



Morphometry

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Overview

• **Voxel-Based Morphometry**

- Morphometry in general
- Volumetrics
- VBM preprocessing followed by SPM
- Tissue Segmentation
- Diffeomorphic Registration
- Longitudinal Registration
- Multivariate Shape Models

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.

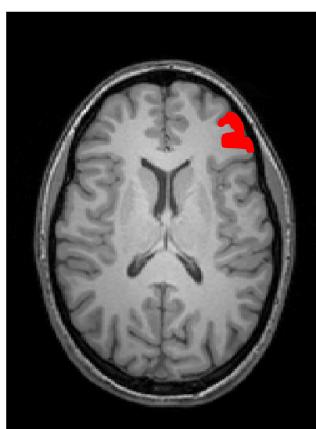
There are many ways to model differences.

- 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.

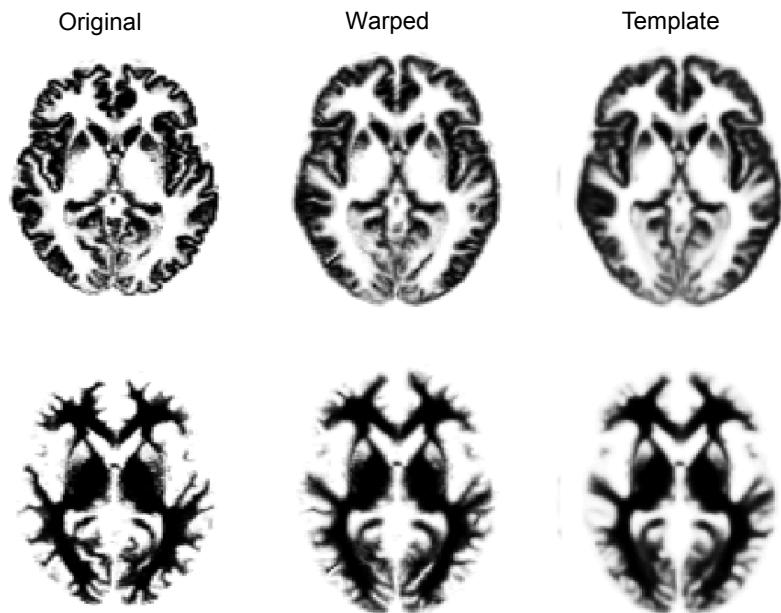
Volumetry



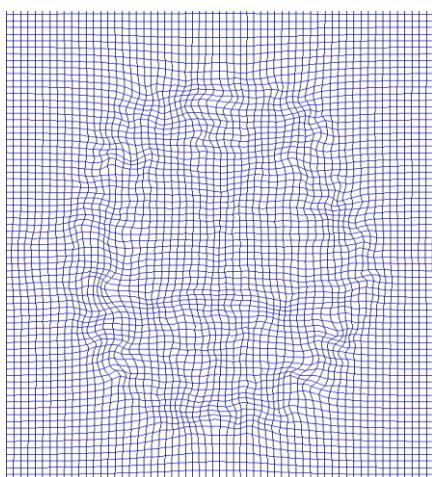
T1-Weighted MRI



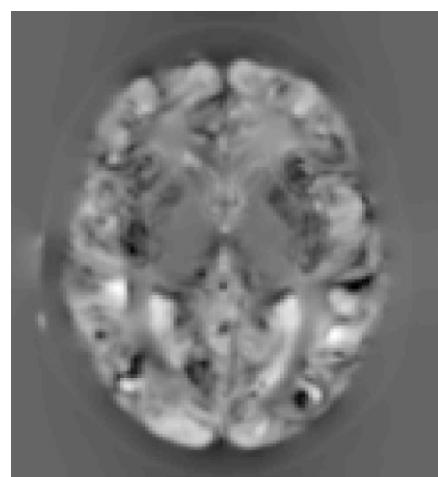
Grey Matter



“Modulation” – change of variables.



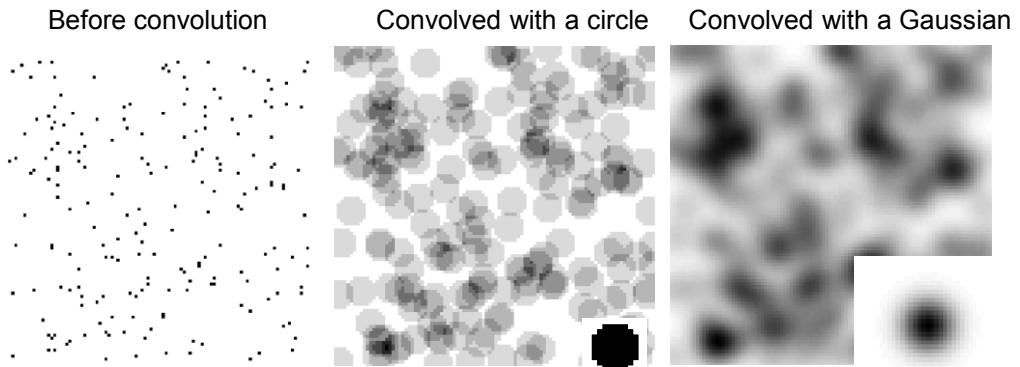
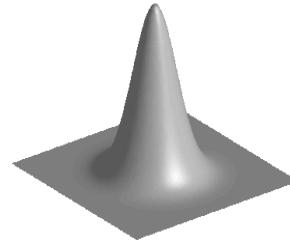
Deformation Field



Jacobians determinants
Encode relative volumes.

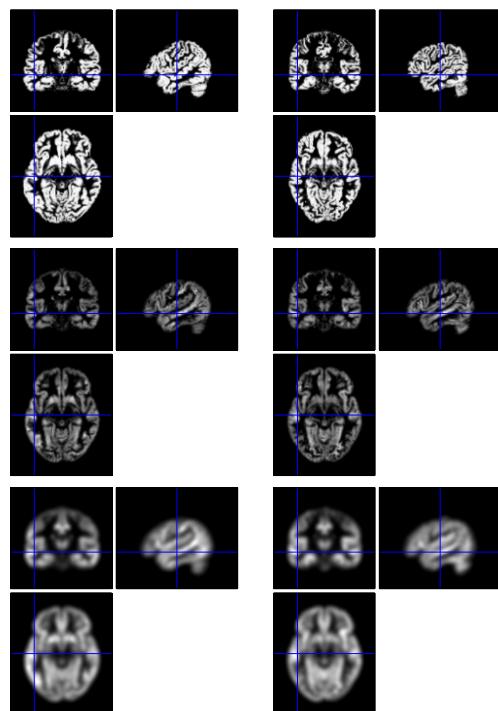
Smoothing

Each voxel after smoothing effectively becomes the result of applying a weighted region of interest (ROI).

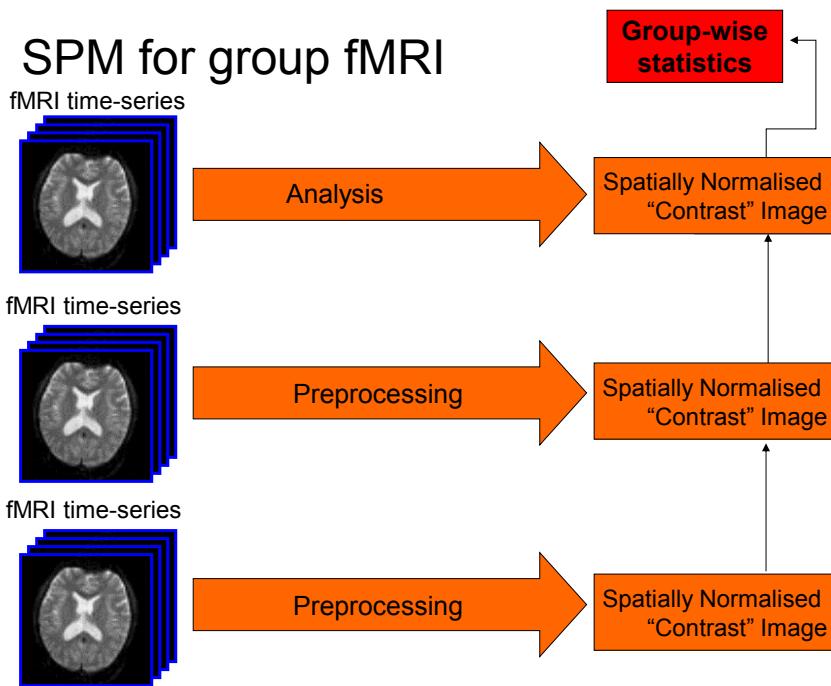


VBM Pre-processing in SPM12

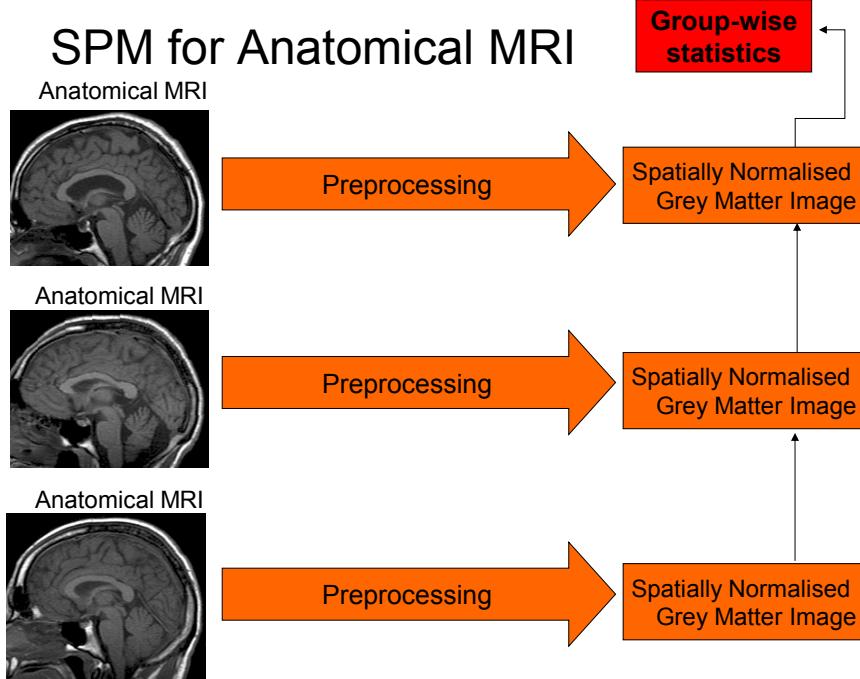
- Use Segment for characterising intensity distributions of tissue classes, and writing out “imported” images that Dartel can use.
- Run Dartel to estimate all the deformations.
- Dartel warping to generate smoothed, “modulated”, warped grey matter.
- Statistics.



