

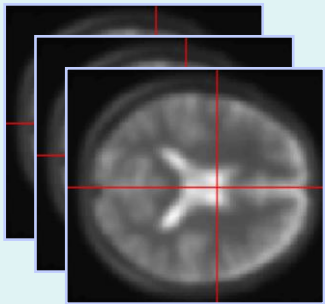
NeuroImaging Data Processing

aka. Statistical Parametric Mapping short course

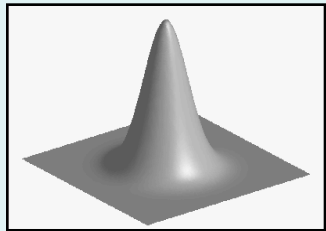
Course 1 & 2:
spatial pre-processing

SPM work flow

Image time-series



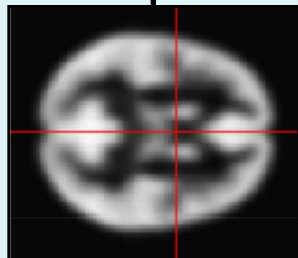
Spatial filter



Realignment

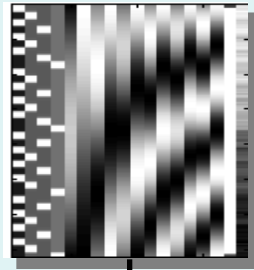
Smoothing

Normalisation

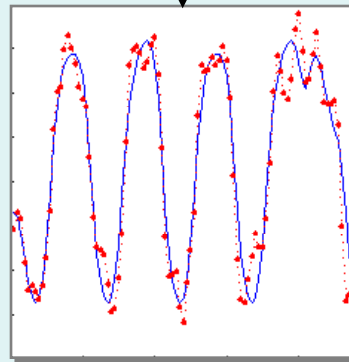


Anatomical reference

Design matrix

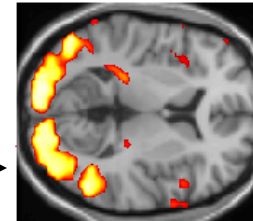
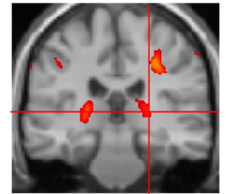
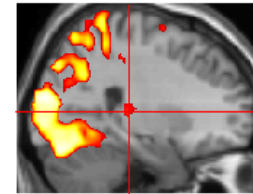


General Linear Model



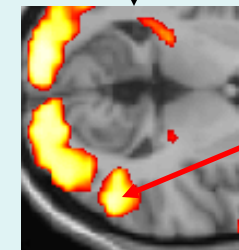
Parameter estimates

Statistical Parametric Map



Statistical Inference

RFT



$p < 0.05$

Content

- **Preliminaries**
- **Within-subject**
- **Between-subject**
- **Smoothing**
- **Conclusion**

Content

- **Preliminaries**

- Introduction
- Rigid-body & affine transformation
- Function optimisation
- Transformations and interpolation
- Pre-processing overview

- **Within-subject**

- **Between-subject**

- **Smoothing**

- **Conclusion**

Image registration

Most “spatial pre-processing” involves aligning images together.

Two components:

- *Registration* –
i.e. Optimise the parameters that describe spatial transformations between the images.
- *Transformation* –
i.e. Re-sample according to the determined transformation parameters.

Label based techniques

- Homologous labels (points, lines, surfaces) in the source and the reference images
 - ➔ find transformations that best superpose them
- Labels are identified (manually/semi-automatically)
 - ➔ time consuming and subjective process
 - ➔ few identifiable discrete points in the brain
- Lines and surfaces, e.g. contours, can be extracted (semi-)automatically
- Best match = minimal **distance**
Question: how do you measure "distance"?

Label based techniques

- Homologous labels (points, lines, surfaces) in the source and the reference images
→ find transformations that best superpose them



Not so obvious in the brain!

Intensity based techniques

By minimizing a “**distance**” between images, i.e. *whole source* image and *whole reference* image

- ➔ Need a scalar measure (=distance) to optimize
- ➔ Depends on the image content...

Finding a best match = global optimum?

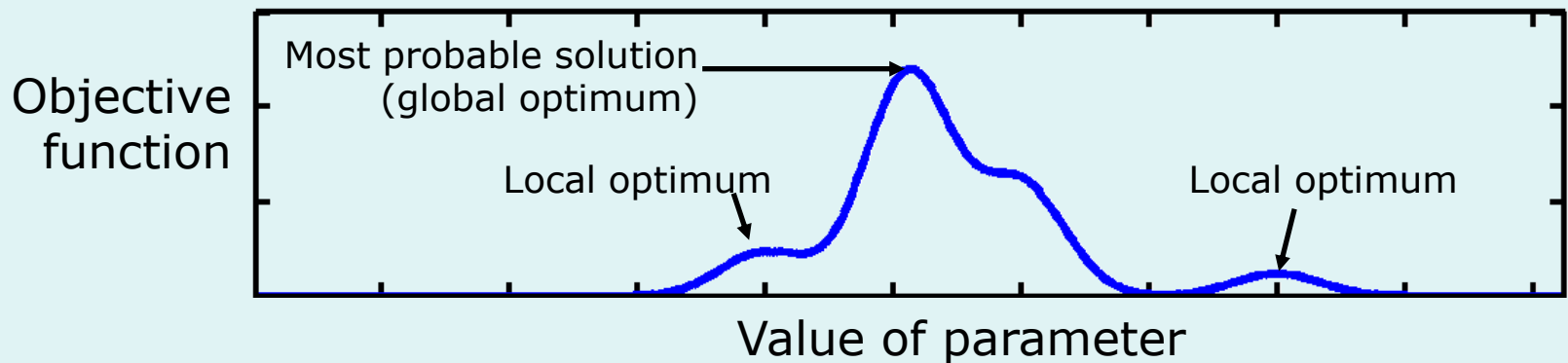
- ➔ but susceptible to poor starting estimates

Hybrid approaches :

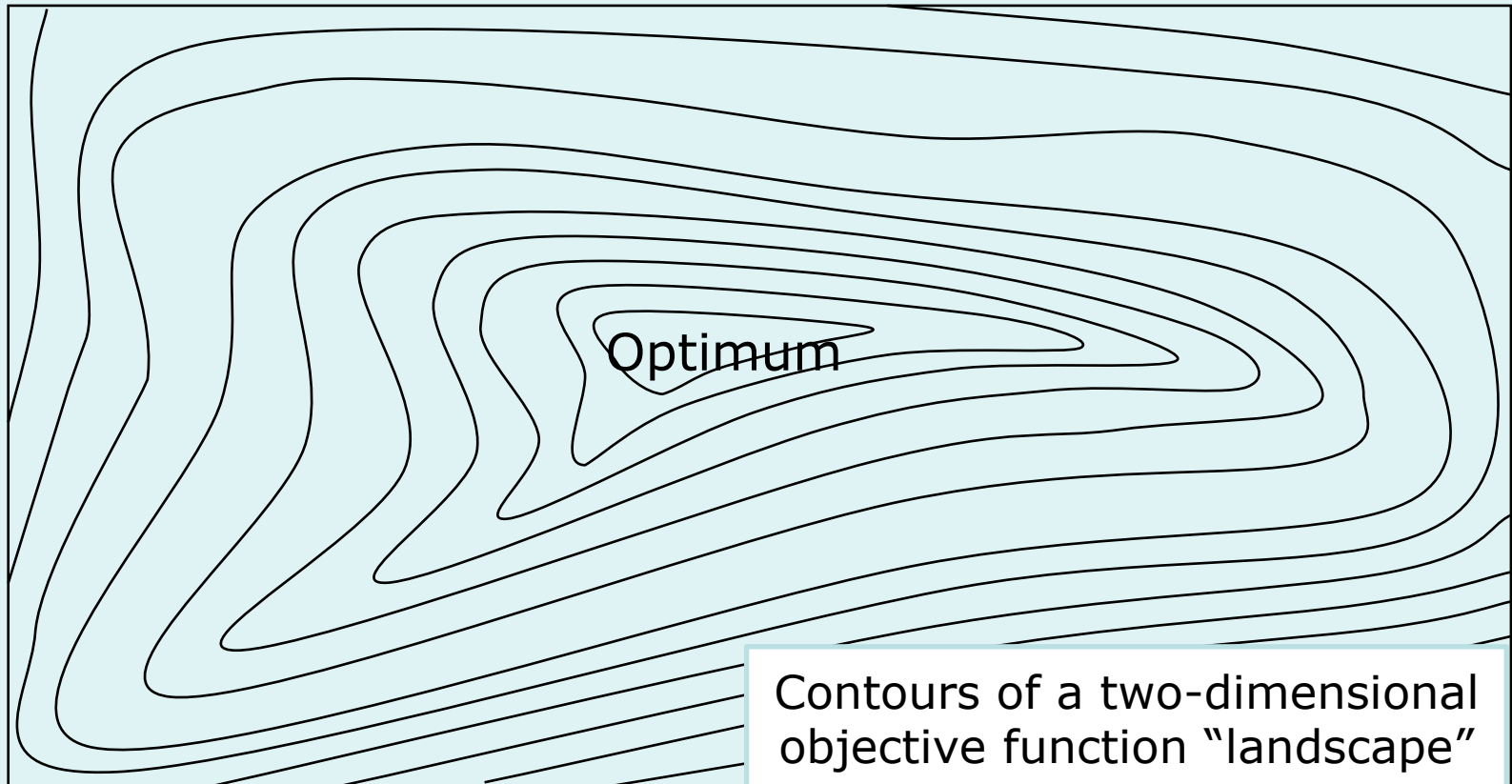
1. label/manual, then
2. intensity based methods

Optimisation

- Image registration is done by **optimisation**.
- Optimisation involves finding some “best” parameters according to an “objective function” (to be either minimised or maximised)



Optimisation, multiple parameters

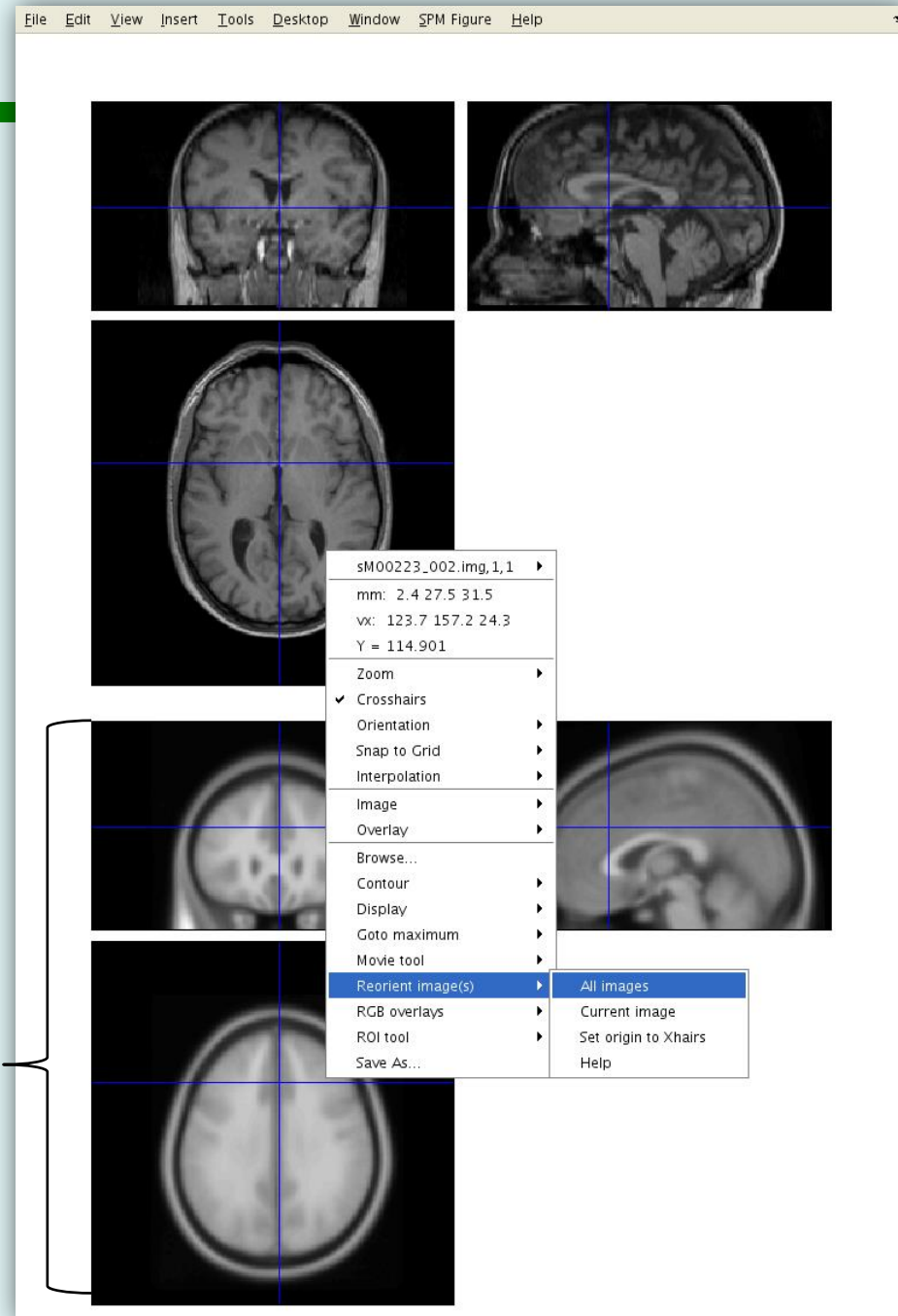


No grid exploration at "high dimension" !

Optimisation

Because registration only finds a *local optimum*, some manual reorienting of the images may be needed before doing anything else in SPM.

An MNI-space image from spm12/canonical directory.



2D Affine Transforms

- Translations by t_x and t_y
 $x_1 = x_0 + t_x$
 $y_1 = y_0 + t_y$
- Rotation around the origin by Θ radians

$$x_1 = \cos(\Theta) x_0 + \sin(\Theta) y_0$$

$$y_1 = -\sin(\Theta) x_0 + \cos(\Theta) y_0$$

- Zooms by s_x and s_y :

$$x_1 = s_x x_0$$

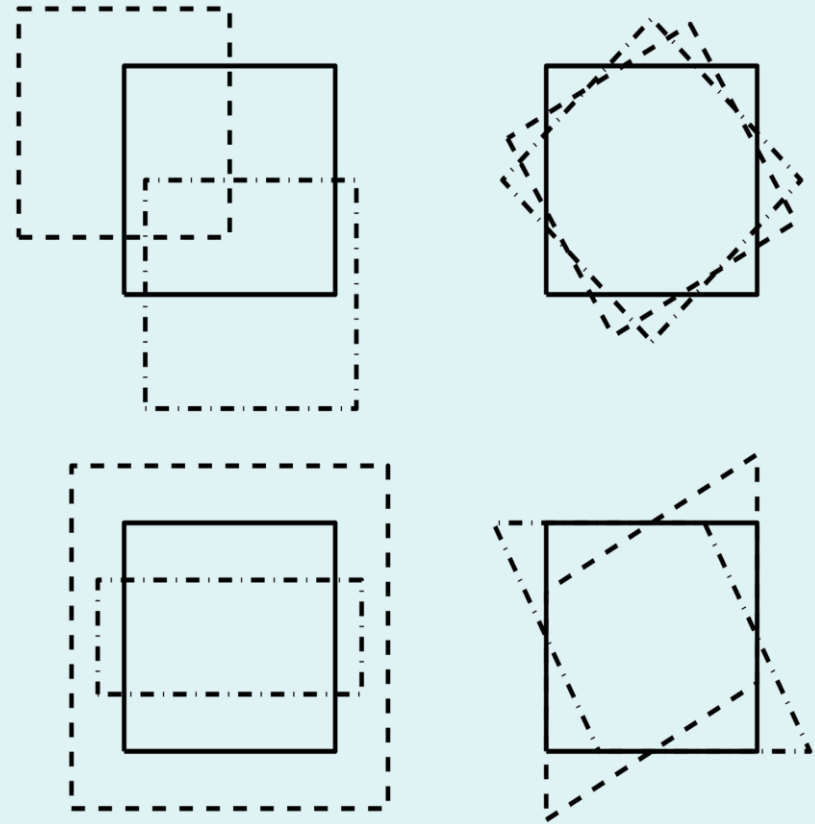
$$y_1 = s_y y_0$$

- Shear h_x

$$x_1 = x_0 + h_x y_0$$

$$y_1 = y_0$$

Same for h_y



2D Affine Transforms

- Translations by t_x and t_y

$$x_1 = 1 x_0 + 0 y_0 + t_x$$

$$y_1 = 0 x_0 + 1 y_0 + t_y$$

- Rotation around the origin by Θ radians

$$x_1 = \cos(\Theta) x_0 + \sin(\Theta) y_0 + 0$$

$$y_1 = -\sin(\Theta) x_0 + \cos(\Theta) y_0 + 0$$

- Zooms by s_x and s_y :

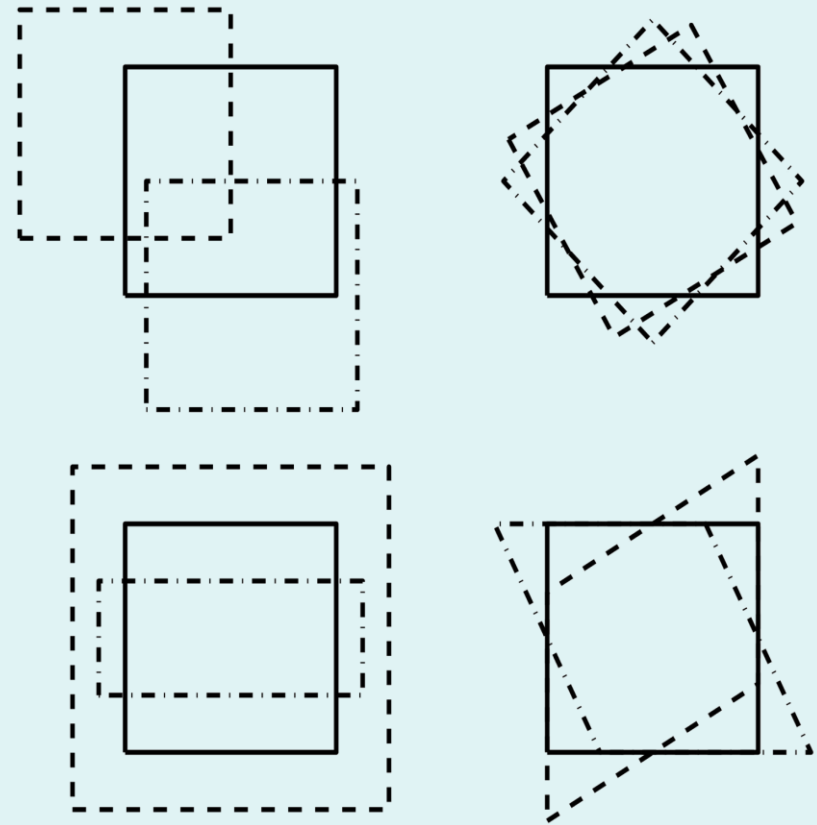
$$x_1 = s_x x_0 + 0 y_0 + 0$$

$$y_1 = 0 x_0 + s_y y_0 + 0$$

- Shear h_x

$$x_1 = 1 x_0 + h_x y_0 + 0$$

$$y_1 = 0 x_0 + 1 y_0 + 0$$



Same for h_y

2D Affine transform

- Operations can be represented by:

$$x_1 = m_{11}x_0 + m_{12}y_0 + m_{13}$$

$$y_1 = m_{21}x_0 + m_{22}y_0 + m_{23}$$

- ...or as matrices:

$$\mathbf{p}_1 = \mathbf{M} \mathbf{p}_0 \quad \begin{bmatrix} x_1 \\ y_1 \\ 1 \end{bmatrix} = \begin{bmatrix} m_{11} & m_{12} & m_{13} \\ m_{21} & m_{22} & m_{23} \\ 0 & 0 & 1 \end{bmatrix} \times \begin{bmatrix} x_0 \\ y_0 \\ 1 \end{bmatrix}$$

- Parallel lines remain parallel

Rigid-body transformations are a subset of “affine transformation”

3D Affine transform

- Operations can be represented by:

$$x_1 = m_{11}x_0 + m_{12}y_0 + m_{13}z_0 + m_{14}$$

$$y_1 = m_{21}x_0 + m_{22}y_0 + m_{23}z_0 + m_{24}$$

$$z_1 = m_{31}x_0 + m_{32}y_0 + m_{33}z_0 + m_{34}$$

- Or as matrices:

$$\mathbf{p}_1 = \mathbf{M} \mathbf{p}_0$$

$$\begin{bmatrix} x_1 \\ y_1 \\ z_1 \\ 1 \end{bmatrix} = \begin{bmatrix} m_{11} & m_{12} & m_{13} & m_{14} \\ m_{21} & m_{22} & m_{23} & m_{24} \\ m_{31} & m_{32} & m_{33} & m_{34} \\ 0 & 0 & 0 & 1 \end{bmatrix} \times \begin{bmatrix} x_0 \\ y_0 \\ z_0 \\ 1 \end{bmatrix}$$

- Parallel lines remain parallel

Rigid-body transformations are a subset of “affine transformation”

Rigid-body transformations

- Assume that brain of the same subject doesn't change shape or size in the scanner.
 - Head can move, but remains the same shape and size.
 - Some exceptions:
 - Image distortions.
 - Brain slops about slightly because of gravity.
 - Brain growth or atrophy over time.
- If the subject's head moves, we need to "match" the images.
 - Do this by image registration.

3D Rigid-body Transform

- A 3D rigid body transform is an affine transform defined by:
 - 3 translations - in X, Y & Z directions
 - 3 rotations - about X, Y & Z axes

$$R = \begin{pmatrix} 1 & 0 & 0 & \mathbf{X}_{\text{trans}} \\ 0 & 1 & 0 & \mathbf{Y}_{\text{trans}} \\ 0 & 0 & 1 & \mathbf{Z}_{\text{trans}} \\ 0 & 0 & 0 & 1 \end{pmatrix} \times \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & \cos f & \sin f & 0 \\ 0 & -\sin f & \cos f & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \times \begin{pmatrix} \cos q & 0 & \sin q & 0 \\ 0 & 1 & 0 & 0 \\ -\sin q & 0 & \cos q & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \times \begin{pmatrix} \cos \Omega & \sin \Omega & 0 & 0 \\ -\sin \Omega & \cos \Omega & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix}$$

Translations
Pitch about x axis
Roll about y axis
Yaw about z axis

- *Note that the the order of the operations matters!*

Voxel-to-world transformation

“Voxel-to-world transforms” =

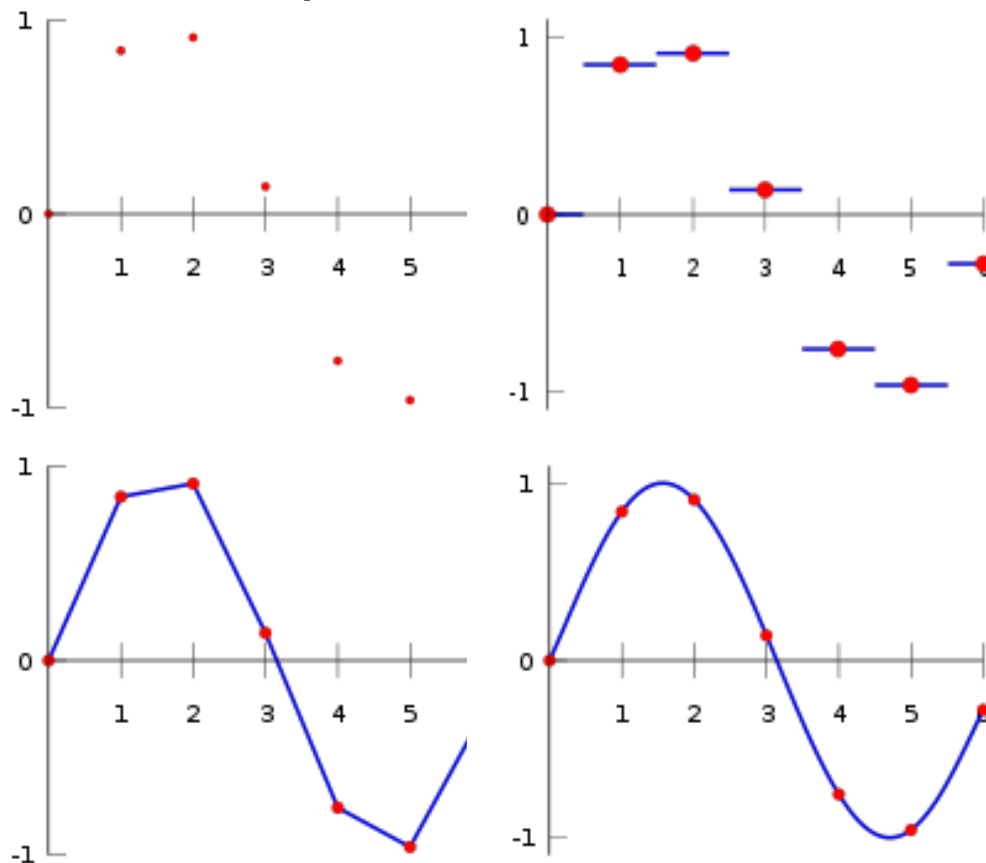
Affine transform **M** associated with each image

- Maps from voxels ($\mathbf{i}=[1...N_i]$, $\mathbf{j}=[1...N_j]$, $\mathbf{k}=[1...N_k]$) to some real world co-ordinate system $[\mathbf{x}, \mathbf{y}, \mathbf{z}]$. e.g.,
 - Scanner co-ordinates (images from DICOM) or MNI coordinates (spatially normalised)
 - Includes *voxel size, head orientation & “space origin”*
- World coordinates are (usually) in millimetres!

Image resampling

A continuous function is represented by a linear combination of basis functions

1D interpolation



2D interpolation kernels

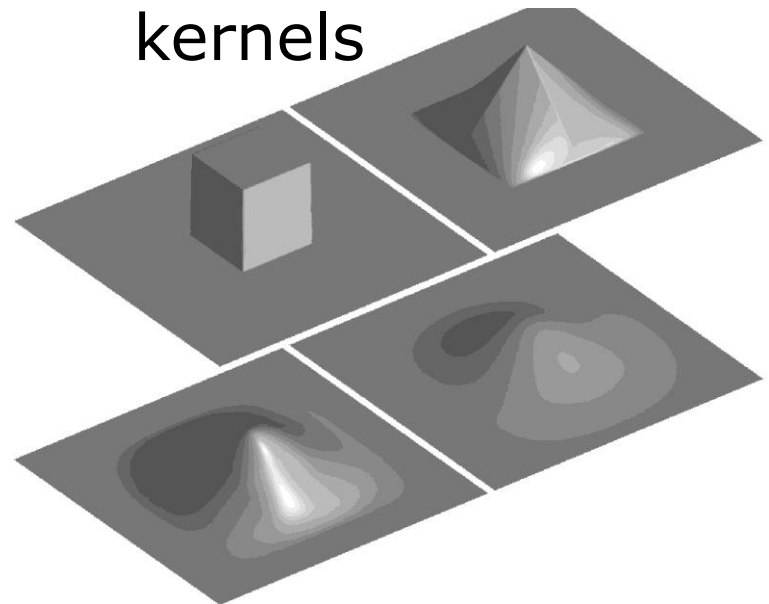


Image resampling

- Nearest neighbour
 - Take the value of the closest voxel
- Tri-linear
 - Just a weighted average of the neighbouring voxels
 - $f_5 = f_1 x_2 + f_2 x_1$
 - $f_6 = f_3 x_2 + f_4 x_1$
 - $f_7 = f_5 y_2 + f_6 y_1$

