BrainMiner: A Visualization Tool for ROI-Based Discovery of Functional Relationships in the Human Brain

Klaus Mueller[1], Tom Welsh[1], Wei Zhu[2], Jeffrey Meade[1], Nora Volkow[3]

[1] Department of Computer Science, State University of New York at Stony Brook
[2] Department of Applied Mathematics and Statistics, State University of New York at Stony Brook
[3] Directorate of Life Sciences, Brookhaven National Laboratory

ABSTRACT

Brain imaging methods used in experimental brain research such as Positron Emission Tomography (PET) and Functional Magnetic Resonance (fMRI) require the analysis of vast amounts of data. Statistical methods are necessary to obtain a reliable measure of a given effect. Typically, researchers report their findings by listing those regions which show significant statistical activity in a group of subjects under some experimental condition or task. These inter-relationships can become rather complex and are best understood in the context of the underlying 3D brain anatomy. In this paper, we present a novel powerful 3D interface that allows the interactive exploration and visual mining of correlational datasets within a common stereotaxic atlas.

Keywords: Information Visualization, Statistics Visualization, Human Brain Mapping, Functional Imaging

1 INTRODUCTION

Although the human brain is no longer the black box it used to be, it is still far from being completely understood. Of particular interest are the functional relationships that exist among different regions of the brain cortex. Having a "wiring schematic" of the brain would enable us to model the effect of pharmaceuticals, environmental stimuli, trauma, diseases, psychological disorders, and many more. Brain researchers investigate and discover functional relationships of different regions of the brain by gathering evidence for these relationships in PET and fMRI studies, involving a representative number of human subjects, both under baseline conditions and under the influence of some drug (in our case Ativan). The functional correlations in the brain activity are then calculated on the basis of predefined anatomical regions-of-interest (ROIs) (for now we model these as spheres). The correlation coefficient is then employed to quantify similarity in response, for various regions during an experimental setting. To account for inter-human anatomical variability, each test subject's volumetric brain data is first transformed into a common anatomical coordinate system (e.g, Talairach-Tournoux [1]). Statistical parameters that can be used to characterize various brain functions include:

- The correlation (including the Pearson product-moment correlations, the partial correlations and the canonical correlations) matrix.
- The ROI clusters from a cluster analysis.
- The principal components (PCA) and the factor analysis (FA) output.
- Differential relationships such as the difference of two correlation matrices (to view the change of functional relationships).

The amount of statistical data that result from such analyses can be quite large, and effective tools are essential for the brain researcher to grasp and discover functional relationships quickly from the statistical data. The *BrainMiner* package currently under development at the State University of New York is a visualization tool that facilitates this task. The nature and domain of the data poses a number of challenging problems which gave rise to some interesting solutions, pertinent to the field of information visualization. To the best of our knowledge, most of these features are not present in other brain visualization software [2].

The rest of the paper is structured as follows: First, in Section 2, we will present a 2D interface that is used as a companion to the 3D interface discussed here. Then, in Section 3, we will introduce the 3D interface. We will illustrate various paradigms we have investigated with the aim of improving the visual and informative power of the three-dimensional display. Finally, Section 4 will present results and conclusions.

2 THE 2D VISUAL INTERFACE

One approach to view statistical brain relationships is by overlaying the statistically significant voxels on top of a high resolution MRI or a brain atlas and view the data as 2D slices, either in flip mode or side-by side. The 2D interface and a description is shown in Fig. 1 towards the end of this paper.

The 2D approach works well as long as the axial dimension is not important. However, the decomposition of the dataset into 2D slices for visualizing 3D relationships becomes limiting when functional relationships are widely spread over the brain. To account for the problems with the 2D approach, we have also developed (in addition to the 2D viewer) a 3D visualization interface. This is described next.

3 THE 3D VISUAL INTERFACE

The 3D visualization interface displays correlational data for each ROI along with an MRI volume as well as a digitized version of the Talairach atlas. Both can be sliced in 3 orthogonal directions and can be overlaid on top of each other. Fig. 2 is a screenshot of the Graphical User Interface (GUI) of the system, where a basic view with a few ROIs is shown.

