

### INTRODUCTION

Defining the location of experimental sections through the brain in relation to a brain atlas, and assigning localization (names and / or coordinates) to structures in the sections, often represent a considerable challenge. We present a novel system for archiving, viewing, and analyzing section-based image data from the rat or mouse brain in standard atlas space. The system is prepared for serial section data (typically high resolution mosaic images of histological sections) and associated metadata, and is also suitable for tomographical image data. Images are co-registered to a common spatial framework, based on a standard stereotaxic coordinate system<sup>1,2</sup>.

Raw images are 1) positioned on the basis of estimated distance from Bregma and major landmarks in the brain, and 2) adjusted to fit standard atlas diagrams using affine transformations. Non-linear warping capabilities can be added to the system. Aiming to serve high-throughput investigations of rodent brain, the present system provides efficient administration of the primary data and metadata, flexible use of one or several atlases, and tools for query and display of results.

### FUNCTIONALITY

Image data are stored and retrieved using localization parameters in overall registration with standard brain atlas coordinates. Images are registered to a global atlas framework following a simple three-step procedure. Metadata / experimental procedures are administered as separate modules at the level of animal, tissue block, and section images. Data queries are either based on graphical search in 2-D / 3-D or experimentally related metadata (e.g., presence of molecules or markers) and compared using 2-D side-by-side viewers. Images and atlas slices may be downloaded for further analyses.

### DESIGN

The database is built on a multiple-tier paradigm, providing different types of user interfaces. A relational database management system provides a framework for storage and complex querying.

### TECHNOLOGIES

- Oracle Designer
- Oracle JDeveloper
- Oracle 10g application server
- Oracle 9i relation database
- Oracle ADF (Application Development Framework)
- Regression testing (Cactus/JUnit)
- MVC (Model View Controller, Struts)
- J2EE Sun Microsystems

### FUNDED BY

- The Centre for Molecular Biology and Neuroscience, University of Oslo
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### REFERENCES

1. Paxinos G, Watson C. (1982) The Rat Brain in Stereotaxic Coordinates, Academic Press, Sydney
2. Paxinos G, Franklin, K.B. (1996) The Mouse Brain in Stereotaxic Coordinates, Academic Press, Sydney
3. Boy J, Leergaard TB, Schmidt T, Odeh F, Bichelmeier U, Nuber S, Holzmann C, Wree A, Prusiner SB, Bujard HB, Riess O, Bjaalie JG (2006) Neurolmage, *In Press*

### Setup

#### REQUIREMENTS

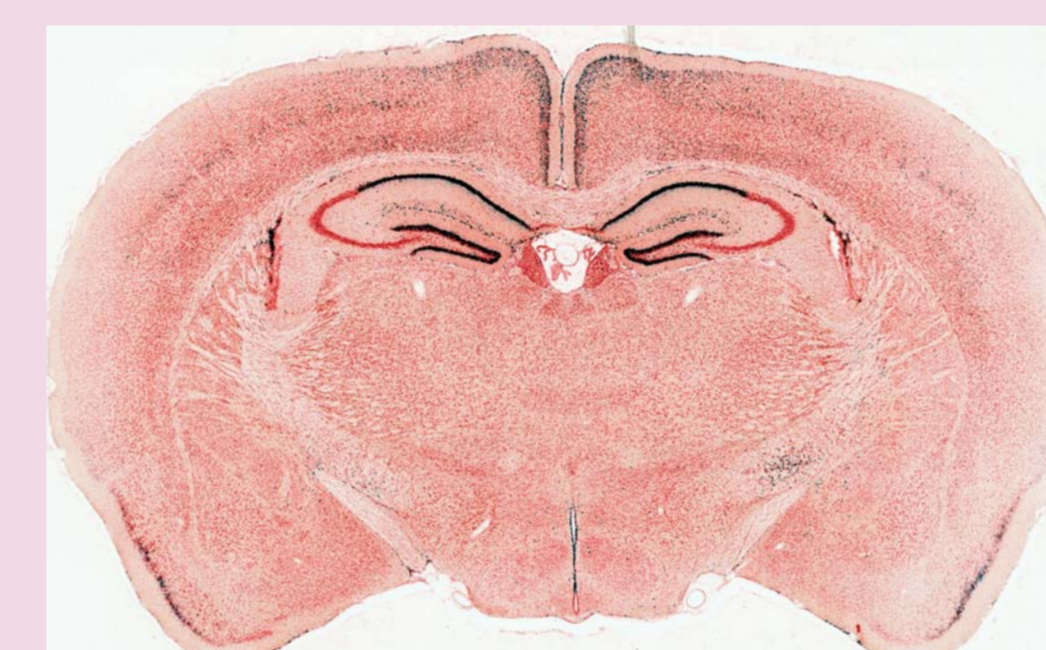
- Digital diagrams from commercial or custom made stereotaxic atlas
- Images must have same orientation as the used atlas diagrams
- High resolution images in TIFF format with LZW compression