SPM for group fMRI

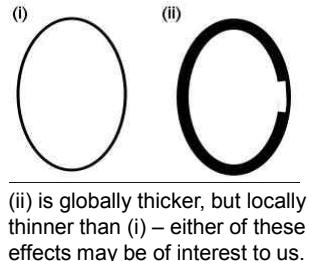


SPM for Anatomical MRI

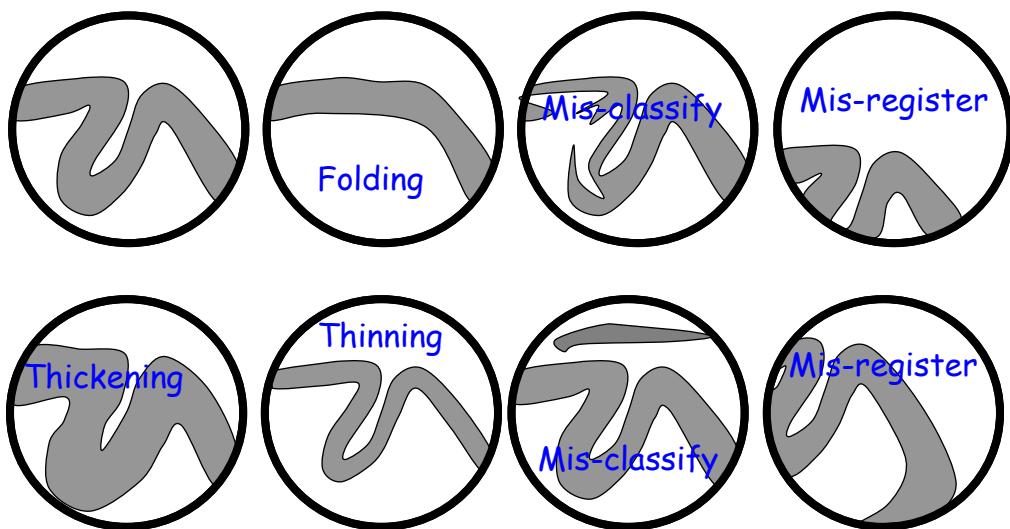


“Globals” for VBM

- 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.
- 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



Selected References

- Wright, McGuire, Poline, Traver, Murray, Frith, Frackowiak & Friston (1995). “A voxel-based method for the statistical analysis of gray and white matter density applied to schizophrenia”. *Neuroimage* 2(4):244-252.
- Ashburner & Friston (2000). “Voxel-based morphometry-the methods”. *Neuroimage* 11(6):805-821.
- Mechelli et al. (2005) “Voxel-based morphometry of the human brain: Methods and applications”. *Current Medical Imaging Reviews* 1(2):105-103.
- Ashburner (2009). “Computational Anatomy with the SPM software”. *Magnetic Resonance Imaging* 27(8):1163-1174.

Overview

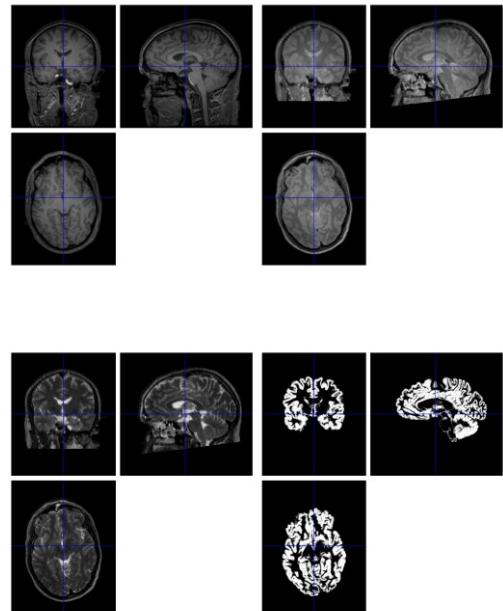
- Voxel-Based Morphometry

● **Tissue Segmentation**

- Gaussian mixture model
- Intensity non-uniformity correction
- Deformed tissue probability maps
- Diffeomorphic Registration
- Longitudinal Registration
- Multivariate Shape Models

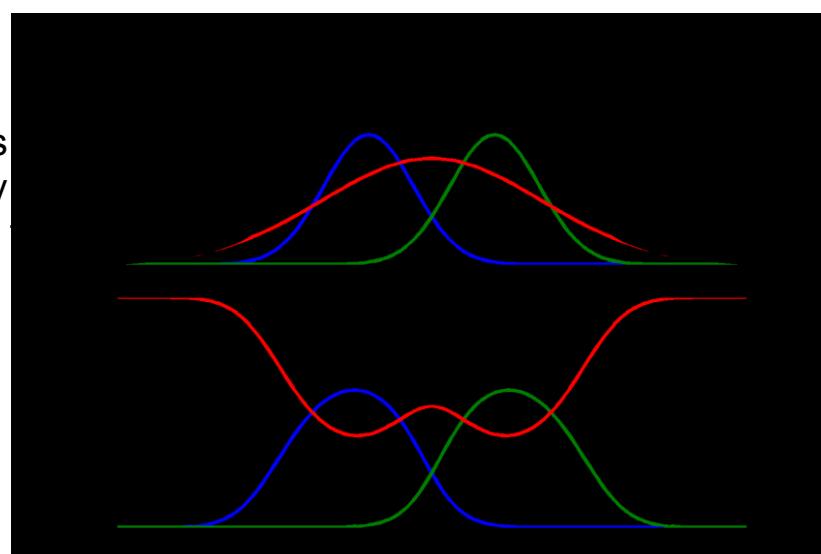
Tissue Segmentation

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



Belonging Probabilities

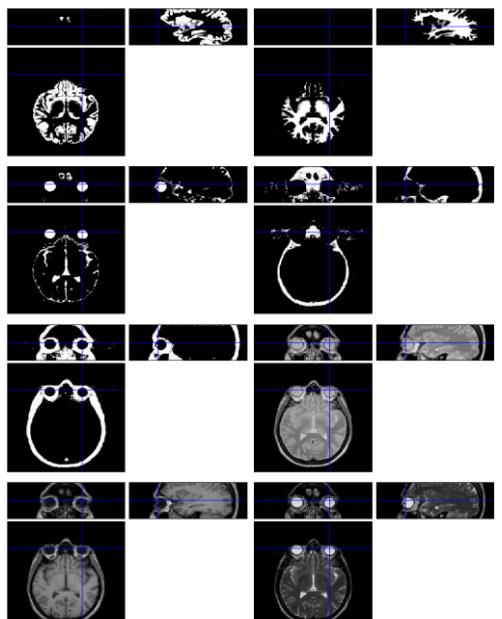
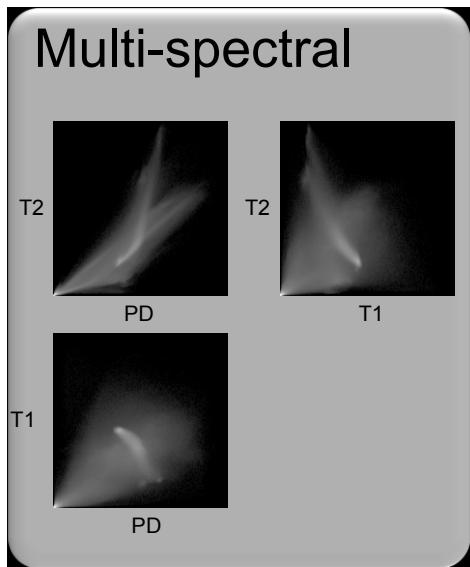
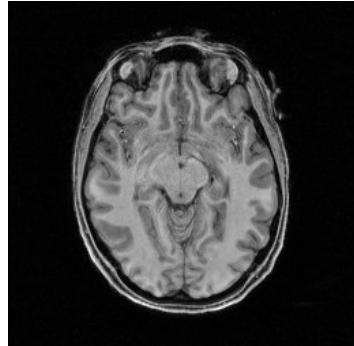
Belonging probabilities assigned by normalising one.



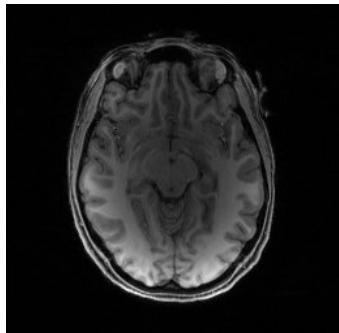
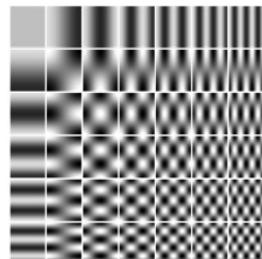
Belonging Probabilities



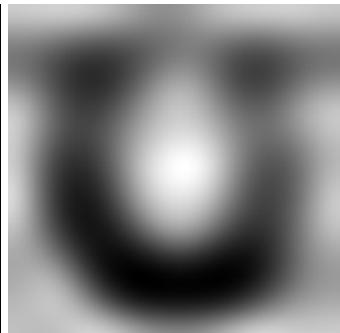
Skull-stripping not needed because information outside the brain is modelled.