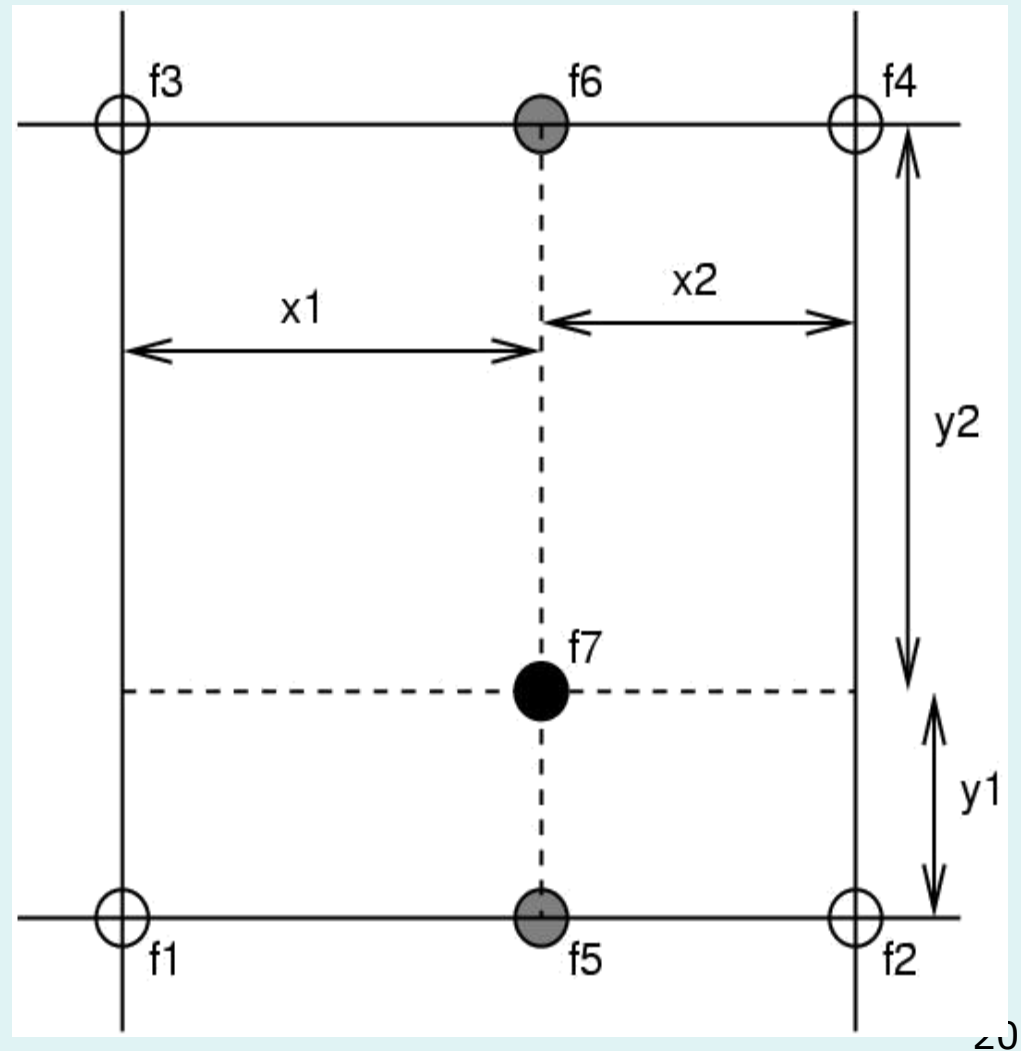


Image resampling, example 1

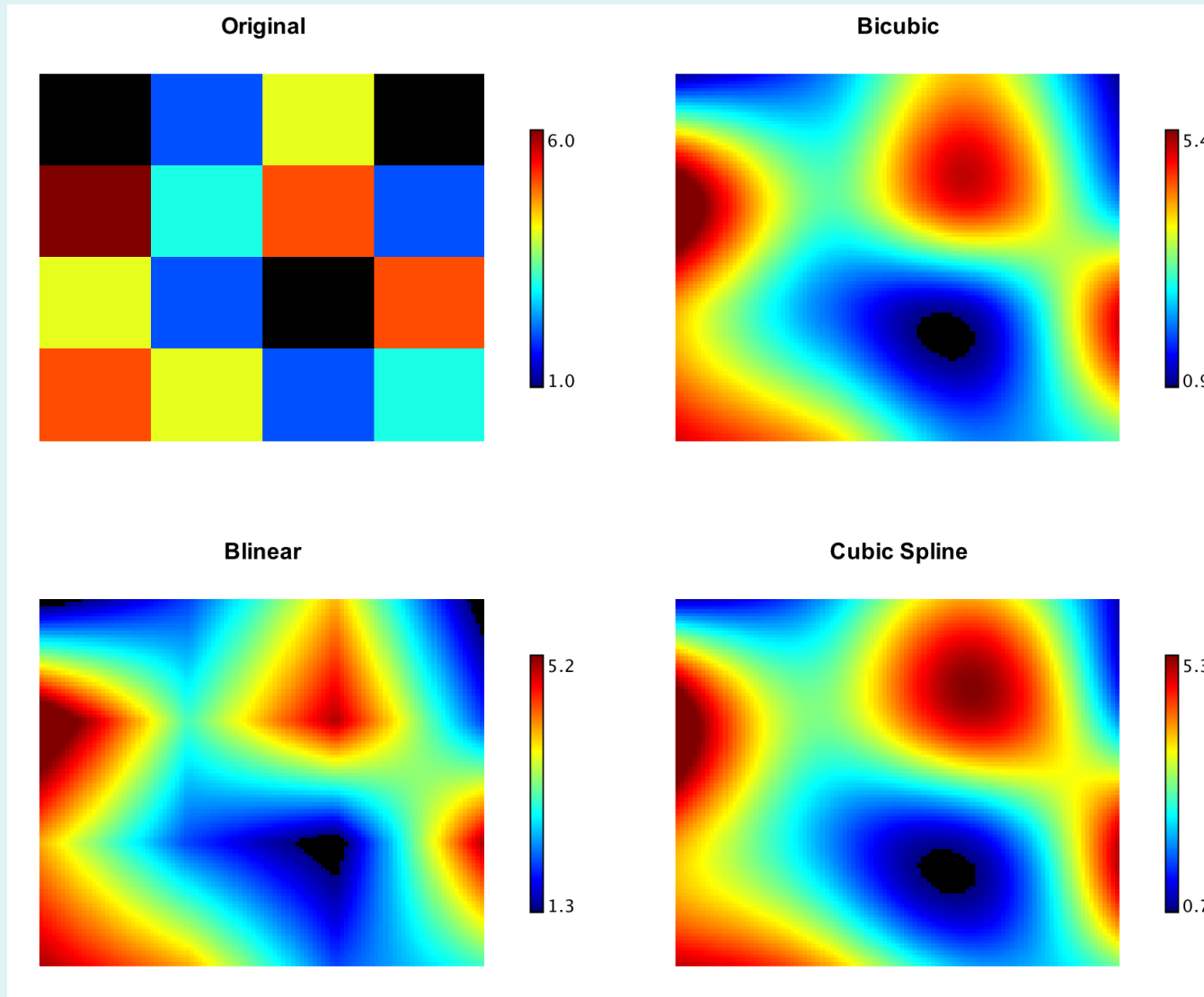
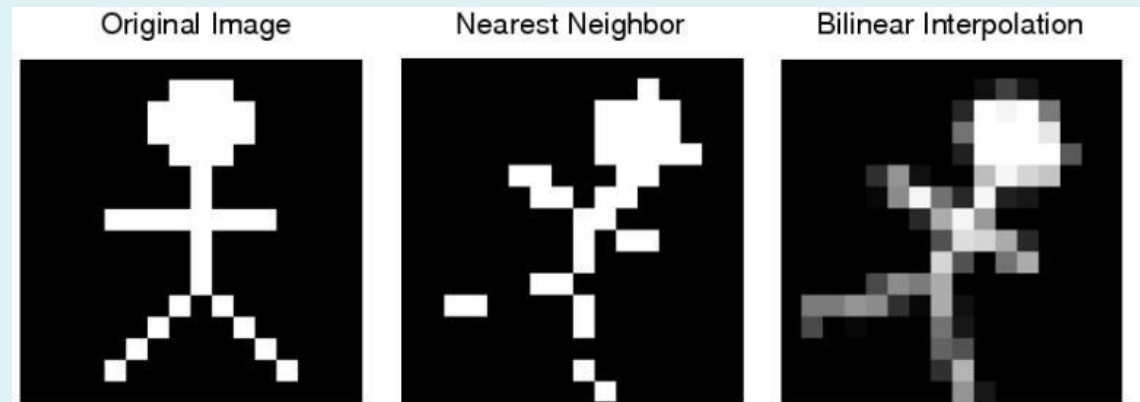
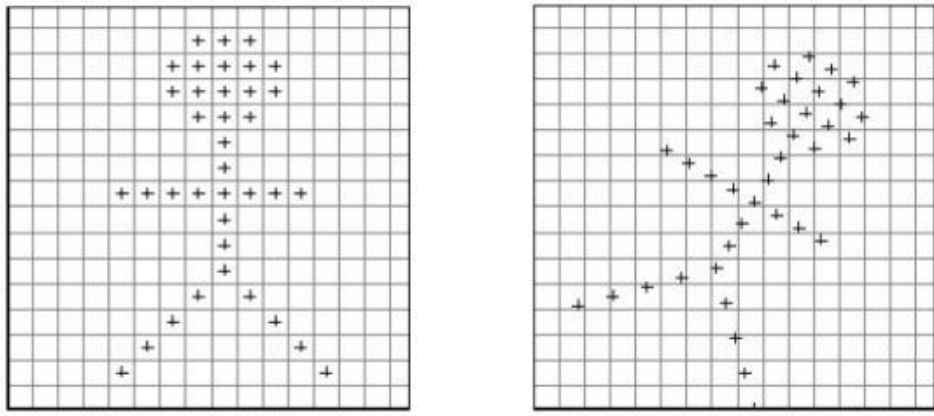


Image resampling, example 2



Binary (or index) image

→ need to preserve property

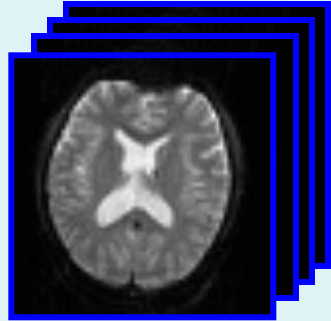
→ no need for smooth interpolation but...

Various registration problems

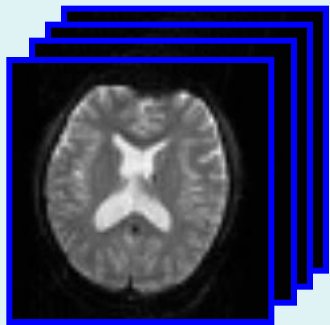
		Rigid body ↓	Image warping ↓
Brain images		Within subject	Between subjects
Same contrast ⇒	Within modality		
Different contrast ⇒	Between modality		

Pre-processing overview: within subject

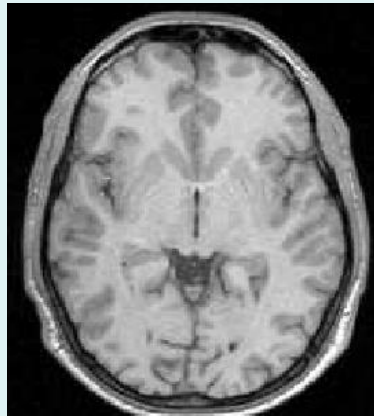
fMRI time-series



Motion (& distortion)
Correction



Anatomical MRI



Coregister

$$\begin{pmatrix} m_{11} & m_{12} & m_{13} & m_{14} \\ m_{21} & m_{22} & m_{23} & m_{24} \\ m_{31} & m_{32} & m_{33} & m_{34} \\ \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{1} \end{pmatrix}$$

Various registration problems

		Rigid body ↓	Image warping ↓
Brain images		Within subject	Between subjects
Same contrast ⇒	Within modality	X	
Different contrast ⇒	Between modality		

Content

- **Preliminaries**

- **Within-subject**

- **Realignment**

- **Minimising mean-squared difference / Residual artifacts**

- **EPI Distortion correction**

- **FieldMap Toolbox / Movement by distortion interaction**

- **Coregistration**

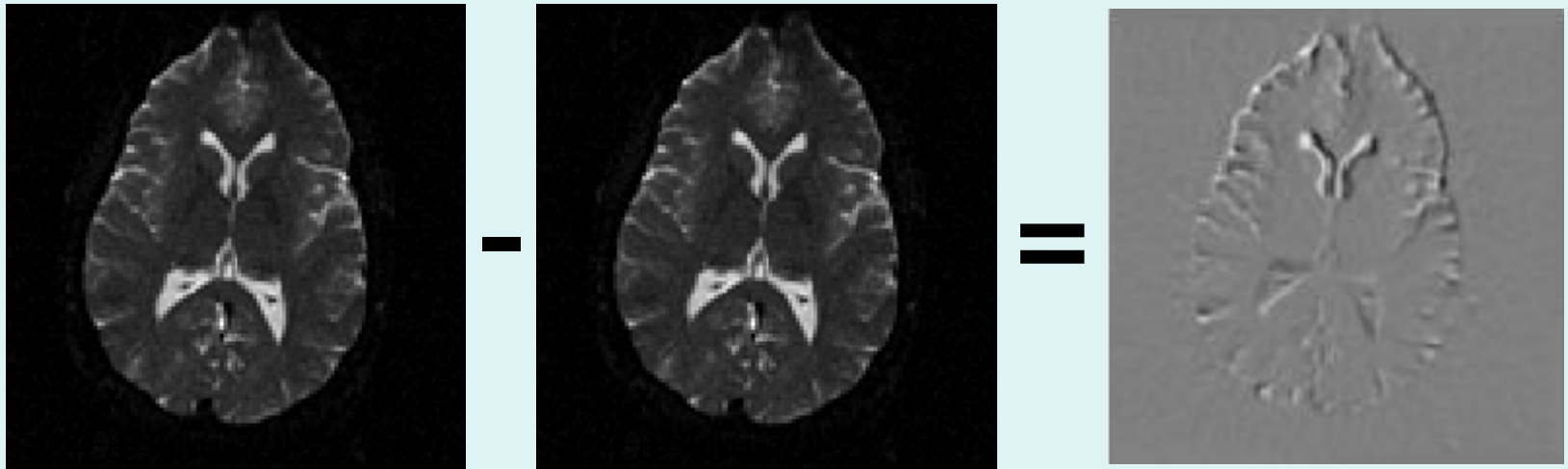
- **Maximising mutual information**

- **Between-subject**

- **Smoothing**

- **Conclusion**

Mean-squared difference



- Minimising mean-squared difference works for intra-modal registration

$$c(I, J) = \sum_{n=1}^N (I_n - J_n)^2$$

- Simple relationship between intensities in one image, versus those in the other
(Assumes normally distributed differences, i.e. residuals)

Within-subject registration

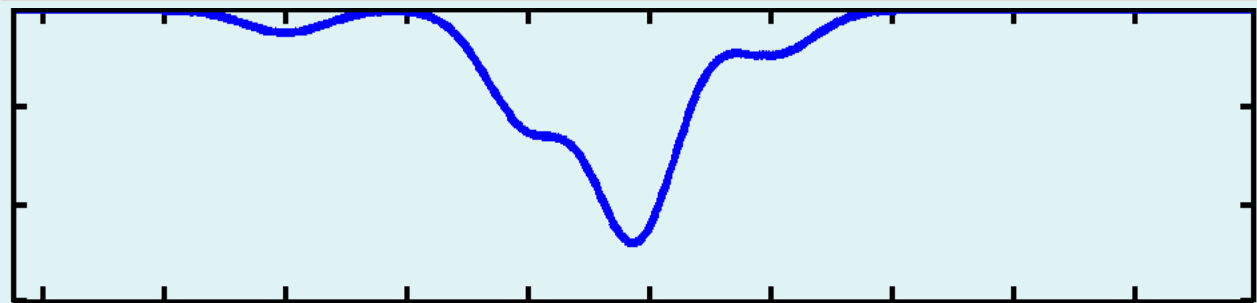
- Realign images I (fixed) and J (moving):
- Criteria to optimize:

$$\rightarrow c(I, J) = \sum_{n=1}^N (I_n - J_n)^2$$

- $c(I, J)$ depends on J 's orientation, which depends on R 's 6 parameters
 - Optimize $c(I, J)$ according to those 6 parameters !

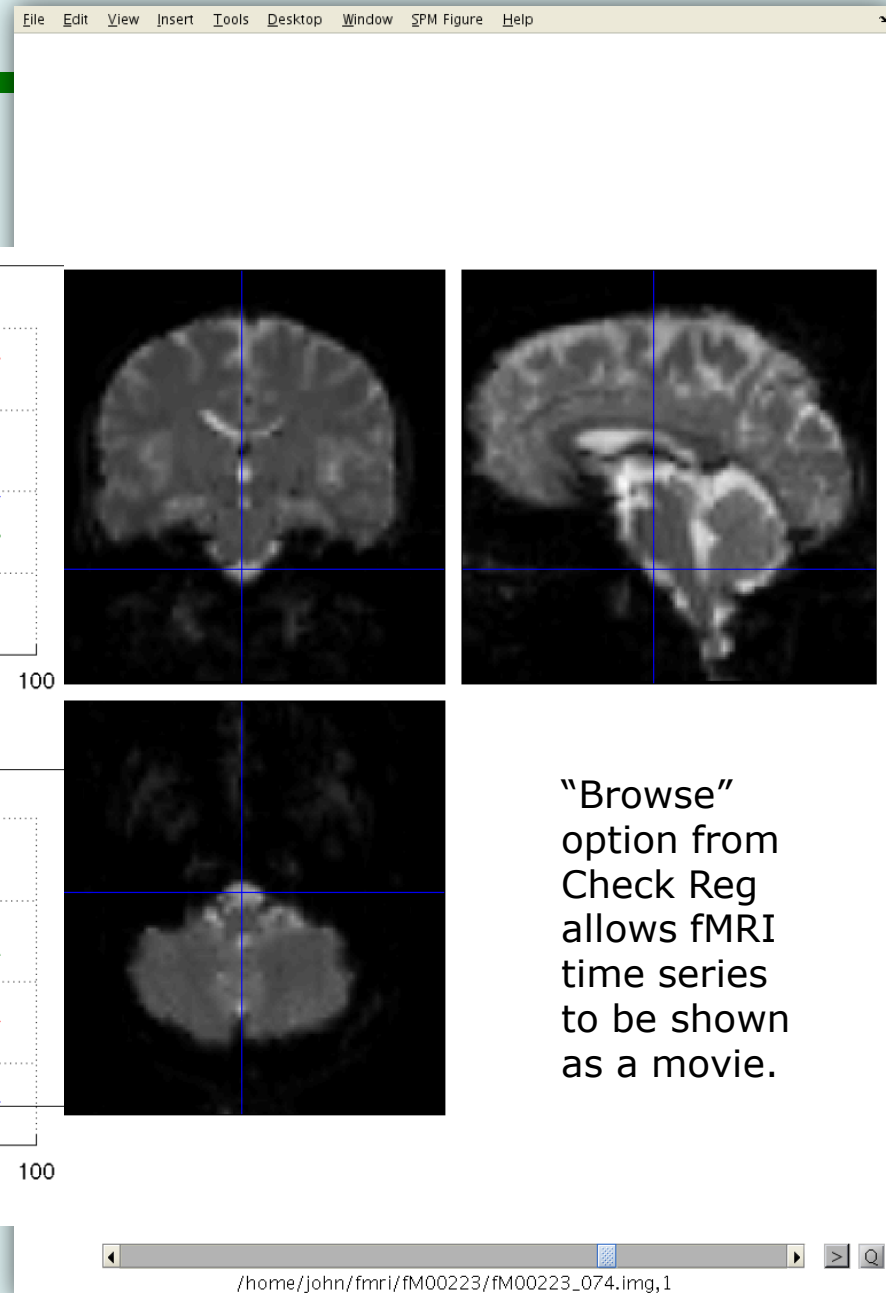
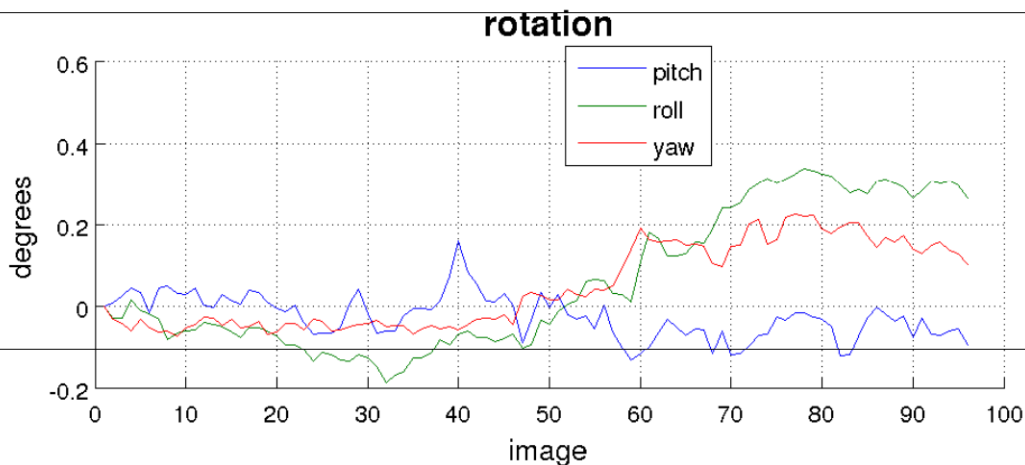
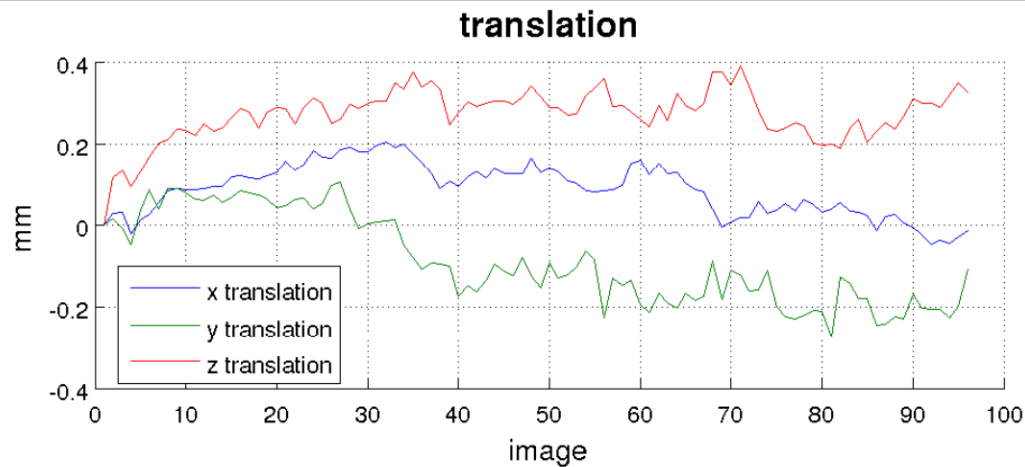
$$R = \begin{pmatrix} 1 & 0 & 0 & X_{\text{trans}} \\ 0 & 1 & 0 & Y_{\text{trans}} \\ 0 & 0 & 1 & Z_{\text{trans}} \\ 0 & 0 & 0 & 1 \end{pmatrix} \times \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & \cos f & \sin f & 0 \\ 0 & -\sin f & \cos f & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \times \begin{pmatrix} \cos q & 0 & \sin q & 0 \\ 0 & 1 & 0 & 0 \\ -\sin q & 0 & \cos q & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \times \begin{pmatrix} \cos \Omega & \sin \Omega & 0 & 0 \\ -\sin \Omega & \cos \Omega & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix}$$

Objective
function



Value of parameter

Motion estimates



Voxel-to-world transformation

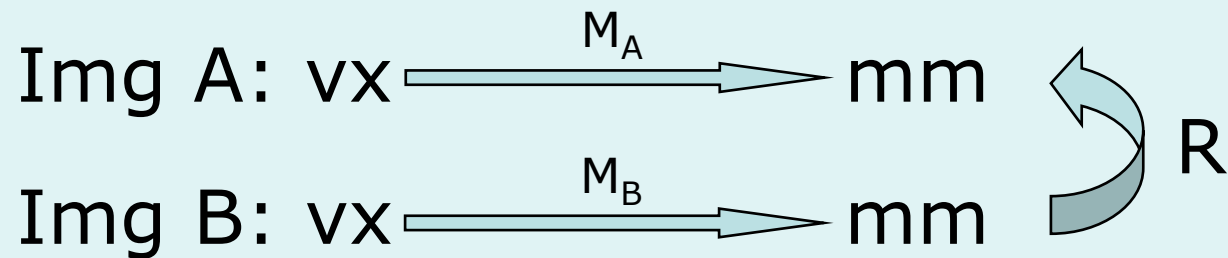
“Voxel-to-world transforms” =

Affine transform **M** associated with each image

- Maps from voxels ($\mathbf{i}=[1...N_i]$, $\mathbf{j}=[1...N_j]$, $\mathbf{k}=[1...N_k]$) to some real world co-ordinate system $[\mathbf{x}, \mathbf{y}, \mathbf{z}]$. e.g.,
 - Scanner co-ordinates (images from DICOM) or MNI coordinates (spatially normalised)
 - Includes *voxel size, head orientation & “space origin”*
- World coordinates are (usually) in millimetres!

Voxel-to-world transformation

- Registering image B (source) to image A (target) will update B's voxel-to-world mapping.



- Mapping from voxels in B to voxels in A is by combining M_B and R : $M_B^* = M_B R$
 - B-to-world using M_B^* , then world-to-A using $M_A^{-1} \Rightarrow M_B^* M_A^{-1}$

Residual errors from aligned fMRI

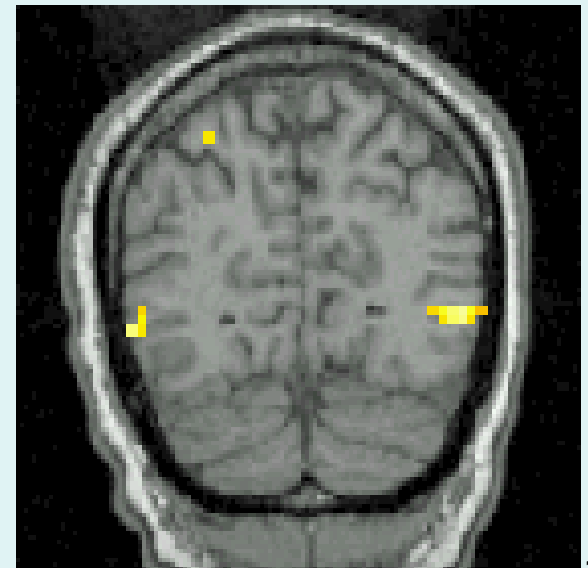
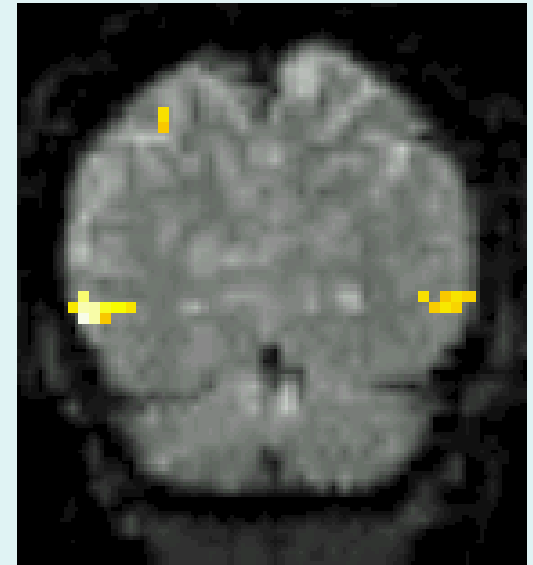
- Re-sampling can introduce interpolation errors
 - tri-linear interpolation $\sim$ smoothing
 - Gaps between slices can cause aliasing artefacts
 - Slices are not acquired simultaneously
 - rapid movements not accounted for by rigid body model
 - Image artefacts may not move according to a rigid body model
 - image distortion, image dropout, Nyquist ghost
 - BOLD signal changes influence the estimated motion.
- ➔ Functions of the estimated motion parameters can be modelled as confounds in subsequent analyses

Various registration problems

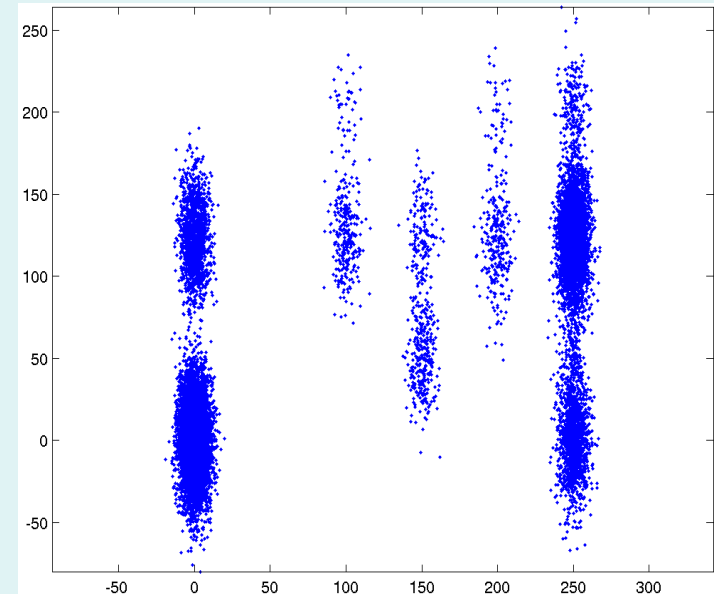
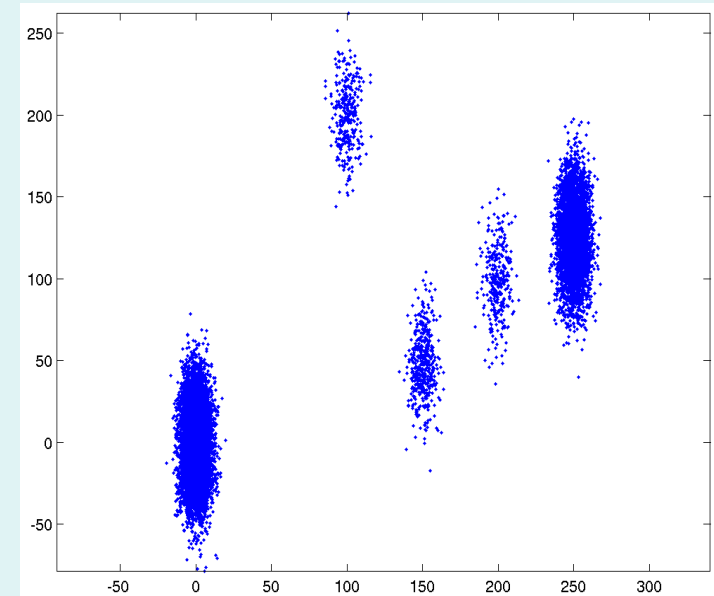
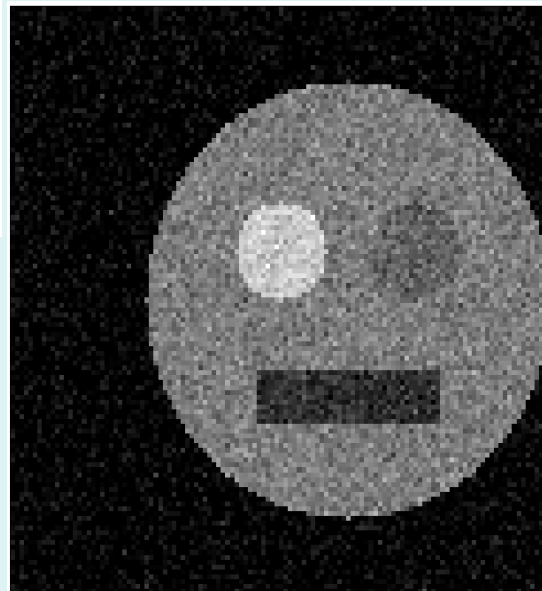
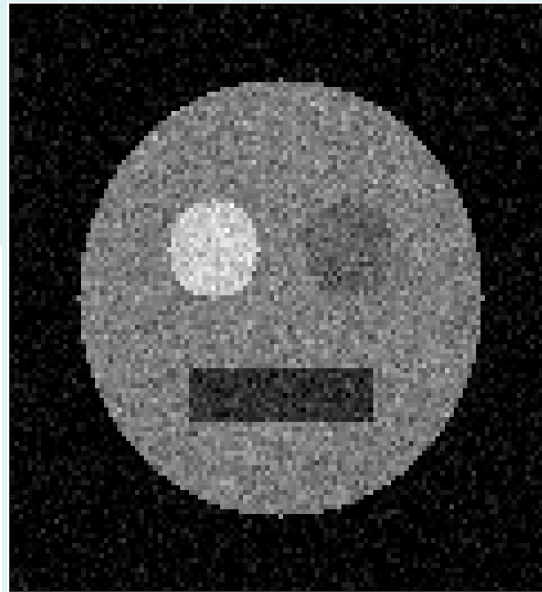
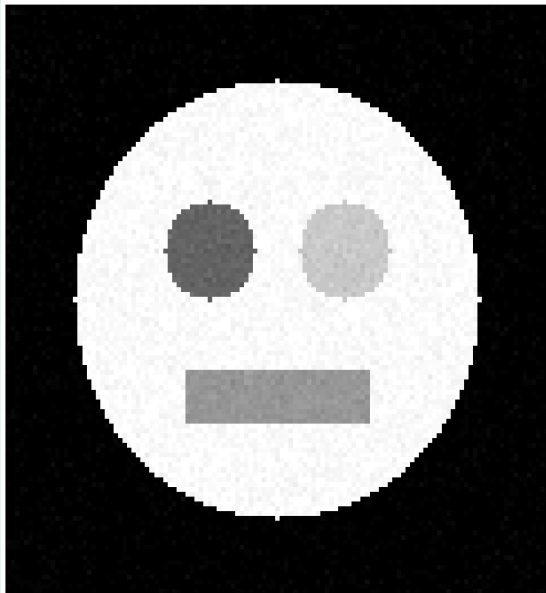
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Brain images		Within subject	Between subjects
Same contrast ⇒	Within modality	X	
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“Coregistration”

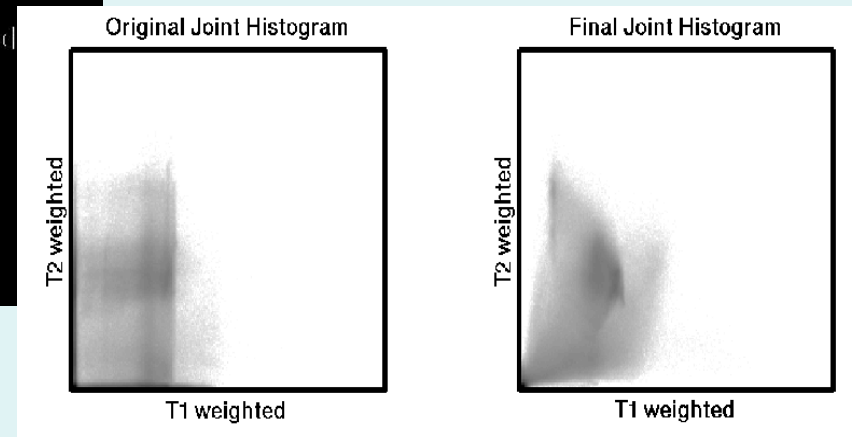
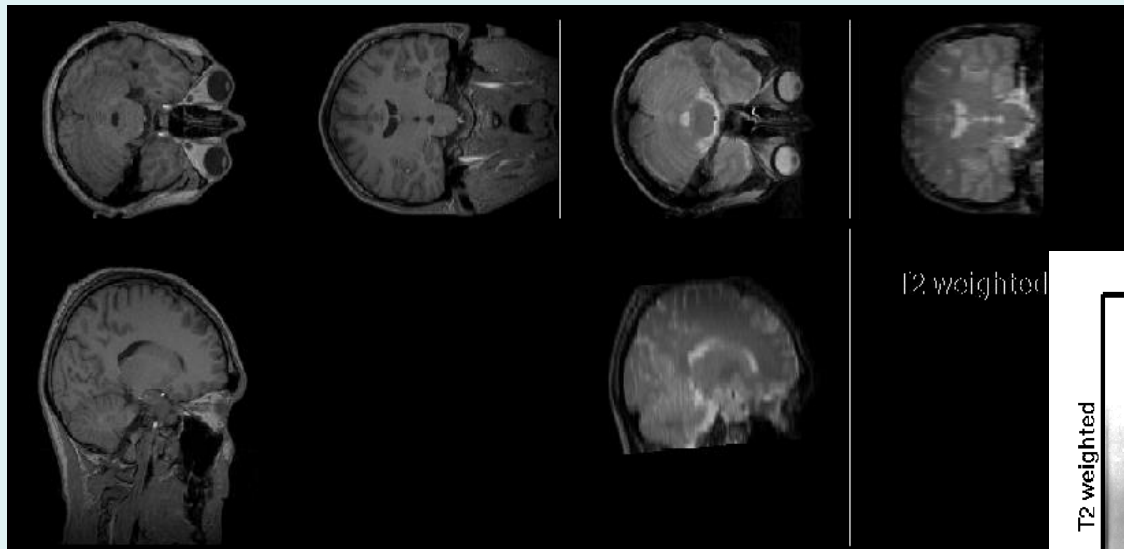
- Inter-modal registration.
- Match images from same subject but different modalities:
 - anatomical localisation of single subject activations
 - achieve more precise spatial normalisation of functional image using anatomical image.



