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Title: MRI VIEW: AN INTERACTIVE COMPUTATIONAL TOOL FOR INVESTIGATION OF BRAIN STRUCTURE AND FUNCTION

Author(s): RANKEN, Douglas M.
GEORGE, John S.

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MRIVIEW: An Interactive Computational Tool for Investigation of Brain Structure and Function

Doug Ranken and John George
Biophysics Group
Los Alamos National Laboratory
Los Alamos, NM 87545

Abstract

MRIVIEW *is a software system which uses image processing and visualization to provide neuroscience researchers with an integrated environment for combining functional and anatomical information. Key features of the software include semi-automated segmentation of volumetric head data and an interactive coordinate reconciliation method which utilizes surface visualization.*

The current system is a precursor to a computational brain atlas. We describe features this atlas will incorporate, including methods under development for visualizing brain functional data obtained from several different research modalities.

1 Introduction

There is a growing need in neuroscience research for computational tools to organize, analyze, and visualize the vast amounts of new information being produced about the structure and function of the brain. Structural information can be at the level of gross anatomy, such as obtained from computed tomography (CT) or magnetic resonance imaging (MRI) [11]; or the microscopic level, such as from studies of neuronal connectivity or synaptic structure. Methods for obtaining functional information at the macroscopic level are electroencephalography (EEG), magnetoencephalography (MEG) [16, 6], and positron emission tomography (PET) [15]. At the microscopic level, numerous techniques are used to study brain function including microelectrode and optical techniques, but these are invasive procedures that are not generally applicable to human subjects.

A primary mission of the Biophysics Group at Los Alamos National Laboratory is to develop MEG as a tool for neuroscience research and clinical applications. This paper outlines some of the capabilities of MRIVIEW, a software tool originally developed to correlate measures of brain function provided by MEG with anatomical information provided by MRI. Neuromagnetic measurement techniques attempt to infer patterns of current within the brain based on noninvasive measurements at the head surface.This inverse problem is ill-posed, but it is possible to localize neural sources with reasonable accuracy by assuming that the underlying current distribution is adequately modeled by a small number of point current generators within the brain [17, 1]. Alternatively, it is possible to generate tomographic, volumetric estimates of current distribution by solving a large underdetermined linear problem [7]. Once an estimate of neuromagnetic source distribution is obtained based on MEG data, sources are mapped onto images of brain anatomy obtained with MRI. The software capabilities required for this task – primarily image processing, volume segmentation, visualization, and coordinate transformation – are also applicable to many other research methods.

2 Computing Environment

MRIVIEW was implemented using the programming language and runtime environment IDL (Interactive Data Language), a product of Research Systems Incorporated (RSI), Boulder Colorado. IDL was designed for interactive data analysis, visualization and image processing. As a programming language, IDL offers dynamic typing and high levels of data abstraction. IDL supports FORTRAN90-like syntax for specification of parallel operations, enabling the use of scalar arithmetic operators with multi-dimensional arrays, or with scalars and arrays. The language specification also provides simple methods for selecting subsets of dimensions to be manipulated in multi-dimensional arrays. A large library of data analysis and display routines is provided with IDL. Mechanisms for calling C and FORTRAN executables are also provided.

IDL can be used as an interactive command interpreter, which is useful for data exploration, one-time visualization tasks, and for software prototype development. Functions and procedures can also be compiled within IDL, allowing a software engineer to adopt a modular programming style.

One disadvantage in using IDL for software development is that the IDL environment is needed to run programs developed with IDL, requiring end-users of these programs to also have IDL on their systems. For our purposes, the disadvantages of IDL are more than offset by the increased efficiency of software development. As a development and computing tool, IDL provides powerful tools for data analysis and display in a flexible environment. It is supported on several X-Windowing platforms. MRIVIEW was developed with IDL on a Sun Sparcstation running Unix and OpenWindows, but is now also used on HP system 700 platforms.

3 System Design Criteria

MRIVIEW was designed as a precursor to a more extensive software project – a computational brain atlas. Because of this, extensibility has been a central consideration during the development of this program. MRIVIEW was also designed to be a comprehensive tool for addressing specific problems in neuroscience research and radiology. The major design criteria used in developing the MRIVIEW system are as follows:

1) The system will present MRI slice images derived from a volumetric MRI data set in standard radiological presentation format.