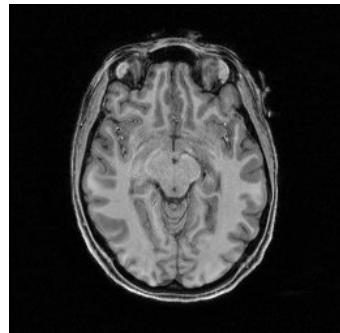
Modelling a bias field



Corrupted image



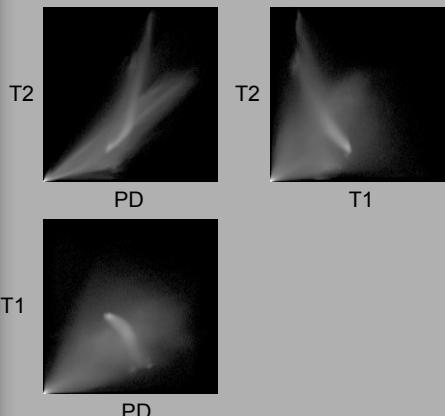
Bias Field



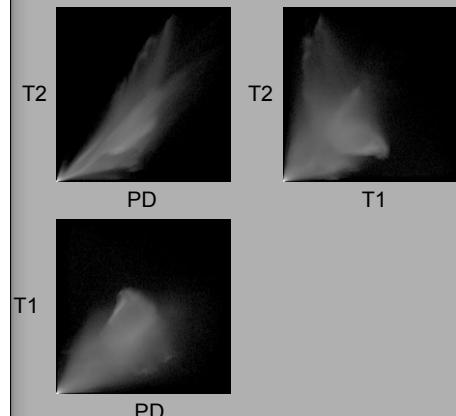
Corrected image

Modelling a bias field

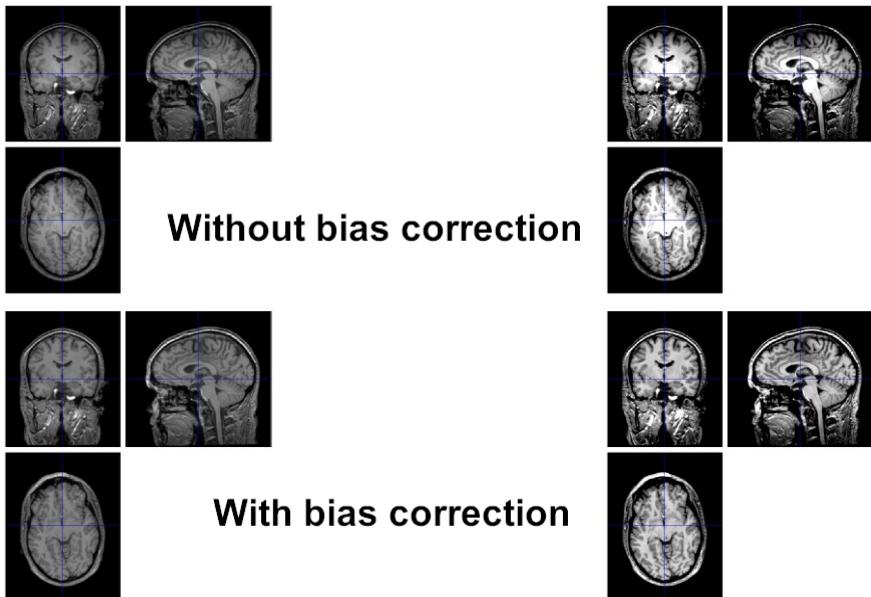
With bias correction



Without bias correction

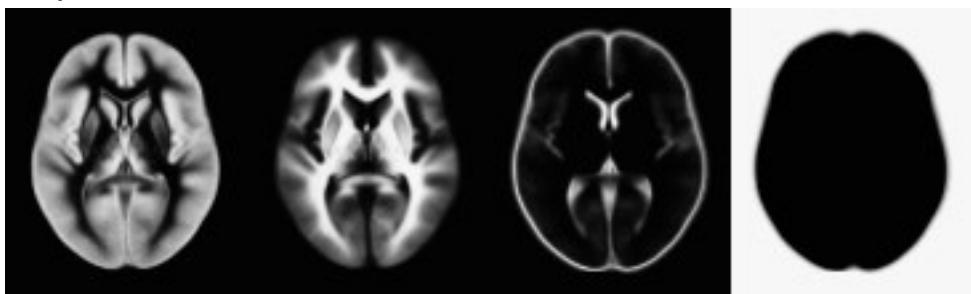


Modelling a bias field



Tissue probability priors

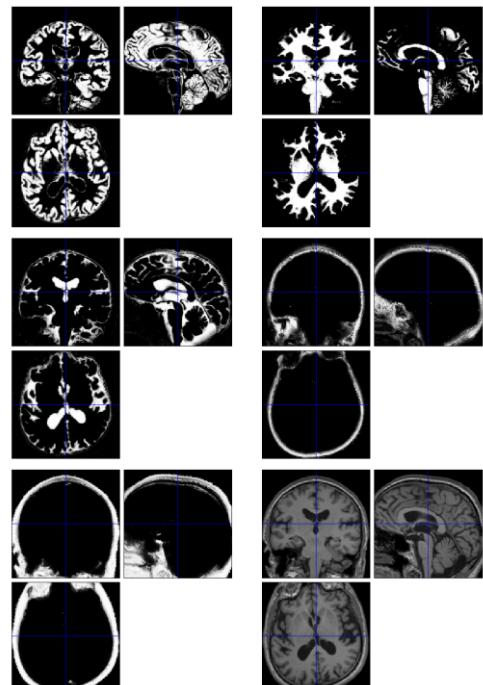
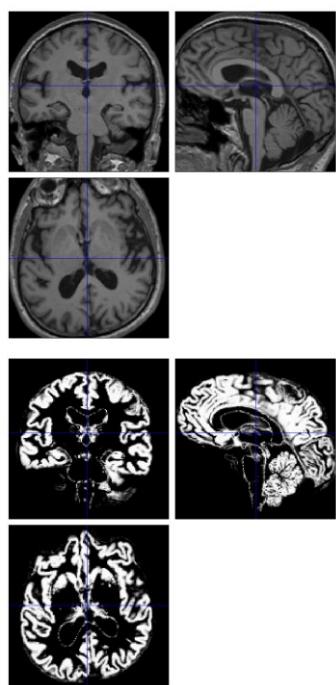
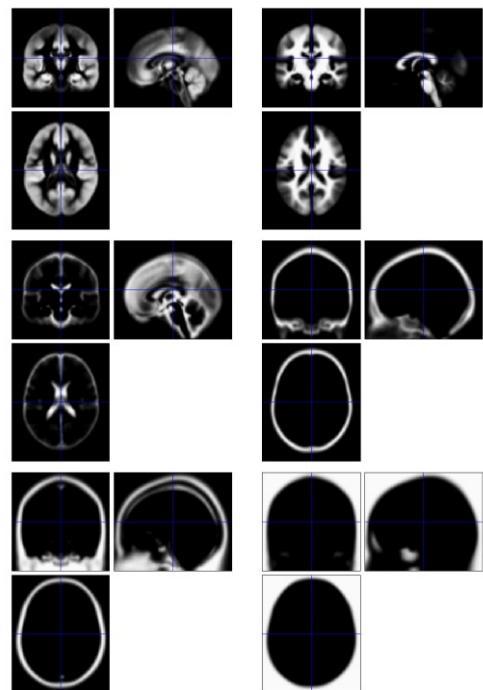
- Tissue probability maps (TPMs) are used instead of the proportion of voxels in each Gaussian as the prior.



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.

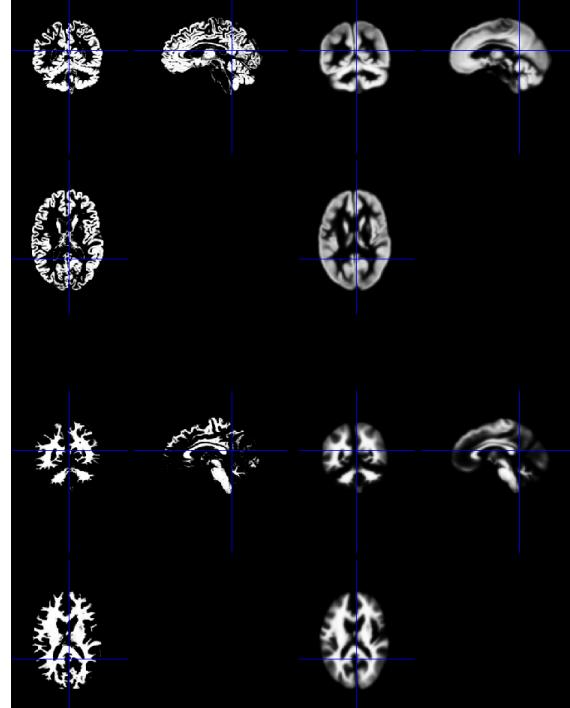
Tissue probability priors in SPM12

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

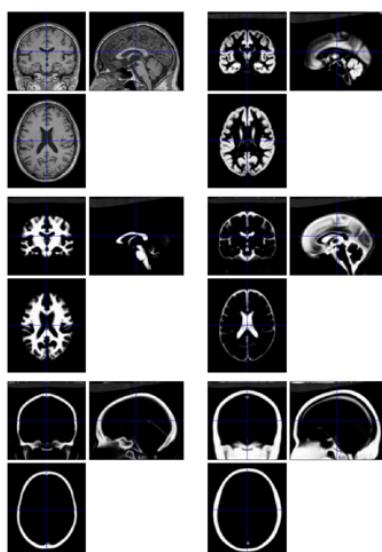


Deformable tissue probability priors

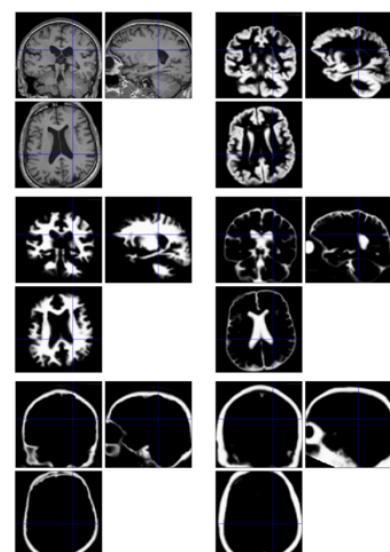
- Tissue probability maps are warped to align with tissues identified in image.



Warping individual to match atlas (spatial normalisation)



Warping atlas to match individual

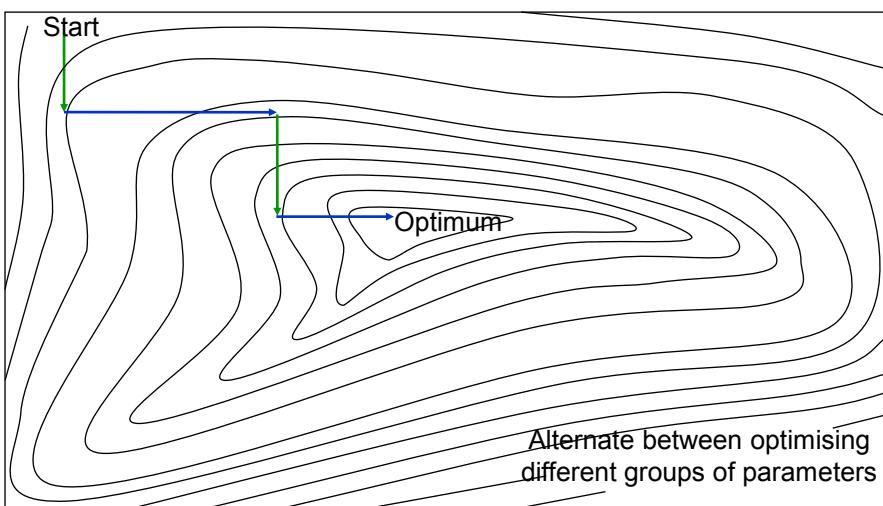


Optimisation

- 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.

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

Descent scheme



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

- Ashburner & Friston (2005). “*Unified Segmentation*”. *NeuroImage* **26**:839-851.