The number of ROIs to be displayed, however, can become quite large (about 120-140), which poses challenging problems in

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the visualization task. We found that in a space too crowded with statistically significant ROIs, it becomes very hard, if not impossible, for the user to tell the 3D positions of the individual ROIs. To overcome these difficulties, a number of techniques were investigated (see Fig. 3 at the end of this paper):

- Superimposing a Talairach atlas slice (or an MRI slice) that can be slid up and down the volume. Fig. 3a shows a movable sheet that maps the slice of the Talairach atlas at the specified height. ROIs that intersect the sheet are highlighted by a ring.

- Placing a single light source above the volume in a fixed position: This provides specular lighting cues for the height and depth of each ROI sphere (see Fig. 2 as well as Fig. 3).

- Enhancing the ROIs by colored halos or coasters, where the colors code their height and depth on a rainbow color scheme (see Fig. 3b). The ROIs are connected by dashed iso-height and iso-depth lines to the MRI volume cuts which suggests the ROIs' position in 3D space.

- Projecting a colored grid of iso-lines onto the two volume cuts, again encoding height and depth in a rainbow map. Colored shadows cast onto the third exposed volume slice provide additional cues (see Fig. 3c).

- Projecting the ROIs onto the brain iso-surface, such as white or grey matter, or skin (see Fig. 3d). Since the ROIs are mostly located close to the brain surface, i.e. on the brain cortex, one can generate a comprehensive, EEG-like, view by projecting the ROIs onto the closest cortex surface and paint the projection in the correlation color.

- Grouping ROI networks into composite polygonal objects, which reduces the object complexity of the scene (see Fig. 3e). For now we simply increased the radius of the ROI spheres until they just touched. This relatively simple approach is quite effective. For the future we plan to estimate the actual hull of a set of ROIs of similar brain function and display this hull as a polymesh.

Finally, Fig. 3f shows a display with just an axial cut. The empty circles on the slice indicate the locations of ROIs with correlations outside the range selected in the legend.

4 RESULTS

To test the software and develop its capabilities, PET fluoro-18-deoxyglucose (FDG) images were analyzed and displayed for two major drug addiction studies. The first study included 30 subjects the second included 40 subjects both under baseline and drug conditions. Metabolic activity was measured for each subject as the average intensity signal for a given ROI defined manually by a trained medical doctor. ROI locations for the first study included 424 anatomically significant regions while the second study included 120 regions. Correlation matrices were generated for each of these ROI datasets. Three major statistical measures were subsequently generated given the correlation matrix for each study: (1) Principle Component Analysis, (2) ROI cluster analysis and (3) Factor Analysis. Visualization software was compiled using libraries for OpenGL, the Fast Light Toolkit (FLTK) [3], and written in C++. Versions were compiled for Irix 6.4, Windows NT 4.0 and Linux and run on an SGI O2/R1000, a Pentium II class laptop and a Pentium 233 respectively. The visualization interface displayed a 3D MRI volume representative of Talairach coordinates which was sliced as three half planes of axial, coronal and saggital views. The slices were drawn using 2D texture mapping. The user could define the slice location along these three axis by dragging each slice with a mouse button. The surface of the brain was also displayed as a polygonal mesh generated from the Marching Cubes algorithm. ROIs were drawn as spheres but were obscured by the surface

depending on the current slice locations. Correlation value was represented for each ROI as a color intensity in relation to a selected "root" ROI. A side window also displayed the current slice as either the Talairach atlas digitized or the MRI volume along with a 2D representation of the ROIs (as circles). In addition, all objects could be rotated together with the mouse (trackball interface) to provide a viewpoint from any direction.

5 CONCLUSIONS

The current system allows interactive exploration of correlational data of with both 120 and 424 ROIs on all platforms. Resident brain researchers use the system routinely in their research, and a public release is planned in the near future.

Future research will concentrate on how 3D relationships can be conveyed even better. For example, one could rock the object slightly back and forth at a user-set frequency, which would employ motion parallax as an additional depth cue [4]. Although the present implementation does allow the user to rotate the object at interactive framerates, an automatic rocking motion would free the user from the possibly distracting interaction with the mouse or joystick.

