Structural Segmentation

- FAST tissue-type segmentation
- FIRST sub-cortical structure segmentation
- FSL-VBM voxelwise grey-matter density analysis
- SIENA atrophy analysis
FAST
FMRIB’s Automated Segmentation Tool

generic tissue-type segmentation and bias field correction

- Input: brain-extracted image(s)
- Segments into different tissue types
- At the same time, estimate bias field
- Robust to noise, because each voxel looks at neighbours
FAST: Input

- First use BET to remove non-brain
  All volumetric results are highly sensitive to errors here.
  For bias-field correction alone the errors do not matter that much

- Input is normally a single image (T1, T2, proton-density....)

- Or several inputs ("multichannel")
- For multi-channel, all must be pre-aligned (FLIRT)
Intensity Model
tissue intensity distributions

- Histogram = voxel count vs. intensity
- Model = mixture of Gaussians
- If well separated, have clear peaks; then segmentation easy
- Overlap worsened by:
  - Bias field
  - Blurring
  - Low resolution
  - Head motion
Probability Model

• Histogram = probability distribution function

• Model = mixture of Gaussians

• Probability determined for each tissue class

For example:
Voxel near WM/GM border

\[ P(CSF) \text{ near zero} \]
\[ P(GM) \text{ low} \]
\[ P(WM) \text{ moderate} \]
Bias Field Correction

Histograms

Original

Bias

Restored
Bias Field Correction

• MRI RF (radio-frequency field) inhomogeneity causes intensity variations across space
• Causes problems for segmentation
• Need to remove bias field before or during segmentation
• Becomes more common and problematic at high field
Use Spatial Neighbourhood Information (MRF)

- Neighbourhood information: “if my neighbours are grey matter then I probably am too”

- Simple classifiers (like K-means) do not use spatial neighbourhood information

- More robust to noise

- Need the right balance between believing neighbours or intensity
Use Spatial Neighbourhood Information (MRF)

Combine with probability based on Gaussian Mixture Model:

Final log probability = \log p(\text{intensity}) + \beta \log p(\text{MRF})

Final result depends on \beta value

This is user-adjustable
Effect of MRF Weighting

\[ \beta = 0 \]

\[ \beta = 0.1 \]

\[ \beta = 0.3 \]

\[ \beta = 0.5 \]
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\[ \beta = 0 \]

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\[ \beta = 0.1 \]

\[ \beta = 0.5 \]
Partial Volume Modelling

- A better model is what fraction of each voxel is tissue X?
- “partial volume” = fraction of CSF, GM or WM

This substantially improves accuracy of volume estimation.
**FAST - The Overview**

- Initial (approximate) segmentation
  - Tree-K-means

- Iterate
  - Estimate bias field
  - Estimation segmentation; iterate
    - Update segmentation (intensity + MRF)
    - Update tissue class parameters (mean and standard deviation)

- Apply partial volume model
  - MRF on mixel-type (how many tissues)
  - PV Estimation
Optional Use of Priors
(tissue probability maps)

- Segmentation priors = average of many subjects’ segmentations
- Can use priors to weight segmentation, but can skew results (e.g. due to misalignment)
- FAST does not use priors by default
- If bias field is very bad, priors can be turned on to help initial segmentation (alternatively, do more iterations)
- Can also be turned on to feed into final segmentation (e.g. to aid segmentation of deep grey .... but see FIRST)
Other Options

FAST:
- **Bias field smoothing** (-l)
  - vary spatial smoothing of the bias field

- **MRF beta** (-H)
  - vary spatial smoothness of the segmentation

- **Iterations** (-I)
  - vary number of main loop iterations

**fsl_anat:**
- This is a new, alternative tool that performs brain extraction and bias field correction (along with other things) in a different way and so is worth trying out too
FIRST
FMRIB’s Integrated Registration & Segmentation Tool
Segmentation of subcortical brain structures
Sub-Cortical Structure Models

Incorporate prior anatomical information via explicit shape models
Have 15 different sub-cortical structures (left/right separately)
Training Data

• Manual segmentations courtesy of David Kennedy, Center for Morphometric Analysis (CMA), Boston

• 336 complete data sets

• T₁-weighted images only

• Age range 4 to 87
  - Adults: Ages 18 to 87, Normal, schizophrenia, AD
  - Children: Ages 4 to 18, Normal, ADHD, BP, prenatal cocaine exposure, schizophrenia.
Model Training: Alignment to MNI152 space

- All CMA data affine-registered to MNI152 space
  - 1 mm resolution, using FLIRT

- 2-stage process:
  - Whole head 12 DOF affine
  - 12 DOF affine with MNI-space sub-cortical mask
Deformable Models

- Model: 3D mesh
- Use anatomical info on shape & intensity (from training)
- Deformation: iterative displacement of vertices
- Maintain point (vertex) correspondence across subjects
The Model: Shape

- Model average shape (from vertex locations)
- Also model/learn *likely variations* about this mean
  - modes of variation of the population; c.f. PCA
  - also call eigenvectors
- Average shape and the modes of variation serve as prior information (known before seeing the new image that is to be segmented)
  - formally it uses a Bayesian formulation
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  - formally it uses a Bayesian formulation

\[ X = \mu_X + U D b_x \]

- mean
- Singular values
- Eigenvectors (modes)
- Shape parameters
The Model: Intensity

- Intensity is then sampled along the surface normal and stored.