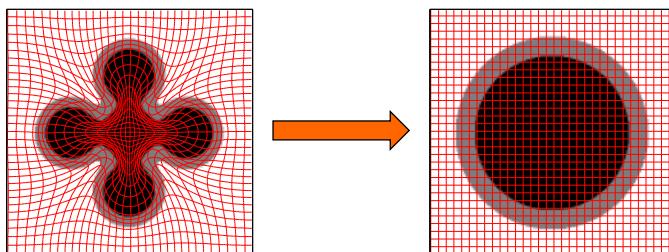
Overview

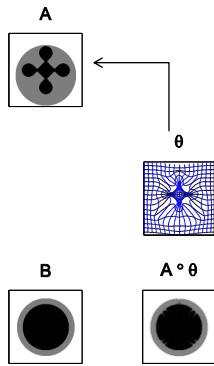
- Morphometry
- Voxel-Based Morphometry
- Tissue Segmentation

• **Diffeomorphic Registration**

- Compositions
- Objective function
- Template creation
- Longitudinal Registration
- Multivariate Shape Models

Diffeomorphic Deformations





Composition

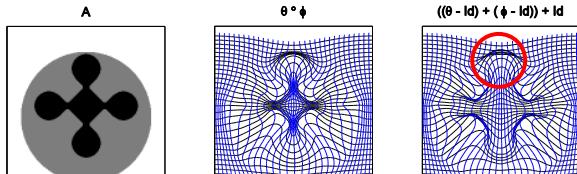
Small Deformation Approximation

The composition:

$$\vartheta \circ \phi$$

Would be approximated with:

$$Id + ((\vartheta - Id) + (\phi - Id))$$

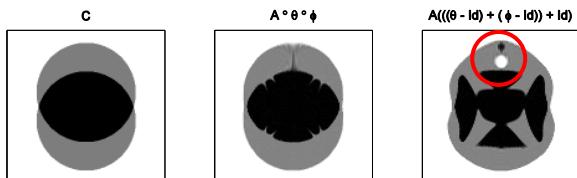


The inversion:

$$\phi^{-1}$$

Would be approximated with:

$$Id - (\phi - Id)$$



Not good approximations for large deformations.

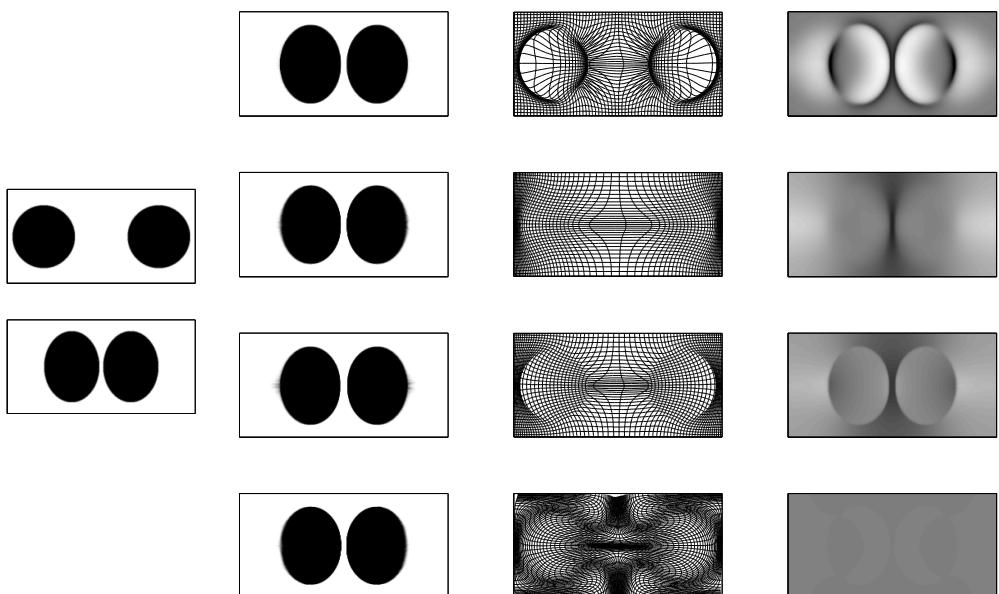
Diffeomorphic Image Registration

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

Because we can not 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.

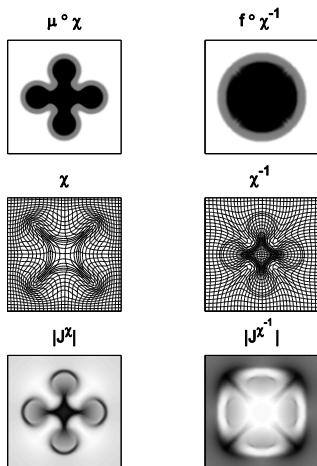
- Uses the same small deformation composed multiple times.
- Faster than Geodesic Shooting.
- Gives similar deformations to Geodesic Shooting.
- Currently more additional utilities.

Geodesic Shooting

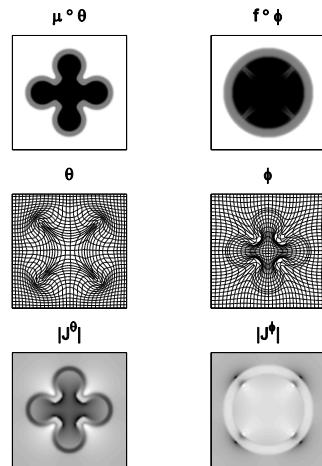
- Uses the optimal series of small deformations, which are composed together.
- More mathematically correct than Dartel.
- Gives nicer maps of volume change than Dartel.
- Likely to replace Dartel in future.

Dartel & GS Compared

Dartel

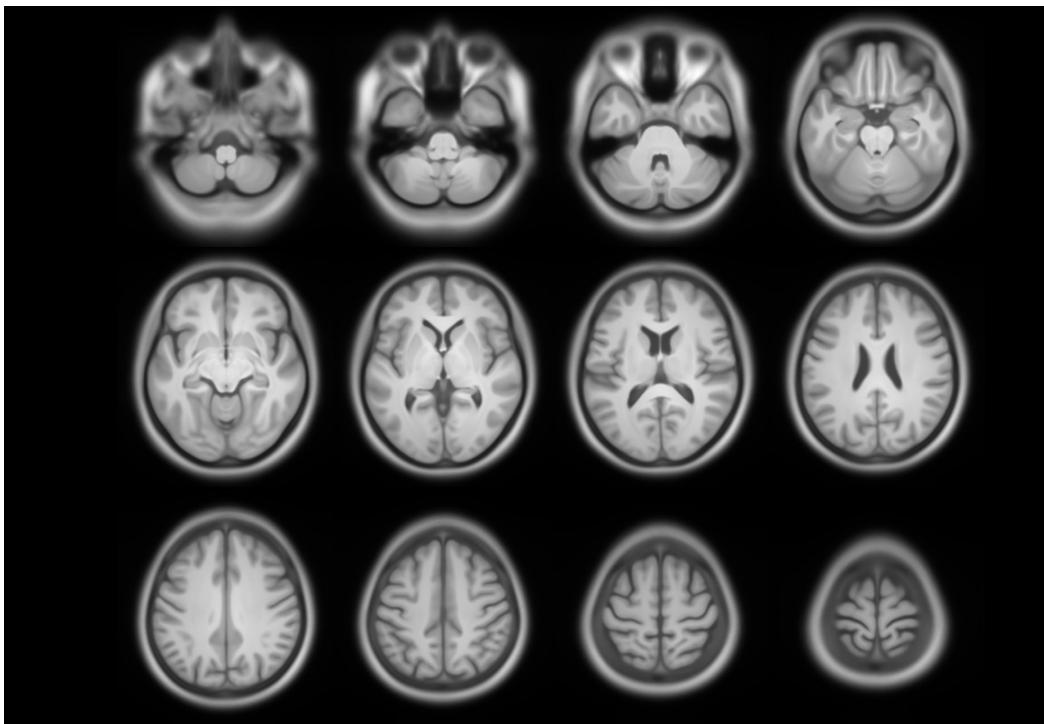
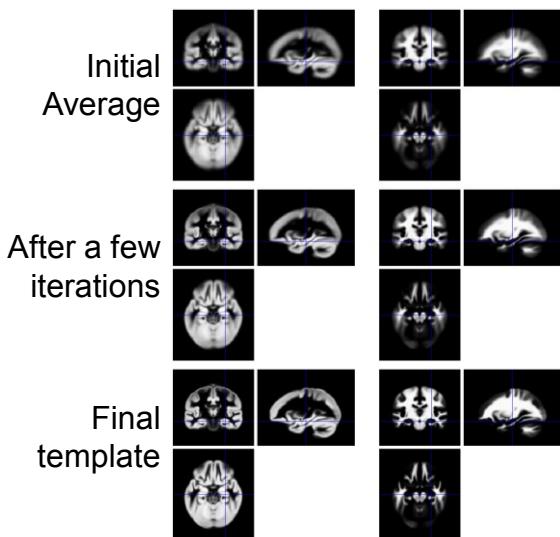


Geodesic Shooting

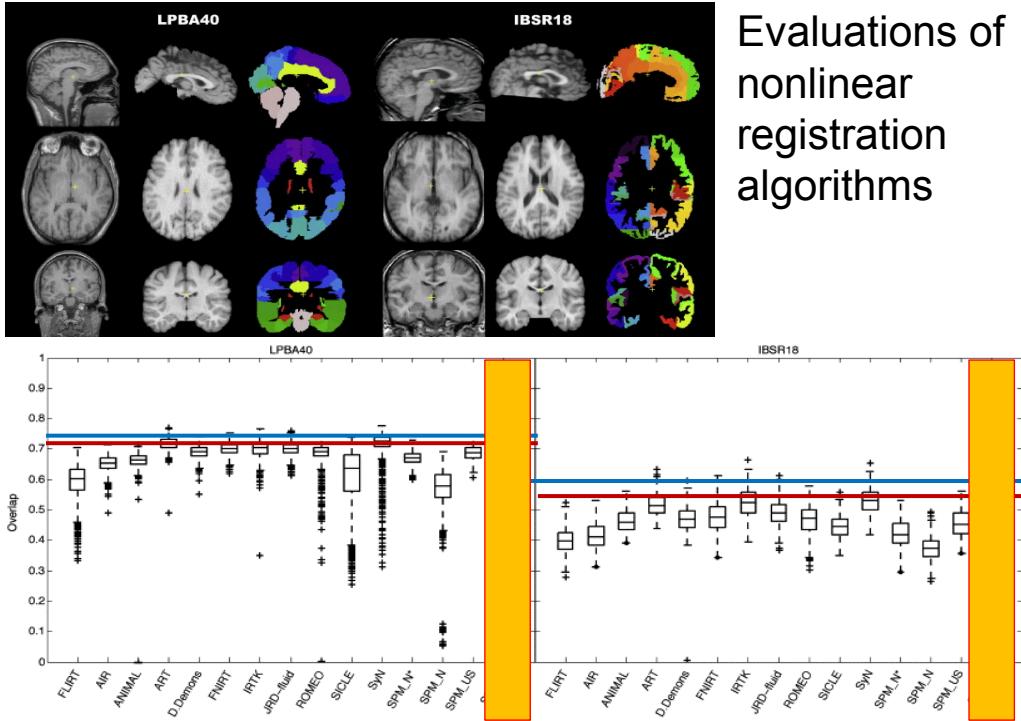


Group-wise alignment

- Template implicitly generated from data in study.
- Findings less biased by choice of template.

