Internet-Enabled Multi-Resolution Brain Mapping and Virtual Microscopy

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Abstract

We describe a novel method for internet-enabled multi-resolution brain mapping and virtual microscopy, and demonstrate its implementation at BrainMaps.org, an interactive zoomable high-resolution digital brain atlas and virtual microscope that is based on more than 10 million megapixels of scanned images of serial sections of both primate and non-primate brains.

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1 Introduction

The immense size of high-resolution neuroanatomical image datasets presents a formidable obstacle to visualization, manipulation, and analysis. Internet technologies have revolutionized the way we access and share data, and make it feasible nowadays to create massive online brain atlases and virtual microscopes.

Here we report on the methodology involved with our implementation at BrainMaps.org, which is an interactive zoomable high-resolution digital brain atlas and virtual microscope that is based on more than 10 million megapixels of scanned images of serial sections of both primate and non-primate brains and that is integrated with a high-speed database for querying and retrieving data about brain structure and function over the internet.

Integration of our atlas with an annotation and information retrieval system permits the user to generate annotations for the atlas (and, in general, for local or web-accessible neuroanatomical images), specify spatial regions of interest, and create metadata. These annotations are stored in a database which may be added to and queried by other neuroscientists.

In sum, our digital primate brain atlas (http://brainmaps.org) is a significant contribution to understanding relationships between different brain regions and cell classes, and provides a solid foundation for further integration of neuroscience and related information within a common neuroanatomical framework.

(Martin & Bowden, 1996)

test (Martone, Gupta, & Ellisman, 2004)

The immense size of high-resolution neuroanatomical image datasets presents a formidable obstacle to visualization, interactive manipulation, and analysis, and has long delayed the production of useful, high-quality, web-accessible cytoarchitectonic primate brain atlases. Here we report on a solution and present several digital cytoarchitectural atlases based on high resolution images of serial sections of primate and non-primate brains cut in the three standard planes. We discuss the issues of, and provide solutions for, (i) handling very large image files; (ii) image alignment and warping other images to a reference atlas; (iii) 3-D rendering and volumetric analysis; and (iv) integration with other types of data and metadata.

BrainMaps.org is an interactive zoomable high-resolution digital brain atlas and virtual microscope that is based on more than 10 million megapixels of scanned images of serial sections of both primate and non-primate brains and that is integrated with a high-speed database for querying and retrieving data about brain structure and function over the internet. Currently featured are complete brain atlas datasets for Macaca mulatta, C. aethiops, Felis catus, and Mus musculus.

The resolution of our images, 0.46 micron per pixel, is higher than any histological
atlases currently available in digital form, and several orders of magnitude better than the resolution of MRI acquired images. Our atlas permits a viewer to zoom in from the gross sectional level to the sub-neuronal level exactly as if viewing them through the microscope. Manipulation and navigation in 3-D space is also possible, thereby providing a more complete understanding of geometric and topographic relationships involving regions of interest.

2 Materials and methods

2.1 Slide Datasets

Various datasets consisting of histochemically- and immunocytochemically-prepared slides were obtained for Macaca mulatta, Chlorocebus aethiops, Homo sapiens, Felis catus, and Mus musculus. These are shown in Table 1.

2.2 Image Acquisition

Slides were scanned in at 20x (0.46 um/pixel) on an Aperio ScanScope T3 scanner and saved in the JPG-compressed TIFF file format, which resulted in an order of magnitude reduction in file size with no perceptible loss of image quality.

Slides are scanned in one pass using an Aperio T3 Scanscope (Aperio Technologies), specially adapted to accommodate 3x2 slides with 20x objective, to generate "virtual slides" (fig. 13). Each virtual slide is a digital image file of 25 GB (uncompressed; 1.5 GB compressed) and width $\leq$100,000 pixels. Virtual slides facilitate data sharing by transmission over computer networks, such as the internet, and offer considerable advantages over glass slides in terms of ease and speed of navigation and inspection of large numbers of slides (13). Virtual slides facilitate data mining and analysis. Virtual slides are converted to a digital format that permits rapid web-based navigation and visualization using software customized for working with very large images (Zoomify Inc.); they are subsequently uploaded to our server and imported to the database. Because conventional image processing software, e.g. Photoshop, will not handle images $\leq$ 2GB, lower resolution versions of the virtual slides will be produced using Aperio’s Digital Slide Studio to allow importation into Adobe Photoshop for labeling, segmentation and registration of section images and plottings (Section 8d.2.3).

2.3 Web Accessibility

Digital slides uploaded to server and tiled to multiple small (256x256 pixels) JPG images to generate composite hierarchically-organized, multiresolution images (see
image pyramid in Figure 1).
Figure 1: Image pyramid

Web-accessibility via Flash front-end for rapid navigation.
PHP used as glue to bring together Flash with HTML, MySQL, and other scripting technologies
A summary of the data acquisition and web accessibility steps is shown in Figure 4.
Figure 3: BrainMaps database schema.
Figure 4: Block diagram outlining the major steps in going from immunohistochemically-processed, slide-mounted sections to web-accessible virtual slides and atlases.

2.4 Online Image Annotation

The terminology employed for online labeling of virtual slides is shown in Figure 5 and is based, to some extent, on NeuroNames (Bowden & Martin, 1995; Bowden & Dubach, 2003).
Figure 5: Terminology used for labeling nonhuman primate brain sections.

3 Results
Figure 6: An example of rapid navigation through high-resolution datasets in stereotaxic coordinates: Starting from a full series of sections through the macaque brain, we select one and subsequently are able to easily and rapidly navigate through the images and zoom in to a maximum resolution of 0.4 microns/pixel. Image sizes for individual sections often exceed 100,000 x 100,000 pixels, and are around 25 GB uncompressed (2.5 GB compressed).

4 Discussion

Conclusions

Web-accessible virtual microscopes and brain atlases may be developed using existing computer and internet technologies that offer universal data-sharing.

Rapid and seamless navigation through vast image datasets may be achieved using hierarchically-organized, multiresolution images in conjunction with a Flash-based front-end.

Relational database integration adds querying capabilities and additional levels of structure for organizing image datasets.

By offering the possibility of data-mining completely digitized brains at the sub-neuronal level, our online tools should prove useful for very large-scale histochemical and stereological analyses.

5 Acknowledgements

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References


Figure 8: Histogram of image tile remote access times for AGM385 (from previous figure). Each image tile is 256x256 pixels in size. n=6788, mean=94.23 ms, std=57.28 ms.
Figure 9: Histogram of image tile local access times (from local server) for AGM385. Each image tile is 256x256 pixels in size. n=8839, mean=87.15 ms, std=67.51 ms.
Figure 10: Histogram of image tile local access times (directly from disk). Each image tile is 256x256 pixels in size. \( n = 9831, \text{ mean } = 2.205 \text{ ms}, \text{ std } = 10.0435 \text{ ms}. \)
Figure 11: Histogram of image sizes as of 2006.05.03.  n=2759, mean=1.2275E9, std=2.264E9
Figure 12: Example

Figure 13: Sample Image.
Figure 14: Sample SMI 32 Image.