BrainSuite

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David W. Shattuck, PhD
Associate Professor
Department of Neurology
David Geffen School of Medicine at UCLA
http://www.loni.ucla.edu/~shattuck/
What is BrainSuite?

• Collection of image analysis tools designed to process structural and diffusion MRI
  • Automated sequence to extract cortical surface models from T1-MRI
  • Tools to register surface and volume data to an atlas to define anatomical ROIs
  • Tools for processing diffusion imaging data, including coregistration to anatomical T1 image, ODF and tensor fitting, and tractography.
  • Visualization tools for exploring these data.
• Runs on Windows, Mac, and Linux*

* GUI for Linux version is not yet released
Overview

Presentation

• Background
• Cortical Surface Extraction
• Surface/Volume Registration
• BrainSuite Diffusion Pipeline
• Visualization Tools

Lab will follow with sample data and exercises
Motivation for Mapping

• It is often the goal to perform comparisons across different brains or brains at different points in time

• For these comparisons to be meaningful, we must be able to establish spatial anatomical correspondence among the data

• Once correspondence is established, we can look for significant differences in various neuroanatomical features
  • Size of structures
  • Cortical thickness
  • Cortical complexity
  • White matter architecture
  • Connectivity relationships
  • How these change over time or in the presence of disease or trauma
Automate all the things?

- One approach to comparative neuroimaging is to manually delineate anatomical structures.
- Drawbacks to manual methods:
  - Raters must be trained to be consistent and to follow a specified protocol
  - Learning effects may bias their processing
  - Raters don’t always visualize 3D relationships when viewing slice-based data
- Human raters still constitute the ‘gold standard’ for many applications
- Automated methods can benefit from the expertise of the rater, which may be superior to an automated algorithm.
- Important to recognize that automated methods may need supervision or correction

A manually delineated brain atlas (BrainSuiteAtlas1)
Image Registration

Goal: identify a transformation that maps from one image to another, such that image features or landmarks are matched.

ICBM452 Atlas, aligned to subject image using AIR affine transform and 5th order warp
Why use surface models?

- Cortex is often represented as a high resolution triangulated mesh with ~700,000 triangles
- Many volumetric-based approaches do not align the cortical anatomy well
- We are often interested in functional areas in the cortex
- Surface-based features, e.g., cortical thickness, are of interest in the study of development or disease processes
- For applications such as EEG/MEG source localization, the location and orientation of the cortical surface can provide additional information
Why diffusion MRI?

• Quantify microstructural tissue characteristics
• Structural connectivity – connectomics (Sporns 2005; Wedeen 2008; Hagmann 2007)
• Clinical – investigation of abnormalities in white matter – e.g., stroke, Alzheimer's disease (Jones 2011; Johansen-Berg 2009)
BrainSuite Workflow

1. **DICOM files**
   - DICOM converter
     - dMRI diffusion parameters
     - sMRI

2. **GUI or Command Line**
   - BrainSuite surface extraction
     - sMRI

3. **Structural Processing**
   - SVReg registration
   - ROI connectivity

4. **Diffusion Processing**
   - Command Line
     - distortion correction
       - brain-only sMRI
       - undistorted DWI
   - tensor/ODF computation
     - fiber tracts
   - BrainSuite tractography
Cortical Surface Extraction
Magnetic Resonance Images

MRI provide noisy, limited resolution representations of brain anatomy

Stained section from a photographic atlas (Roberts et al.)

T1 weighted MRI
Nonuniformity and Noise

- The intensity of voxel would ideally be given only by the tissues present in that voxel.
- Imperfections in the scanner hardware, as well as susceptibility variations in the subject, introduce magnetic field artifacts that produce shading in the image.
- Other noise in the system will also confound the classification process.
Partial Volume Effects

- Finite resolution of MRI is insufficient for some neuroanatomical details.
- Each measurement is an average of the tissue signals in the voxel.
In the ideal case:
- An extracted brain would contain only GM, WM, and CSF.
- We would measure a single intensity value for each type of tissue present in the image.
- The resolution would be sufficient that each voxel would be composed of a single tissue type.