REFERENCES

[1] J. Talairach, *Co-Planar Stereotactic Atlas of the Human Brain*, Thieme:Stuttgart, 1988.
[2] see http://hendrix.imm.dtu.dk/software/brainsoftware.html for a comprehensive list of existing brain research related software.
[3] freely available at http://www.fltk.org.
[4] private conversation with Robert van Liere at NPIVM 2000.
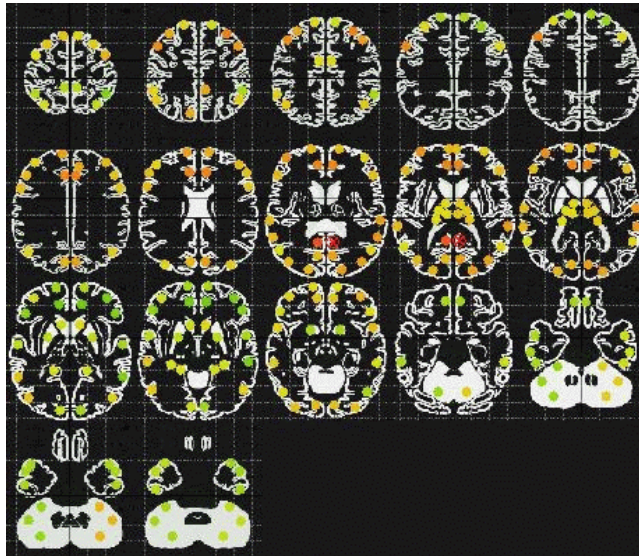
Figure 1: The 2D visual interface that complements our 3D interface. The user can move existing or define new ROIs freely. The circular ROIs are colored according to their correlation with respect to a root-ROI, marked by a red cross. A rainbow color legend is used to encode the correlations: the color blue stands for highly negative correlation and the color red stands for highly positive correlation. Green and yellow tones encode mildly negative or positive correlations, respectively. There are apparently no extremely strong correlations in the configuration shown here.
