

Introduction à la statistique médicale

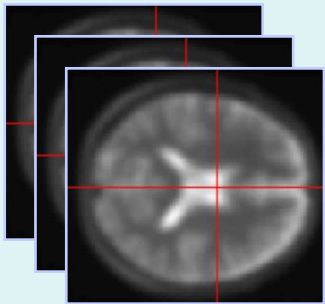
Statistical Parametric Mapping short course

Course 1: spatial pre-processing

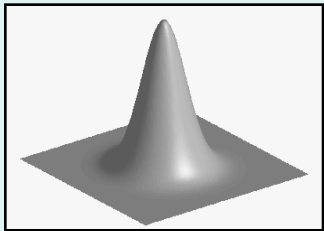
Christophe Phillips, Ir PhD
GIGA – CRC *In Vivo* Imaging &
GIGA – *In Silico* Medicine

SPM work flow

Image time-series



Spatial filter

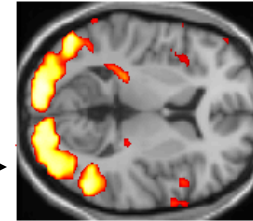
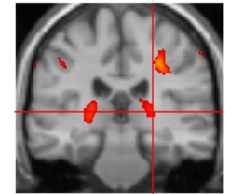
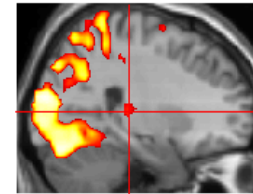


Realignment

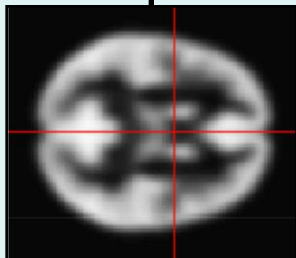
Smoothing

General Linear Model

Statistical Parametric Map

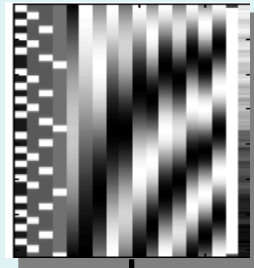


Normalisation

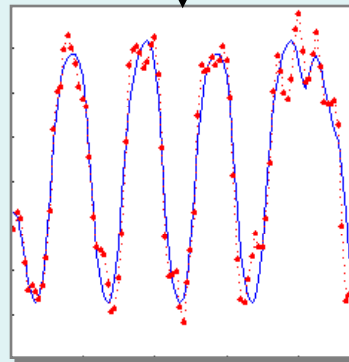


Anatomical reference

Design matrix

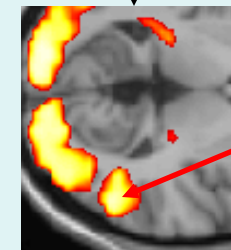


Parameter estimates



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 “preprocessing” 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
 - 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...

Intensity based techniques

By minimizing a « **distance** » between the whole *source* image and the whole *reference* image:

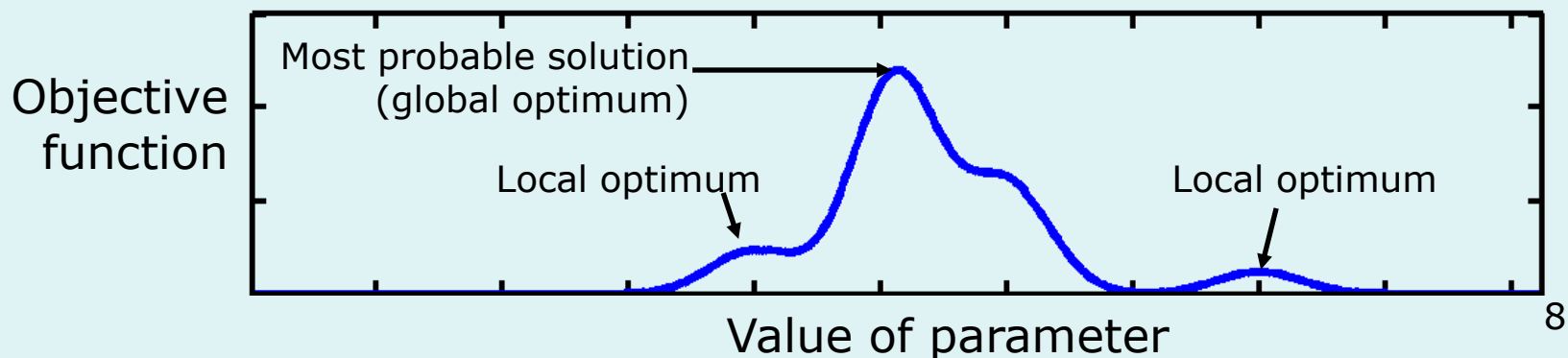
- Need a scalar measure to optimize
- Susceptible to poor starting estimates

➔ Hybrid approaches :

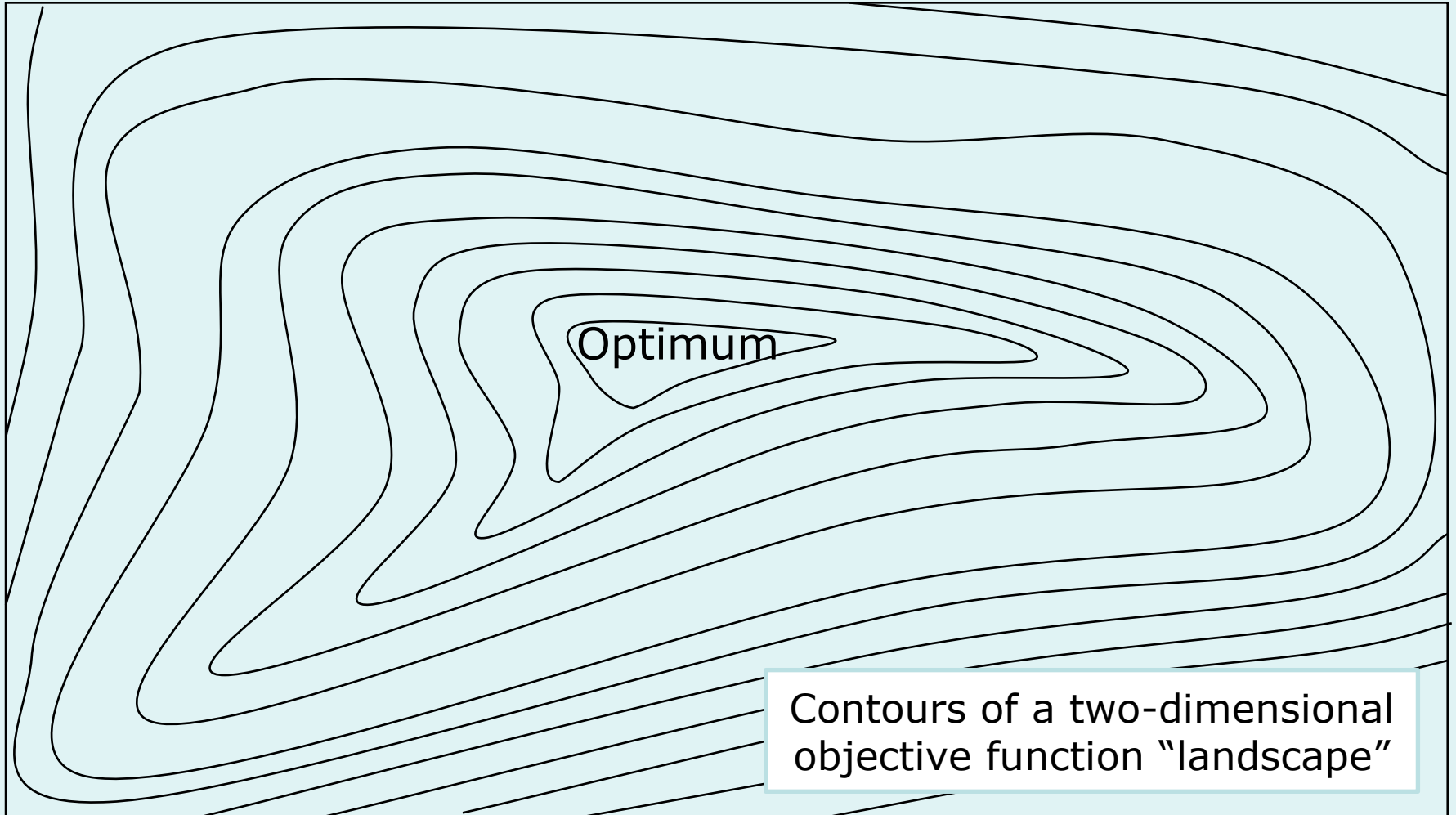
label/manual + intensity based methods

Optimisation

- Image registration is done by **optimisation**.
- Optimisation involves finding some “best” parameters according to an “objective function”, which is either minimised or maximised
- The “objective function” is often related to a probability based on some model



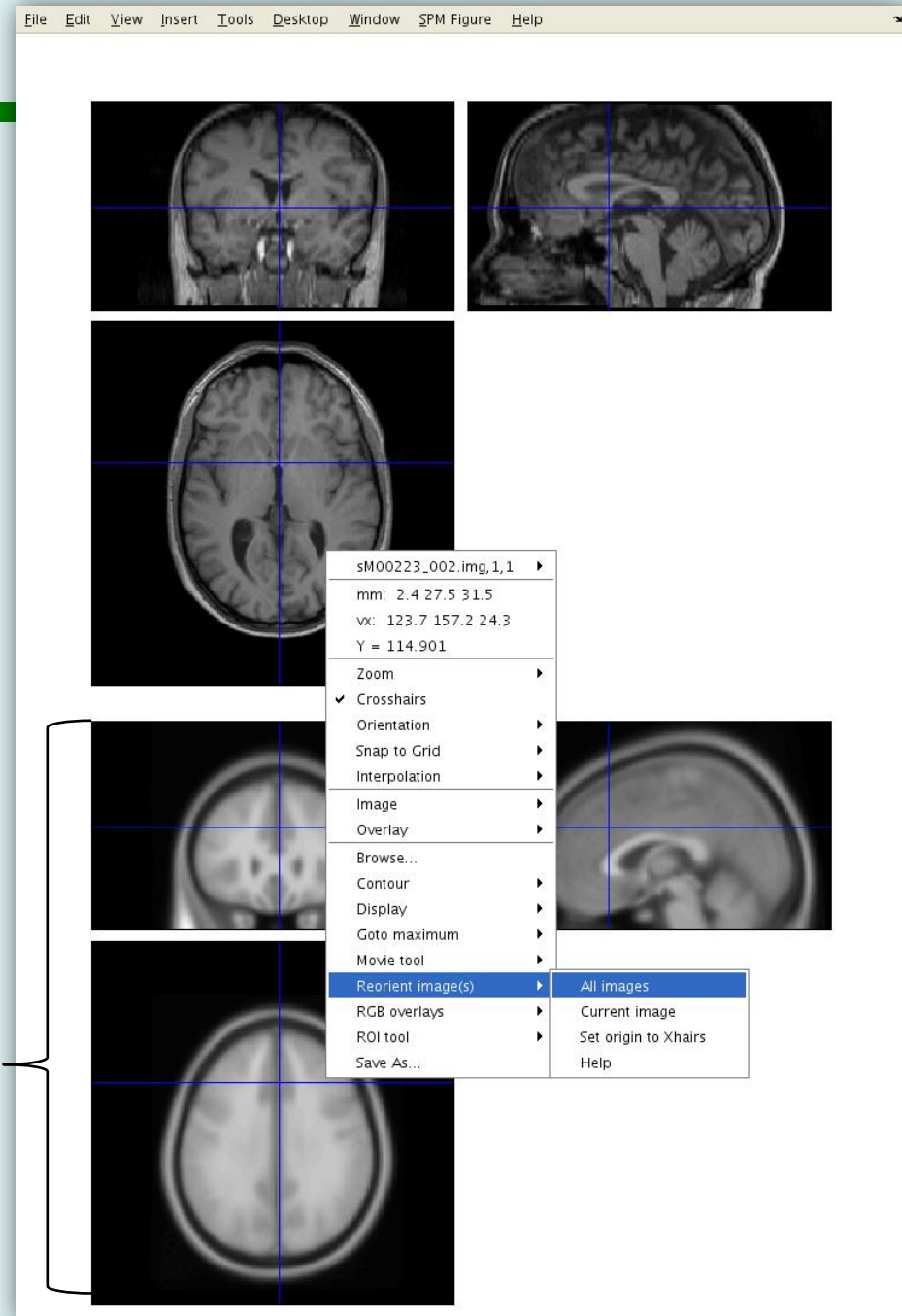
Optimisation, multiple parameters



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.



Rigid-body transformations

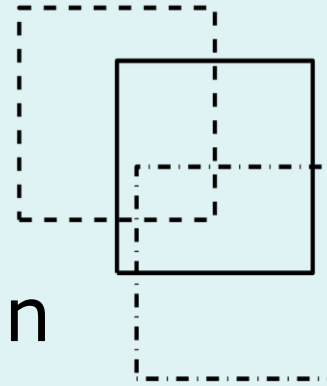
- Assume that brain of the same subject doesn't change shape or size in the scanner.
 - Head can move, but remains the same shape and size.
 - Some exceptions:
 - Image distortions.
 - Brain slops about slightly because of gravity.
 - Brain growth or atrophy over time.
- If the subject's head moves,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

2D Affine Transforms

- Translations by t_x and t_y

$$x_1 = x_0 + t_x$$

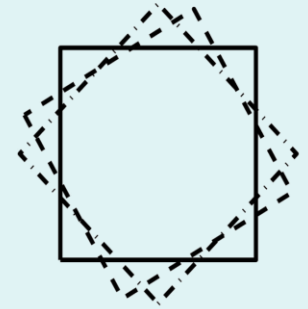
$$y_1 = y_0 + t_y$$



- Rotation around the origin by Θ radians

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

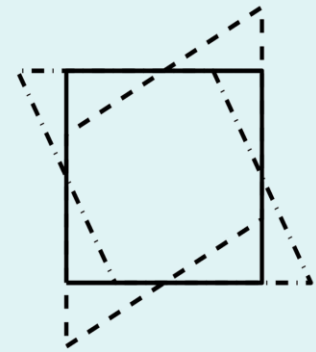
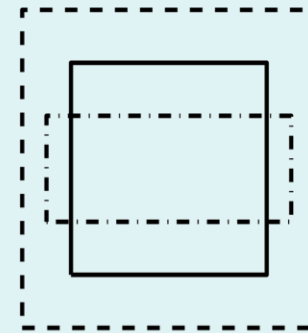
$$y_1 = -\sin(\Theta) x_0 + \cos(\Theta) y_0$$



- 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 :

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

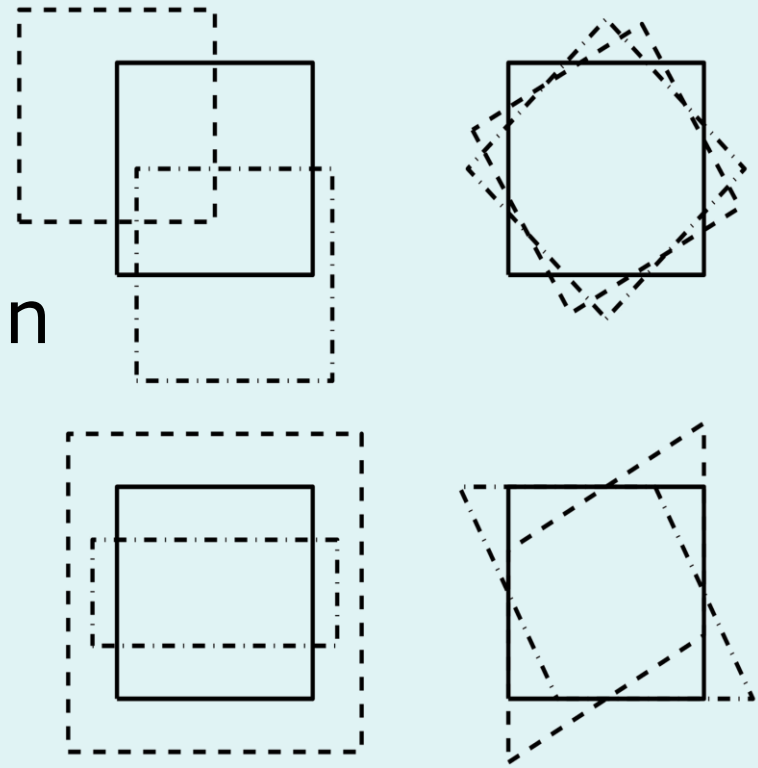
$$y_1 = 0 x_0 + s_y y_0 + 0$$

- Shear h_x

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

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

Same for h_y



2D Affine transform

- Rigid-body transformations are a subset of “affine transformation”
- Parallel lines remain parallel
- 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:

$$\mathbf{y} = \mathbf{M} \mathbf{x}$$

$$\begin{bmatrix} x_1 \\ y_1 \\ 1 \end{bmatrix} = \begin{bmatrix} m_{11} & m_{12} & m_{13} \\ m_{21} & m_{22} & m_{23} \\ 0 & 0 & 1 \end{bmatrix} \times \begin{bmatrix} x_0 \\ y_0 \\ 1 \end{bmatrix}$$

3D Affine transform

- Rigid-body transformations are a subset of “affine transformation”
- Parallel lines remain parallel
- 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:

$$\mathbf{y} = \mathbf{M} \mathbf{x}$$

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

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
- The order of the operations matters

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

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

Voxel-to-world transformation

“Voxel-to-world transforms” =

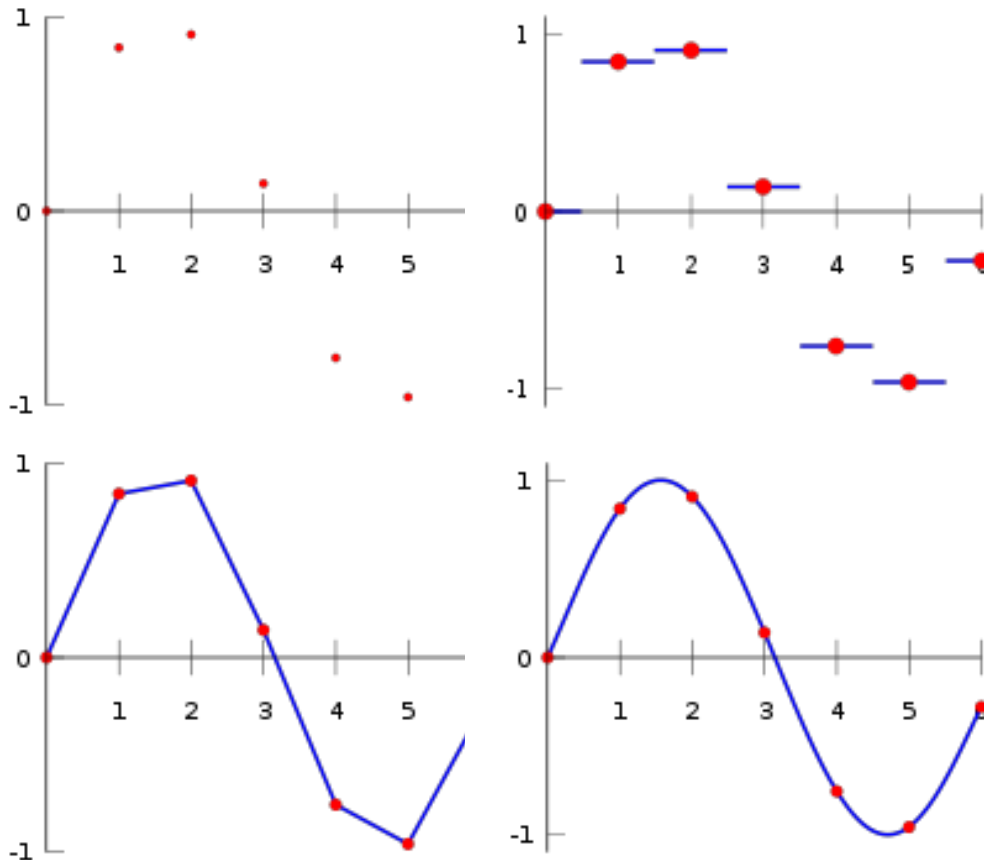
Affine transform **M** associated with each image such that

- Maps from voxels ($\mathbf{x}=[1\dots N_x]$, $\mathbf{y}=[1\dots N_y]$, $\mathbf{z}=[1\dots N_z]$) to some world co-ordinate system. e.g.,
 - Scanner co-ordinates - images from DICOM toolbox
 - T&T/MNI coordinates - spatially normalised
- 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

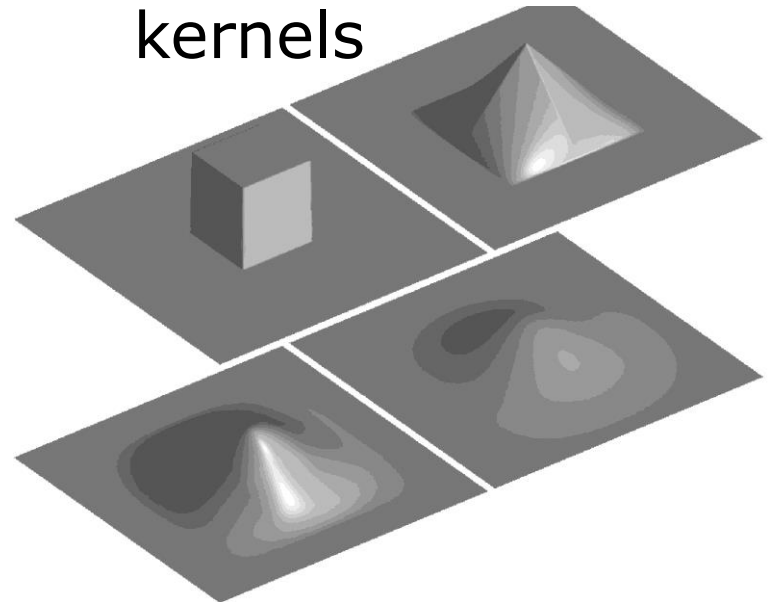
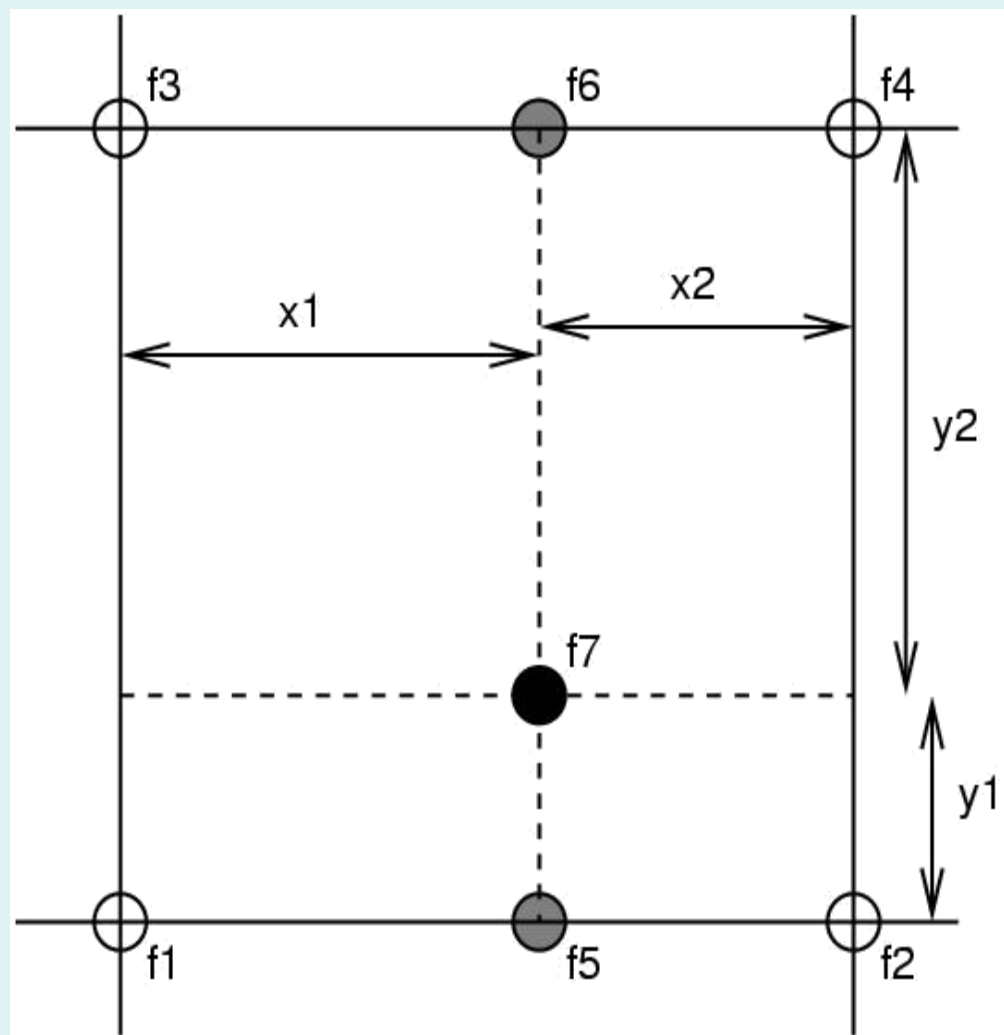
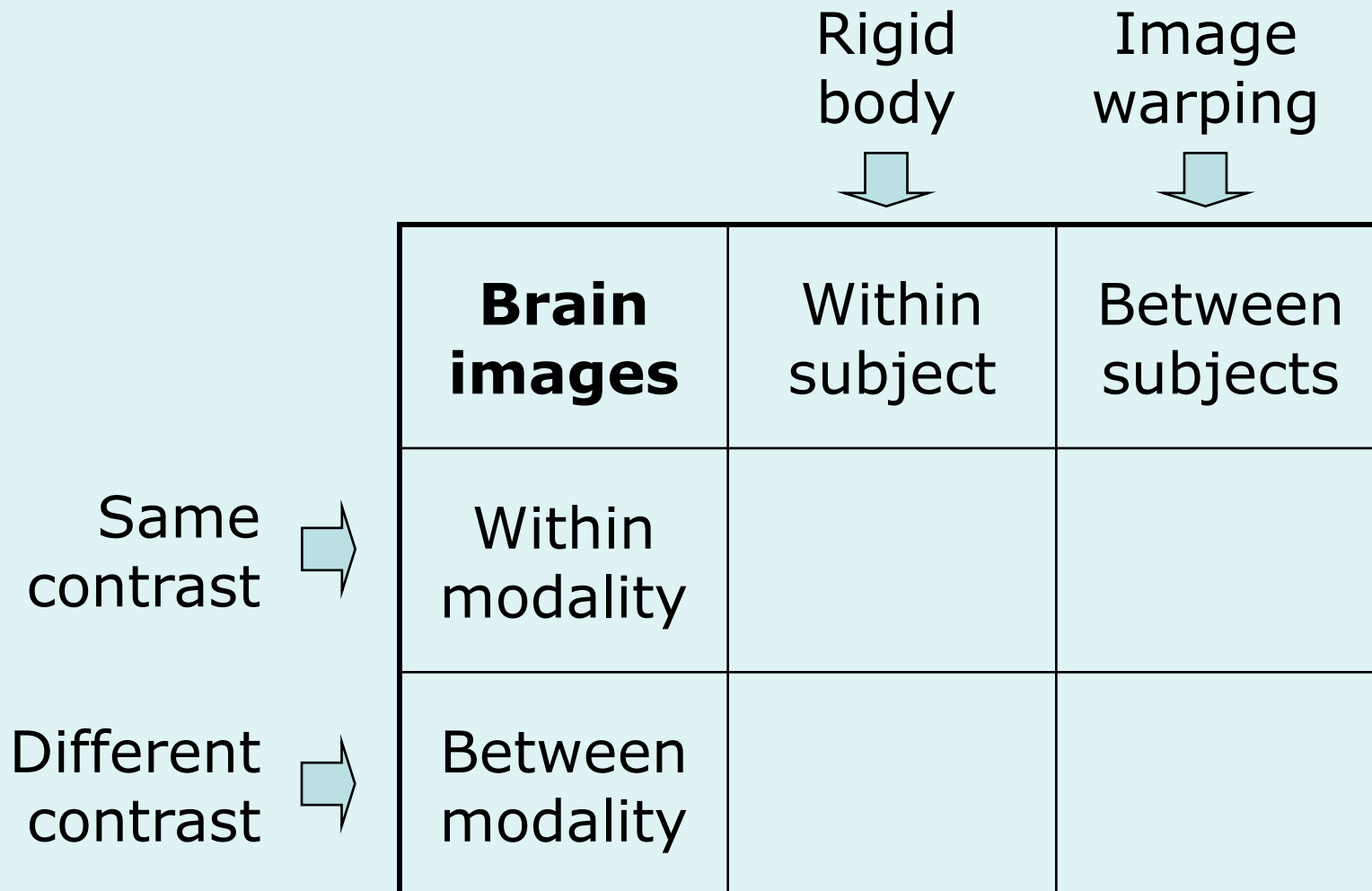