2) Flexibility must be provided, so that MRI volumetric datasets of different sizes or voxel resolution, or acquired with different acquisition protocols can be used with the system.

3) Volume model segmentation should be fast and easy, and efficient methods for storing segmented structures should be provided.

4) A simple method to define data coordinate transformations should be provided to allow registration of volumetric data sets.

5) Three dimensional viewing capabilities should be available, and a method for tracking three dimensional surfaces in standard radiological two dimensional views should be implemented.

6) The software should perform adequately for interactive use on relatively inexpensive general-purpose workstations.

7) The system should be extensible to new data types and to new analysis and visualization tasks.

4 System Implementation

User Interface

The user interface for MRIVIEW consists of an MRI viewing window, a series of pop-up menus, and a text window used to print messages to the user and obtain keyboard input. With the 2-D viewing and editing operations, the viewing window contains a sequence of eight consecutive slice images. When the 3-D viewing routines are used, a combination of 2-D slice images and 3-D surfaces is presented (see Figure 4) (colorplate). An MRIVIEW user's manual is available, which contains a more complete description of the operation of MRIVIEW, and of its user interface.

MRI Data Resolution

MRI volumetric acquisitions of the head typically consist of a series of 32 to 128 slices, each having 128^2 to 256^2 pixels, with inter-slice spacing from 1.5 to 5.0 millimeters. Three standard orientations are generally used. These are sagittal, in which image planes are vertically oriented, with front-to-back slices; coronal, which are also vertically oriented, but with side to side slices; and horizontal (or axial) views in which slices are oriented as horizontal planes (see Figure 1).

For neuroscience or clinical research purposes, a series of 128 1.5 to 2.0 millimeter thick slices acquired in the sagittal plane provides sufficient resolution to identify structures of interest in the brain. In MRIVIEW, the underlying representation of the MRI data is a volumetric model. A full resolution volumetric model requires 8 Mb. Because of memory limitations on some hardware platforms, and for performance reasons, a reduced resolution model (128^3) is often useful. This reduced model provides isotropic two millimeter resolution in the three standard orthogonal views, which is adequate for most purposes. MRIVIEW accommodates these two model sizes transparently to the user.

Two Dimensional Viewing and Segmentation

To present the standard radiological views, the volume passes through a 3-D to 2-D transformation function which extracts slices based on slice numbers and the current viewing orientation. This function creates temporary arrays used for screen presentation as well as in image processing and editing. These temporary arrays provide a mechanism allowing a user to first process or edit slices, and then to decide whether or not to make the changes permanent. A 2-D to 3-D transformation function provides the necessary inverse function to the above function, so that changes to the slice data are incorporated correctly in the volume model. The two major editing options, flooding and layer removal, each provide an efficient, semiautomated method for performing volume segmentation tasks.

The Flood Edit routines implement a 3-D region growing procedure. After adjusting a low and high threshold to isolate a structure of interest, a user can either flood this structure in one slice, or start a 3-D flood. The 3-D flood begins by flooding an initial slice, and proceeds slicewise allowing interactive supervision of the process by the user. If the process goes awry, the user can stop the procedure, make necessary modifications to the temporary image using the image editing tools, and restart the process. If there is a reasonable degree of morphological continuity between slices, this technique works well; two millimeter inter-slice distance usually provides sufficient continuity. However, with low resolution data, the variations in the shape of structures between slices may make it difficult to isolate a structure of interest across multiple slices. The Flood Edit capabilities allow the user to work with any desired set of 2-D views. In practice the procedure is best-behaved when working from the top of the head through a series of axial slices. To help confine labelling to the structure of interest, a mechanism is provided to utilize a gradient mask when flooding the slice. An interactive routine lets the user adjust the gradient threshold of a Robert's filter of a slice image. This mask can be further modified using the interactive toolset. These capabilities allow the user to set the edge of the flood plain, determining the density of edges in the gradient mask and repairing residual breaches. Once the edge mask is set, it is applied to that slice before it is sent to the flood subroutine. Often, threshold values that are optimal for isolating the whole brain can produce some in-filling of anatomical fine details such as sulci. We have found that post-processing procedures based on simple image processing or morphological analysis strategies allow us to recover much of the structural detail.

