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Registration of a 3D mouse brain atlas with brain microstructure data

Wonryull Koh*, Bruce H. McCormick

Department of Computer Science, Texas A&M University, College Station, TX 77843-3112, USA

Abstract

The brain tissue scanner http://research.cs.tamu.edu/bnl/ is being used to explore the topology and geometry of mouse brain architecture at two levels: its gross anatomy and its microstructure. Aligned volume data set acquisition using this instrument is described. A 3D atlas of mouse brain partitions the gross anatomical structures of brain by a solid model. When registered with the microstructure data, the model serves to organize and index the microstructure data. Volume element partitioning of the mouse brain data can provide a common coordinate framework for visualization and morphological modeling of neurons and can serve as containers to grow synthetic neurons.

Keywords: 3D brain atlas; Brain microstructure; Brain data registration

1. Objectives

Our objectives are to

- build an annotated solid model (3D atlas) of a mouse brain gross anatomy,
- register this model with the brain microstructure data, and thereby
- organize and index the microstructure data.

* Corresponding author.
E-mail addresses: wkoh@cs.tamu.edu (W. Koh), mccormick@cs.tamu.edu (B.H. McCormick).

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2. Introduction

We use the *brain tissue scanner* [7] to explore the topology and geometry of brain's architecture at two levels: its microstructure and its gross anatomy. Aligned volume data set acquisition using this instrument is described, and the methodology extends to volume data acquisition by confocal and two-photon microscopes as well. At the microstructure level, we have designed an exoskeleton microstructure database [4,5] that supports 3D reconstruction and modeling of neurons and cortical networks. At the gross anatomy level, we are building a solid model of the mouse brain, which exhibits cortical areas and brain nuclei and can also accommodate the gross anatomical description of encapsulated fibers in nerve tracts and blood vasculature.

The solid model of a mouse brain organizes and indexes microstructure data. We partition the solid model following the gross anatomical structures of brain. We contend that such a volume element partitioning of the 3D mouse brain model can provide a common coordinate framework for visualization and morphological modeling of neurons [1,8], and can also serve as containers to grow the synthetic neurons, using stochastic models derived from observed biological neurons. The global indexing and organization of the microstructure data at the gross anatomy level are possible because we assign each neuron to the *big voxel* (see Section 3.1) that houses its soma, and position each big voxel within a solid model of brain.

For rat and mouse brains, there are 2D brain atlases (e.g., [3,13,14,17,9]), some with more than 1000 individual structures listed. We are constructing 3D atlases for the rat and mouse brains, modeled from both the 2D structures and additional partitioning by hexahedral finite elements [1]. This solid modeling, annotated by neuroanatomical nomenclature, will facilitate later integration of our system with other anatomical, electrophysiological, and neurochemical database systems (e.g., [11,12,19]).

3. Methods

3.1. Collection of the volume data

The mouse brain is embedded in a specimen block that is 15 mm A–P × 12 mm M–L × 9 mm D–V (Fig. 1). The brain tissue scanner [7] concurrently sections and scans the brain tissue at a nominal 0.5 μm thickness with a nominal 0.625 mm effective knife width. For horizontal scanning, the volumetric data is obtained from scanning a total of 360,000 aligned sections.

The brain tissue scanner [7] uses knife-edge scanning to generate an aligned image stack from consecutive serial sections. Each stroke of knife is the full length of the specimen block, and therefore the length of each section is 15 mm. The width of each section is nominally 0.625 mm for the 40× objective, 2.5 mm for the 10× objective. The effective knife width of 0.625 mm represents the digitized portion of the field of view (FoV) of the 40× objective, i.e., the diameter of the largest circular area that can be simultaneously viewed by the linear sensor array of a line-scan camera. For horizontal color and monochrome scanning using the 40× objective, each section

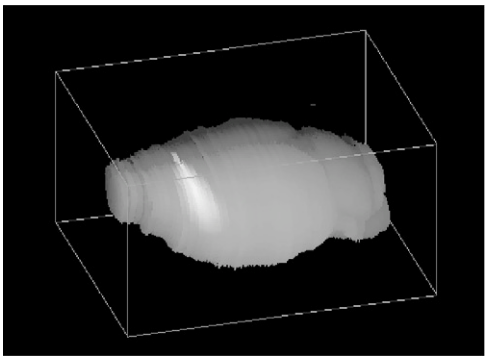

Fig. 1. Schematic of a mouse brain embedded in a specimen block.