Image resampling

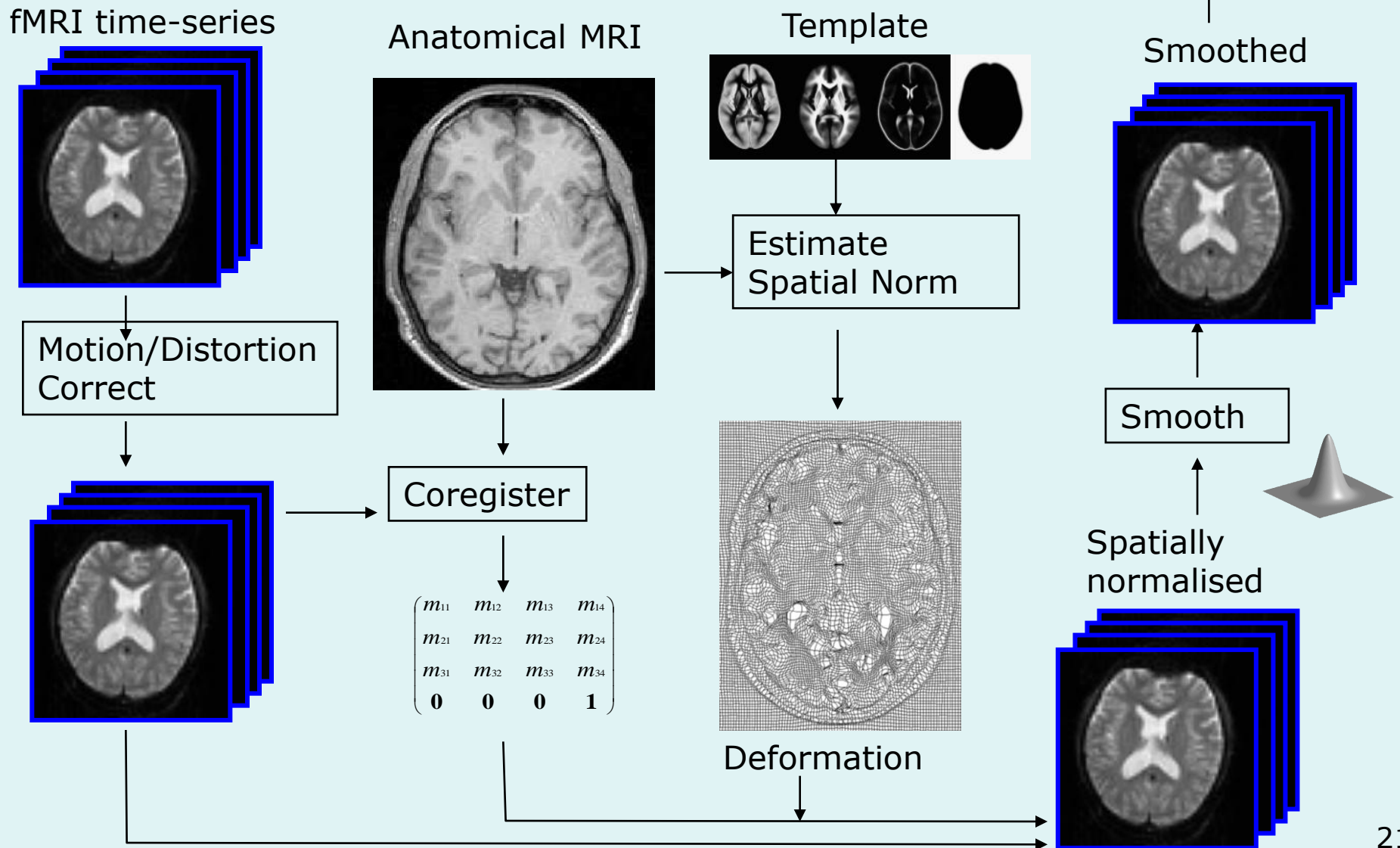
- Nearest neighbour
 - Take the value of the closest voxel
- Tri-linear
 - Just a weighted average of the neighbouring voxels
 - $f_5 = f_1 x_2 + f_2 x_1$
 - $f_6 = f_3 x_2 + f_4 x_1$
 - $f_7 = f_5 y_2 + f_6 y_1$



Various problems



Pre-processing overview



Content

- **Preliminaries**

- **Within-subject**

- **Realignment**

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

- **EPI Distortion correction**

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

- **Coregistration**

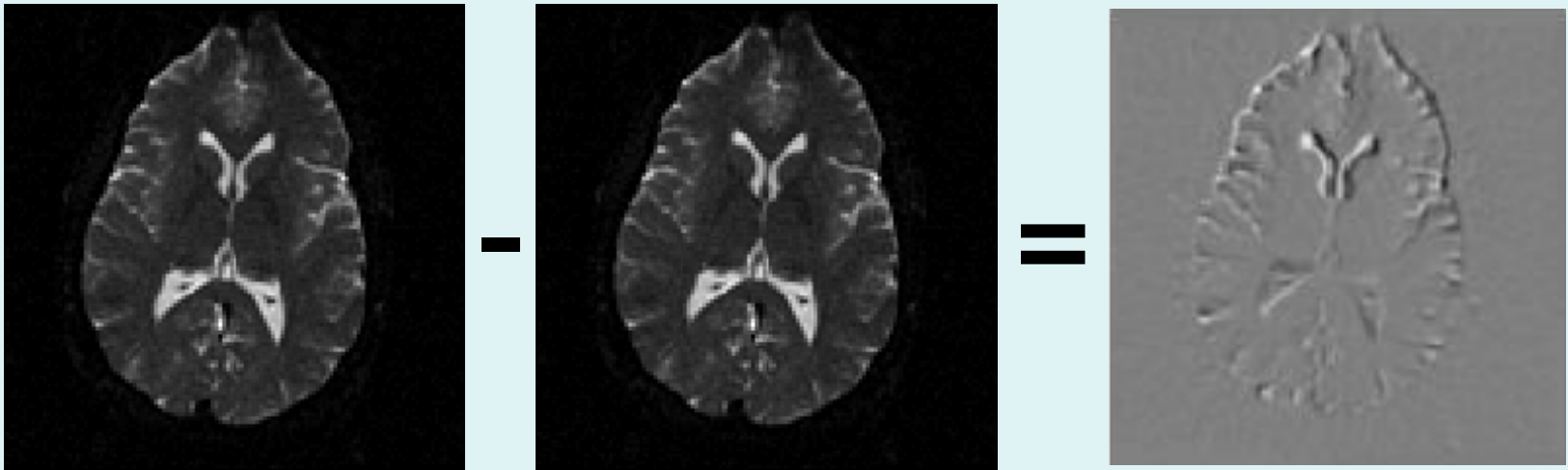
- **Maximising mutual information**

- **Between-subject**

- **Smoothing**

- **Conclusion**

Mean-squared difference



- Minimising mean-squared difference works for intra-modal registration (realignment)

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

- Simple relationship between intensities in one image, versus those in the other
 - Assumes normally distributed differences

Within-subject registration

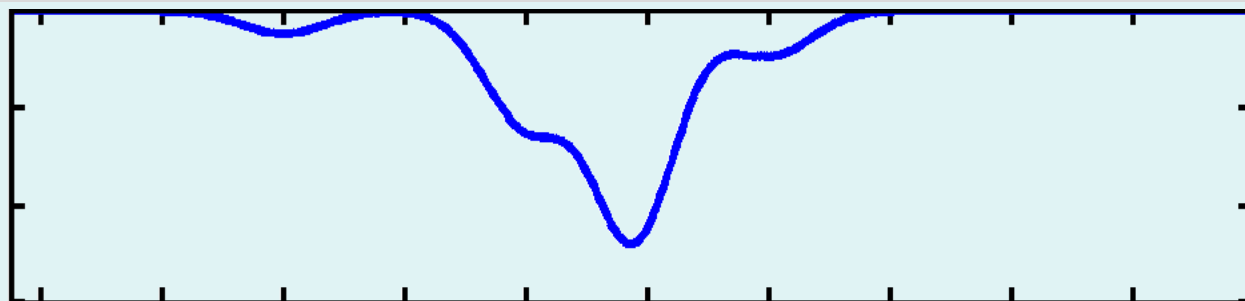
- Realign images I (fixed) and J (moving):
- Criteria to optimize:

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

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

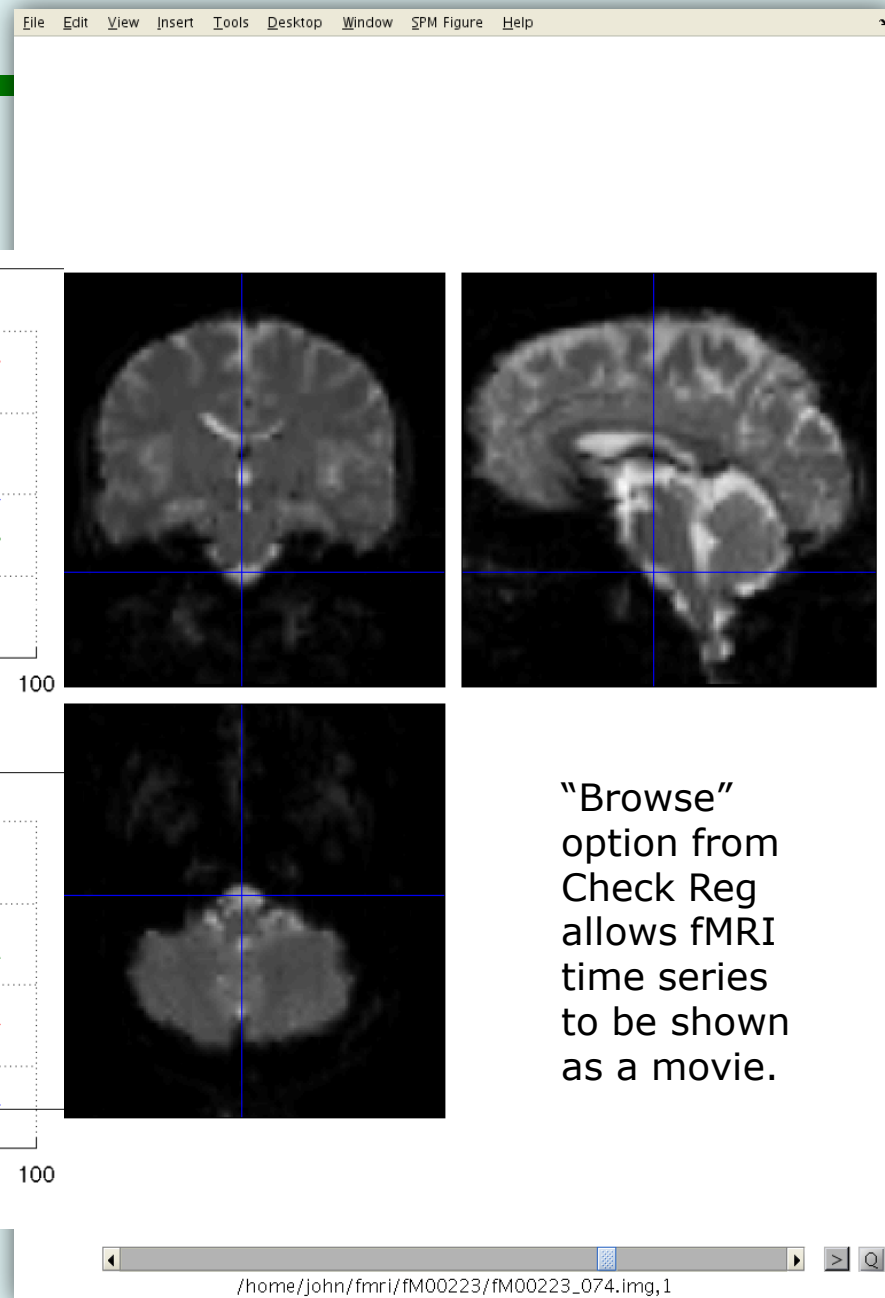
$$R = \begin{pmatrix} 1 & 0 & 0 & X_{\text{trans}} \\ 0 & 1 & 0 & Y_{\text{trans}} \\ 0 & 0 & 1 & Z_{\text{trans}} \\ 0 & 0 & 0 & 1 \end{pmatrix} \times \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & \cos f & \sin f & 0 \\ 0 & -\sin f & \cos f & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \times \begin{pmatrix} \cos q &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

Objective function

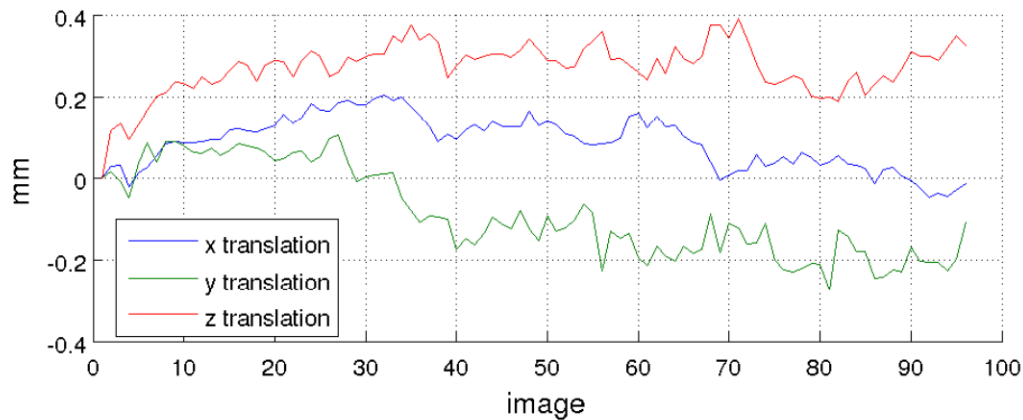


Value of parameter

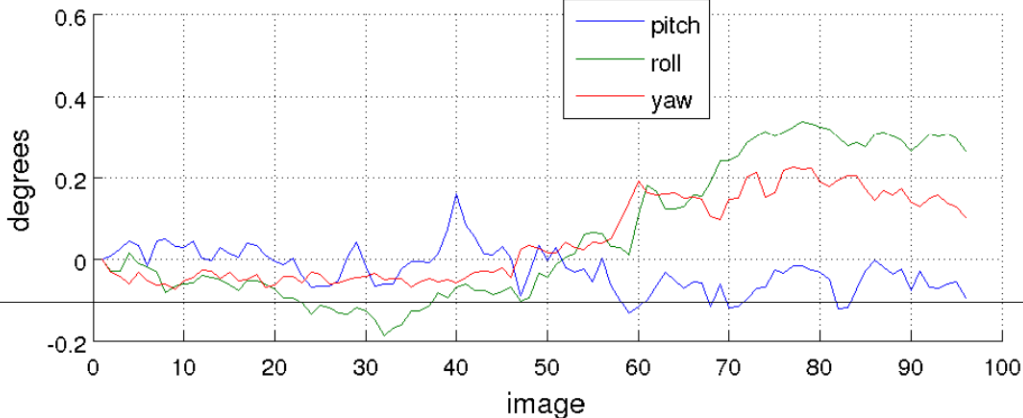
Motion estimates



translation



rotation



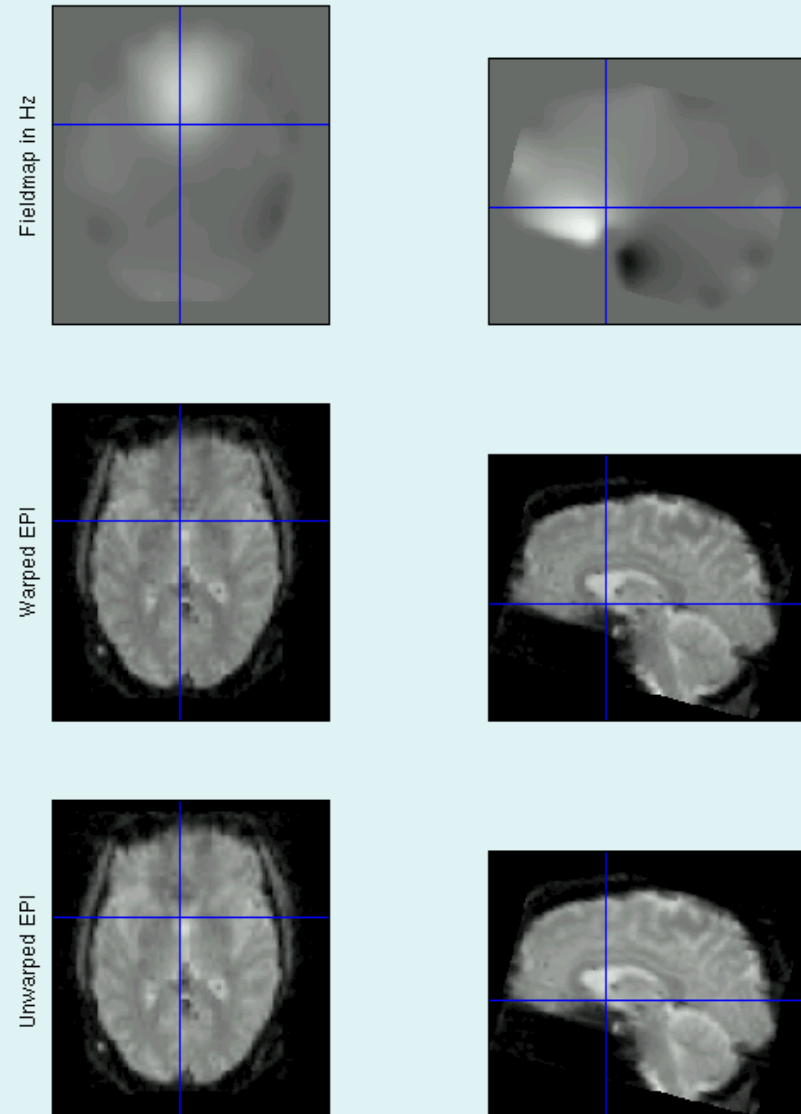
“Browse” option from Check Reg allows fMRI time series to be shown as a movie.

