NeuroImaging Data Processing

aka. Statistical Parametric Mapping short course

Course 1 & 2:

spatial pre-processing

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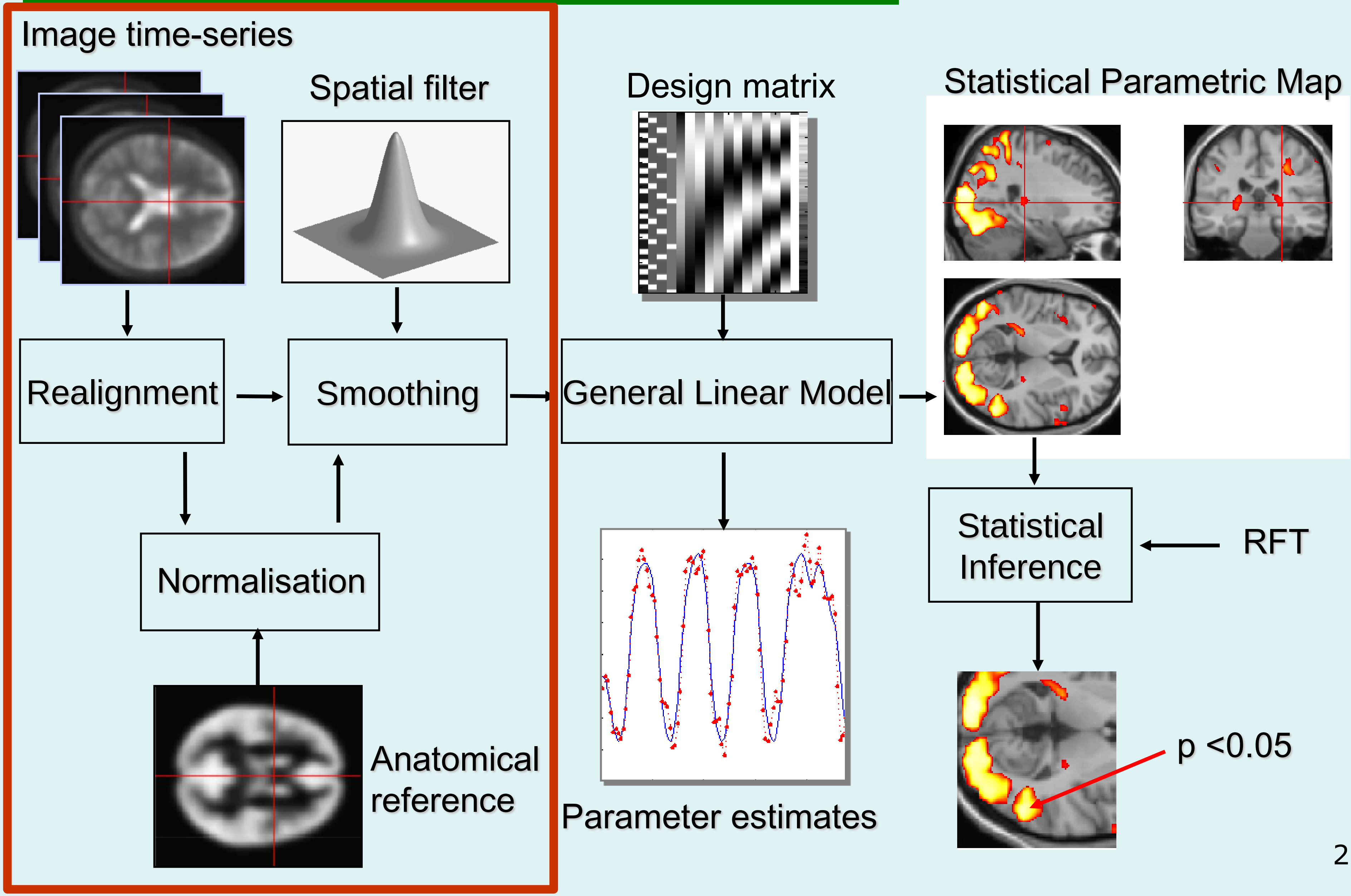
SPM work flow



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 the whole *source* image and the 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

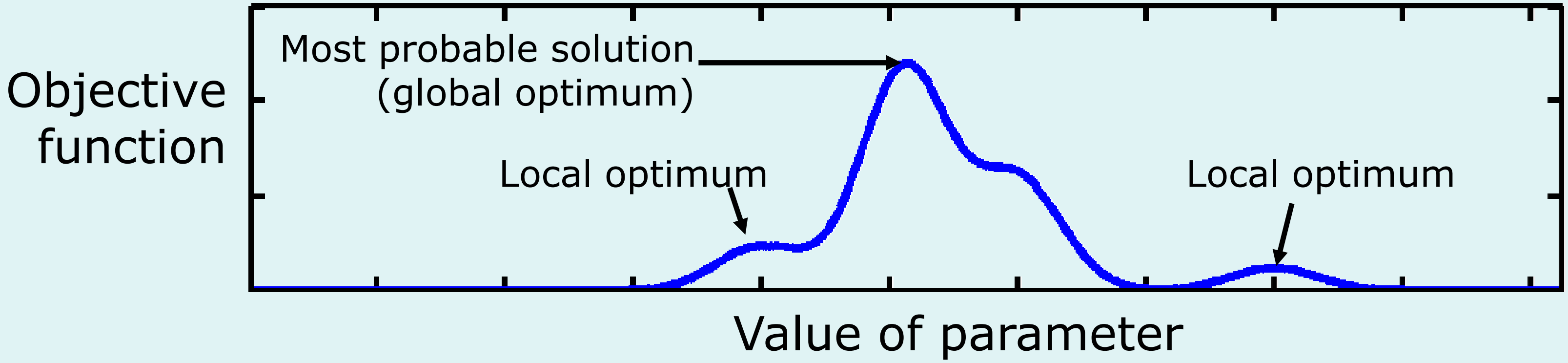
Hybrid approaches :

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

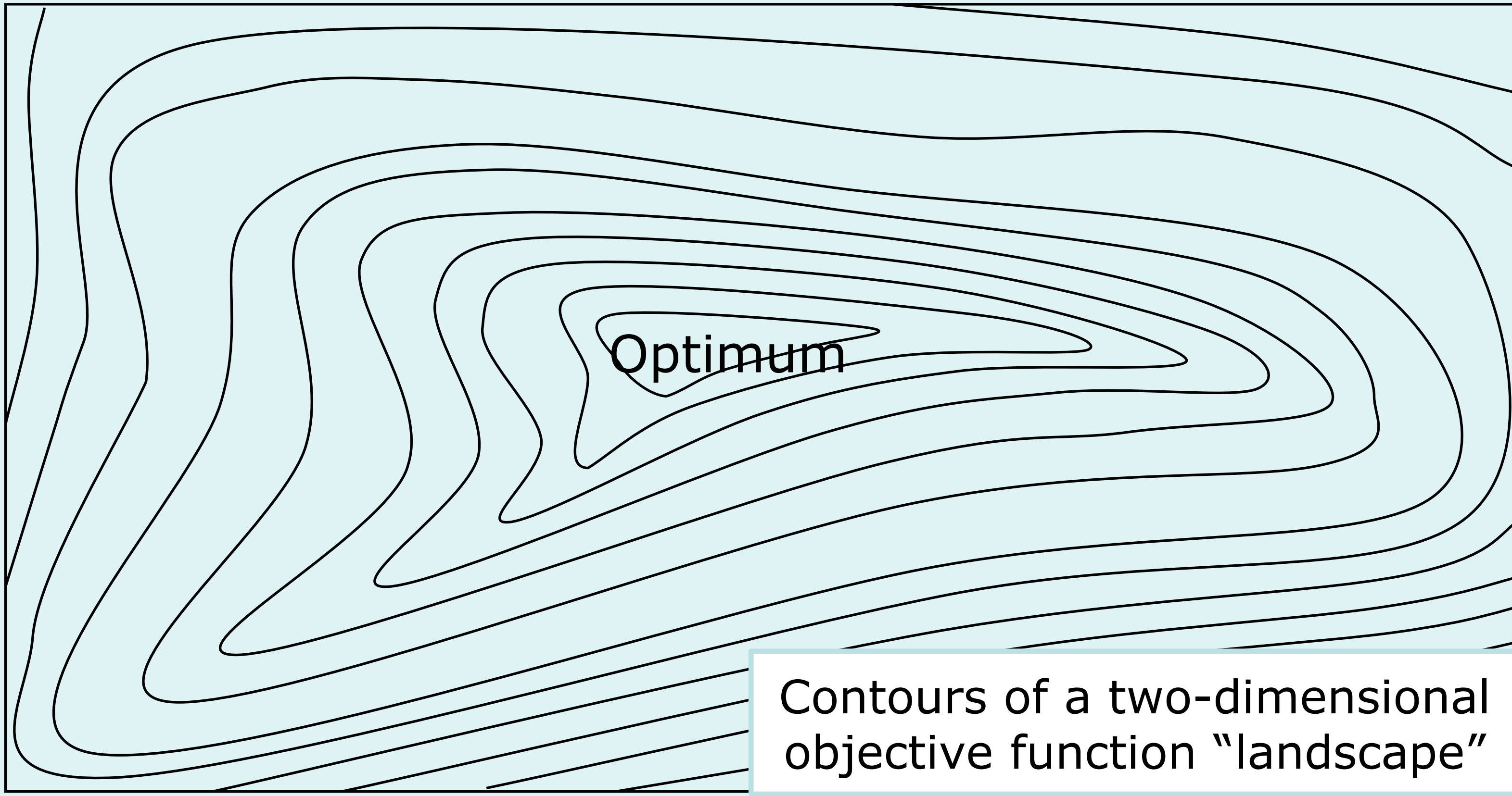
Optimisation

- Image registration is done by **optimisation**.

- Optimisation involves finding some "best" parameters according to an "objective function" (to be either minimised or maximised)



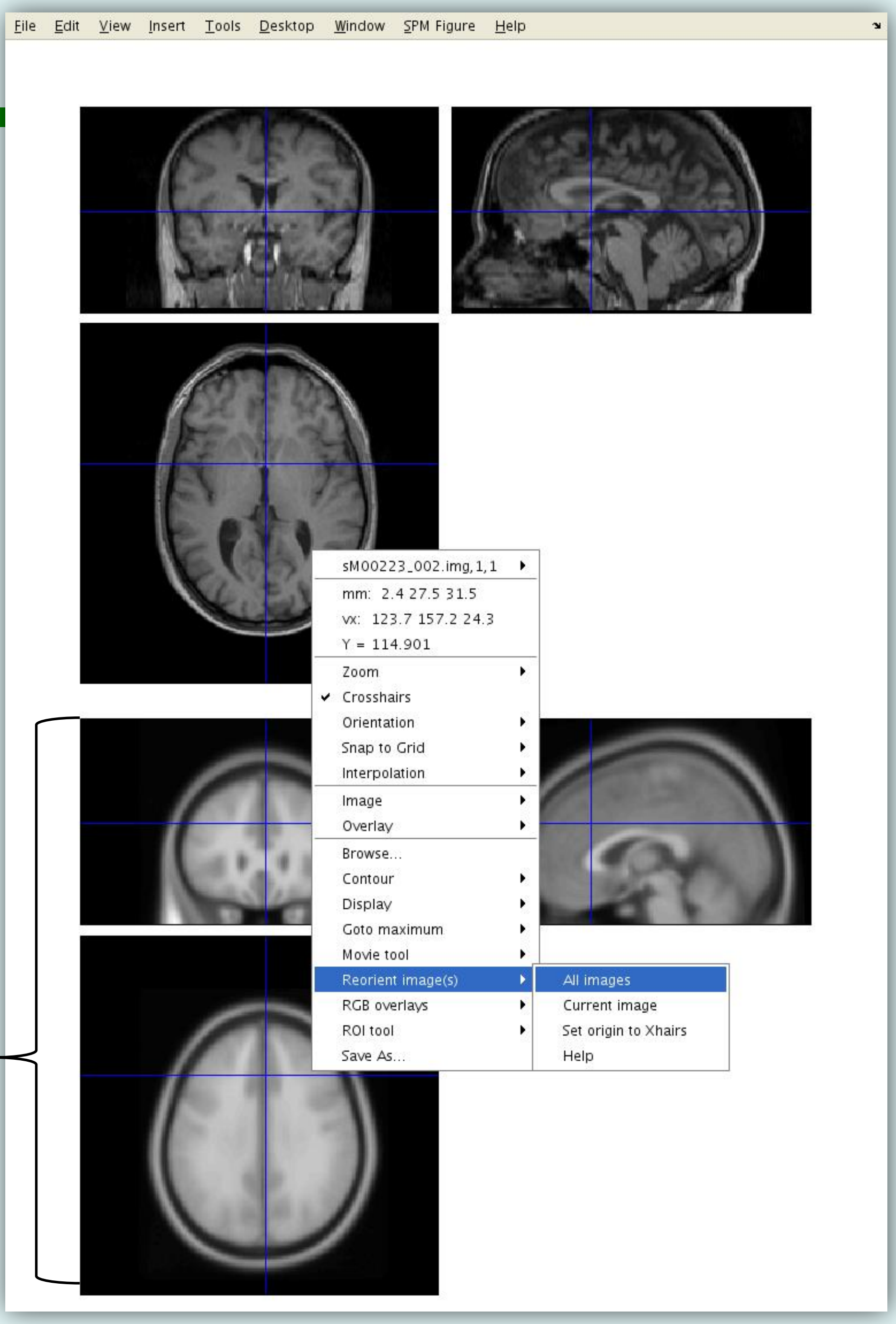
Optimisation, multiple parameters



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:

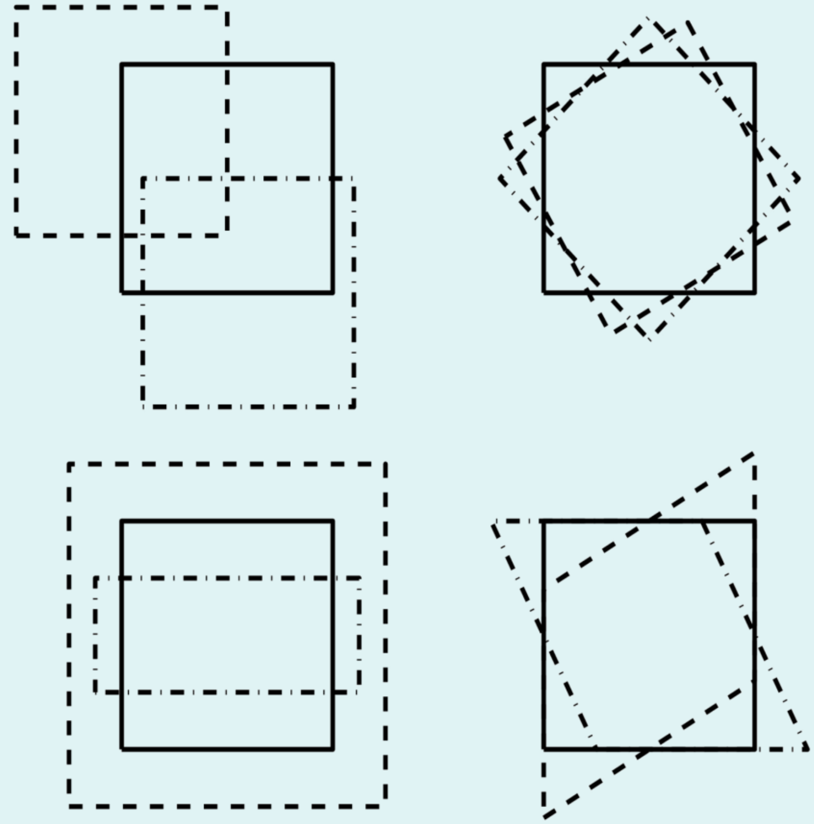
  $x_1 = s_x\, x_0$

  $y_1 = s_y\, y_0$

- 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:

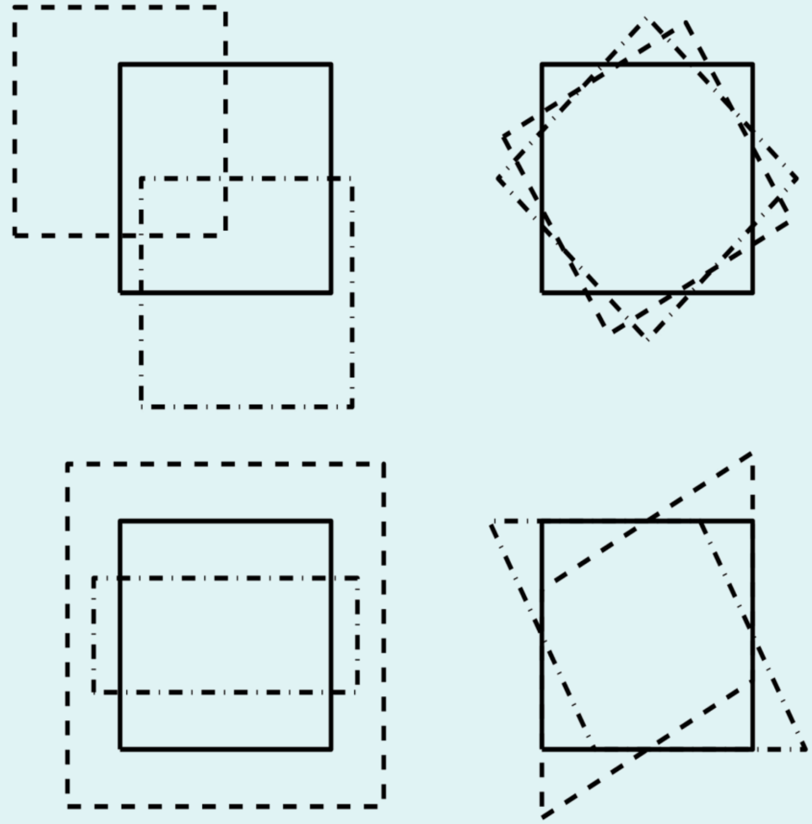
  $x_1 = s_x\ x_0 + 0\ y_0 + 0$

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

- 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:

  $\mathbf{p_1} = \mathbf{M}\ \mathbf{p_0}$

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

- 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

- The order of the operations matters!

Voxel-to-world transformation

"Voxel-to-world transforms" =

Affine transform **M** associated with each image

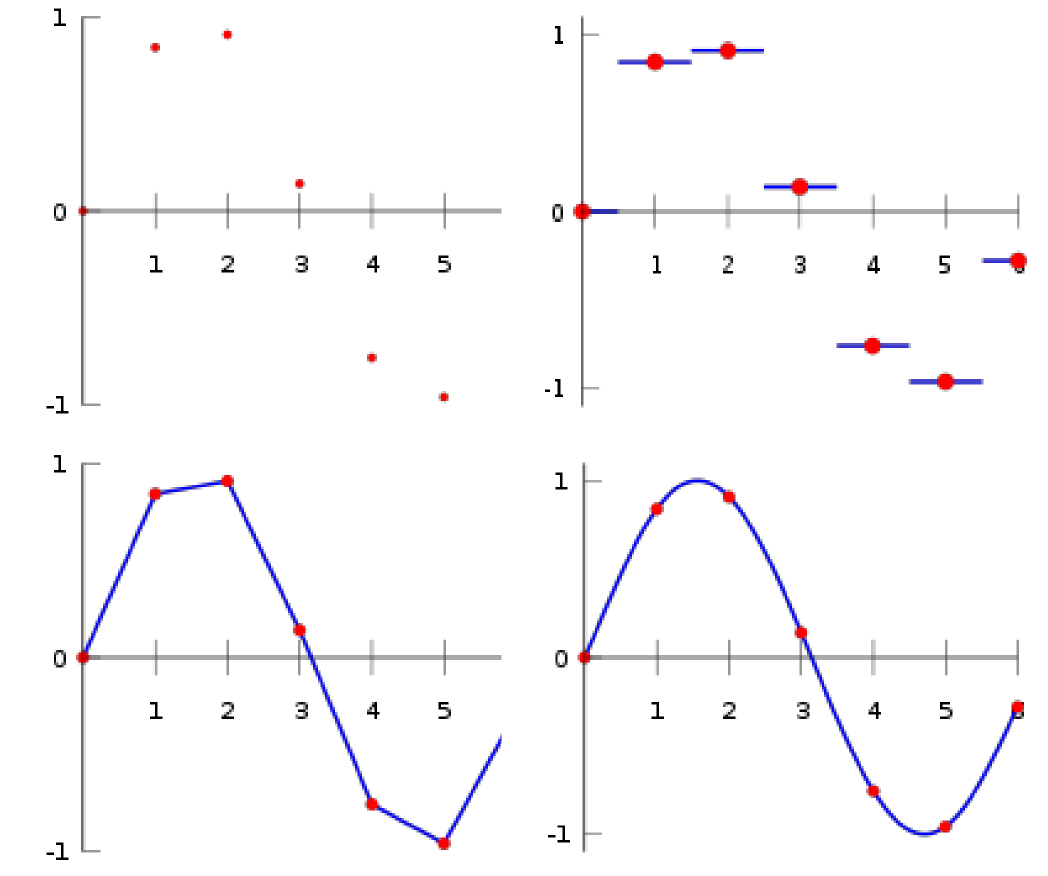
- Maps from voxels (**i**=$[1 \ldots N_i]$, **j**=$[1 \ldots N_j]$, **k**=$[1 \ldots N_k]$) to some real world co-ordinate system [**x**, **y**, **z**]. e.g.,
  - Scanner co-ordinates (images from DICOM) or MNI coordinates (spatially normalised)
  - Includes *voxel size*, *head orientation* & *"space 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

