DMN) or how the brain responds when no external stimuli or task is given. The main feature of DMN function is strong interregional coordination of baseline oscillatory activities between its participant nodes. Core DMN brain regions are the ventromedial and dorsomedial prefrontal cortex, the posterior cingulate, the precuneus, the lateral temporal cortex and the hippocampus. Our results show that in depression (Figure 6) there is strong coupling between the precuneus and hippocampus in the resting-state topological space, in line with extensive evidence supporting the involvement of these two regions in DMN functional organization [3, 32].

When using the *BIGExplorer* to explore the DMN in the averaged brain of 10 healthy controls and the averaged brain of 15 subjects with depression, an insight clinicians had when they looked at the functional connectome is the differential patterns of interaction between the hippocampus, thalamus, and putamen. They found that within the control participants these regions tended to be mixed together, suggesting functional coupling. By contrast, in the depressed participants cohort, the hippocampus and the thalamus demonstrated a tend towards separating from the putamen, creating a separate cluster that is closer to the precuneus. This behaviour is clearly visible in Figure 6. Previous literature supports this idea of tight clustering of the hippocampus and thalamus regions in depressed patients, more so than healthy controls [12]. This could be a unique signature for major depression and



(a) Functional Connectome (b) Healthy Subjects (c) Depressed Subjects

Figure 6. This figure compares the intrinsic topology of the functional connectome in healthy versus depressed subjects. In Figure (b) it is clear that the hippocampus and thalamus regions (blue and red nodes) tend to create a cluster apart from other regions. On the contrary, in healthy subjects the same regions are mixed together with putamen regions (green nodes).

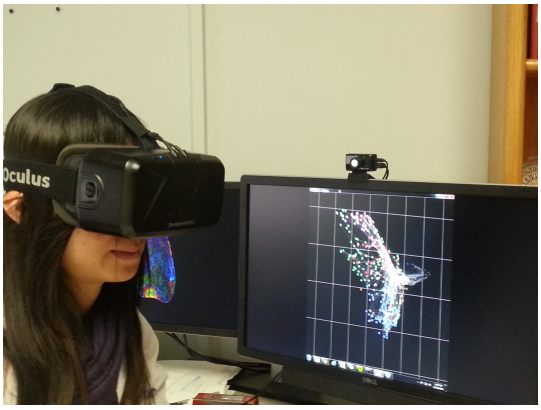


Figure 7. A photo of a neuroimaging researcher exploring the intrinsic geometry of the brain with the *BIGExplorer* application in immersive 3D using an Oculus Rift headset.

offers some insight into the behaviour of depressed subjects, especially their tendency to ruminate on their past and unsuccessful life events.

6.3 Discussion

Since in the intrinsic space spatial vicinity equates to stronger connectivity, the user is able to explore freely and easily the terrain of brain connectivity, either functional or structural. Indeed, the real advantage of exploring in the intrinsic space (especially when coupled with virtual-reality technology), is the ability for experts to understand the connectivity relationship among a number of brain regions, as neuroimagers unfold complex high-dimensional connectivity data into easily understandable and relatable configurations in 3D. This is evident in the resting state fMRI case study where the default mode network (DMN) connectivity alterations in regions including precuneus and hippocampus can be easily appreciated. Experts also think this tool transforms connectivity matrices in an engaging and easily digestible way. By converting fiber count or functional connectivity into a distance measure, this visualization software creates a "road map" of the human brain. While the actual connectivity matrix can be parsed—much like knowing the distance to any stop of a road trip— it is hard to comprehend these strict numerical quantities without a map to help guide relative locations. *BIGExplorer* allows for such an appreciation to occur and provides methods for interacting with individual nodes to discover highly integrated circuits in both functional and structural connectomes. Moreover, by inducing virtual lesions, one can compare the relative importance of certain brain regions and graph theoretical metrics by the subsequent changes in the visualization's topographical shape.

7 Conclusion and Future Work

This paper introduced *BIGExplorer*, a novel visualization application that enables a user to interactively explore the human brain connectome. Being able to select edges on demand allows users to explore the entire connectivity network while limiting the visual clutter typical of highly connected node-link diagrams. Moreover, the analytics tools provided by *BIGExplorer* make it easier to investigate the most relevant parts of the network according to the users current goals. Additionally, it enables users to view and compare the intrinsic geometry of connectome datasets in a number of different topological spaces in order to enable new understandings of the data.

Although, as described in Section 6, *BIGExplorer* has enabled us to explore the intrinsic geometry of the brain and to make interesting medical insights, there are still many aspects of the application that we want to improve. For instance, it would be useful to allow users to add or remove nodes interactively and then apply dimensionality reduction techniques directly to only the currently visible nodes. We also plan to continue our investigation into the use of virtual reality systems. One current exploration involves combining the Occulus Rift and Leap Motion[6] devices together to enable gesture interaction within an immersive environment to enable a more engaging exploration with the brain's intrinsic geometry. Finally, we are very excited about the potential utility of immersive connectome visualization as part of a biofeedback process that can provide users with the ability to see and control their connectome. Currently, we can use the DTI and fMRI data to track long term changes in the brain and follow macroscale neuroplastic changes within the brain. Due to the flexible nature of the inputs into *BIGExplorer*, a future goal is to also map changes to the connectome using electroencephalography (EEG) and provide feedback in real-time to patients to promote changes in the brain through treatment.

[6] https://www.leapmotion.com

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