(15 mm × 0.625 mm × 0.5 μm) line sampled at 305 nm intervals yields an image that is 49,152 line samples of 2048 pixels. Assuming 3 bytes/pixel, each color image then contains 0.302 GB of data in the worst case. This data size is less than 2 GB (the memory size on our servers), and therefore the data can be kept concurrently in memory for filtering and extraction of the regions of interest (ROIs). Moreover, when the strips are cut parallel to *M–L* or *D–V* axis, the data size contained in each image section decreases, and the data acquisition can be easily accommodated. For storage and data organization, each section is divided into square images (0.625 mm × 0.625 mm) by uniformly dividing the length of each section by the width of the knife. For example, for a specimen block length of 15 mm, each section is partitioned into 24 images. Each square image is stored in an image stack that constitutes a *big voxel* whose dimensions are 0.625 mm × 0.625 mm × 0.625 mm.

3.2. Organization of the volume data

The volumetric data is organized as a collection of $24 \times 20 \times 15 = 7200$ big voxels where each big voxel is cubic and 0.625 mm × 0.625 mm × 0.625 mm in size (Fig. 2). This collection of big voxels forms a block (15 mm × 12.5 mm × 9.375 mm) whose dimensions are nearly identical to those of the specimen block in which the mouse brain was embedded for scanning. Following the conventions employed by the National Library of Medicine's Visible Human Project [6,10], we can then visualize our volume data as serial coronal slices (perpendicular to the *A–P* axis). We can also assemble sagittal slices (perpendicular to the *M–L* axis) or horizontal slices (perpendicular to the *D–V* axis). The big voxels located at the outer boundaries of the block are treated as "dark" big voxels, i.e., as big voxels that contain no data but that facilitate storage and organization of the big voxels.

The FoV of the objective determines the voxel dimensions of 0.625 mm. Hence, when the volumetric data is obtained from confocal or two-photon microscopy, or from the BTS with a different effective knife width, the physical dimensions of the big voxel and the total number of big voxels would change depending on the objective.

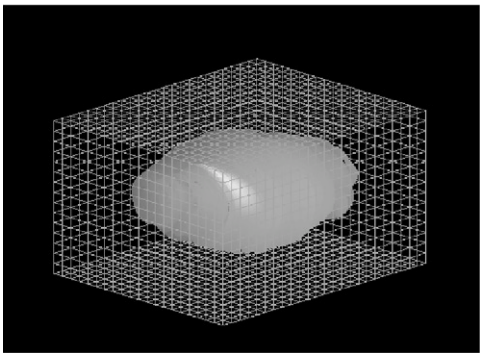

Fig. 2. Volumetric data organization as a collection of 7200 *big voxels*.

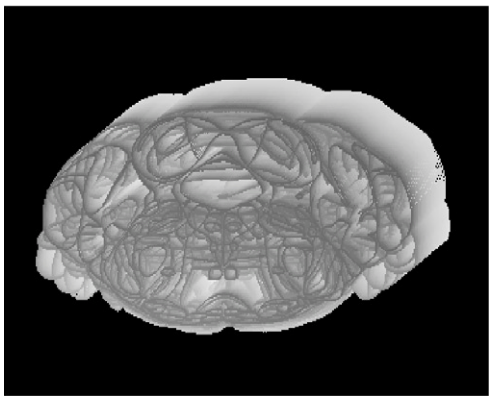

Fig. 3. Partial 3D modeling of mouse cerebellum and medulla, based on Paxinos and Franklin's 2D coronal diagrams [13].