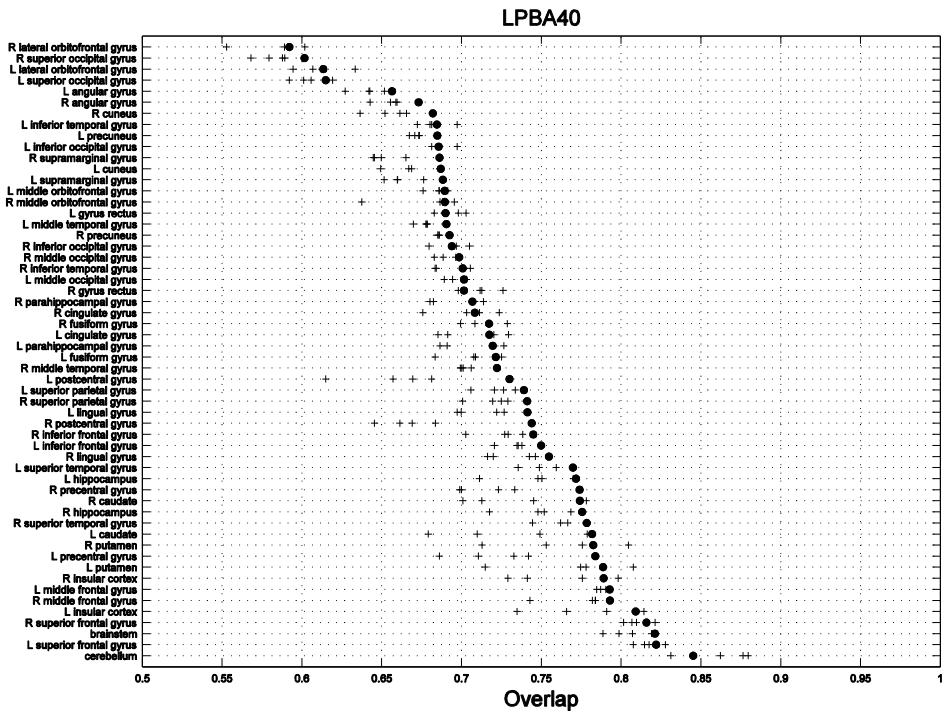


Evaluations of nonlinear registration algorithms



Tissue map averages





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

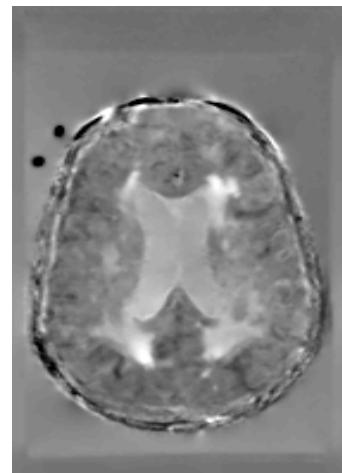
- Beg, Miller, Trouvé & Younes (2005). “*Computing large deformation metric mappings via geodesic flows of diffeomorphisms.*” International journal of computer vision 61(2):139-157.
- Ashburner (2007). “*A Fast Diffeomorphic Image Registration Algorithm*”. NeuroImage 38:95-113.
- Ashburner & Friston (2009). “*Computing Average Shaped Tissue Probability Templates*”. NeuroImage 45:333-341.
- Klein et al (2009). “*Evaluation of 14 nonlinear deformation algorithms applied to human brain MRI registration*”. NeuroImage 46(3):786-802.
- Ashburner & Friston (2011). “*Diffeomorphic registration using geodesic shooting and Gauss-Newton optimisation*”. NeuroImage 55(3):954-967

Overview

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

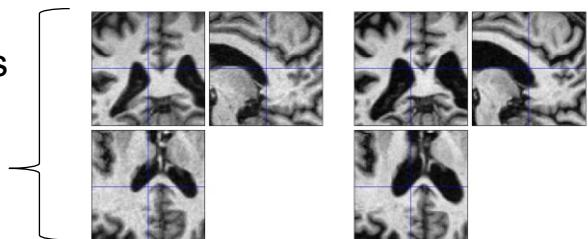
Longitudinal Registration

- Unified model combines:
 - Nonlinear diffeomorphic registration.
 - Rigid-body registration.
 - Intensity inhomogeneity correction.



Two Longitudinal Scans

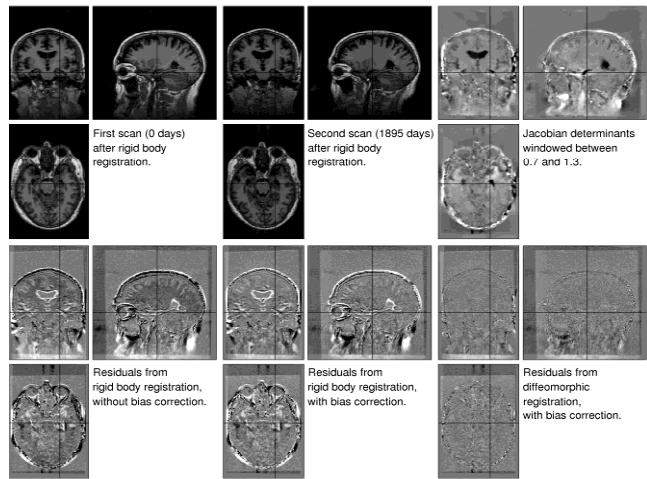
Two scans taken 6 years apart
(after rigid registration).



Oasis Data

OAS2 0002

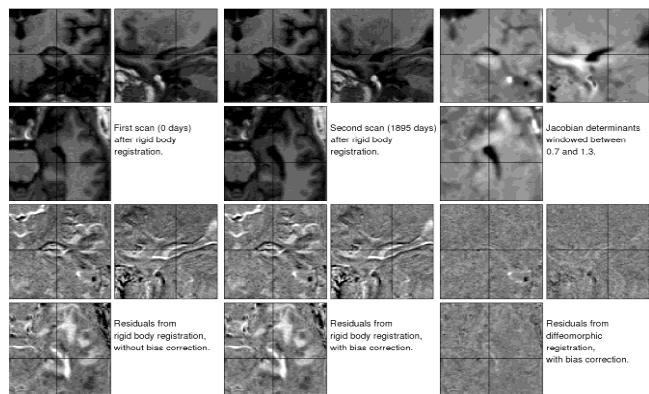
75 year old male,
with MCI
(MMSE=22,
CDR=0.5).



Oasis Data

OAS2 0002

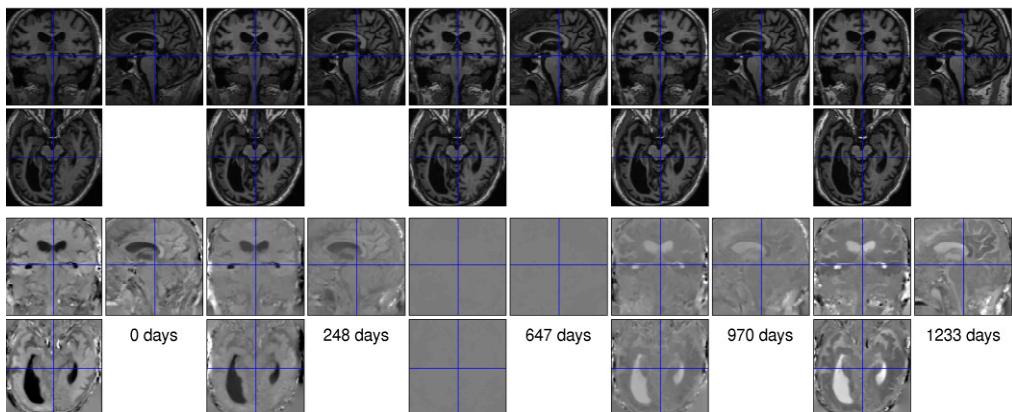
75 year old male,
with MCI
(MMSE=22,
CDR=0.5).



Oasis Data

OAS2 0048

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



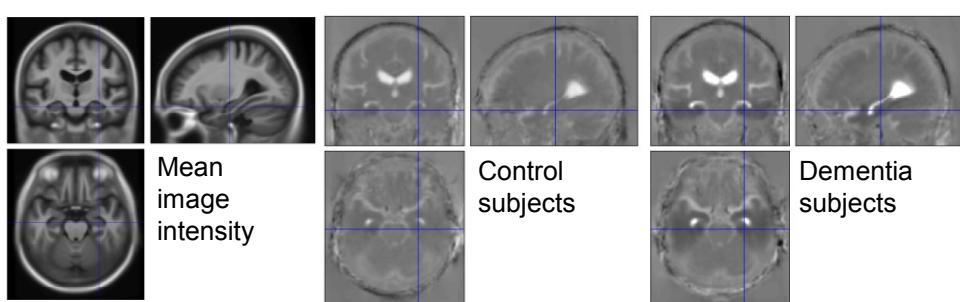
Oasis Data

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

- Fox, Ridgway & Schott (2011). “*Algorithms, atrophy and Alzheimer's disease: cautionary tales for clinical trials*”. Neuroimage 57(1):15-18.
- Ashburner & Ridgway (2013). “*Symmetric diffeomorphic modelling of longitudinal structural MRI*”. Frontiers in Neuroscience 6(197).

Overview

- Morphometry
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- Tissue Segmentation
- Diffeomorphic Registration
- Longitudinal Registration

• **Multivariate Shape Models**

- Multivariate nature of shape
- “Scalar momentum”
- Some evaluations

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)
[Mechelli, Friston, Frackowiak & Price. Structural covariance in the human cortex. Journal of Neuroscience 25\(36\):8303-8310 \(2005\).](#)
- We should work with the most accurate modelling assumptions available.
 - If a model is accurate, it will make accurate predictions.

Argument from authority I

"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).

