

Simultaneously Probing Functional and Structural Brain Connectivity in Real-time

Fibernavigator: An Interactive Tool for Brain Visualization

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1 OBJECTIVES

The human brain can be viewed as a collection of parallel networks. Those highly specialized networks can be conceptualized to as a set of nodes (gray matter functional areas) linked together by edges (for example white matter axonal structure). Functional MRI (fMRI) can provide 4D whole-brain images that indicates changes in cortical blood flow, volume and oxygen ratio as well (Blood-Oxygenation-Level-Dependant or BOLD signal) caused by cerebral activity across time (Bandettini et al. 1993; Kwong et al. 1992; Turner 1992). The spontaneous low fluctuations (< 0.1 Hz) present in the BOLD signal allow the detection of temporally correlated spatial patterns, also known as Resting State Networks (RSNs) when the brain is at rest (Biswal et al. 1995; Damoiseaux et al. 2006). A common method of obtaining those networks is to extract the BOLD time course from an a priori region of interest (ROI) and perform the temporal correlation with all other voxels of the brain. The result is a correlation map or a functional connectivity map based on the location of the seed ROI.

Some have proposed a tool for voxel-wise brain connectivity visualization but it often requires the pre-calculation of a correlation matrix to be held in memory (Dixhoorn 2012). Great effort was also made towards GPU implementation of functional connectivity exploration (Eklund et al. 2011) However, the proposed software restrict the user from placing their reference ROI directly into the 3D space which greatly reduces the level of interactivity. Another tool was proposed for neurosurgical application which quickly allows the user to interrogate data for pre-surgical planning

(Böttger et al. 2011). Here, the user is forced to move the ROI solely on 2D anatomical slices, thus only revealing activations present on those selected slices.

In this work, we propose an interactive tool for the exploration of functional connectivity in a fully 3D fashion, which can be coupled with our existing real-time fiber tracking module inside the *Fibernavigator* (Chamberland et al. 2014). Using a healthy volunteer dataset, we qualitatively demonstrate how both functional and structural modules can be merged together for efficient brain mapping exploration.

2 METHODS

Our new real-time functional exploration tool is implemented on CPU and runs on a single core computer, which does not require any specific hardware. It works on any functional data (e.g resting-state) that is preferably pre-processed. For anatomical reference, the user has to first load a subject-specific T1-weighted image. By placing a ROI in the 3D environment, one can instantaneously activate the functional correlation module while dragging the ROI everywhere in the brain. The mean signal is first extracted from the voxels encompassed by the ROI, and then statistically compared to the rest of the brain. The correlation coefficient (CC) between voxels x and y is denoted as:

$$CC = \text{cov}(x,y)/\sigma_x\sigma_y \quad (1)$$

where $\text{cov}(x, y)$ is the covariance of any two signals and σ_x σ_y are the standard deviation of the time series. CCs are then converted to z-scores and

rendered at each voxel as small particles like in the following OpenGL example:

```

glEnable(GL_BLEND) //Activate blending
glBlendFunc(...) //Blending function
glEnable(GL_POINT_SPRITE) //Render ON
glPointSize(size * z_Score) //Pt size

glColor4f(r, g, b, alpha * z_Score)
glBegin(GL_POINTS)
    glVertex3f(x, y, z) //3D points
glEnd();
glDisable(GL_POINT_SPRITE) //Render OFF
glDisable(GL_BLEND) //Deactivate blend

```

To reduce cluttering, the opacity (alpha) of each particle is weighted by its z-score value. A transfer function is also responsible for the mapping between z-scores and color display (using a hot colormap). Interactive z-threshold and cluster-level sliders are also available for visualization purpose. Finally, the user can save and export the generated activation map into a 3D nifti file. As one can see, the computation step is performed in the native space (i.e fMRI space) while the rendering stage is done at the anatomical level (T1-space) using the transformation matrix coming from fMRI-T1 registration of the datasets.

2.1 Datasets

Continuous functional recording was carried out on a Siemens 1.5 Tesla (T) imaging system using a standard echo-planar imaging (EPI) sequence. 35 axial slices were obtained with a 64 x 64 matrix, TR/TE 2730/40 msec, for a voxel size of 3.4 x 3.4 x 4.2 mm. Diffusion data was acquired using a single-shot echo-planar (EPI) spin echo sequence (TR/TE = 11700/98 ms, GRAPPA factor 2), with b-value of 1000 s/mm² and 64 uniform directions (128 x 128, 2 mm isotropic spatial resolution, upsampled to 1 mm³).