#### ATLAS IMPORT

Rodent Brain Navigator accommodates any 2-D serial stereotaxic rat or mouse brain atlas as well as 3-D atlas models. 2-D diagrams (e.g. from CD) are imported and registered to conventional stereotaxic space<sup>1,2</sup> on basis of major anatomical landmarks with use of affine transformations. 3-D atlas models are registered by transformation to standard coordinate space.

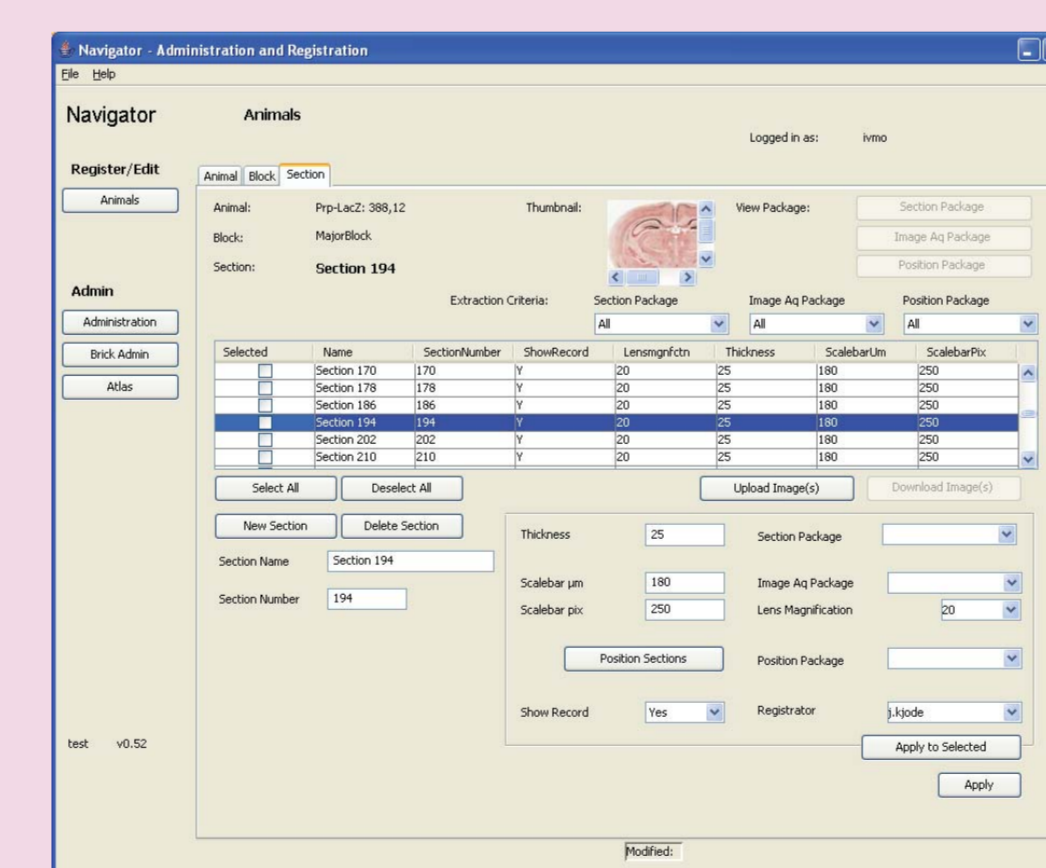
#### IMAGE REGISTRATION

Full image series or solitaire images are submitted together with metadata (animal, tissue block, section level) via a data entry interface. Images are automatically converted from TIFF to ZOOMIFY format. Data are made public following review by a curator.