Residual errors from aligned fMRI

- Re-sampling can introduce interpolation errors
 - especially tri-linear interpolation
- 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

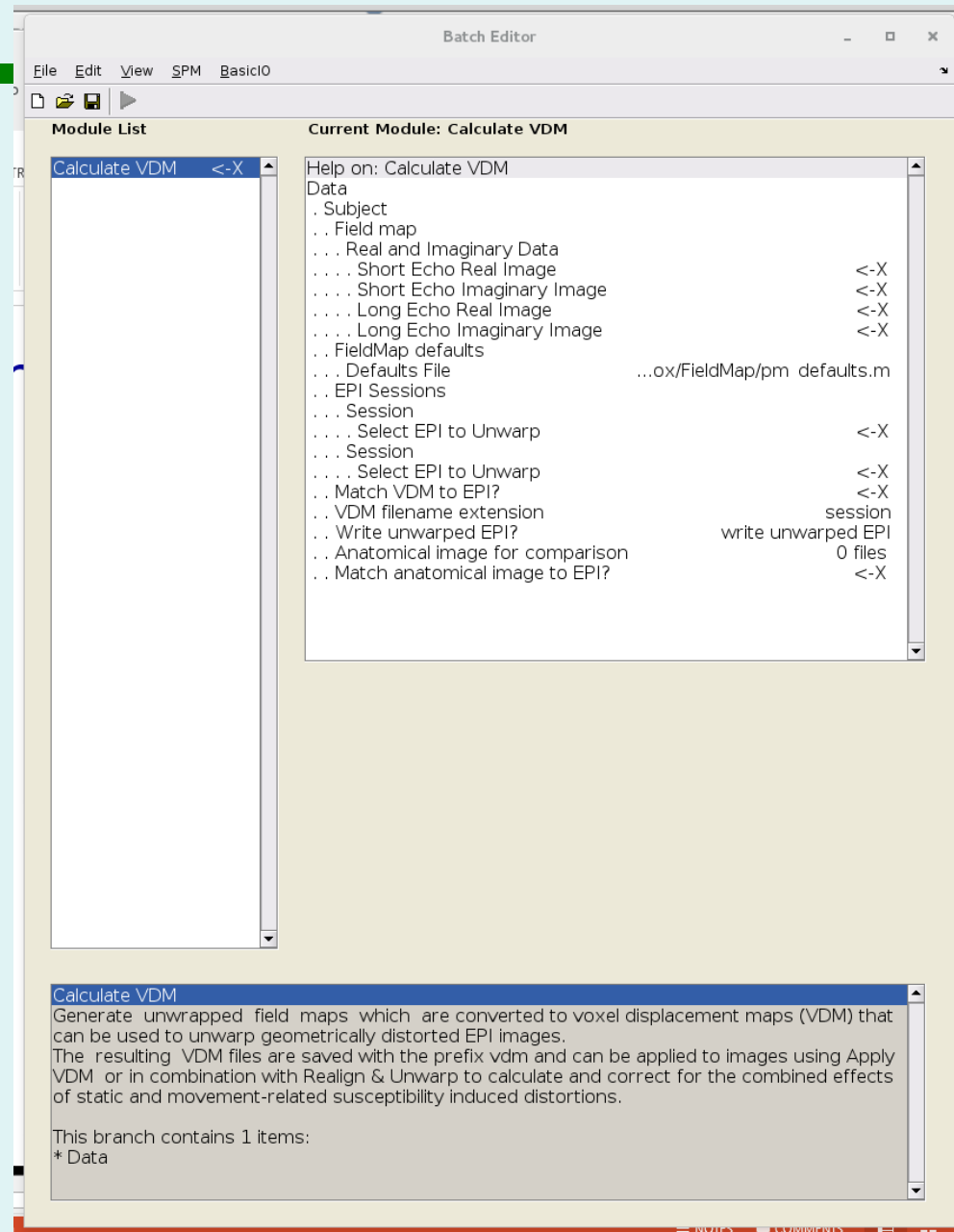
EPI distortion

- Magnetic susceptibility differs among tissues.
- Greatest difference is between air and tissue.
- Subject disrupts B0 field, rendering it inhomogeneous
- Distortions in phase-encode direction



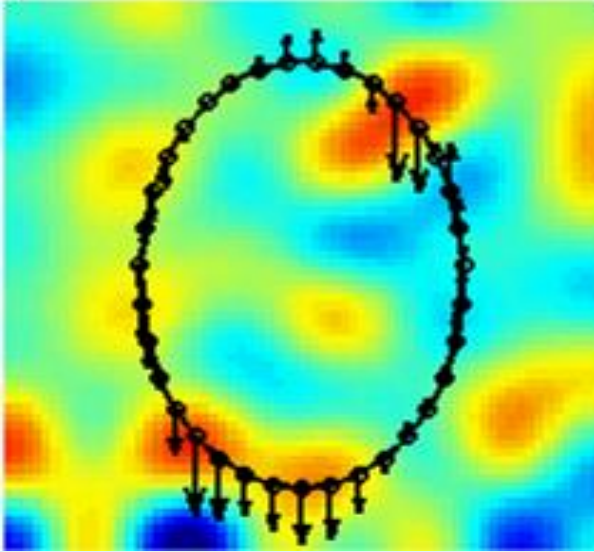
FieldMap toolbox

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

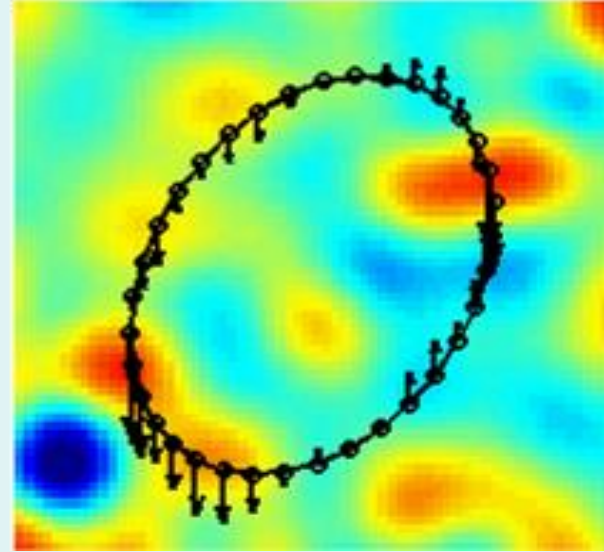


Movement-by-distortion interaction

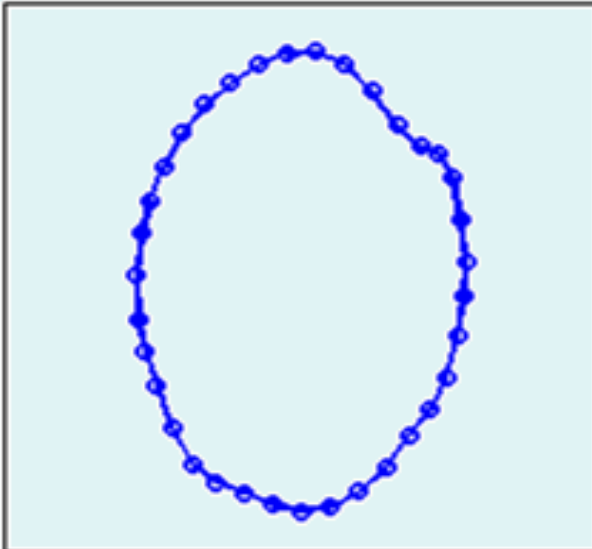
Original position



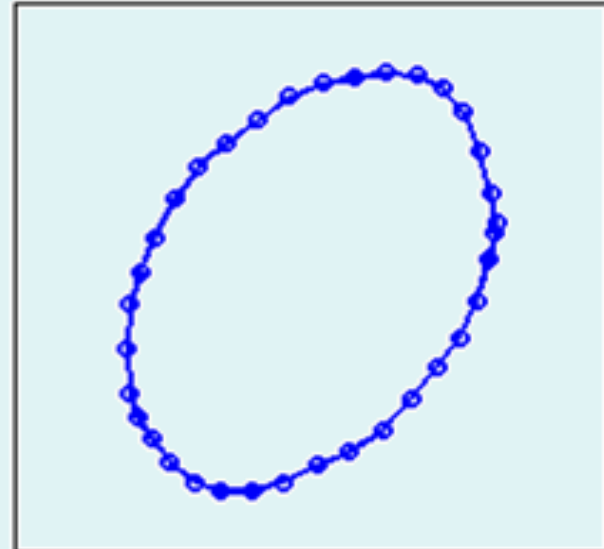
After rotation



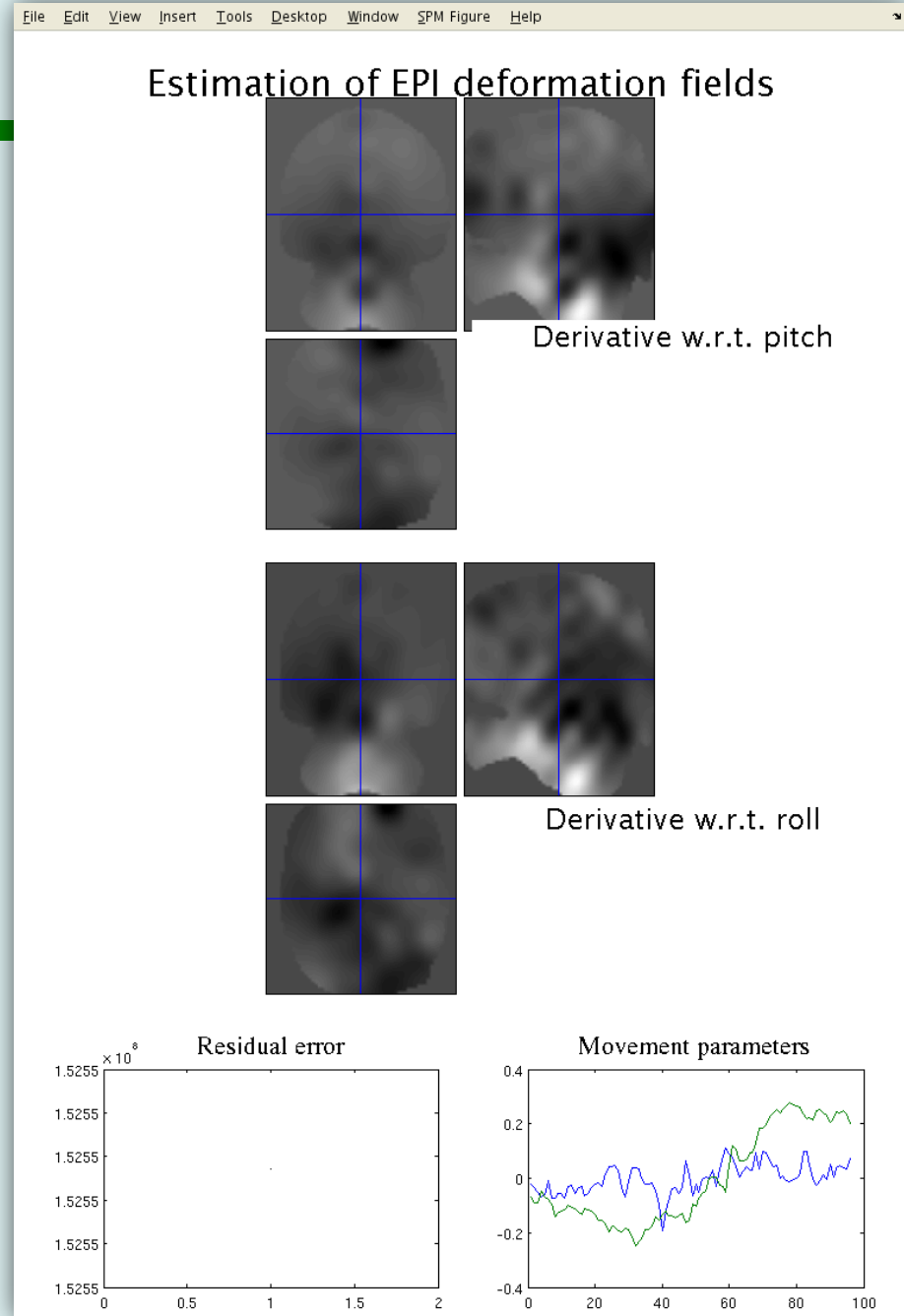
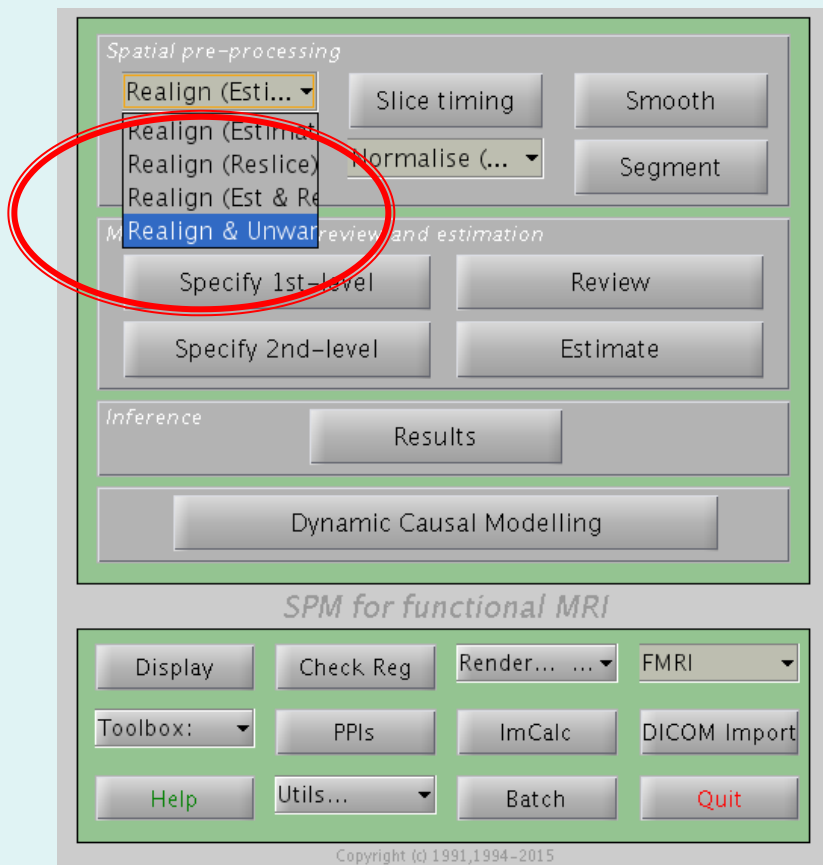
Original position



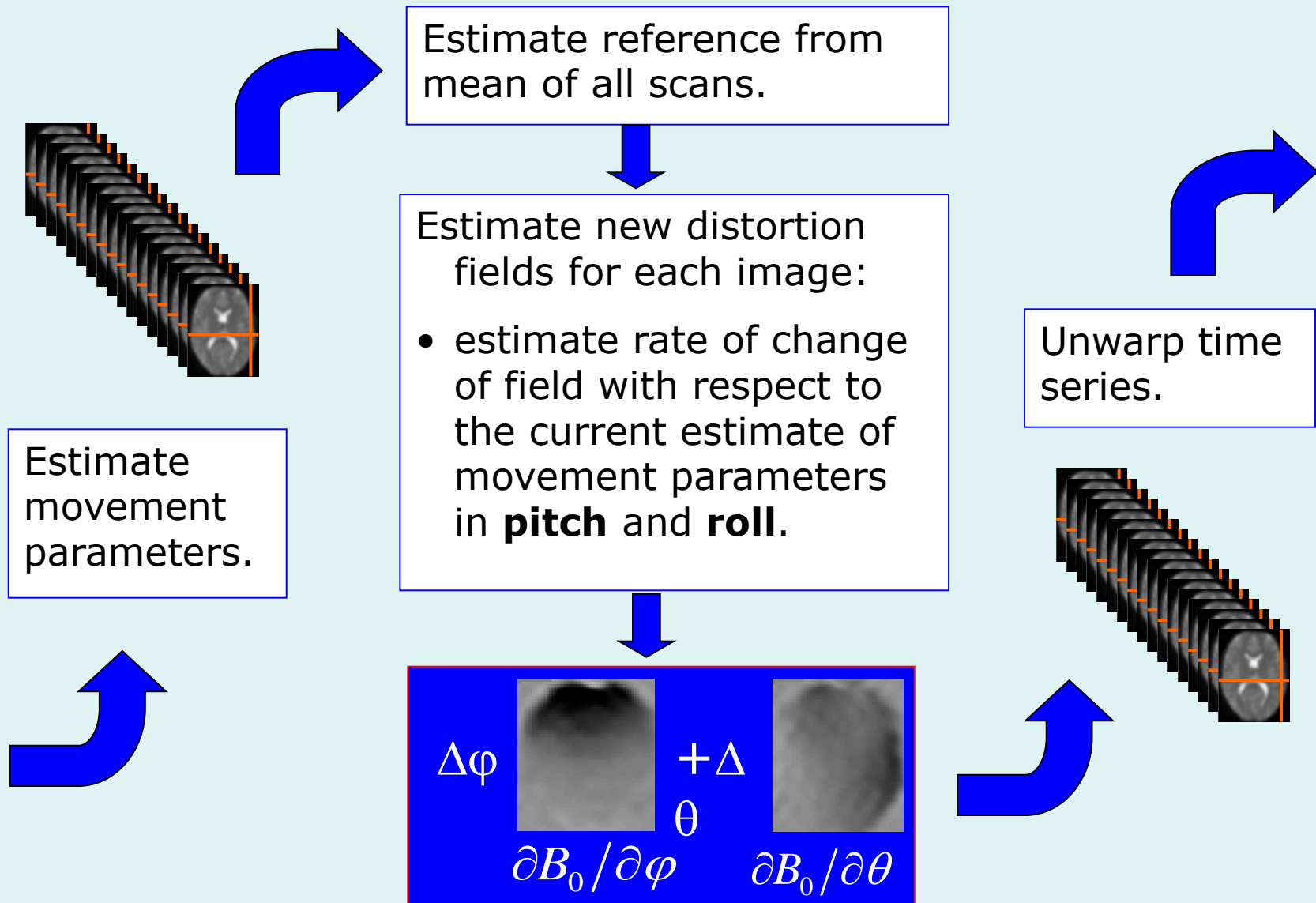
After rotation



Realign & Unwarp

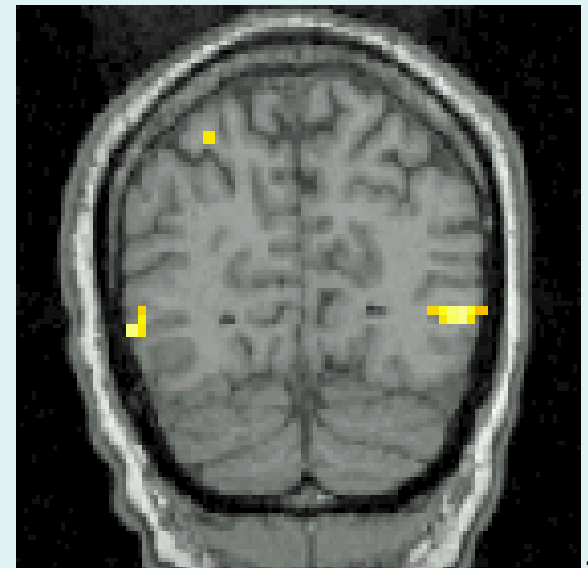
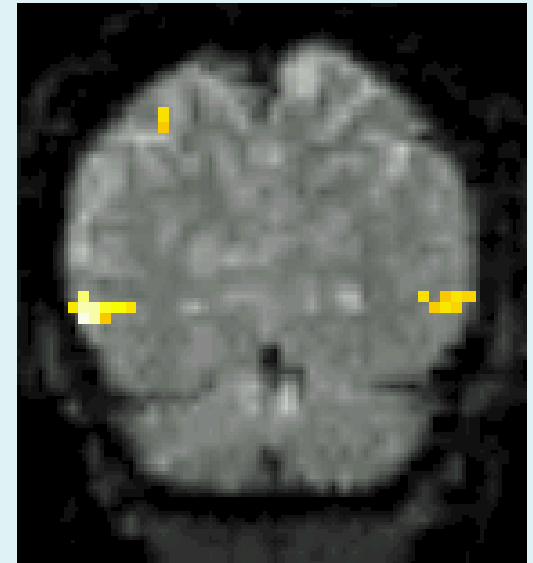


Correcting for distortion changes

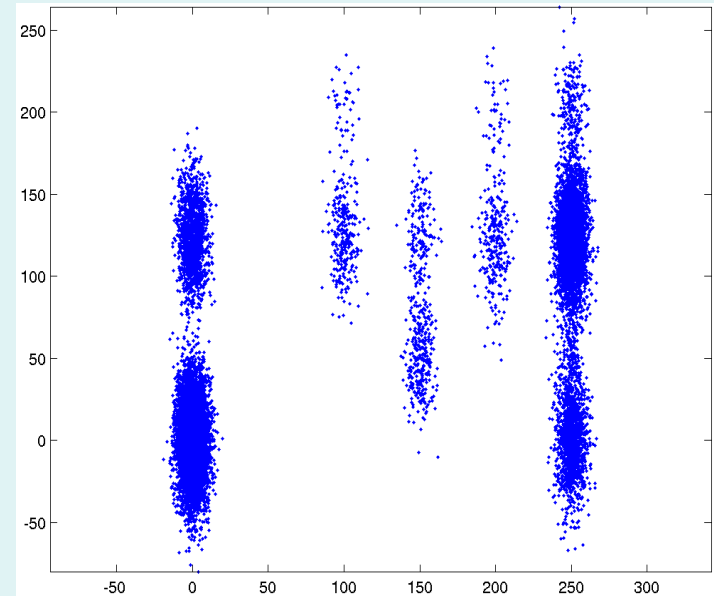
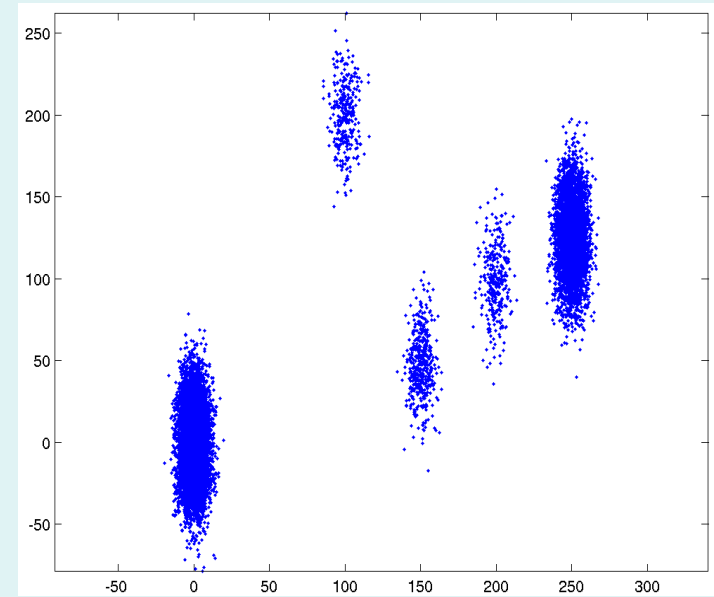
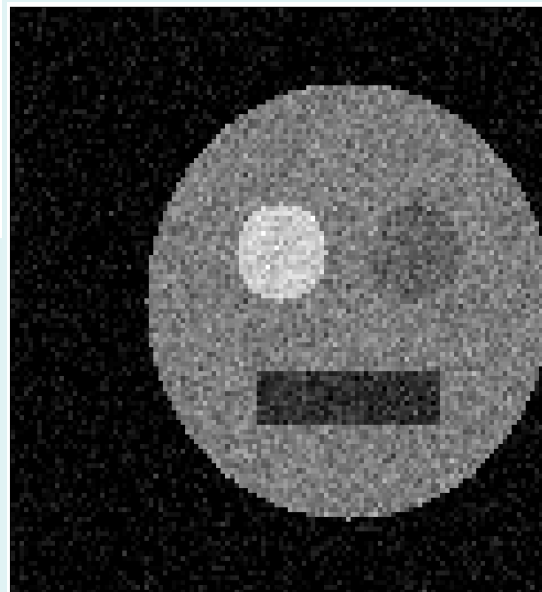
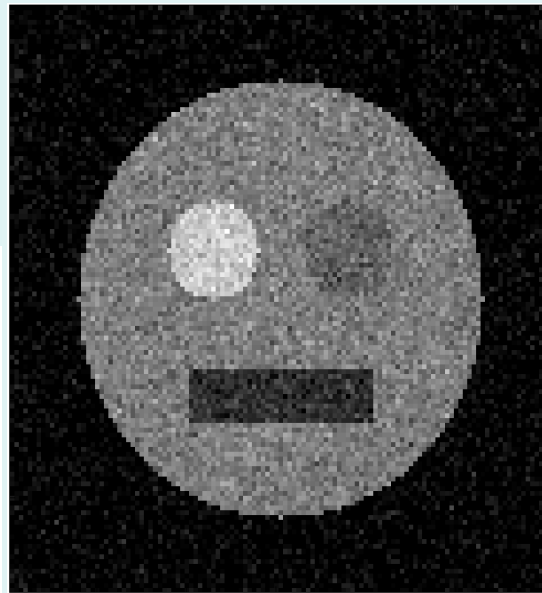
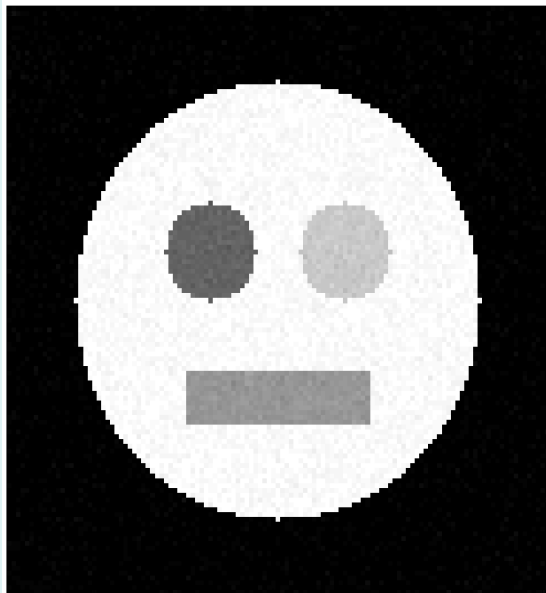


Coregistration

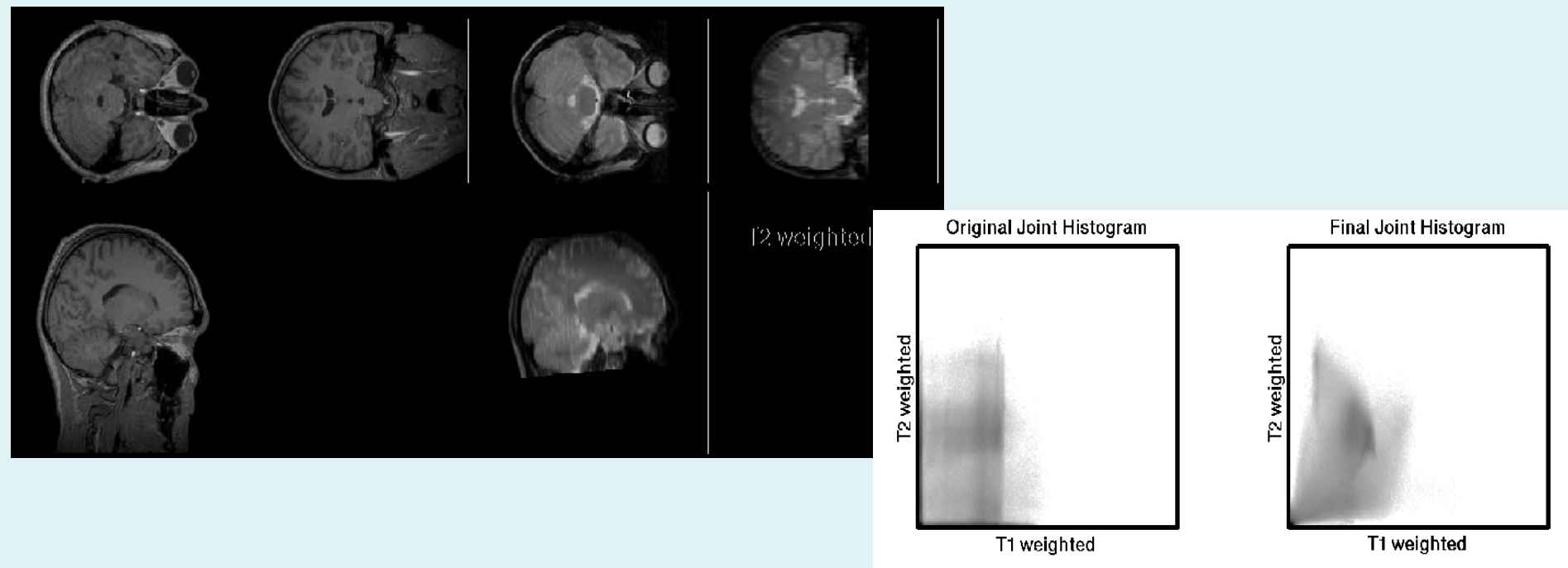
- Inter-modal registration.
- Match images from same subject but different modalities:
 - anatomical localisation of single subject activations
 - achieve more precise spatial normalisation of functional image using anatomical image.