3 RESULTS

Figure 1 illustrates the functional connectivity tool on its own. It shows the well-known “Default Mode Network” (Raichle et al. 2001) obtained by placing a 4 mm³ ROI at the junction of the posterior cingulate cortex and precuneus (z-score > 2). As one can see, the expected 4 nodes of the network are well represented, namely the medial prefrontal cortex and the bilateral inferior parietal lobes.

Figure 2 demonstrates how the functional connectivity tool can be coupled with our existing real-time fiber tracking module. A 20 x 10 x 10 mm

ROI was interactively placed in the left lateral motor cortex, revealing associated right activations (namely known as the motor RSN, z-score > 2) with underlying corticospinal tract and corpus callosum. Tractography parameters are shown in Table 1.

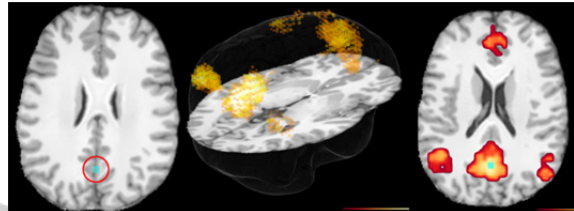


Figure 1: Default Mode Network. Left: Seed ROI (circled) interactively placed in the posterior cingulate cortex. Middle: 3D rendering of co-activated nodes. Right: 2D view of the activation map generated.

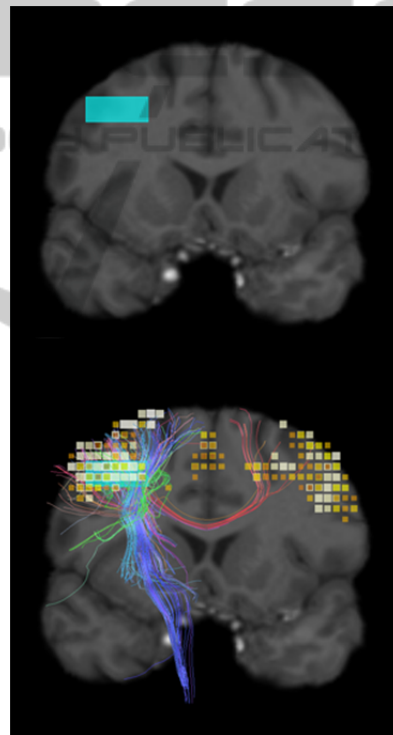


Figure 2: Motor activation and associated fiber pathway (corticospinal tract / corpus callosum). By launching seeds and CC from the ROI (blue), the user can observe a joint functional/structural network, without the need of precomputing CC matrices.

Table 1: Tractography parameters.

Step size	1.0 mm
Max. Angle (θ)	35°
Threshold	0.15 (Frac.Anis.)
Min. Length	10 mm
Max. Length	200 mm
# of seeds	500

Experimentation was done on a laptop with the following specs: System: Linux Mint 32-bit, Video card: Geforce GT 640M memory 2GB, NVIDIA Driver: 306.97, CPU: Intel(R)Core(TM) i7-3632QM @ 2,20GHz, 16GB RAM. Mean frame-per-second (FPS) ratio remained above 20 when moving the ROI in the 3D space which indicates no latency.

4 DISCUSSION

We present here a new real-time interactive feature of the *Fibernavigator* that allows fast visualization of functional and structural organization of the brain in a 3D fashion. It gives convincing results on the fly and is an important tool to better understand how connections lie behind functional networks. It can also serve as a quality assurance tool at the individual level for close inspection of data prior launching massive analysis.

Since the 2 modules work independently, it allows the user to either look at structural, functional, or as described here, combined brain connectivity. If one is interested in visualizing brain connectivity without performing real-time fiber tracking, it is possible to load a set of precomputed tracts. In this case, the ROI will serve as a selection object, only displaying streamlines that pass through it.

Finally, our real-time technique will shortly be introduced in a clinical setup and is achievable without complex GPU programming. One possible extension would be to not only initiate tractography from the draggable ROI but also launch seed from the generated functional clusters to fully visualize the total extent of the underlying network.

SUPPLEMENTARY MATERIAL

Supplementary video data showing the real-time functional tool in action can be found online at: www.youtube.com/watch?v=HmlxktmVSPA.

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