Modeling and Visualization of Computational Neuroanatomy—Part II

1st author
John C. Mazziotta, MD, Ph.D.
Chair, Department of Neurology
Director, Brain Mapping Center
David Geffen School of Medicine at UCLA
660 Charles Young Drive South
Los Angeles, CA 90095

2nd author
Arthur W. Toga, Ph.D.
Director, Laboratory of Neuro Imaging
Department of Neurology
Co-Director, Brain Mapping Center
David Geffen School of Medicine at UCLA
635 Charles Young Drive South, Suite 225
Los Angeles, CA 90095

Abstract

Rapid and convenient access to digital image archives, as well as archive-based computational tools, are fundamental to many hypothesis-driven investigations of brain anatomy and function in health and disease. The complexity and density of brain image data requires the design of intelligent tools which allow scientific and clinical data, collected at numerous research centers, to be compared, integrated, and disseminated. We describe our results in the development of image data navigational tools, image analysis software, and strategies to represent populations of brain image data involving atlas descriptions of its variance.

Keywords*:* Brain mapping; anatomical modeling

1. Informatics and Human Brain Mapping

Brain mapping is a multidisciplinary science whose goal is the integration of information describing brain structure and function. From microscopic to whole brain organization, data are acquired at many scales from subjects in various experimental conditions, at differing ages and in a range of developmental or disease states. Very high resolution post mortem techniques, such as cryosectioning, can be used to bridge the gap between lower resolution *in vivo* techniques, such as magnetic resonance imaging (MRI), and ultra high resolution methods, such as neurochemical and molecular mapping. In this manner, brain mapping permits the characterization of regional anatomy and the integration of functional information at a very fine structural level.

Unlike most reductionistic approaches in medical science, where great increases in information have resulted in ever increasing subspecialization and diversity, brain mapping integrates many sources of information to produce a holistic view, combining the technical skills of experts in neuroscience, computer science and informatics. A pre- requisite to the success of such an effort is the development of advanced technologies to open information superhighways to brain researchers and clinicians, by providing an array of information tools for the analysis and representation of brain structure and function [1]. These include digital brain atlases, mathematical and computational tools for analyzing multi-modality image databases and technologies for such information to be managed, integrated, and shared over networks.

The ultimate goal of brain mapping is to provide a means by which investigators and students can learn about brain function in health and disease, through the integrated data sets collected and stored in digital brain libraries. In this paper, we describe the development of a battery of internet -based resources ranging from new computational tools to digital image archives. These resources are designed to allow rapid and convenient access to archives of brain images in various modalities, while the accompanying software provides methods for comparing and integrating brain data obtained at geographically disparate research centers. Archive-based computer algorithms are described which allow globally-networked sites to benefit directly from large repositories of image data collected at remote research centers. Applications include the detection and quantification of structural abnormalities in brain scans from incoming patients, and the complex transformation of neuroanatomic atlases onto new patients ' scans to compensate for the normal structural variations of different individuals. With these methods, computer databases which continually benefit from the addition of new information, as well as new tools for analyzing this information, will better characterize normal brain function, disease states, and the detailed circuitry of the brain's component parts.

2. Brain Atlas Databases

Accurate clinical diagnosis often requires the severity of subtle deviations from normal brain structure and function to be quantified precisely. This exercise is especially difficult in the brain, because its internal geometry is highly individual in character. Striking variations exist, across normal subjects, in the size, configuration, and complexity of brain substructures [5] .These complex variations have complicated the goals of comparing and integrating functional data from many subjects and of developing standardized atlases of the human brain. In what follows, we describe recent developments in neuroscience and informatics which may offer viable solutions to each of these two problems. First, we describe the design of software tools, available to globally-networked research centers via the Internet, which make it easier to compare and integrate experimental findings about brain structure and function across subjects and imaging modalities. Secondly, we describe research projects directed towards the eventual development of publicly available anatomical templates and expert diagnostic systems which retain comprehensive information on inter-subject variations in brain architecture

3. Deformable Brain Atlases

In view of the complex structural variability between individuals, a fixed digital atlas, representing the anatomy of a single human brain, will fail to serve as a faithful representation of the brains of new subjects. It would, however, be ideal if an atlas could be elastically deformed to fit a new image set from an incoming patient. Transforming individual datasets into the shape of a single reference anatomy, or onto a 3D digital brain atlas, removes subject-specific shape variations, and allows subsequent comparison of brain function between individuals [6]. Conversely, high-dimensional warping algorithms can also be used to transfer all the information in a 3D digital brain atlas onto the scan of any given patient, while respecting the intricate patterns of structural variation in their anatomy. Such deformable atlases [7,8] can be used to carry 3D maps of functional and vascular territories into the coordinate system of different patients, as well as information on different tissue types and the boundaries of cytoarchitectonic fields and their neurochemical composition.