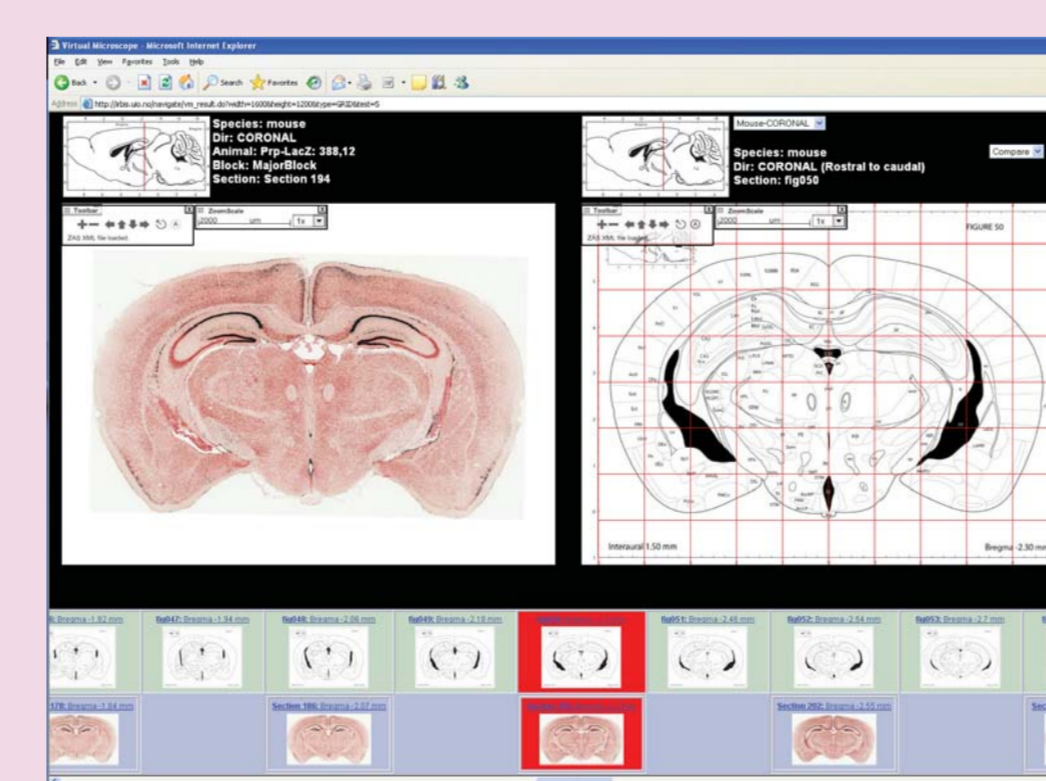


Example: Mosaic image of coronal brain section showing distribution of a prion protein promoter in double transgenic mice<sup>from 3</sup>.

