Morphometry

John Ashburner

Wellcome Trust Centre for Neuroimaging,
12 Queen Square, London, UK.
Overview

• Voxel-Based Morphometry
  • Morphometry in general
  • Volumetrics
  • VBM preprocessing followed by SPM
• Tissue Segmentation
• Diffeomorphic Registration
• Longitudinal Registration
• Multivariate Shape Models
• Current Work
Measuring differences with MRI

• What are the significant differences between populations of subjects?
• What effects do various genes have on the brain?
• What changes occur in the brain through development or aging?

• A significant amount of the difference (measured with MRI) is anatomical.
There are many ways to model differences.

- Usually, we try to localise regions of difference.
  - **Univariate models**.
  - Using methods similar to SPM
  - Typically localising volumetric differences

- Some anatomical differences can not be localised.
  - Need **multivariate models**.
  - Differences in terms of proportions among measurements.
  - Where would the difference between male and female faces be localised?

- Need to select the best model of difference to use, before trying to fill in the details.
Voxel-Based Morphometry

- Based on comparing **regional volumes of tissue**.
- Produce a map of statistically significant differences among populations of subjects.
  - e.g. compare a patient group with a control group.
  - or identify correlations with age, test-score etc.
- The data are pre-processed to sensitise the tests to regional tissue volumes.
  - Usually grey or white matter.

- Suitable for studying focal volumetric differences of grey matter.
Volumetry

T1-Weighted MRI

Grey Matter
“Modulation” – change of variables.

Deformation Field

Jacobians determinants
Encode relative volumes.
Smoothing

Each voxel after smoothing effectively becomes the result of applying a weighted region of interest (ROI).
VBM Pre-processing in SPM12

- Use Segment for characterising intensity distributions of tissue classes, and writing out “imported” images that Dartel can use.
- Run Dartel to estimate all the deformations.
- Dartel warping to generate smoothed, “modulated”, warped grey matter.
- Statistics.
SPM for group fMRI

fMRI time-series

Preprocessing

Spatially Normalised “Contrast” Image

Group-wise statistics

Spatially Normalised “Contrast” Image

Preprocessing

Spatially Normalised “Contrast” Image

Preprocessing

Spatially Normalised “Contrast” Image

Analysis
SPM for Anatomical MRI

Preprocessing

Spatially Normalised Grey Matter Image

Group-wise statistics
“Globals” for VBM

• Shape is really a multivariate concept
  • Dependencies among different regions

• SPM is mass univariate
  • Combining voxel-wise information with “global” integrated tissue volume provides a compromise
  • Either ANCOVA or proportional scaling.

(ii) is globally thicker, but locally thinner than (i) – either of these effects may be of interest to us.

• Total intracranial volume (TIV) integrates GM, WM and CSF, or attempts to measure the skull-volume directly
  • Can still identify global brain shrinkage (skull is fixed!)
  • Can give more powerful and/or more interpretable results

• See also Pell et al (2009) doi:10.1016/j.neuroimage.2008.02.050
Some Explanations of the Differences

- Thickening
- Thinning
- Folding
- Mis-classify
- Mis-register
- Mis-register
Selected References

Overview

• Voxel-Based Morphometry

Tissue Segmentation

• Gaussian mixture model
• Intensity non-uniformity correction
• Deformed tissue probability maps

• Diffeomorphic Registration
• Longitudinal Registration
• Multivariate Shape Models
• Current Work
Tissue Segmentation

• It uses a **generative model**, which involves:
  • Mixture of Gaussians (MOG)
  • Bias Correction Component
  • Warping (Non-linear Registration) Component
Belonging Probabilities

Belonging probabilities are assigned by normalising to one.
Belonging Probabilities

Skull-stripping not needed because information outside the brain is modelled.
Modelling a bias field
Modelling a bias field

With bias correction

Without bias correction
Modelling a bias field

Without bias correction

With bias correction
Tissue probability priors

- Tissue probability maps (TPMs) are used instead of the proportion of voxels in each Gaussian as the prior.

**ICBM Tissue Probabilistic Atlases.** These tissue probability maps are kindly provided by the International Consortium for Brain Mapping, John C. Mazziotta and Arthur W. Toga.
Tissue probability priors in SPM12

Includes additional non-brain tissue classes (bone, and soft tissue)
Deformable tissue probability priors

- Tissue probability maps are warped to align with tissues identified in image.
Warping individual to match atlas (spatial normalisation)

Warping atlas to match individual
Optimisation

- The “best” parameters are those that minimise this objective function.
- Optimisation involves finding them.
- Begin with starting estimates, and repeatedly change them so that the objective function decreases each time.