Layer removal routines are used successively to peel away 1-pixel-deep outer layers from the MRI head data. Referring to Figure 4, the bright boundary of the heads in the slice images is scalp data. The dark band between this and the brain is skull. Removal of the scalp data allows a simple ray-tracing algorithm to generate images of the cortical surface. The layer removal is accomplished with a contour following algorithm. A series of mouse button selections are used to control the depth of the layer removal. The semiautomated layer removal option provides a means of quickly paging through and editing the slices of the volume model, using a series of mouse button presses. For the upper part of the head (above the eyes), the outer tissue is of nearly uniform thickness. In this region, the layer removal routines work well. The surface images in Figure 4 were derived from a data set in which layer removal was applied to the horizontal slices of the upper portion of the head.

In the future we expect segmentation procedures to become more efficient and automatic, incorporating more sophisticated image processing strategies as well as knowledge-based constraints which utilize a statistical atlas of brain anatomy. These capabilities will facilitate the bootstrap development of such an atlas by allowing efficient segmentation of new individual datasets which can then be added to the atlas database.

Object Storage

Once structures are labelled with the flood routines, the segmented volume model can be saved, or tagged structures can be saved individually, providing some of the functionality needed for a computational brain atlas. An individual object is saved by storing its x, y, and z extents followed by a three dimensional run length encoding. This encoding consists of x, y, and z start points, and the length of the run in a selected dimension. For most types of objects observed in volumetric MRI data, run length encoding is more efficient than storing the object as an array of binary values, yet it is relatively simple to implement.

For other purposes, alternative encoding strategies such as octree encoding [8] may have significant advantages. Given the variability of obtainable neuromagnetic current reconstruction resolution as a function of distance from the sensor array, the octree appears to be a useful computational framework for structuring inverse calculations and for storing the results.

Three Dimensional Capabilities

Coordinate transformations can be obtained with MRIVIEW using a method of tracking 3-D surfaces in the standard 2-D orthogonal MRI views. To facilitate high performance surface tracking and rendering we extract and encode isosurfaces as six 2-D arrays, equivalent to the z-buffer values for ray traced isosurface rendering from each face of the data volume. Surface images are rendered using the depth information to assign pixel gray-levels. The surface images in Figure 4 were generated using this technique. By combining the surface and surface image information, an interactive system is provided for exploring the MRI data volume. Referring to Figure 4, the location of the cursor in the 3-D viewing window selects the corresponding location in the appropriate orthogonal MRI slice images.

This surface tracking capability allows a user to quickly identify reference points in the volumetric model, which can then be used to set up a coordinate transformation from a coordinate system used for MEG, PET, or other data to the implicit coordinate system of the MRI volumetric model. For example, the MEG head centered coordinate system is based on three external anatomical landmarks that are easily identifiable in the surface views. The selection of one of these landmarks is shown in Figure 4. Using these landmarks and the MRI data resolution information, a homogeneous transformation matrix is constructed. Once a transformation has been obtained, a user can enter dipole locations in MEG coordinates, and view these locations on the orthogonal MRI slices of the volumetric model (see Figure 1).

The surface labelling routines use surface tracking to allow a user to trace features on the 3-D surface images and label the volumetric model at the identified locations. The labelled surface can be saved to a file in the same format as flood-edited volumetric objects are saved. One use of this is to label important sulci in the volumetric model.

An oblique slicer is provided which uses the 3-D viewing window in Figure 4 and a rubberband cursor to provide the user with a method of selecting slices through the data volume at arbitrary angles. An isosurface viewer is also provided, which allows the user to rotate and view the volumetric model. The isosurface is constructed with an IDL-supplied routine which implements the tesselation algorithm of Klemp et al. [10]. This algorithm is similar to the marching cubes algorithm [4].