If this were true, then classification would be simple.
Image Formation: Reality

- Some other types of tissue are likely to be present (vessels, sinuses, etc.)

- Image artifacts produce variations in the measured intensity for the tissues
  - Slow spatial gain variation
  - Spatially independent noise

- Neuroanatomical detail is much too fine for the mm$^3$ voxel size typical in MRI

Histograms of: (top) a whole-head MRI (middle) a skull-stripped MRI (bottom) non-uniformity corrected skull-stripped MRI
<table>
<thead>
<tr>
<th>Step</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI</td>
<td>&lt;2 sec</td>
</tr>
<tr>
<td>skull stripping</td>
<td>&lt;2 sec</td>
</tr>
<tr>
<td>bias field correction</td>
<td>40s - 4 mins</td>
</tr>
<tr>
<td>tissue classification</td>
<td>&lt;5 sec</td>
</tr>
<tr>
<td>cerebrum identification</td>
<td>&lt;20 sec</td>
</tr>
<tr>
<td>topology correction</td>
<td>&lt;40 sec</td>
</tr>
<tr>
<td>tessellation</td>
<td>&lt;2 sec</td>
</tr>
<tr>
<td>pial surface generation</td>
<td>&lt;10 mins</td>
</tr>
</tbody>
</table>

Cortical Surface Extraction
Brain Surface Extractor (BSE)

- Extracts the brain from non-brain tissue (skull-stripping)
- We apply a combination of:
  - anisotropic diffusion filtering
  - edge detection
  - mathematical morphological operators
- This method can rapidly identify the brain within the MRI
Skull and Scalp Modeling

- We can apply thresholding, mathematical morphology, and connected component labeling to MRI to identify skull and scalp regions.
  - The method builds upon the BSE skull stripping result.
  - The volumes produced by this algorithm will not intersect.
  - We can produce surface meshes from the label volume.

- The results are suitable for use in MEG/EEG source localization.
Bias Field Corrector

- Performs non-uniformity correction by analyzing regional histograms
- Sub-volumes have dramatically different profiles.
- Regional histograms reflect this.

Two cubic regions of interest (ROIs)

3D rendering of the ROIs
 Bias Field Corrector

• We can fit a tunable model of the tissue profiles to many ROIs spaced throughout the brain.
• This allows us to estimate the local gain variation.
Bias Field Corrector

- Estimate bias parameter at several points throughout the image.
- Remove outliers from our collection of estimates.
- Fit a tri-cubic B-spline to the estimate points.
- Divide the image by the B-spline to make the correction.
Maximum Likelihood Classifier

• We can compute a maximum likelihood classification from our measurement model.

• At each voxel, we simply compute the probability of the intensity value belonging to a particular tissue, and then select the label that has the highest likelihood.

• This maps each intensity value to a specific label, and it thus very fast.

• Does not take into account any of the surrounding labels.
Partial Volume Classifier (PVC)

- We can construct a model that computes a score for local neighborhoods
  - Higher scores for pixel configurations that are similar
  - Lower scores for unlikely combinations (e.g., WM next to CSF)
- We use this model to produce a maximum a posteriori (MAP) classifier
- We maximize this function using the Iterated Conditional Modes (ICM) algorithm
  - Initialize ICM with a maximum likelihood labeling.
  - Iteratively update each individual label to maximize
PVC Tissue Fraction Estimation

- For each brain voxel, we estimate the tissue fraction as follows:
  - Pure voxels are 100%.
  - Each mixed tissue voxel is assigned a fractional value based on where its signal intensity falls between the class means.
Cerebrum Identification

• For the cortical surface, we are interested in the cerebrum, which we separate from the rest of the brain.