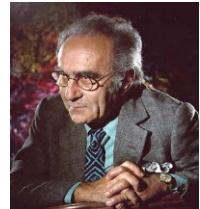
Argument from authority II

"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."

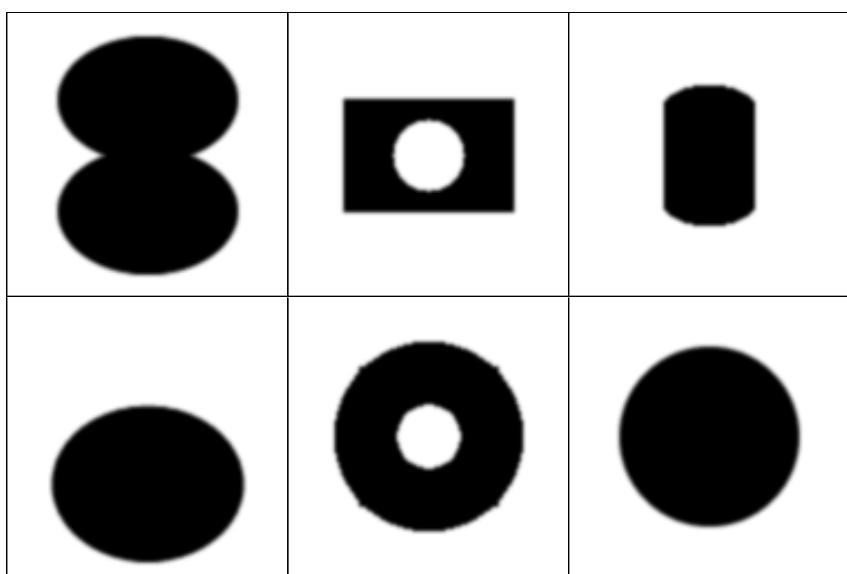
Jacob Bronowski & W.M. Long (Nature, 1951).

"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."

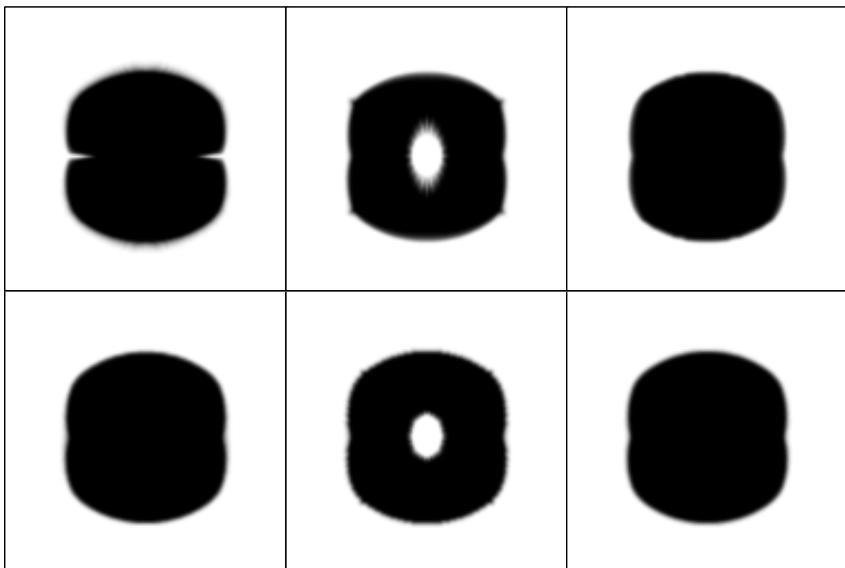
Jacob Bronowski & W.M. Long (Nature, 1951).



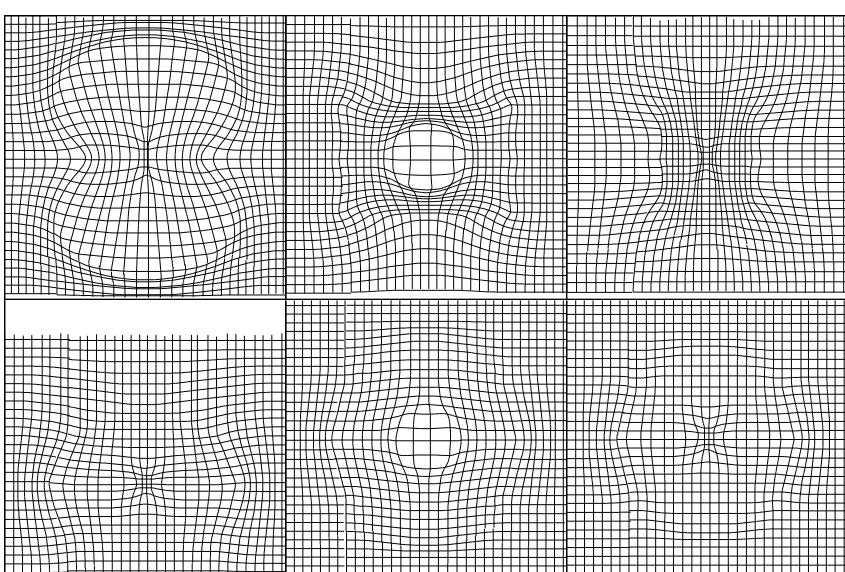
Some 2D Shapes



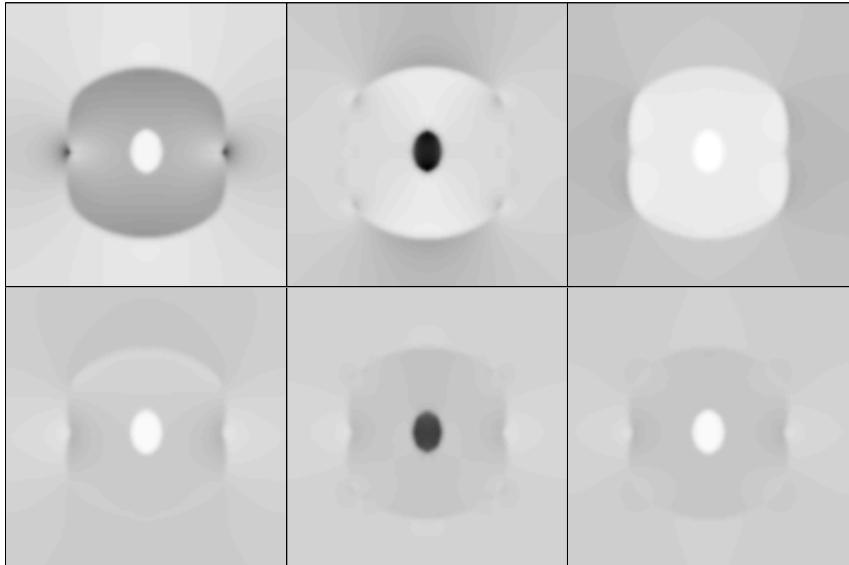
Shapes aligned to their average



These were the deformations for that

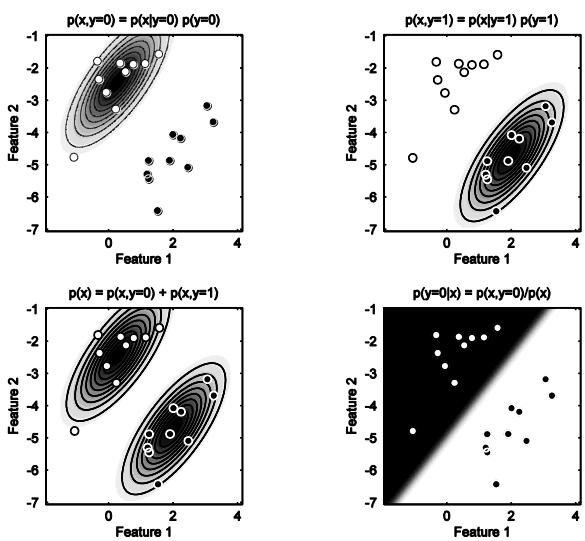


and these are the Jacobian determinants



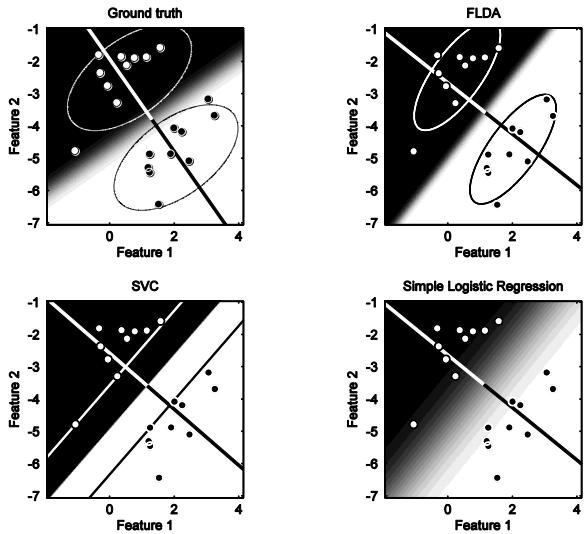
Fisher's Linear Discriminant Analysis

- A multivariate model.
- Special case of canonical variates analysis.
- A **generative** model.



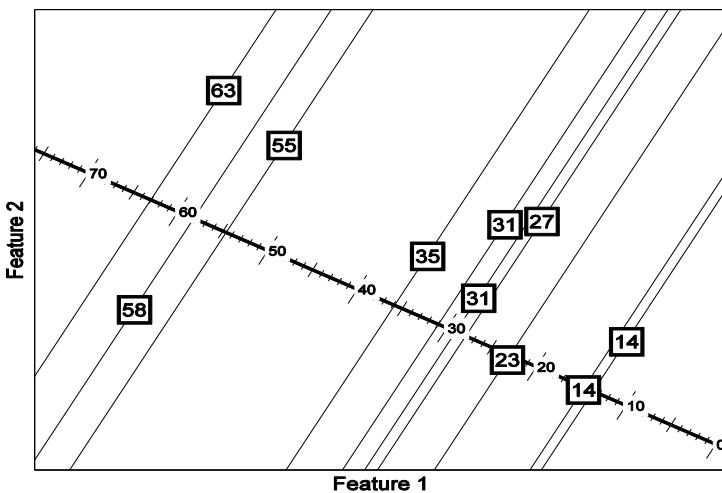
Other linear discrimination approaches

- 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:

$$y = a_1 \times x_1 + a_2 \times x_2 + a_3 \times x_3 + \dots + b$$

where: y is the prediction

x_1, x_2, x_3 etc are voxels in the image to classify

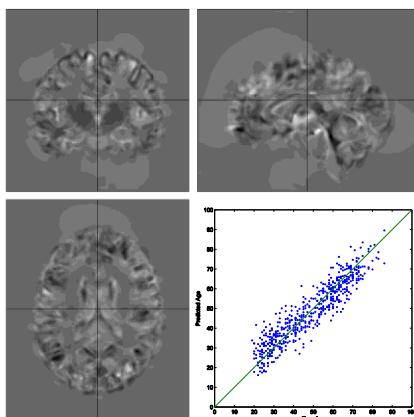
a_1, a_2, a_3 etc are voxels in a weight map

b is a constant offset.