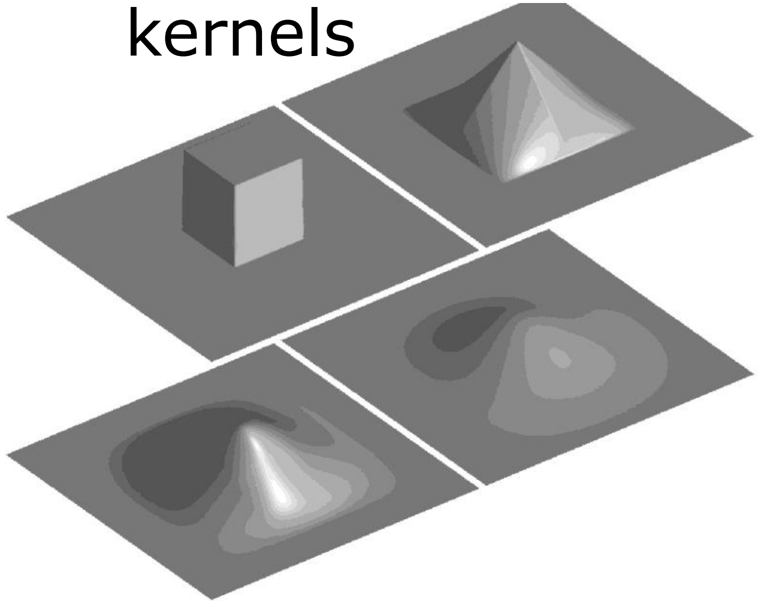


Image resampling

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

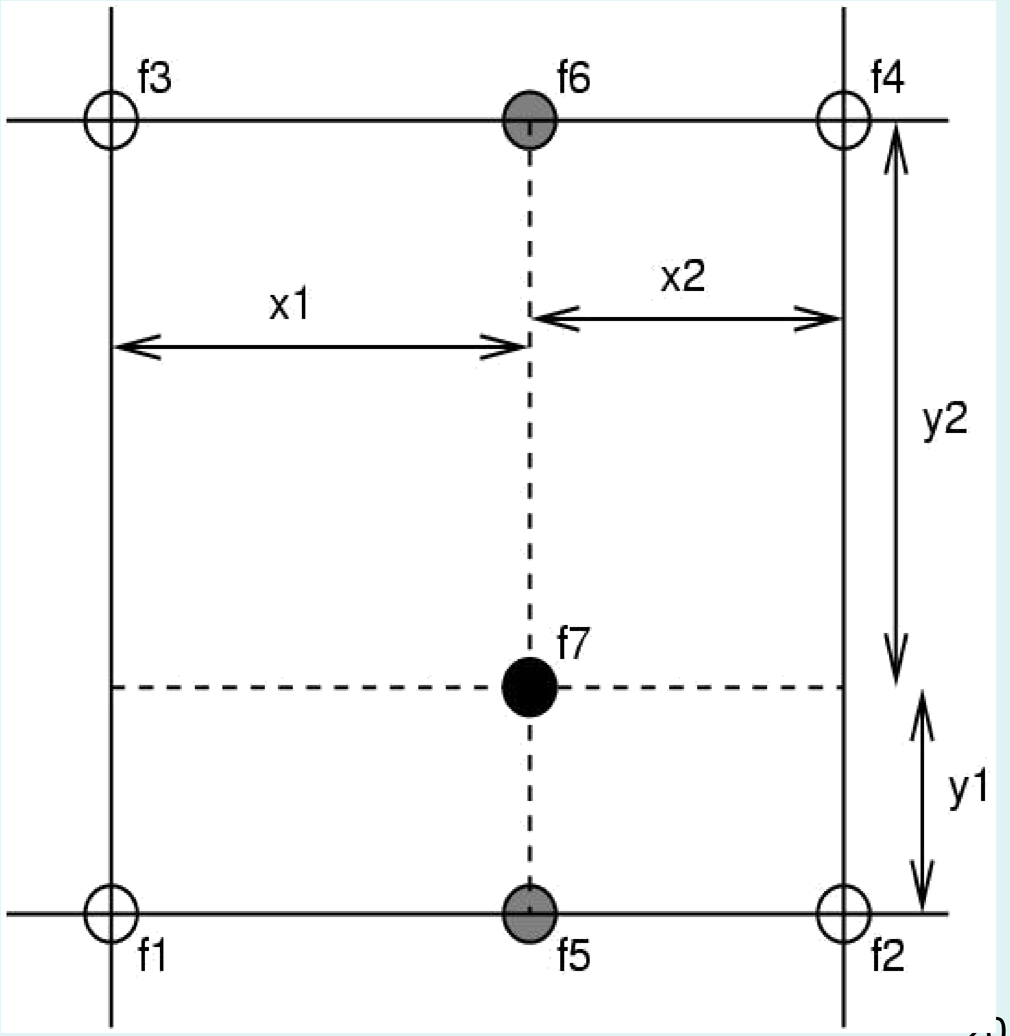


Image resampling, example 1

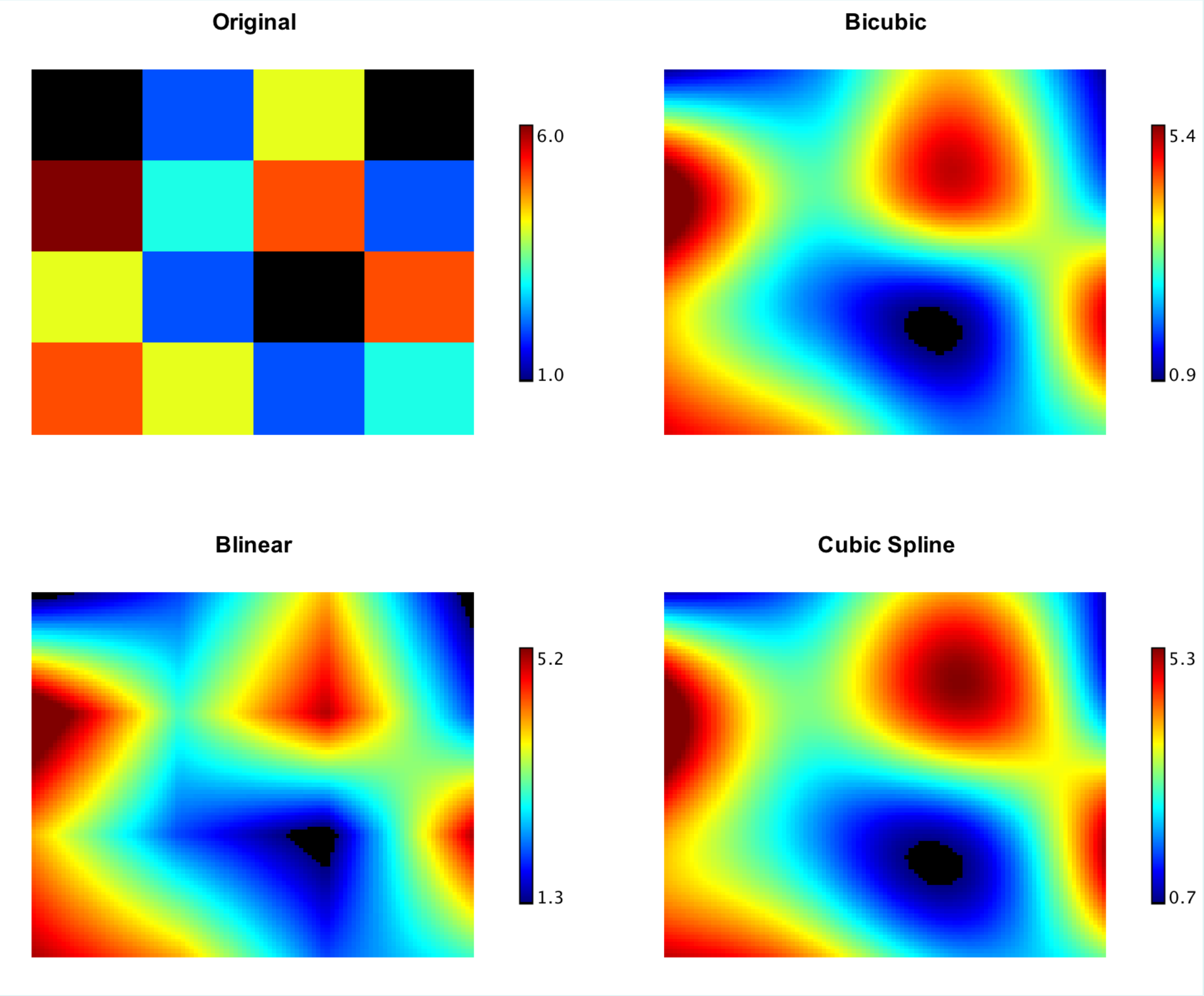
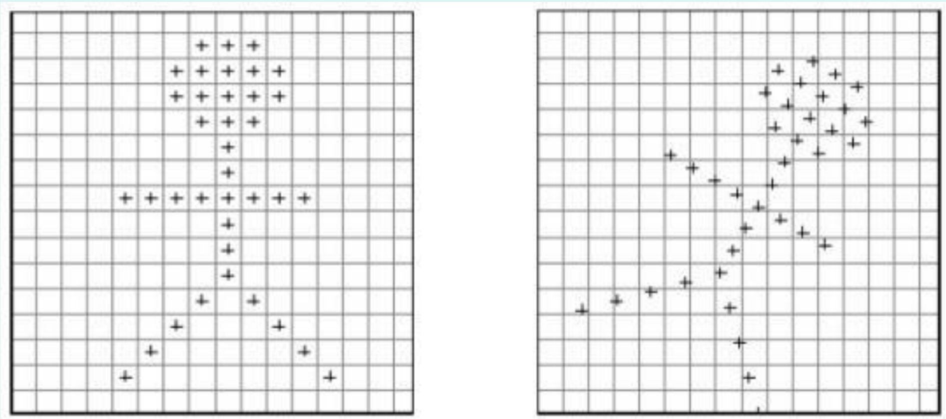
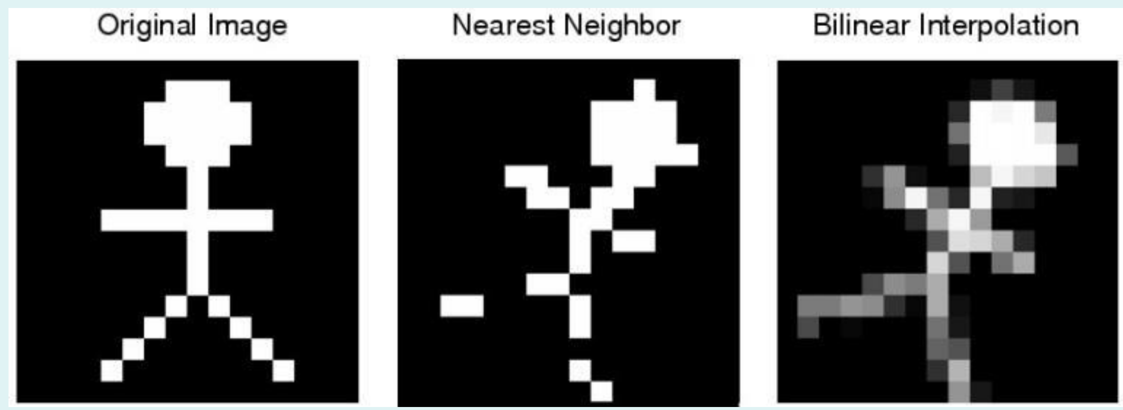


Image resampling, example 2





Binary (or index) image

→ need to preserve property

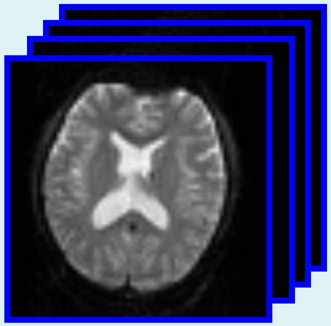
→ no need for smooth interpolation but…

Various registration problems

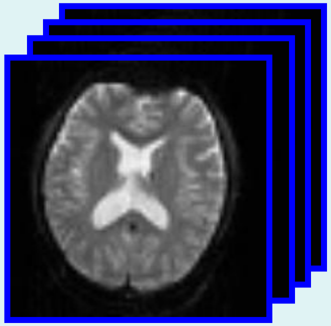
		Rigid body	Image warping
	Brain images	Within subject	Between subjects
Same contrast	Within modality		
Different contrast	Between modality		

Pre-processing overview

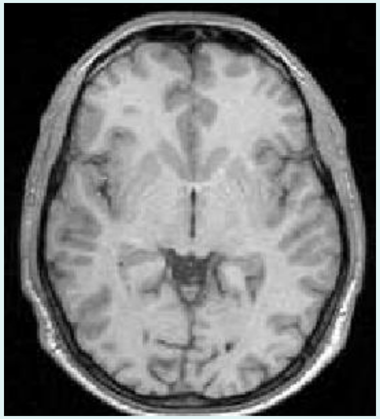
fMRI time-series



Motion (& distortion)
Correction



Anatomical MRI



Coregister

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

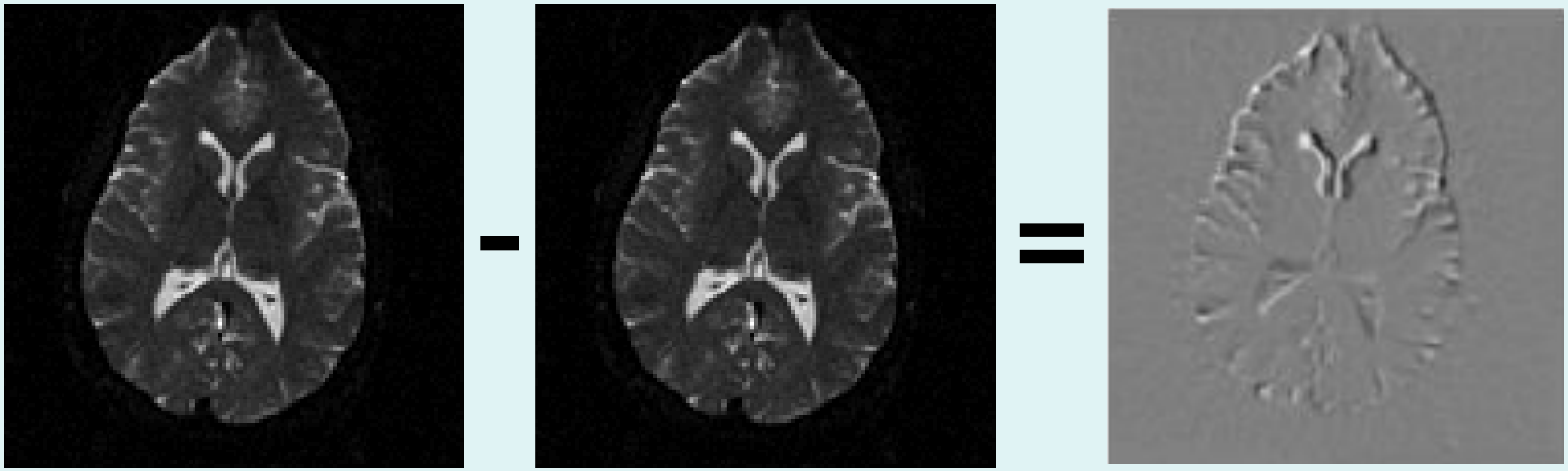
Various registration problems

		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

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

- Simple relationship between intensities in one image, versus those in the other

  (Assumes normally distributed differences, i.e. residuals)

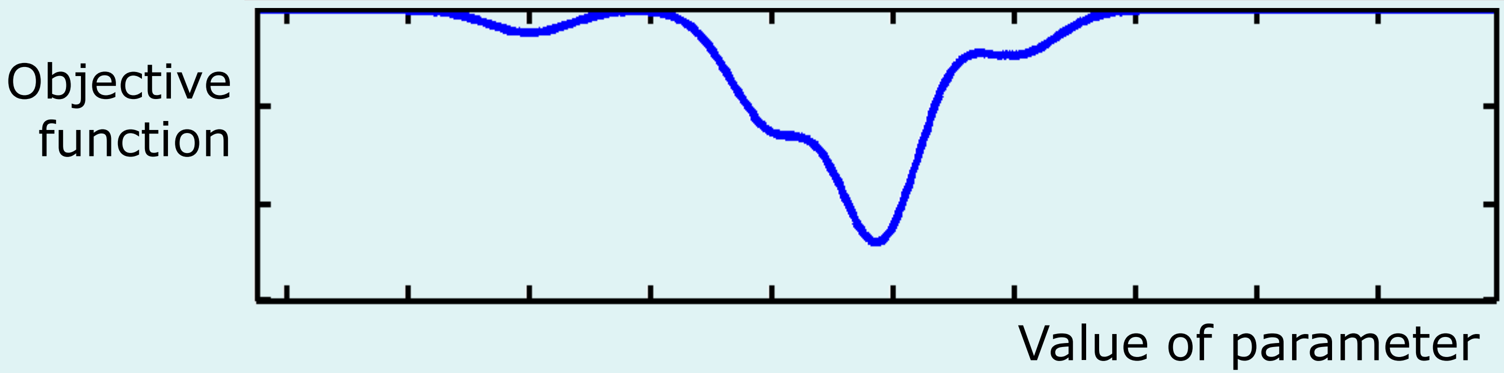
Within-subject registration

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

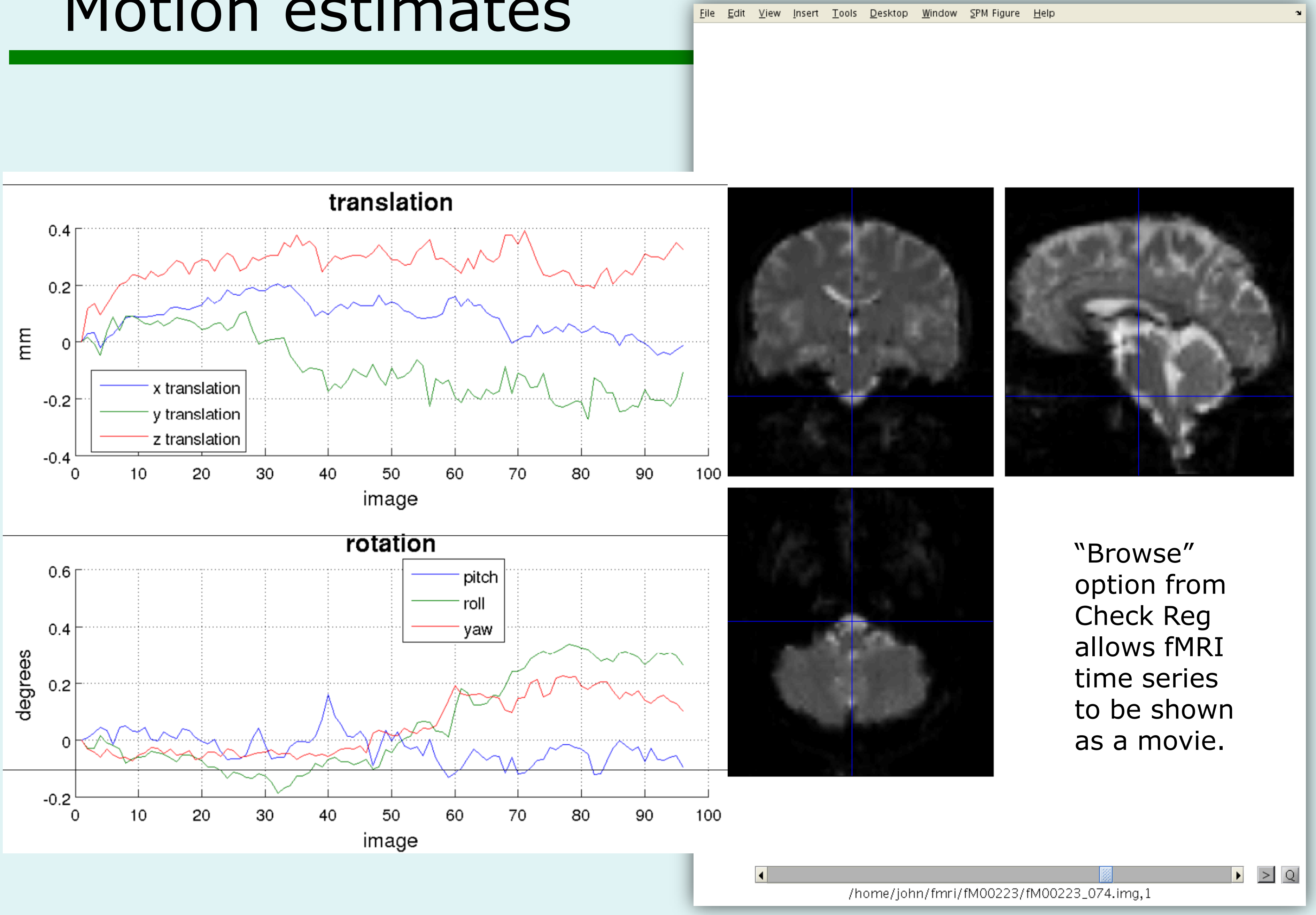
$$\rightarrow \quad c(I,J) = \sum_{n=1}^{N} \left(I_n - J_n\right)^2$$

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

$$R = \begin{pmatrix} 1 & 0 & 0 & \mathrm{Xtrans} \\ 0 & 1 & 0 & \mathrm{Ytrans} \\ 0 & 0 & 1 & \mathrm{Ztrans} \\ 0 & 0 & 0 & 1 \end{pmatrix} \times \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & \cos f & \sin f & 0 \\ 0 & -\sin f & \cos f & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \times \begin{pmatrix} \cos q & 0 & \sin q & 0 \\ 0 & 1 & 0 & 0 \\ -\sin q & 0 & \cos q & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \times \begin{pmatrix} \cos\Omega & \sin\Omega & 0 & 0 \\ -\sin\Omega & \cos\Omega & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix}$$