- Learn average shape/intensity and “modes of variation” about both.

- Aside: the intensities are re-scaled to a common range and the mode of the intensities in the structure is subtracted.
Fitting the Model

• Find the “best” shape by searching along *modes of variation*
  - these efficiently describe the ways in which the structure’s shape varies most typically over a population

Average shape  1st mode of variation  2nd mode of variation
Boundary Correction

- FIRST models all structures by meshes
- Converting from meshes to images gives two types of voxels:
  - boundary voxels
  - interior voxels
- Boundary correction is necessary to decide whether the boundary voxels should belong to the structure or not
- Default correction uses FAST classification method and is run automatically (uncorrected image is also saved)
Vertex Analysis

• Use a univariate test at each vertex to measure difference in location (e.g. between means of two groups of subjects)
Vertex Analysis

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Controls

Disease

Consider each vertex in turn
Vertex Analysis

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Controls

Disease

Consider each vertex in turn

Do a test on distance of these vertices to average shape
Vertex Analysis

- Use a univariate test at each vertex to measure difference in location (e.g. between means of two groups of subjects) using distance along surface normals

- Results are now given as *images* and statistics done with *randomise*

- Can do analysis in MNI space or native structural space

- MNI space analysis *normalises for brain size*
Running FIRST

• Inputs:
  - $T_1$-weighted image
  - Model (built from training data) - provided with FSL

• Applying FIRST
  - A single command: `run_first_all`
    1. registers image to MNI152 1mm template
    2. fits structure models (meshes) to the image
    3. applies boundary correction (for volumetric output)

• Analysis:
  - Use command: `first_utils`
    • volumetric analysis (summary over whole structure)
    • vertex analysis (localised change in shape and/or size)
FSL-VBM
Voxel-Based Morphometry with FSL tools

→ To investigate GM volume differences voxel-by-voxel across subjects
Voxel-based analysis of GM volume

• Somewhat controversial approach

• BUT it gives some clues for:
  - volume/shape difference between subjects/populations
  - correlations with (e.g.) clinical score
  - fMRI/PET results “caused” by structural changes

• Currently the simplest and most widely-used approach for such information (~1,500 papers published to date)
Voxel-based analysis of GM volume

• No a priori required = whole-brain unbiased analysis
• Automated = Reproducible intra/inter-rater
• QUICK!

• Localisation of the GM differences across subjects
  ⇒ non-linear registration

• Trade-off:
  - not enough non-linear = no correspondence
  - too much non-linear = no difference
Voxel-based analysis of GM volume

- Standard protocol (Ashburner et al., 2000)
  - Non-linearly register T1 images to ICBM-T1 template
Voxel-based analysis of GM volume

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  - Segment into GM probability map
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  - Smooth with a Gaussian filter
Voxel-based analysis of GM volume

- Standard protocol (Ashburner et al., 2000)
  - Non-linearly register T1 images to ICBM-T1 template
  - Segment into GM probability map
  - Smooth with a Gaussian filter
  - Voxelwise statistical analysis across \#n subjects
Voxel-based analysis of GM volume

- **Standard protocol**

- Optimised protocol (Good et al., 2001)

1) Segment: BET then FAST to get GM probability map
Voxel-based analysis of GM volume

- Optimised protocol (Good et al., 2001)

2) Study-specific template
Voxel-based analysis of GM volume

- Optimised protocol (Good et al., 2001)

3) “Modulation”: compensates for the non-linear part of the registration (FNIRT)
Voxel-based analysis of GM volume

• Jacobian modulation
Voxel-based analysis of GM volume

- Jacobian modulation
Voxel-based analysis of GM volume

• Jacobian modulation

~1 mm² in original space

Jacobian ~ 1

1 mm² in warped space
Voxel-based analysis of GM volume

- Jacobian modulation

~3mm² in original space

Jacobian ~3

1mm² in warped space
Voxel-based analysis of GM volume

- Jacobian modulation

\[ \text{Jacobian } \approx \frac{1}{3} \]

\[ \approx \frac{1}{3} \text{mm}^2 \text{ in original space} \]

\[ 1 \text{mm}^2 \text{ in warped space} \]
Voxel-based analysis of GM volume

Jacobian map: correction for local expansion/contraction

Uncorrected GM results

Results in "correct" amount of local GM
Voxel-based analysis of GM volume

- Optimised protocol (Good et al., 2001)
Voxel-based analysis of GM volume

smooth=5mm

↓

smooth=8mm
Voxel-based analysis of GM volume

• Controversial approach - back to the issues:

1) Interpretation of the results - real loss/increase of volume?