• We achieve this by registering a multi-subject average brain (ICBM452) to the individual brain using AIR (R. Woods)

• We have labeled this atlas:
  • cerebrum / cerebellum
  • subcortical regions
  • left / right
Cortex Extraction

- We combine our registered brain atlas with our tissue map
  - retain subcortical structures, including nuclei
  - identify the inner boundary of the cerebral cortex
Topological Errors

- In normal human brains, the cortical surface can be considered as a single sheet of grey matter.
- Closing this sheet at the brainstem, we can assume that the topology of the cortical surface is equivalent to a sphere, i.e., it should have no holes or handles.
- This allows us to represent the cortical surface using a 2D coordinate system.
- Unfortunately, our segmentation result will produce a surface with many topological defects.
Topological Errors

• We can identify topological loops in the volume segmentation by representing it with two graphs.
• If these graphs have cycles, then topological handles exist in the object.
Topological Editing

- By analyzing the graphs, we can identify locations in the object where we can either remove or add voxels in order to break a cycle in the graph.
- We can make our decisions of where to edit based on making small changes to the object.
- This method allows us to rapidly remove all topological defects and produce a volumetric segmentation that will yield a genus zero surface mesh.
Topology Correction

Cortical surface model produced from binary masks
• (top right) close-up view of a handle on the surface generated from the volume before topological correction
• (bottom right) close-up view of the same region on the surface generated from the same volume after topology correction.
Digital Object Filtering
Pial Surface

- Expand inner cortex to outer boundary
- Produces a surface with 1-1 vertex correspondence from GM/WM to GM/CSF
  - Preserves the surface topology
  - Provides direct thickness computation
  - Data from each surface maps directly to the other
Pial Surface

Contour view showing the inner (blue) and outer (orange) boundaries of the cortex.
SVReg: Surface-constrained Volumetric Registration
Surface-constrained Volumetric Registration
BrainSuite Atlas

Single subject atlas labeled at USC by expert neuroanatomist

26 sulcal curves per hemisphere

98 volumetric regions of interest (ROIs), 35*2=70 cortical ROIs

Included with BrainSuite13 as ‘BrainSuiteAtlas1’
Cortical Surface Parameterization

Each hemisphere is mapped to the unit square using an energy-minimization technique.
Curvature-based Registration

subject

atlas
3D Alignment

Input mid surface

Smoothed surfaces

Atlas Subject

Atlas Subject

AIR transformation

Matching based on L2 penalty
Multi-resolution Surface Matching

Input mid surface

Smoothed surfaces

Cumulative curvature computation for multi-resolution representation

Elastic matching for atlas and subject flat maps
Curvature Weighting

- Shown is the color-coded curvature variance, as computed by aligning 100 normal adult brains.
- Inverse of curvature variance is used as a weighting on the curvature cost function to reduce the influence of highly variable areas.
Curvature Weighting Results

No curvature variance weighting

With curvature-variance weighting
Refinement of labels and sulci

Original labels plotted on a smoothened representation of a cortical surface

Labels after geodesic curvature flow plotted on a smoothened representation of a cortical surface

Animation of the geodesic curvature flow for sulcal refinement
Surface Registration Methods

+ Accurate sulcal alignment
- Doesn’t define volumetric correspondence
Motivation for Surface-constrained Volumetric Registration

Alignment of 2 brains by AIR (5th order)

+ Good alignment of subcortical structures
- Sulcal alignment inaccurate
Extension to Volumetric Registration

Accurate Sulcal Alignment

Accurate Subcortical Feature Alignment

Intensity-based Alignment

Solves the difficult problem of surface/sulcal registration in 3D volume

Surface registration

Extrapolation to volume

Volumetric intensity registration

Surface and Volume Registration (SVReg) method performs accurate alignment of both cortical surfaces as well as subcortical volumes.

**Atlas**

(top) Surface and volume views of the BrainSuite13 anatomical atlas, delineated into anatomical regions of interest. (bottom) Similar views of an automatically labeled subject dataset.