Motion estimates



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

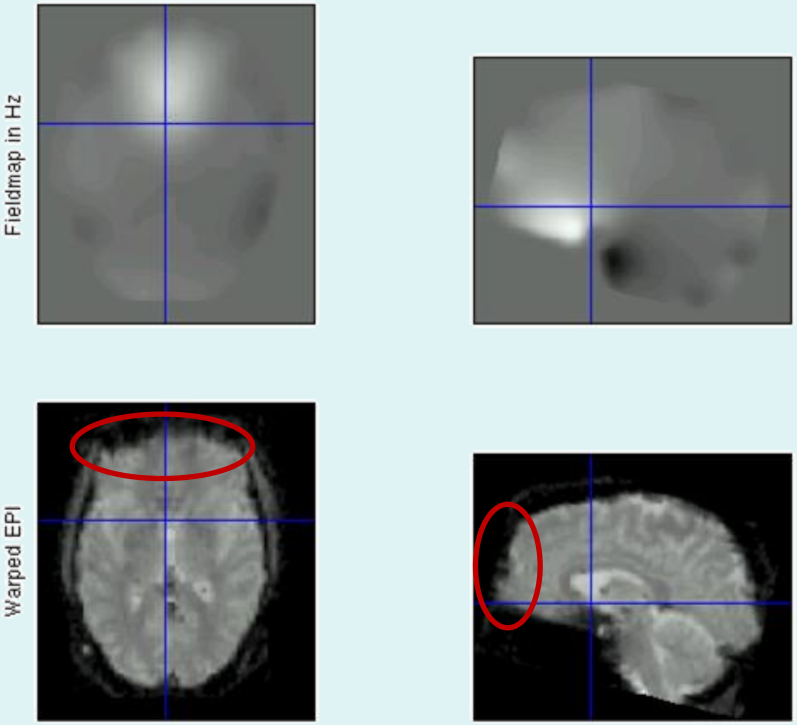
Residual errors from aligned fMRI

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

EPI distortion

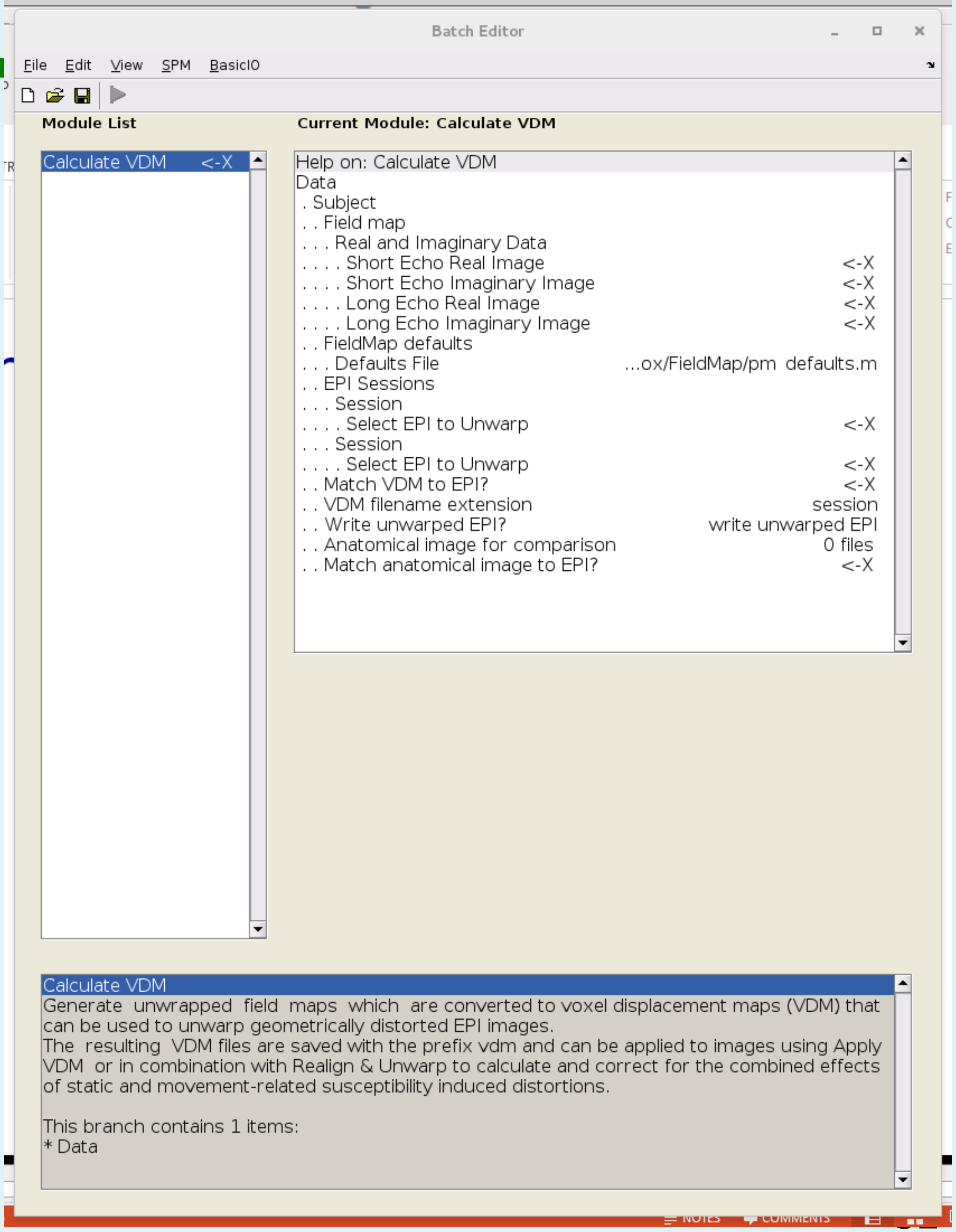
- Magnetic susceptibility differs among tissues.
- Greatest difference is between air and tissue.
- Subject disrupts B_0 field, rendering it inhomogeneous
- Distortions in phase-encode direction



FieldMap toolbox

- Computes a voxel-displacement map (VDM) from "fieldmap" scans.

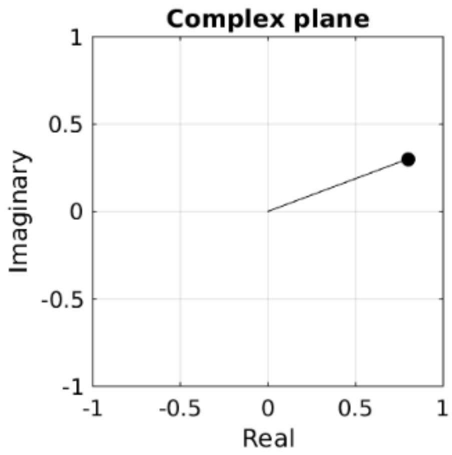
- Used to correct distortions in EPI.

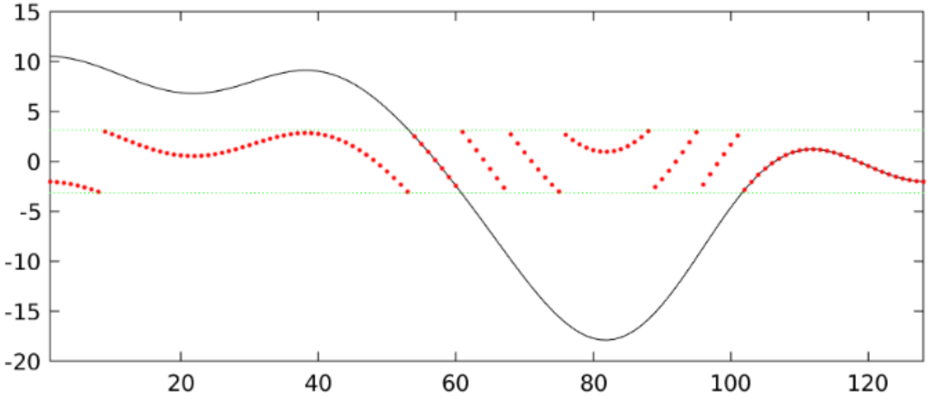


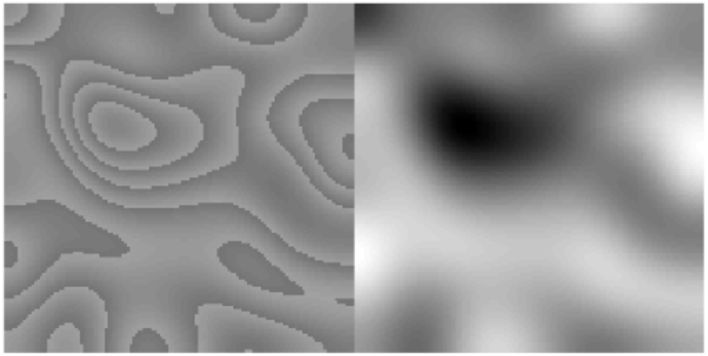
Phase unwrapping

- Phase of complex data used.
- $-\pi < \text{phase} < \pi$
- Phase-unwrapping needed.
- Phase is poorly defined when magnitude is small relative to noise

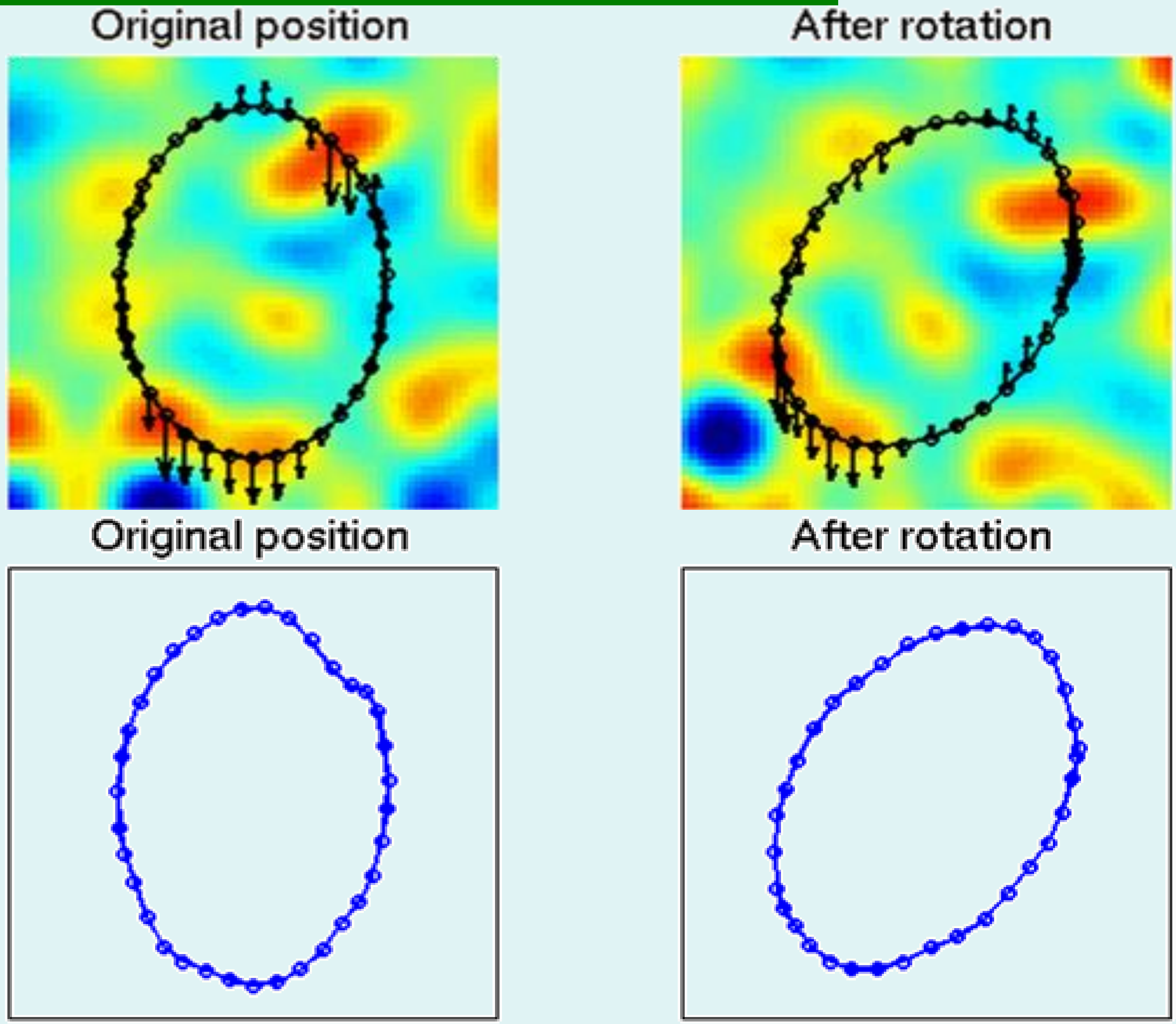
➔ Part that is most likely to go wrong.



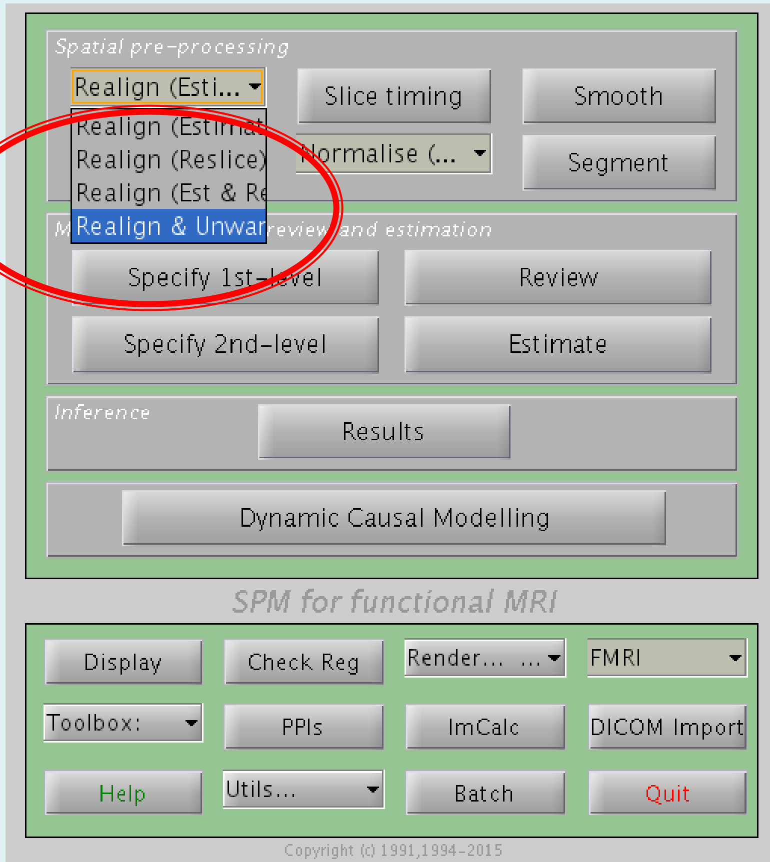


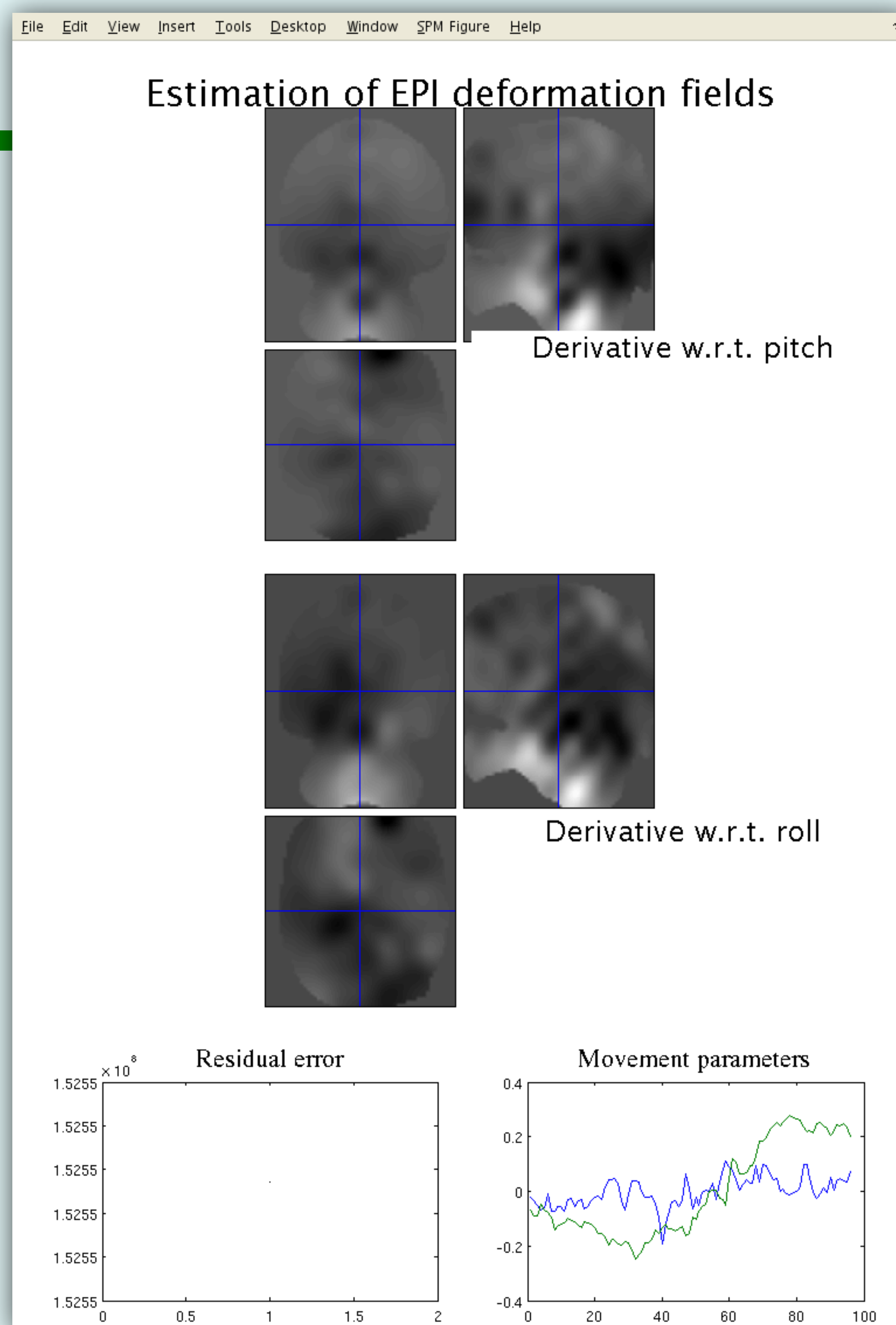


Movement-by-distortion interaction



“Realign & Unwarp”



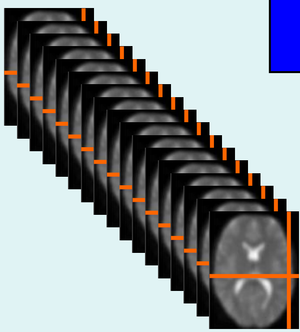


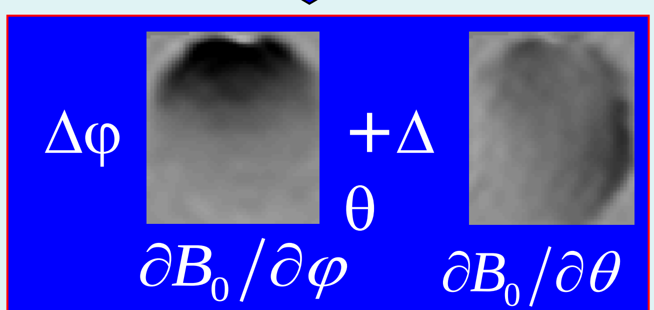
Correcting for distortion changes

Estimate reference from mean of all scans.

Estimate new distortion fields for each image:

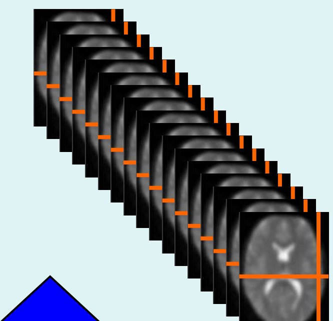
- estimate rate of change of field with respect to the current estimate of movement parameters in **pitch** and **roll**.





Estimate movement parameters.

Unwarp time series.