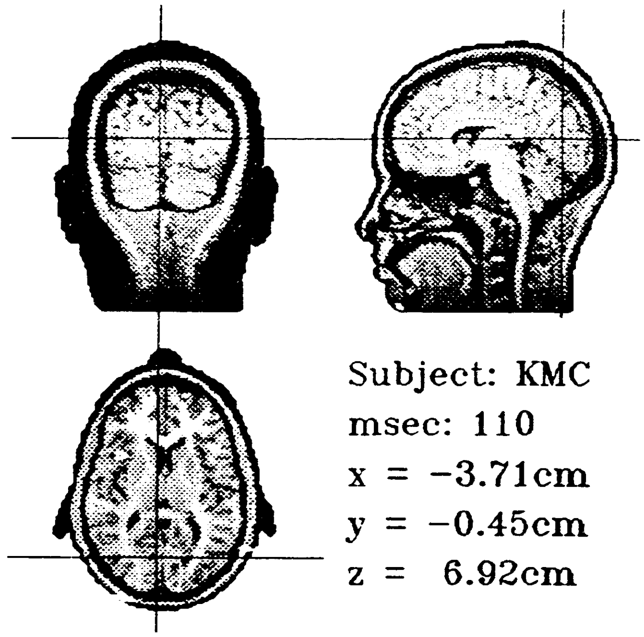

Figure 1: An example of MEG source localization based on point current dipole modeling.

5 Extensions To MRIVIEW

MRIVIEW is intended to be a precursor to a computational brain atlas, which would be a comprehensive package for supporting neuroscience research. This atlas would have as its underpinning a statistical volumetric representation of brain anatomy based on many individual subjects. The atlas would incorporate information from many modalities, providing the necessary database technology, and incorporating methods for analyzing and visualizing this information.

The design and implementation of MRIVIEW allow easy transitions between the MRIVIEW environment and the IDL command interpreter, making it possible to use MRIVIEW tools together with interpreted commands and custom or prototype software not incorporated into the package. This allows MRIVIEW to be very flexible and extensible without causing constant evolution of the core program or spawning multiple specialized versions. Capabilities found to be generally useful can be developed to relative maturity within the hybrid environment and subsequently incorporated into the package. The following paragraphs outline some of the capabilities currently being developed and explored by these mechanisms.

Data Fusion and Visualization of Multidimensional Data

Increasingly, we encounter a need to work with multiple volumetric or other high dimensional datasets. For example, in order to estimate the uncertainty in point source localization based on MEG measurements we typically utilize Monte Carlo techniques [12] adding noise to the best fitting theoretical field distributions and refitting these noisy distributions. For visualization purposes, the resulting solutions are summarized in a smoothed 3-D histogram, which can be visualized in conjunction with anatomical data. Other MEG analysis procedures produce volumetric or tomographic source estimates. The MUSIC algorithm produces a point by point estimate of source probability over a specified grid by projecting the field distribution associated with an optimally oriented current element at each node onto a subspace of the measured signal data [13]. Other procedures solve a large underdetermined linear problem to find a current distribution that accounts for the measurements. In this case, the multidimensional data set consists of three current vectors associated with each point within a defined reconstruction volume. Such reconstructions can be improved by limiting the reconstruction space to the thin layer of grey matter over the convoluted surface of the neocortex, and further improved by constraining the orientation of the net current vector to be normal to the local cortical surface [5]. Extensions to MRIVIEW allow these derivative datasets to be calculated and visualized.

Alternative 3-D models such as the Monte Carlo histogram, the volumetric MUSIC metric, or current density estimates based on tomographic reconstruction procedures can be visualized by co-registering the volume models with the MRI data and in some way combining the information from the two datasets. A useful general strategy is to employ color (hue and saturation) to encode one form of information while employing intensity to encode another. Figure 5 (colorplate) illustrates Monte Carlo histogram data above a threshold, superimposed on a 3-D rendering of the volumetric MRI , with slice data mapped onto cutplane surfaces. Figure 6 (colorplate) illustrates MUSIC data superimposed on a depth cued head surface rendering. In this case a maximum intensity projection was used for the functional data; variations in intensity allow the underlying anatomy to be visible. For slice images we often find it less ambiguous to construct a mask based on the segmented anatomical structure, and to display the functional data as a color map embedded in a grey scale depiction of the surrounding anatomy.

In order to visualize vector field data, we have developed a strategy based on a colored light source model. Red, green and blue illumination sources are arrayed along the three orthogonal axes of the viewing space model, and this space is rotated so that the view axis lies along the net vector formed by addition of the three unit vectors (i.e. the 45,45,45 axis). The object or field distribution to be visualized is located at the center of the viewing space model and may be rotated relative to it. This strategy provides a useful general strategy for representation of vector field data, particularly when the data is localized to a particular surface or cut plane. Figure 7 is an example of this procedure, illustrating brain surface norms calculated by a local convolution operation.