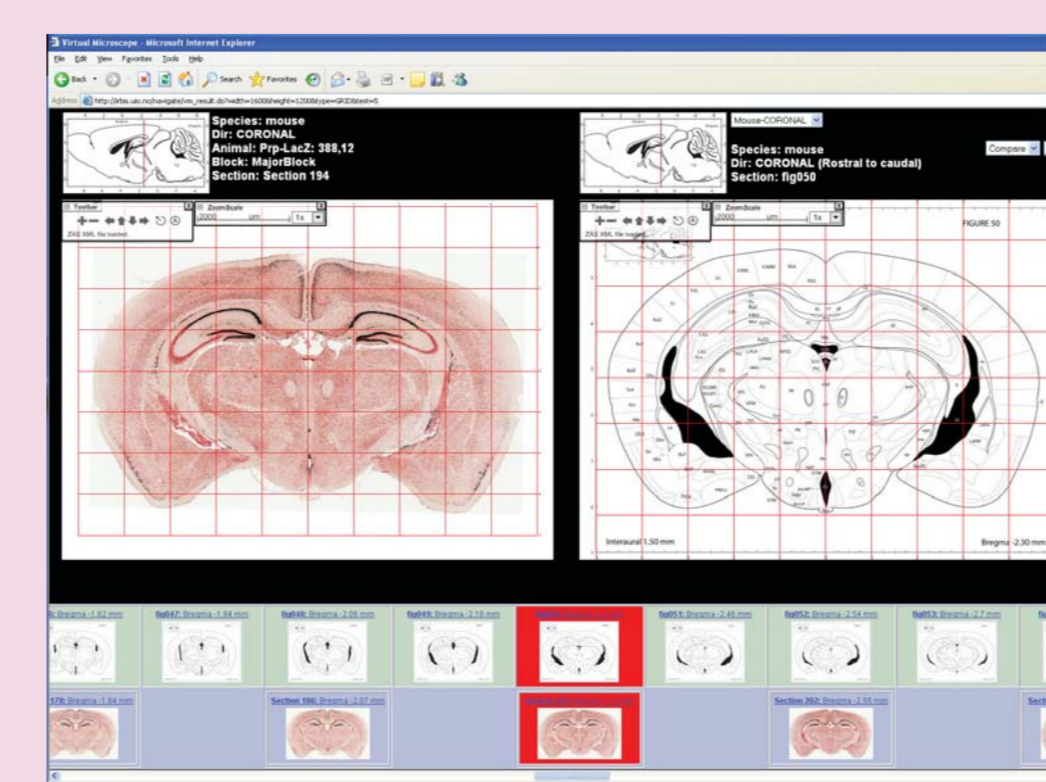
#### REGISTRATION PROCEDURE



Step 1)  
**Upload** images and metadata using data entry interface.



Step 2)  
**Anchor images** to atlas using major landmarks. When 2 (remote) images are anchored, remaining images are positioned automatically. After validation, procedure is repeated as needed.

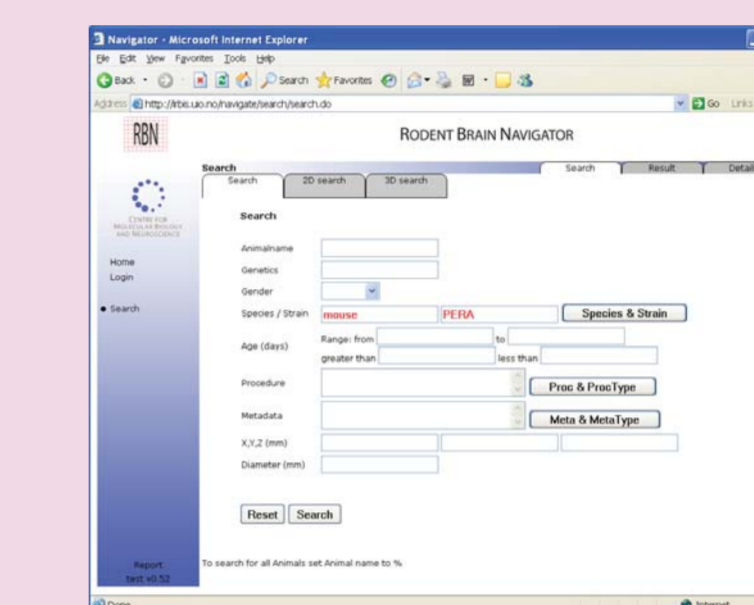


Step 3)  
**Apply coordinate system grid.** The grid overlying the images (representing stereotaxic space) is size adjusted to correspond with the atlas grid, thus adjusting for *in-plane* size