Thickening

Thinning

Courtesy of John Ashburner
Voxel-based analysis of GM volume

- Controversial approach - back to the issues:

1) Interpretation of the results - real loss/increase of volume?
- Difference in the contrast?
- Difference in gyrification pattern?
- Problem with registration?

Or ...

- Thickening
- Thinning

Courtesy of John Ashburner

- Mis-classify
- Folding
- Mis-register
Voxel-based analysis of GM volume

• Controversial approach - back to the issues:

1) Interpretation of the results - real loss of volume?
   - Difference in the contrast?
   - Different in gyrification pattern (developmental)?
   - Problem with registration (Bookstein 2001)?

2) Continuum of results, depending on:
   - Smoothness (Jones 2005)
   - DOF of the nonlinear registration (Crum 2003)
   - Template?
   - Software?

→ See Ridgway et al., NeuroImage 2008 for best practice
Voxel-based analysis of GM volume

• Useful literature/examples:
  - Optimised protocol: Good et al., NeuroImage 2001
  - Optimised protocol in FSL (and comparison across softwares): Douaud et al., Brain 2007

- Comparison of VBM (FSL) versus surface-based approach (FS): Voets*, Hough* et al., NeuroImage
Voxel-based analysis of GM volume

- Useful literature/examples:
  - Longitudinal protocol in FSL: Douaud et al., Brain 2009
  - Comparisons of longitudinal protocols and
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<th>Original global-only estimation</th>
<th>Voxelwise local-only estimation</th>
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<td>SIENA</td>
<td>Longitudinal FSL-VBM</td>
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<td>Single timepoint</td>
<td>SIENAX</td>
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<td>(atrophy state)</td>
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SIENA

Longitudinal atrophy estimation

- Atrophy of cortical grey-matter between two timepoints
- Works well for a range of acquisitions (e.g. slice thicknesses)
- Correction for scanner geometry drift (skull-based)
- Accuracy is 0.2 PBVC (% brain volume change)
- Global calculation provides increased sensitivity (c.f. VBM)
SIENA Step 1

BET: brain extraction

- Separate brain from non-brain (approx.)
- Use rough estimates of exterior skull surface
  - good enough to fix scaling in registration stage (assumes no change in skull)
- Applied to both timepoints
SIENA Step 2
FLIRT : registration

- Register brains (affine, 12 DOF)
- Use skull to constrain scaling
- Fits rotation and translation given this constraint
- Work in half-way space
  - similar interpolation blurring for both images
SIENA Step 3
Atrophy estimation using edge motion

- Find brain/non-brain boundaries using FAST (GM-CSF)
SIENA Step 3

Atrophy estimation using edge motion

- Find brain/non-brain boundaries using FAST (GM-CSF)
- Sample normal profile per edge point (pre-BET images)
- Same for timepoint 2
SIENA Step 3
Atrophy estimation using edge motion

- Find brain/non-brain boundaries using FAST (GM-CSF)
- Sample normal profile per edge point (pre-BET images)
- Same for timepoint 2
- Take derivative of both profiles
SIENA Step 3
Atrophy estimation using edge motion

- Find brain/non-brain boundaries using FAST (GM-CSF)
- Sample normal profile per edge point (pre-BET images)
- Same for timepoint 2
- Take derivative of both profiles
- Correlate with subvoxel accuracy (to give shift)
SIENA Step 4
Convert to % brain volume change

- Using derivative correlation:
  - perpendicular motion is found at each point (noisy per point)
  
  Blue=atrophy   Red="growth"

- Estimate mean over all edge points (mean reduces the noise)

- Convert to PBVC (% Brain Volume Change)
  - uses “auto-calibration”
  - based on scaling one image artificially and correlating with mean edge motion
Scan-Rescan Error Rate

- 16 normals each scanned twice
- Range of slice thicknesses
- Error not very dependent on thickness
- Error approximately 0.2%
A-B + B-C vs. A-C

• 39 MS patients scanned at 3 timepoints
• Accuracy tested by (A-B + B-C) vs. (A-C)

Data: Val Stevenson & D Miller, ION, London
SIENAX

Cross-sectional atrophy estimation

- Atrophy state at a single timepoint
- Registration-based measure of NBV (normalised brain volume)
- Error approximately 0.5-1% in NBV
- Subject variability halved by normalising for head size
SIENAX

1. BET : find brain and skull
2. FLIRT : register to standard space using skull for scaling
3. Use standard-space masking to remove residual eyes/optic nerve
4. FAST : partial volume segmentation of tissues
5. Output : normalised brain volume (NBV)

Note: NBV is useful for including as a head/brain-size covariate in other structural analyses (e.g. FIRST, VBM, etc.)
The End

- FAST tissue-type segmentation
- FIRST sub-cortical structure segmentation
- FSL-VBM voxelwise grey-matter density analysis
- SIENA atrophy analysis