Joint histogram & Mutual information



Mutual Information, real case



- Used for between-modality registration
 - Derived from joint histograms
 - $MI = \int_{ab} P(a,b) \log_2 [P(a,b) / (P(a) P(b))]$
 - Related to entropy: $MI = -H(a,b) + H(a) + H(b)$
- Where $H(a) = -\int_a P(a) \log_2 P(a)$ and $H(a,b) = -\int_{ab} P(a,b) \log_2 P(a,b)$

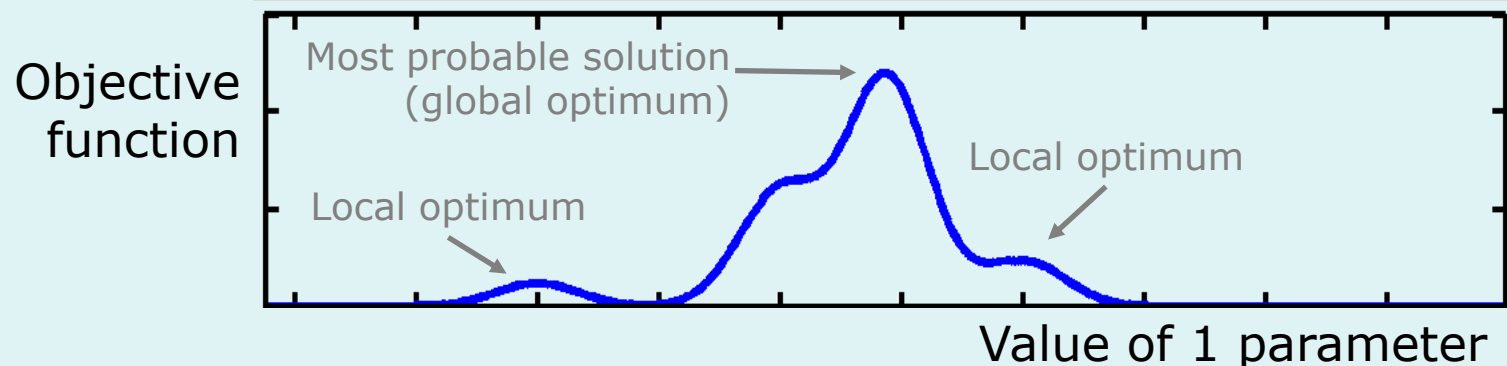
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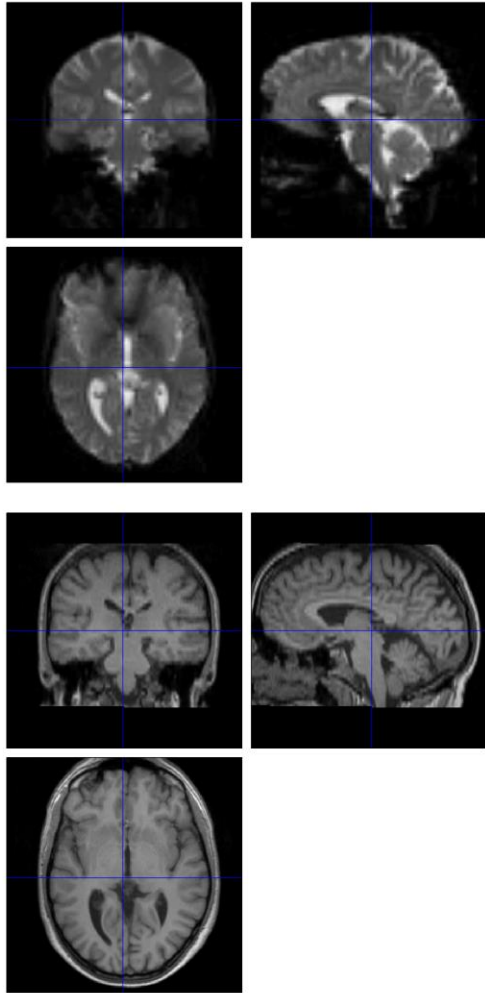
$$\rightarrow c(I, J) = MI(I, J)$$

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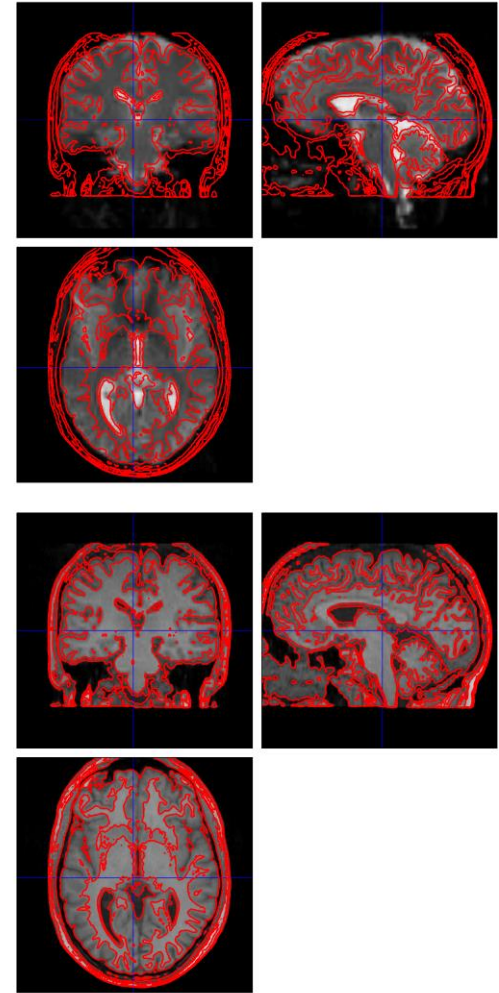
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“CheckReg” to assess alignment



CheckReg allows
contours from one
image to be shown
superimposed on
another



Voxel-to-world transformation

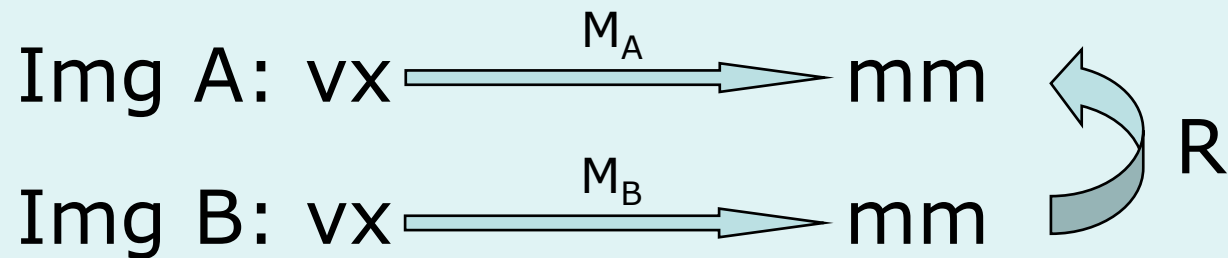
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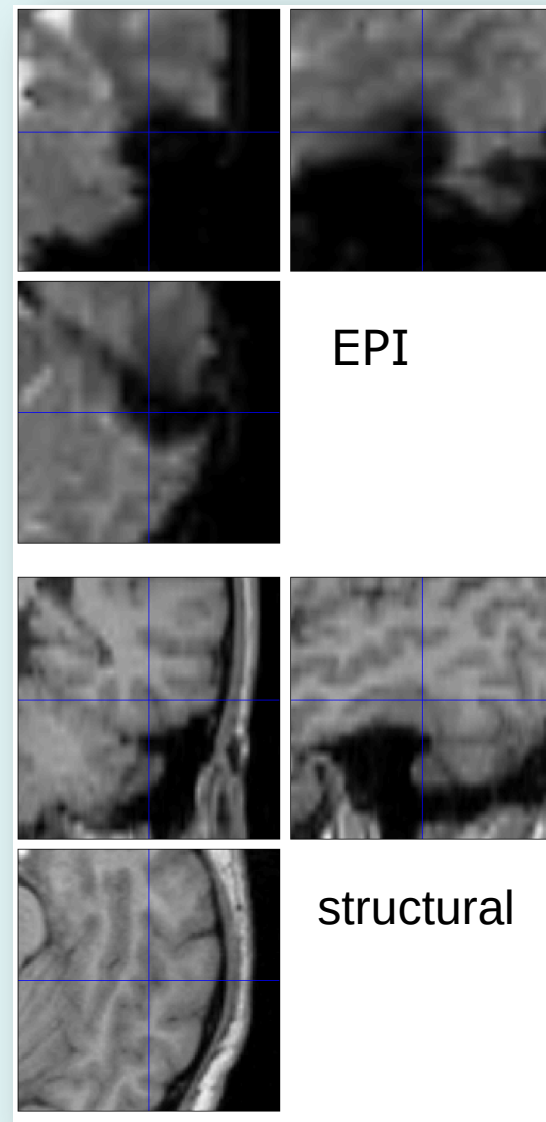
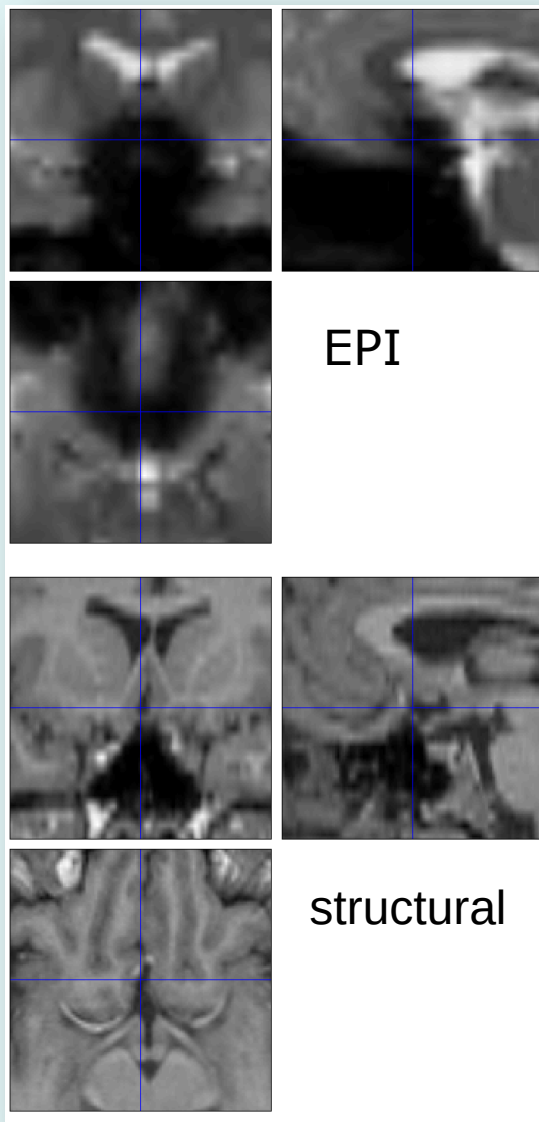
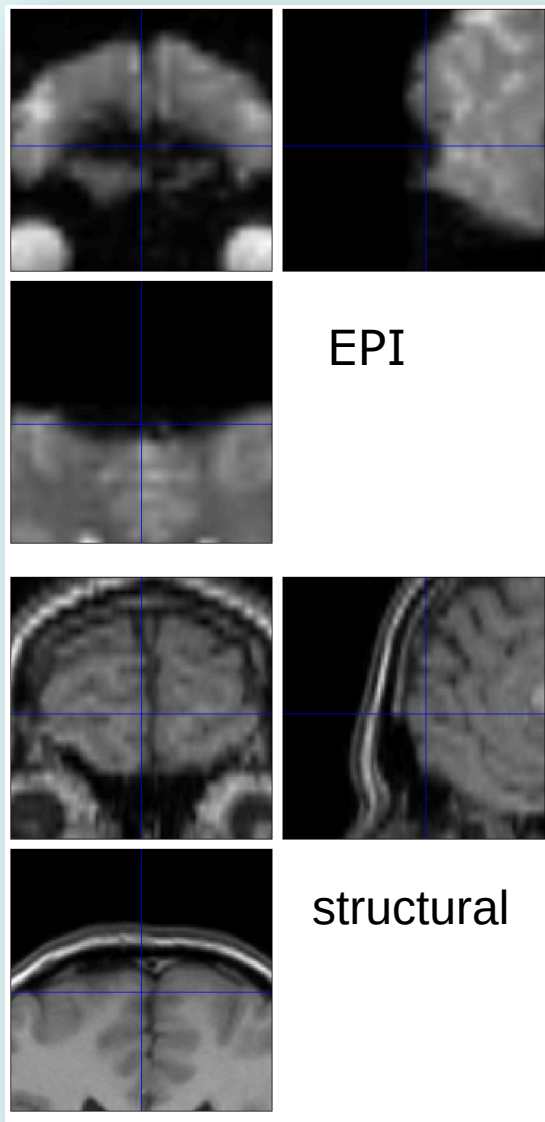
Voxel-to-world transformation

- Registering image B (source) to image A (target) will update B's voxel-to-world mapping.



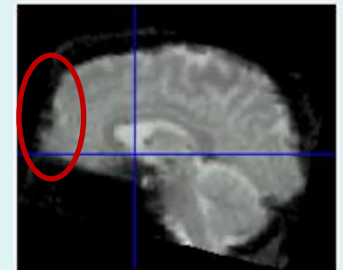
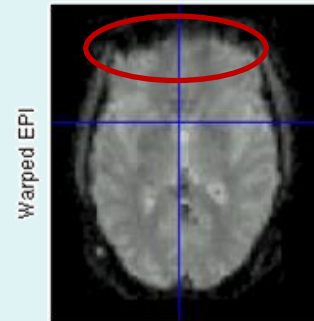
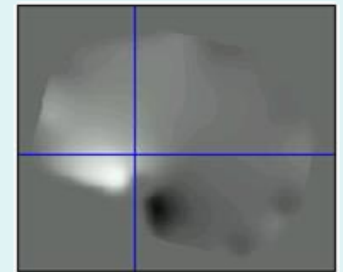
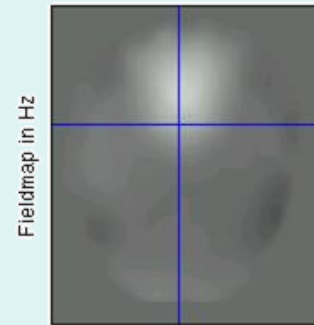
- Mapping from voxels in B to voxels in A is by combining M_B and R : $M_B^* = M_B R$
 - B-to-world using M_B^* , then world-to-A using $M_A^{-1} \Rightarrow M_B^* M_A^{-1}$

EPI dropout and distortion



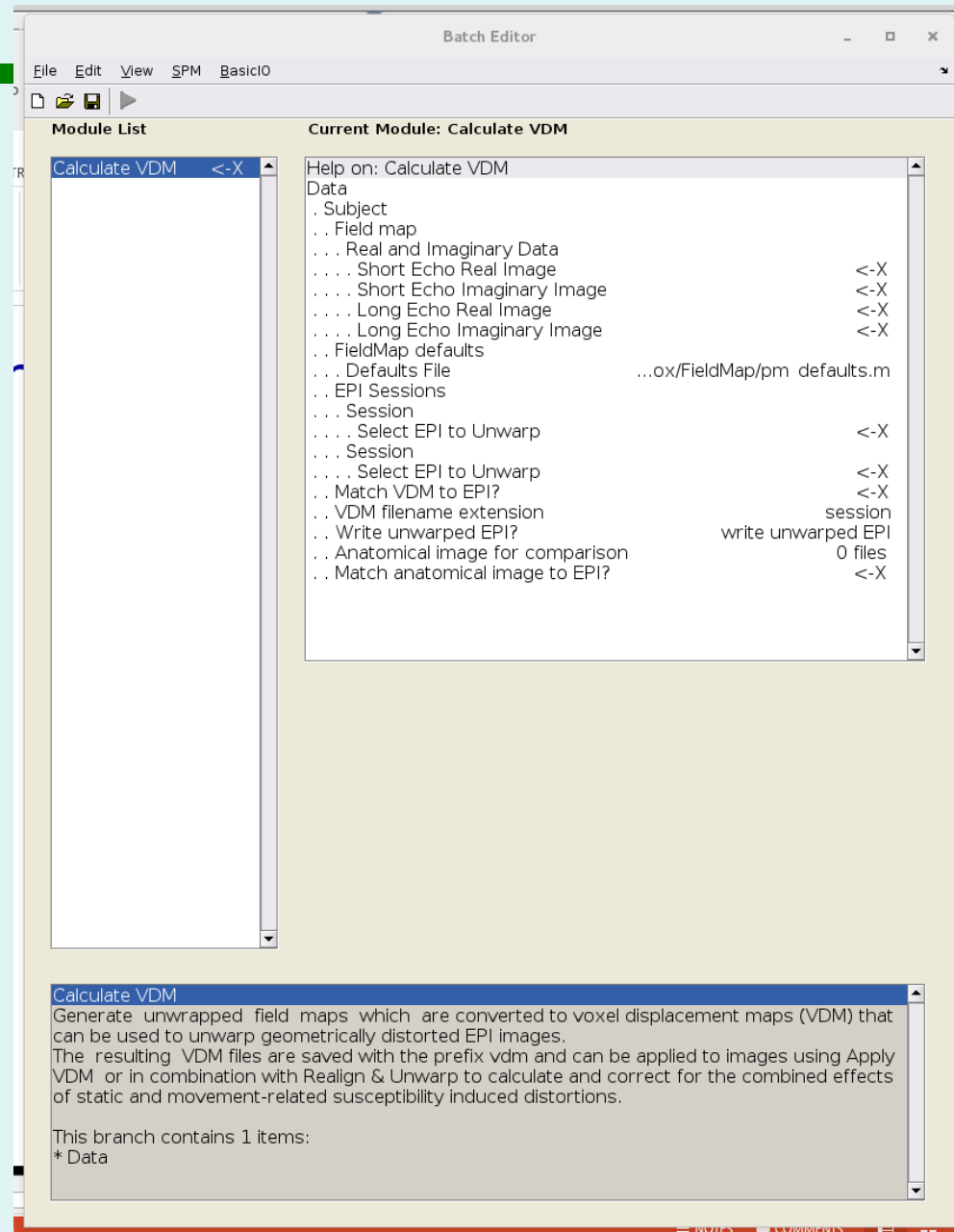
EPI distortion

- Magnetic susceptibility differs among tissues.
- Greatest difference is between air and tissue.
- Subject disrupts B_0 field, rendering it inhomogeneous
- Distortions in phase-encode direction



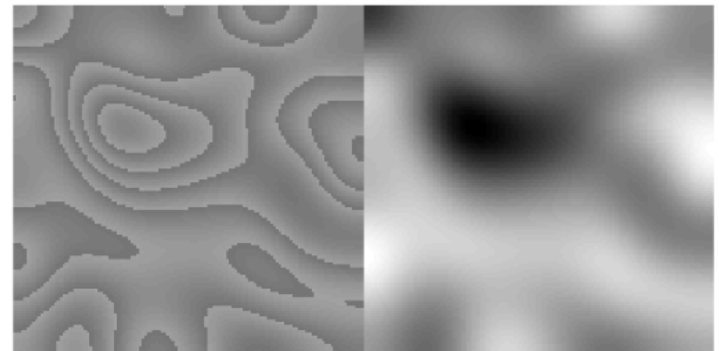
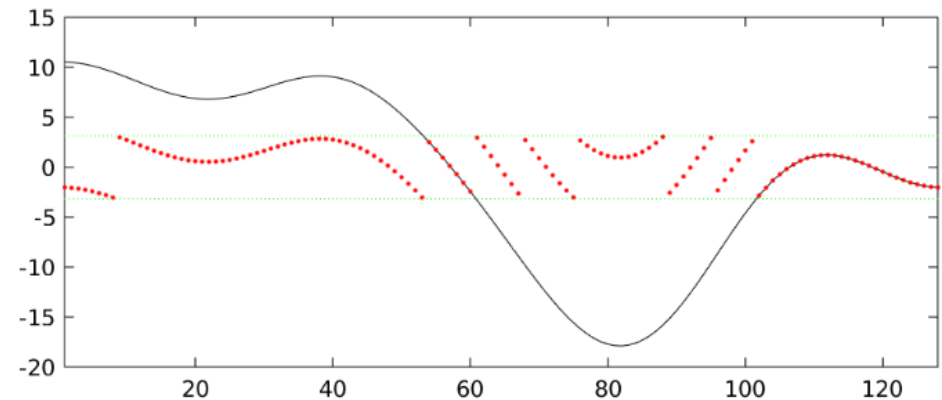
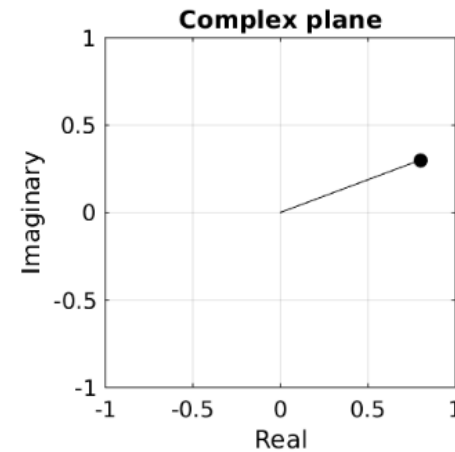
FieldMap toolbox

- Computes a voxel-displacement map (VDM) from “fieldmap” scans.
- Used to correct distortions in EPI.



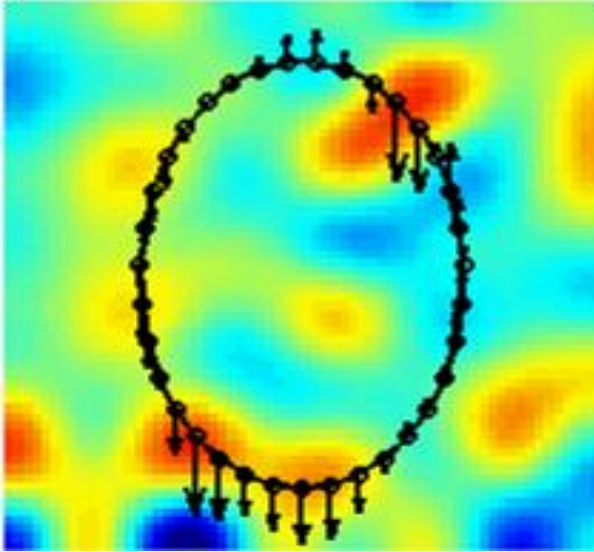
Phase unwrapping

- Phase of complex data used.
 - $-\pi < \text{phase} < \pi$
 - Phase-unwrapping needed.
 - Phase is poorly defined when magnitude is small relative to noise
- ➔ Part that is most likely to go wrong.

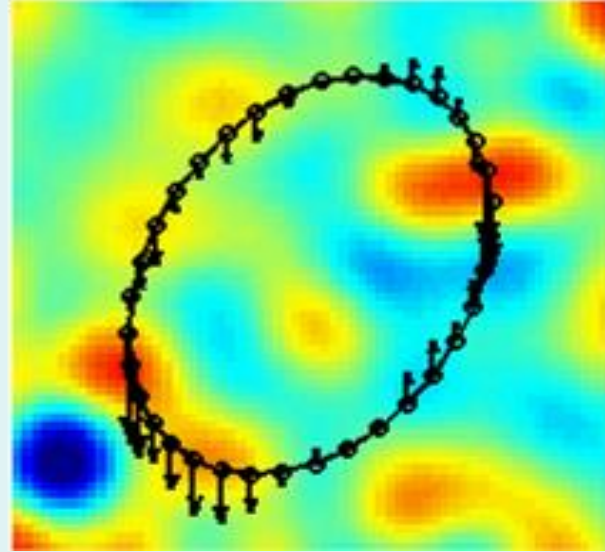


Movement-by-distortion interaction

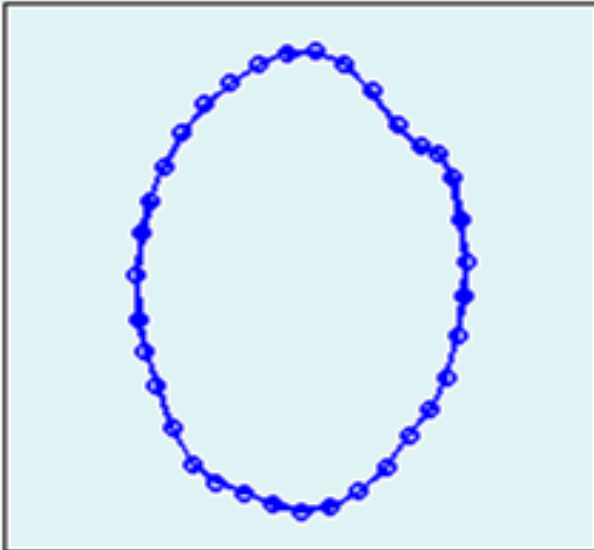
Original position



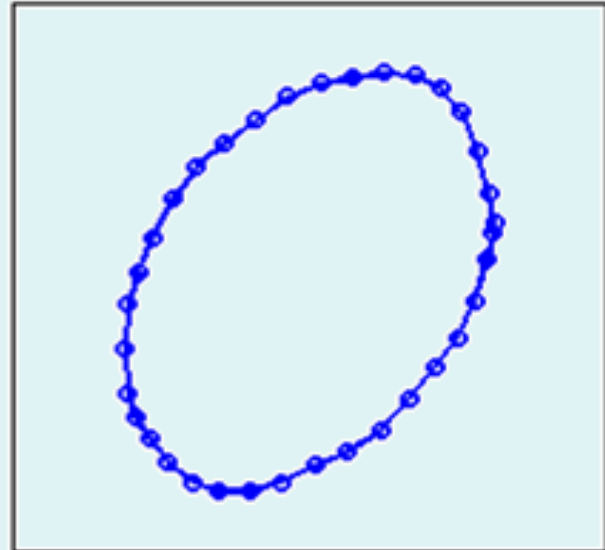
After rotation



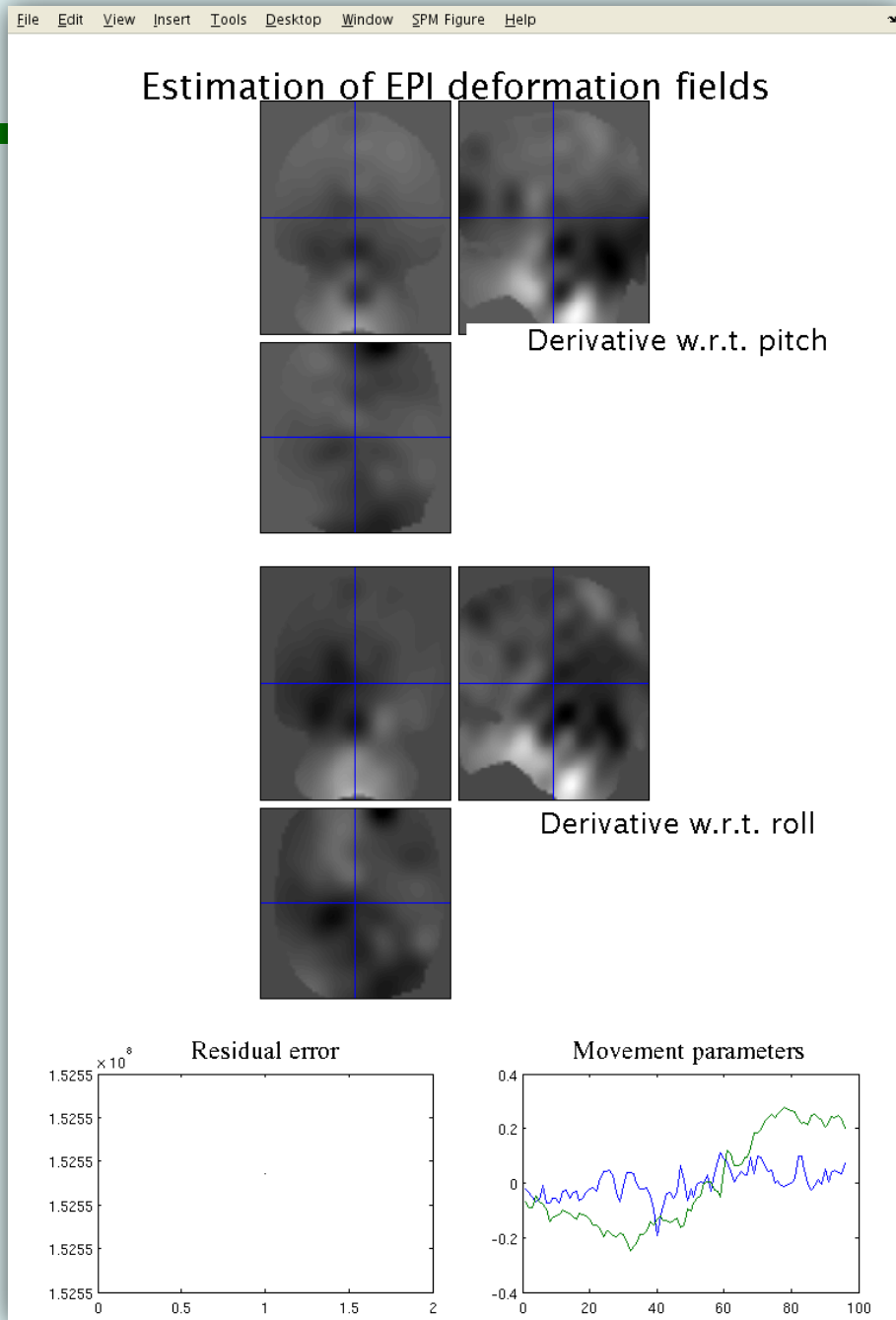
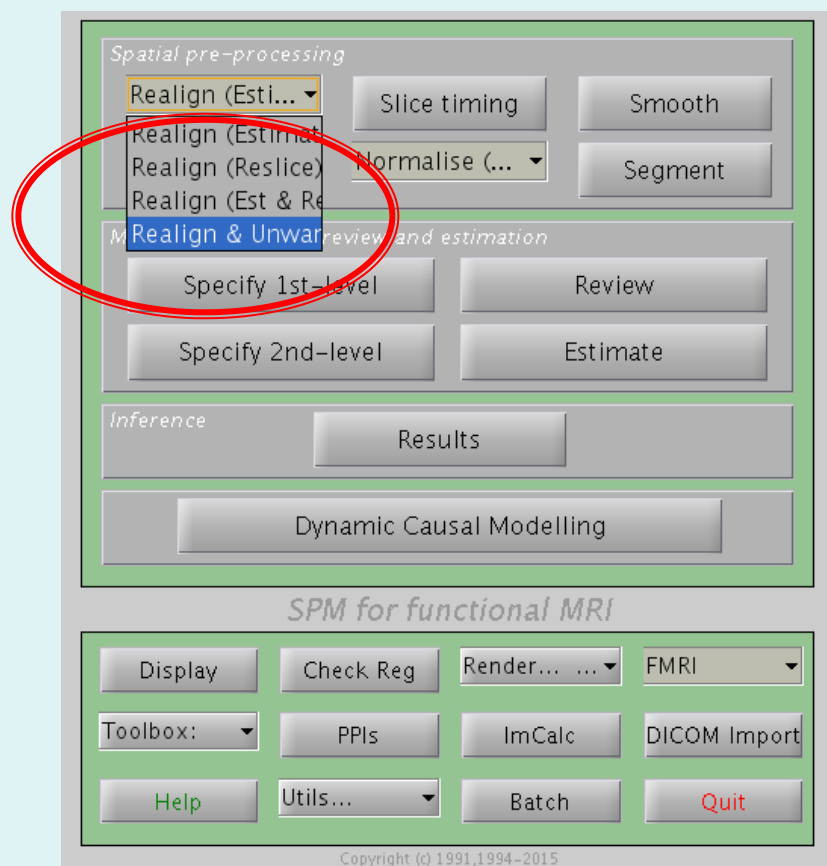
Original position