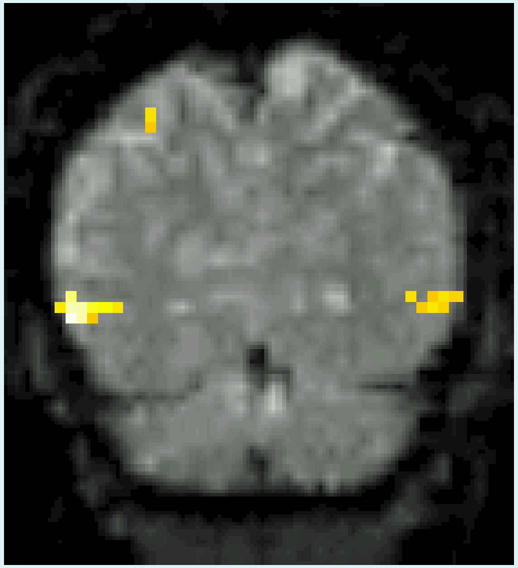
Andersson et al, 2001

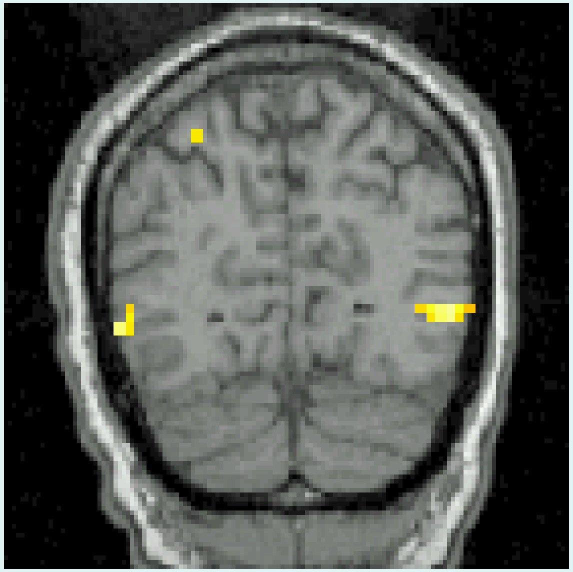
Various registration problems

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

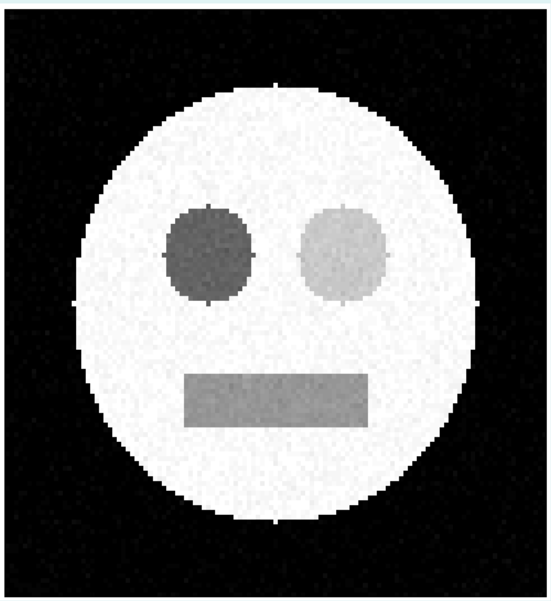
"Coregistration"

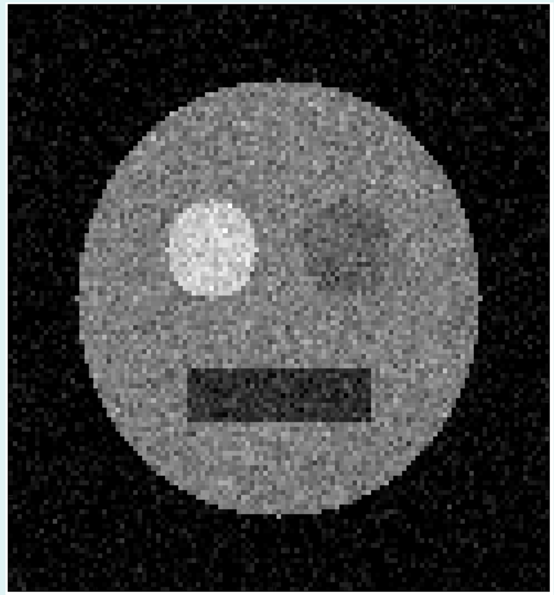
- Inter-modal registration.
- Match images from same subject but different modalities:
  - – anatomical localisation of single subject activations
  - – achieve more precise spatial normalisation of functional image using anatomical image.

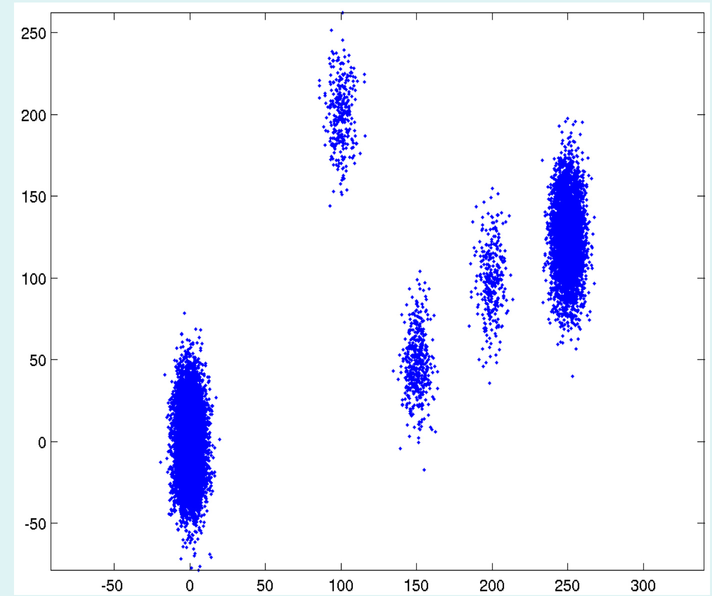


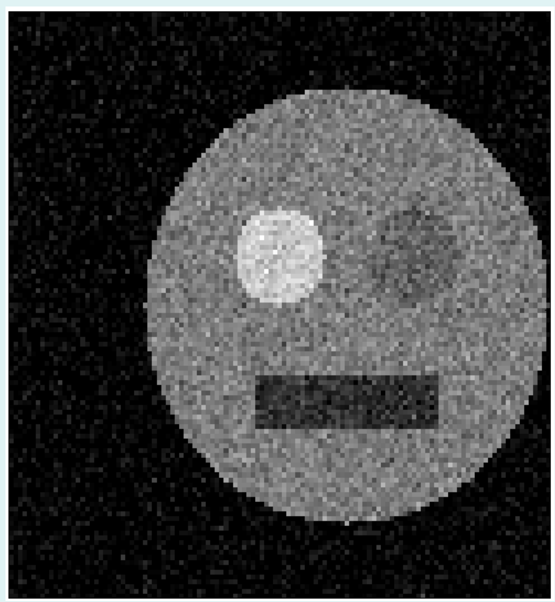


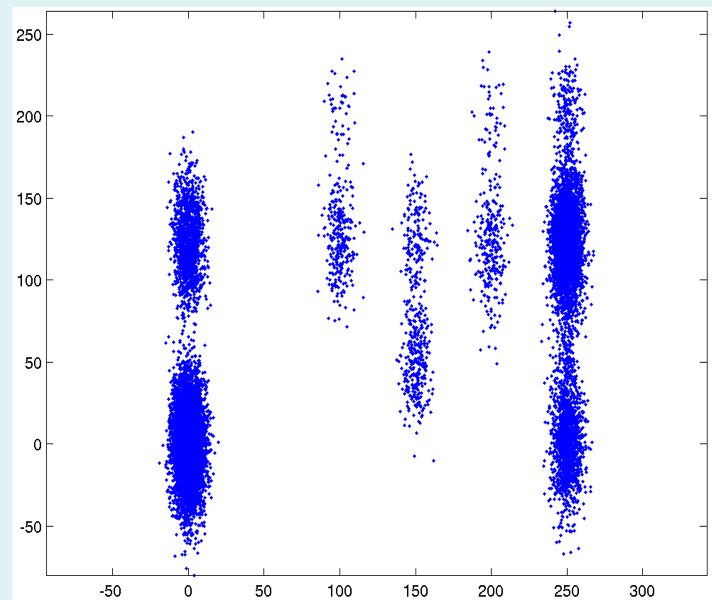
Joint histogram & Mutual information



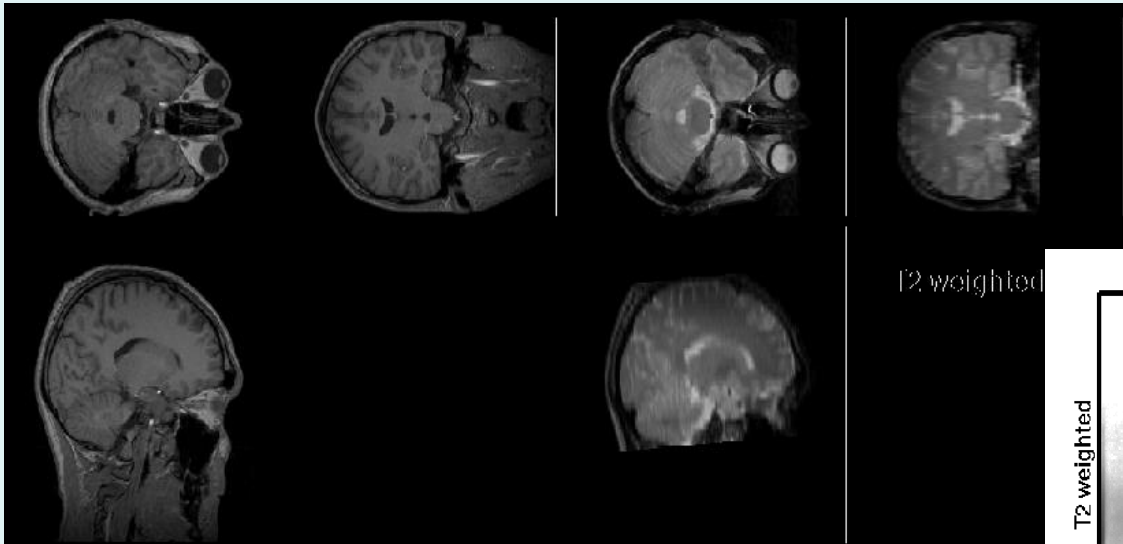


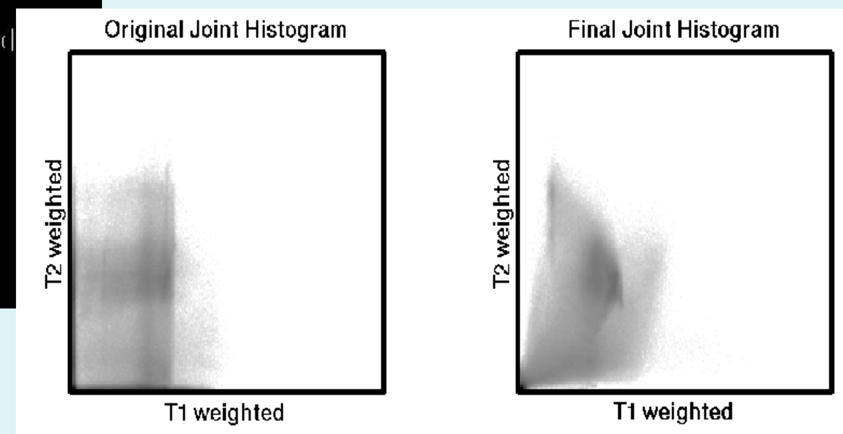






Mutual Information, real case





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

Within-subject registration

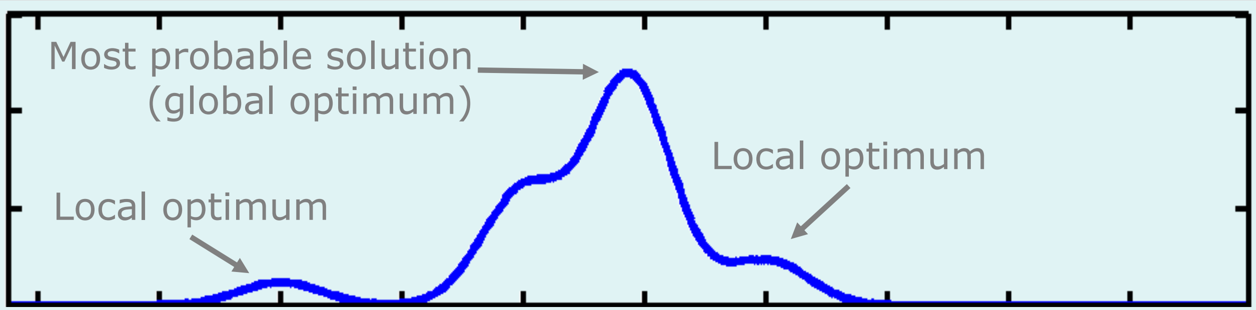
- Realign images *I* (fixed) and *J* (moving):
- Criteria to optimize:

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

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

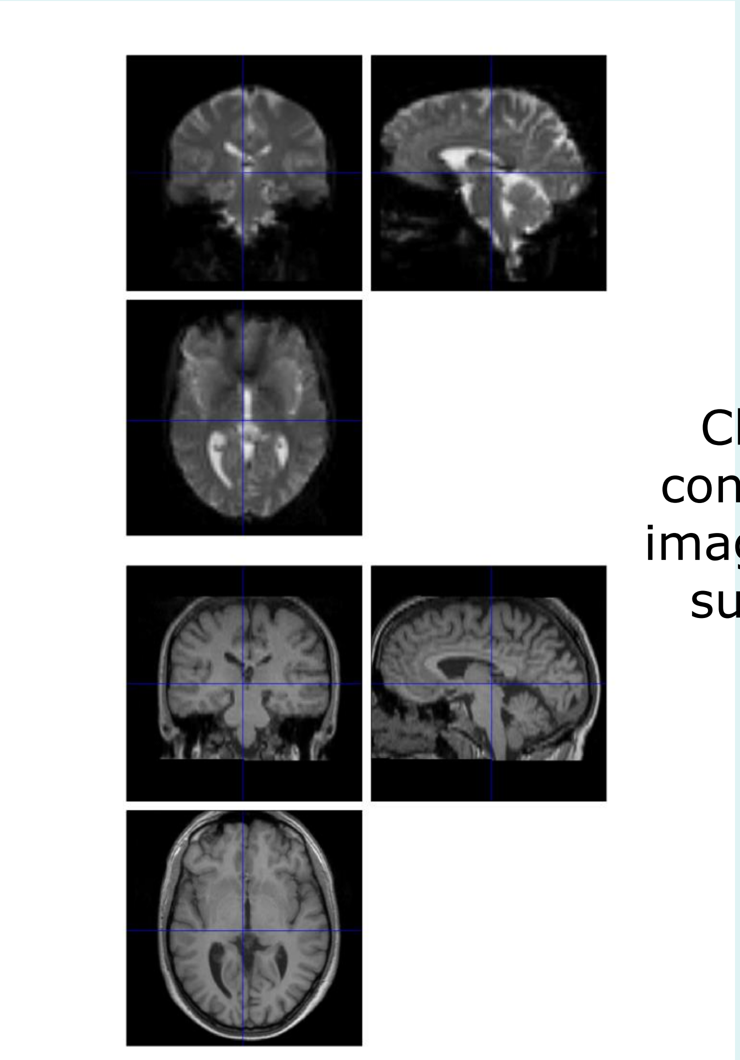
$$R = \begin{pmatrix} 1 & 0 & 0 & X_{trans} \\ 0 & 1 & 0 & Y_{trans} \\ 0 & 0 & 1 & Z_{trans} \\ 0 & 0 & 0 & 1 \end{pmatrix} \times \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & \cos f & \sin f & 0 \\ 0 & -\sin f & \cos f & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \times \begin{pmatrix} \cos q & 0 & \sin q & 0 \\ 0 &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

Objective function

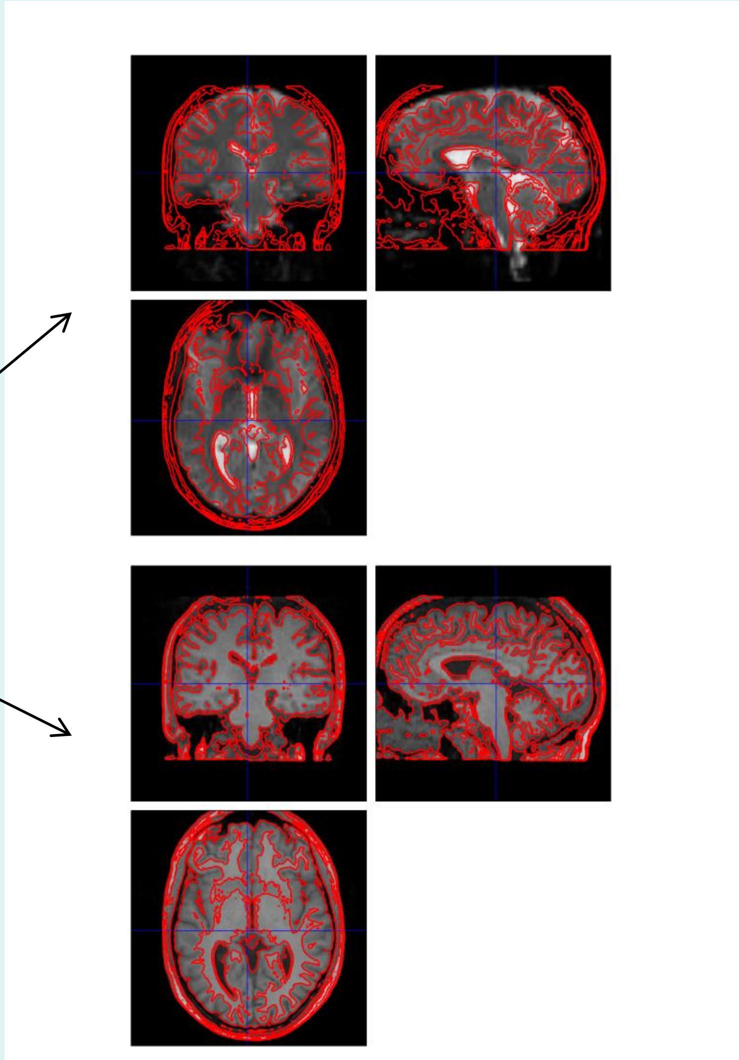


Value of 1 parameter

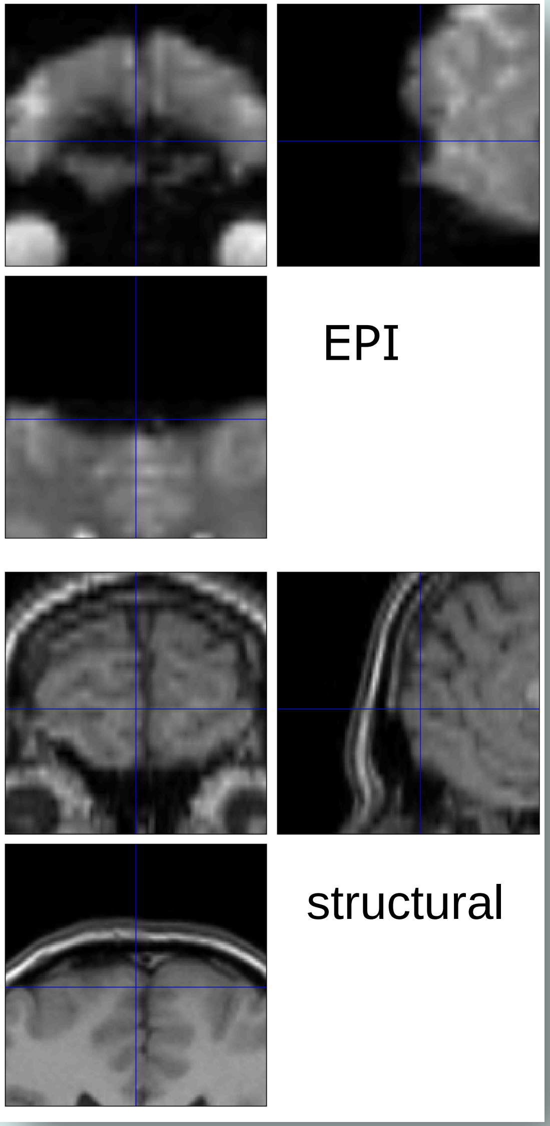
"CheckReg" to assess alignment

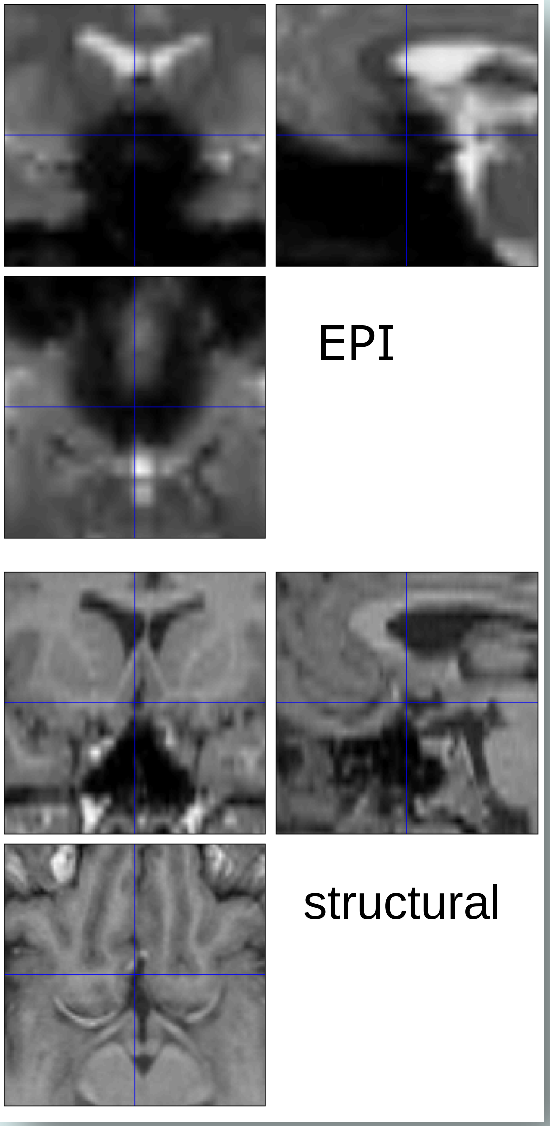


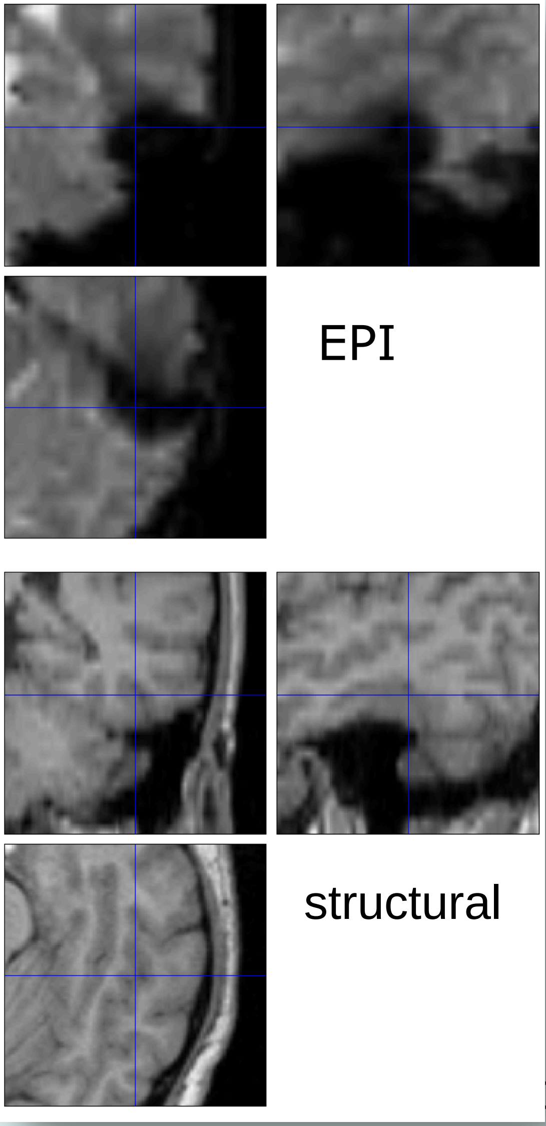
CheckReg allows contours from one image to be shown superimposed on another