Mutual Information, example



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 $H(a,b) = -\int_{ab} P(a,b) \log_2 P(a,b)$

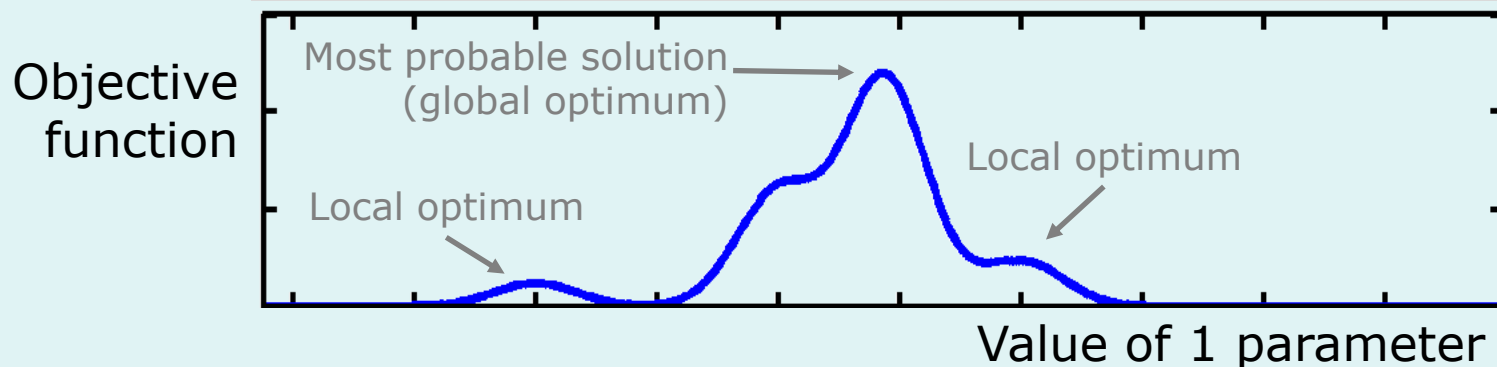
Within-subject registration

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

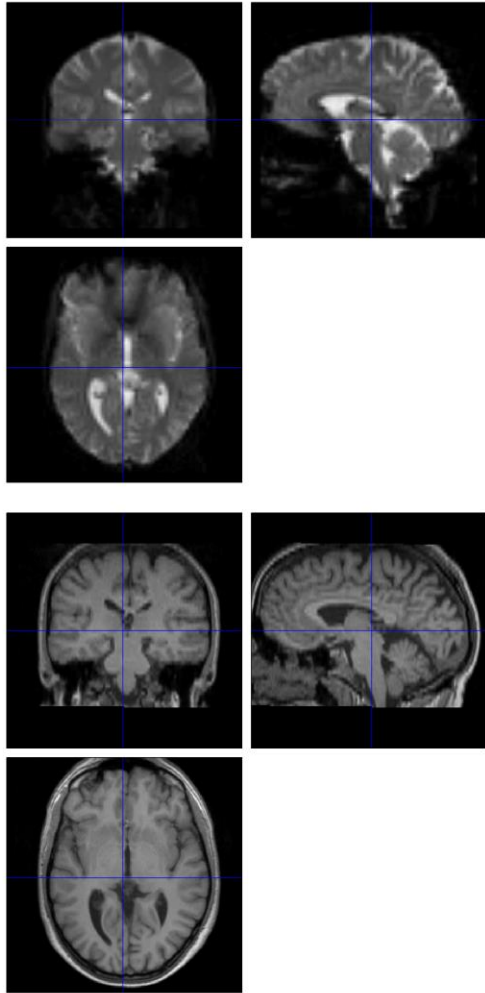
$$\rightarrow c(I, J) = MI(I, J)$$

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

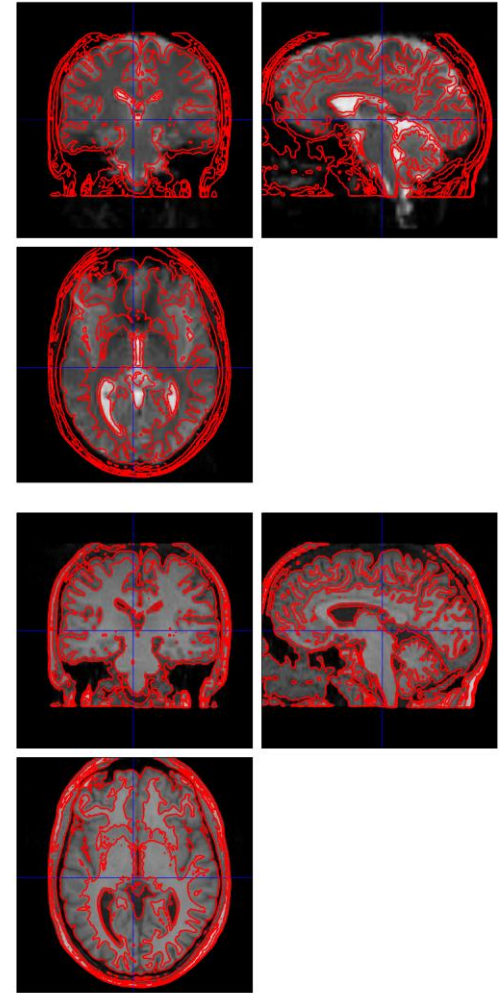
$$R = \begin{pmatrix} 1 & 0 & 0 & X_{\text{trans}} \\ 0 & 1 & 0 & Y_{\text{trans}} \\ 0 & 0 & 1 & Z_{\text{trans}} \\ 0 & 0 & 0 & 1 \end{pmatrix} \times \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & \cos f & \sin f & 0 \\ 0 & -\sin f & \cos f & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \times \begin{pmatrix} \cos q &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



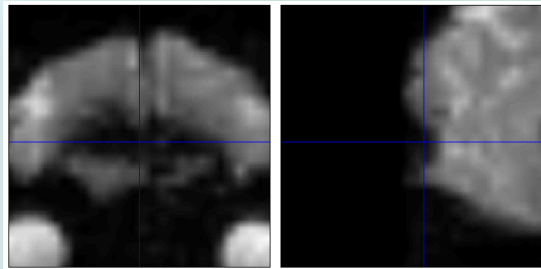
“CheckReg” to assess alignment



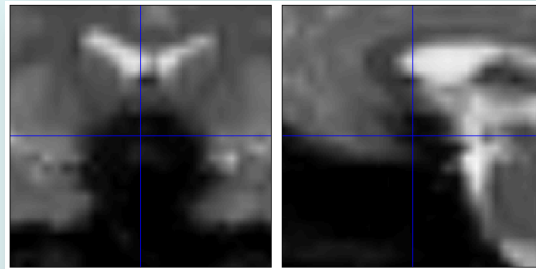
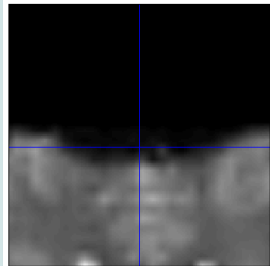
CheckReg allows contours from one image to be shown superimposed on another



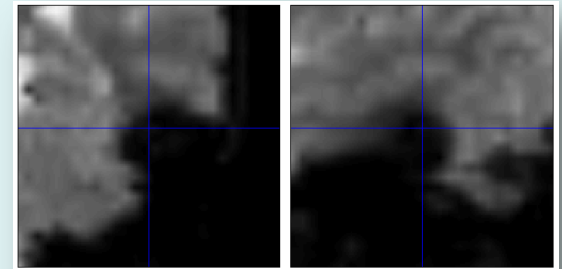
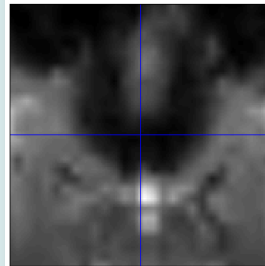
EPI dropout and distortion



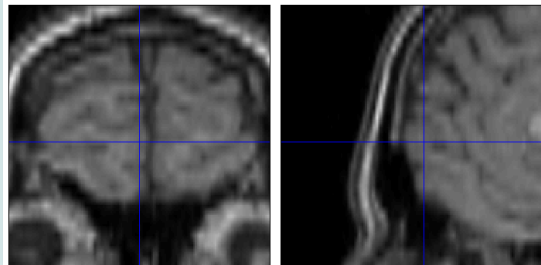
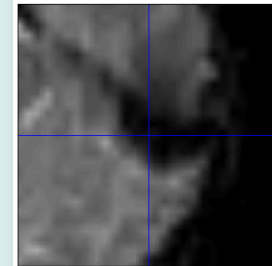
EPI



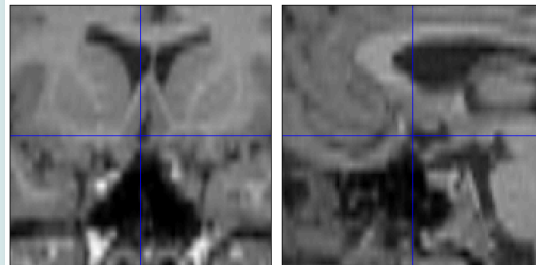
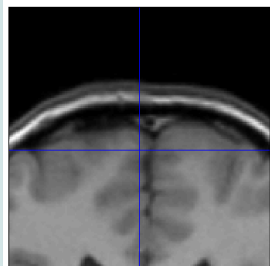
EPI



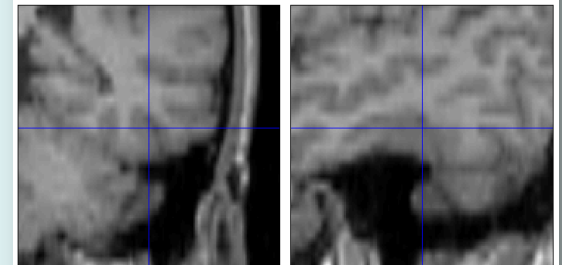
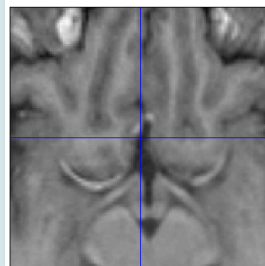
EPI



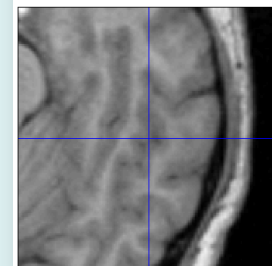
structural



structural

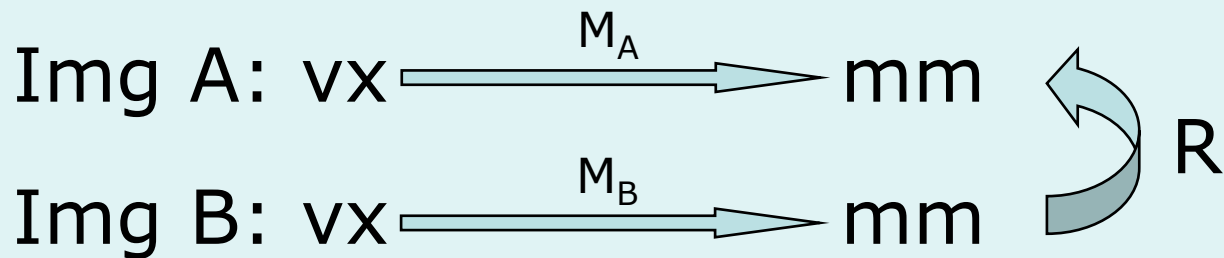


structural



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 $M_A^{-1} \Rightarrow M_B^* M_A^{-1}$

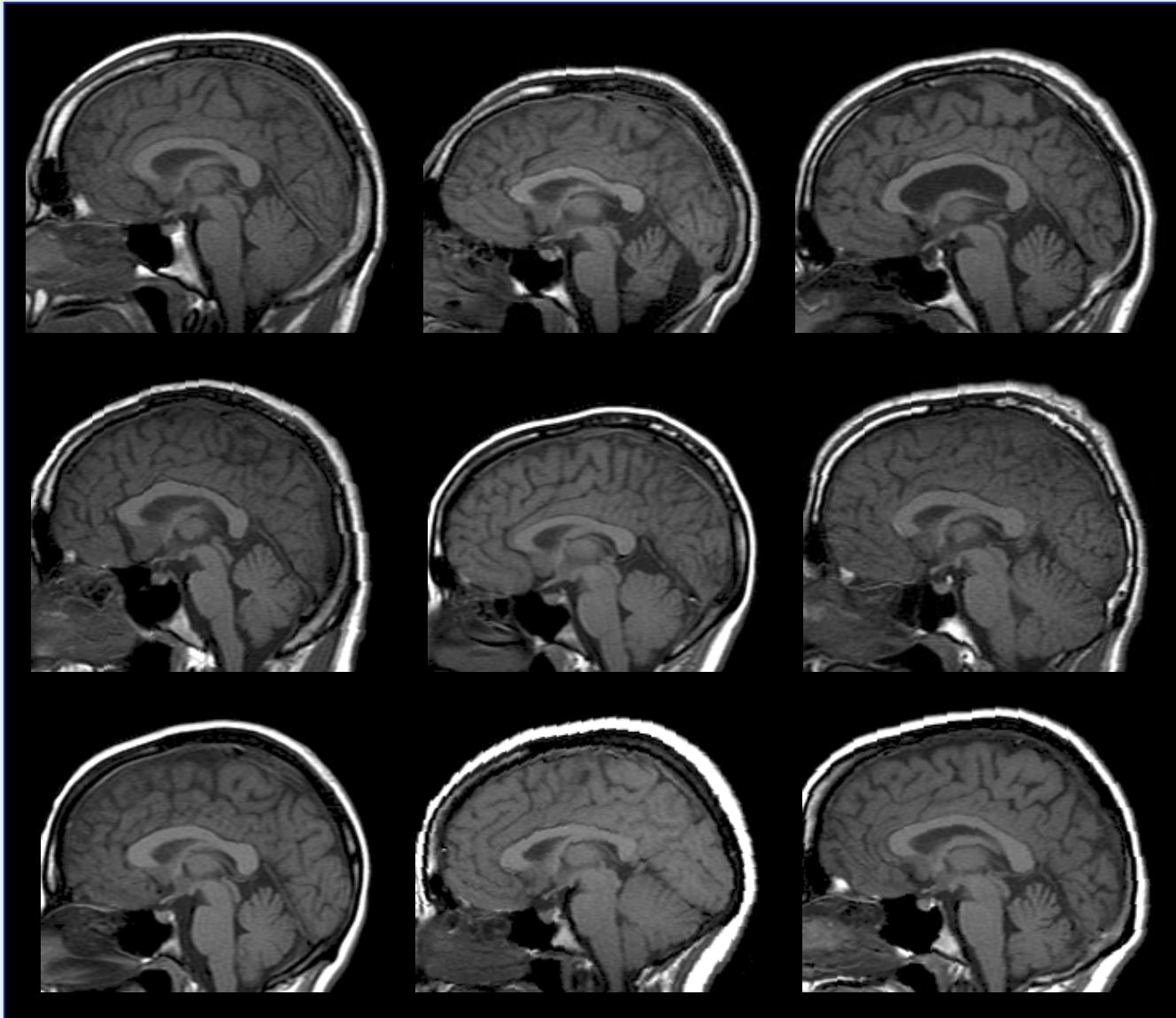
Content

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

Between subjects

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

Between subjects



Between subjects

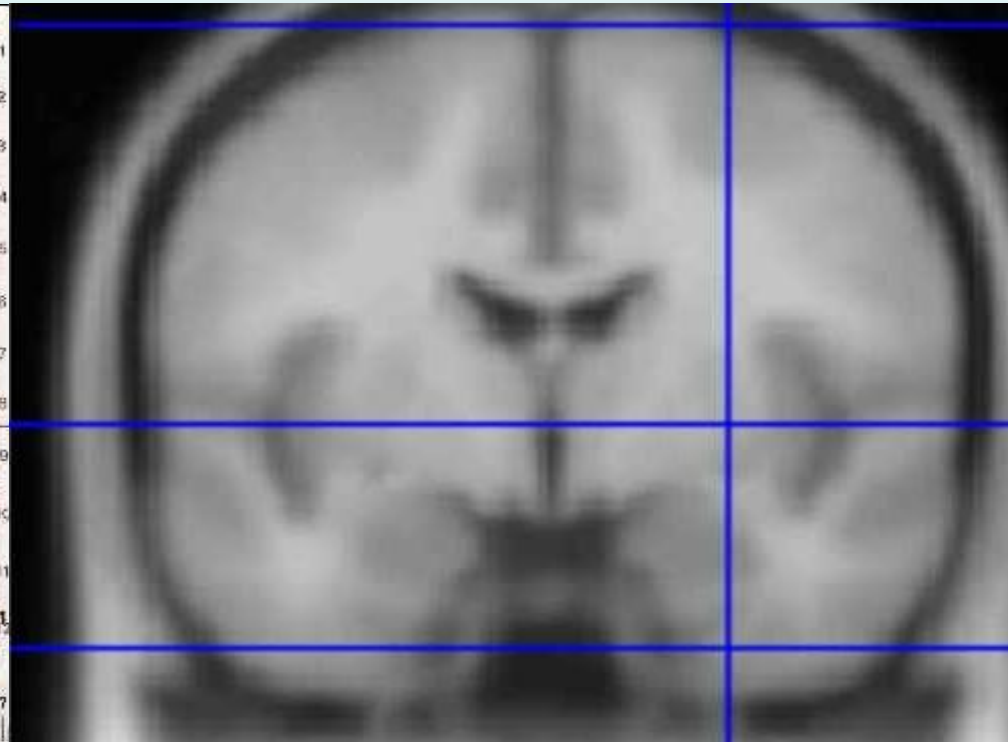
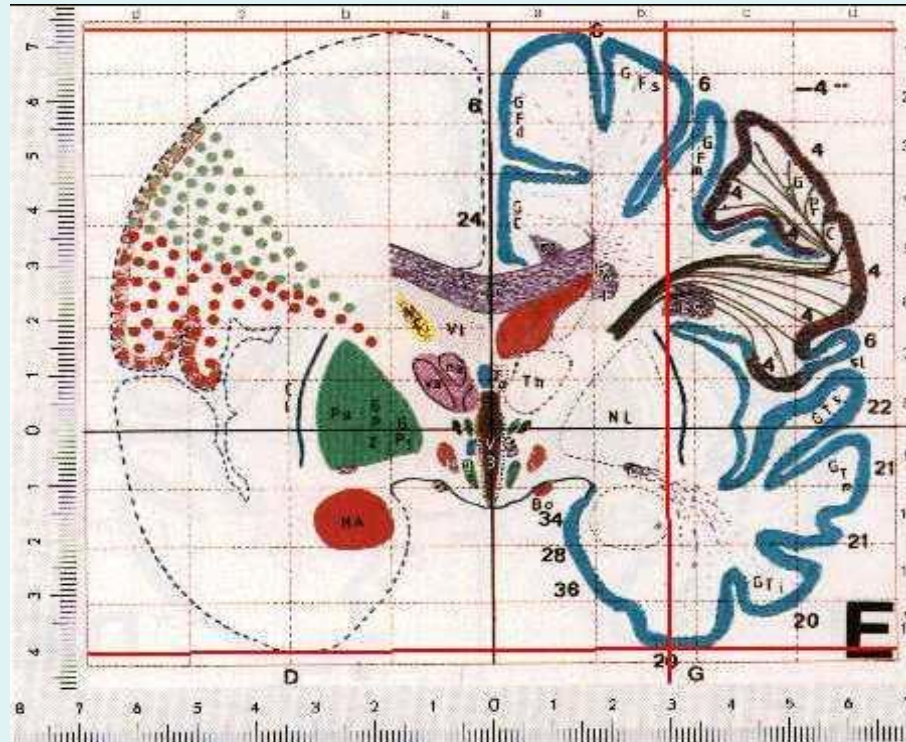
Brains of different subjects vary in *shape* and *size*.

- 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)

Between subjects

The Talairach Atlas

The MNI/ICBM AVG152 Template



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

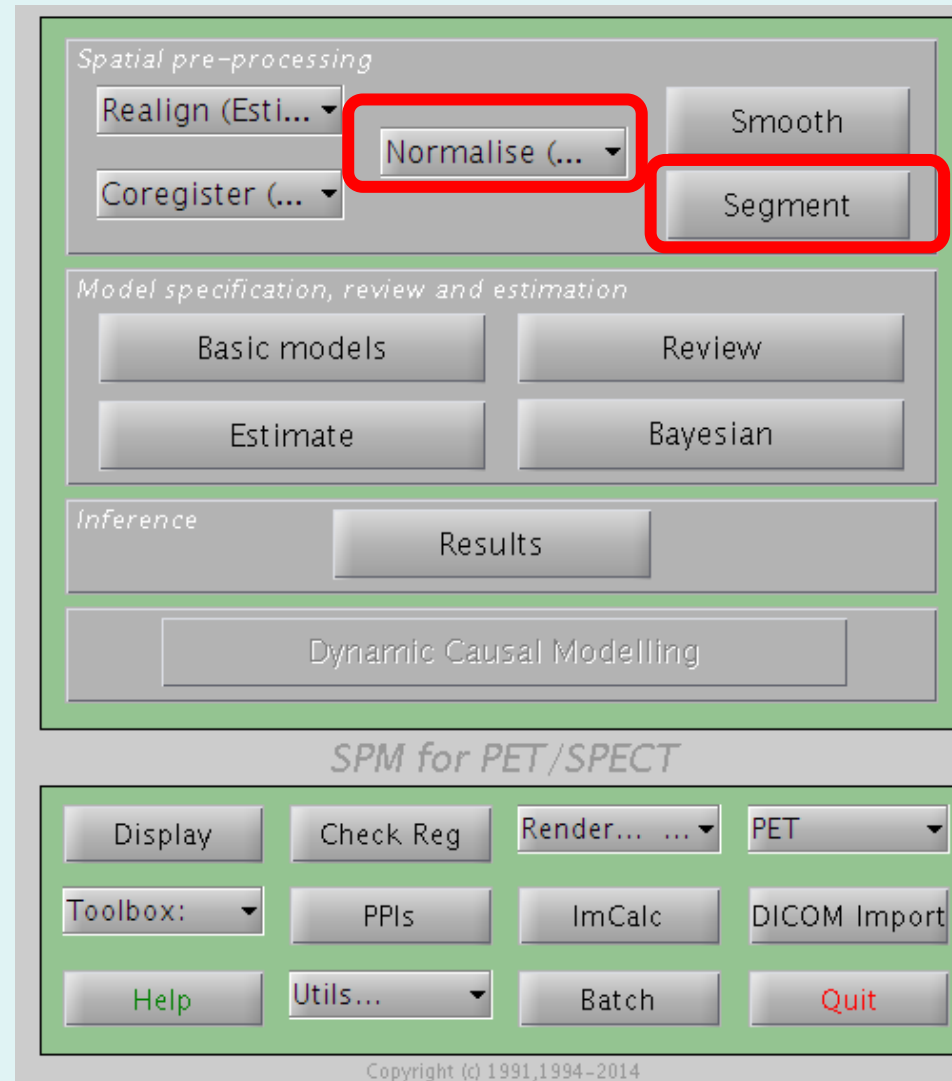
Recommended reading: <http://imaging.mrc-cbu.cam.ac.uk/imaging/MniTalairach>

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 SPM12, alignment is achieved by matching GM with GM and WM with WM.
 - With possible alignment of other tissues.