\[
E = -\sum_{i=1}^{I} \log \left[ \rho_i(\beta) \sum_{k=1}^{K} \frac{\gamma_k b_{ik}(\alpha)}{\sum_{j=1}^{K} \gamma_j b_{ij}(\alpha)} \frac{1}{\sqrt{2\pi}\sigma_k} \exp \left( - \frac{(\rho_i(\beta) y_i - \mu_k)^2}{2\sigma_k^2} \right) \right]
\]
Descent scheme

Alternate between optimising different groups of parameters
Limitations of the current model

- Assumes that the brain consists of only the tissues modelled by the TPMs
  - No spatial knowledge of lesions (stroke, tumours, etc)
- Prior probability model is based on healthy brains (IXI dataset from London).
  - Less accurate for subjects outside this population
- Needs reasonable quality images to work with
  - No severe artefacts
  - Good separation of intensities
  - Reasonable initial alignment with TPMs.
Selected References

Overview

- Voxel-Based Morphometry
- Tissue Segmentation

**Diffeomorphic Registration**

- Compositions
- Objective function
- Template creation

- Longitudinal Registration
- Multivariate Shape Models
- Current Work
Diffeomorphic Deformations
Composition
Small Deformation Approximation

The composition:

\[ \vartheta \circ \phi \]

Would be approximated with:

\[ \text{Id} + ((\vartheta - \text{Id}) + (\phi - \text{Id})) \]

The inversion:

\[ \phi^{-1} \]

Would be approximated with:

\[ \text{Id} - (\phi - \text{Id}) \]

Not good approximations for large deformations.
Diffeomorphichic Image Registration

- Minimises two terms:
  1. A measure of distance between images
  2. A measure of the amount of distortion.

Because we cannot simply add displacement fields, large deformations are generated by composing many small deformations.

The amount of distortion is computed by summing up the distortion measures from the small displacements.
Effect of Different Distortion Measures
Two diffeomorphic approaches in SPM

**Dartel.**
- Uses the same small deformation composed multiple times.
- Faster than Geodesic Shooting.
- Gives similar deformations to Geodesic Shooting.
- Currently more additional utilities.

**Geodesic Shooting**
- Uses the optimal series of small deformations, which are composed together.
- More mathematically correct than Dartel.
- Gives nicer maps of volume change than Dartel.
- Likely to replace Dartel in future.
Dartel & GS Compared

**Dartel**

\[ \mu \circ \chi \]
\[ f \circ \chi^{-1} \]
\[ \chi \]
\[ \chi^{-1} \]
\[ |J^\chi| \]
\[ |J^{\chi^{-1}}| \]

**Geodesic Shooting**

\[ \mu \circ \theta \]
\[ f \circ \phi \]
\[ \theta \]
\[ \phi \]
\[ |J^\theta| \]
\[ |J^\phi| \]
Group-wise alignment

- Template implicitly generated from data in study.
- Findings less biased by choice of template.
Evaluations of nonlinear registration algorithms
Tissue map averages

LPBA40

IBSR18
Limitations of spatial normalisation

- Cortical folding variability precludes accurate one-to-one mapping.
- Assumptions that we must “spatially normalise” may be impeding progress.
- Should instead be thinking about how best to model the data generatively.
Selected References

Overview

- Voxel-Based Morphometry
- Tissue Segmentation
- Diffeomorphic Registration
- **Longitudinal Registration**
- Multivariate Shape Models
- Current Work
Longitudinal Registration

• Unified model combines:
  • Nonlinear diffeomorphic registration.
  • Rigid-body registration.
  • Intensity inhomogeneity correction.
Two Longitudinal Scans

Two scans taken 6 years apart (after rigid registration).
Oasis Data

**OAS2 0002**

75 year old male, with MCI (MMSE=22, CDR=0.5).
Oasis Data

**OAS2 0002**

75 year old male, with MCI (MMSE=22, CDR=0.5).
Oasis Data

OAS2 0048

66 year old male, with MCI (MMSE=19, CDR=1).
Oasis Data

Data from first 82 subjects (OAS2 0001 to OAS2 0099).
Computed average expansion/contraction rates for each subject.
Warped all data to common anatomical space.
Generated averages.
Selected References


Overview

• Morphometry
• Voxel-Based Morphometry
• Tissue Segmentation
• Diffeomorphic Registration
• Longitudinal Registration

• Multivariate Shape Models
  • Multivariate nature of shape
  • “Scalar momentum”
  • Some evaluations
• Current Work
Multivariate shape models

- In theory, assumptions about structural covariance among brain regions are more biologically plausible. Form determined (in part) by spatio-temporal modes of gene expression.