EPI dropout and distortion







Voxel-to-world transformation

"Voxel-to-world transforms" =

Affine transform **M** associated with each image

- Maps from voxels ($\mathbf{i}=[1 \ldots N_i]$, $\mathbf{j}=[1 \ldots N_j]$, $\mathbf{k}=[1 \ldots N_k]$) to some real world co-ordinate system [**x**, **y**, **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.

$$\begin{tikzcd} \text{Img A: vx} \arrow[r, "M_A"] & \text{mm} \\ \text{Img B: vx} \arrow[r, "M_B"] & \text{mm} \arrow[u, bend right, "R"'] \end{tikzcd}$$

- 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} $\Rightarrow M^*_B\, M_A^{-1}$

Various registration problems

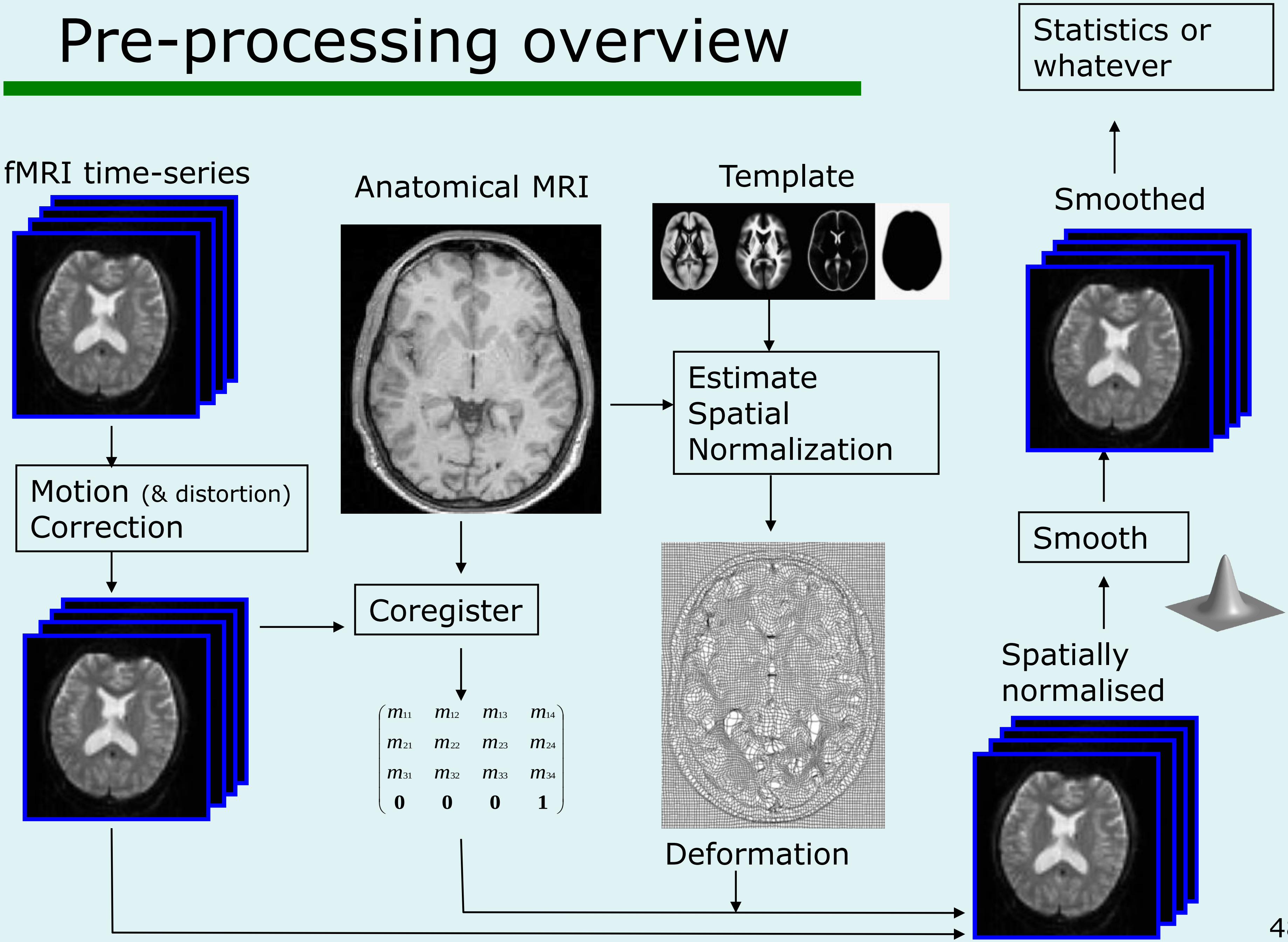
		Rigid body	Image warping
	Brain images	Within subject	Between subjects
Same contrast	Within modality	**X**	X
Different contrast	Between modality	**X**	

Content

- **Preliminaries**
- **Within-subject**
- **Between-subject**

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

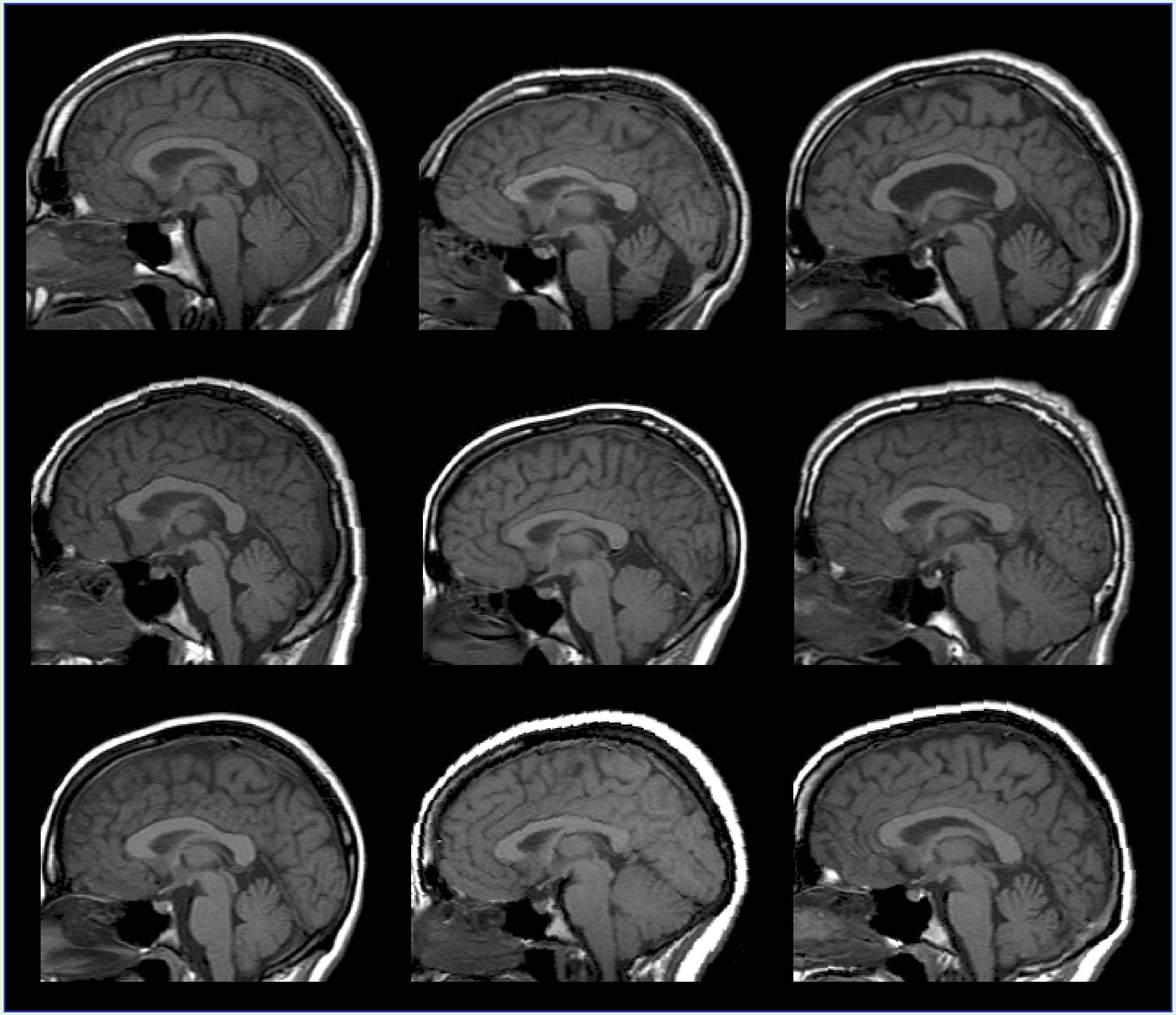
Pre-processing overview



Between subjects

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

Between subjects



Between subjects

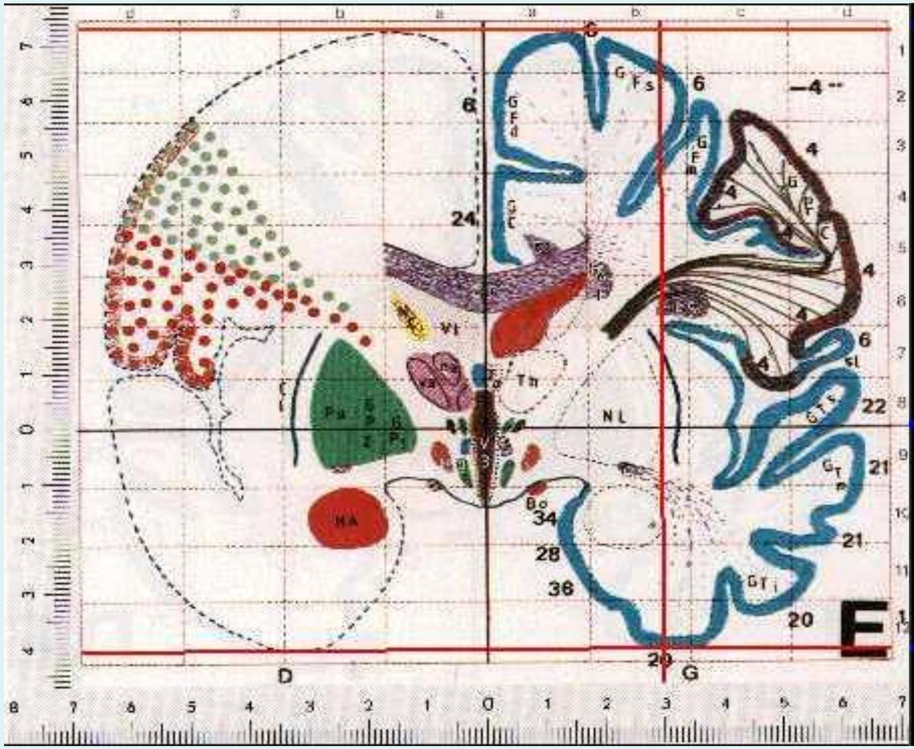
Brains of different subjects vary in *shape* and *size*.

→ Need to bring them all into a common anatomical space.

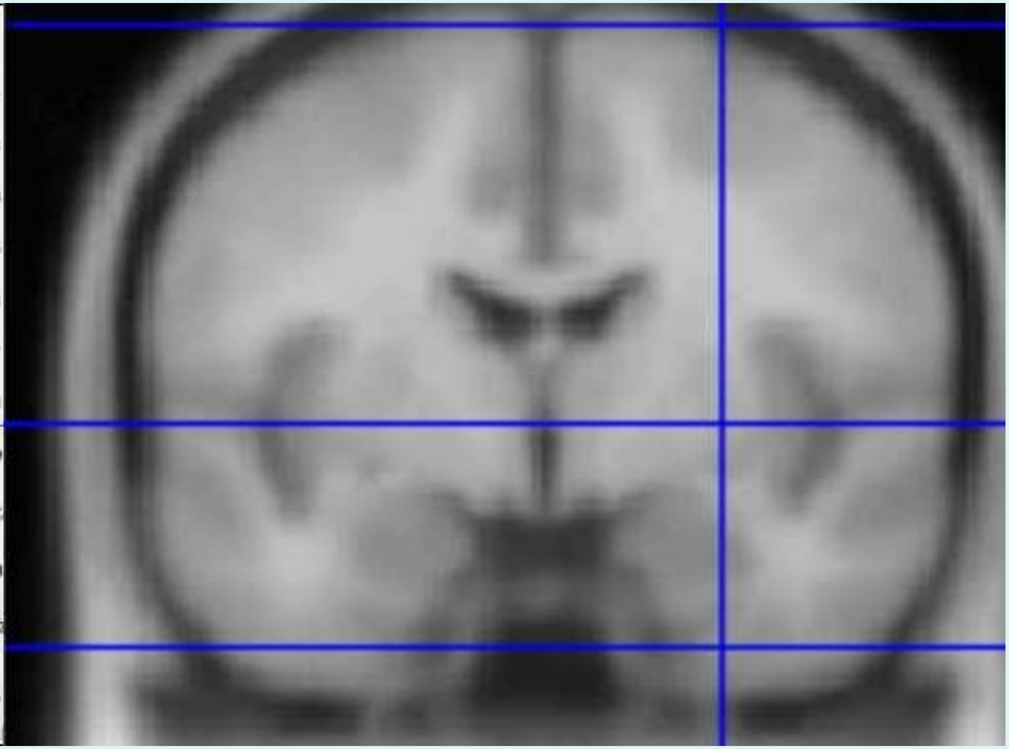
- Examine homologous regions across subjects
  - Improve anatomical specificity
  - Improve sensitivity
- Report findings in a common anatomical space (e.g. MNI space)

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*

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

Between subjects

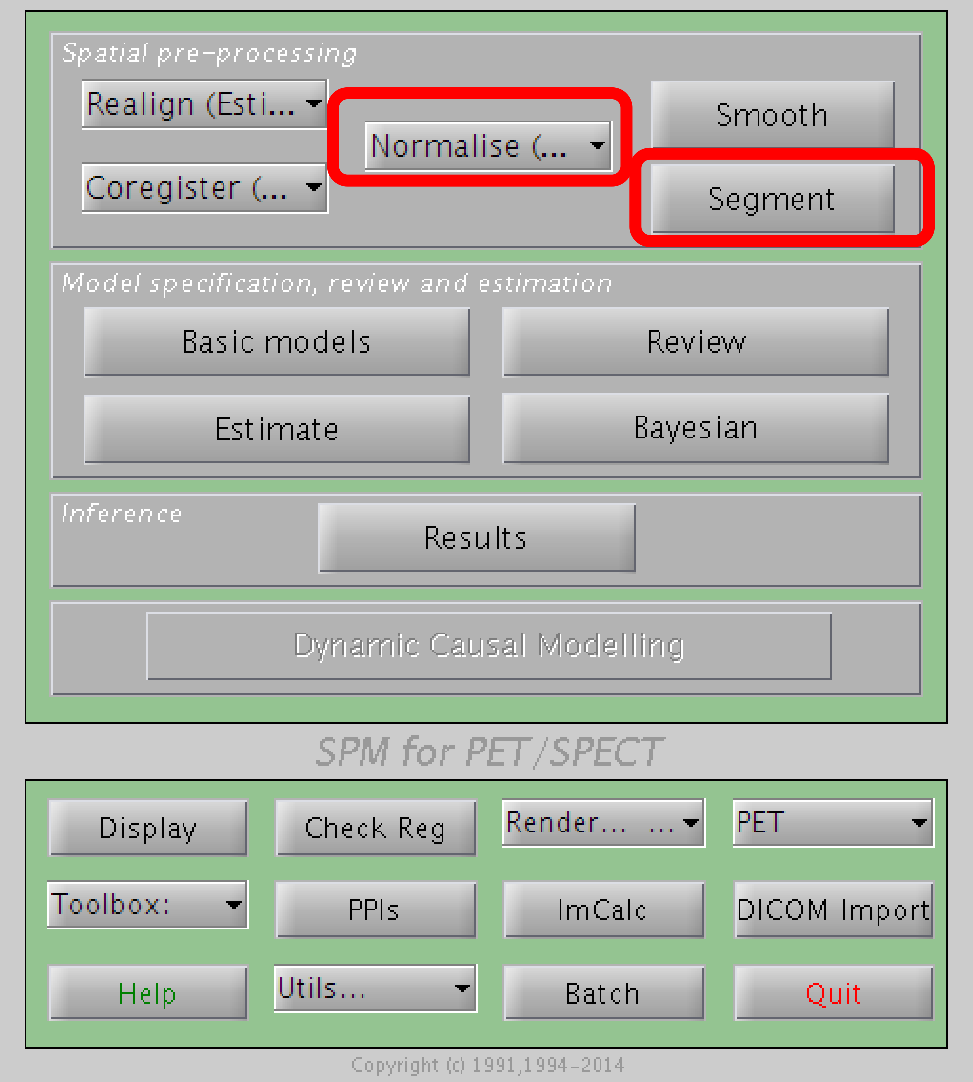
- Brains of different subjects vary in *shape* and *size*.
  → Need to bring them all into a common anatomical space.
  - Examine homologous regions across subjects
    - Improve anatomical specificity
    - Improve sensitivity
  - Report findings in a common anatomical space (e.g. MNI space)

- In SPM12, alignment is achieved by matching tissue classes, i.e. GM with GM, WM with WM,…

Normalise/Segment

- This is the same algorithm as for tissue segmentation.

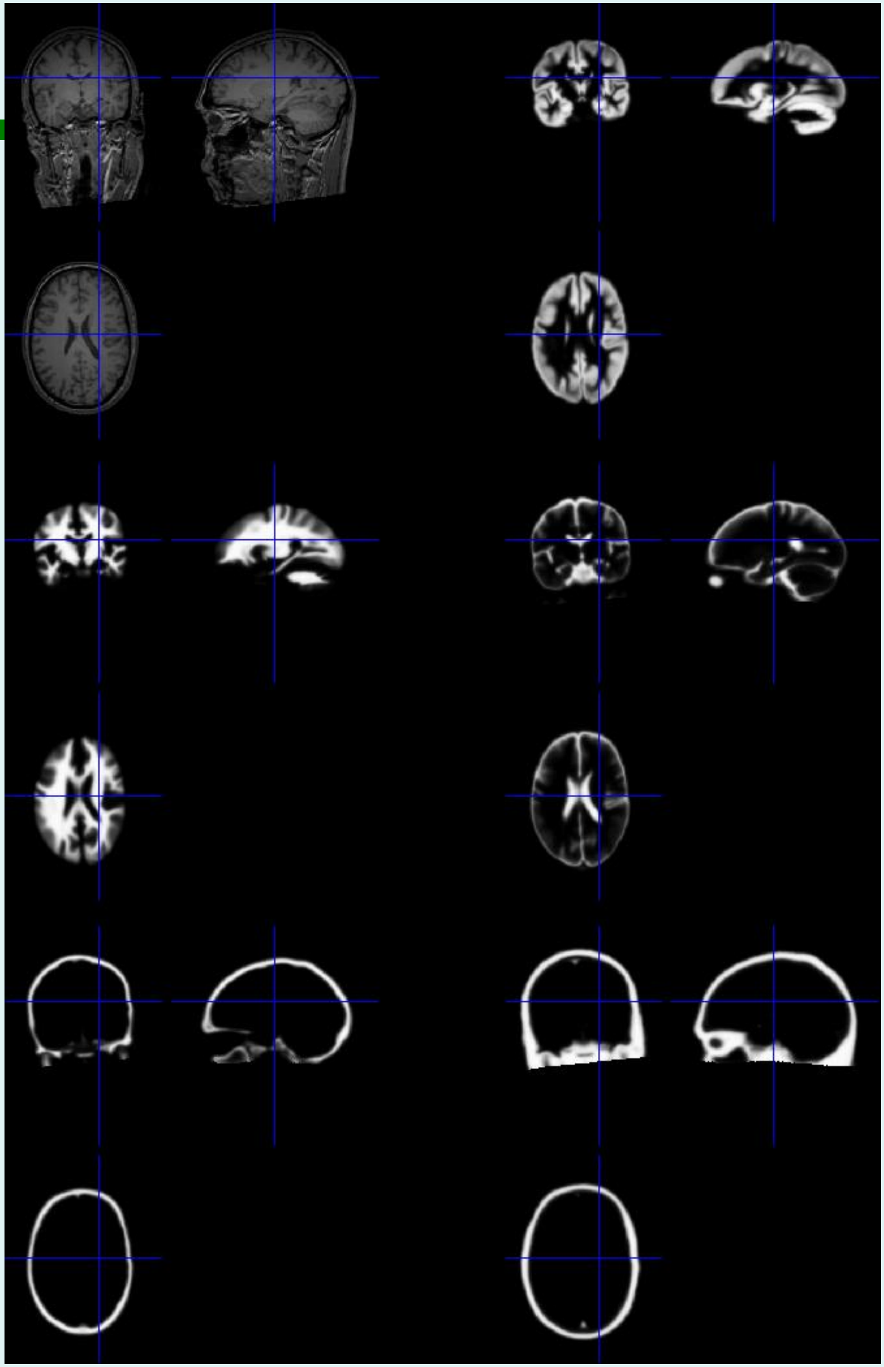
- Combines:
  - Mixture of Gaussians (MOG)
  - Bias Correction Component
  - Warping (Non-linear Registration) Component



Spatial normalisation

- Default spatial normalisation in SPM12 estimates nonlinear warps that match tissue probability maps to the individual image.

