Visualizing Connectomes Elucidated from Dimensionality Reduction in an Immersive Virtual Reality Environment (CAVE2™)

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Target audience – Members of the MR community who are interested in novel methods and technologies for interpreting and visualizing connectome data based on diffusion tensor MRI and tractography.

Purpose – Complex interactions between different regions of the brain have necessitated the development and growth of the field of connectomics. The brain connectome is typically mathematically represented using connectivity matrices, which describe either structural or functional interaction among different brain regions. Most current connectome study designs - based on brain connectivity matrices - involve the computation of summarizing statistics on a global or nodal level.[1] However, current methods visually represent this data using somewhat arbitrary or heuristic methods.[2] In this study, we attempt to fundamentally address this issue by proposing a novel framework that realizes the intrinsic complexity and geometry of a brain network. To this end, we posit that dimensionality reduction techniques coupled with new visualization technologies may be optimal for properly exploring the brain's intrinsic connectivity patterns. Thus, we propose to use the CAVE automatic virtual environment (CAVE2™), a 24 feet wide, 8 feet tall, large scale state-of-the-art hybrid virtual reality environment[3]. When compared to conventional neuroimaging visualization technologies, the CAVE2 environment has several advantages, namely, stereoscopic viewing, multi-dimensional capability, and the ability to interact real-time with neuroimaging data in an immersive manner.

Methods – Forty-six healthy control subjects (HC, 20 male/26 female; age: 59.7 +/- 14.6) were scanned on a Philips 3.0T Achieva scanner (Philips Medical Systems, Best, The Netherlands) using an 8-channel SENSE head coil under an approved IRB protocol. DTI images were acquired with a single shot EPI sequence (FOV = 240 mm; voxel size = 0.83 x 0.83 x 2.2 mm; TR/TE = 6,994/71ms; Flip angle = 90^o). Sixty seven contiguous axial slices aligned to the anterior commissure–posterior commissure (AC-PC) line were collected in 32 gradient directions with b=700s/mm^2 and one acquisition without diffusion (B0 image). We then generated structural brain networks using several steps: correcting for eddy currents followed by the computation of diffusion tensors and deterministic tractography using the fiber assignment by continuous tracking algorithm.[4] T1-weighted images were used to generate label maps using the Freesurfer software (http://surfer.nmr.mgh.harvard.edu). These 87 Freesurfer ROI labels 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. For testing purposes, we chose thresholds of 1500 voxels and 800 voxels, which upsampled ROIs by ~5 and ~10 times, respectively. The resulting data converted 87 regions into 412 and 770 sub regions for the two parameters we tested. 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 all 46 brain networks to obtain a group average network. Next, using the Dijkstra algorithm, we created the graph distance matrix of the average network[5]. Using this graph distance matrix we explored brain's intrinsic geometry by feeding these distances into dimensionality reduction algorithms[6] including MDS, Isomap and t-SNE. For the sake of space in this abstract, we will only present Isomap results.

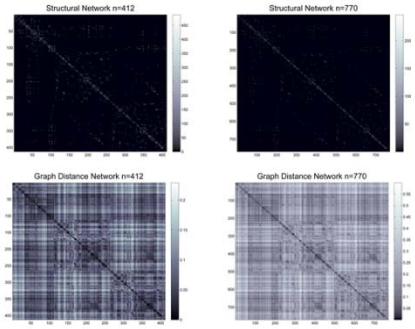

Figure 1. Connectivity matrices for n=412 and n=770 nodes for both structural networks and for graph distance networks.

Results and Discussion– Figure 1 shows the results of structural networks and their corresponding graph distance matrices. These were the starting point for all of our dimensionality reduction techniques. By using graph distance between regions as inputs, we are able to obtain unique and intrinsic structures of the brain based on tractographic information alone. In order to relate the computed intrinsic geometry to the original neuroanatomical space, we compared the nodal path length, between any two regions, to their Euclidean distance in the anatomical space (the Cartesian distance) and the Euclidean distance in the Isomap space. These results are plotted in figure 2, showing that the Euclidean distance in the Isomap space better corresponds to the graph distance (i.e., intrinsic) than the Cartesian or extrinsic distance (r=.4691 versus .7473). Furthermore, we examined the location of "rich club" regions[7] of the brain (these are regions that exhibit high interconnectivity with each other as well as with other non-rich club regions in the brain). We observed the rich club located in the center of our recreated Isomap space as expected. Finally, we implemented these structures in CAVE2, thus allowing us to visualize connectome data in a novel 3D immersive manner. This point cannot be under-emphasized as true stereoscopic assimilation of brain data allows for greater comprehension of relationships between regions in new dimensionality reduced structures. CAVE2 also allows us to view higher dimensions by introducing higher degrees of freedom such as Euclidean position, color, opacity, shape, etc., freeing an even greater amount of separation between regions of the brain.

Conclusion – We propose a novel framework for exploring the intrinsic geometry of brain networks. Using such techniques, we posit that researchers in the future will be able to deduce white matter pathologies in the brain by observing an alteration in this intrinsic geometry with novel visualization technologies such as CAVE2. The present work consists primarily of methodological development, and although applied to a dataset of human subjects remains relatively qualitative in nature. Future work will include the further development of necessary mathematical and statistical theories for group and/or longitudinal studies.

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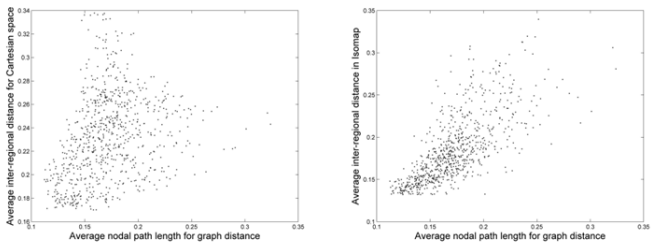

Figure 2: This figure compares the average nodal path length versus the average inter-regional Euclidean distance in the physical Cartesian space (r = 0.4691) and Isomap space (r = 0.7473), right, for all 770 nodes.

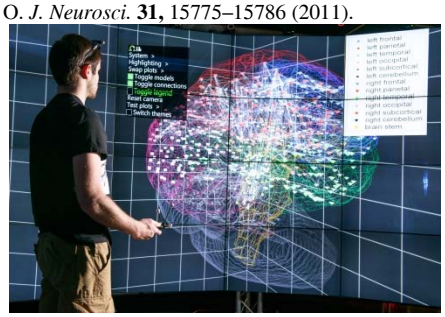

Figure 3: An example of the immersive 3D scope of CAVE2.