3.3. Partitioning the brain solid model by anatomical structure

A 3D model of mouse brain cortical areas and nuclei has been reconstructed from the contours extracted from the 2D image scans and diagrams of Paxinos and Franklin [13], where the image scans oriented perpendicular to any of the three axes are provided. Each volume element is modeled from the compilation of 2D contours associated with an anatomical structure. Our brain solid model is partitioned by these volume elements, each based on a delineated anatomical structure within a common coordinate system. Fig. 3 shows a 3D coronal section of mouse brain that contains the cerebellum, pons and medulla. Fig. 4 models a 3D coronal section of mouse brain showing parts of the corpus callosum, hippocampus, thalamus, hypothalamus and cerebral cortex.

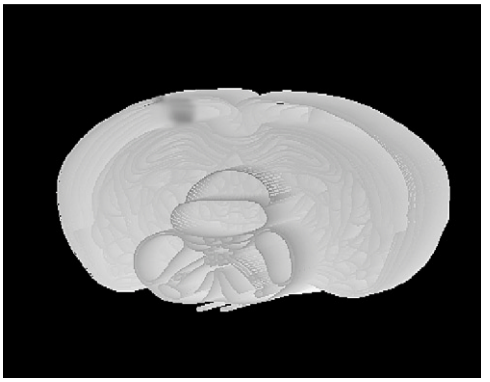

Fig. 4. Partial 3D modeling of mouse thalamus, hypothalamus, and hippocampus, based on Paxinos and Franklin's 2D coronal diagrams [13].

3.4. Registration of the brain solid model with the microstructure data

We spatially decompose the mouse brain, embedded in a 15 mm × 12 mm × 9 mm block, into a mesh of 7200 *big voxels*, where each big voxel is 0.625 mm × 0.625 mm × 0.625 mm in size. Microstructure data then are registered with our mesh of big voxels by assigning each neuron to the big voxel that houses its soma. The reconstructed microstructure data is then organized and indexed by the 3D brain atlas by superimposing our brain solid model over the mesh of big voxels. This registration allows global indexing and organization of microstructure data within a common coordinate framework at the gross anatomy level.

Our initial big voxels are equal sized and may intersect more than one gross anatomical structure when superimposed with the brain solid model. To accommodate the registration of finite elements that are smaller than our initial big voxel size, we use an octree-based refinement algorithm that is an extension of the grid-based algorithm [2,15]. The octree is a well-known tool for organizing spatial data with applications in solid modeling, mesh generation, and various other fields [18]. We use a modified octree concept [16,18], the "27-tree" method [16], where we start with a big voxel from the initial decomposition above. The big voxel is then split up into 27 sub-voxels (octants) that are refined recursively until the sizes of all octants fall below a predefined threshold that is set by the size of the smallest anatomical structure to be represented.

Acknowledgements

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W. Koh is a Ph.D. candidate in Computer Science at Texas A&M University. She received her B.S. degree in Computer Science and Mathematics from the University of Texas at Austin, and M.S. degree in Computer Science at Texas A&M University. Her research interests include computer graphics, brain mapping, cortical networks, visualization, and computational neuroscience.

B.H. McCormick received his B.S. and Ph.D. degrees in Physics from MIT and Harvard University, respectively. He was Professor of Computer Science and Physics at the University of Illinois at Urbana-Champaign. At the University of Illinois at Chicago and Texas A&M University, he headed the Information Engineering and the Computer Science departments, respectively. Currently, he is a professor of Computer Science and director of the Brain Networks Laboratory, at Texas A&M University. His research areas include computer graphics and visualization, brain mapping, and neural networks. His attention is currently focused on the brain tissue scanner and its potential to generate data for biologically accurate 3D reconstruction of brain networks.