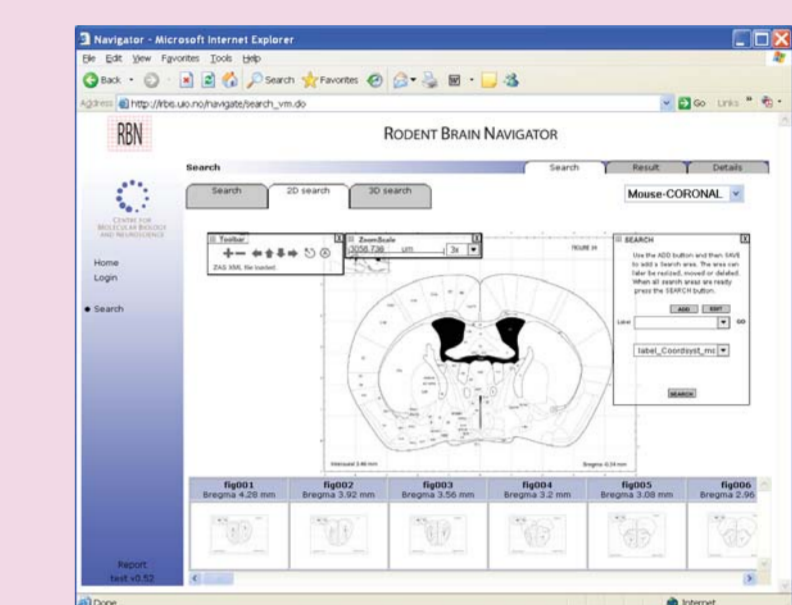
### Use

#### QUERY

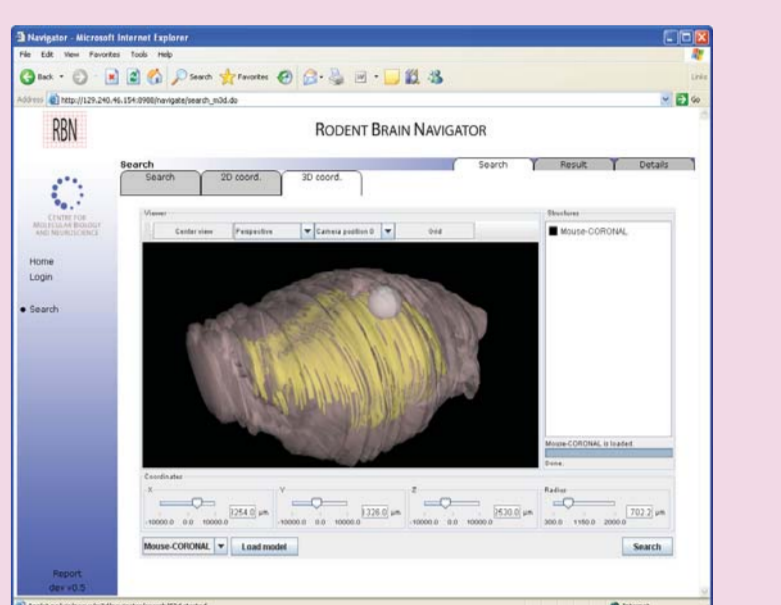
The database can be accessed using textual and / or graphical search. The text search is related to data registered to the animal or experiment. The graphical search gives the opportunity to search within an identified section image or model using a graphical selection cursor to define an area of interest.



GUI for text search allowing queries for animal / experimental parameters or location (X, Y, Z coordinates and diameter)



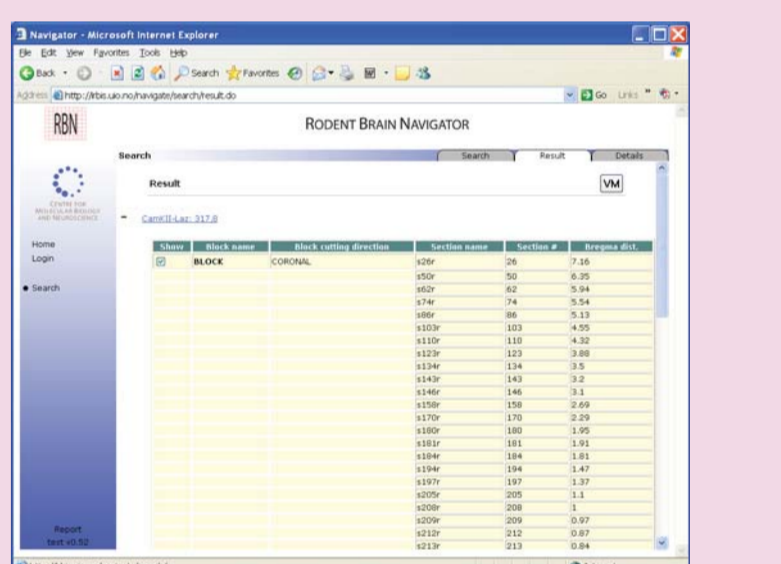
GUI for 2D graphical search provides a circular cursor tool for defining location in a selected atlas diagram.