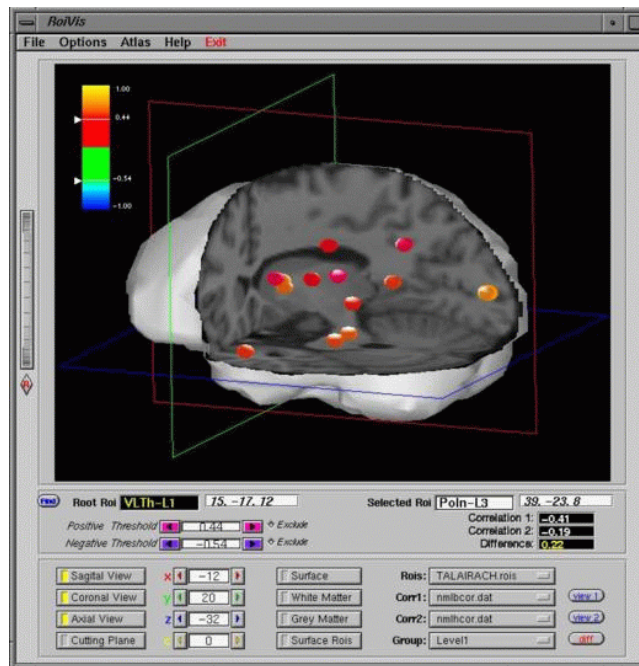
Figure 2: The 3D visual interface, along with a basic view of a small number of ROIs embedded into a cut-out area of a normalized/ standardized MRI brain. At present, all ROIs are spherical in shape. Similar to the 2D viewer, the colors of the ROIs denote the strength of the correlational relationship, on a rainbow scale. The root ROI is colored in yellow. A legend is shown on the left to illustrate the color mapping. The two pointers in the legend can be used to select the range of statistical significance. Only ROIs within that range are displayed. The GUI also allows the user to slide the cutting planes up and down and back and forth, to rotate the volume, and to select certain brain surfaces, such as white matter, grey matter, and skull to be semi-transparently superimposed. The correlation thresholds can be selected by moving the pointers in the color bar