3-D to 2-D Topological Transformations

2-D cartographic representations of the cortical surface are important because the most significant functional organization of cortex is two-dimensional. We have begun to extend and automate the procedures described by [9]. Their technique, termed the "straight line 2-D" (SL2D) method involved manual tracing of the cortical surface. Contours traced from a single section were essentially straightened out - i.e., represented by a straight line segment of proportional length with reference points marked at appropriate intervals. Our procedures automatically extract contours from volumetric data segmented using the MRIVIEW tools. Sequential contours derived from a tomographic series are represented by a series of parallel bands with width equal to the interslice distance. The stacked bands can be realigned along any chosen set of reference points. Corresponding reference points from adjacent sections may be color or intensity coded to define the anatomical or functional organization. For example, in Figure 8 (colorplate), gray-scale intensity is used to encode the z coordinate of the surface voxel in the 3-D volume, and color based on the MUSIC metric describing the probability of a point source at a given location.

Any computational or mechanical procedure to flatten a complex 3-dimensional surface in two dimensions will introduce some distortion [20, 14]. In the SL2D technique, angular distortion is the most significant problem. This can be minimized by choosing a reference line through the region of interest.

3-D Normalization and a Statistical Atlas

An important goal of the proposed computational models is to compare the locations of anatomical or functional structures between individuals, and to permit the development of computational atlases. We refer to the generalized 3-D mapping capabilities required for such applications as anatomical normalization. The most influential and widely utilized strategy of this sort was pioneered by Talairach [19]. In his procedure, the brain is divided into six compartments defined by the anterior and posterior commissures, the

Figure 2: The proportional grid of the Talairach system, based on a set of anatomical landmarks and the peripheral extents of the neocortex.

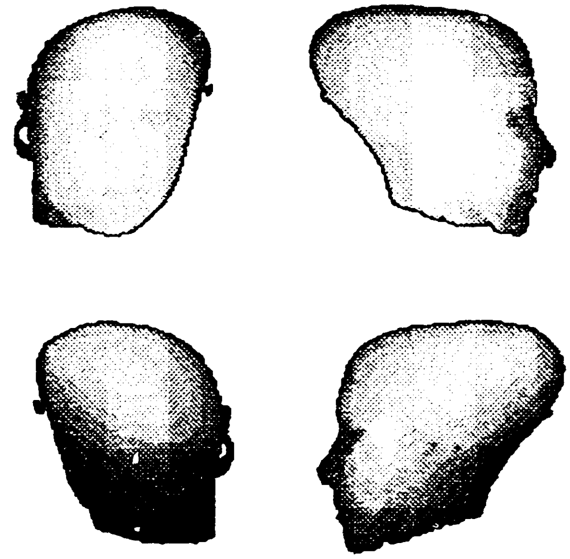

Figure 3: A nonlinear warp of volumetric MRI data to match anatomical landmarks with arbitrary coordinates.

horizontal plane containing them, and the perpendicular (i.e. vertical) planes containing each of the control points (see Figure 2). Each of the compartments is scaled independently in each dimension to match the desired template. A significant problem with the Talairach procedure is that it typically introduces discontinuities at compartment boundaries. For this reason, we are exploring continuous transforms which might accomplish the same basic ends. One such procedure is the 3-D affine transform which allows translation, rotation and scaling of an object. For some purposes more powerful nonlinear warping procedures are necessary which require specification of three or more corresponding points in both the native and target coordinate systems. We are exploring procedures based on polynomials [2] or 3-D thin plate splines [3]. Such algorithms align the control points and compute the mapping for any other arbitrary point according to an underlying system of equations (see Figure 2).

6 Summary

MRIVIEW explores the use of a volumetric model derived from magnetic resonance images to provide an integrated system for editing and viewing MRI head data, and for combining this data with brain functional information.

Methods were developed for displaying and segmenting the MRI data in the volumetric model in any of the three standard radiological 2-D formats. Combined with the 3-D capabilities in MRIVIEW , a method is provided for identifying and tracking features in head and brain surface anatomy. Using the surface tracking procedure, anatomical landmarks can be located on the MRI data, and coordinate transformations can be defined. Surface tracking also provides a method for following anatomical features, such as gyri, which can be difficult to trace between the slices of the standard 2-D views without 3-D surface information.