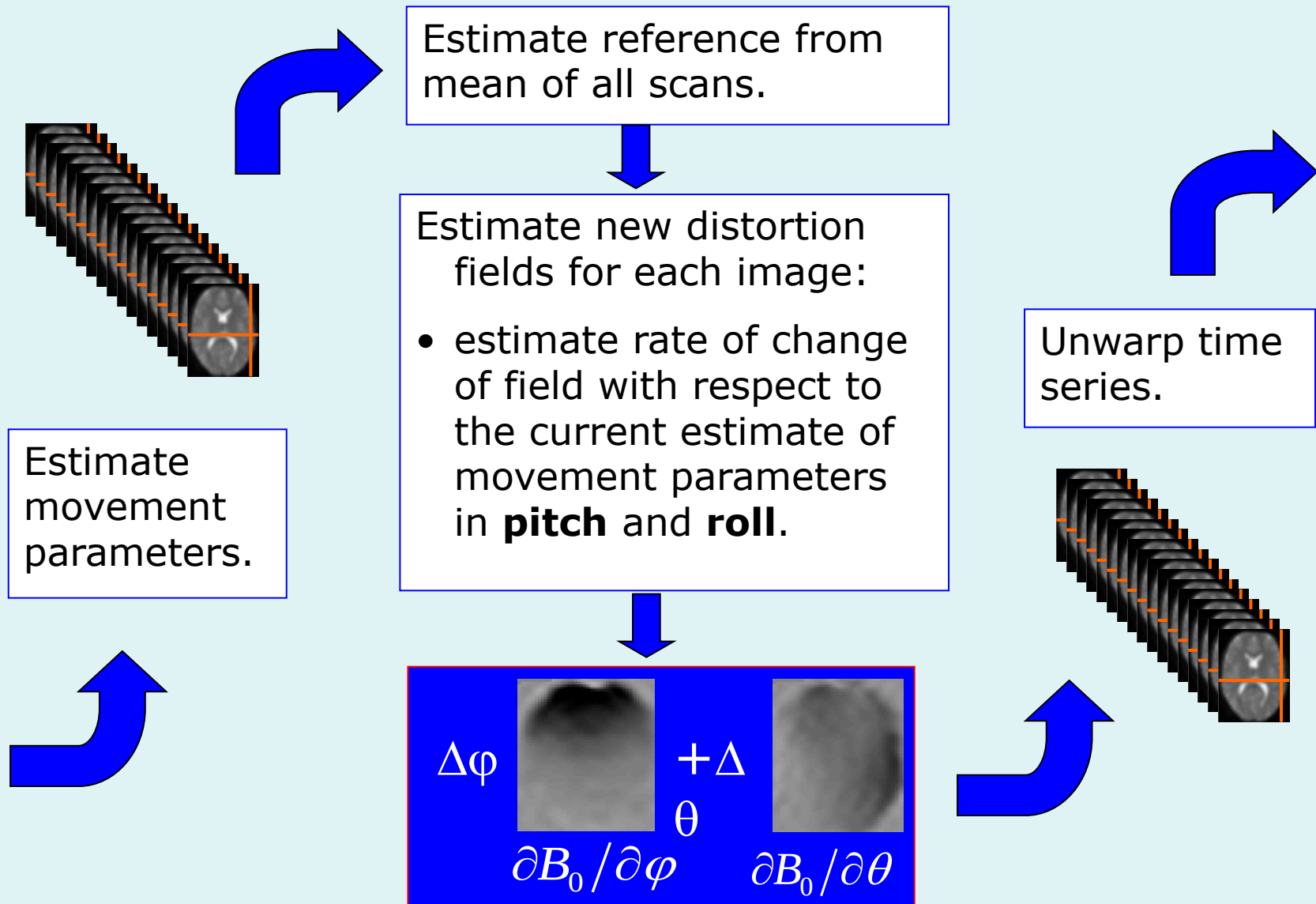
After rotation



"Realign & Unwarp"



Correcting for distortion changes



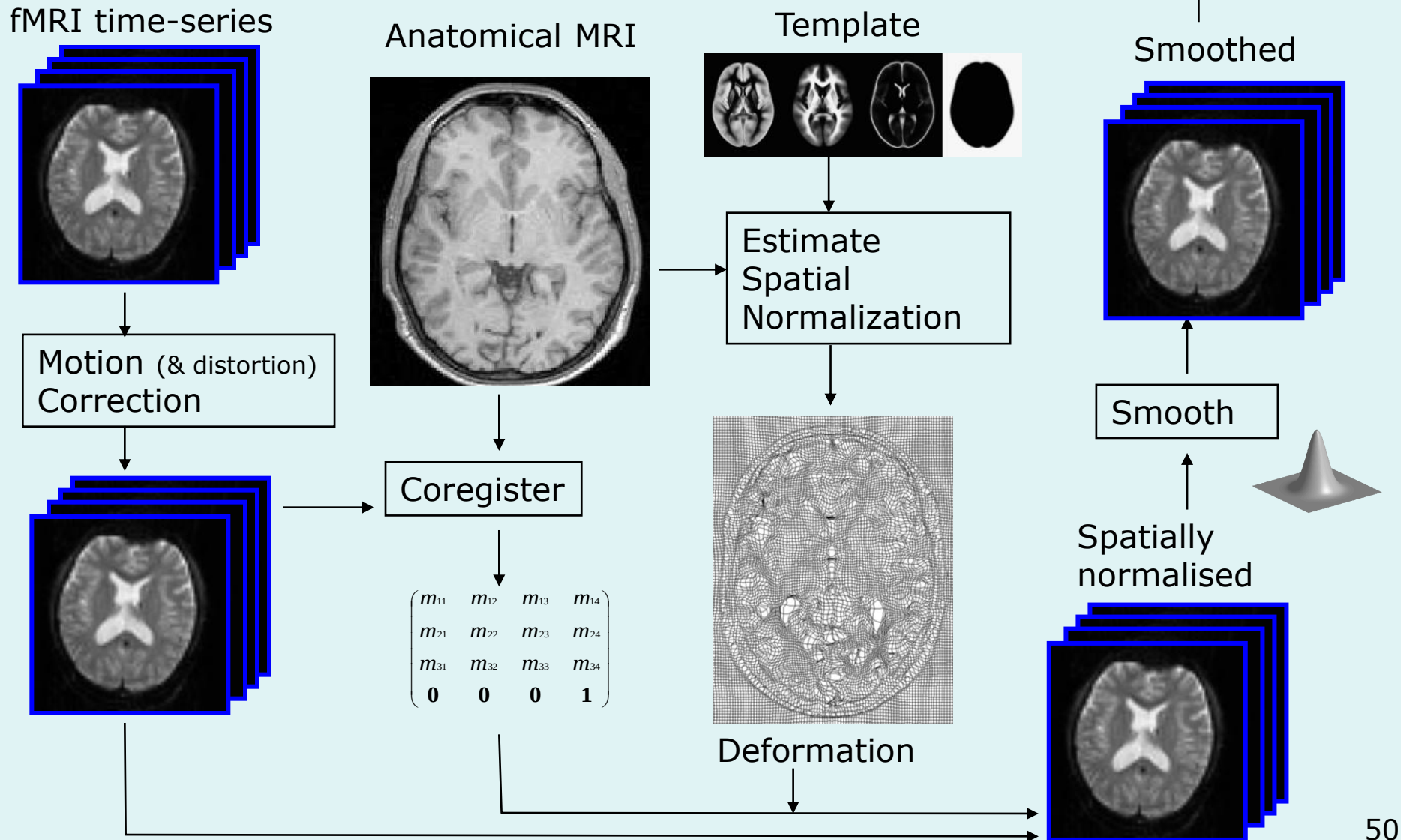
Various registration problems

		Rigid body ↓	Image warping ↓
Brain images		Within subject	Between subjects
Same contrast ⇒	Within modality	X	X
Different contrast ⇒	Between modality	X	

Content

- Preliminaries
- Within-subject
- **Between-subject**
 - Unified segmentation for spatial normalisation**
 - Gaussian mixture model
 - Intensity non-uniformity correction
 - Deformed tissue probability maps
- Smoothing
- Conclusion

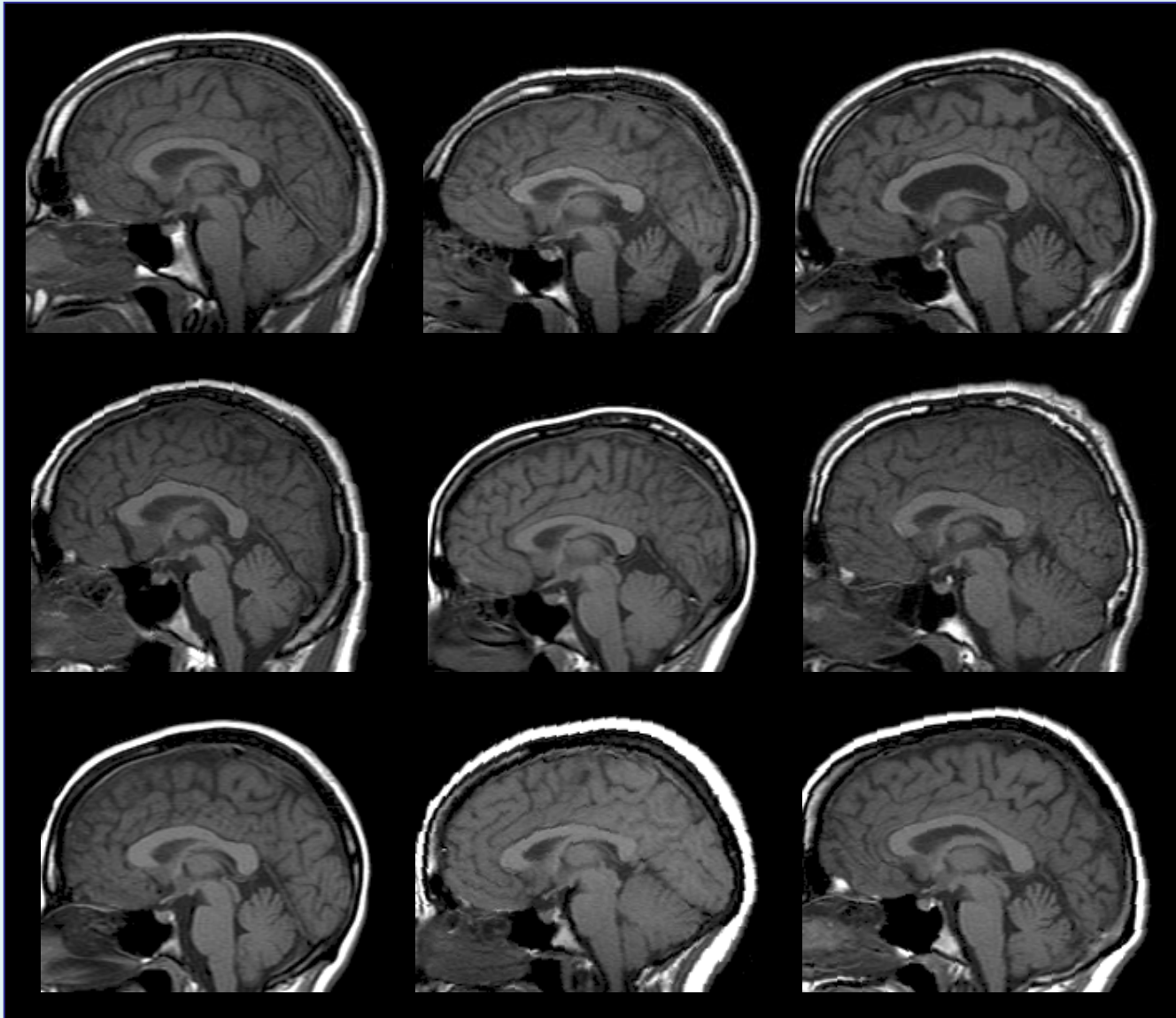
Pre-processing overview



Between subjects

Brains of different subjects vary in *shape* and *size*.

Between subjects



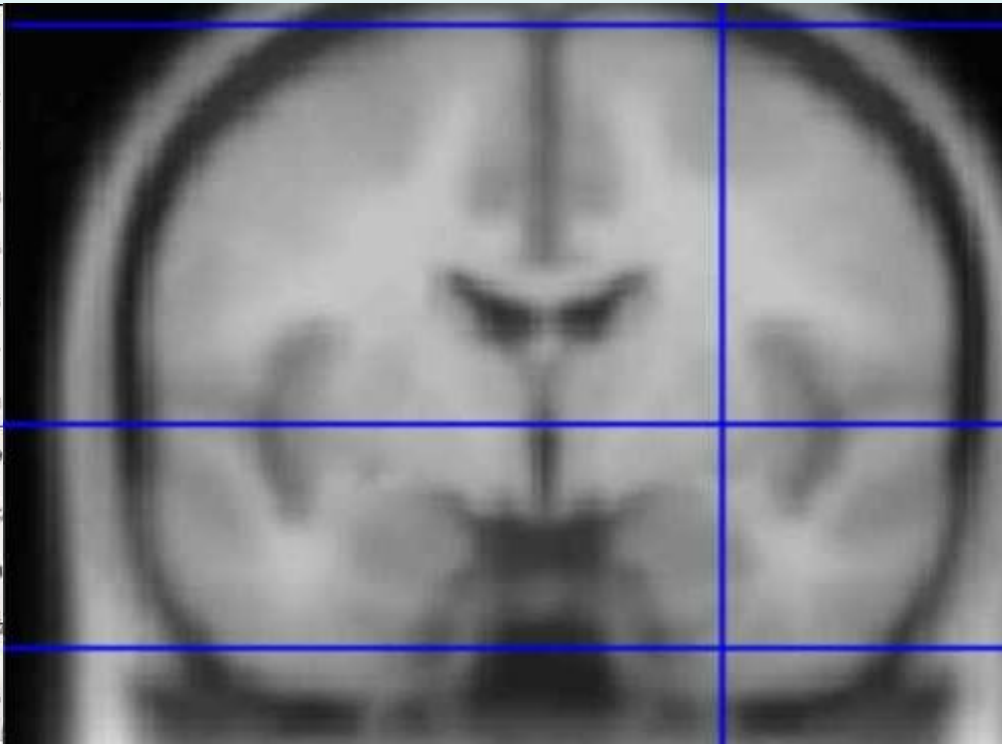
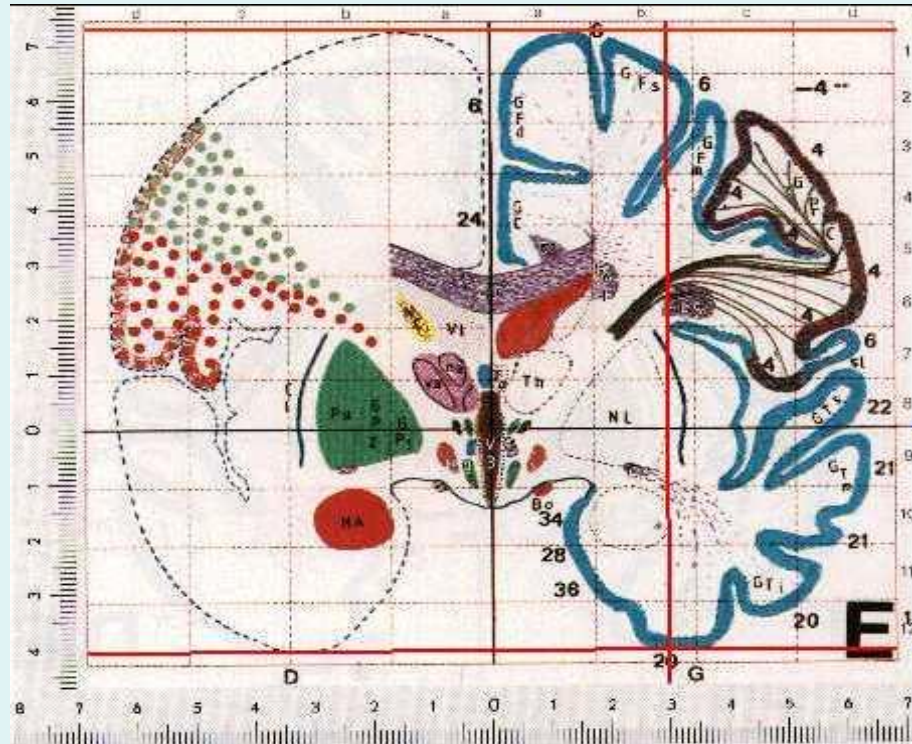
Between subjects

Brains of different subjects vary in *shape* and *size*.

- Need to bring them all into a common anatomical space.
 - Examine homologous regions across subjects
 - Improve anatomical specificity
 - Improve sensitivity
 - Report findings in a common anatomical space (e.g. MNI space)

T&T atlas vs MNI template

The Talairach & Tournoux Atlas The MNI/ICBM AVG152 Template



The MNI template follows the *convention* of T&T, but does NOT match the *particular brain* of T&T

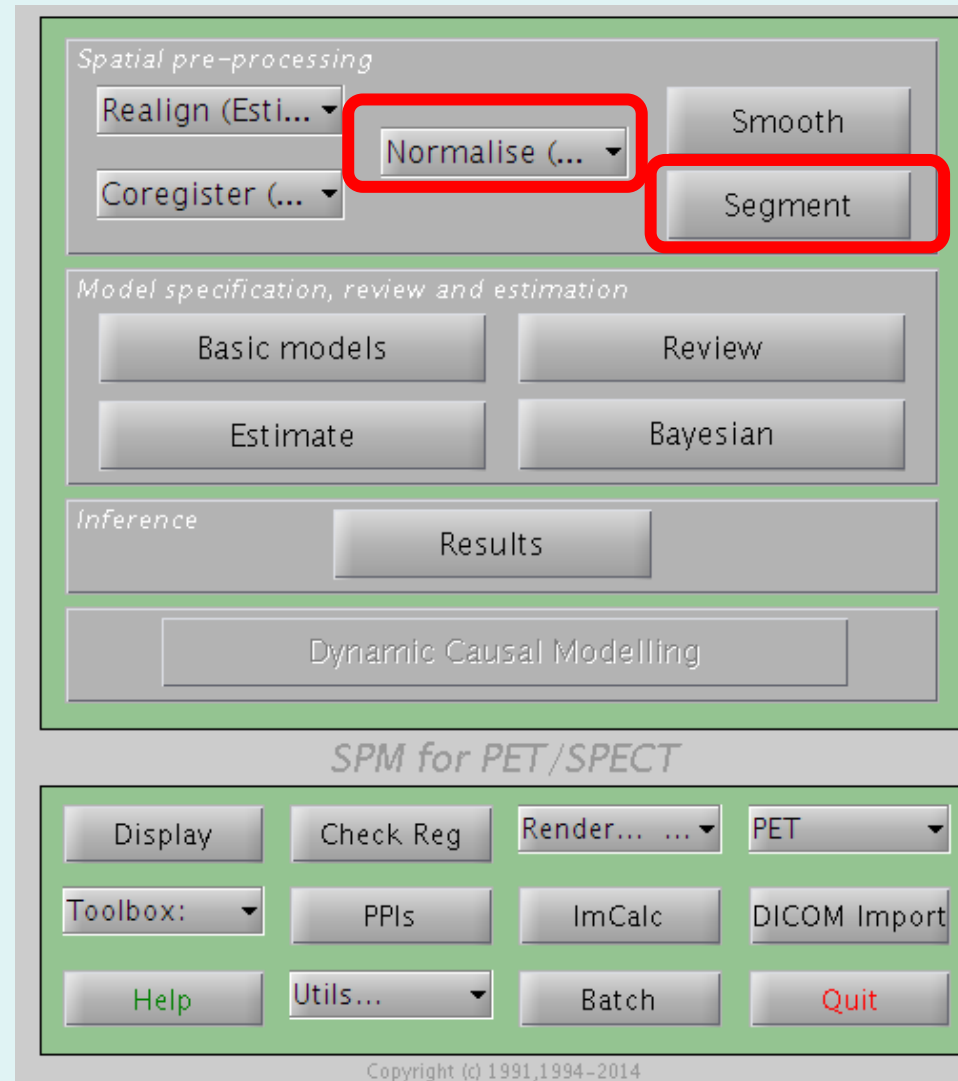
Recommended reading: <http://imaging.mrc-cbu.cam.ac.uk/imaging/MniTalairach>

Between subjects

- Brains of different subjects vary in *shape* and *size*.
 - Need to bring them all into a common anatomical space.
 - Examine homologous regions across subjects
 - Improve anatomical specificity
 - Improve sensitivity
 - Report findings in a common anatomical space (e.g. MNI space)
- In SPM12²⁵, alignment is achieved by matching tissue classes, i.e. GM with GM, WM with WM,...

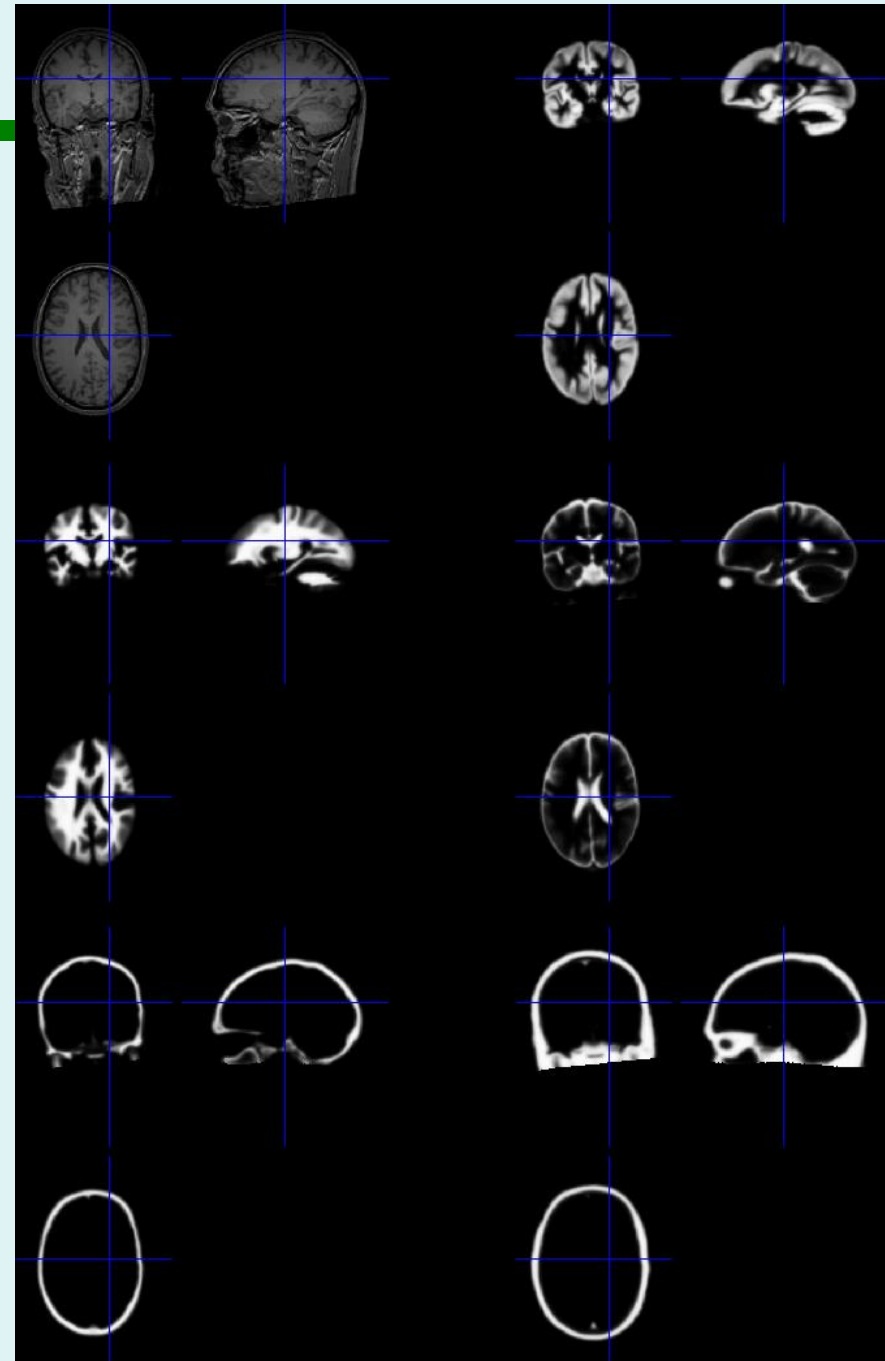
Normalise/Segment

- This is the same algorithm as for tissue segmentation.
- Combines:
 - Mixture of Gaussians (MOG)
 - Bias Correction Component
 - Warping (Non-linear Registration) Component



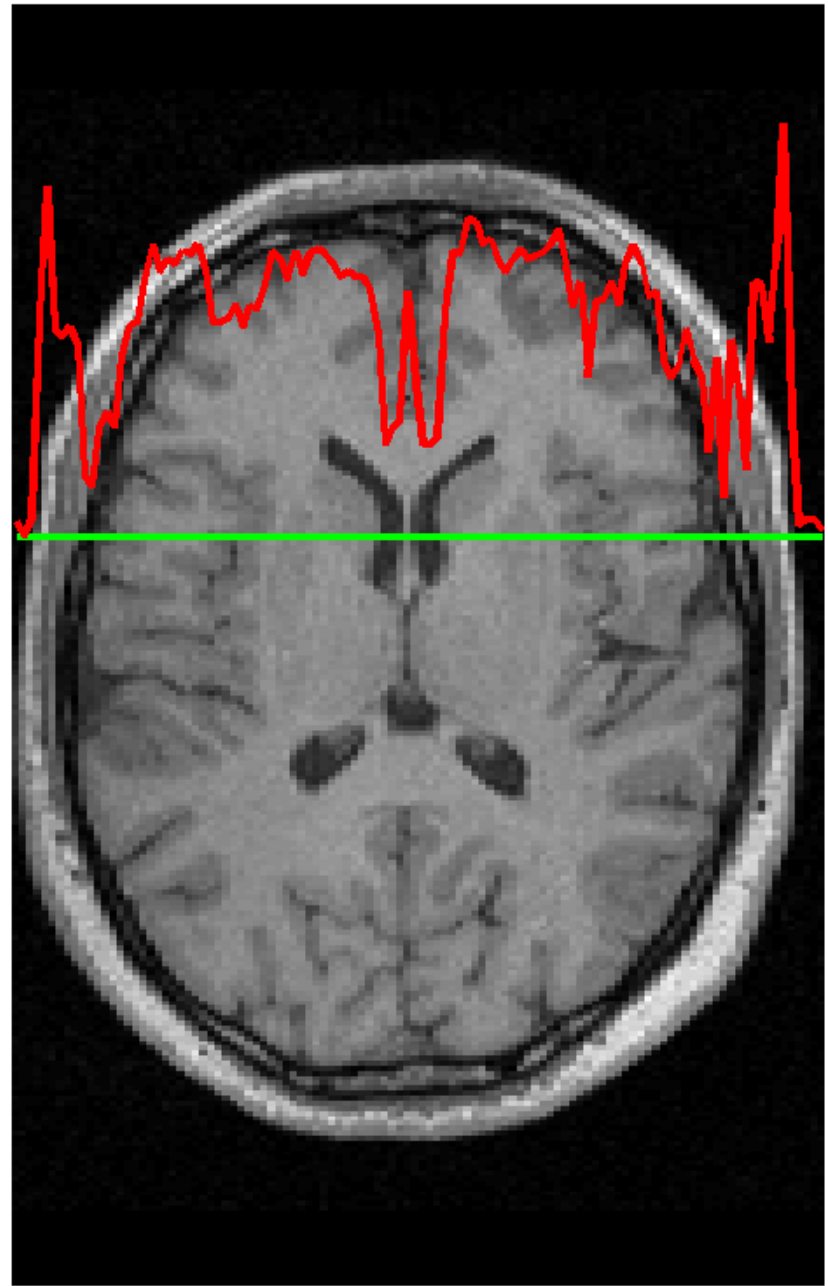
Spatial normalisation

- Default spatial normalisation in SPM12 estimates nonlinear warps that match tissue probability maps to the individual image.
- Spatial normalisation achieved using the inverse of this transform.