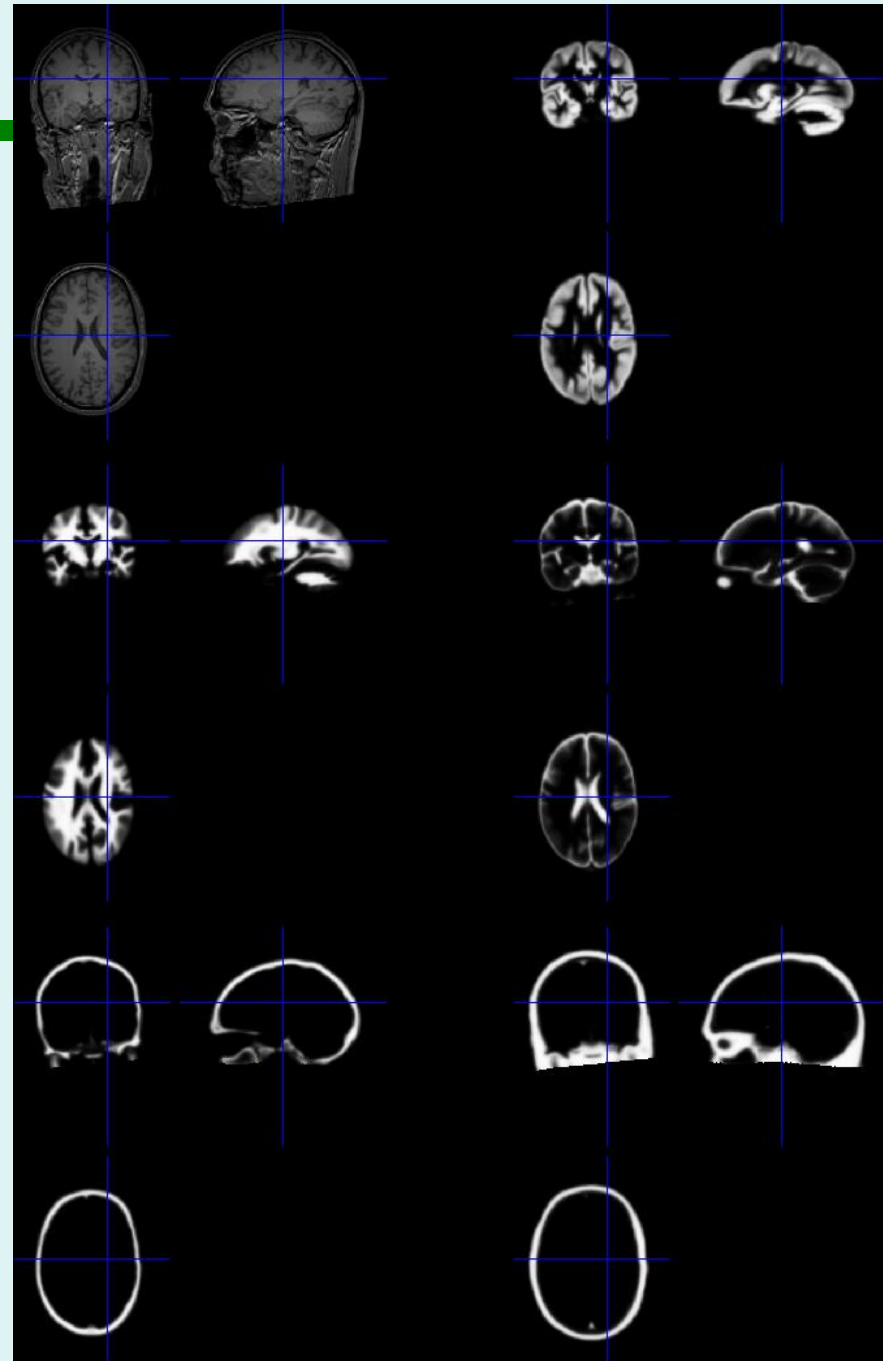
Normalise/Segment

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



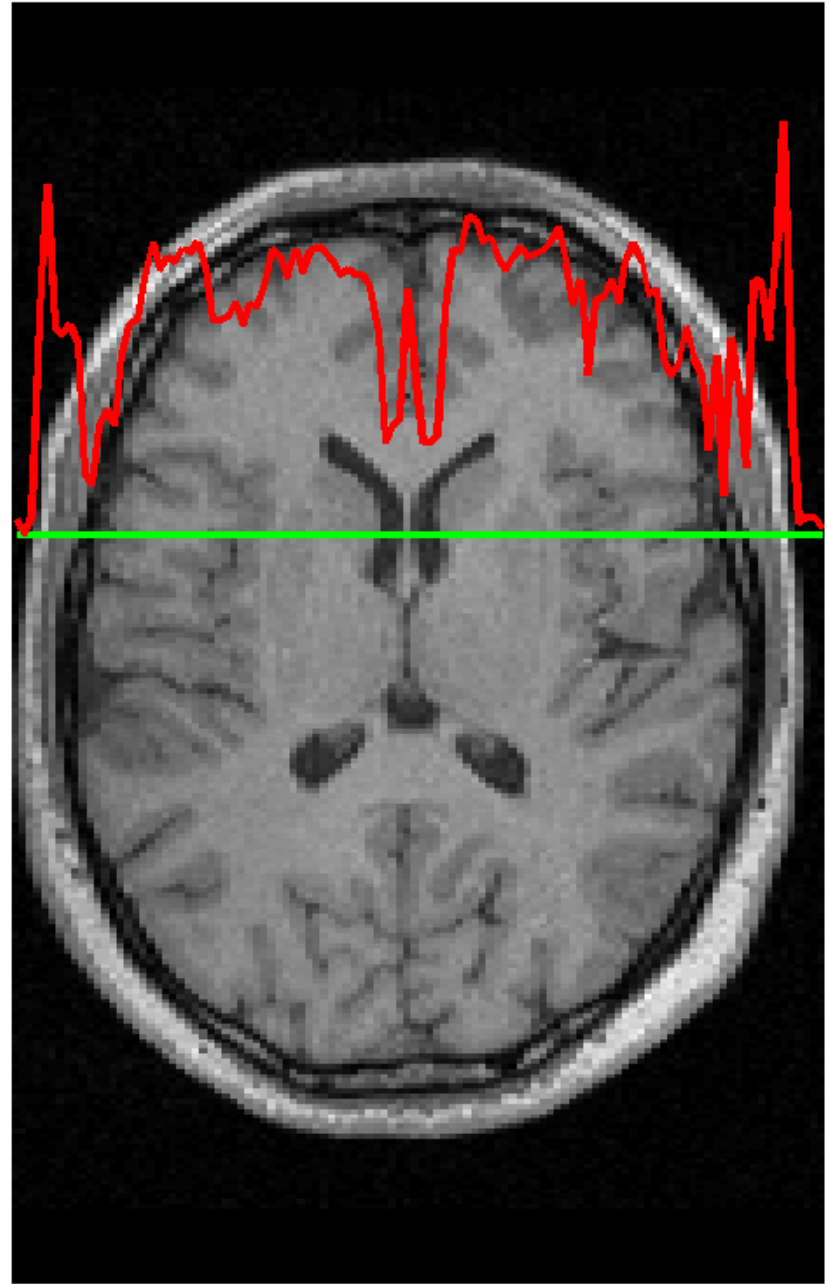
Spatial normalisation

- 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.

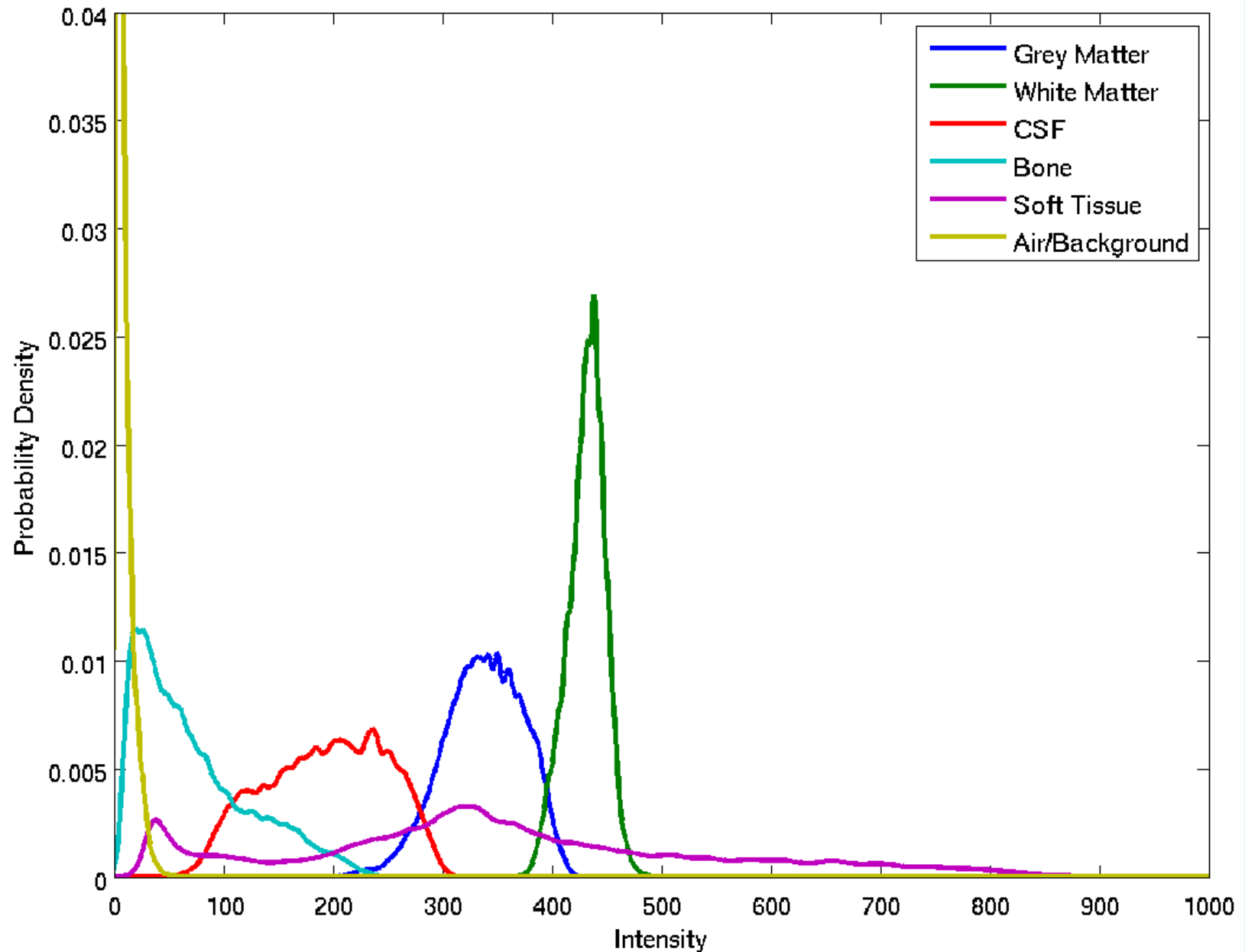


Segmentation

- 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



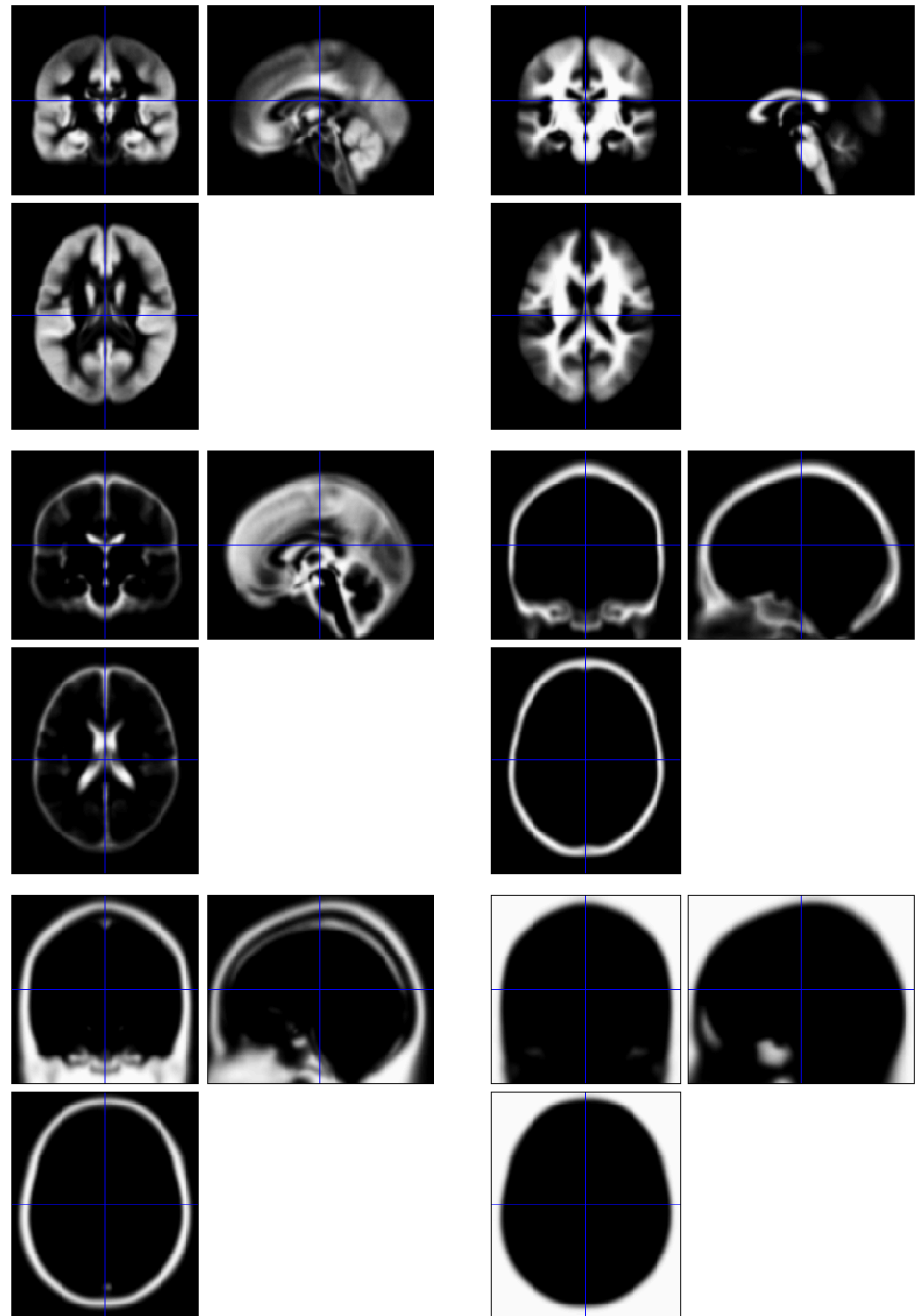
Tissue intensity distributions (T1w-MRI)



TPM's

Tissue probability maps in SPM12.

- GM, WM & CSF
- Additional non-brain tissue classes



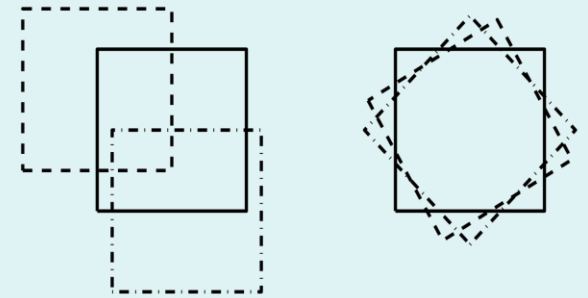
Modelling deformations, affine transform

12 parameter affine transform

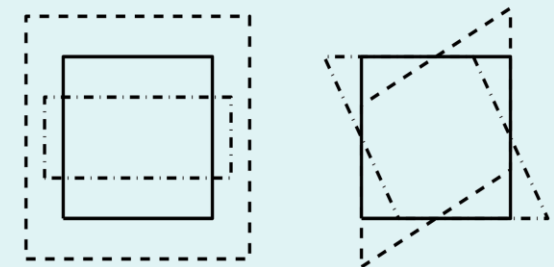
- 3 translations
- 3 rotations
- 3 zooms
- 3 shears

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

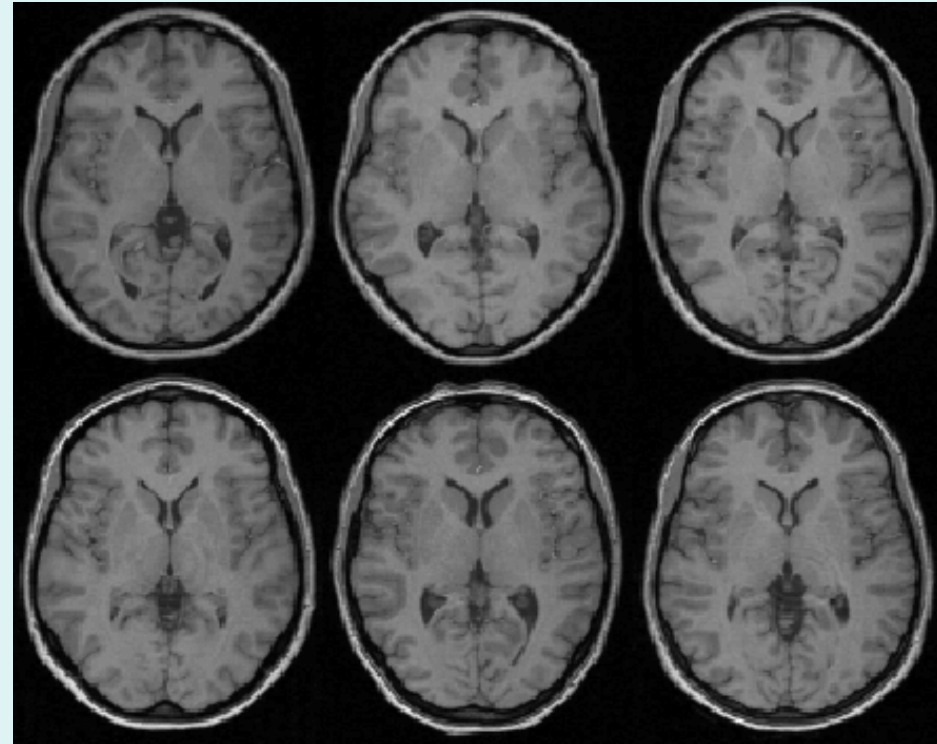
→ Fits overall shape and size



→ Need *warping* for local deformation



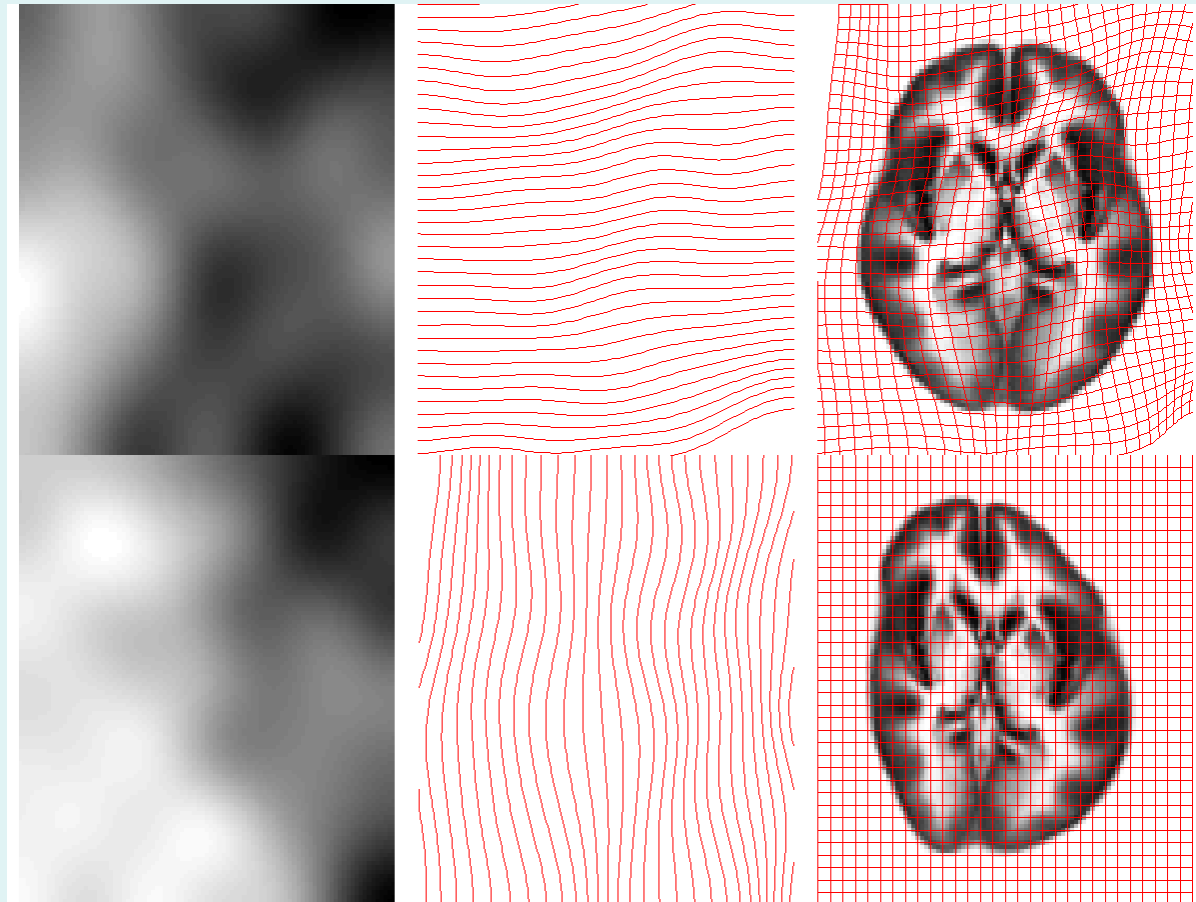
Spatial normalisation results



Affine registration

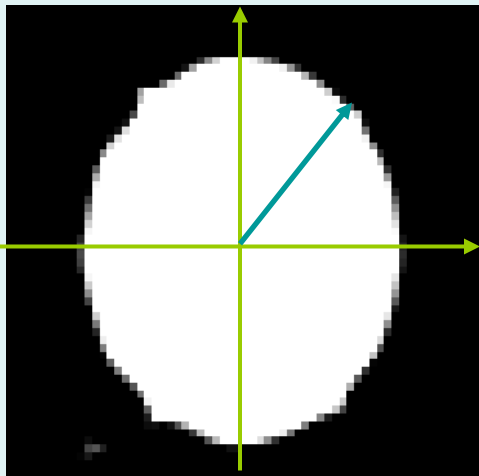
Modelling deformations, warps

- Tissue probability images are warped to match the subject
- The inverse transform warps to the TPMs
- Warps are constrained to be reasonable by penalising various distortions (energies)

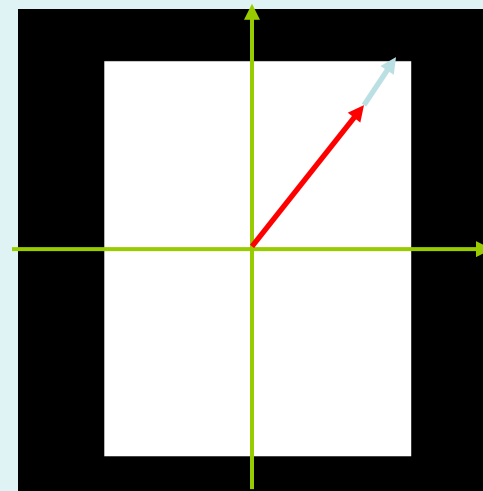


Non-linear warping, example

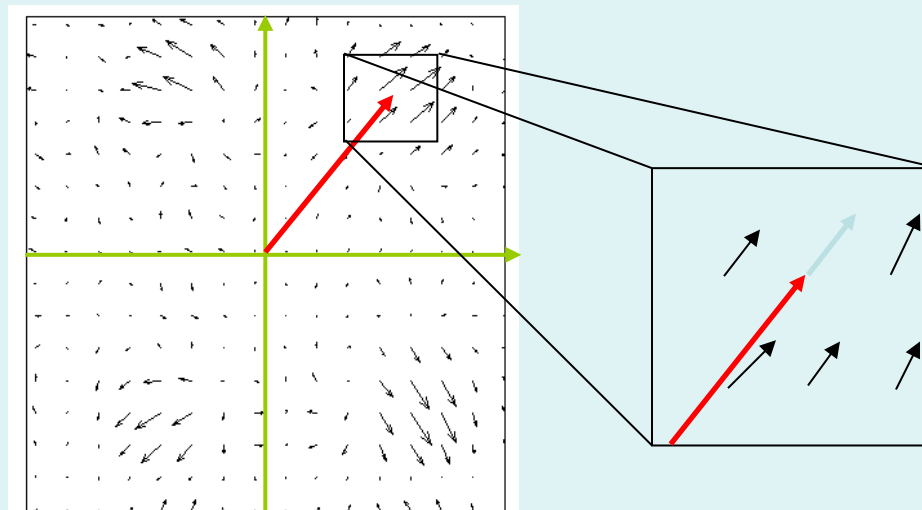
For every voxel position in blank sheet



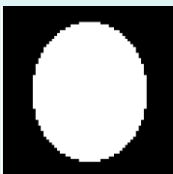
Go to original image and find intensity at warped co-ordinate



Get position in original space by adding pertinent displacement

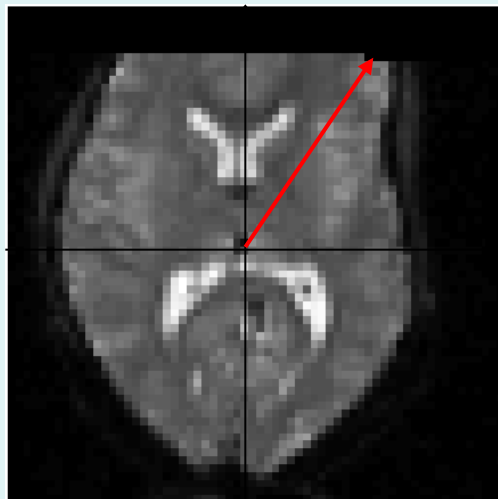


Template



Non-linear warping, example

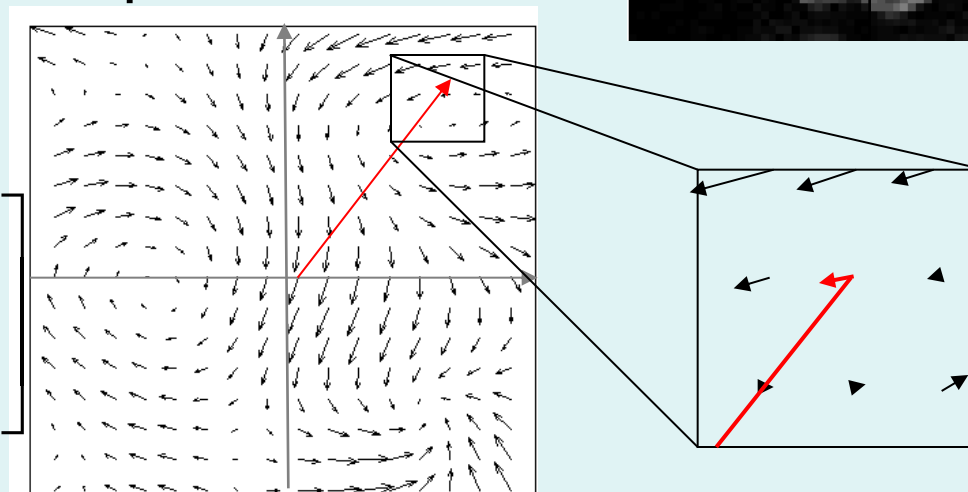
For each voxel-centre in blank sheet.