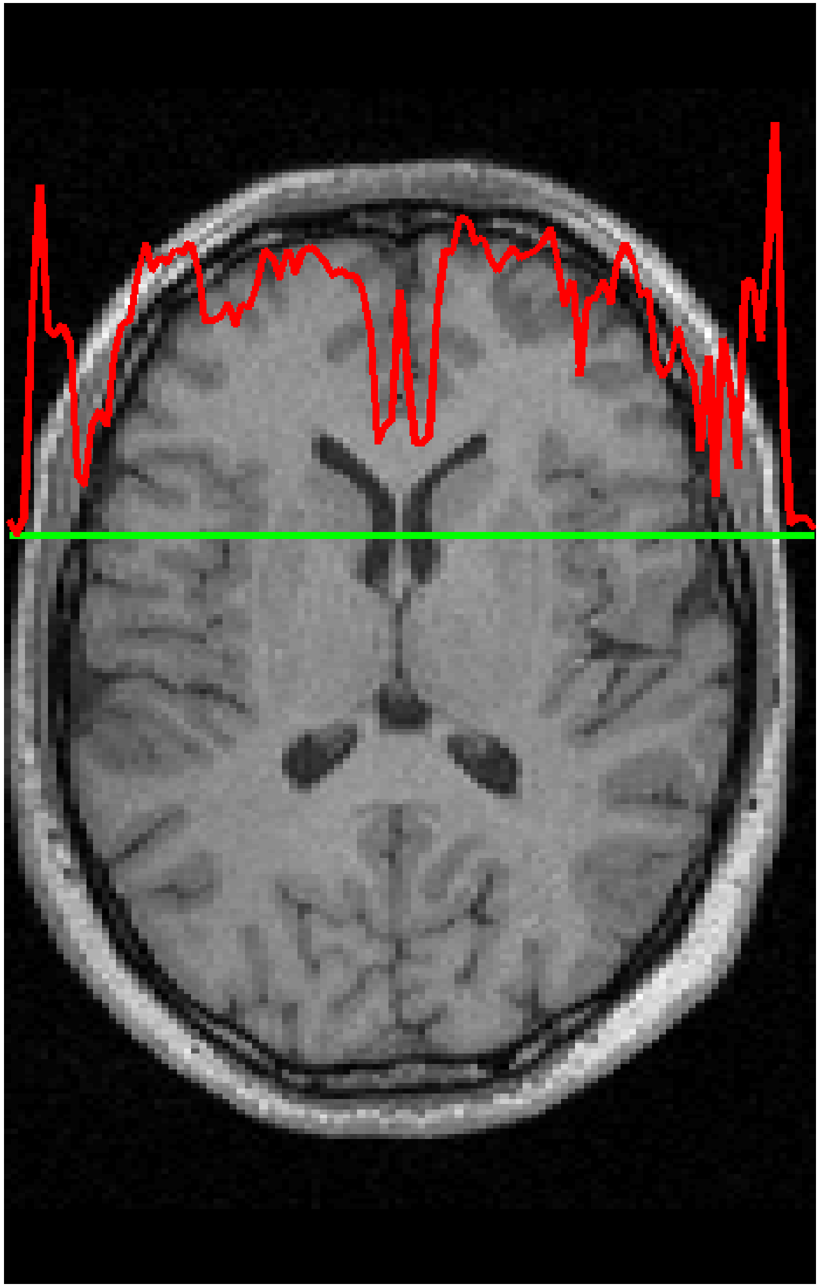
- Spatial normalisation achieved using the inverse of this transform.



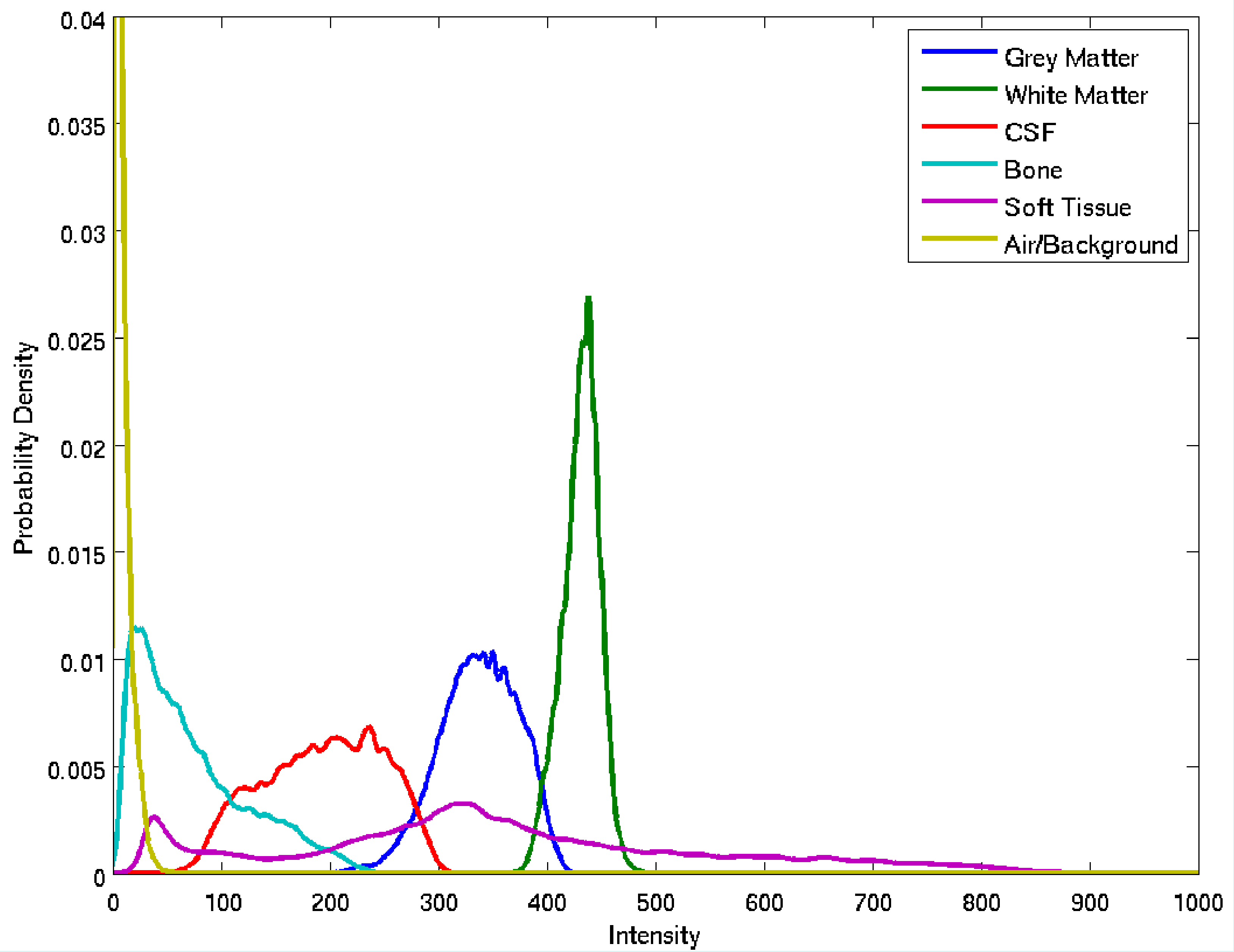
Segmentation

- 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)

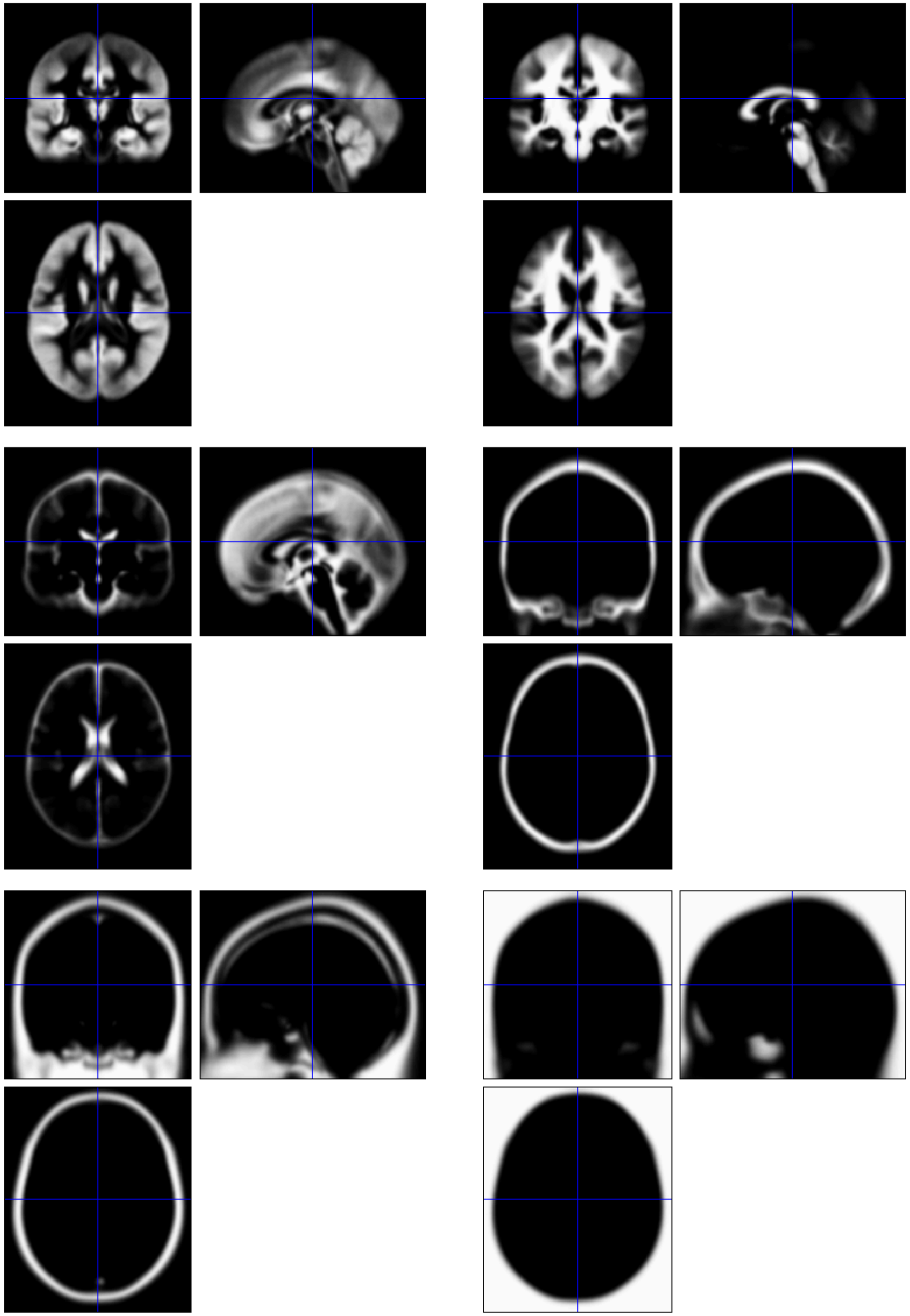


TPM’s

Tissue probability maps in SPM12.

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

➔ **defines the template space = reference!**



Modelling deformations, affine transform

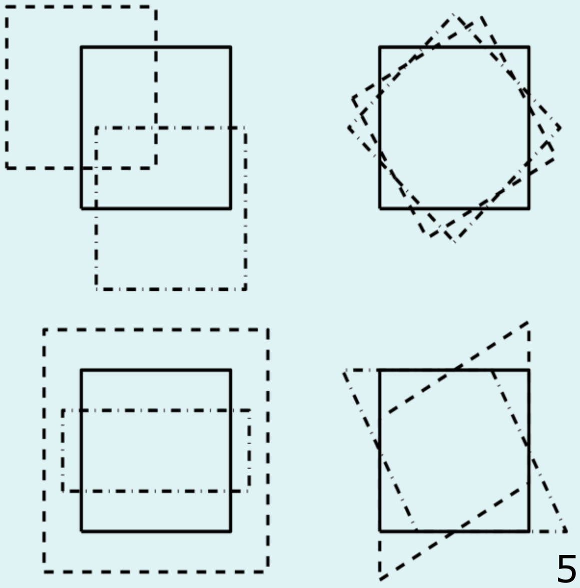
12 parameter affine transform

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

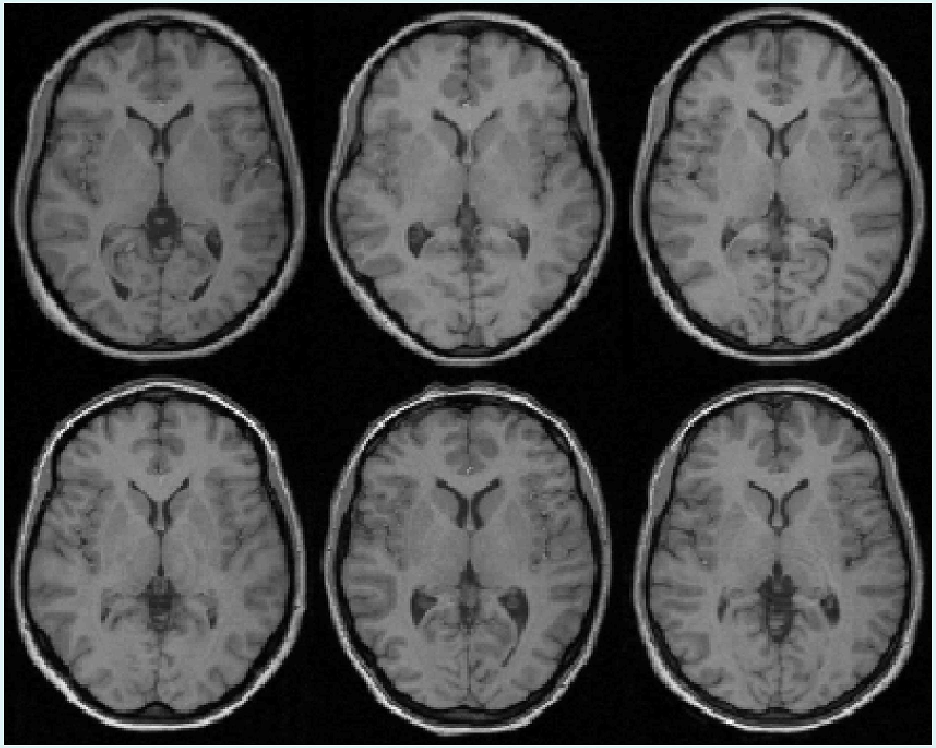
$$\begin{bmatrix} x_1 \\ y_1 \\ z_1 \\ 1 \end{bmatrix} = \begin{bmatrix} m_{11} & m_{12} & m_{13} & m_{14} \\ m_{21} & m_{22} & m_{23} & m_{24} \\ m_{31} & m_{32} & m_{33} & m_{34} \\ 0 & 0 & 0 & 1 \end{bmatrix} \times \begin{bmatrix} x_0 \\ y_0 \\ z_0 \\ 1 \end{bmatrix}$$

➔ Fits **overall** shape and size

➔ Need *warping* for local deformation



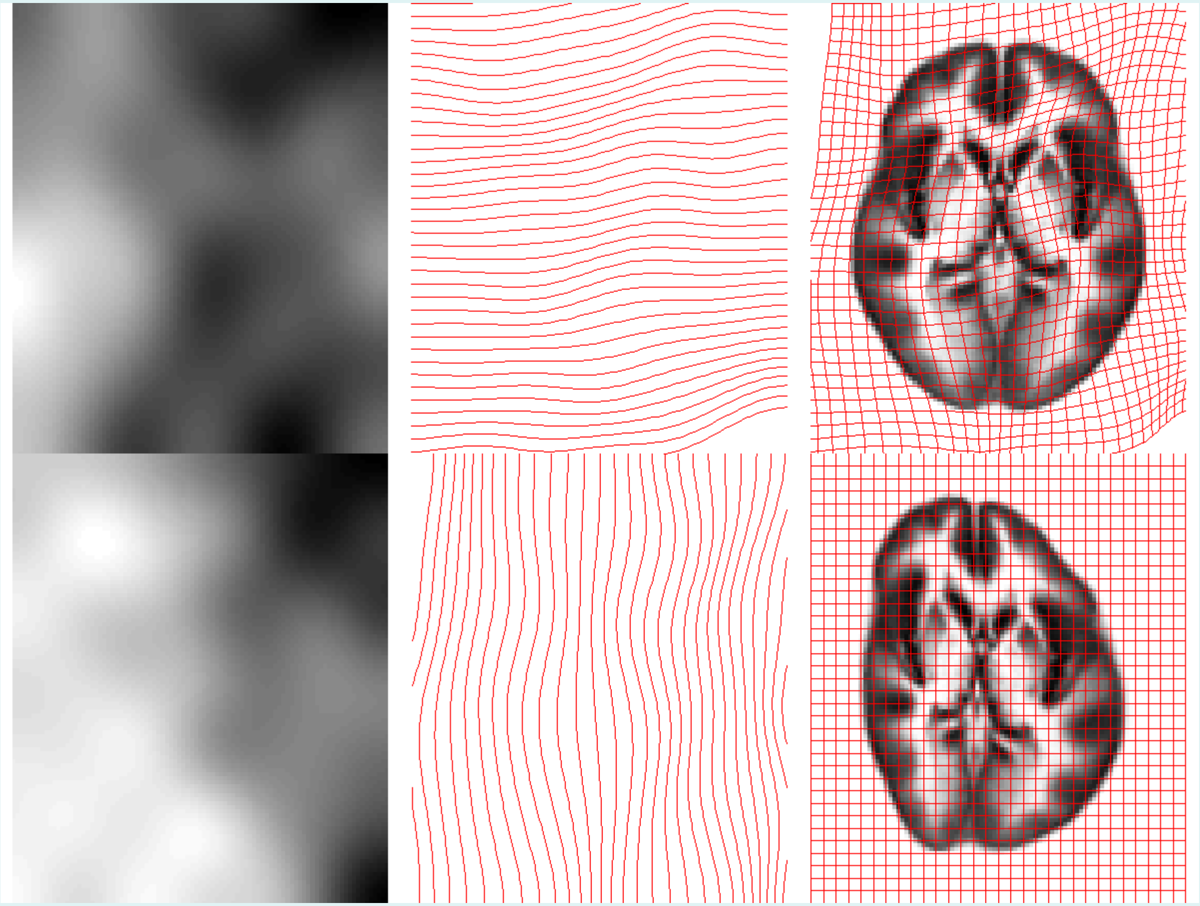
Spatial normalisation results



Affine registration

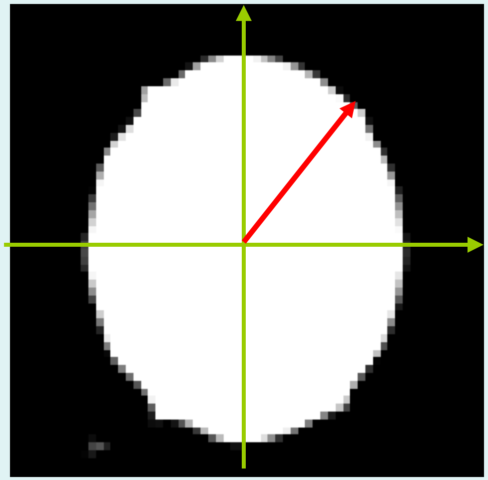
Modelling elastic deformations, “warps”