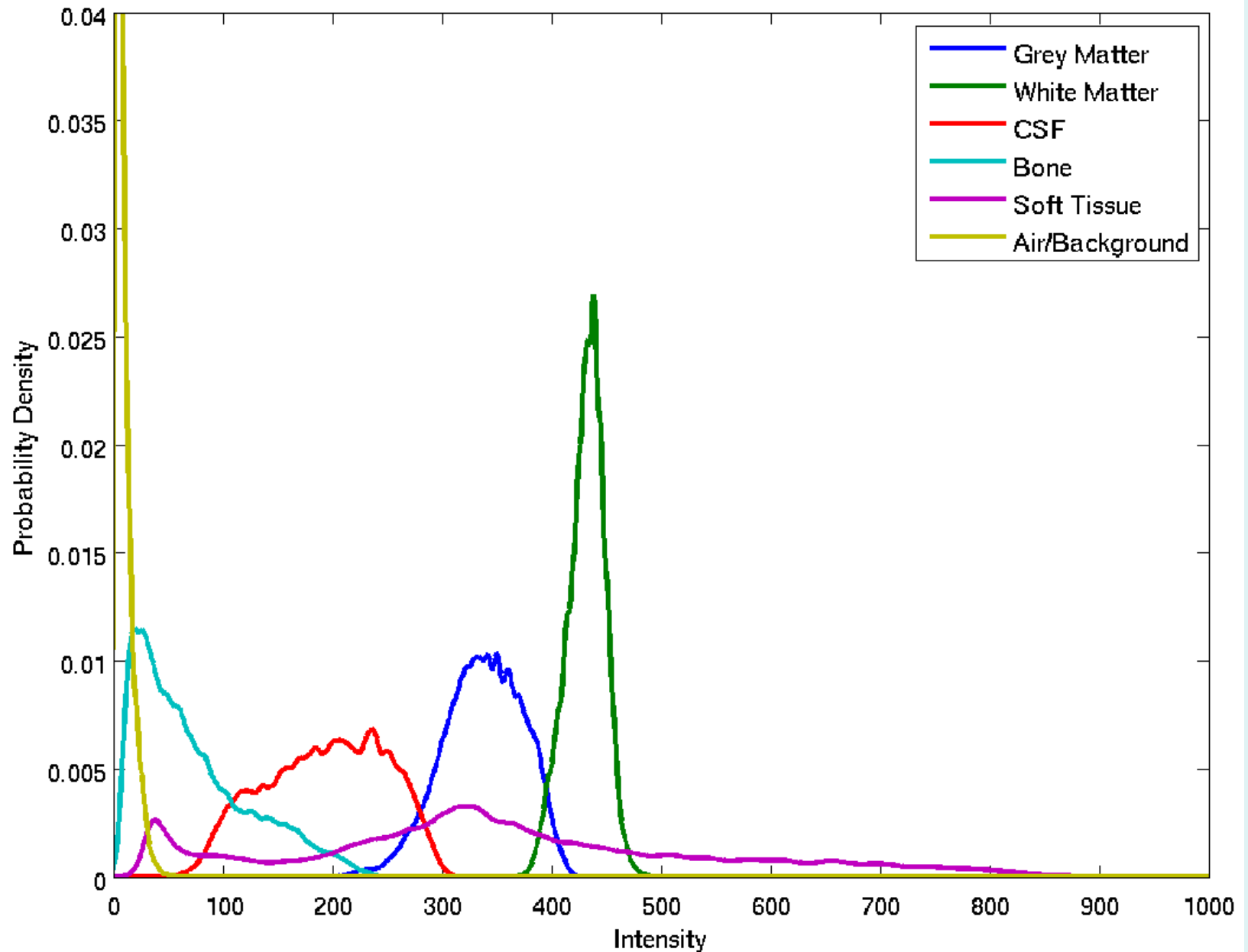


Segmentation

- Segmentation in SPM12 also estimates a spatial transformation that can be used for spatially “normalising” images.
- It uses a **generative model**, which involves:
 - Mixture of Gaussians (MOG)
 - Warping (Non-linear Registration) Component
 - Bias Correction Component



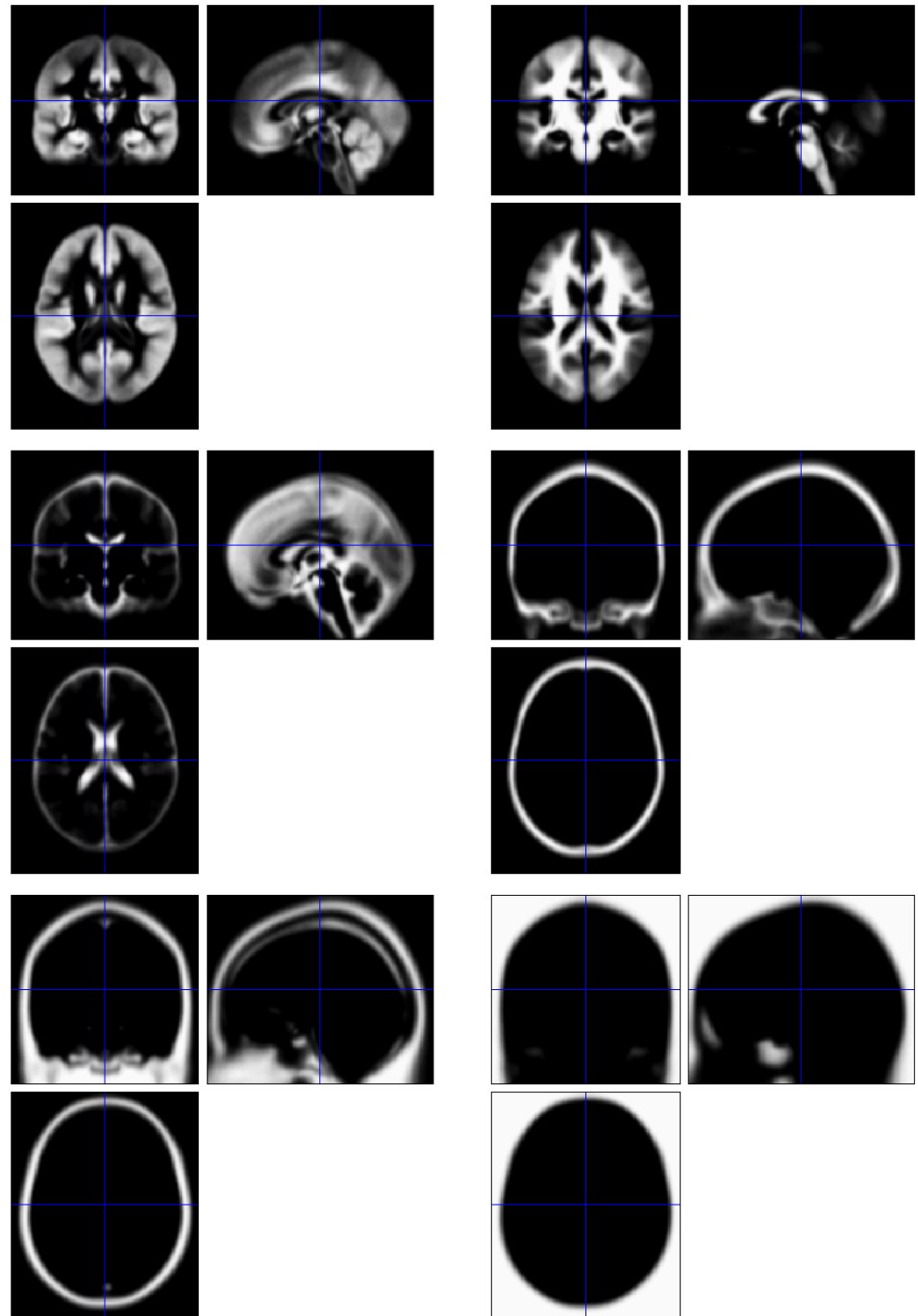
Tissue intensity distributions (T1w-MRI)



TPM's

Tissue probability maps in SPM12.

- GM, WM & CSF
 - additional non-brain tissue classes
- defines the template space = reference!



Modelling deformations, affine transform

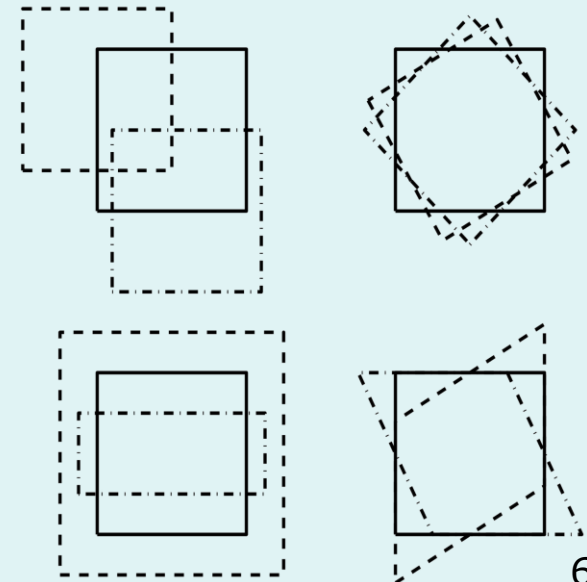
12 parameter affine transform

- 3 translations
- 3 rotations
- 3 zooms
- 3 shears

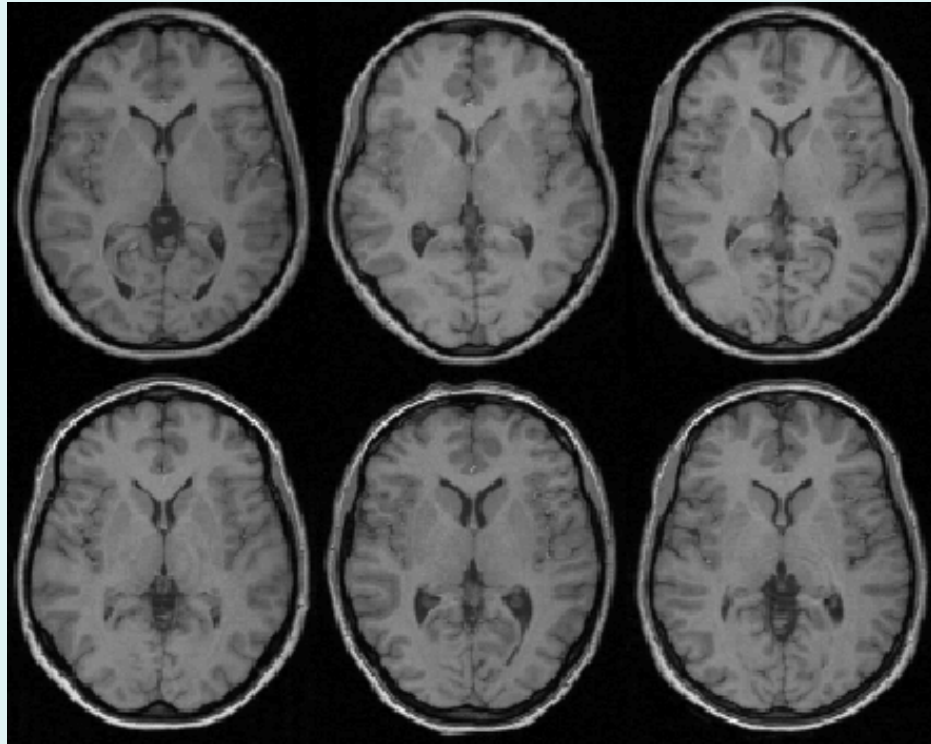
$$\begin{bmatrix} x_1 \\ y_1 \\ z_1 \\ 1 \end{bmatrix} = \begin{bmatrix} m_{11} & m_{12} & m_{13} & m_{14} \\ m_{21} & m_{22} & m_{23} & m_{24} \\ m_{31} & m_{32} & m_{33} & m_{34} \\ 0 & 0 & 0 & 1 \end{bmatrix} \times \begin{bmatrix} x_0 \\ y_0 \\ z_0 \\ 1 \end{bmatrix}$$

→ Fits **overall** shape and size

→ Need *warping* for local deformation

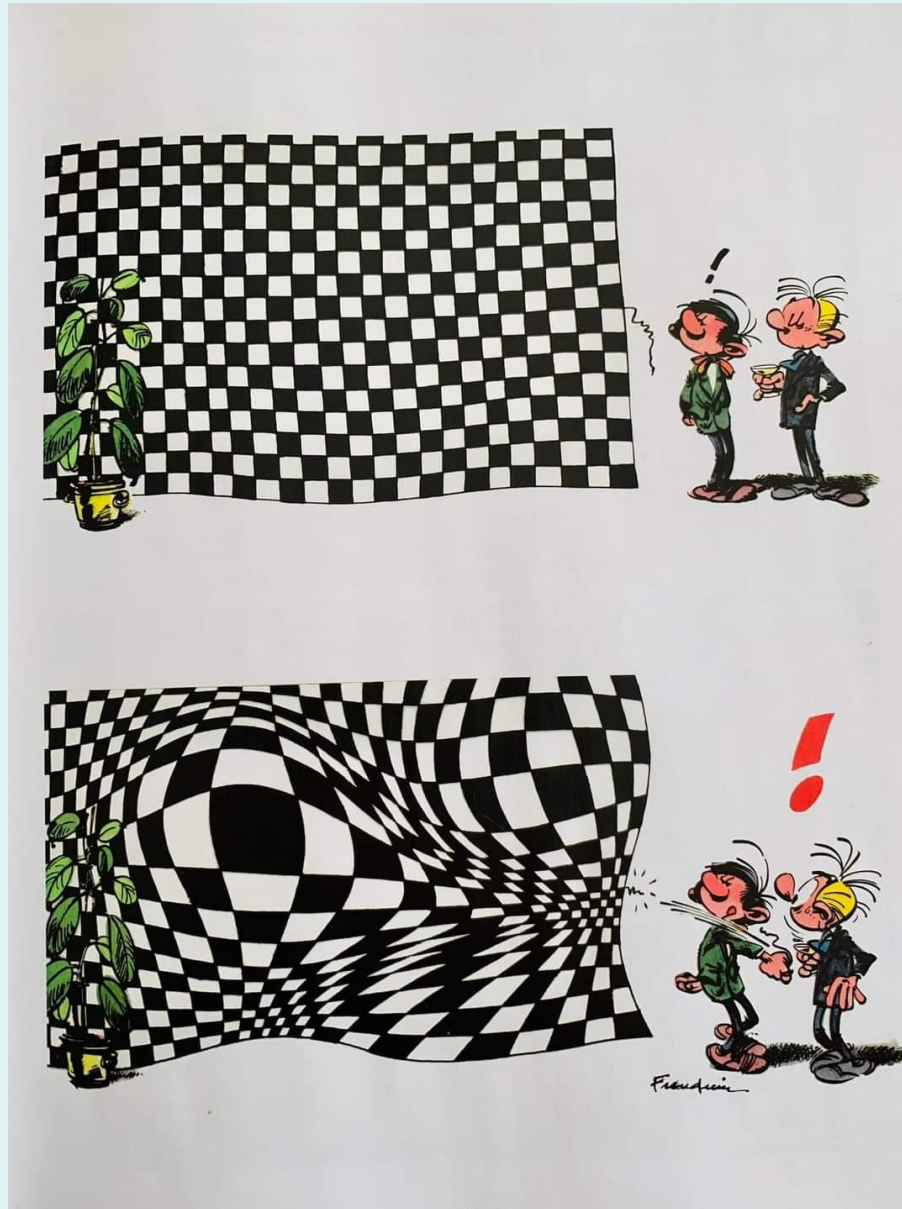


Spatial normalisation results



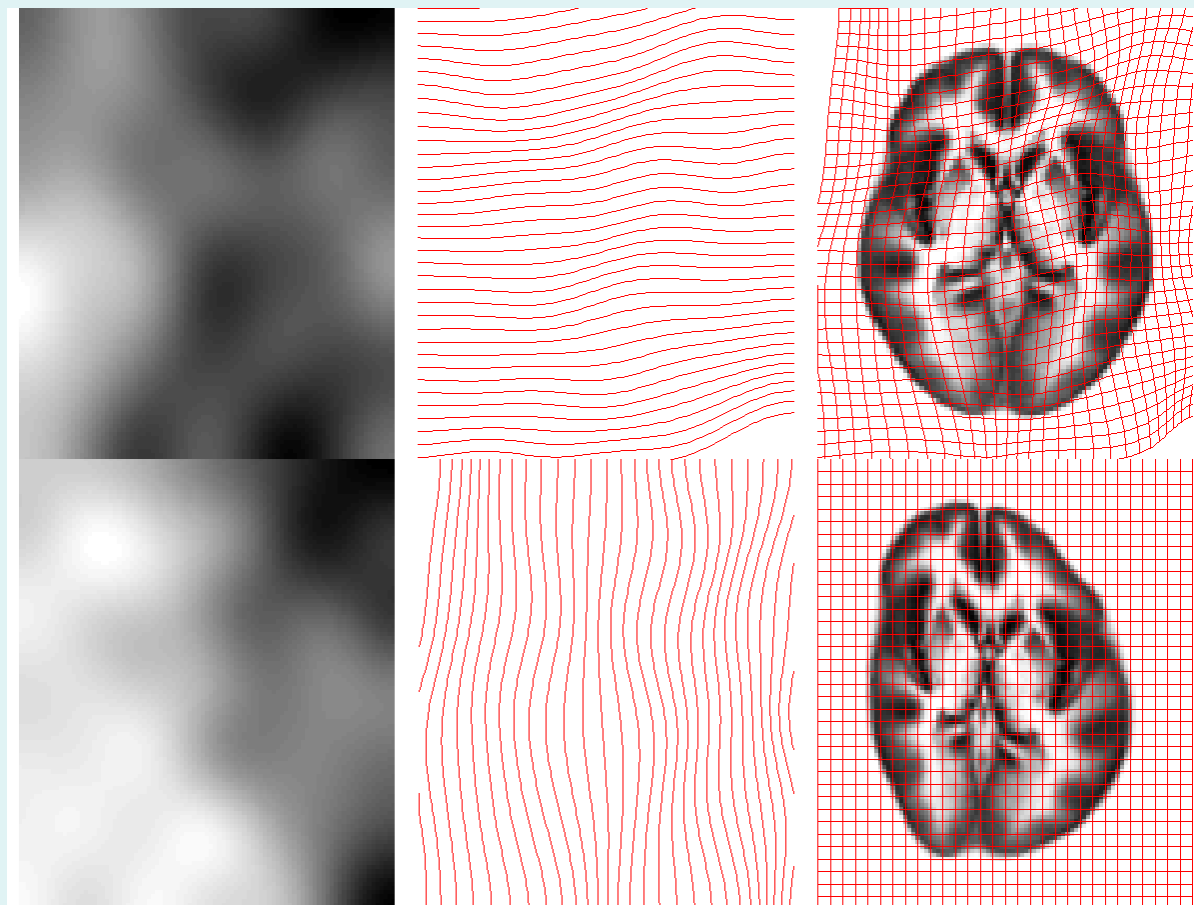
Affine registration

Modelling elastic deformations, "warps"



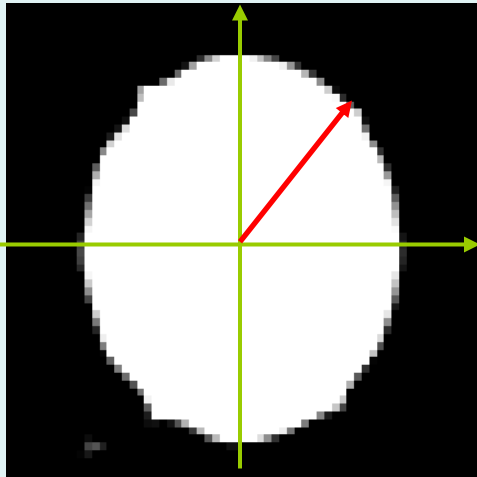
Modelling elastic deformations, “warps”

- Tissue probability images are warped to match the subject
- The inverse transform warps from subject space to the TPM space
- Warps are constrained to be *reasonable* by penalising extreme distortions (bending energy)



Non-linear warping, example

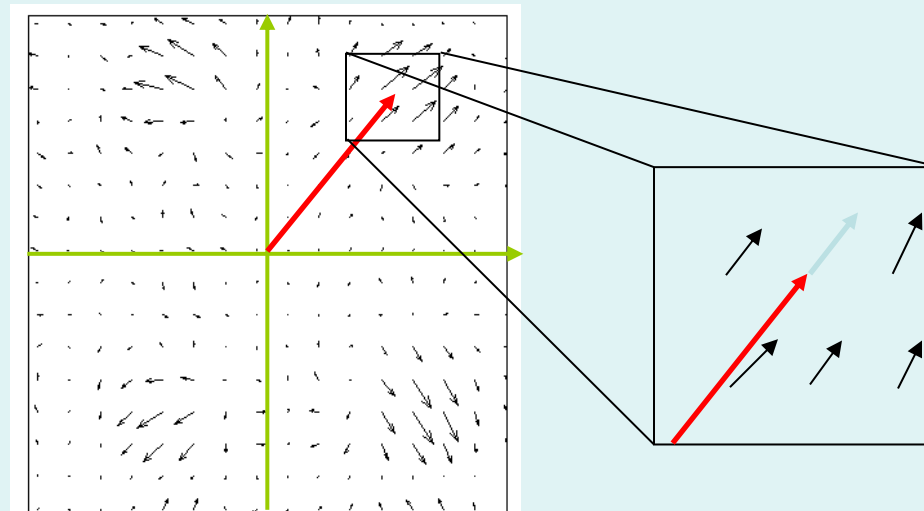
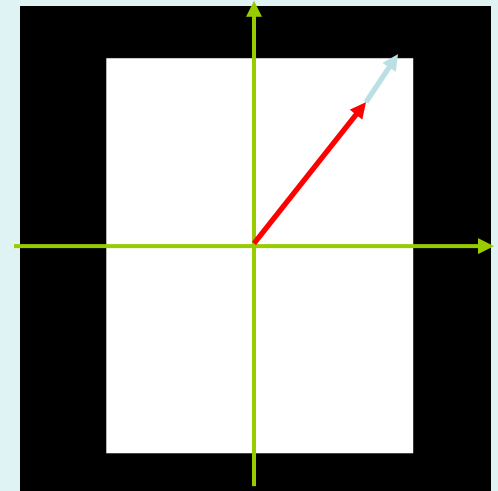
For every voxel
position in blank
sheet



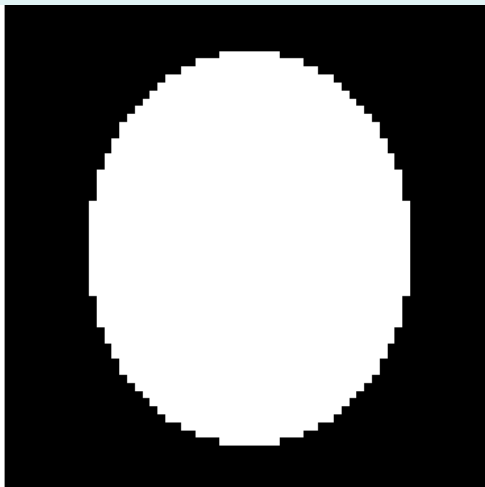
$$\begin{bmatrix} x' \\ y' \end{bmatrix} = \begin{bmatrix} x \\ y \end{bmatrix} + \begin{bmatrix} d_x(x, y) \\ d_y(x, y) \end{bmatrix}$$

Get position in
original space by
adding pertinent
displacement

Go to original image
and find intensity at
warped co-ordinate

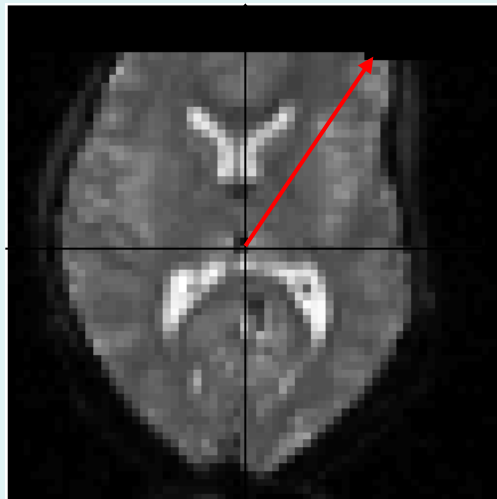


Target

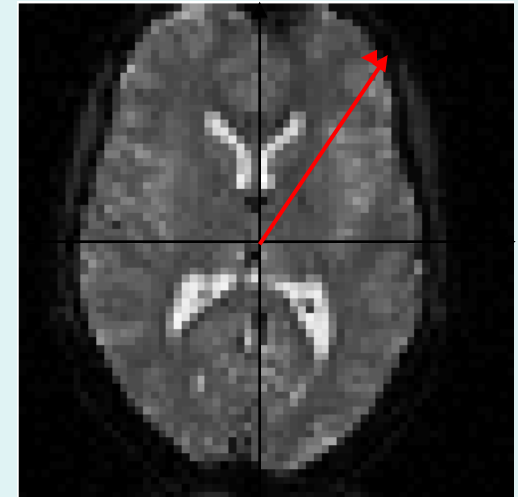


Non-linear warping, example

For each voxel-centre in blank sheet.

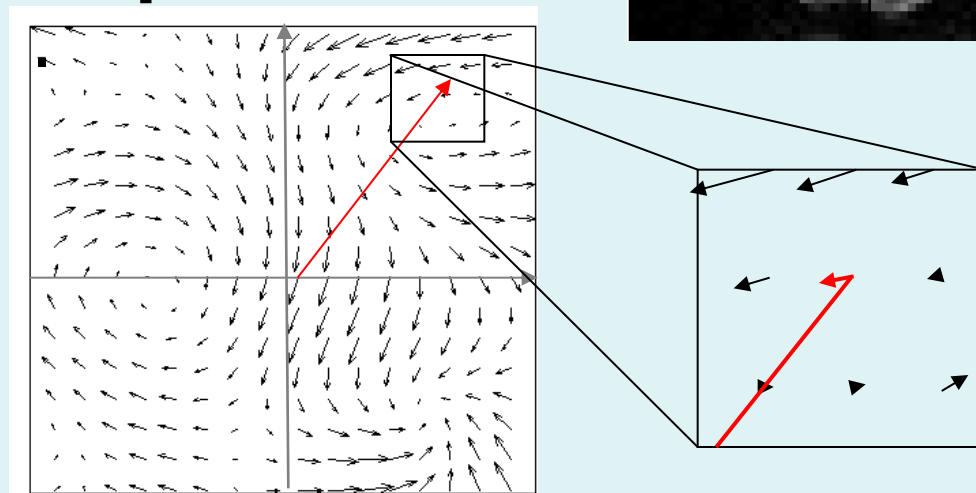


Go to original image and find intensity at "warped" co-ordinate

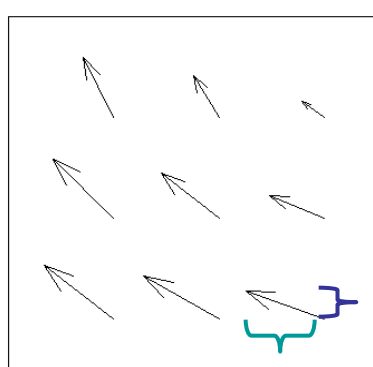
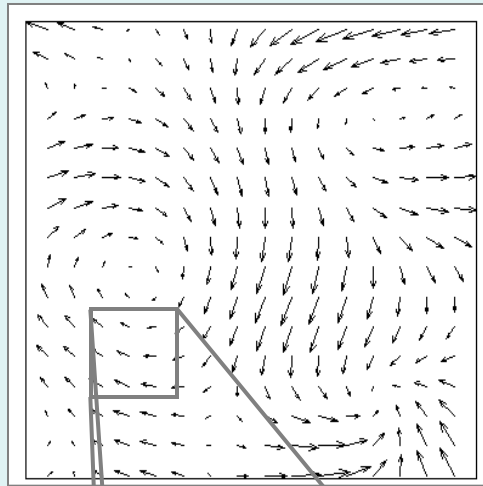


Get position in original space by adding pertinent **displacement**

$$\begin{bmatrix} x' \\ y' \end{bmatrix} = \begin{bmatrix} x \\ y \end{bmatrix} + \begin{bmatrix} d_x(x, y) \\ d_y(x, y) \end{bmatrix}$$

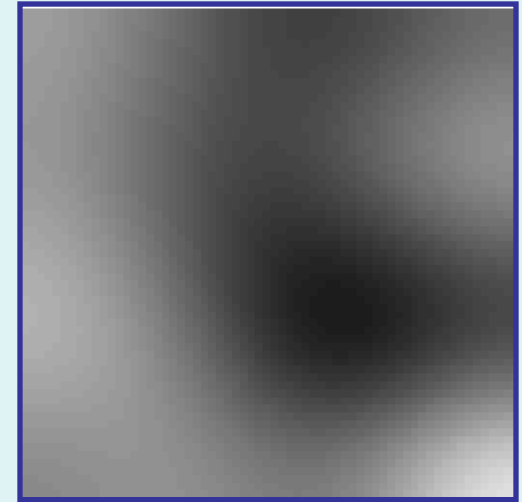


Displacement map

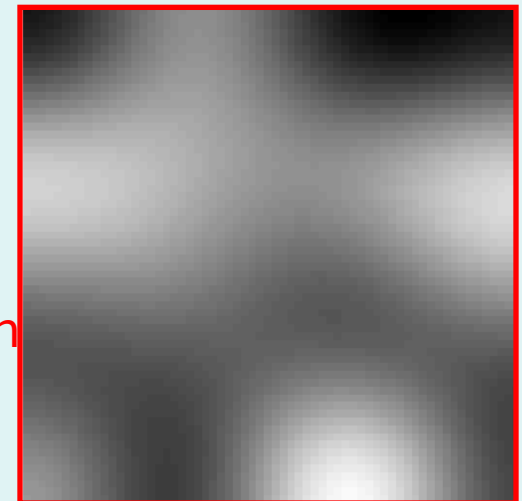


x-displacement

y-displacement,
black: downward
translation
white: upward
translation
grey: no translation

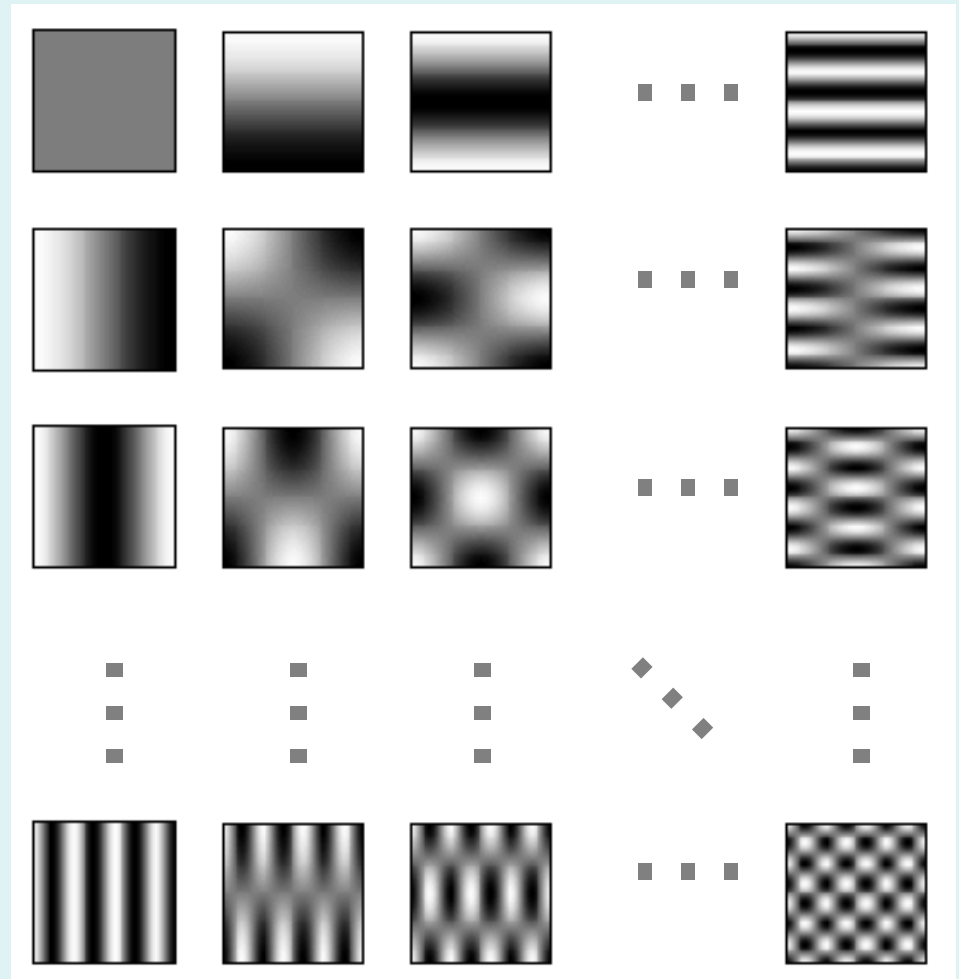


x-displacement,
black: leftward
translation
white: rightward
translation
gray: no translation



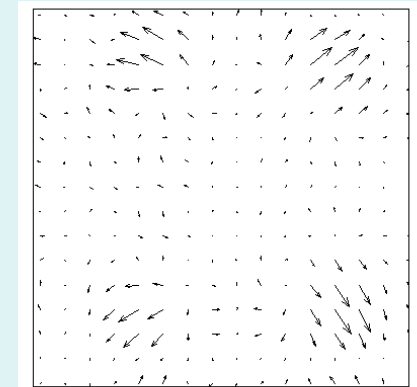
Displacement map modelling

- To prevent impossible deformations we restrict it to be a linear combination of permitted basis-warps.
- For example use the discrete cosine set $\rightarrow$ smooth deformation!