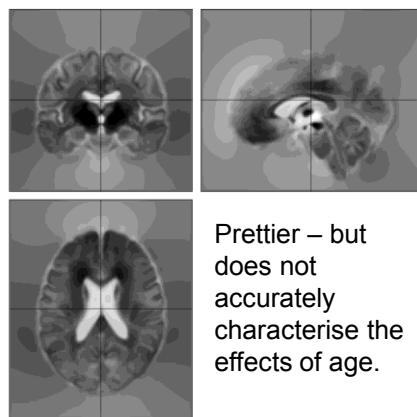
The weight map can be visualised

Maps

Multivariate weight map



Simple T statistic image

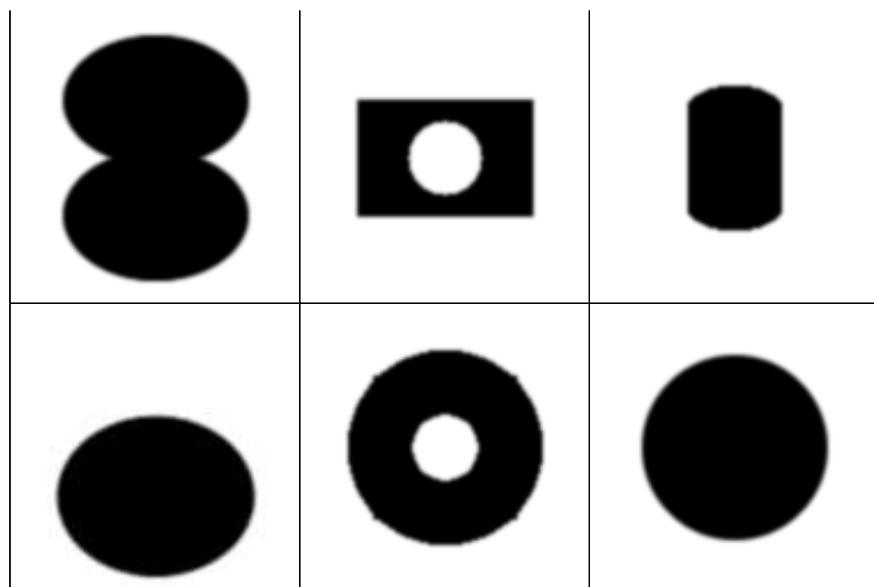


Prettier – but
does not
accurately
characterise the
effects of age.

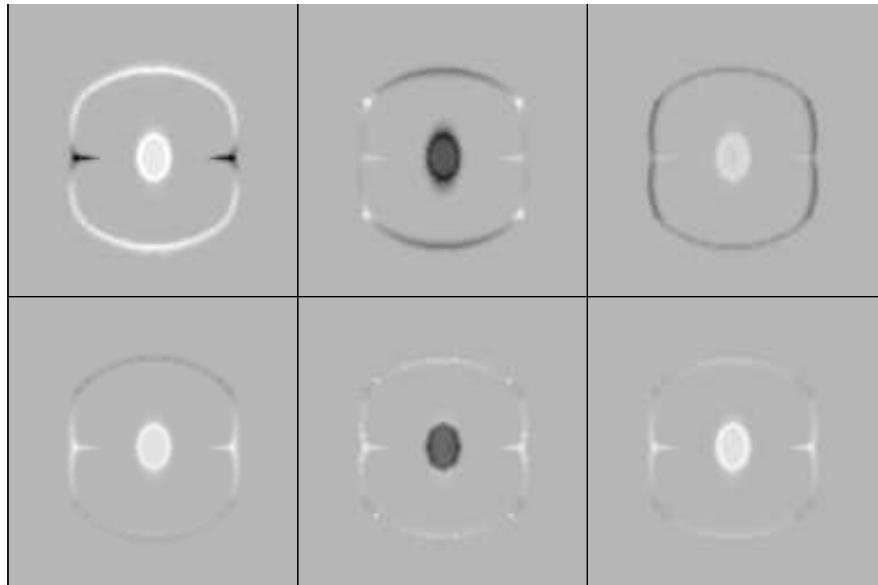
“Scalar Momentum”

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

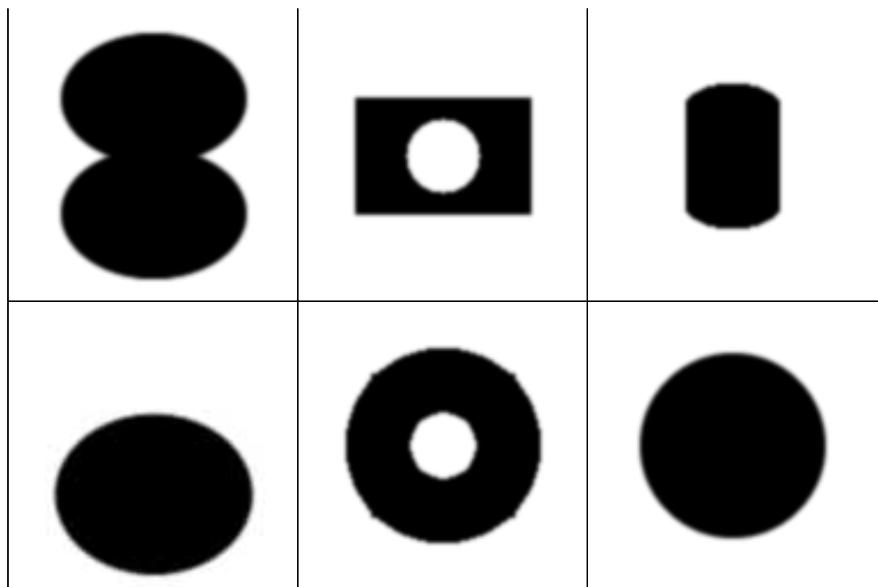
The 2D shapes (again)



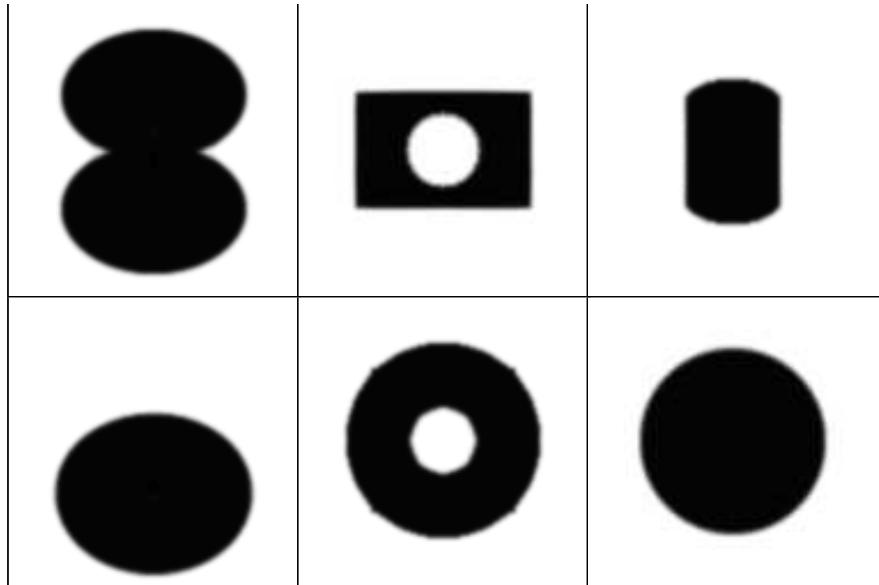
“Scalar momentum” $| \det d\varphi |(I_0 - I_1 \circ \varphi)$



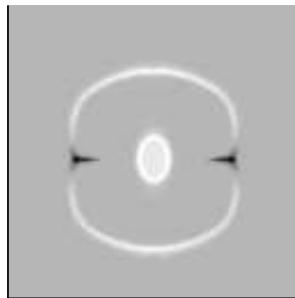
The 2D shapes (yet again)

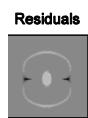


Reconstructed from scalar momentum and template.



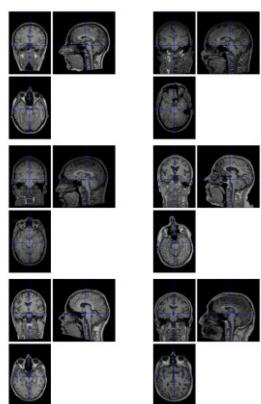
“Scalar momentum” – encodes the original shapes



