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## **Human Brain Mapping: Experimental and Computational Approaches**

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### **Abstract**

This is the final report of a three-year, Laboratory-Directed Research and Development (LDRD) project at the Los Alamos National Laboratory (LANL). This program development project combined Los Alamos' and collaborators' strengths in noninvasive brain imaging and high performance computing to develop potential contributions to the multi-agency Human Brain Project led by the National Institute of Mental Health. The experimental component of the project emphasized the optimization of spatial and temporal resolution of functional brain imaging by combining: (a) structural MRI measurements of brain anatomy; (b) functional MRI measurements of blood flow and oxygenation; and (c) MEG measurements of time-resolved neuronal population currents. The computational component of the project emphasized development of a high-resolution 3-D volumetric model of the brain based on anatomical MRI, in which structural and functional information from multiple imaging modalities can be integrated into a single computational framework for modeling, visualization, and database representation.

### **Background and Research Objectives**

Understanding the structural and functional organization of the human brain is one of the foremost challenges in contemporary science. The advancement of neuropsychiatric medicine and of neuroscience in the next century will require an expanded knowledge of normal brain organization and variability between normal individuals, as well as an enhanced understanding of the relationship between brain abnormalities (e.g. tumors, abnormal neuronal circuitry, neurochemical imbalances) and behavioral and psychological disorders (e.g. Alzheimer's disease, Parkinson's disease, schizophrenia). Such information will permit improved therapeutic approaches, including surgery, drug therapy, and radiotherapy.

In view of this scientific challenge, and in view of the 50 million people affected each year by neurological and psychiatric disorders and the resulting \$350 billion annual economic burden, Congress and the President declared the 1990s the "Decade of the Brain." A key component of the effort to understand normal and abnormal brain function and for developing

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effective therapeutic interventions is the need to map brain function onto brain structure: This problem is the focus of the Brain Mapping Project, national initiative of a consortium of ten federal agencies led by the National Institute of Mental Health (also including NIH, NSF, NASA, ONR, the National Library of Medicine, and DOE, among others). The goal of the initiative is a significant improvement in brain mapping capabilities by means of the integration of noninvasive brain imaging techniques with advanced computer visualization, modeling, and database techniques. The Brain Mapping Initiative is based on the recommendations of a National Academy of Sciences working group (Mapping the Brain and its Functions: Integrating Enabling Technologies into Neuroscience Research, National Academy Press, Washington, 1991).

This LDRD Program Development project accomplished both experimental and computational objectives targeted toward the Human Brain Project: (a) Experimental Objectives: to achieve significant improvements in the spatial and temporal resolution of noninvasive brain imaging techniques by combining structural MRI measurements of brain anatomy, functional MRI measurements of brain hemodynamic responses, and MEG measurements of neuronal currents; and (b) Computational Objectives: to develop high-resolution 3-D volumetric models of the brain based on anatomical MRI in which structural and functional information from multiple imaging modalities can be integrated into a single computational framework for visualization, segmentation, modeling, and representation in distributed database form.

### **Importance to LANL's Science and Technology Base and National R&D Needs**

This project contributed significantly to the enhancement of the Laboratory's core competencies in Bioscience and Biotechnology and in Theory, Modeling, and High-Performance Computing. The work helped achieve a number of Strategic Directions in the Los Alamos Strategic Plan, including Strategic Direction 5 in the Health and Biotechnologies Subsector: Significantly increase the Laboratory's basic research and technology development programs in minimally invasive diagnostics and therapeutics. The relation of this project to National R&D needs has been addressed in detail above. To summarize, the project contributed significantly to the goals of the NIMH-led Human Brain Project in which DOE is a consortium member.

### **Scientific Approach and Accomplishments**

A principal accomplishment of this project is the continued development and enhancement of MRIVIEW (Ranken and George, 1997), a computational system for the integration of structural and functional imaging modalities. MRIVIEW includes tools for reconciliation of coordinate systems from different modalities and provides capabilities for MRI

visualization in a variety of formats: 2-D multipanel "light box" displays (in a selected slice orientation); 3 orthogonal slices in a 3-D volume (engineering style isometric rendering) and slices of arbitrary orientation. The package also supports 3-D visualization in a variety of formats: surface and volume renderings employing depth cued and light source models. The system implements a volume cursor used to select locations on surfaces or within arbitrary volumes.

MRVIEW accommodates anatomical and functional imagery from a variety of sources. FMRI data can be combined with high resolution anatomy and rendered in slices, surfaces, maximum intensity projections. Computed MEG sources can be rendered as point sources, confidence intervals, or derived current distributions (Figure 1). Anatomical geometry extraction is an important capability for many of the analytical and rendering strategies supported by MRVIEW. The package provides interactive and automatic segmentation techniques based on image volume processing methods. These tools allow the precise and efficient identification of anatomical volumes and edges including the principal conductivity boundaries within the head (the inner and outer surfaces of the skull) and the surface of cortex (Figure 2).

A second important accomplishment is the development of a new approach to the electromagnetic inverse problem based on Bayesian inference (Schmidt, George, and Wood, in press). This approach explicitly addresses the ambiguity associated with the ill-posed character of the electromagnetic inverse problem. Rather than calculating a single "best" solution according to some criterion, our approach produces a large number of likely solutions that both fit the data and any prior information that is used. While the range of the different likely results is representative of the ambiguity in the inverse problem even with prior information present, features that are common across a large number of the different solutions can be identified and are associated with a high degree of probability. This approach is implemented and quantified within the formalism of Bayesian inference which combines prior information with that from measurement in a common framework using a single measure. In addition, we have applied this approach to single-time-point MEG data using a general neural activation model we constructed that includes a variable number of extended regions of activation and can incorporate a great deal of prior information on neural current such as information on location, orientation, strength and spatial smoothness. Taken together, this activation model and the Bayesian inferential approach yield estimates of the probability distributions for the number, location, and extent of active regions (Figures 3 and 4).

## Publications

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3. Gorodnitsky, I., George, J.S., and Rao, B. Neuromagnetic source imaging with FOCUSS: A recursive weighted minimum norm algorithm. *Electroenceph. Clin. Neurophysiol.* 95:231-251 (1995)
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7. Ranken, D. and George, J.S. .MRIVIEW: A Software Tool for Integrating Brain Structural and Functional Information. *NeuroImage*, Vol. 5, No. 4, p. S388, 1997.
8. Schmidt, D.M., George, J.S., and Wood, C. C.. Estimating Active Regions of Variable Extent from MEG Data. *NeuroImage*, Vol. 5, No. 4, p.S433, 1997.
9. Schmidt, D.M., George, J.S., and Wood, C. C. Bayesian inference applied to the electromagnet inverse problem. *Human Brain Mapping*, in press.

Figure 1. MRIVIEW 3-D rendering of MRI data, combined with estimates of activity derived from analysis of MEG data (represented in color).

Figure 2. MRIVIEW's segmentation capabilities.

Figure 3. Bayesian estimates (below) of simulated current sources (above) illustrating the approach's ability to identify the number, location, and relative size of regions of brain activity from MEG data.

Figure 4. Bayesian estimates of regions of activity derived from real MEG data in response to visual stimulation.