- Empirical evidence in (eg)


- We should work with the most accurate modelling assumptions available.
  - If a model is accurate, it will make accurate predictions.
“The morphologist, when comparing one organism with another, describes the differences between them point by point, and “character” by “character”. If he is from time to time constrained to admit the existence of “correlation” between characters, yet all the while he recognises this fact of correlation somewhat vaguely, as a phenomenon due to causes which, except in rare instances, he cannot hope to trace; and he falls readily into the habit of thinking and talking of evolution as though it had proceeded on the lines of his own descriptions, point by point, and character by character.”

D’Arcy Thompson (Growth and Form, 1917).
“This unhappy result can be traced to the piecemeal tests which have hitherto been used. A bone or a tooth is a unit; it is not a discrete assembly of independent measurements.”


“The right statistical method must treat the set of variates as a single coherent matrix; and this is, in fact, the technique of multivariate analysis.”

Some 2D Shapes
Shapes aligned to their average
These were the deformations for that
and these are the Jacobian determinants
Fisher’s Linear Discriminant Analysis

- A multivariate model.
- Special case of canonical variates analysis.
- A generative model.
Other linear discrimination approaches

- Can also use **discriminative models**.
- Anatomical differences are encoded by the vector orthogonal to the separating hyper-plane.
- The most accurate model of difference is the one that best separates the groups.
Regression

- For predicting a continuous variable
Weight Map

For linear classifiers, predictions are made by:

\[ y = a_1 \times x_1 + a_2 \times x_2 + a_3 \times x_3 + ... + b \]

where:
- \( y \) is the prediction
- \( x_1, x_2, x_3 \) etc are voxels in the image to classify
- \( a_1, a_2, a_3 \) etc are voxels in a weight map
- \( b \) is a constant offset.

The weight map can be visualised
Maps

Multivariate weight map

Simple T statistic image

Prettier – but does not accurately characterise the effects of age.
“Scalar Momentum”

- For diffeomorphic registration by least-squares matching, the warps ($\varphi$) are encoded by an initial velocity ($v(0)$):

$$Lv(0) = \frac{1}{\sigma^2} \left| \text{det } d\varphi \right| (I_0 - I_1 \circ \varphi) \nabla I_0$$

- Initial Momentum
- Jacobian determinants
- Template
- Warped individual
- Gradient of template
The 2D shapes (again)
“Scalar momentum” \[ |\det d\varphi| (I_0 - I_1 \circ \varphi) \]
The 2D shapes (yet again)
Reconstructed from scalar momentum and template.
“Scalar momentum” – encodes the original shapes
Residuals
IXI Data

Original Images

Rigidly Aligned Grey Matter
VBM-type Features

Warped Grey Matter

“Modulated” Warped GM
Volumetric Measures from Deformation Fields

**Jacobian determinants**

**Initial Velocity Divergence**
Scalar Momentum

1st Component

2nd Component
Age Prediction - Best Result
Age Prediction – Comparison Among Features

8-Fold Cross-Validation

- Jacobians
- Divergences
- Rigid GM
- Unmodulated GM
- Modulated GM
- Scalar Momentum

RMS error (years) vs. Smoothing (mm)
Differences > 4.6 indicate “decisive” evidence in favour of one approach over another.
Sex Prediction – Best Result
Sex Prediction – Best Result

ROC Curve (AUC=0.9769)
Sex Prediction – Comparison Among Features
Differences > 4.6 indicate “decisive” evidence in favour of one approach over another.
Selected References

Overview

• Voxel-Based Morphometry
• Tissue Segmentation
• Diffeomorphic Registration
• Longitudinal Registration
• Multivariate Shape Models

Current Work

• Privacy-preserving factorisation of large image datasets
Privacy-preserving image factorisation

Data ($F$)  Features ($Z$)

Hospital 1

$F_1$

$F_2$

Features ($Z$)

$z_1$

$z_2$

Hospital 2

Spatial basis functions ($W$)

$W$

Privacy-preserving image factorisation

Data ($F$)  Features ($Z$)

Hospital 1

$F_1$

$F_2$

Features ($Z$)

$z_1$

$z_2$

Hospital 2

Spatial basis functions ($W$)

$W$
Shape and appearance “eigen-modes”

First of 50 eigenmodes

First of 64 eigenmodes
Data (only 2D)

Faces (64 out of 490)

Grey matter maps (64 of 581)
Full model fit

Shape and appearance

Shape and appearance (logistic)
Shape model only

Warped average face

Warped average GM
Full model fit

Shape and appearance

Shape and appearance (logistic)
Appearance model only

Appearance fit (no warping)

Appearance fit (no warping)
For the harmony of the world is made manifest in Form and Number, and the heart and soul and all the poetry of Natural Philosophy are embodied in the concept of mathematical beauty.

D'Arcy Thompson
On Growth and Form
(Dundee, 1917)