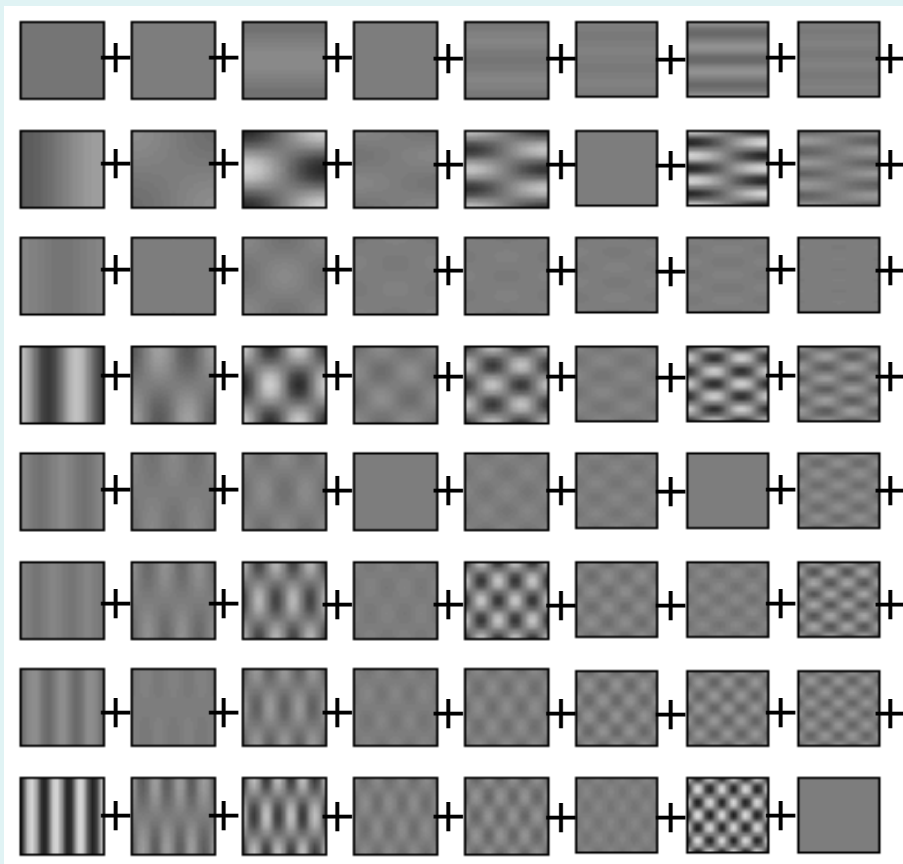


Displacement maps, example

Square-to-ellipse map

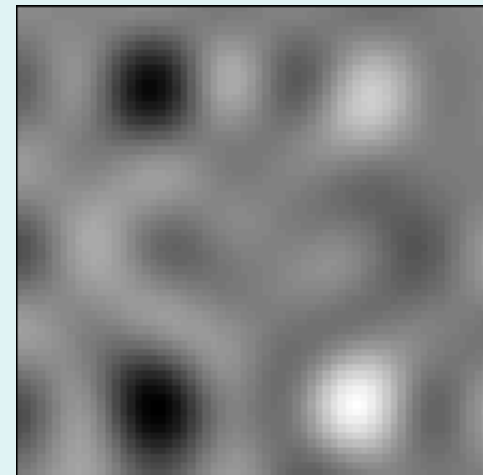


Each basis-warp multiplied by a weight



x-component of
square-to-ellipse map

=

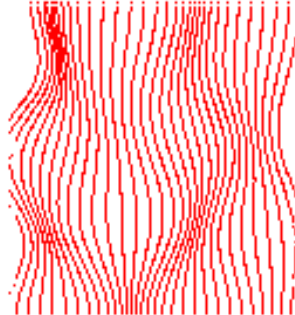


Displacement maps, example

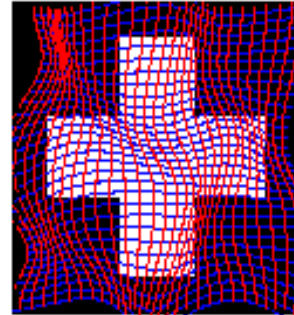
Dark – shift left, Light – shift right



Deformation Field in X



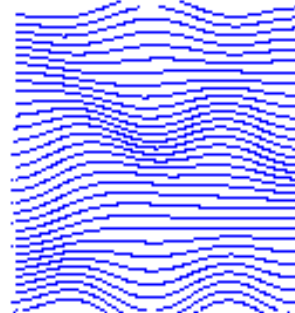
Field Applied To Image



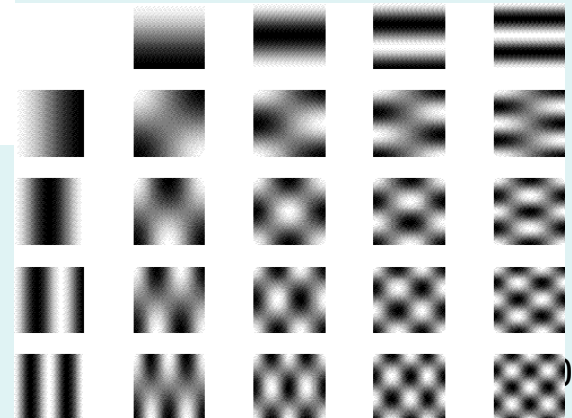
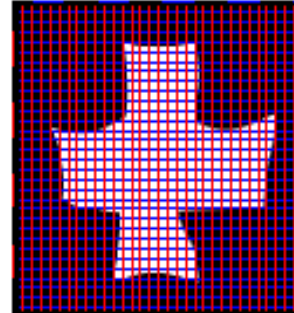
Dark – shift down, Light – shift up



Deformation Field in Y

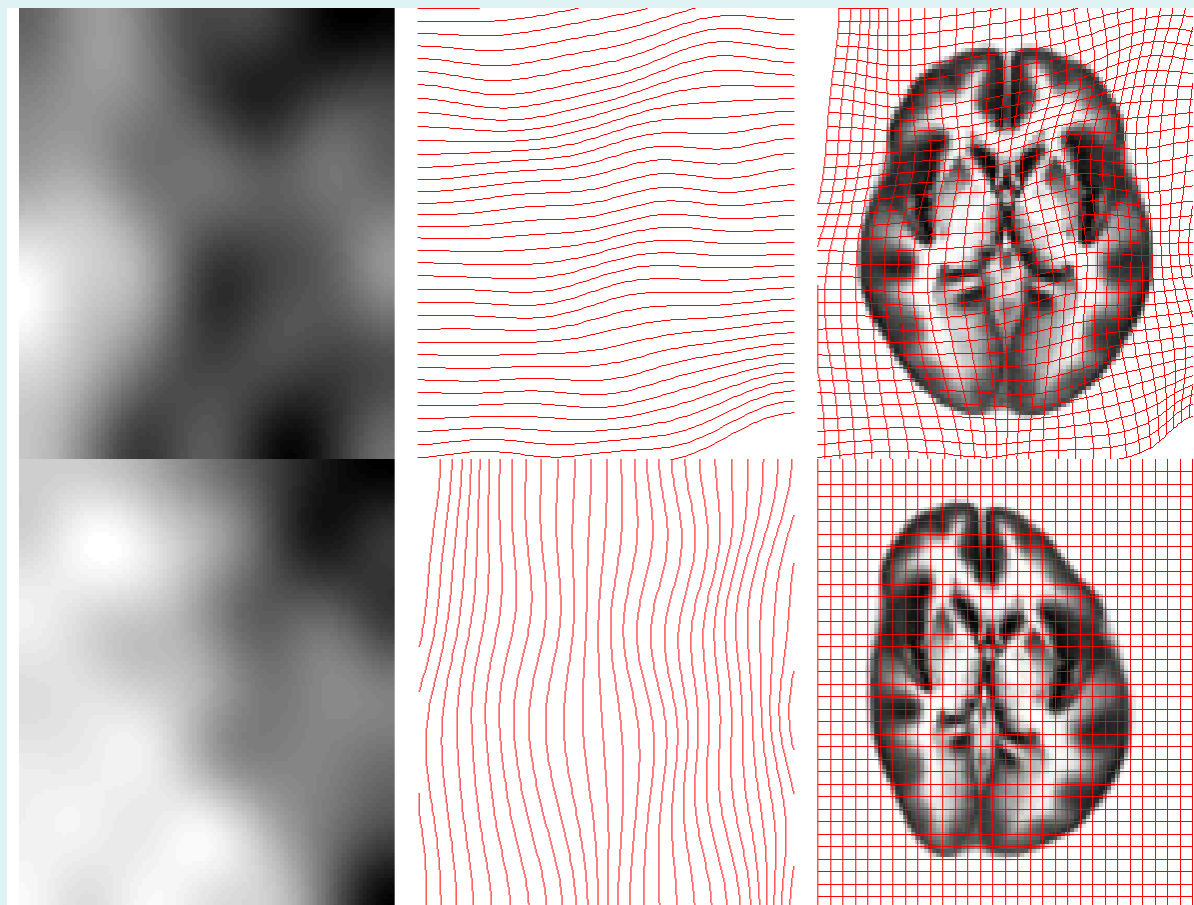


Deformed Image

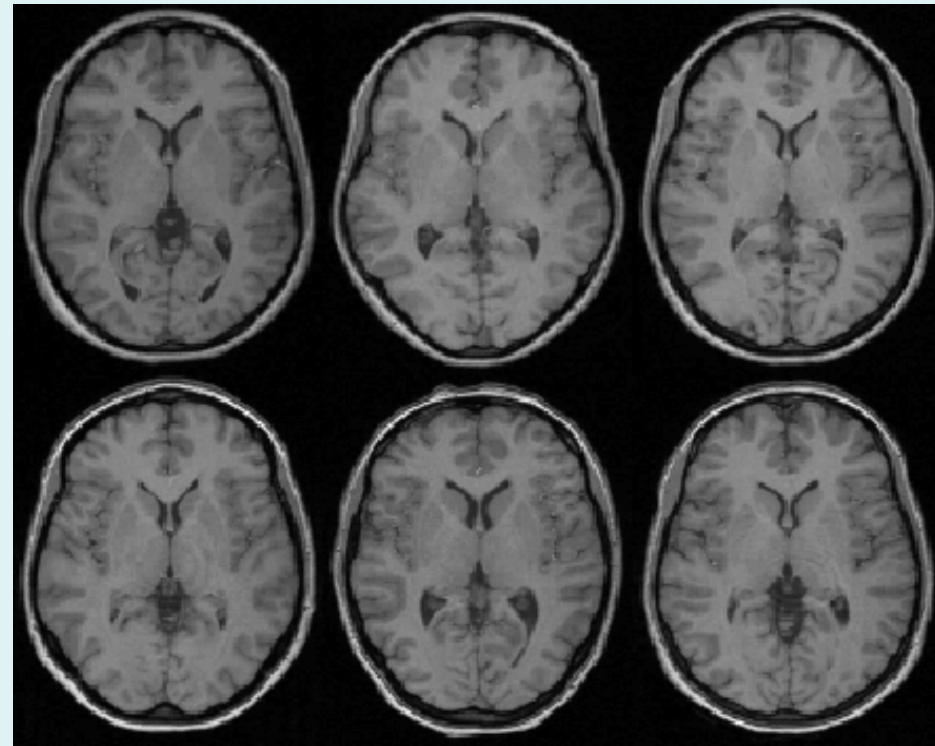


Modelling elastic deformations, “warps”

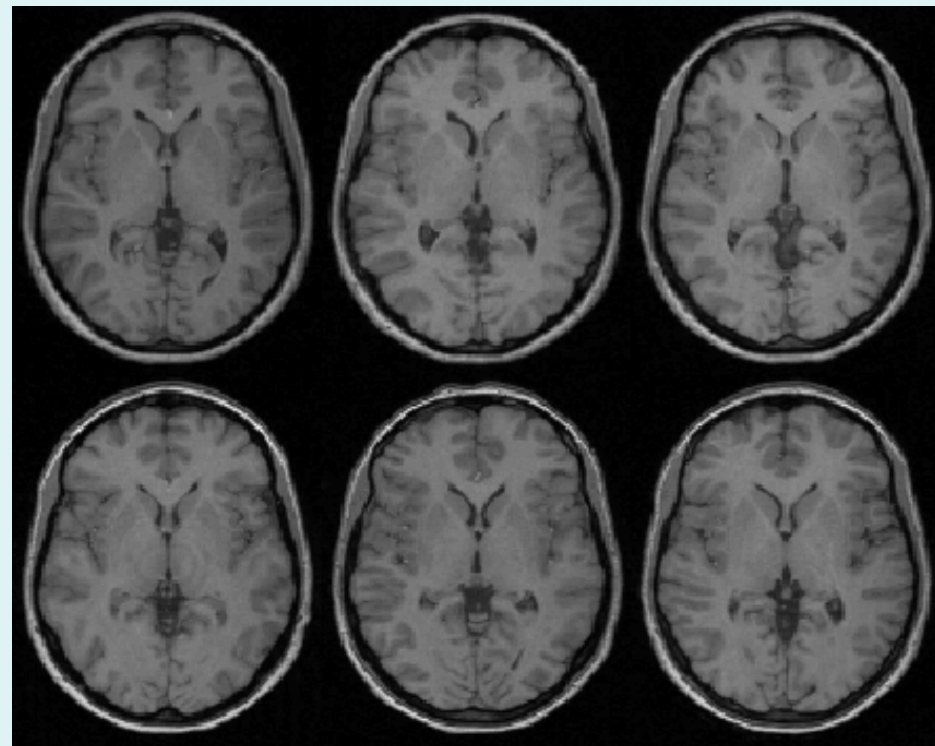
- Tissue probability images are warped to match the subject
- The inverse transform warps from subject space to the TPM space
- Warps are constrained to be *reasonable* by penalising extreme distortions (bending energy)



Spatial normalisation results



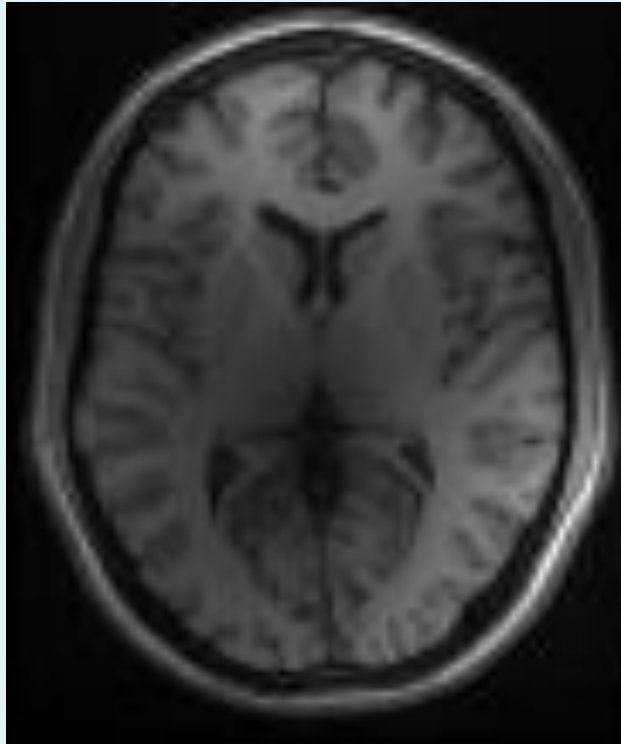
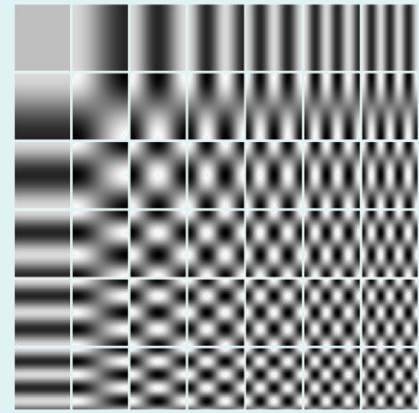
Affine registration



Non-linear registration

Modelling inhomogeneity

A multiplicative bias field is modelled as a spatially smooth image



Corrupted image



Bias Field



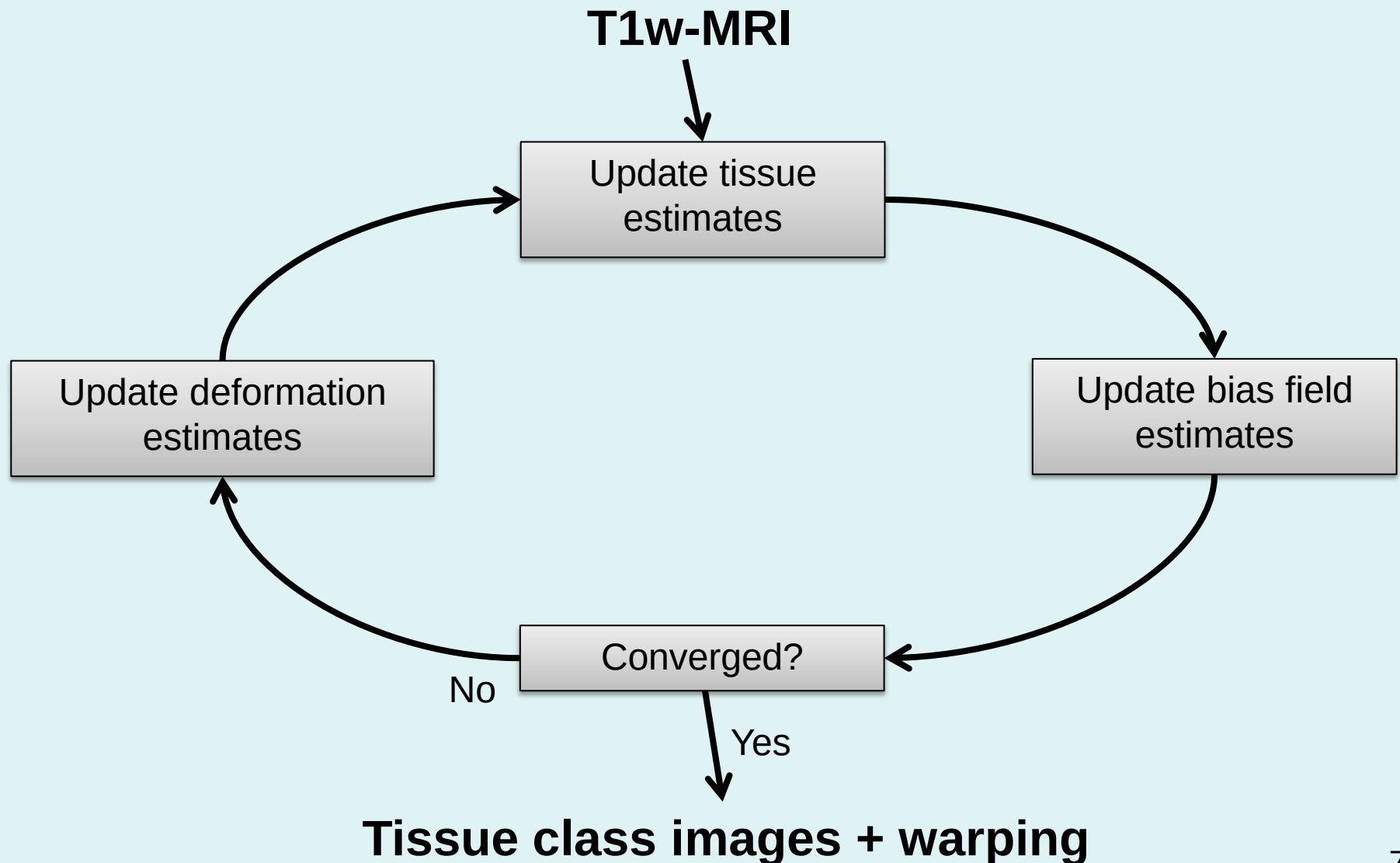
Corrected image

Normalisation & Unified Segmentation

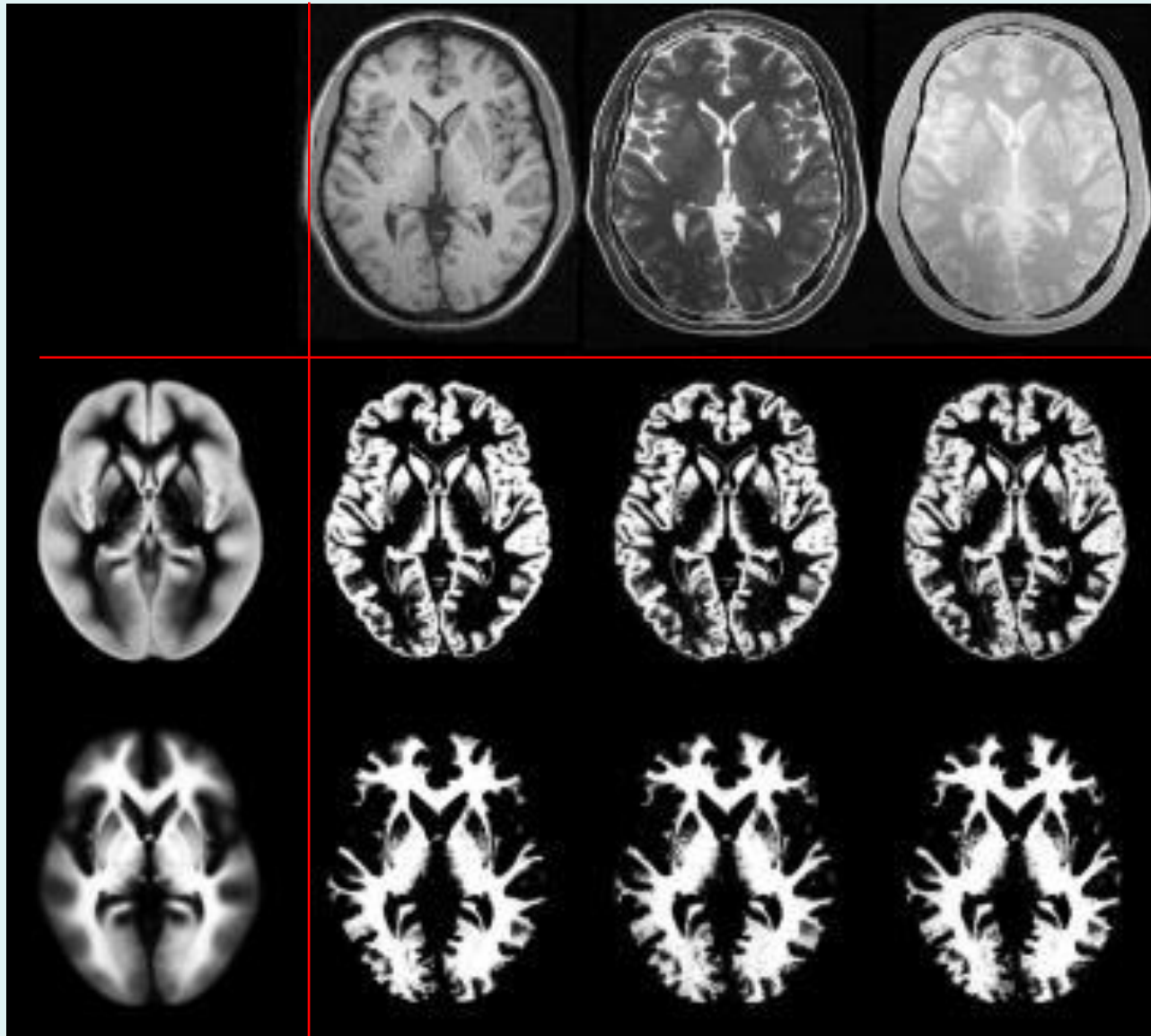
- MRI imperfections make normalisation harder
 - Differences between sequences, artefacts
 - Intensity inhomogeneity or “bias” field
- Normalising *segmented tissue maps* should be more robust and precise than using the original images (GM-onGM, WM-on-WM, etc.)...
- ... Tissue segmentation benefits from spatially-aligned *prior tissue probability maps* (from other segmentations)

→ Circular reasoning!

Iterative optimisation scheme



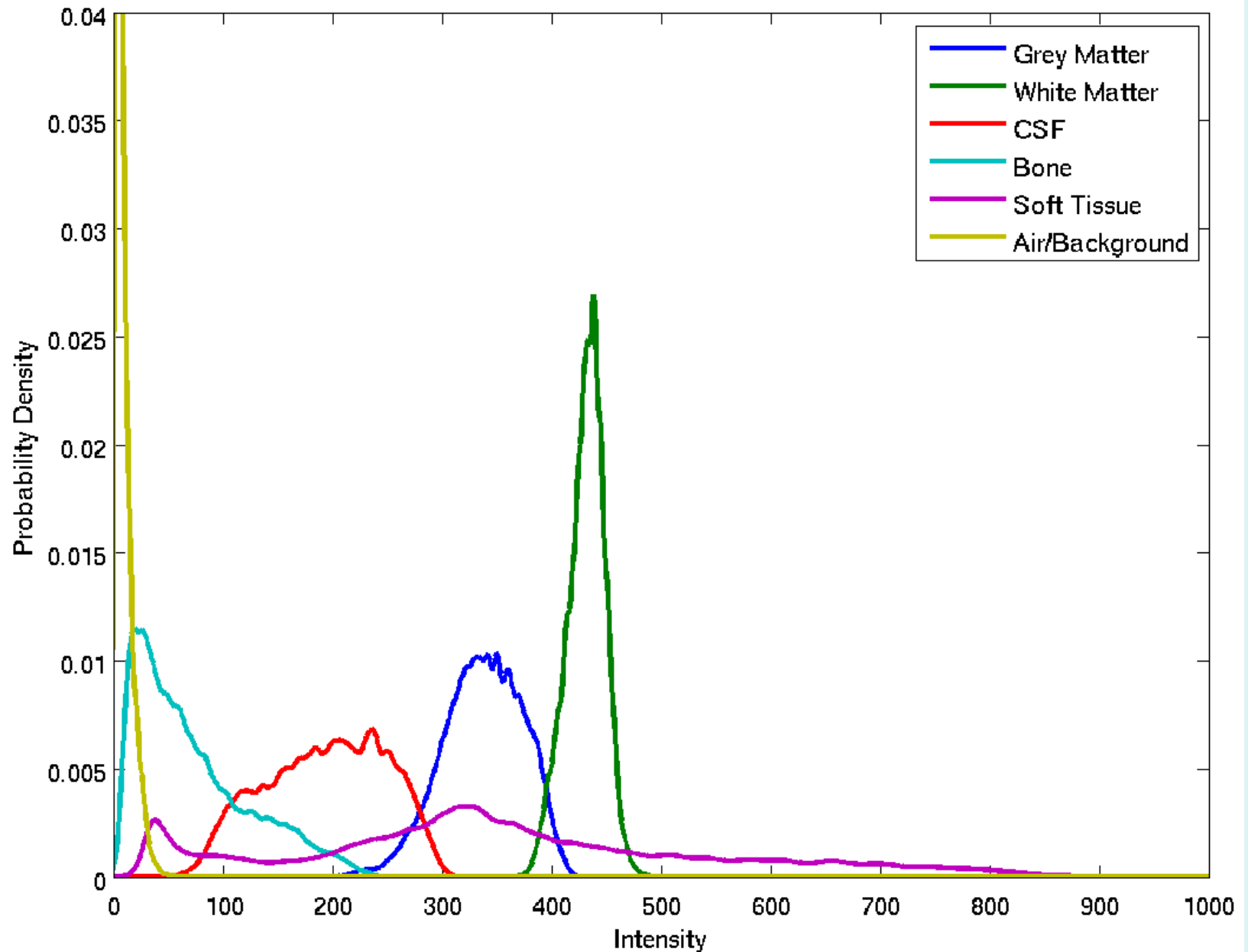
Segmentation results



Spatially
normalised
BrainWeb
phantoms
(T1, T2,
PD)

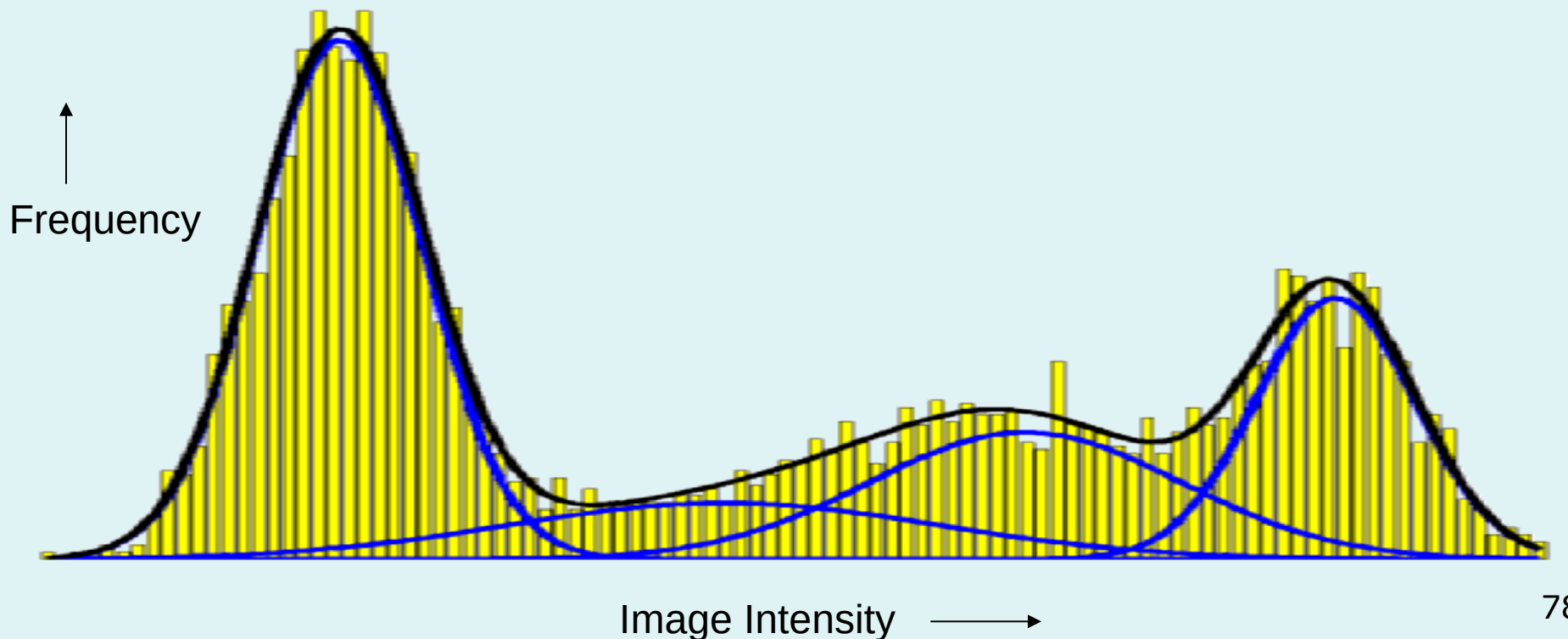
Tissue
probability
maps of
GM and
WM

Tissue intensity distributions (T1w-MRI)



Mixture of Gaussians (MoG)

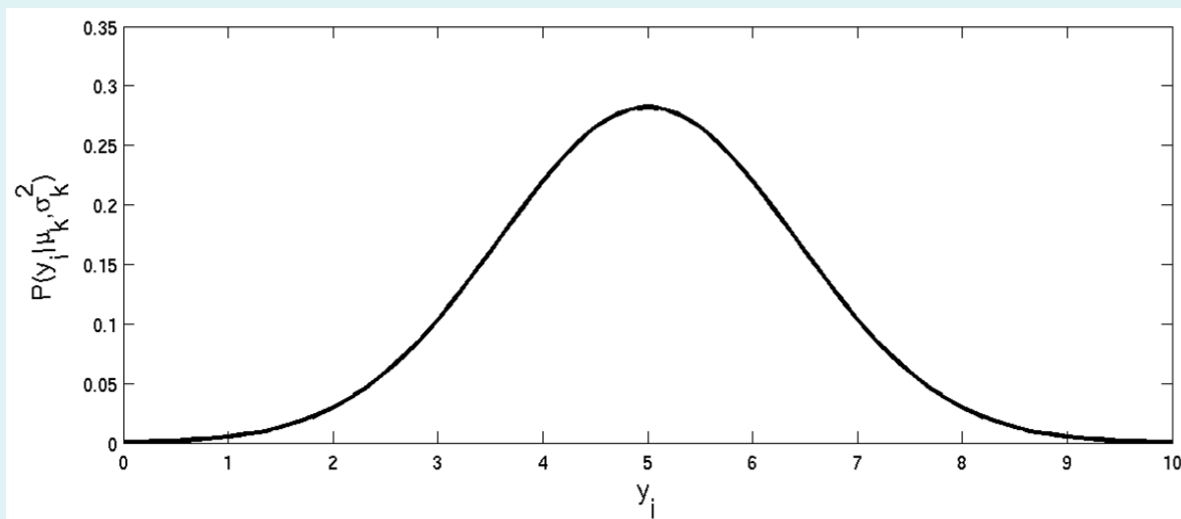
Classification is based on a Mixture of Gaussians model (MOG), which represents the intensity probability density by a number of **Gaussian distributions**.