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



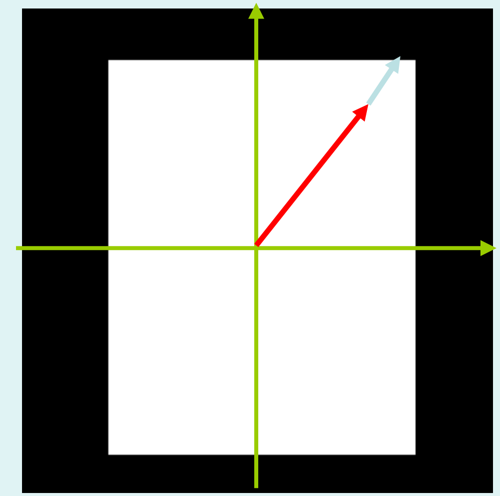
Non-linear warping, example

For every voxel position in blank sheet



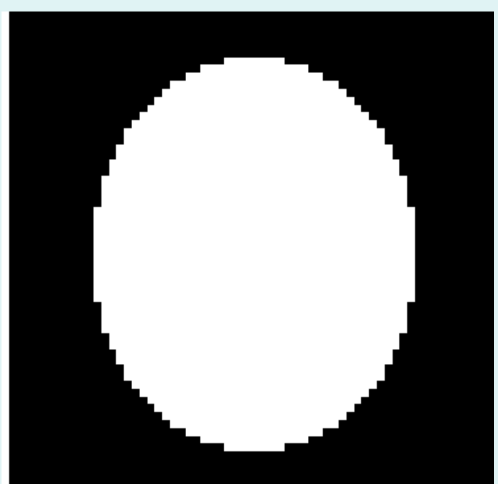
$$\begin{bmatrix} x' \\ y' \end{bmatrix} = \begin{bmatrix} x \\ y \end{bmatrix} + \begin{bmatrix} d_x(x,y) \\ d_y(x,y) \end{bmatrix}$$

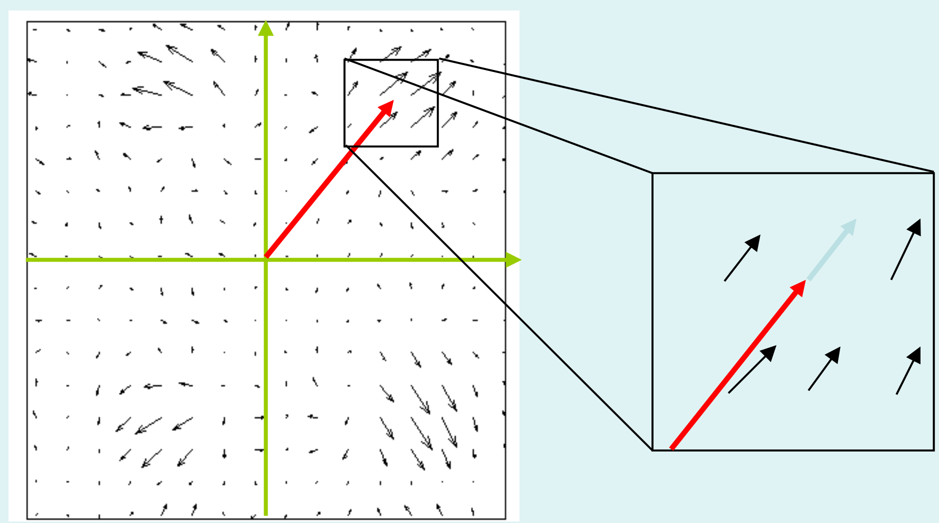
Go to original image and find intensity at warped co-ordinate



Get position in original space by adding pertinent displacement

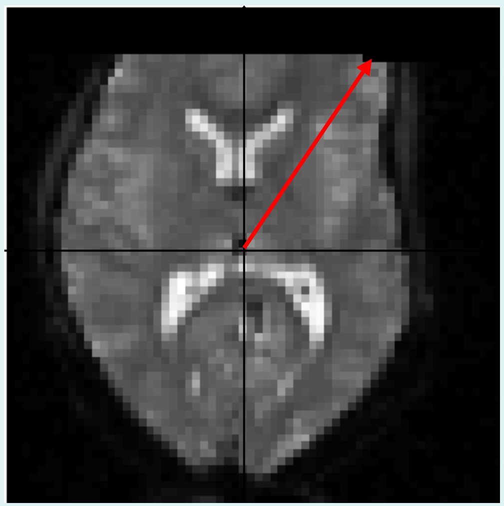
Target



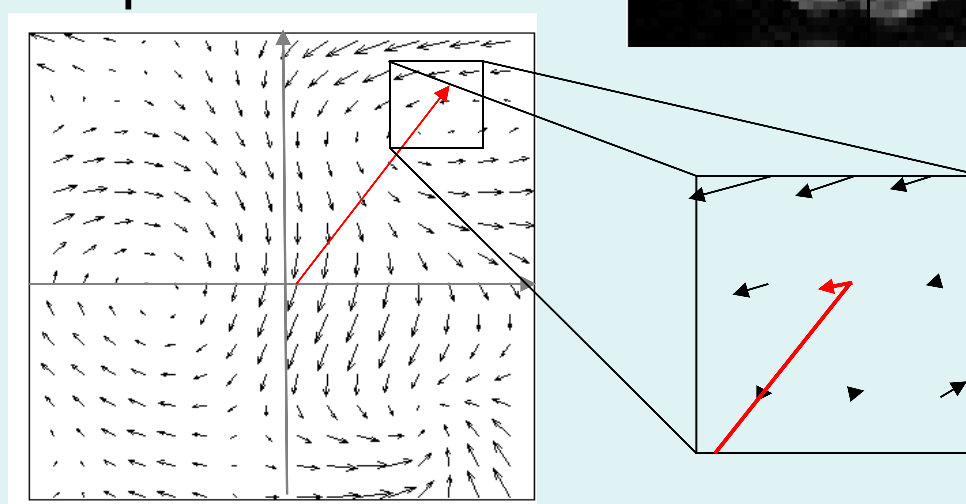


Non-linear warping, example

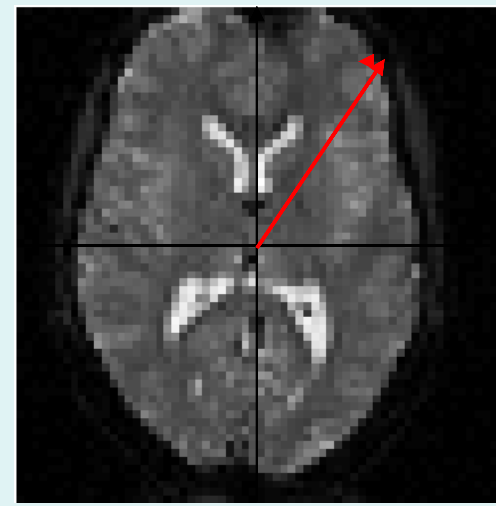
For each voxel-centre in blank sheet.



Get position in original space by adding pertinent displacement.

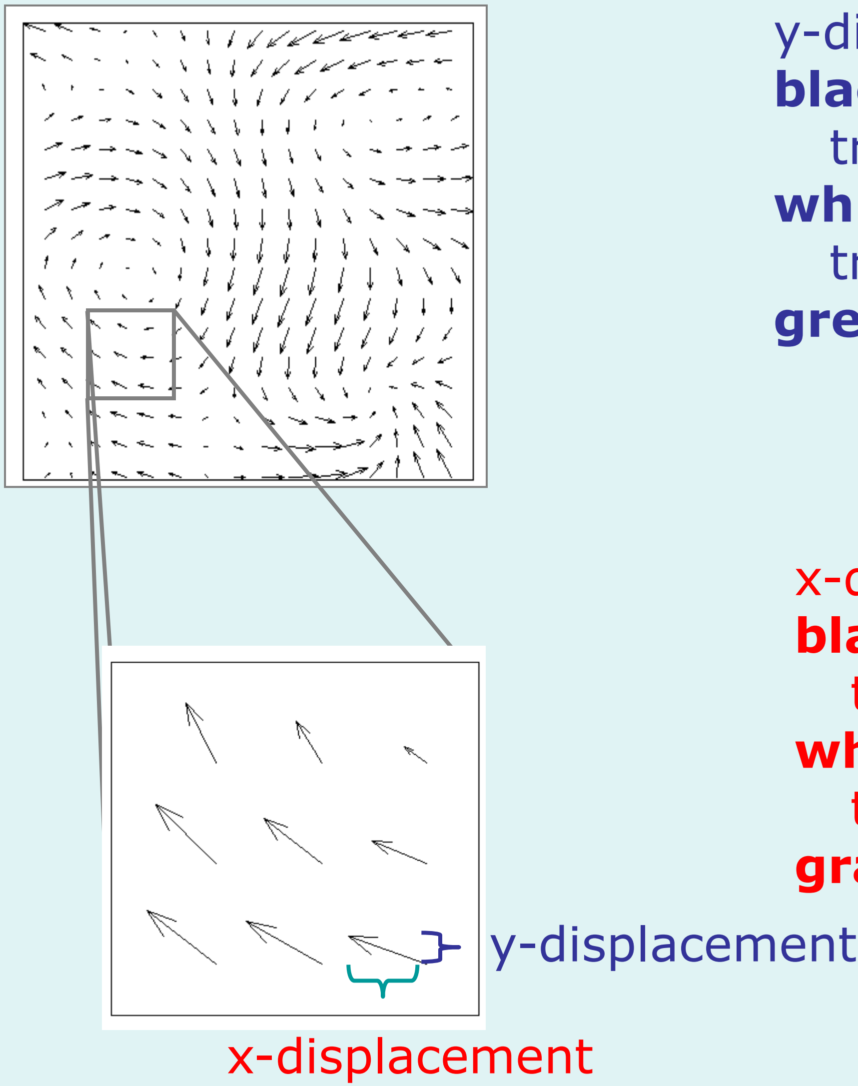


Go to original image and find intensity at “warped” co-ordinate

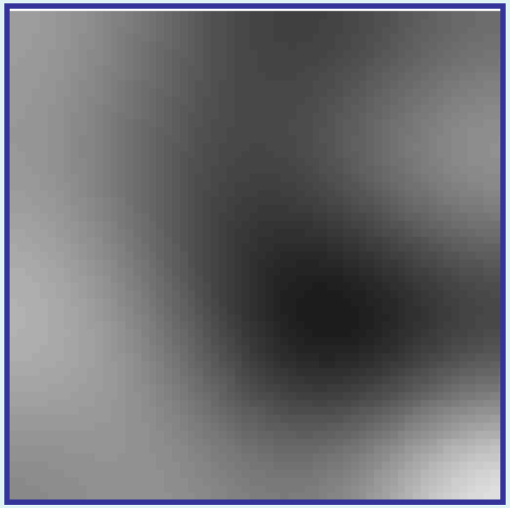


$$\begin{bmatrix} x' \\ y' \end{bmatrix} = \begin{bmatrix} x \\ y \end{bmatrix} + \begin{bmatrix} d_x(x,y) \\ d_y(x,y) \end{bmatrix}$$

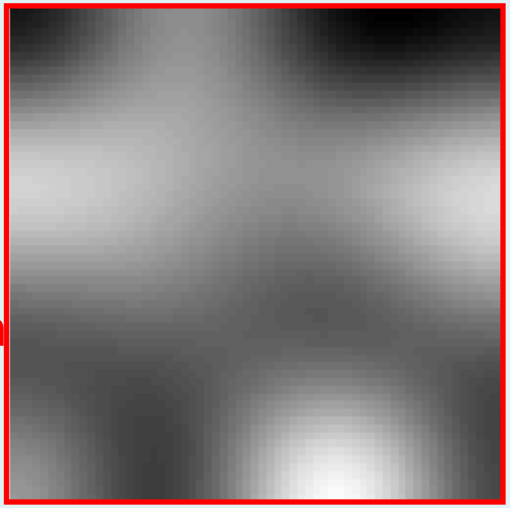
Displacement map



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

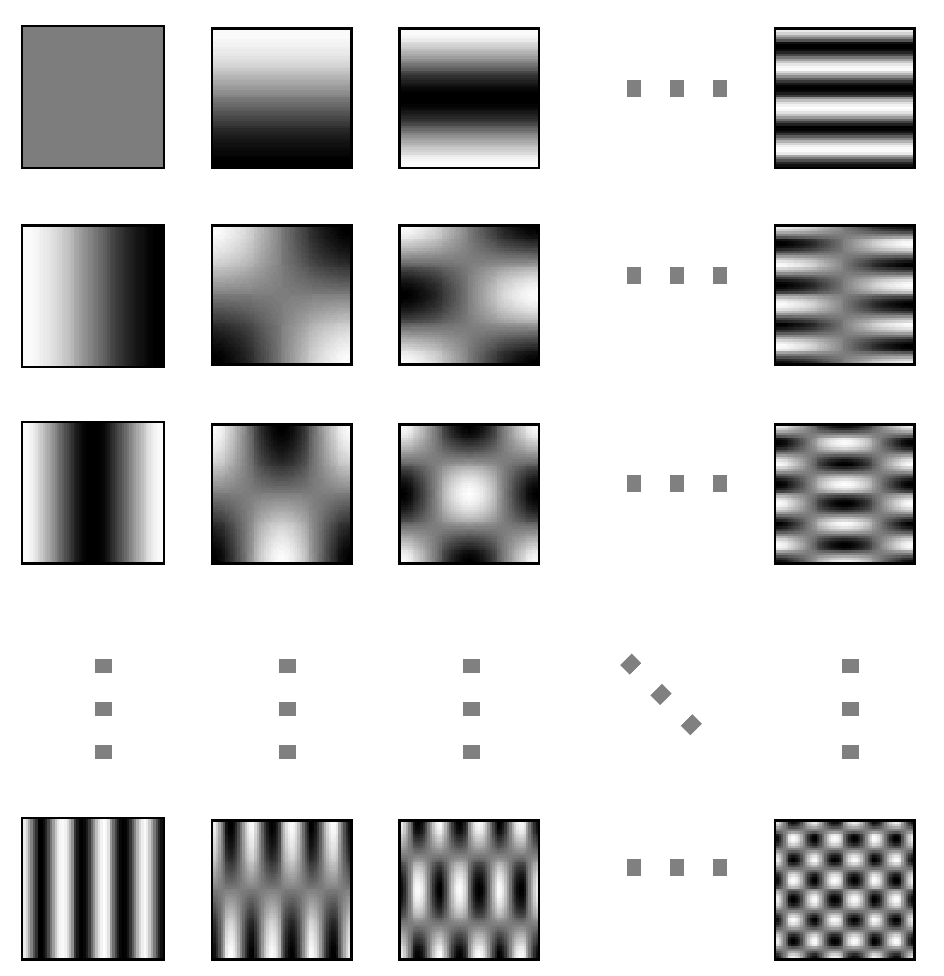


x-displacement,
black: leftward translation
white: rightward translation
gray: no translation