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

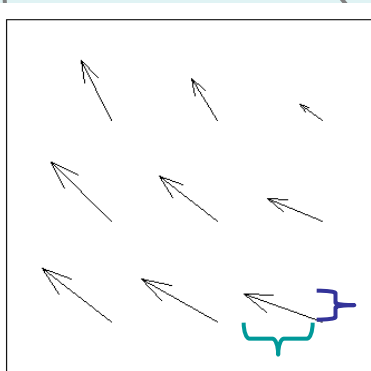
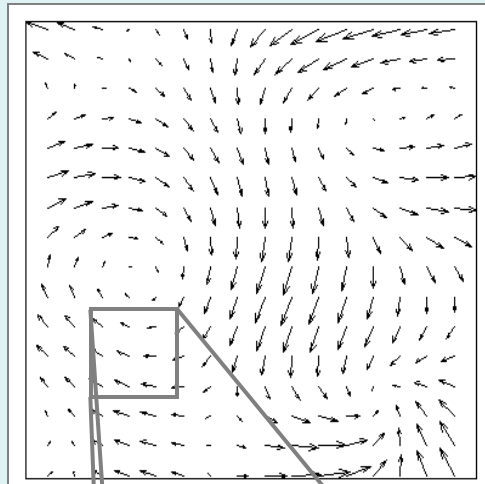


Get position in original space by adding pertinent displacement.



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

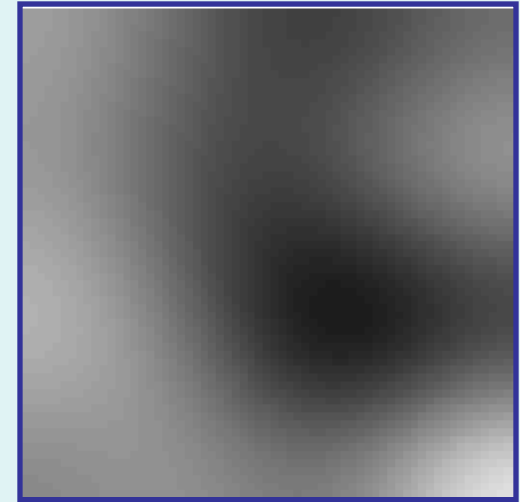
Displacement map



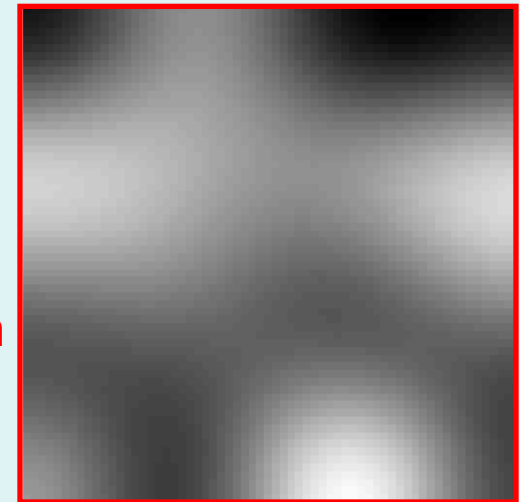
x-displacement

y-displacement

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

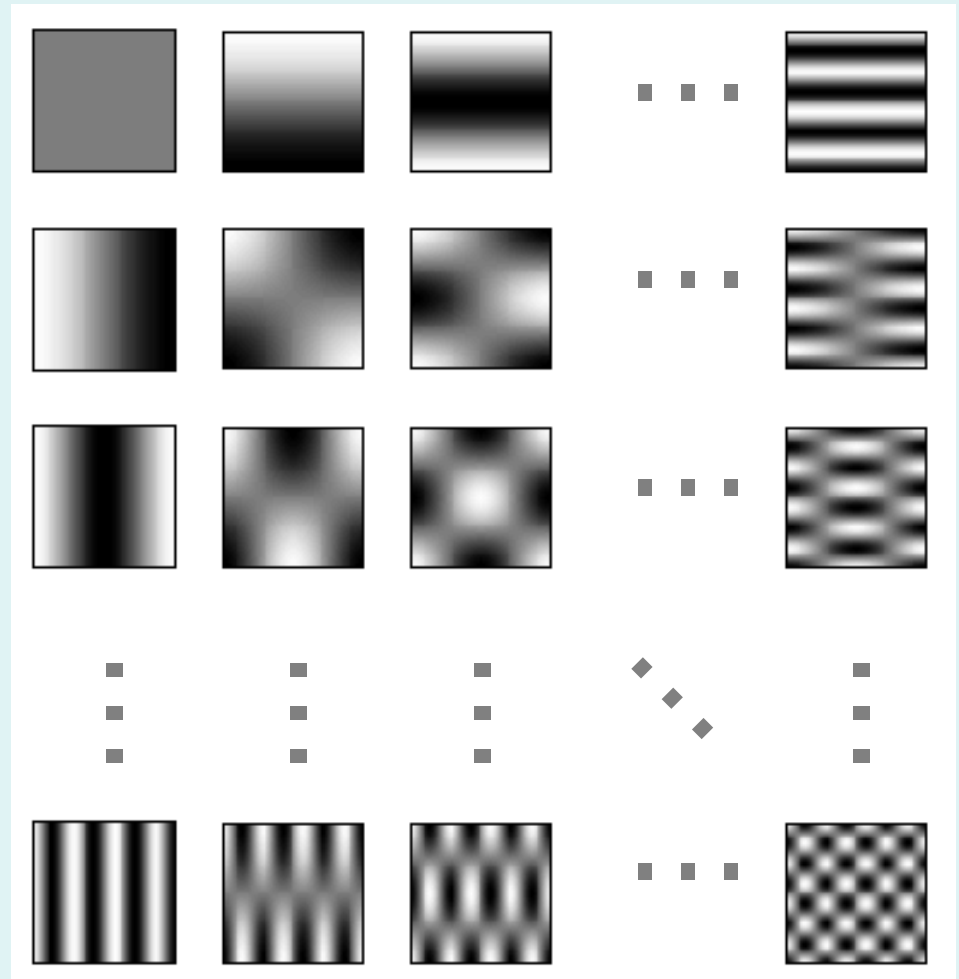


x-displacement,
black: leftward
translation
white: rightward
translation
gray: no translation



Displacement map modelling

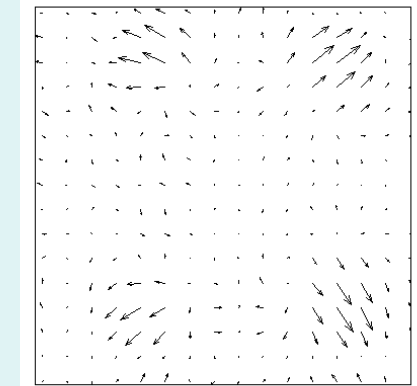
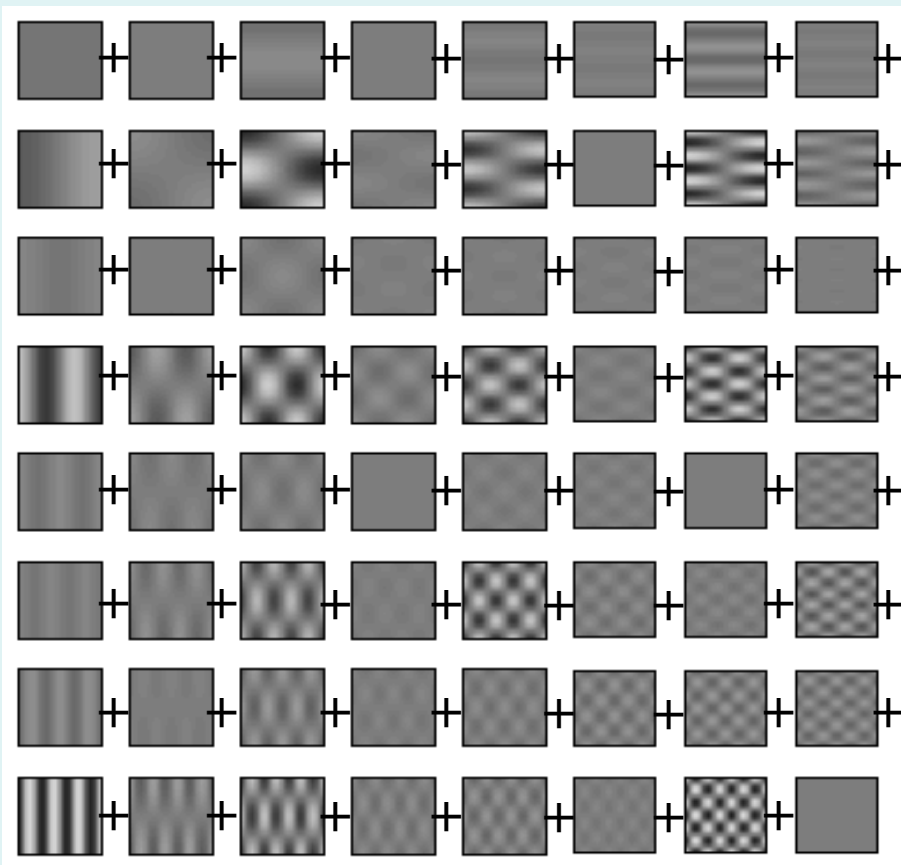
- To prevent impossible deformations we restrict it to be a linear combination of permitted basis-warps.
- For example use the discrete cosine set \rightarrow smooth deformation!



Displacement maps, example

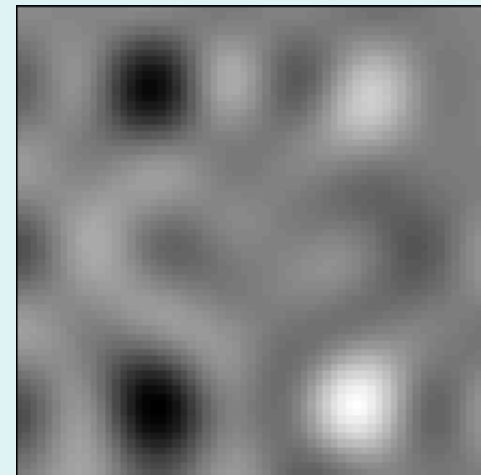
Square-to-ellipse map

Each basis-warp multiplied by a weight



x-component of
square-to-ellipse map

=

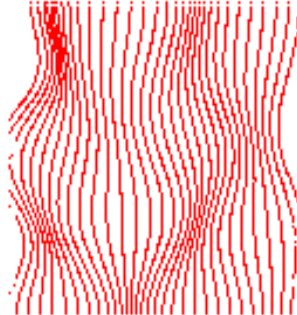


Displacement maps, example

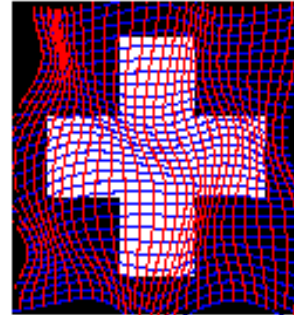
Dark - shift left, Light - shift right



Deformation Field in X



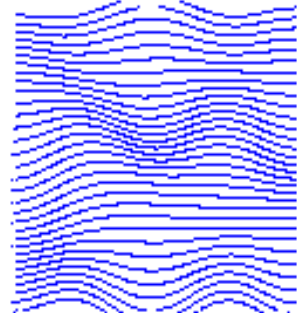
Field Applied To Image



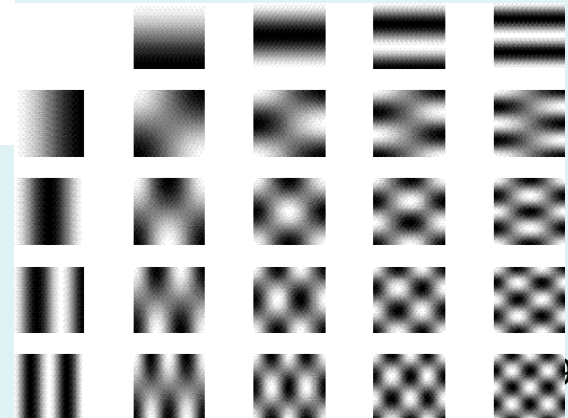
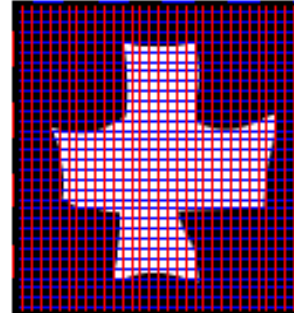
Dark - shift down, Light - shift up



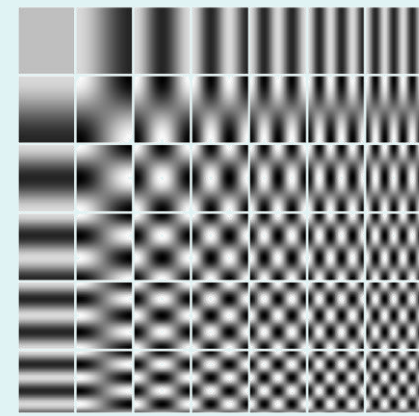
Deformation Field in Y



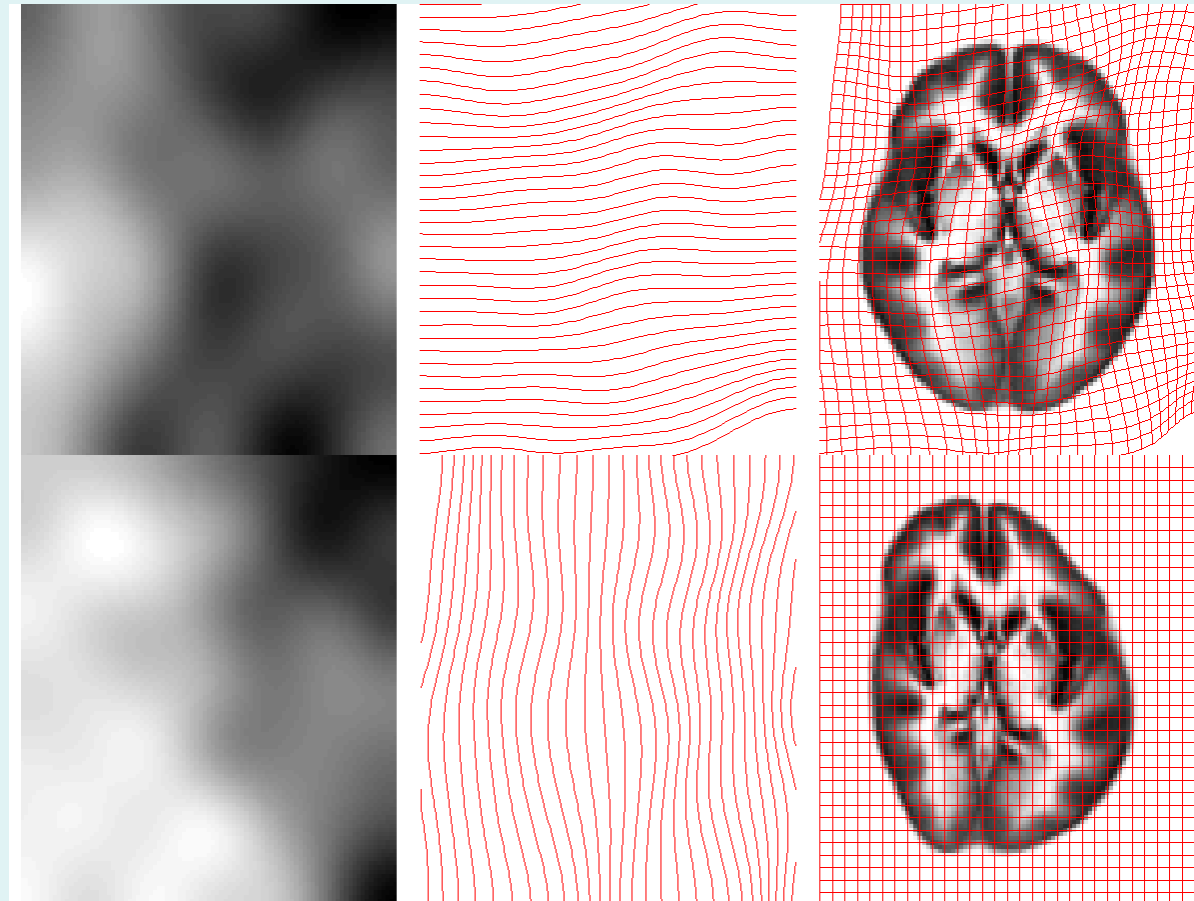
Deformed Image



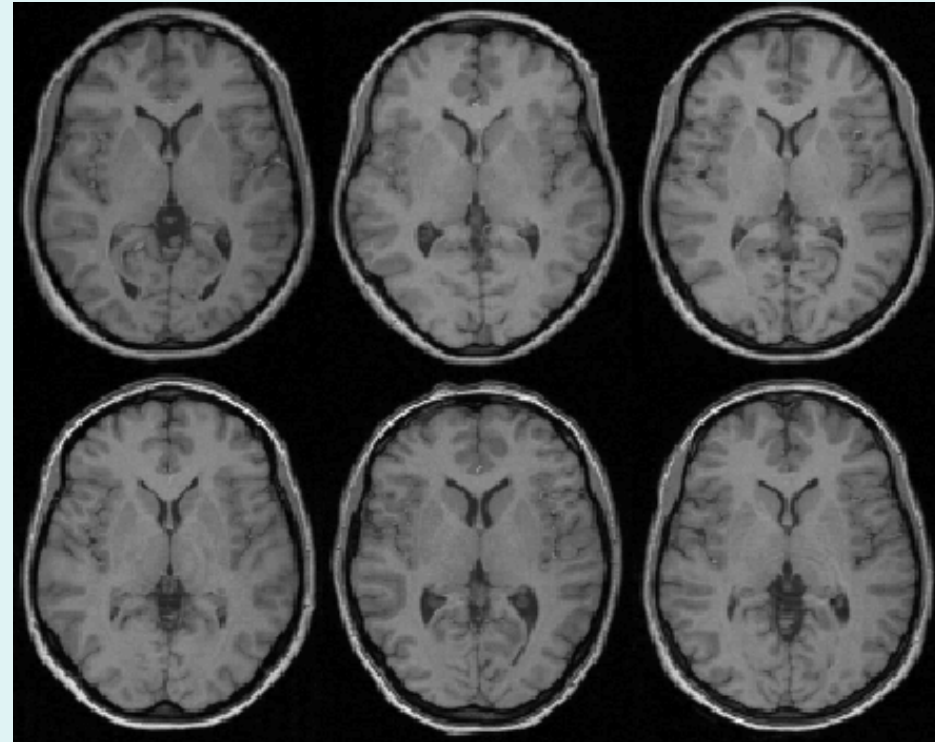
Modelling deformations, warps



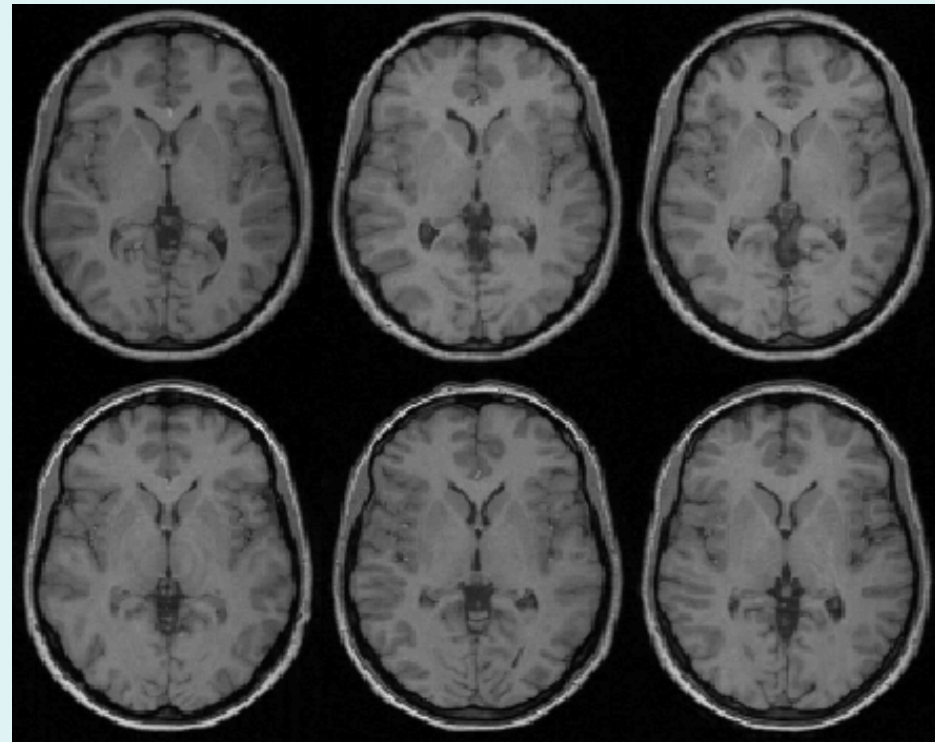
- Tissue probability images are warped to match the subject
- The inverse transform warps to the TPMs
- Warps are constrained to be reasonable by penalising various distortions (energies)



Spatial normalisation results



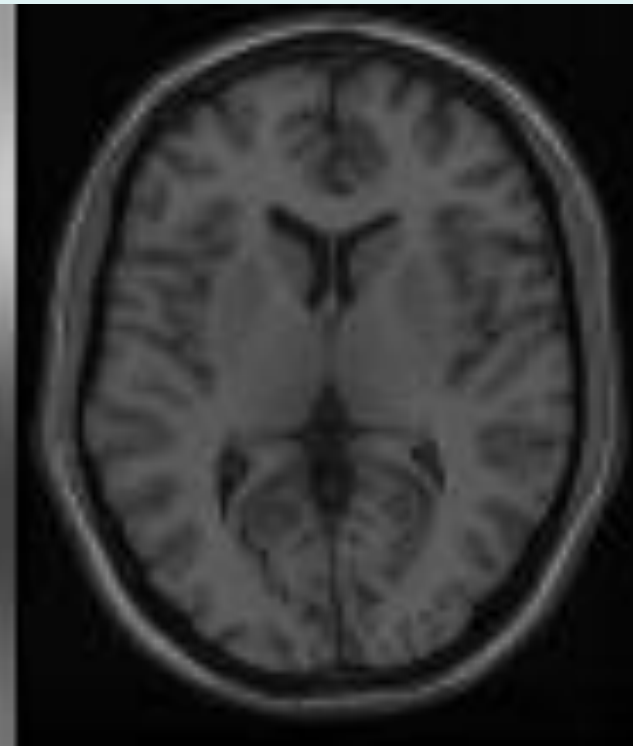
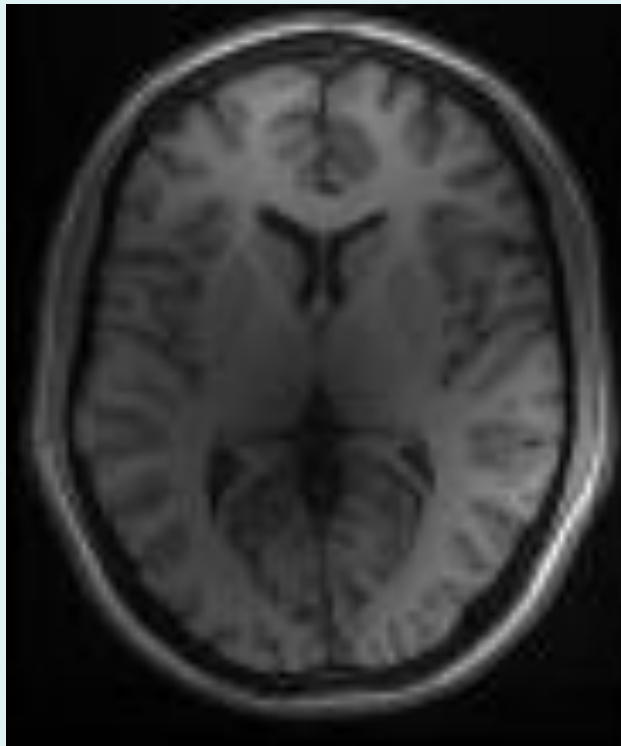
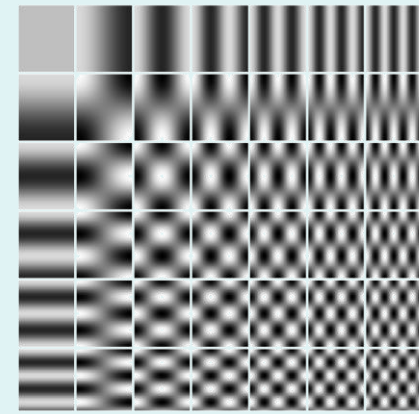
Affine registration