Gaussian probability density

If intensities are assumed to be Gaussian of mean μ_k and variance σ_k^2 , then the probability of a value y_i is:

$$P(y_i | \mu_k, \sigma_k^2) = \frac{1}{\sqrt{2\pi\sigma_k^2}} \exp\left(-\frac{(y_i - \mu_k)^2}{2\sigma_k^2}\right)$$

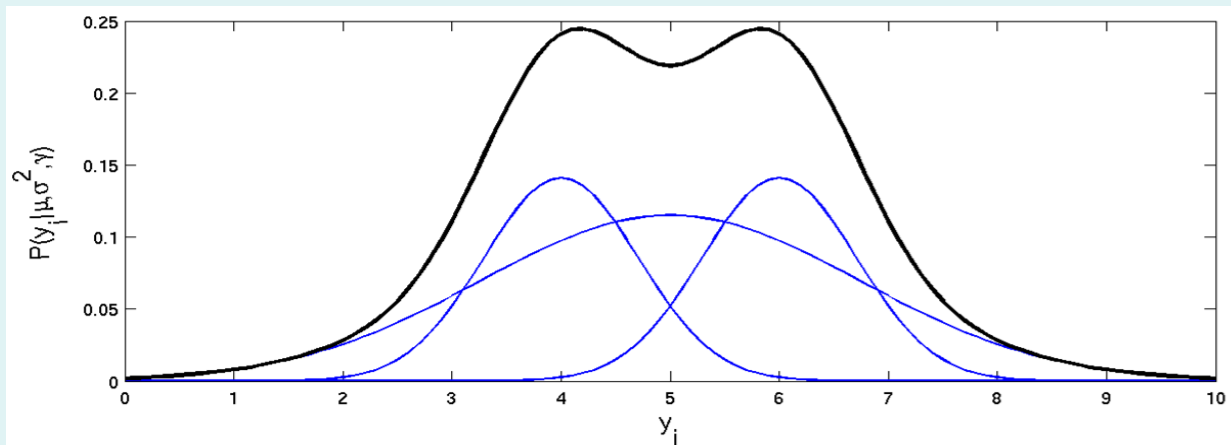


Non-Gaussian probability density

A non-Gaussian probability density function can be modelled by a Mixture of Gaussians (MOG):

$$P(y_i | \mu, \sigma^2, \gamma) = \sum_{k=1}^K \gamma_k \frac{1}{\sqrt{2\pi\sigma_k^2}} \exp\left(-\frac{(y_i - \mu_k)^2}{2\sigma_k^2}\right)$$

Mixing proportion - positive and sums to one

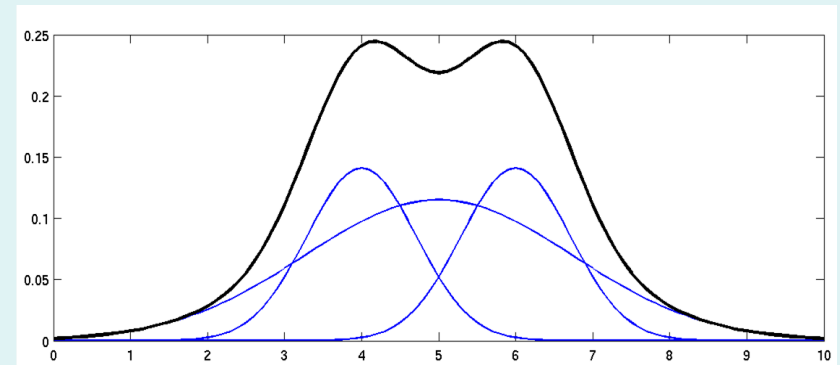


Mixing proportions

- The mixing proportion γ_k represents the prior probability of a voxel being drawn from class k - irrespective of its intensity.

$$P(c_i = k \mid \gamma) = \gamma_k$$

- So:



$$\begin{aligned} P(y_i \mid \mu, \sigma^2, \gamma) &= \sum_{k=1}^K P(y_i, c_i = k \mid \mu, \sigma^2, \gamma) \\ &= \sum_{k=1}^K P(c_i = k \mid \gamma) P(y_i \mid c_i = k, \mu, \sigma^2) \end{aligned}$$

Probability of whole image

- If the voxels are assumed to be independent, then the probability of the whole image is the product of the probabilities of each voxel:

$$P(\mathbf{y} \mid \mu, \sigma^2, \gamma) = \prod_{i=1}^I P(y_i \mid \mu, \sigma^2, \gamma)$$

- It is often easier to work with negative log-probabilities:

$$-\log(P(\mathbf{y} \mid \mu, \sigma^2, \gamma)) = -\sum_{i=1}^I \log(P(y_i \mid \mu, \sigma^2, \gamma))$$

Modelling a bias field

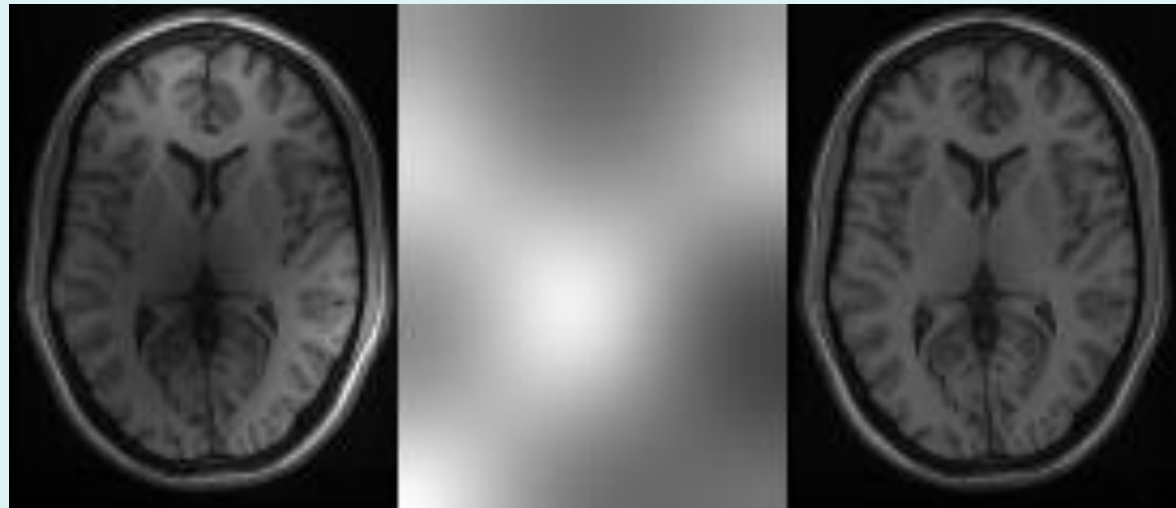
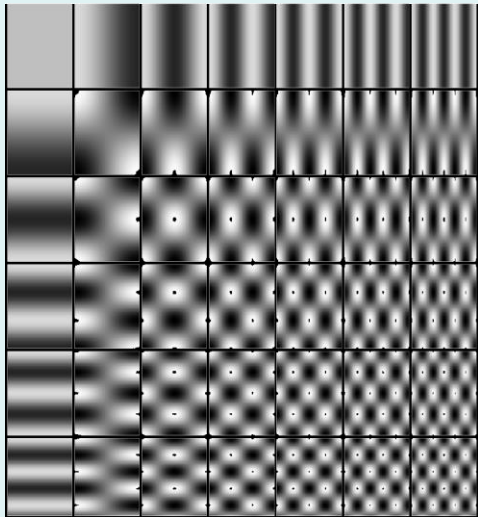
- A bias field is included, such that the required scaling at voxel i , parameterised by β , is $\rho_i(\beta)$.
- Replace the means by $\mu_k / \rho_i(\beta)$
- Replace the variances by $(\sigma_k / \rho_i(\beta))^2$

$$P(y_i \mid c_i = k, \mu, \sigma^2, \beta) = \frac{1}{\sqrt{2\pi(\sigma_k / \rho_i(\beta))^2}} \exp\left(-\frac{(y_i - \mu_k / \rho_i(\beta))^2}{2(\sigma_k / \rho_i(\beta))^2}\right)$$

Modelling a bias field

After rearranging:

$$P(y_i | c_i = k, \mu, \sigma^2, \beta) = \frac{\rho(\beta)}{\sqrt{2\pi\sigma_k^2}} \exp\left(-\frac{(y_i \rho(\beta) - \mu_k)^2}{2\sigma_k^2}\right)$$



y

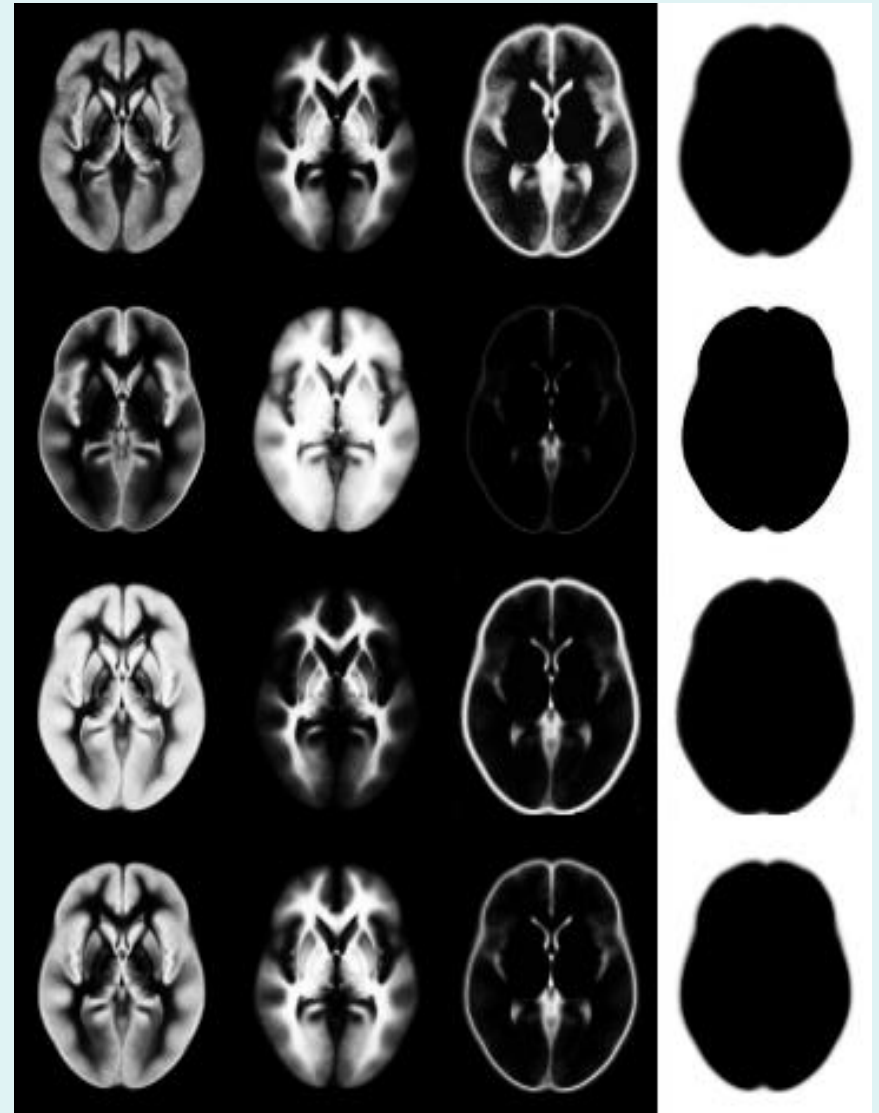
$\rho(\beta)$

$y \rho(\beta)$

“Mixing proportions”

- Tissue probability maps for each class are included.
- Priors depend on location in the brain
- The probability of obtaining class k at voxel i , given weights γ is then:

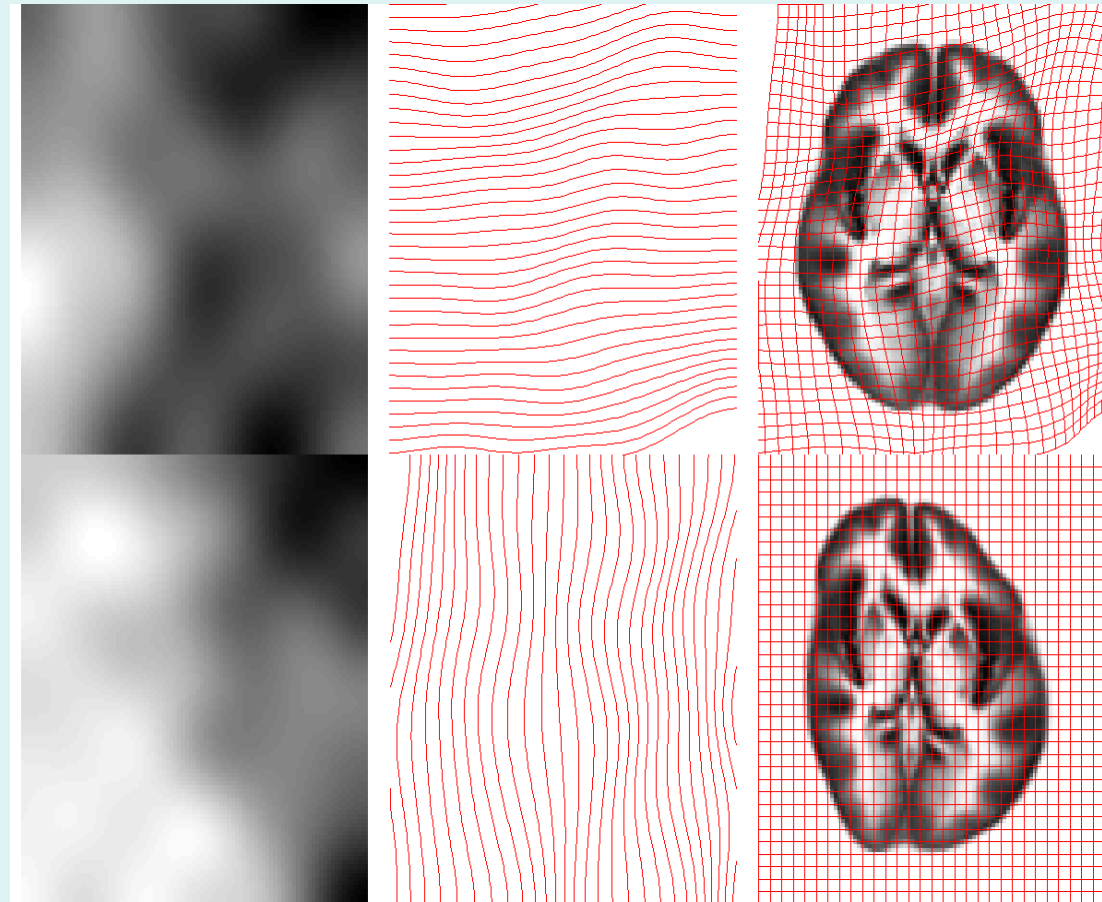
$$P(c_i = k \mid \gamma) = \frac{\gamma_k b_{ik}}{\sum_{j=1}^K \gamma_j b_{ij}}$$



TPMs deformation

- Tissue probability images are deformed according to parameters α .
- The probability of obtaining class k at voxel i , given weights γ and parameters α is then:

$$P(c_i = k \mid \gamma, \alpha) = \frac{\gamma_k b_{ik}(\alpha)}{\sum_{j=1}^K \gamma_j b_{ij}(\alpha)}$$



The extended US model

- By combining the modified $P(c_i=k|\theta)$ and $P(y_i|c_i=k,\theta)$, the overall objective function (E) becomes:

$$E = -\sum_{i=1}^I \log[P(y_i|\theta)] = -\sum_{i=1}^I \log \left[\sum_{k=1}^K P(c_i = k | \theta) P(y_i | c_i = k, \theta) \right]$$

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

The Objective Function

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.

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

Optimisation strategy

Repeat until convergence...

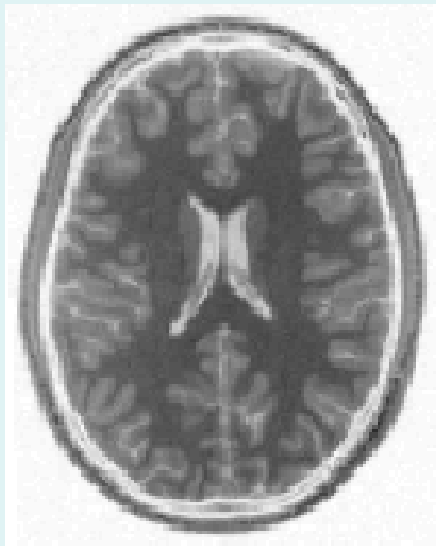
- Hold γ , μ , σ^2 and α constant, and minimise E w.r.t. β (i.e. bias field)
Levenberg-Marquardt strategy, using $dE/d\beta$ and $d^2E/d\beta^2$
- Hold γ , μ , σ^2 and β constant, and minimise E w.r.t. α (i.e. spatial deformation)
Levenberg-Marquardt strategy, using $dE/d\alpha$ and $d^2E/d\alpha^2$
- Hold α and β constant, and minimise E w.r.t. γ , μ and σ^2 (i.e. segmentation parameters)
Use an Expectation Maximisation (EM) strategy.

end

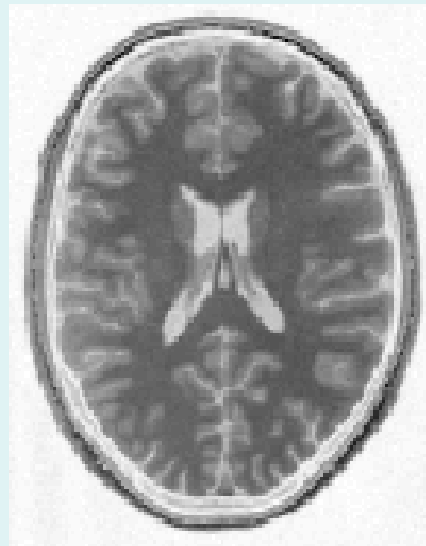
Spatial normalisation, overfitting

Without regularisation, the non-linear spatial normalisation can introduce unnecessary warps.

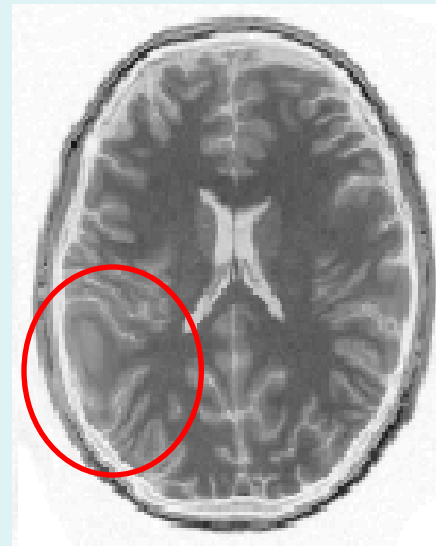
Template
image



Affine
registration.



Non-linear
registration
without
regularisation.



Linear regularisation

- Some bias fields and distortions are more probable (a priori) than others.
- Encoded using Bayes rule:

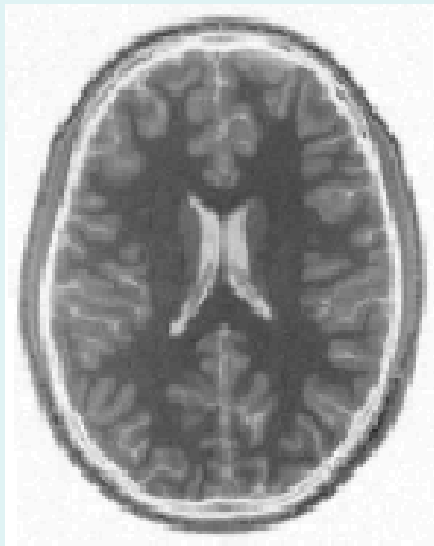
$$-\log[P(\theta, \mathbf{y})] = -\log[P(\mathbf{y}|\theta)] - \log[P(\theta)]$$

- Prior probability distributions can be modelled by a multivariate normal distribution.
 - Mean vector μ_a and μ_b
 - Covariance matrix Σ_a and Σ_b
 - $-\log[P(\mathbf{a})] = (\mathbf{a} - \mathbf{m}_a)^T \mathbf{S}_a^{-1} (\mathbf{a} - \mathbf{m}_a) + \text{const}$

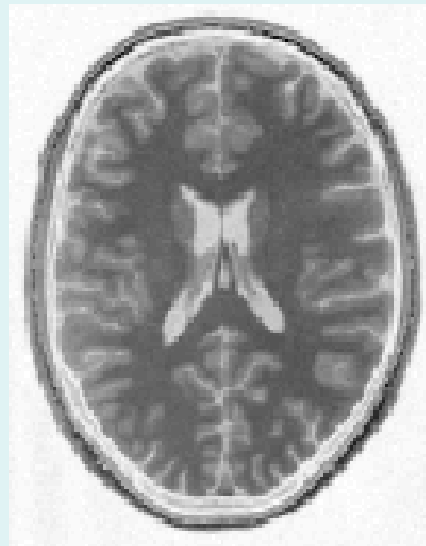
Spatial normalisation, overfitting

Without regularisation, the non-linear spatial normalisation can introduce unnecessary warps.

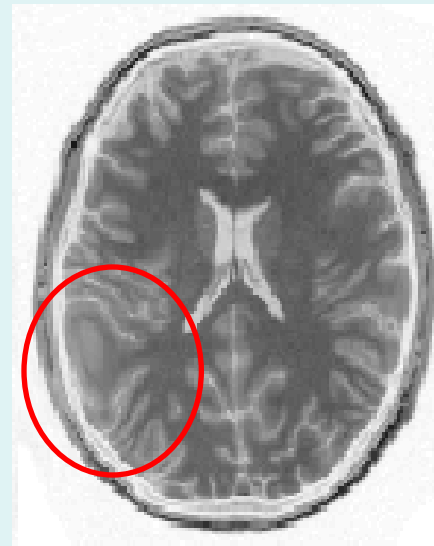
Template image



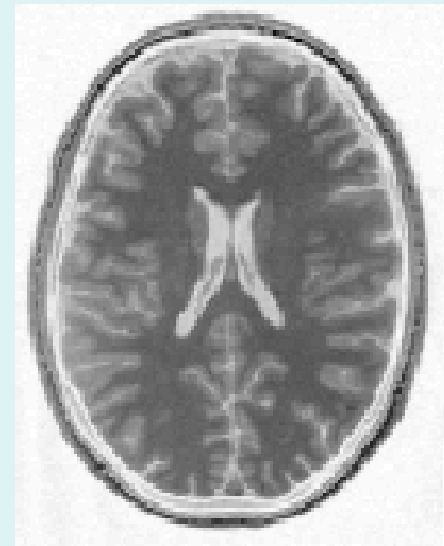
Affine registration.



Non-linear registration without regularisation.

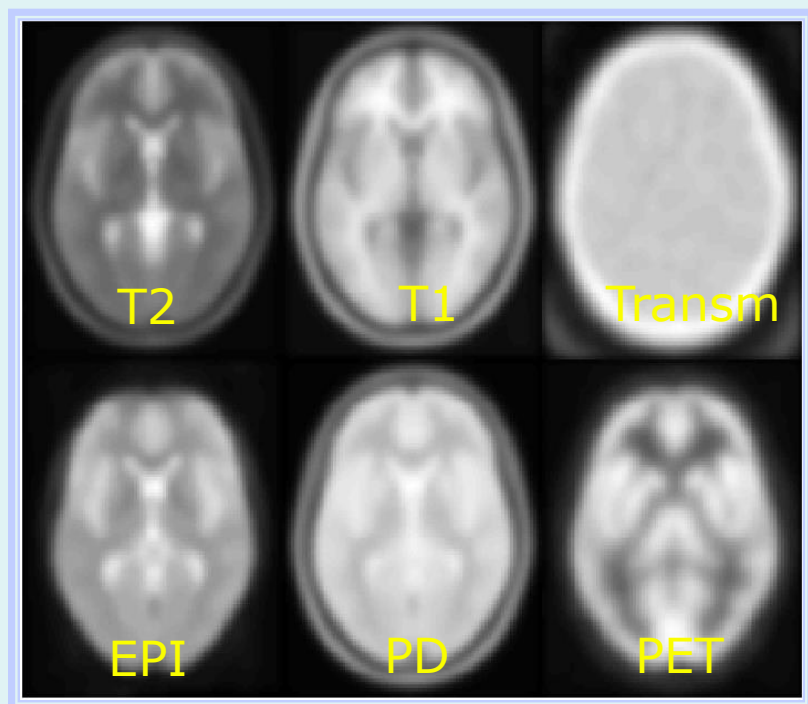


Non-linear registration using regularisation.



Old fashioned template matching

Minimise mean squared difference from image to template image(s)



Template Images



Spatial normalisation can be weighted so that non-brain voxels do not influence the result.

Similar weighting masks can be used for normalising lesioned brains.

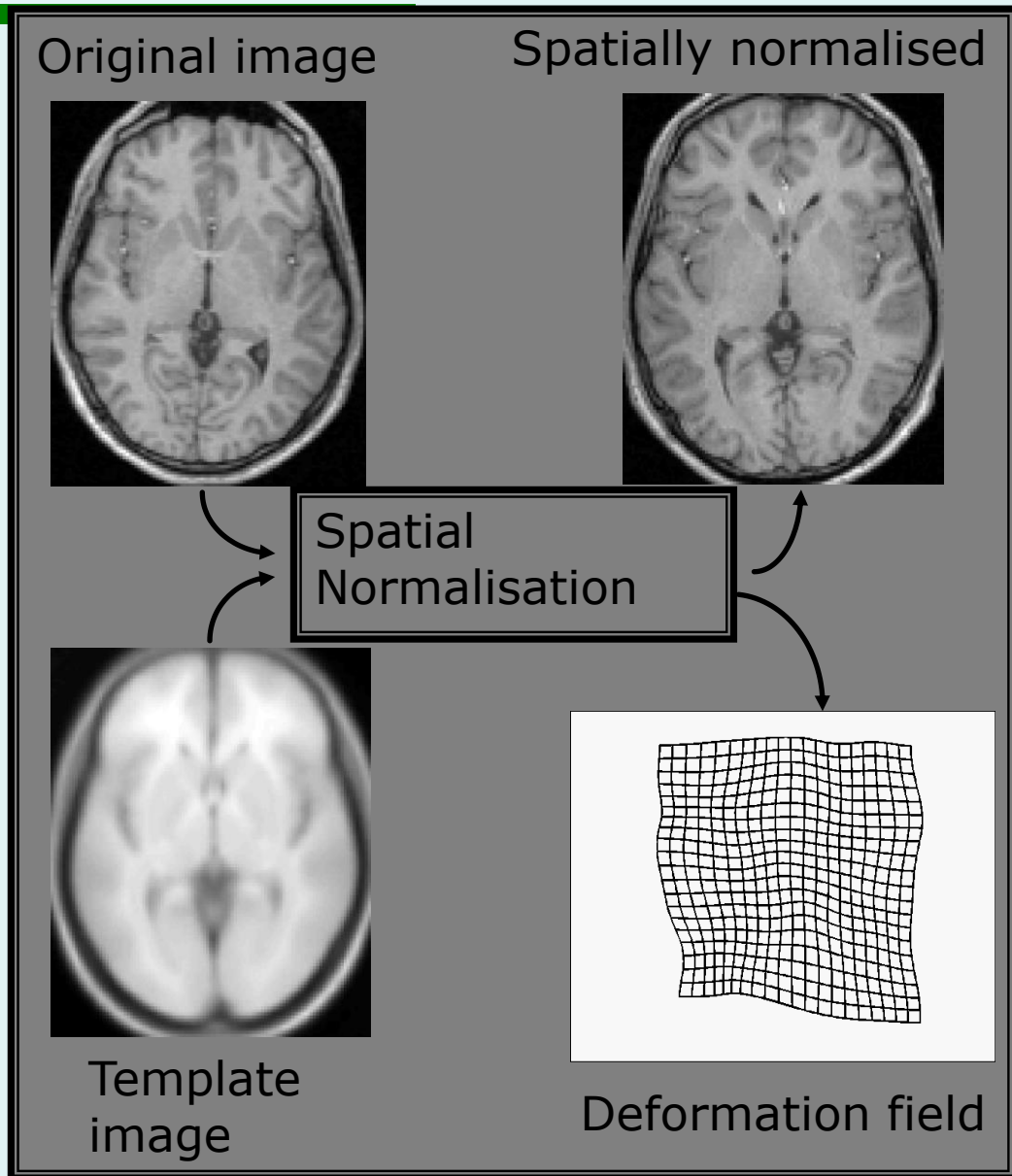
Old fashioned template matching

Determine the spatial transformation that minimises the sum of squared difference between an image and a linear combination of one or more templates.

Begins with an affine registration to match the size and position of the image.

Followed by a global non-linear warping to match the overall brain shape.

Uses a Bayesian framework to simultaneously minimize the bending energies of the warps.



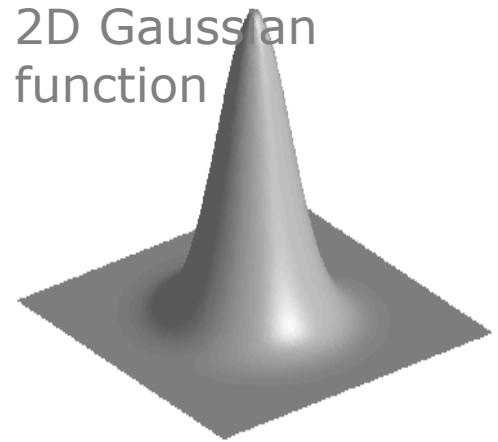
Content

- Preliminaries
- Within-subject
- Between-subject
- **Smoothing**
- Conclusion

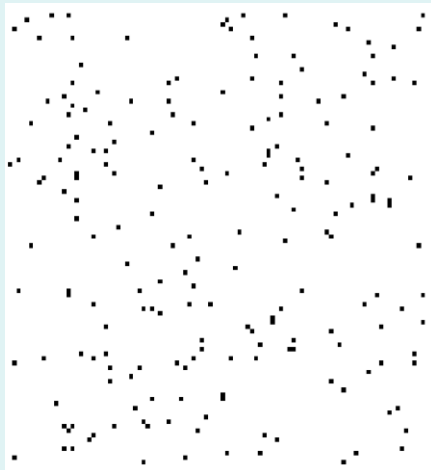
Smoothing, principle

- Smoothing is done by convolution.
- Each voxel after smoothing effectively becomes the result of applying a weighted region of interest (ROI).
- Gaussian function, defined by its “*full width at half maximum*” (FWHM)

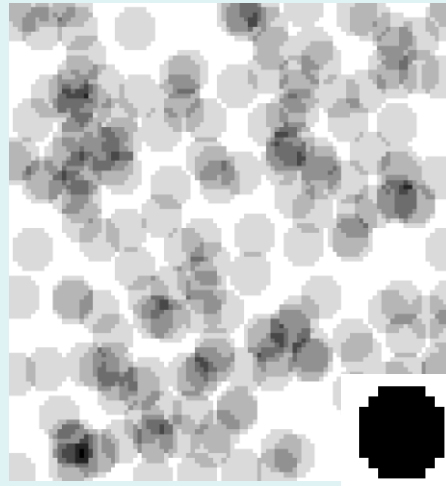
2D Gaussian function



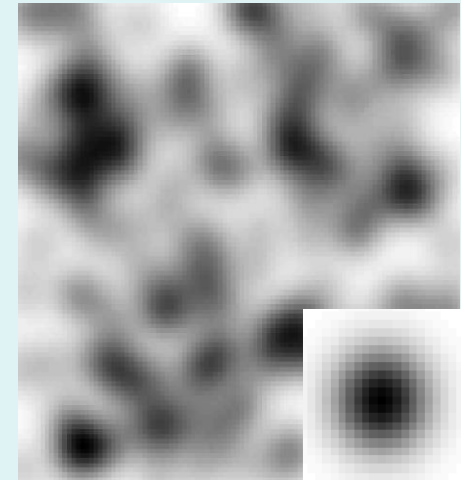
Before convolution



Convolved with a circle

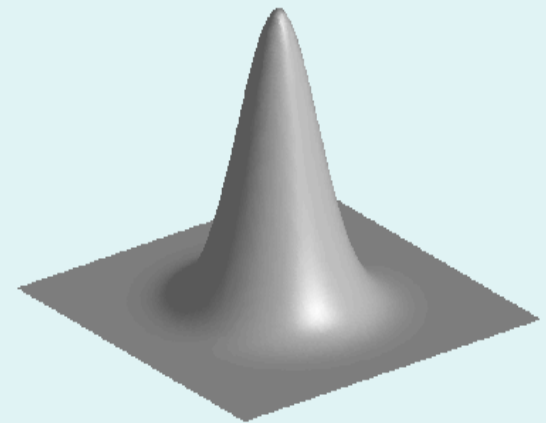


Convolved with a Gaussian



Smoothing, why blur the data?