Deformable atlases rely on high-dimensional warping algorithms to drive them into precise structural correspondence with target brain images [9]. This algorithm was designed to calculate the high-dimensional deformation field relating the brain anatomies of an arbitrary pair of subjects. The resulting 3D deformation maps may be used to quantify anatomic differences between subjects or within the same subject over time and to transfer functional information between subjects or integrate that information on a single anatomic template. High spatial accuracy is guaranteed by using a large set of corresponding anatomic surfaces to constrain the complex transformation of one subject's anatomy into the shape of another. These surfaces include critical functional interfaces such as the ventricles and cortex, as well as numerous cytoarchitectonic and lobar boundaries in 3 dimensions. The construction of extremely complex surface deformation maps on the internal cortex is made easier by building a generic surface structure to model it. Connected systems of parametric meshes model several deep internal fissures, or sulci, whose trajectories represent critical functional boundaries. These sulci are sufficiently extended inside the brain to reflect subtle and distributed variations in neuroanatomy between subjects. The parametric form of the system of connected surface elements allows us to represent the relation between any pair of anatomies as a family of high-resolution displacement maps carrying the surface system of one individual onto another in stereotaxic space. The algorithm then calculates the high-dimensional volumetric warp deforming one 3D scan into structural correspondence with the other. Integral distortion functions are used to extend the deformation field required to elastically transform these surface systems into structural correspondence with their counterparts in the target scan.

3D warping algorithms provide a method for calculating local and global shape changes and give valuable information to scientists studying normal and abnormal growth and development. Deformable atlases not only account for the anatomic variations and idiosyncrasies of each individual patient, but they offer a powerful strategy for exploring and classifying age-related, developmental or pathologic variations in anatomy. More fundamentally, they also provide a method for spatially normalizing the anatomies of different brains. Further automation of warping algorithms may ultimately allow extramural users to submit their own images for normalization, instead of downloading the source code directly. Such normalization software supplies a basis for comparing experimental or clinical data obtained from different subjects or different research centers.

4. Probabilistic Brain Atlases

Probabilistic atlasing [11,12,13] is a research strategy whose goal is to generate anatomical templates and expert diagnostic systems which retain quantitative information on inter-subject variations in brain architecture. The recent interest in comprehensive brain mapping also stresses that the comparisons between subjects, both within and across homogeneous populations, are required to understand normal variability and genuine structural and functional differences. Initial attempts to derive average representations of neuroanatomy have underscored the power of this approach in both clinical and research settings [14,15].

We have developed and implemented an approach for constructing a probabilistic surface atlas of the brain. This performs a statistical analysis of deep surface structures in the brain (in a reference database of normal scans), and then automatically quantifies and maps distributed patterns of abnormality in the same system of anatomic surfaces in new subjects. Once again, connected systems of parametric meshes model deep fissures in the brain, whose trajectories represent critical functional and lobar boundaries. Additional surface analysis algorithms construct a probability space of random transformations (based on the theory of 3D Gaussian random fields) reflecting the variability in stereotaxic space of the connected system of anatomic surfaces. Automatic parametrization of the surface anatomy of new subjects has enabled the detection and mapping of subtle shape and volume abnormalities in the brains of patients with metastatic tumors. These shape changes can be visualized in the form of probability maps on a graphical surface model of the subject's anatomy. The resulting surface system can be rotated, magnified and animated interactively for detailed examination and clinical diagnosis.

5. Visualization

Advances in the science and technology of computing have engendered unprecedented improvements in scientific, biomedical and clinical research. Continuing and accelerating these advancements will require people to comprehend vast amounts of data and information being produced from a multitude of sources. Visualization, namely helping people explore or explain data through software systems that provide static or interactive visual representation, will be critical in achieving this goal. Visualization is a process of analysis and interpretation of information, both quantitative and qualitative, with the end goal of presenting data to convey the salient features most clearly. Visualization designers exploit the high-bandwidth channel of human visual perception to allow people to comprehend information orders of magnitude more quickly than they could through reading raw numbers or text.

Figure 1. Visualization of multi-disciplinary data showing activations of the visual system in the brain.

Visualization can:

- Clarify huge volumes of data in applications such as the surveillance of public health at a regional or national level in order to track the spread of infectious diseases
- Assess application problems such as in biomedical imaging, to generate new knowledge that crosses traditional disciplinary boundaries
- Explain models of complex phenomena, such as multilevel models of human physiology from DNA to whole organs
- Highlight effective business and medical practices, thereby garnering hospitals a competitive edge
- Improve education by training the next generation of scientists as cross-disciplinary researchers

Advances in visualization enable researchers to analyze and understand unprecedented amounts of experimental, simulated, and observational data and through this understanding to address problems previously deemed intractable or beyond imagination. Visualization creates a transparency between fields, enabling a collaborative culture of strong multidisciplinary groups and a clarifying voice through the abundant yield of technology. Many talk about multi-disciplinary collaboration, but few are actually successful at sustaining attempts to see what will happen. We believe visualization is key to success in multidisciplinary collaboration and critical to uncovering unexplored areas of innovation.