**Subject**

BrainSuite ROI Labeling (top) Surface and volume views of the BrainSuite13 anatomical atlas, delineated into anatomical regions of interest. (bottom) Similar views of an automatically labeled subject dataset.
SVReg Outputs
- Labeled cortical surfaces
- Labeled brain volume
- Measurements for each ROI (area, volume)
- Mappings to atlas space
- Mapped sulcal curves
Integration with BrainStorm

BrainSuite Cortical Surface Model with ROIs Labeling imported into BrainStorm. The BrainSuite parcellation can be directly imported into BrainSuite, where the ROIs are useful for interpreting current sources.

see also: http://neuroimage.usc.edu/brainstorm/Tutorials/SegBrainSuite
BDP: BrainSuite Diffusion Pipeline
Diffusion Image Acquisition

- A set of diffusion-weighted images is acquired with diffusion-sensitizing magnetic field gradients
- Gradients are oriented in different directions
- A 3D volume image is acquired for each direction
- Reconstruction methods are used to estimate the local diffusion properties

Diffusion Tensor Imaging (DTI)

- With at least six directions and a baseline image, a tensor model can be estimated.
- Different types of tissue will have different diffusion properties
  - Oriented along nerve fibers
  - Free diffusion in CSF and grey matter
- Visualization of scalar properties (e.g., fractional anisotropy)
- Visualization of major eigenvector using direction encoded color (DEC) maps
  - Red: x, left/right
  - Green: y, anterior/posterior
  - Blue: z, inferior/superior

L/R

A/P

I/S
DTI Visualization

Often visualized using ellipsoids

- Spherical shapes indicate isotropic diffusion
- Elongated shapes indicate directionality
- Flat discs are suggestive of the crossing or junction of nerve fibers

L/R
A/P
I/S
High Angular Resolution Diffusion Imaging (HARDI)

- The tensor model is limited in what it can resolve
- Fiber tracts may cross in a voxel, presenting ambiguities in determining the meaning of the diffusion pattern
- By sampling in many more directions, we can get a more complete picture of the diffusion pattern
- Examples include Q-Ball imaging (Tuch, 2004)
- Can be processed and visualized using spherical harmonics

BrainSuite Diffusion Pipeline

A framework to:
- Read diffusion data from DICOM images
- Align diffusion and MPRAGE image
- Correct diffusion data for distortions
- Fit different diffusion models – tensor and ODFs
- Compute different quantitative diffusion parameters
- Compute diffusion tracks and connectivity matrix
• Scanner saved DICOM images, as input
• De-mosaic the diffusion images
• Extracts diffusion parameters
  • bmat, bval, bvec
• Re-orient diffusion gradients to voxel coordinates
• Writes standard 4D nifti files
• Diffusion MRI uses fast acquisition – Echo planar Imaging (EPI)
• EPI is sensitive to magnetic field ($B_0$) inhomogeneity ➔ Localized geometric distortion
• Distortions result in misalignment with structural scans by several millimeters
• Limits the accuracy of multi-modal analysis
• Corrects the distortion in diffusion (EPI) images using non-rigid registration

• No fieldmap is required for correction

Each figure shows (left) distorted and (right) corrected b=0 image, overlaid with the edge-map (red outline) generated from the T1-weighted image. Arrows indicate areas of significant correction.

- Estimates diffusion tensors
  - FA, MD, color-FA
- Axial, Radial Diffusivity
- ODFs using FRT and FRACD
- FRACD (Haldar and Leahy, 2013)
  - improved accuracy
  - higher angular resolution
- Fiber tracking in T1-structural space
- ROI-based connectivity analysis
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Questions
The software is available online at: http://brainsuite.loni.ucla.edu/

Additional documentation at: http://www.loni.ucla.edu/~shattuck/brainsuite/

User forum: http://forum.loni.ucla.edu/brainsuite

More details for the methods described in this talk can be found in the following papers:

**Segmentation**

References

Registration and Curve Delineation


References

Diffusion MRI