Non-linear registration

Modelling inhomogeneity

A multiplicative bias field is modelled as a spatially smooth image



Corrupted image

Bias Field

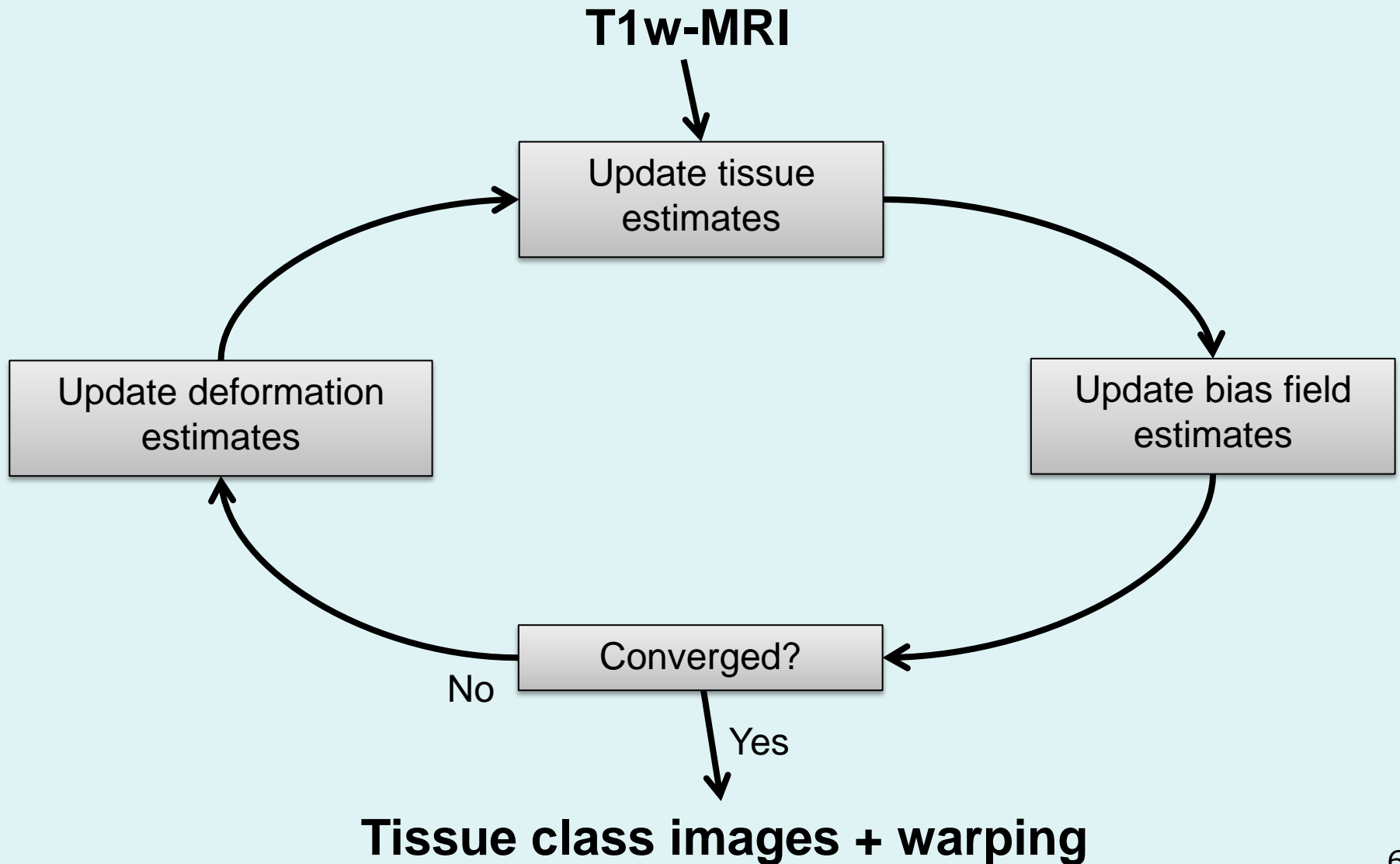
Corrected image

Normalisation & Unified Segmentation

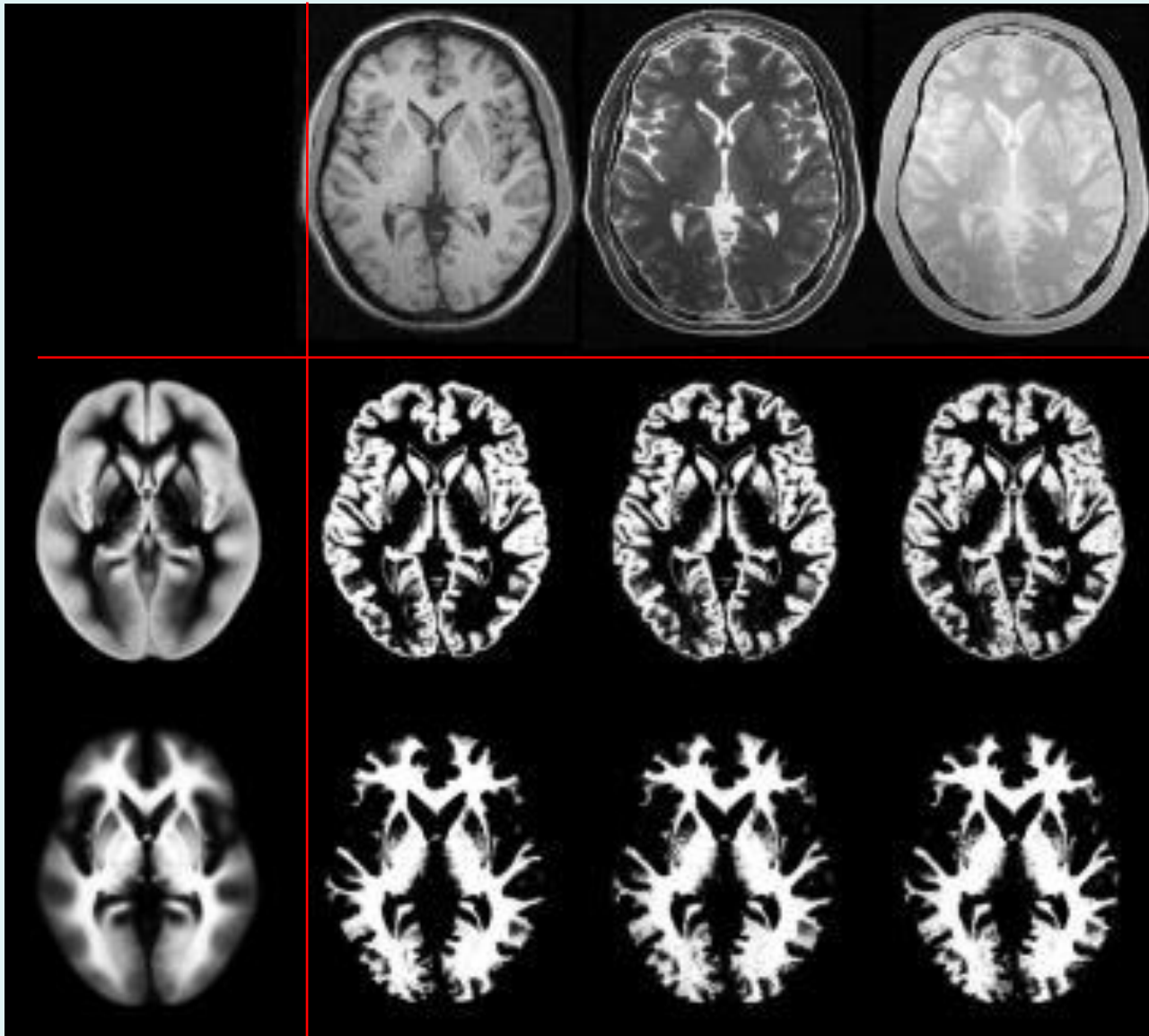
- MRI imperfections make normalisation harder
 - Differences between sequences, artefacts
 - Intensity inhomogeneity or “bias” field
- Normalising *segmented tissue maps* should be more robust and precise than using the original images ...
- ... Tissue segmentation benefits from spatially-aligned *prior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

→ Circular reasoning!

Iterative optimisation scheme



Segmentation results

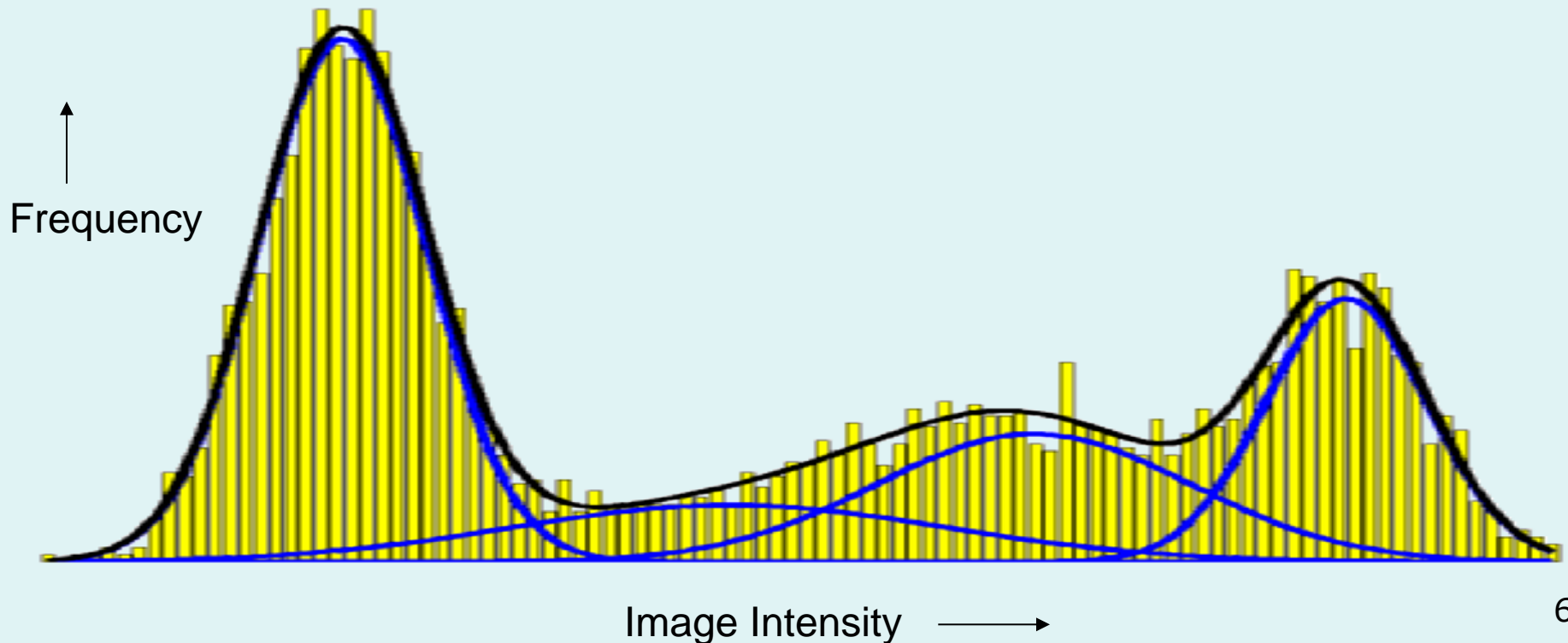


Spatially
normalised
BrainWeb
phantoms
(T1, T2,
PD)

Tissue
probability
maps of
GM and
WM

Mixture of Gaussians (MoG)

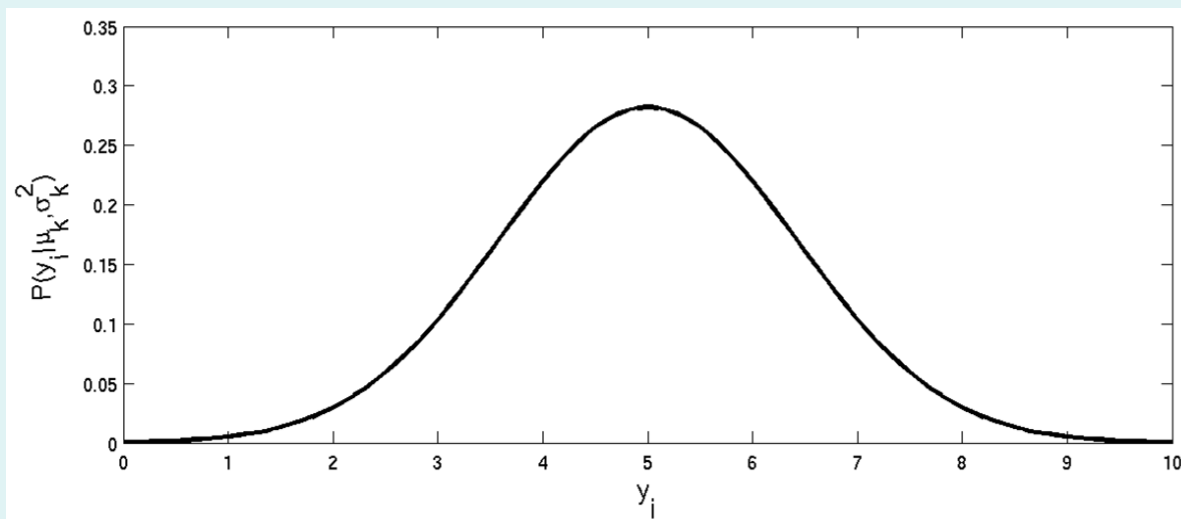
Classification is based on a Mixture of Gaussians model (MOG), which represents the intensity probability density by a number of Gaussian distributions.



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:

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

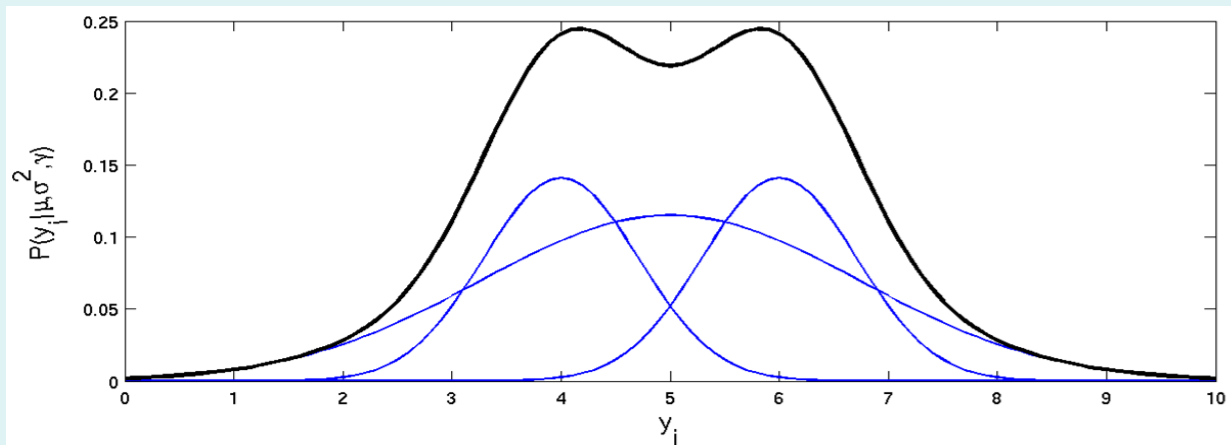


Non-Gaussian probability density

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

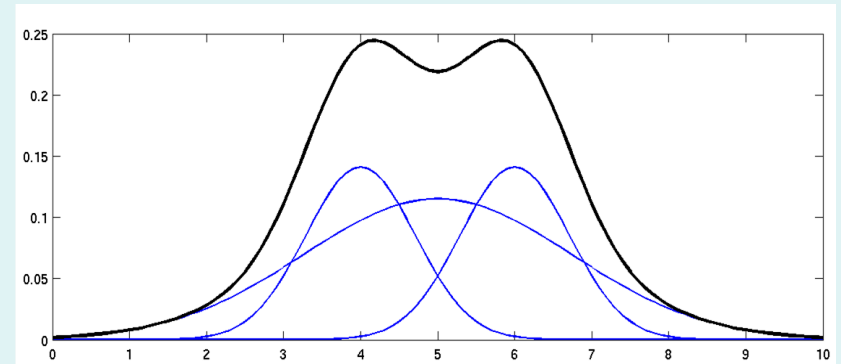


Mixing proportions

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

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

- So:



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

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

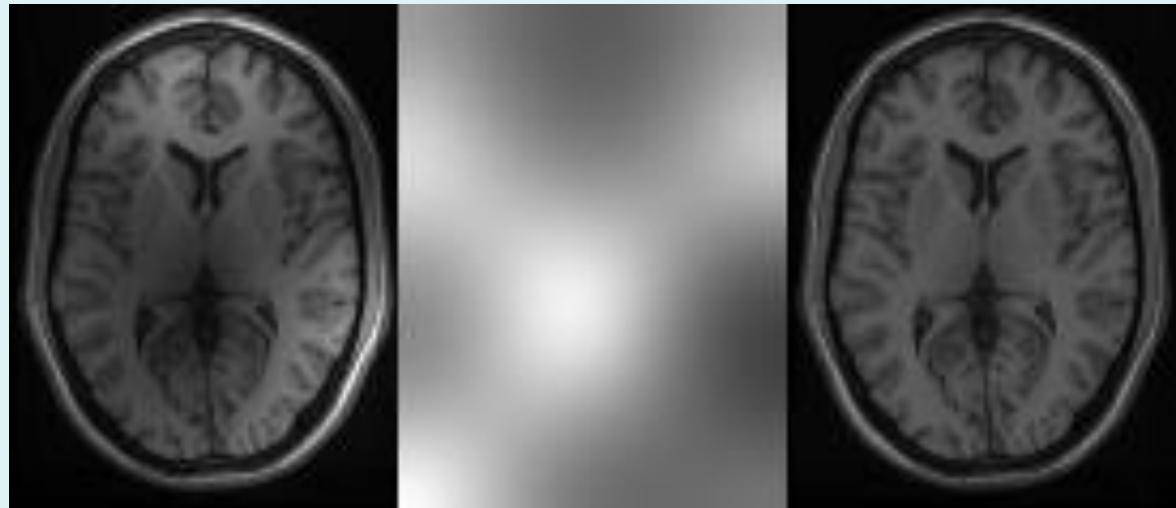
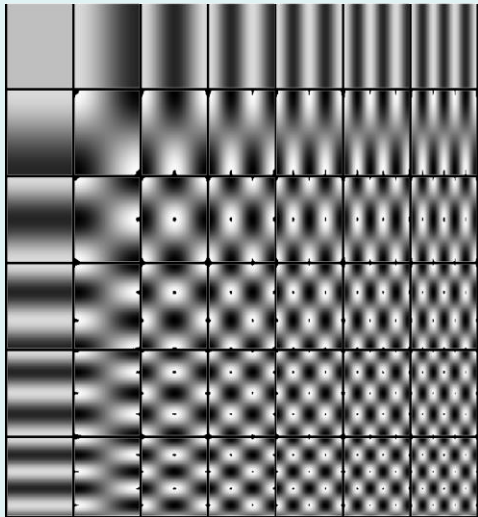
- A bias field is included, such that the required scaling at voxel i , parameterised by β , is $\rho_i(\beta)$.
- Replace the means by $\mu_k / \rho_i(\beta)$
- Replace the variances by $(\sigma_k / \rho_i(\beta))^2$

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

Modelling a bias field

After rearranging:

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



y

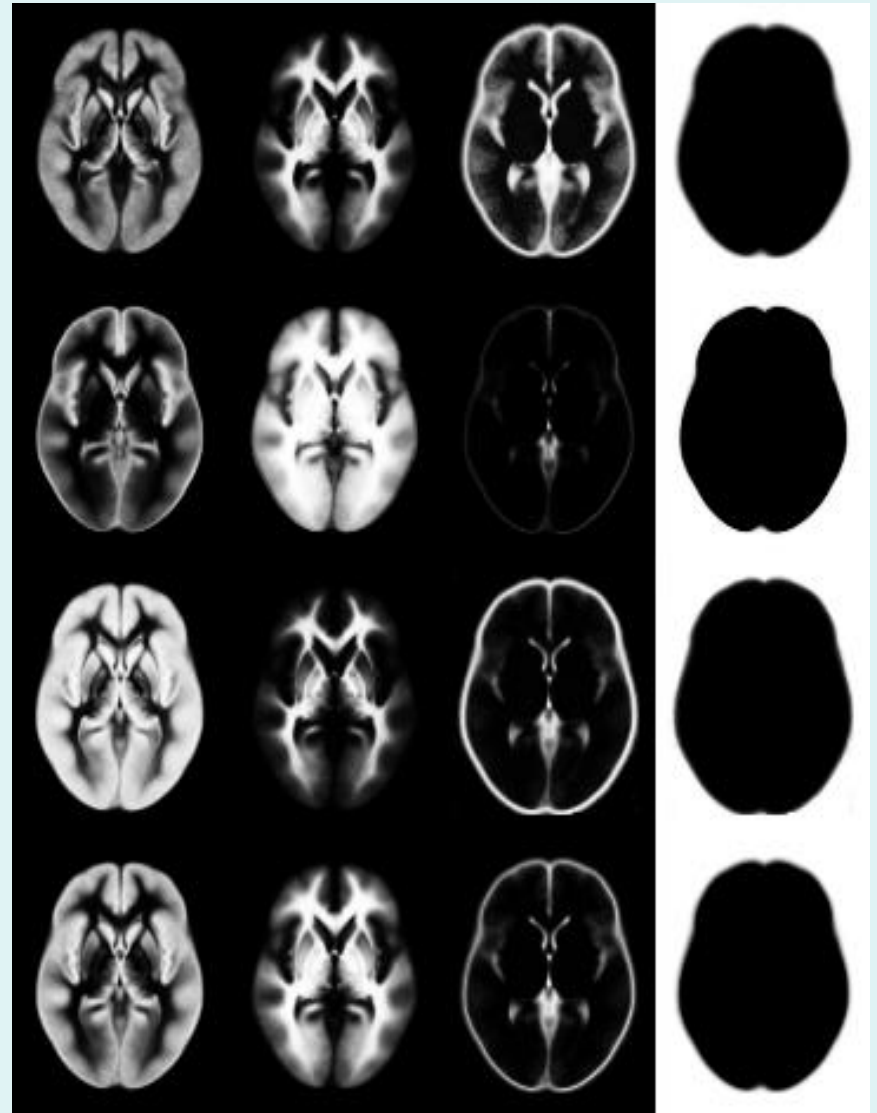
$\rho(\beta)$

$y \rho(\beta)$

“Mixing proportions”

- Tissue probability maps for each class are included.
- The probability of obtaining class k at voxel i , given weights γ is then:

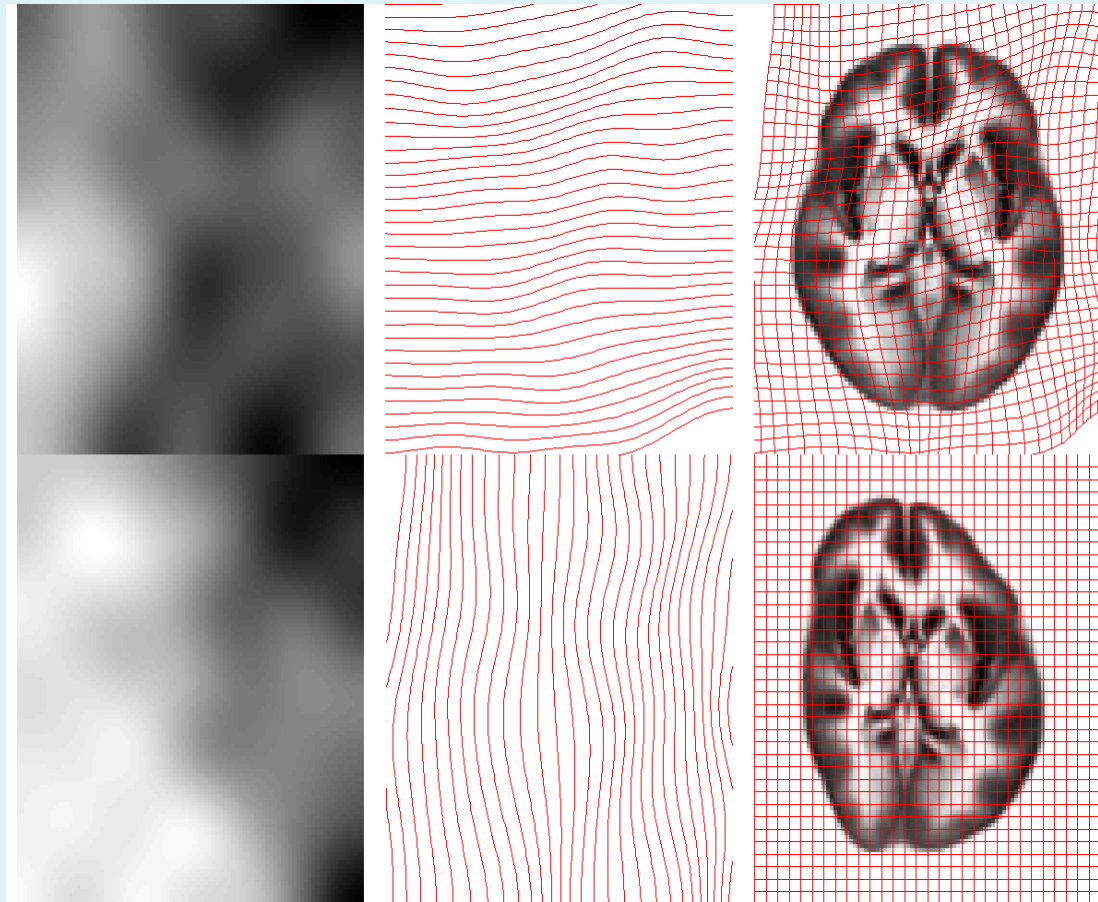
$$P(c_i = k | \gamma) = \frac{\gamma_k b_{ik}}{\sum_{j=1}^K \gamma_j b_{ij}}$$



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:

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



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...