in the upper left corner of the display. When the sliders are moved, the application adjusts the color range such that the entire range of rainbow colors is always utilized. Two studies (baseline and drug) can be loaded simultaneously. The display can then be switched between three correlation matrices: those of the two loaded studies as well as the difference correlation matrix. The latter display shows the ROIs that have changed, under the influence of the drug, their statistical relationship with respect to the selected root ROI. Finally, the 2D interface discussed in Section 2 can be popped up, if so desired.
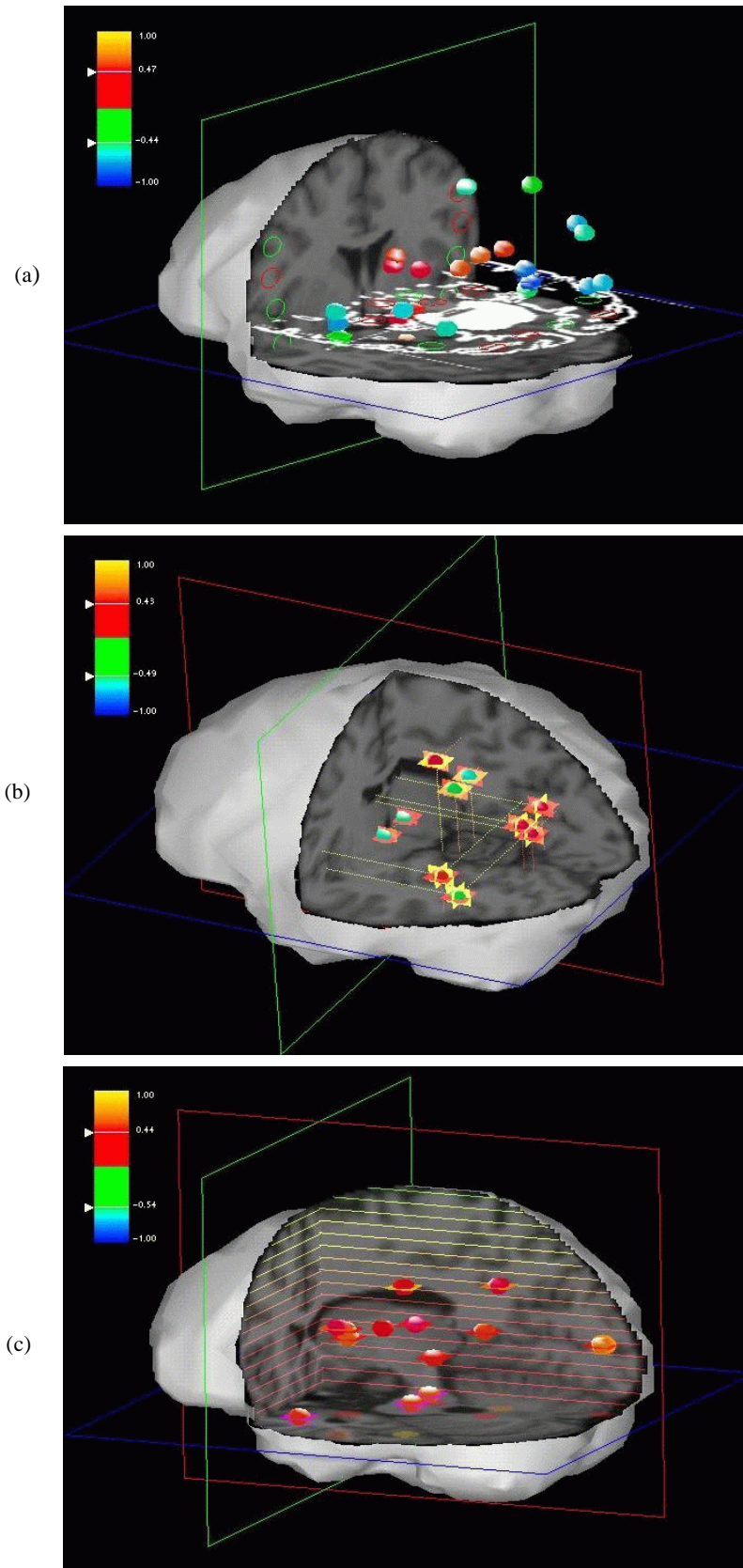
Figure 3: Screenshots of various 3D visualization paradigms of *BrainMiner*. Detailed descriptions are given in Section 3.
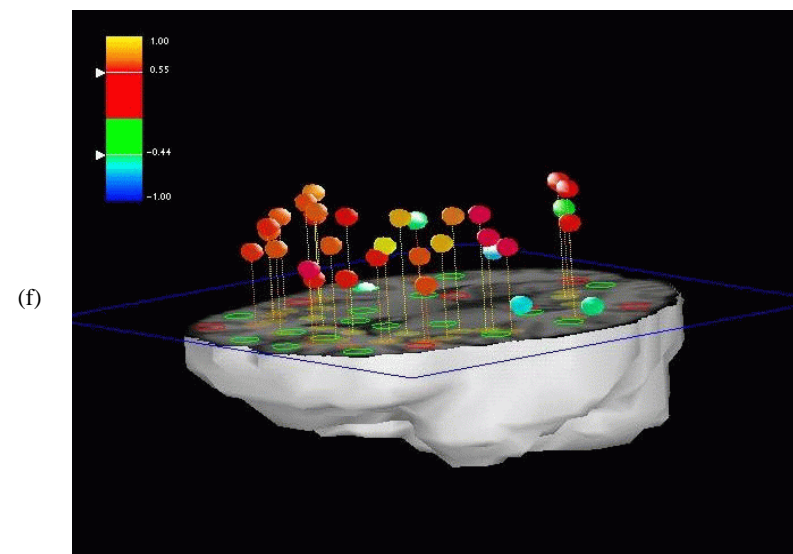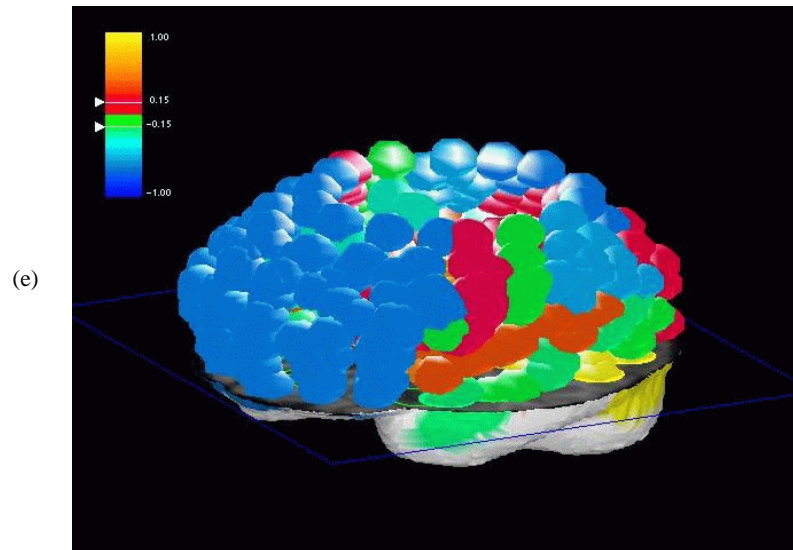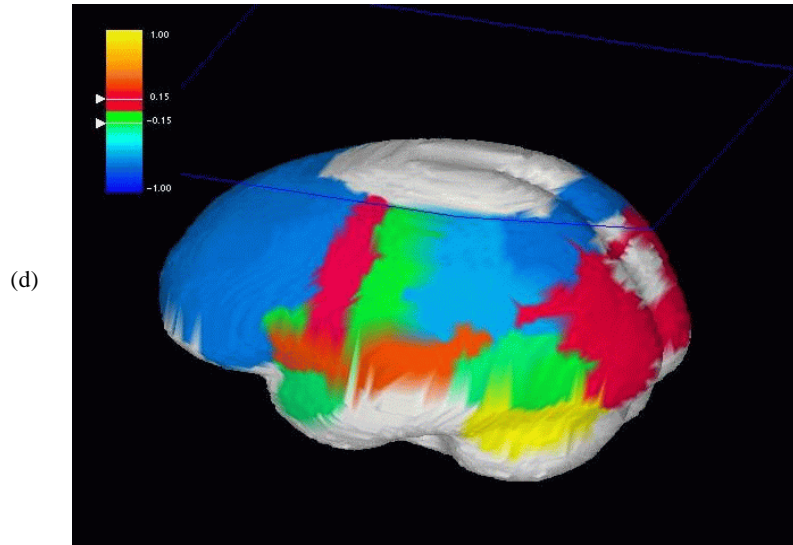
(d)

(e)

(f)

Figure 3 continued.