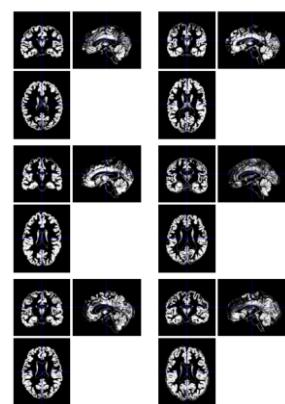


IXI Data

Original Images

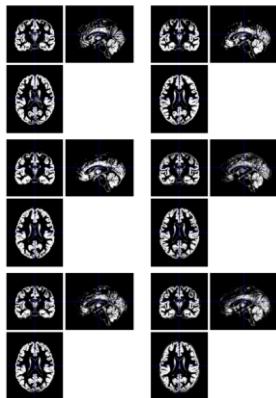


Rigidly Aligned Grey Matter

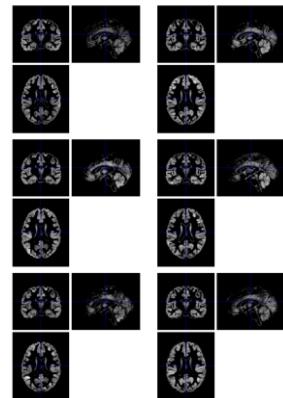


VBM-type Features

Warped Grey Matter

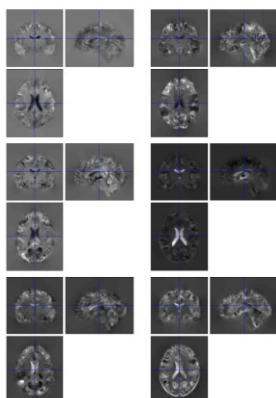


“Modulated” Warped GM

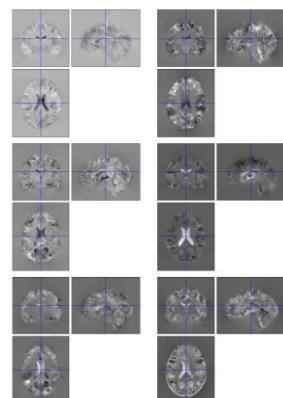


Volumetric Measures from Deformation Fields

Jacobian determinants

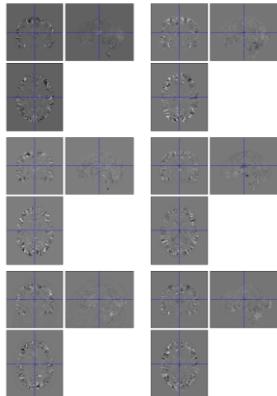


Initial Velocity Divergence

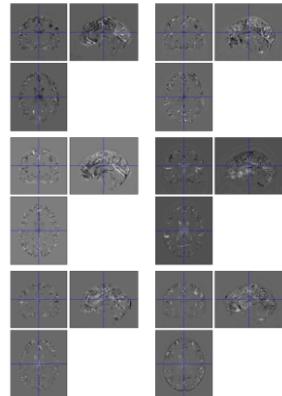


Scalar Momentum

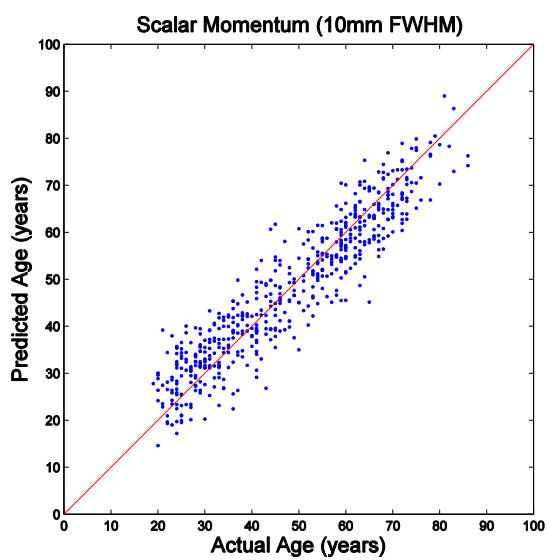
1st Component



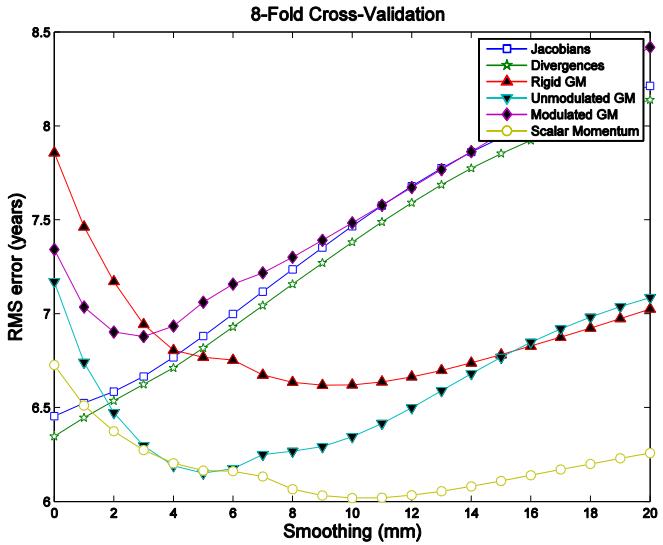
2nd Component



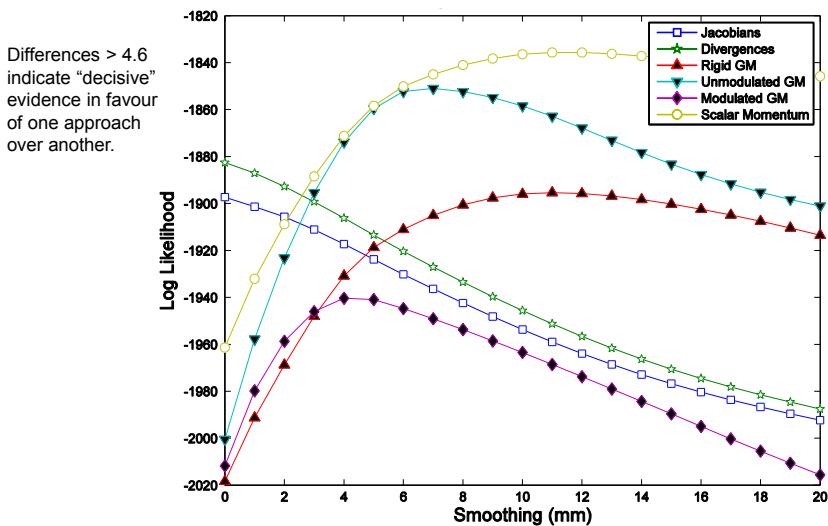
Age Prediction - Best Result



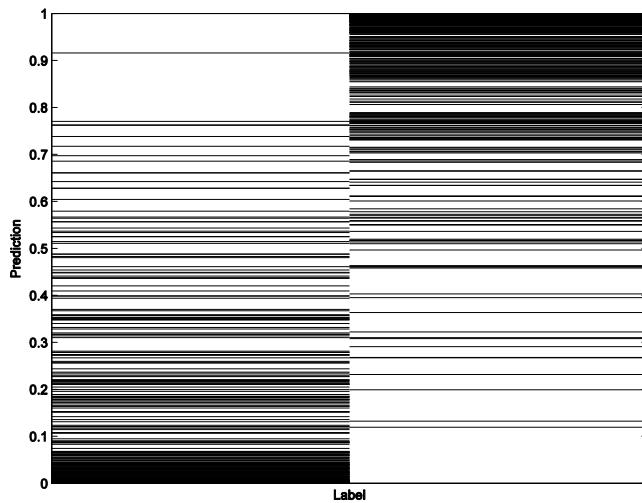
Age Prediction – Comparison Among Features



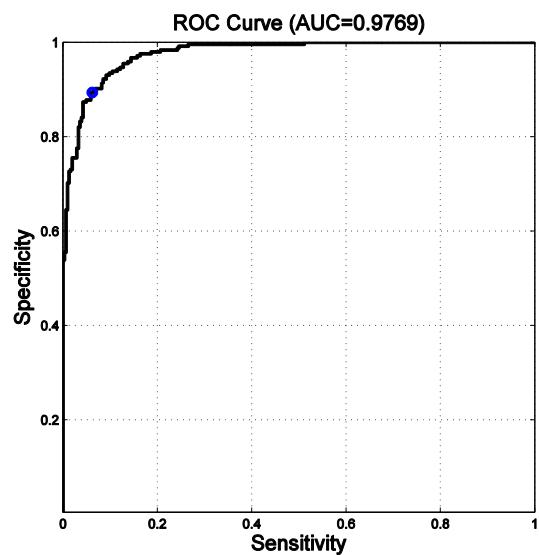
Age Prediction – Model Log Likelihoods



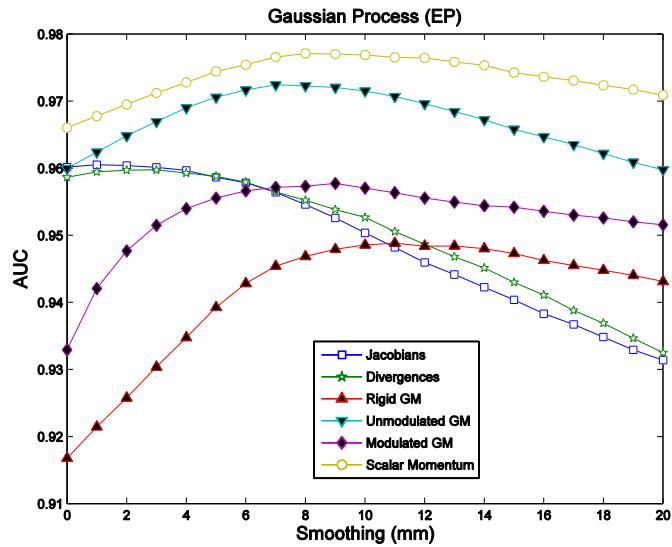
Sex Prediction – Best Result



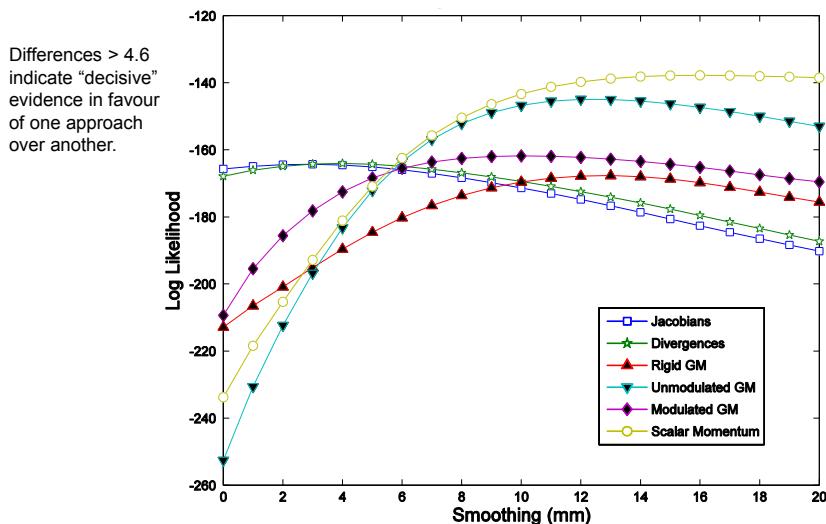
Sex Prediction – Best Result



Sex Prediction – Comparison Among Features



Sex Prediction – Model Log Likelihoods



Selected References

- Bishop. *Pattern Recognition and Machine Learning*. 2006.
- Rasmussen & Williams. *Gaussian Processes for Machine Learning*. MIT Press, 2006. ISBN-10 0-262-18253-X, ISBN-13 978-0-262-18253-9.
<http://www.gaussianprocess.org/gpml/>
- Younes, Arrate & Miller. "Evolutions equations in computational anatomy". *NeuroImage* 45(1):S40-S50, 2009.
- Singh, Fletcher, Preston, Ha, King, Marron, Wiener & Joshi (2010). *Multivariate Statistical Analysis of Deformation Momenta Relating Anatomical Shape to Neuropsychological Measures*. T. Jiang et al. (Eds.): MICCAI 2010, Part III, LNCS 6363, pp. 529–537, 2010.
- Ashburner & Klöppel (2011). "Multivariate models of inter-subject anatomical variability". *NeuroImage* 56(2):422-439.