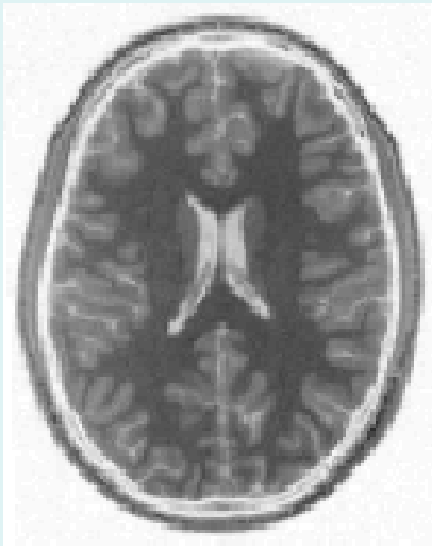
- Hold γ , μ , σ^2 and α constant, and minimise E w.r.t. β
Levenberg-Marquardt strategy, using $dE/d\beta$ and $d^2E/d\beta^2$
- Hold γ , μ , σ^2 and β constant, and minimise E w.r.t. α
Levenberg-Marquardt strategy, using $dE/d\alpha$ and $d^2E/d\alpha^2$
- Hold α and β constant, and minimise E w.r.t.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

end

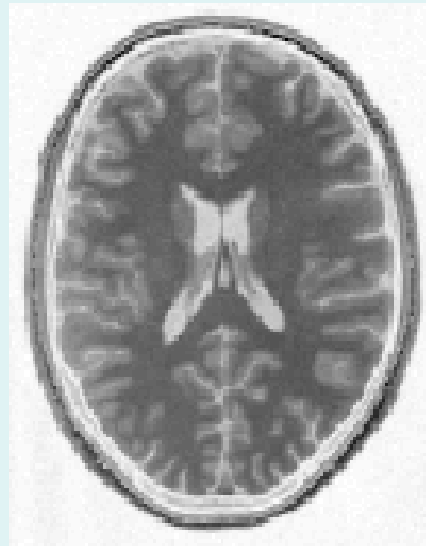
Spatial normalisation, overfitting

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

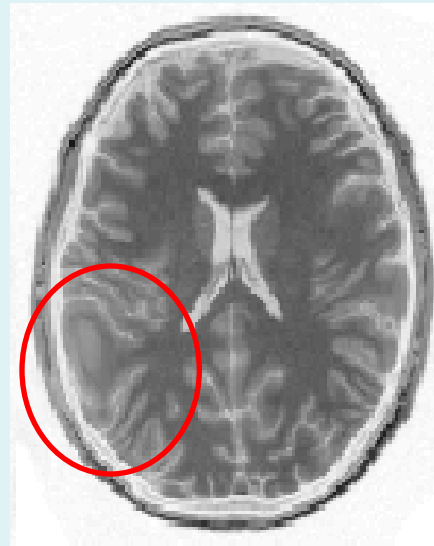
Template image



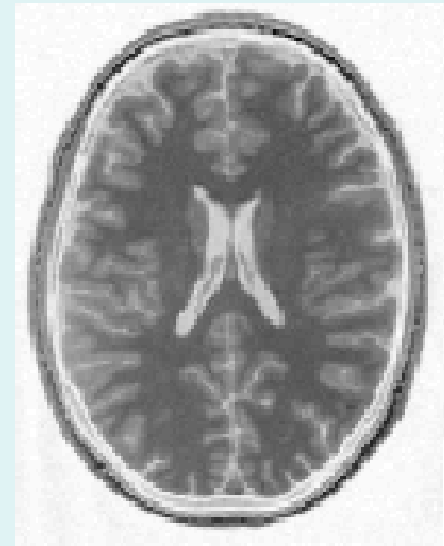
Affine registration.



Non-linear registration without regularisation.



Non-linear registration using regularisation.



Linear regularisation

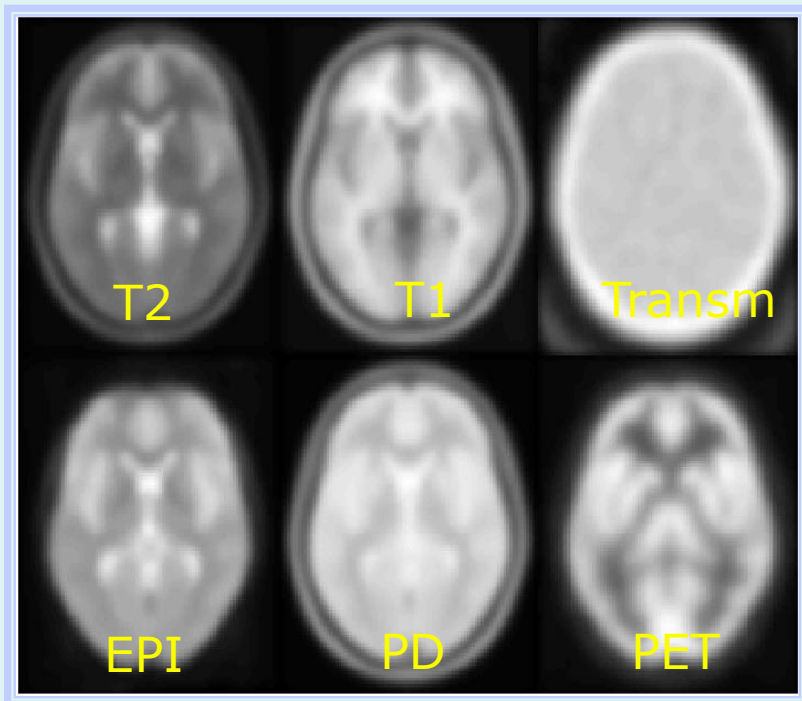
- Some bias fields and distortions are more probable (a priori) than others.
- Encoded using Bayes rule:

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

- 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
 - $-\log[P(\mathbf{a})] = (\mathbf{a} - \mathbf{m}_a)^T \mathbf{S}_a^{-1} (\mathbf{a} - \mathbf{m}_a) + \text{const}$

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.

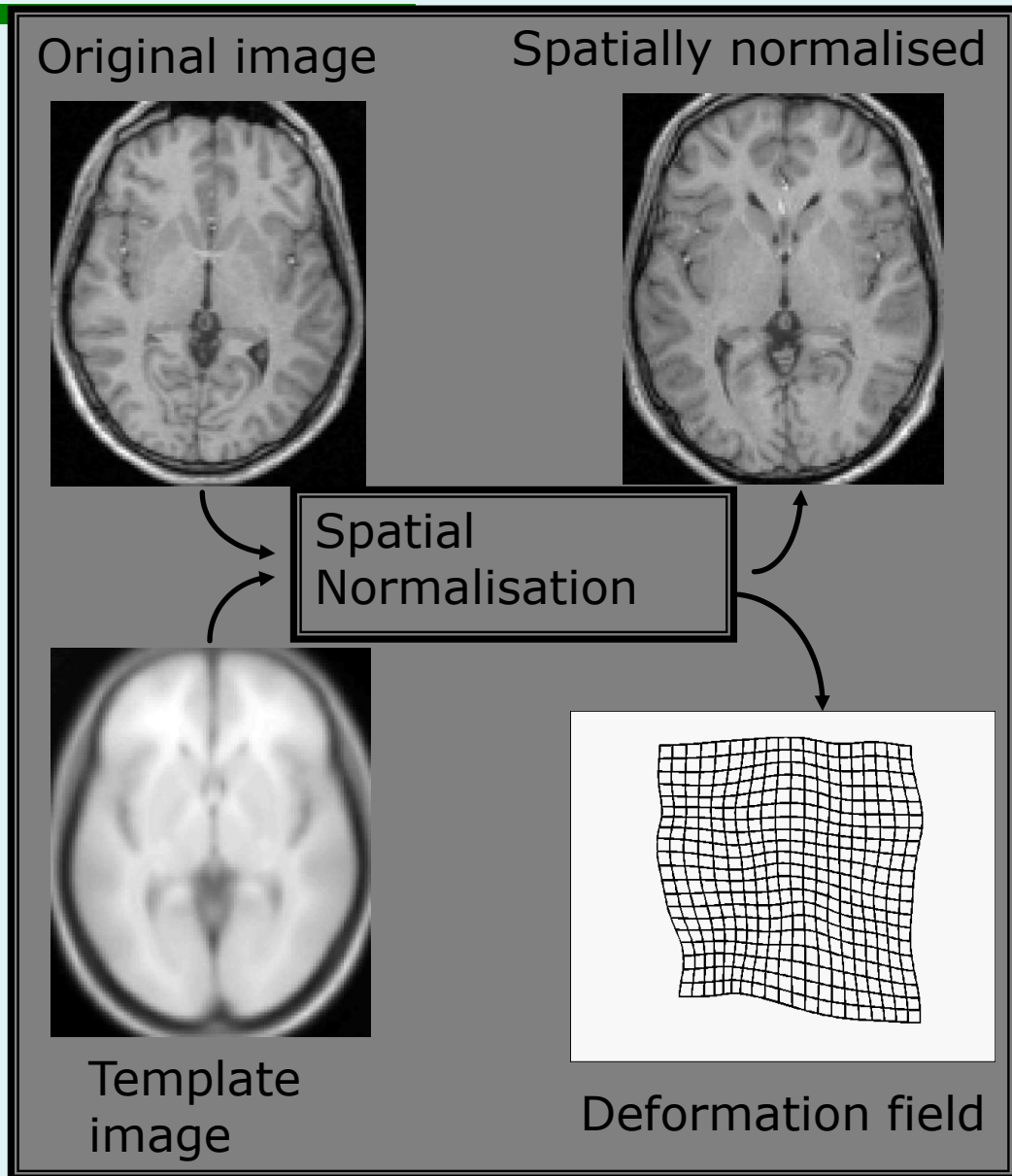
Old fashioned template matching

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.



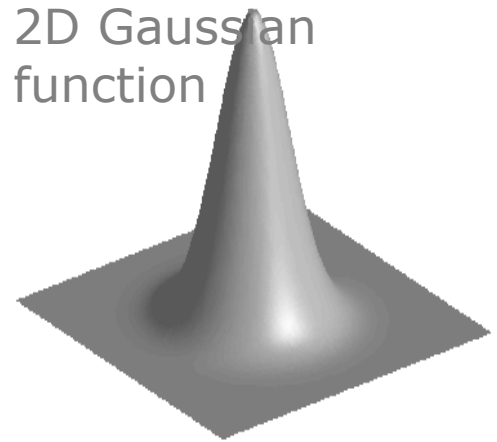
Content

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

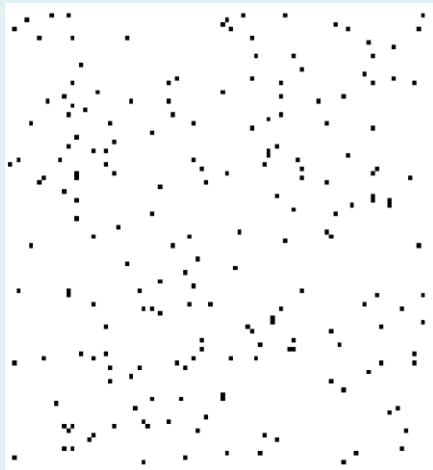
Smoothing, principle

- 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)

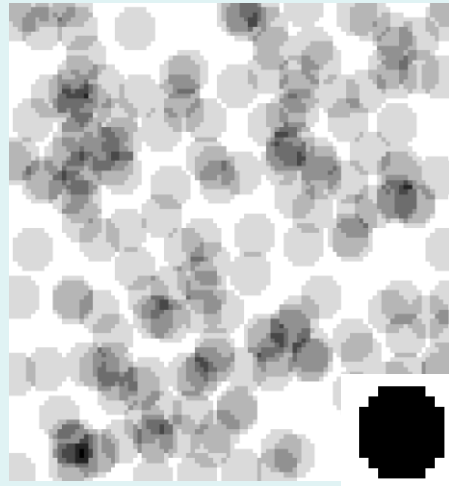
2D Gaussian function



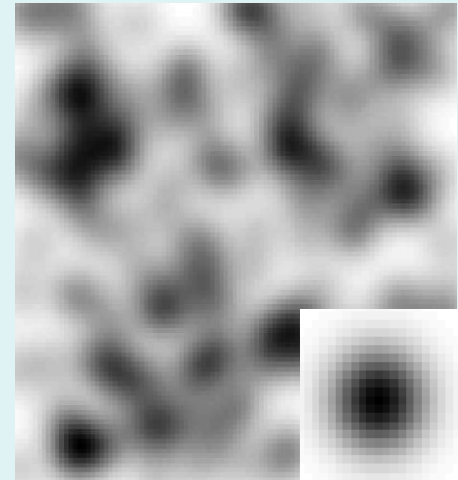
Before convolution



Convolved with a circle

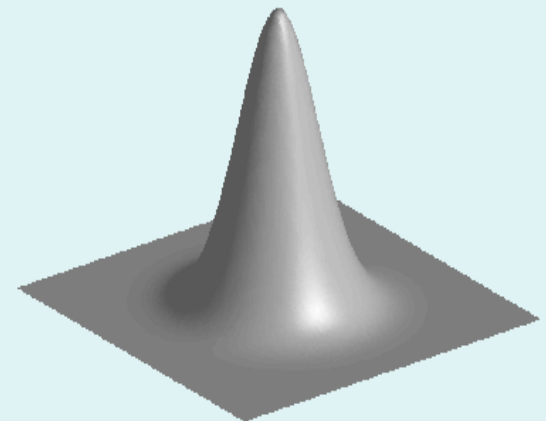


Convolved with a Gaussian



Smoothing, why blur the data?

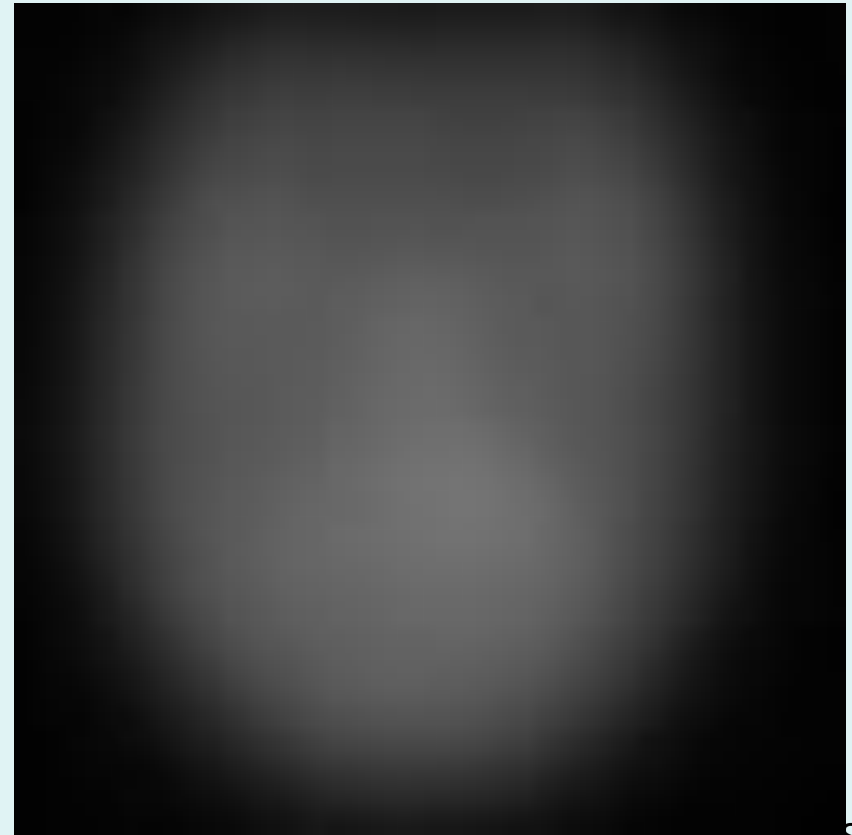
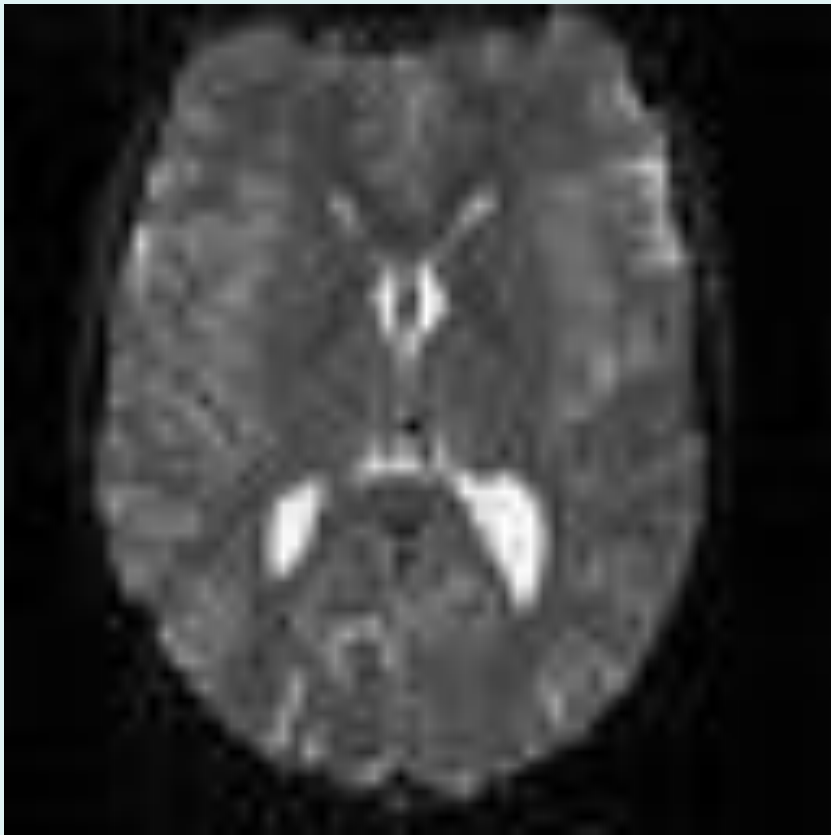
- Improves spatial overlap by blurring over minor anatomical differences and registration errors
- Averaging neighbouring voxels suppresses noise
 - matched filter theorem
- Makes data more normally distributed (central limit theorem)
- Reduces the effective number of multiple comparisons



Smoothing, kernel size

Decide *a priori*, based on:

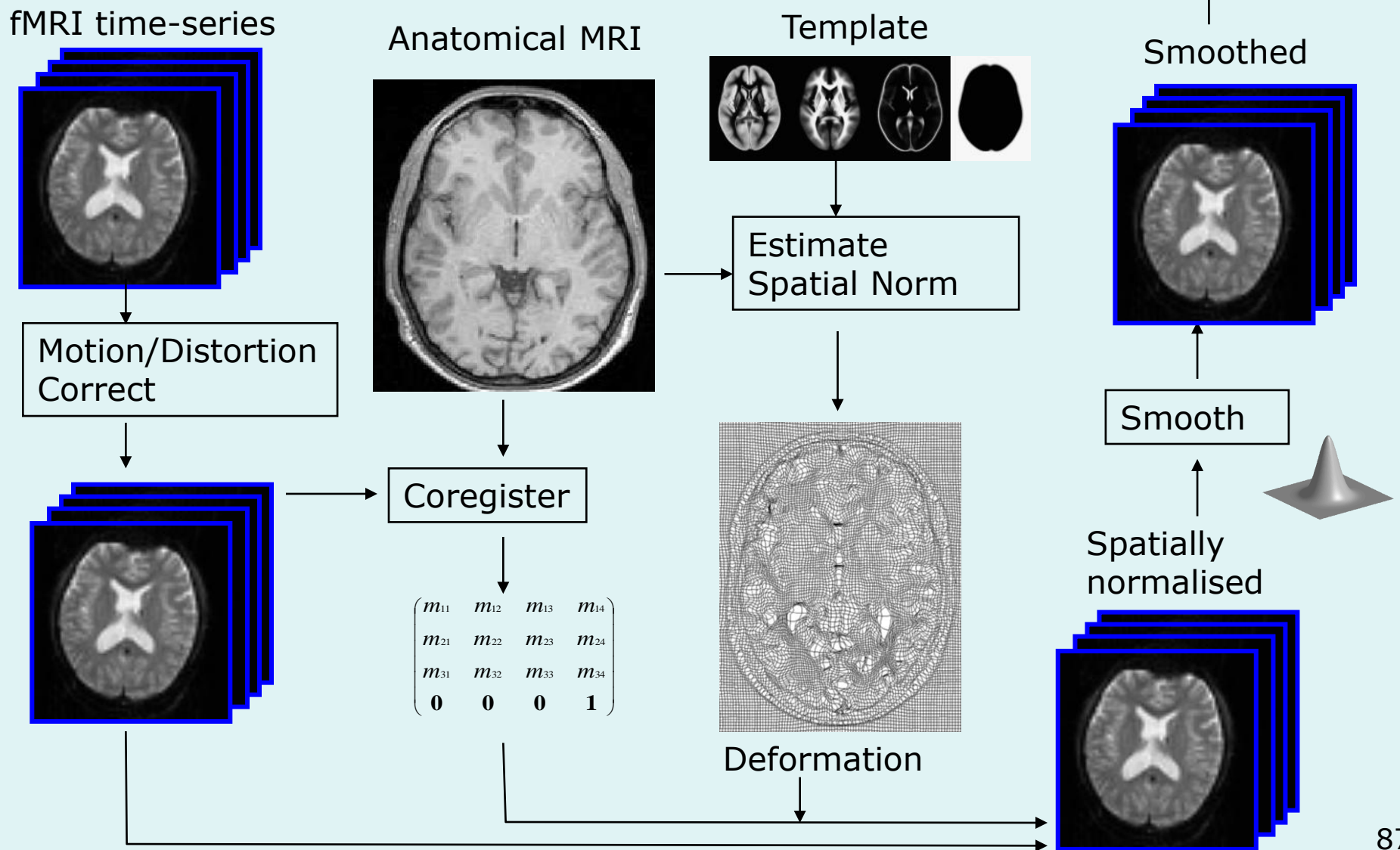
- Population, i.e. noise & inter-subject variability
- Expected activation size



Content

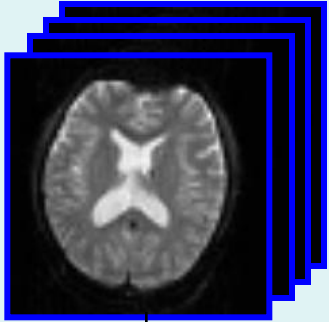
- **Preliminaries**
- **Within-subject**
- **Between-subject**
- **Smoothing**
- **Conclusion**

Pre-processing overview

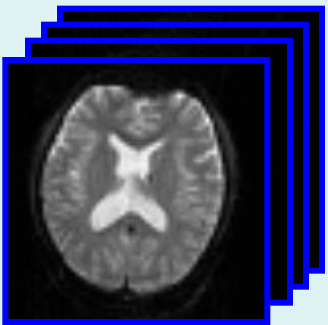


Alternative pipeline

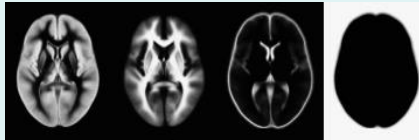
fMRI time-series



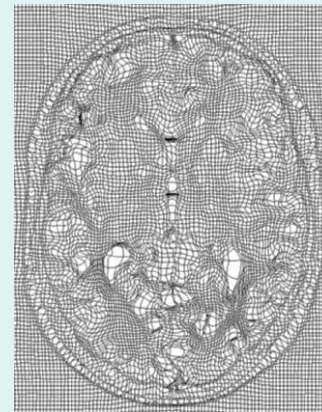
Motion/Distortion Correct



Template



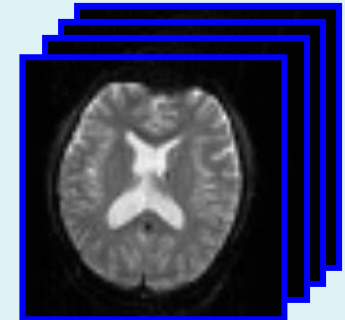
Estimate Spatial Norm



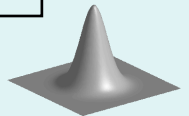
Deformation

Statistics or whatever

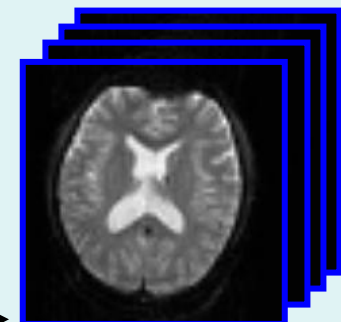
Smoothed



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).