GUI for 3D graphical search provides a spherical cursor tool for defining location in the 3-D atlas model / coordinate system.

#### RESULT:

Images of interest are selected from the result list sent to a visualization tool

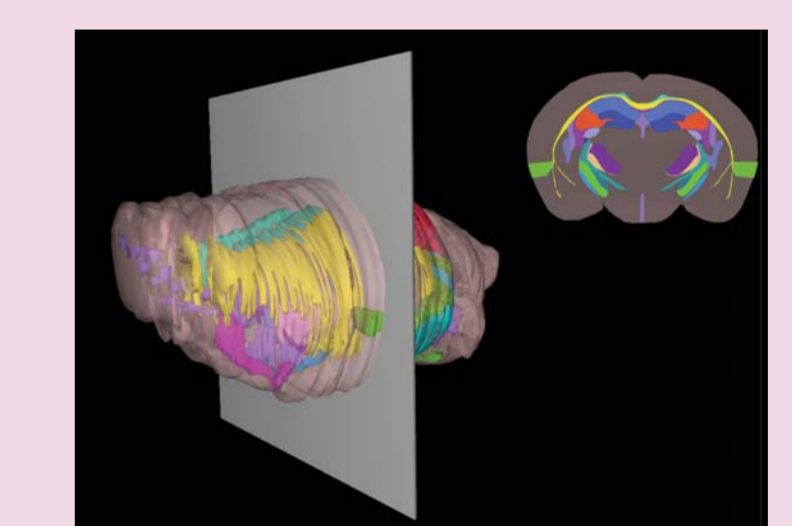


#### VISUALIZATION

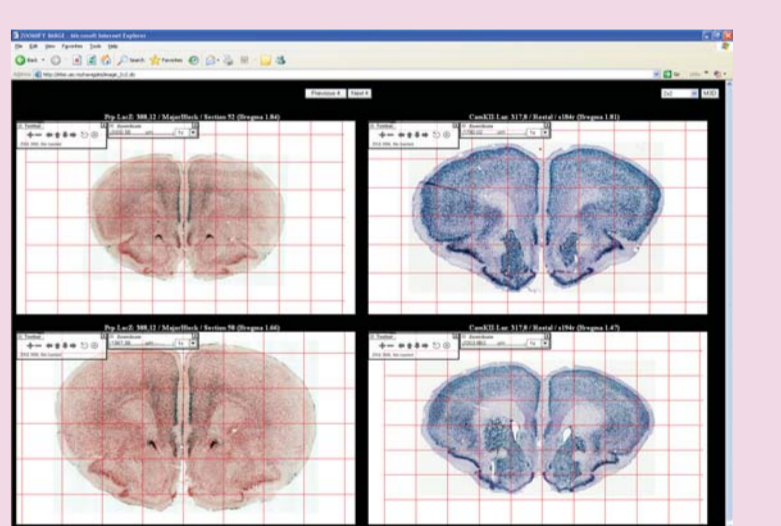
The present version allows 2-D and 3-D visualization of the results. Images may be downloaded for more detailed analyses, e.g. image overlay and local co-registration.



Dual 2-D viewer for side-by-side comparison of images and atlas diagrams. Zoomify technology provides virtual microscope functionality. The horizontal scroll bar allows rapid browsing for neighboring diagrams or images.



3-D viewer applet for dynamic visualization of surface-rendered atlas structures. The orientation of selected images are illustrated in the model. The 3-D atlas models allows generation atlas slices with same orientation as section images.



Multiviewer for comparison of multiple images. Slices from the resultset can be viewed together in 2x2 or 3x3.

#### FUTURE IMPLEMENTATIONS

- Structure search, both graphical and textual
- Visualization tools allowing
  - image overlay
  - options to toggle between different atlases
- Support for 3-D image volumes (tomographic, confocal etc.)
- Handling of images from sections cut at any angle

#### SUMMARY

Rodent Brain Navigator is an open access system providing:

- 1) improved management of serial section image data
- 2) rapid query and visualization of images
- 3) improved analysis by use of multiple atlases
- 4) capability to use 3-D digital brain atlases
- 5) capability to re-slice 3-D reconstructions in order to provide customized atlas diagrams at any chosen angle