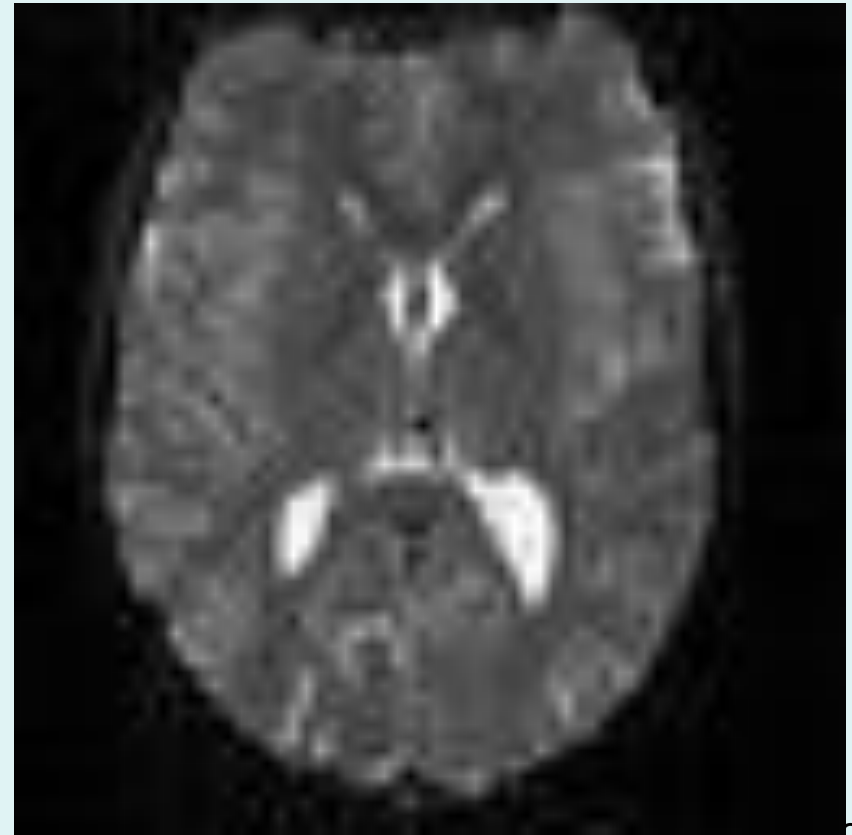
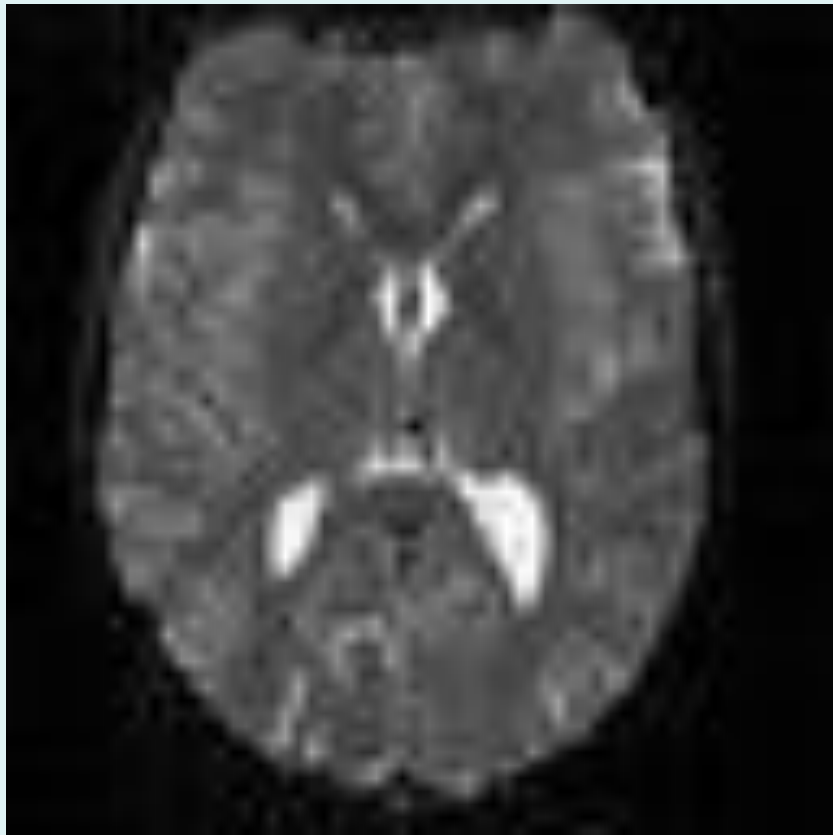
- Improves spatial overlap by blurring over minor anatomical differences and registration errors
- Averaging neighbouring voxels suppresses noise (matched filter theorem)
- Makes data more normally distributed (central limit theorem)
- Reduces the effective number of multiple comparisons



Smoothing, kernel size

Decide *a priori*, based on:

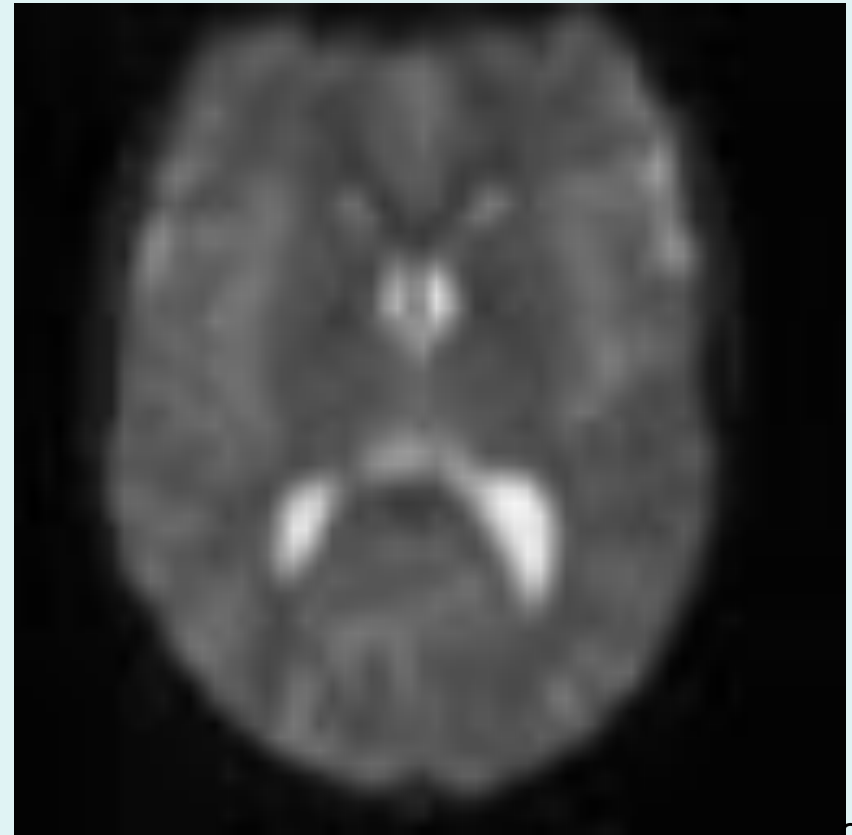
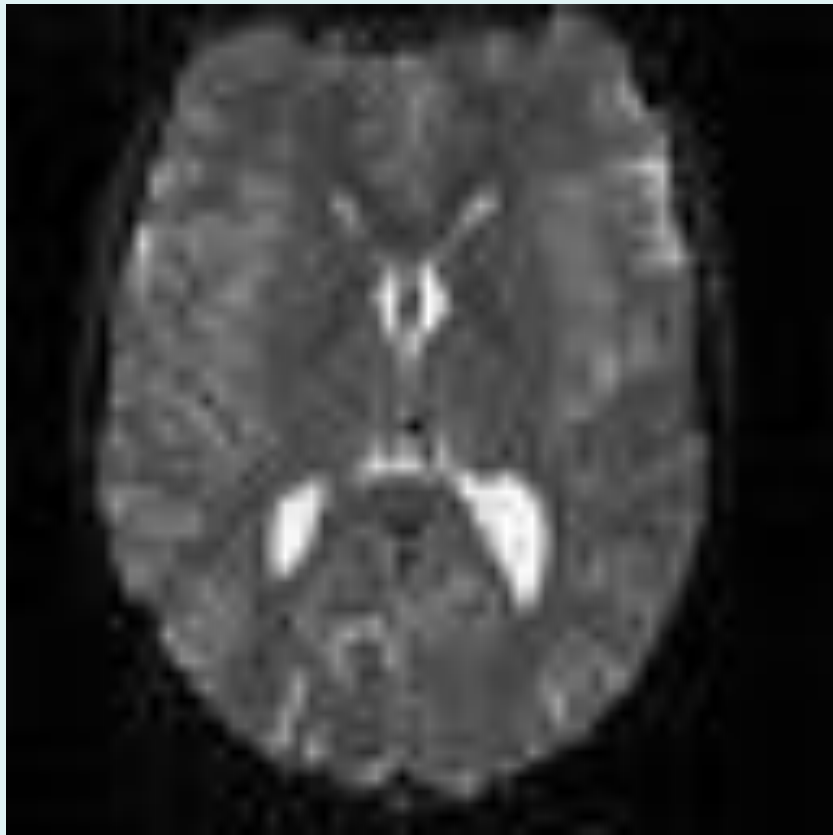
- Population, i.e. noise & inter-subject variability
- Expected activation size



Smoothing, kernel size

Decide *a priori*, based on:

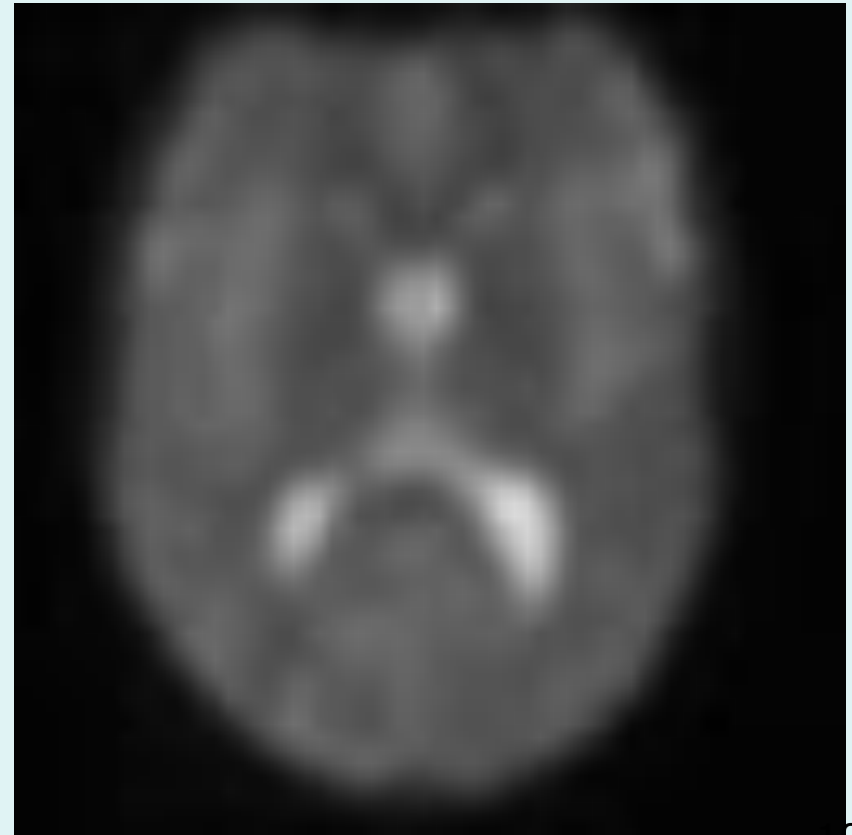
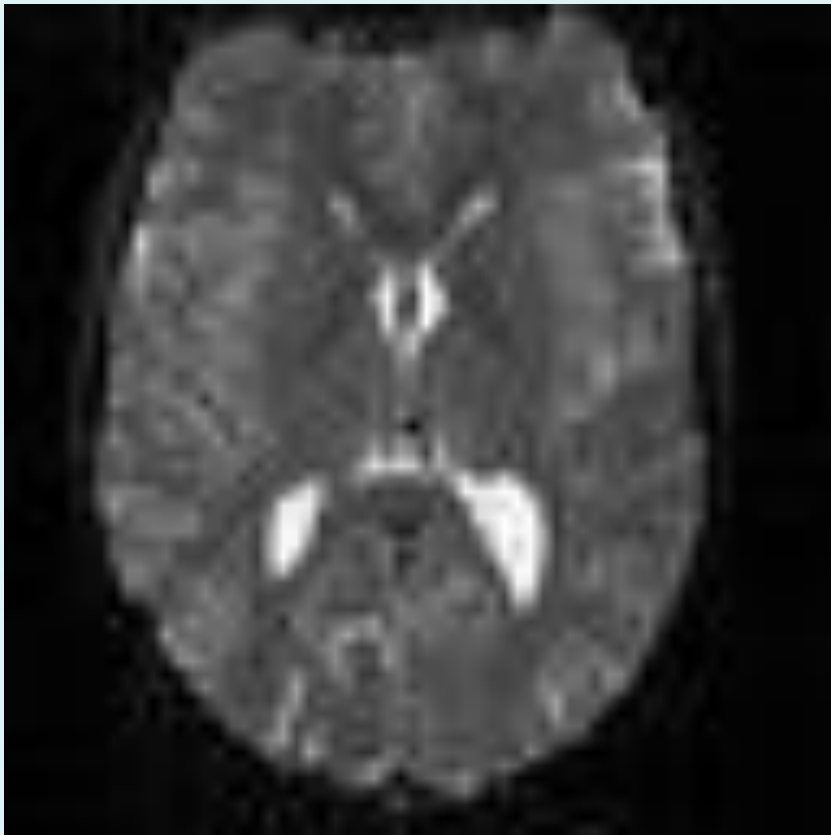
- Population, i.e. noise & inter-subject variability
- Expected activation size



Smoothing, kernel size

Decide *a priori*, based on:

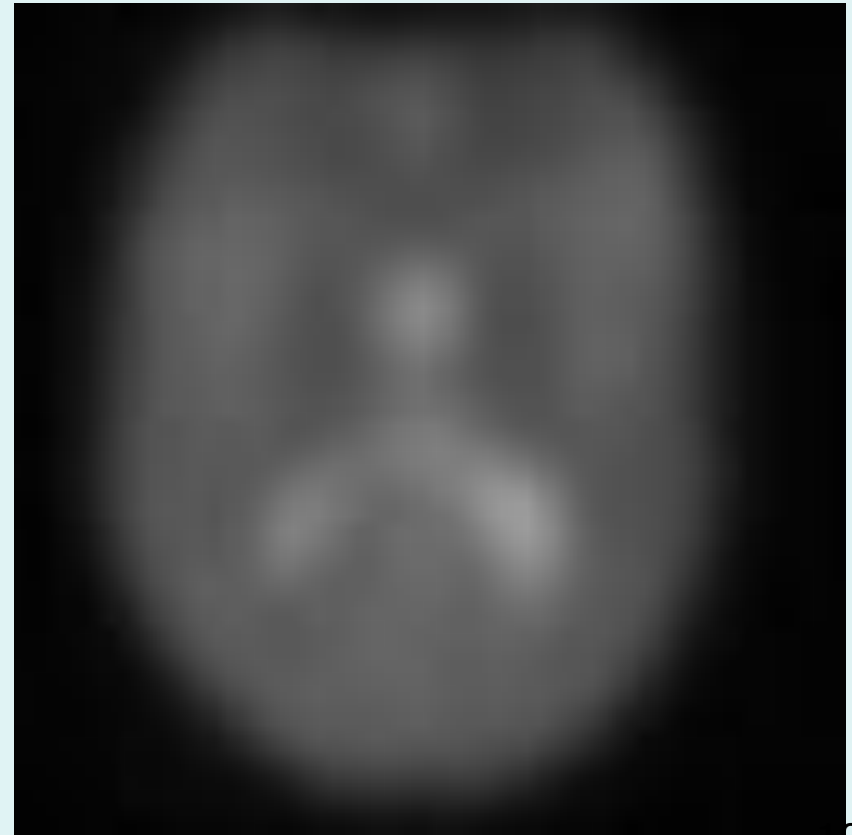
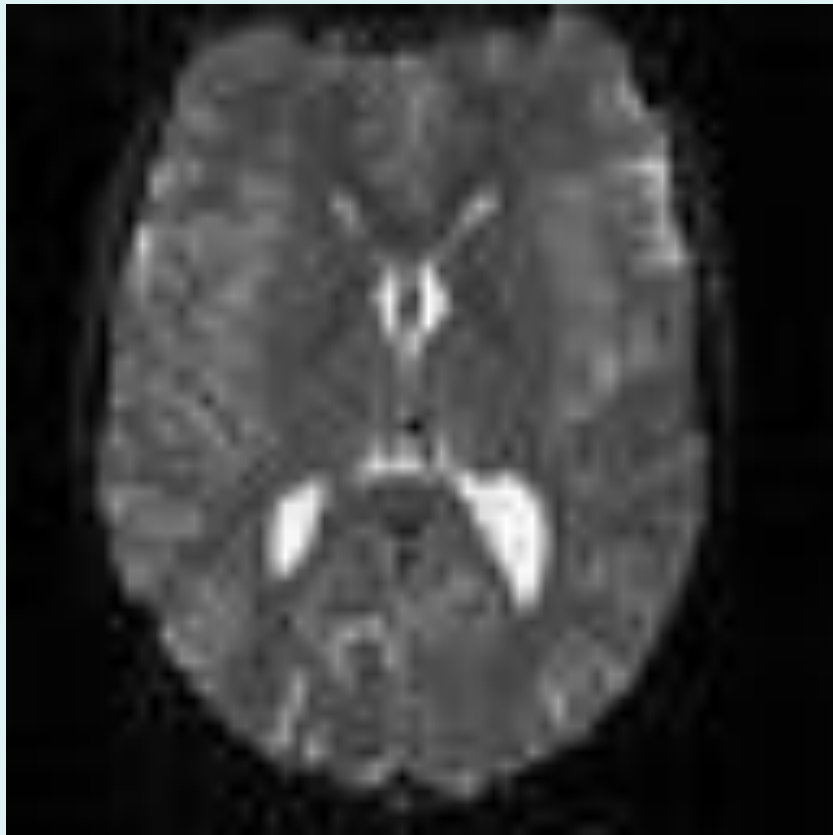
- Population, i.e. noise & inter-subject variability
- Expected activation size



Smoothing, kernel size

Decide *a priori*, based on:

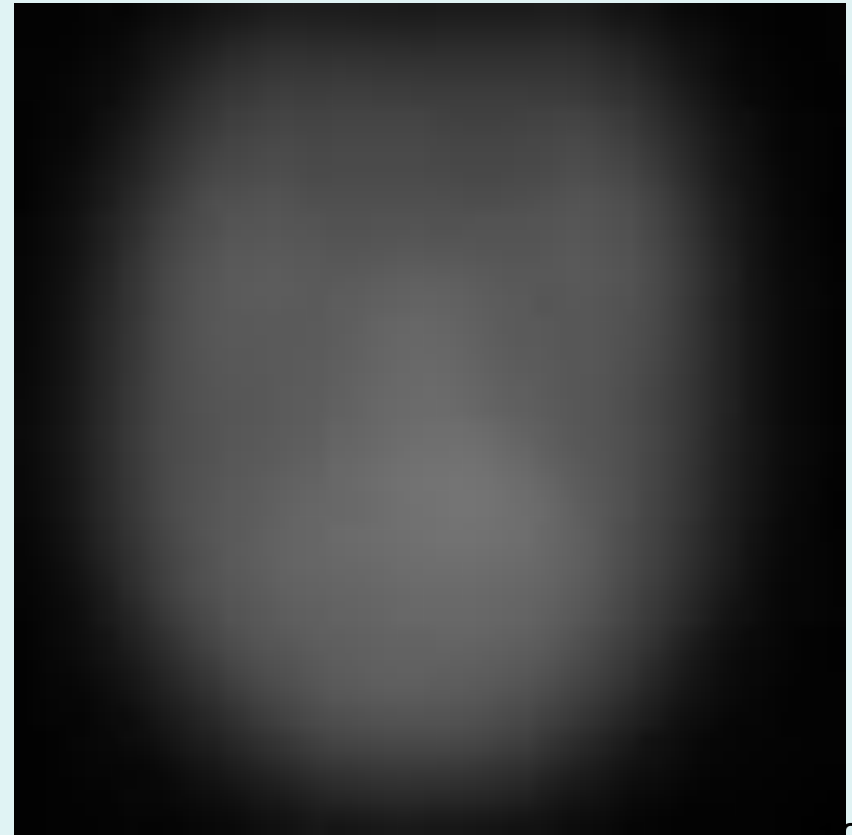
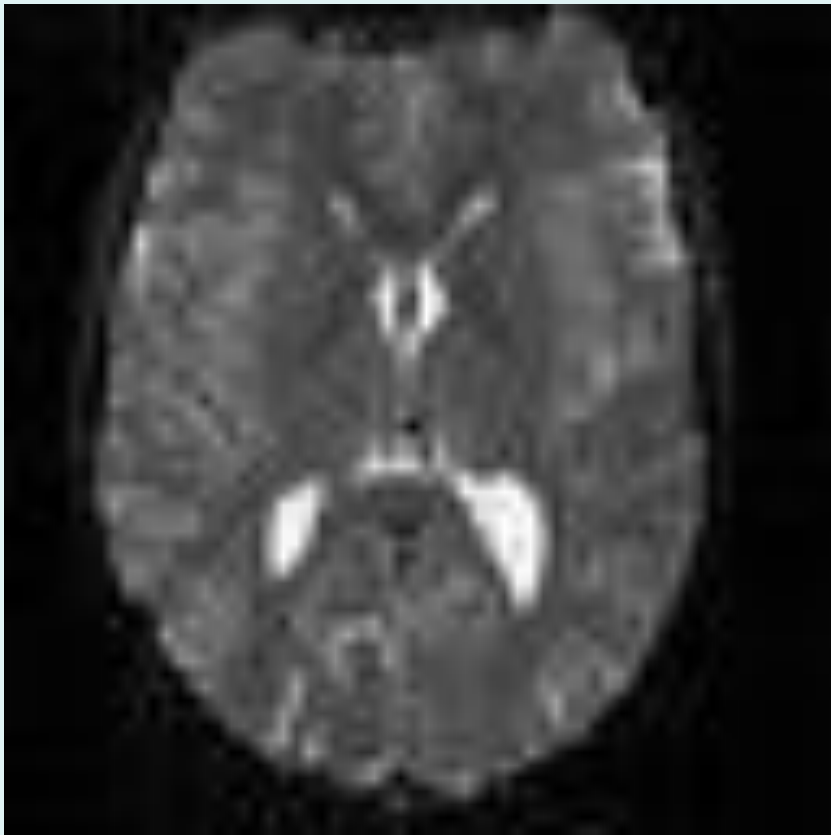
- Population, i.e. noise & inter-subject variability
- Expected activation size



Smoothing, kernel size

Decide *a priori*, based on:

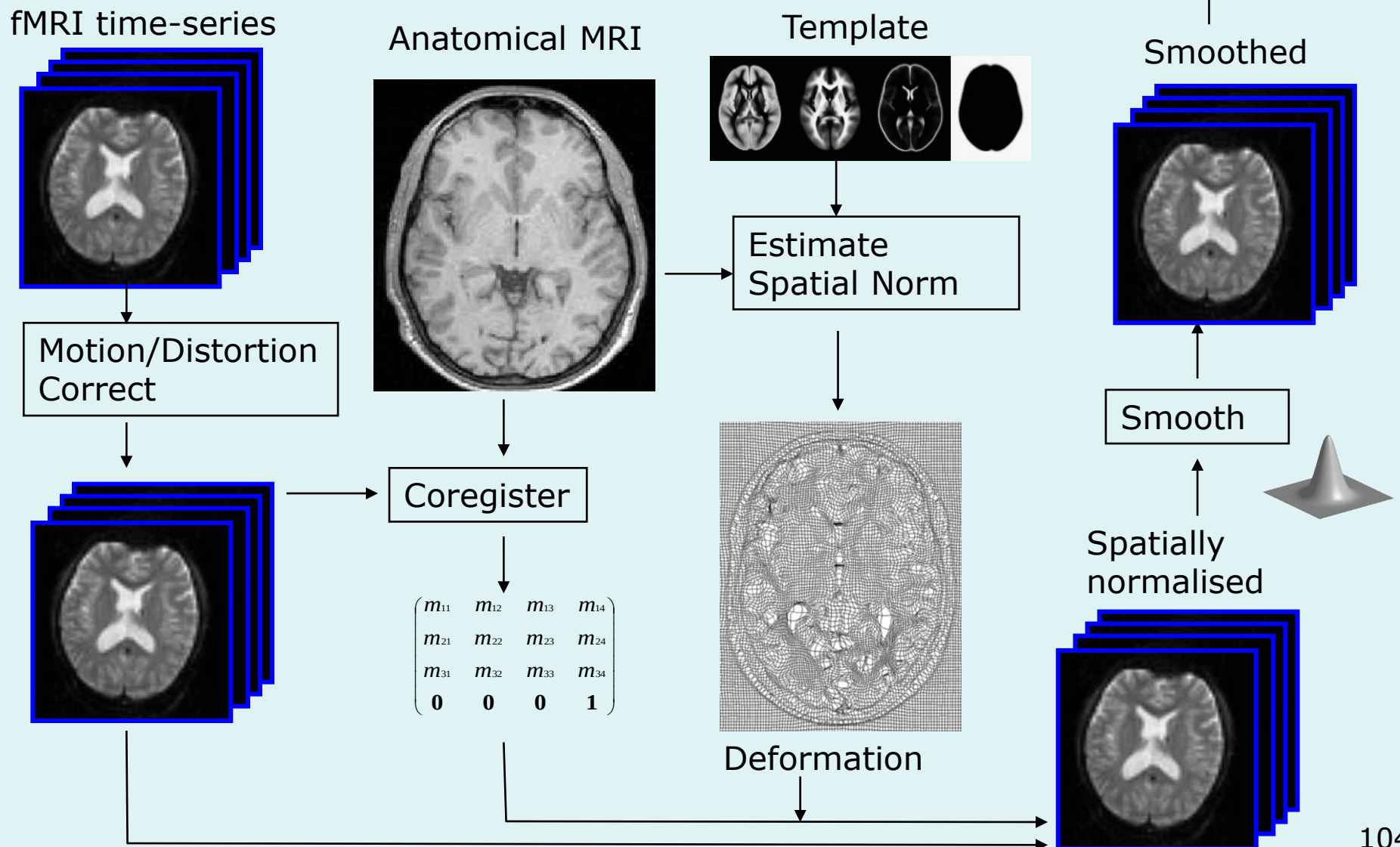
- Population, i.e. noise & inter-subject variability
- Expected activation size



Content

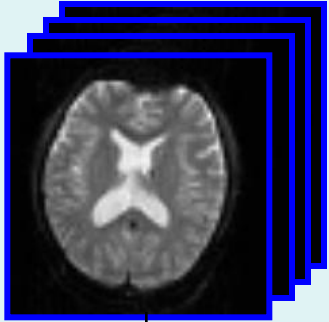
- Preliminaries
- Within-subject
- Between-subject
- Smoothing
- Conclusion

Pre-processing overview

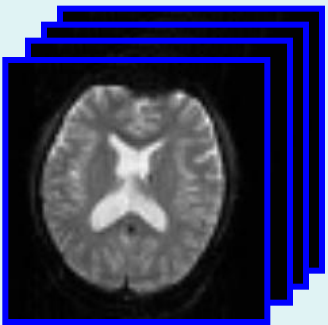


Alternative pipeline

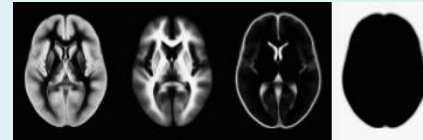
fMRI time-series



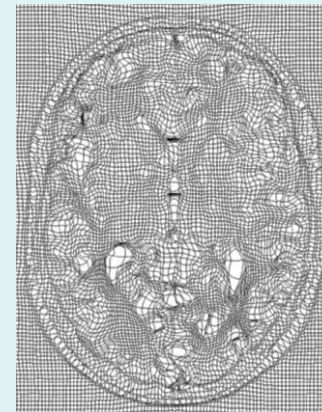
Motion/Distortion
Correct



Template



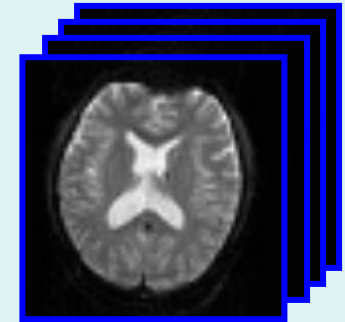
Estimate
Spatial Norm



Deformation

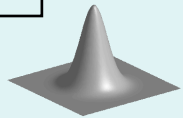
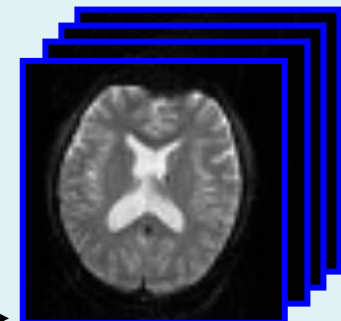
Statistics or
whatever

Smoothed



Smooth

Spatially
normalised



References

- Friston et al. Spatial registration and normalisation of images. Human Brain Mapping 3:165-189 (1995).
- Collignon et al. Automated multi-modality image registration based on information theory. IPMI'95 pp 263-274 (1995).
- Thévenaz et al. Interpolation revisited. IEEE Trans. Med. Imaging 19:739-758 (2000).
- Andersson et al. Modeling geometric deformations in EPI time series. Neuroimage 13:903-919 (2001).
- Hutton et al. Image distortion correction in fMRI: a quantitative evaluation. NeuroImage 16:217-240 (2002).
- Ashburner & Friston. Unified Segmentation. NeuroImage 26:839-851 (2005).