6. Discussion

In the future, rapid access to digital image archives, as well as archive-based computational tools, will be fundamental to many hypothesis-driven investigations of brain anatomy and function in health and disease. The establishment of powerful brain atlasing approaches, together with methods for guaranteeing the comparability of research findings from different laboratories, are central to the task of comprehensive brain mapping. Internet repositories of software tools, such as those for creating deformable neuroanatomic atlases [6,8,9], will enable the transfer of multi-subject 3D functional, vascular and histologic maps onto a single anatomic template, the mapping of 3D brain atlases onto the scans of new subjects, and the rapid detection, quantification and mapping of local shape changes in 3D medical images in disease and during normal or abnormal growth and development.

7. Acknowledgements

This work was supported by research grants from the National Institutes of Health, Roadmap Initiative for Bioinformatics and Computational Biology, (U54-RR21813), National Center for Research Resources (P41 RR13642 and M01 RR00865), and by a Human Brain Project grant to the International Consortium for Brain Mapping, funded jointly by NIMH, NINDS and NIBIB (5P01 EB001955). Additional support was provided by the National Library of Medicine (LM/MH05639) and the Biomedical Informatics Research Network (BIRN, http://www.nbirn.net), which is funded by the National Center for Research Resources at the National Institutes of Health (NIH).)

8. References

[1]. Human Brain Project Main Server, http://wwwhbp.scripps.edu/.
[2]. Talairach J, Tournoux P *Co-planar Stereotaxic Atlas of the Human Brain*. New York: Thieme, 1988.
[3]. *Nomina Anatomica* International Congress of Anatomists, New York: Elsevier,1977.
[4]. Bowden DM, Martin RF *NeuroNames Brain Hierarchy*, NeuroImage 2(1):63-84,1995.
[5]. Thompson PM, Schwartz C, Lin RT, Khan AA, Toga A W *3D Statistical Analysis of Sulcal Variability in the Human Brain*, Journal of Neuroscience, 16(13):4261-4274, 1996a.
[6]. Christensen GE, Miller MI, Marsh JL, Vannier MW *Automatic Analysis of Medical Images using a Deformable Textbook*, in: Lemke HU *et al*., [eds.], Comp. Assist. Radiol.: Proc. Internat'l Symposium on Computer and Communication Systems for Image-Guided Diagnosis and Therapy, Springer, Berlin, 146-151, 1995.
[7]. Toga AW, Thompson PM *Visualization and Mapping of Anatomic Abnormalities Using a Probabilistic Brain Atlas Based on Random Fluid Transformations*, Lecture Notes in Computer Science, 1131:383-392, 1996b.
[8]. Evans AC, Dai W, Collins L, Neelin P, Marrett S *Warping of a Computerized 3D Atlas to Match Brain Image Volumes for Quantitative Neuroanatomical and Functional Analysis*, SPIE Med.lmag. III, 264-274, 1991.
[9]. Thompson PM, Toga AW *A Surface-Based Technique for Warping 3-Dimensional Images of the Brain*, IEEE Transactions on Medical Imaging, 15(4):1-16, 1996c.

[10]. Mega MS, Chen SS, Thompson PM, Woods RP, Karaca TJ, Tiwari A, Vinters HV, Small GW & Toga AW *Mapping histology to metabolism: Coregistration of stained whole-brain sections to premortem PET in Alzheimer's Disease*, NeuroImage, 5(2):147-153, 1997.
[11]. Mazziotta JC, Toga A W, Evans AC, Fox P, Lancaster J *A Probabilistic Atlas of the Human Brain: Theory and Rationale for its Development*, NeuroImage 2:89-101, 1995.
[12]. Evans AC, Kamber M, Collins DL, MacDonald D *An MRI-Based Probabilistic Atlas of Neuroanatomy*, in: Magnetic Resonance Scanning and Epilepsy, Shorvon SD et al. [eds.], Plenum Press, New York, 263-274, 1994.
[13]. Thompson PM, Schwartz C, Toga AW *High-Resolution Random Mesh Algorithms for Creating a Probabilistic 3D Surface Atlas of the Human Brain*, NeuroImage 3:19-34, 1996d.
[14]. Evans AC, Collins DL, Milner B *An MRI- based Stereotactic Brain Atlas from 300 Young Normal Subjects*, Soc. Neuroscience Abstracts 22:408, 1992.
[15]. Andreasen NC, Arndt S, Swayze V, Cizadlo T, Flaum M, O'Leary D, Ehrhardt JC, Yuh WTC *Thalamic Abnormalities in Schizophrenia Visualized through Magnetic Resonance Image Averaging*, Science, 14 October 1994, 266:294-298, 1994.