MRIVIEW supplies a subset of the features needed in a computational brain atlas. Additional features needed for a brain atlas include improved editing, segmentation, and rendering capabilities, as well as volume warping and database capabilities. The strategy used to implement MRIVIEW allows simple extension of the package to accommodate new data types or new analysis or visualization capabilities.

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Color Figure Captions

Figure 4: The MRIVIEW 3D viewing window. The cursor is positioned over an external anatomical landmark.

Figure 5: Monte Carlo histogram of dipole model displayed on MRI-derived anatomy.

Figure 6: A MUSIC metric distribution projected on a depth-cued head surface.

Figure 7: Visualization of vector data using red, green and blue light sources.

Figure 8: Unfolded cortical surface showing a MUSIC metric distribution.

FIGURE 4

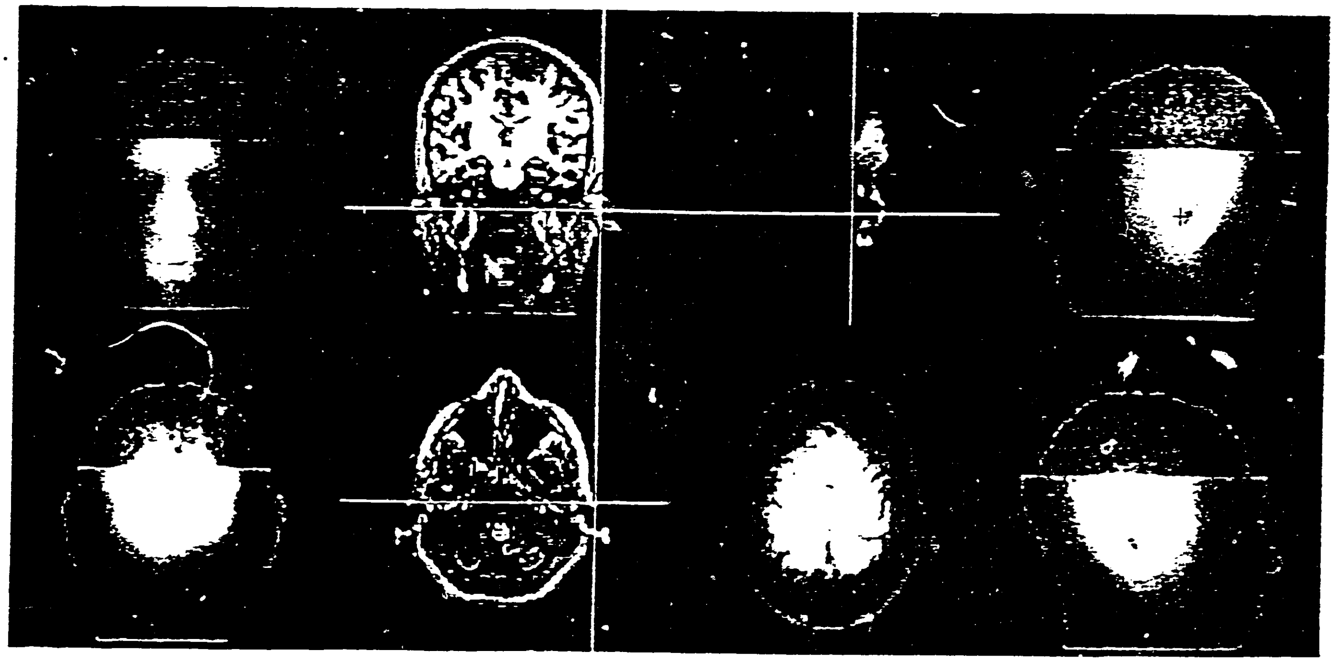


FIGURE 5

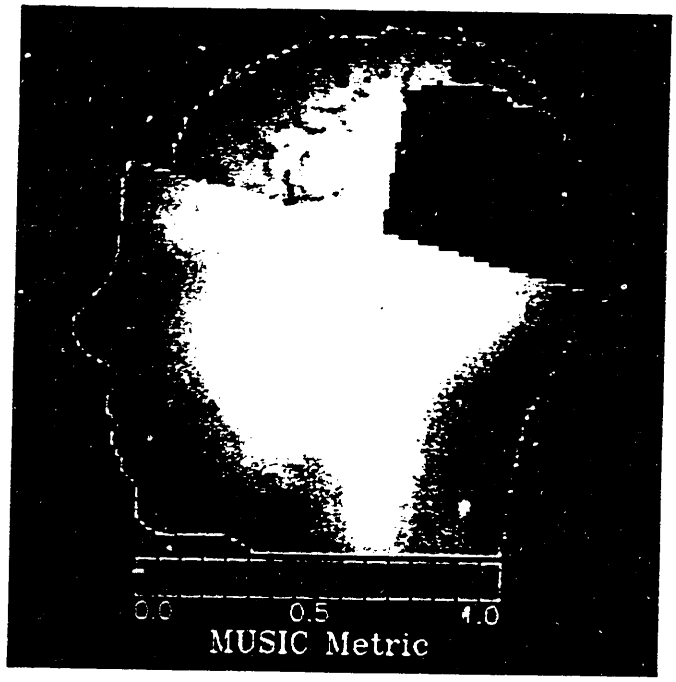
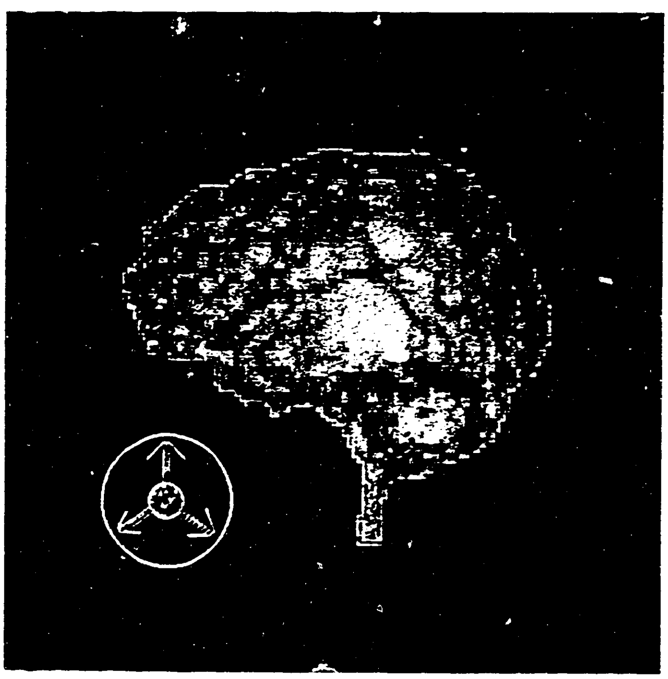


FIGURE 6

FIGURE 7



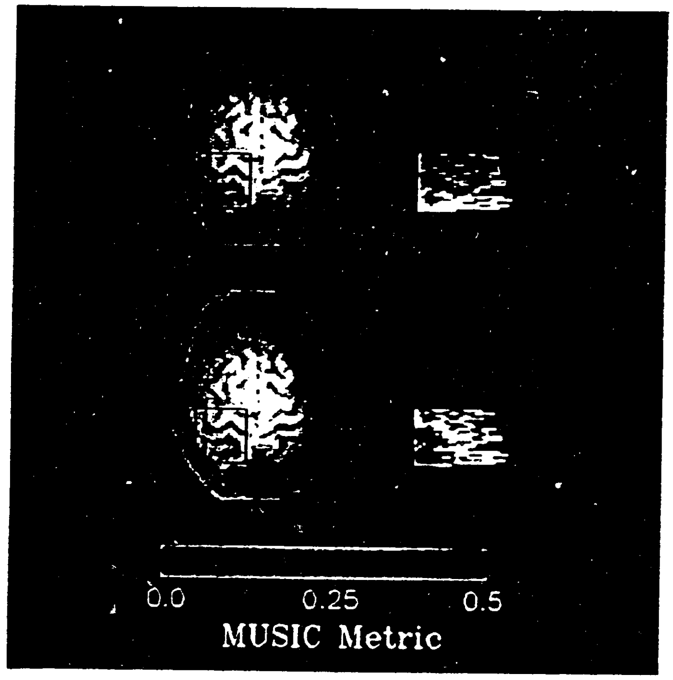


FIGURE 8

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