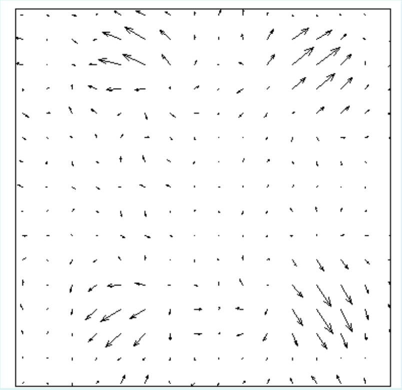
Displacement map modelling

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

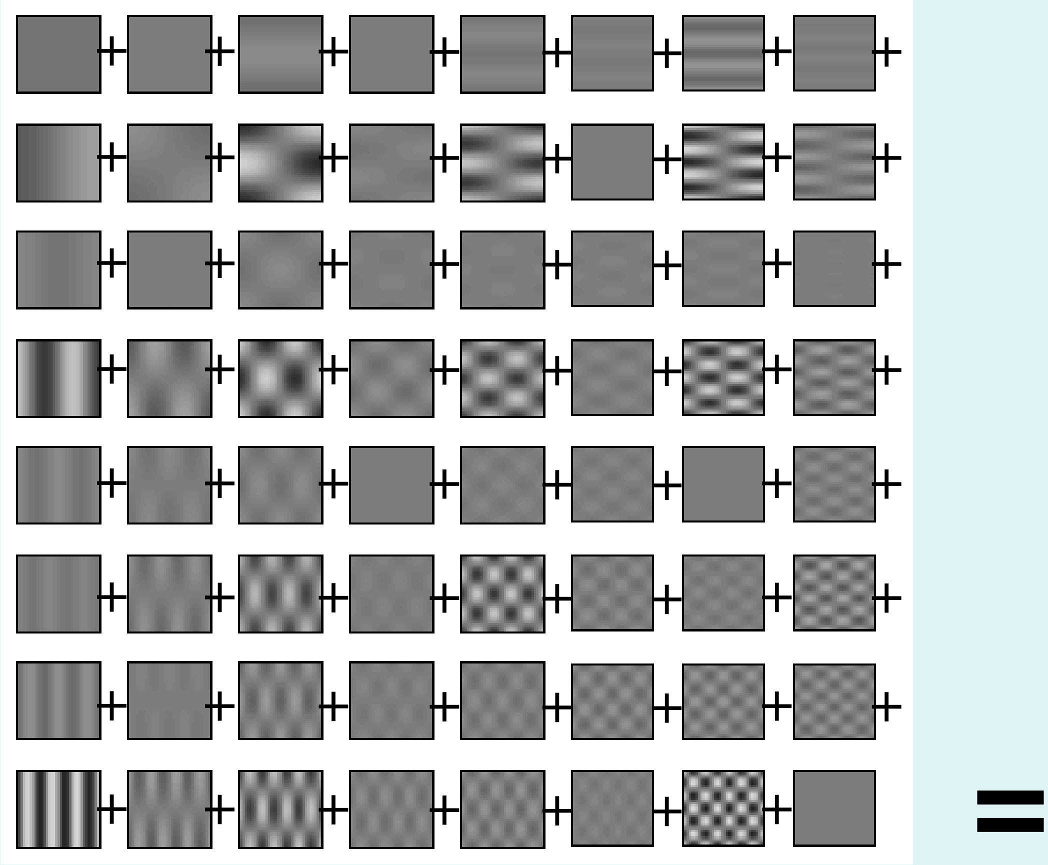


Displacement maps, example

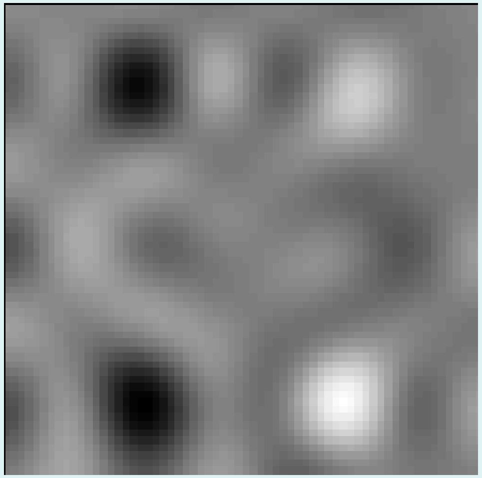
Square-to-ellipse map



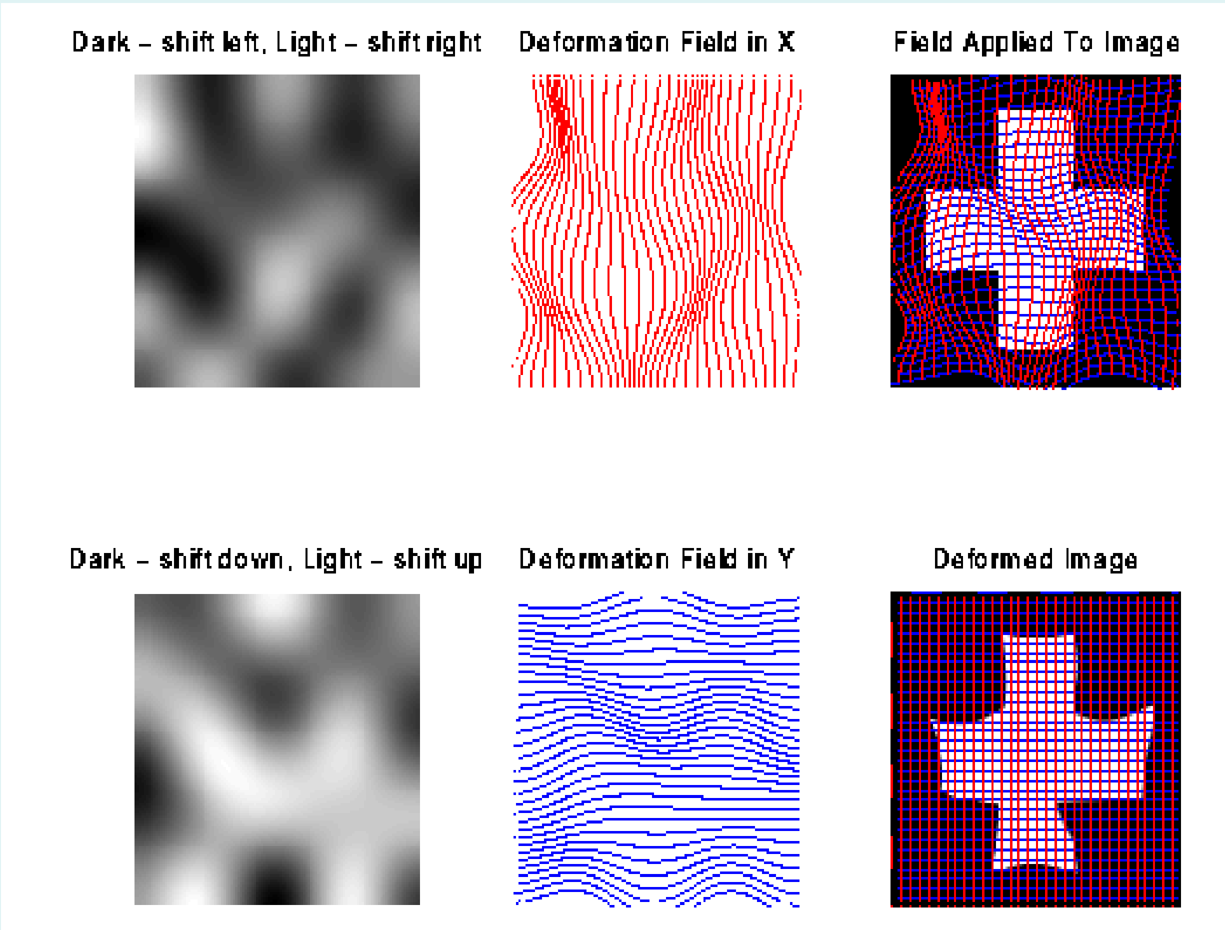
Each basis-warp multiplied by a weight

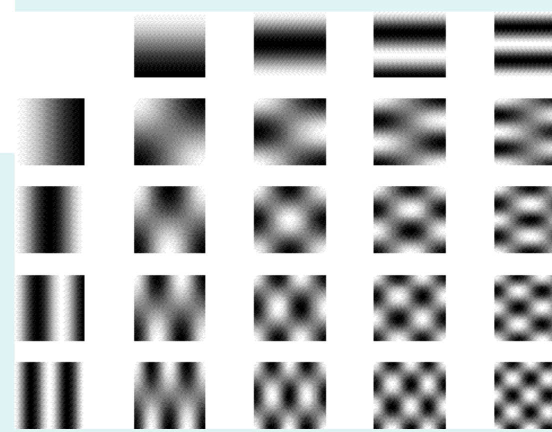


x-component of
square-to-ellipse map

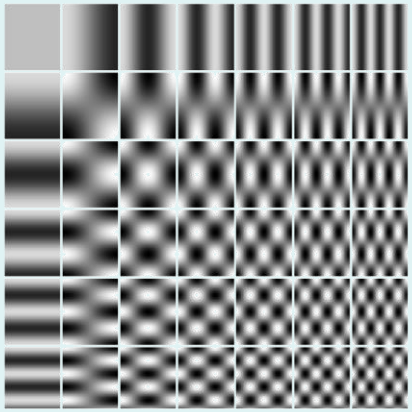


Displacement maps, example

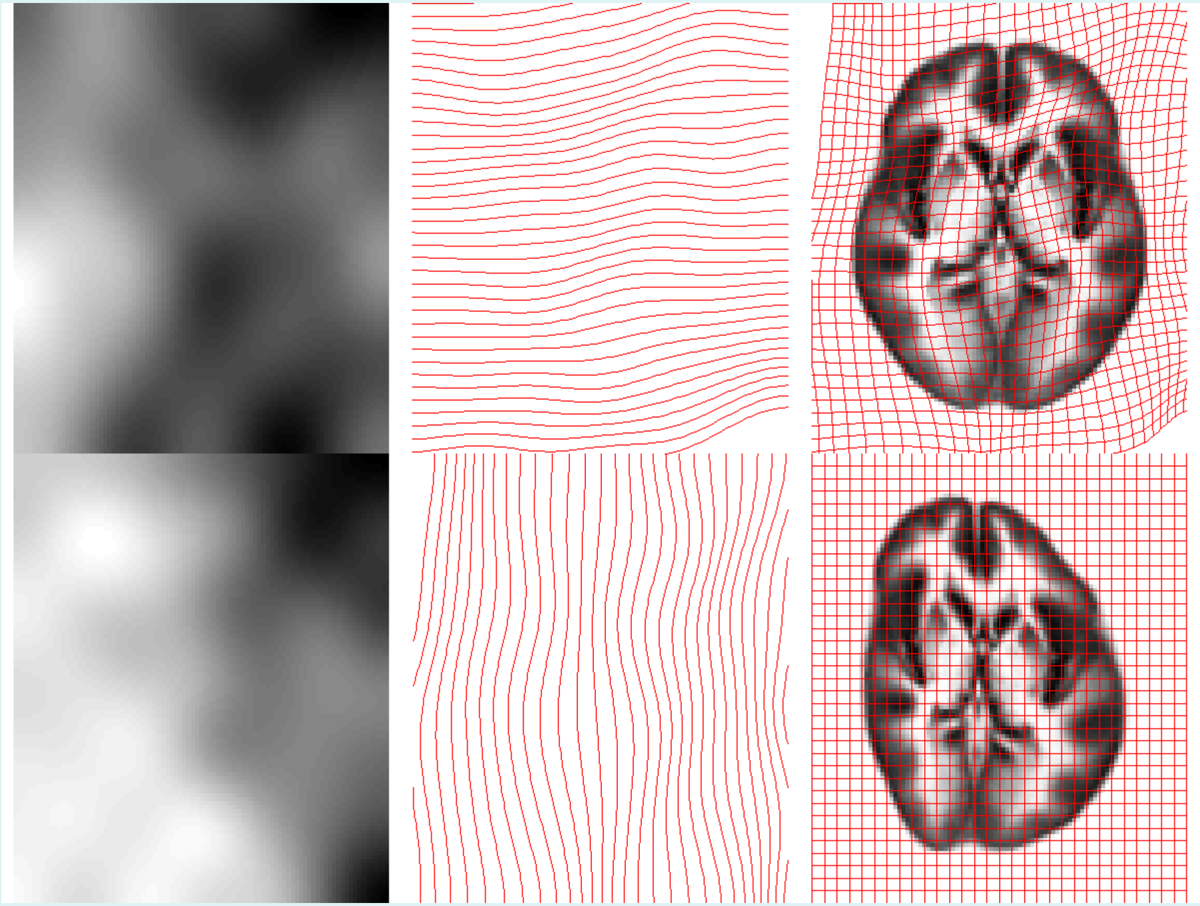




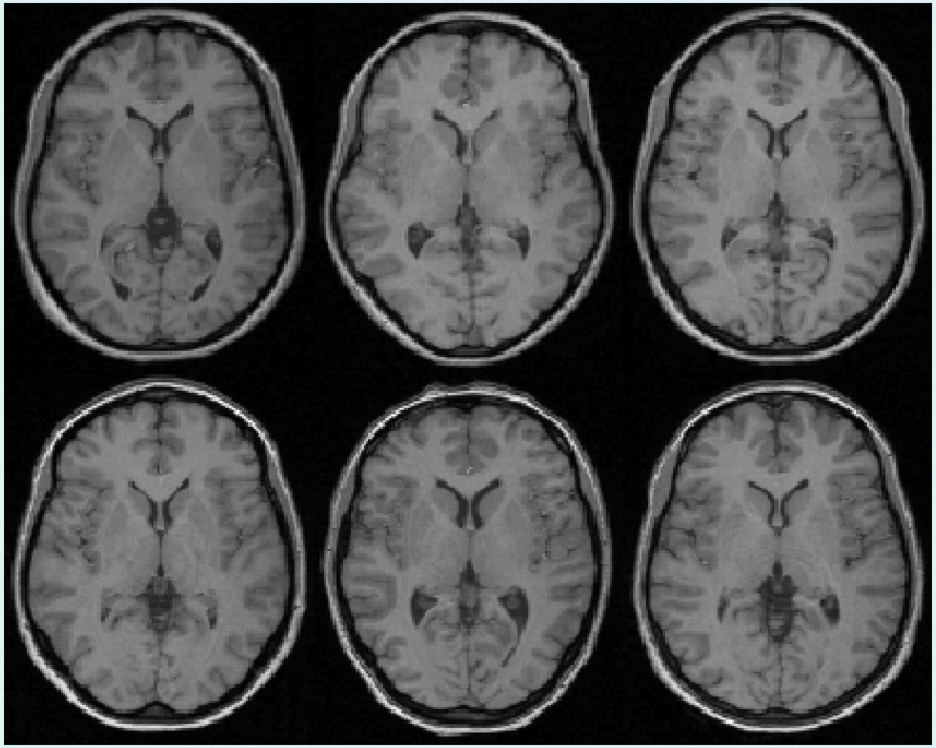
Modelling deformations, warps



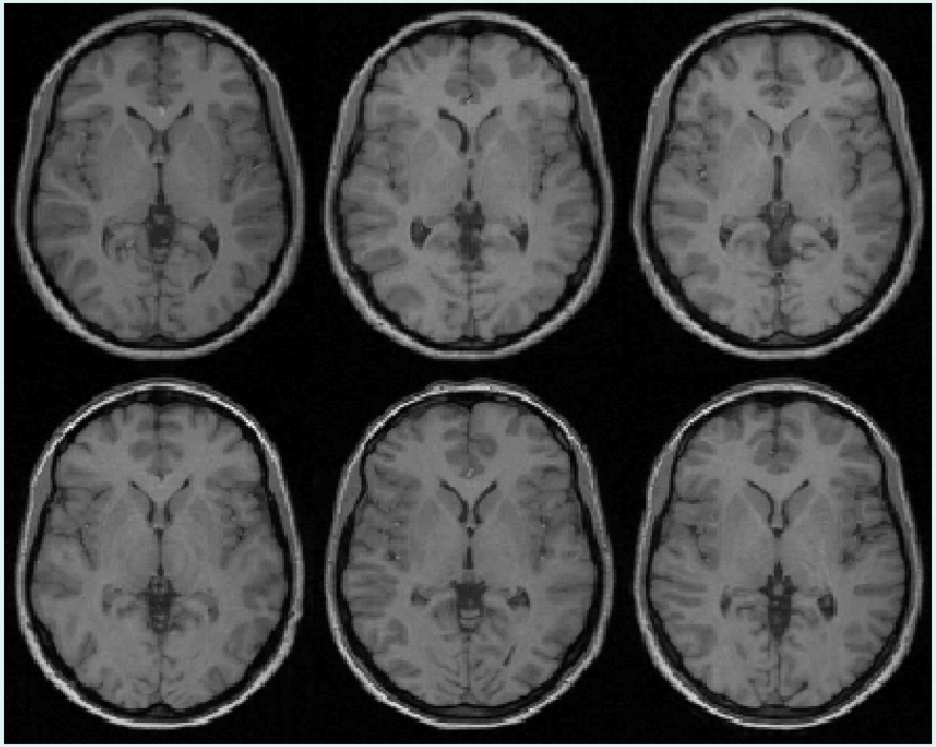
- Tissue probability images are warped to match the subject
- The inverse transform warps to the TPMs
- Warps are constrained to be reasonable by penalising various distortions (energies)



Spatial normalisation results

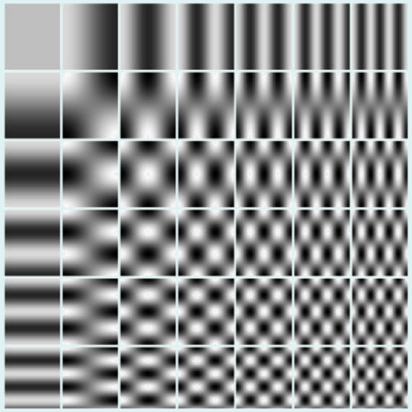


Affine registration

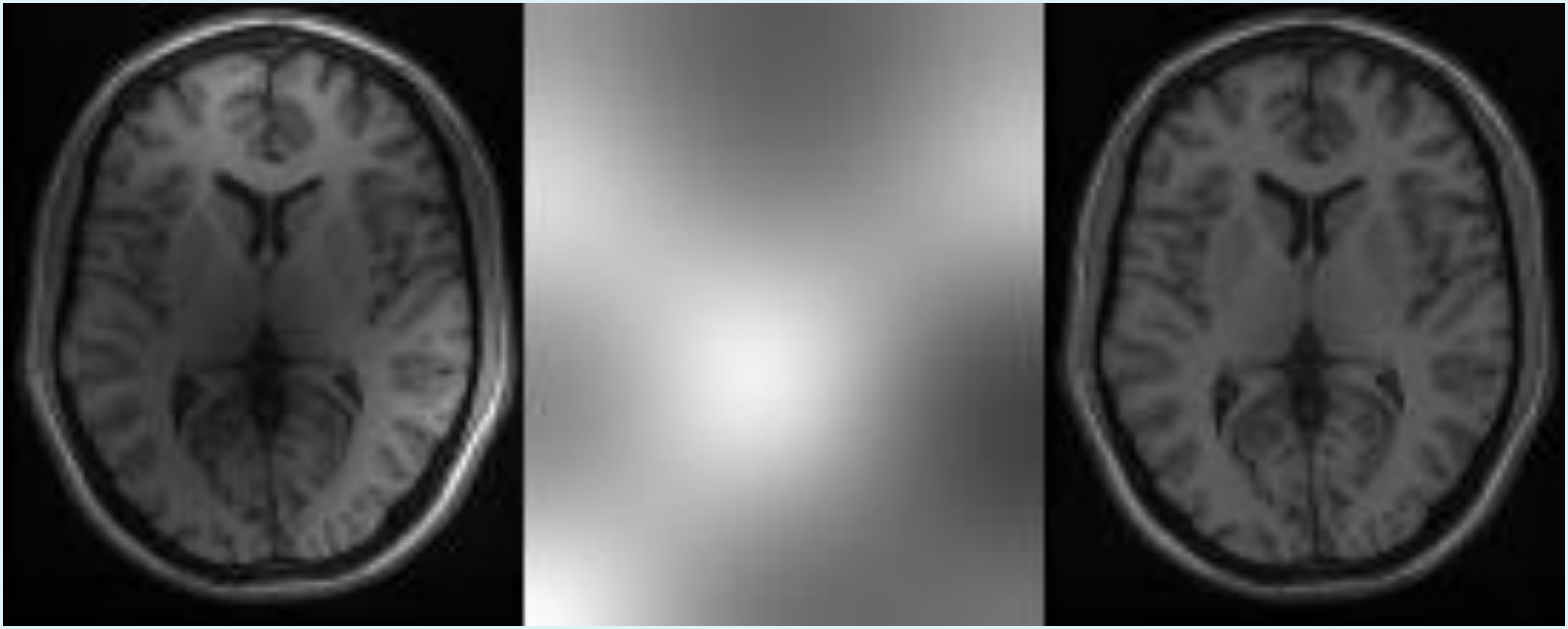


Non-linear registration

Modelling inhomogeneity



A multiplicative bias field is modelled as a spatially smooth image



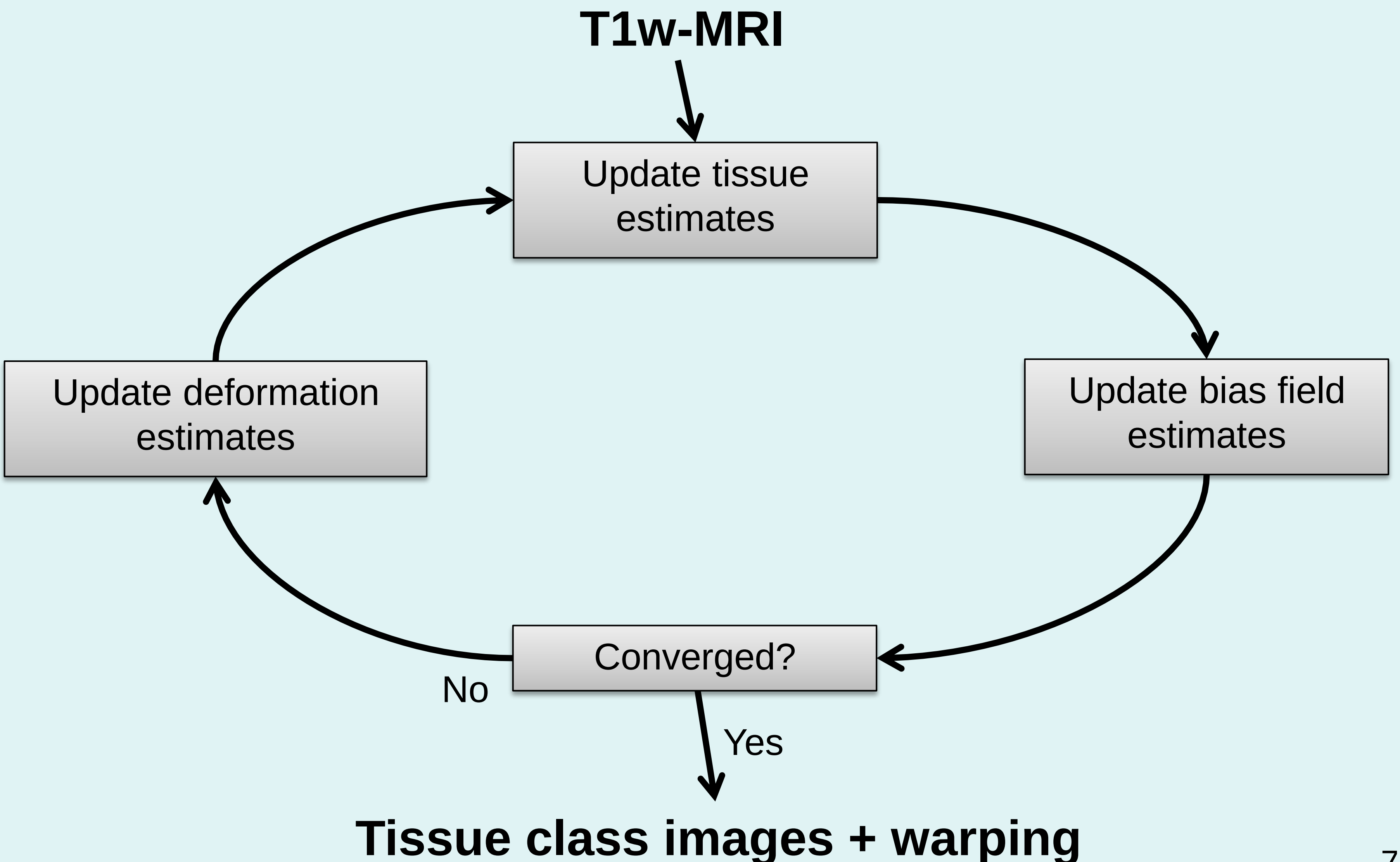
Corrupted image **Bias Field** **Corrected image**

Normalisation & Unified Segmentation

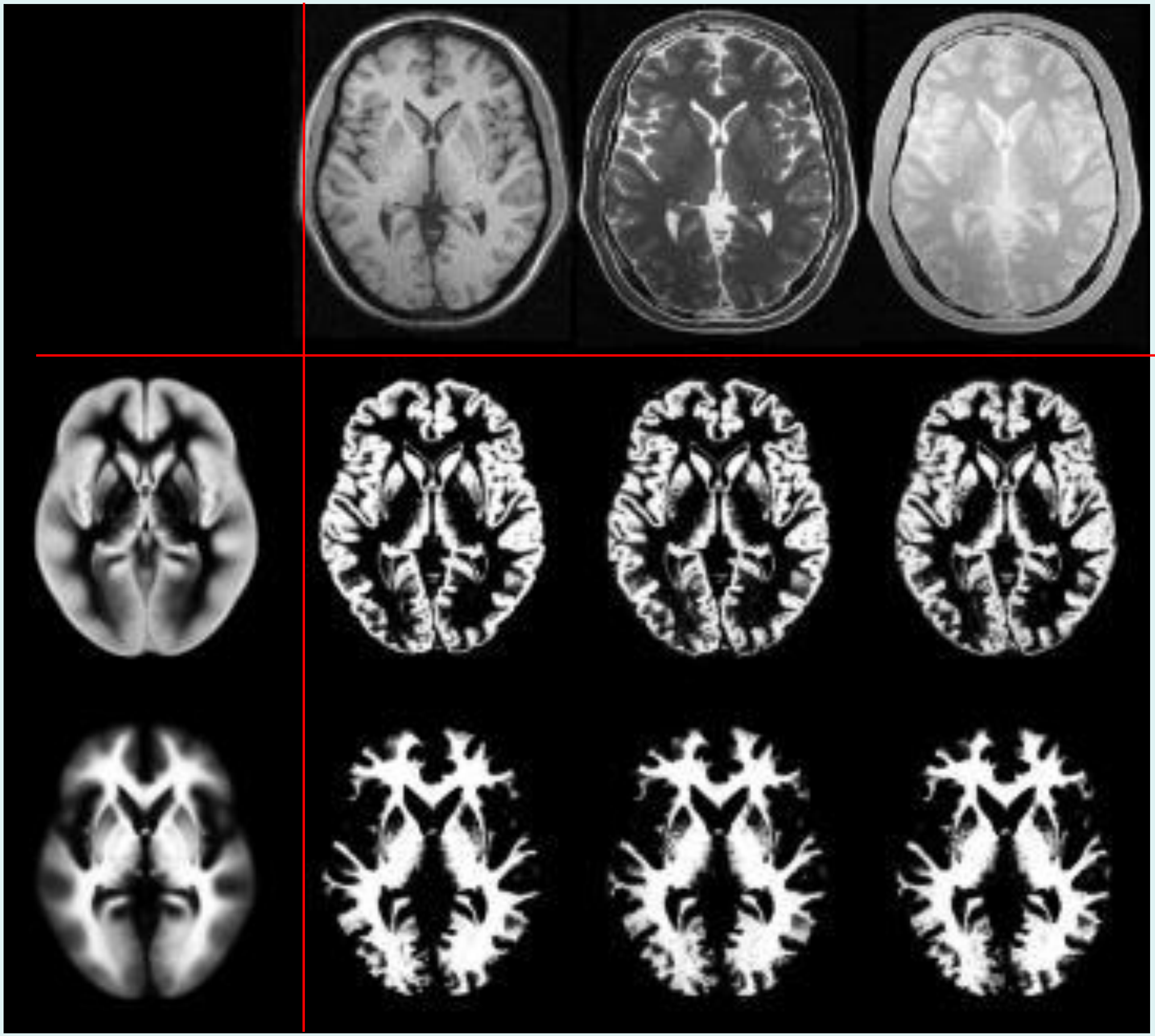
- MRI imperfections make normalisation harder
  - Differences between sequences, artefacts
  - Intensity inhomogeneity or “bias” field
- Normalising *segmented tissue maps* should be more robust and precise than using the original images (GM-onGM, WM-on-WM, etc.)...
- … Tissue segmentation benefits from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

→ Circular reasoning!

Iterative optimisation scheme



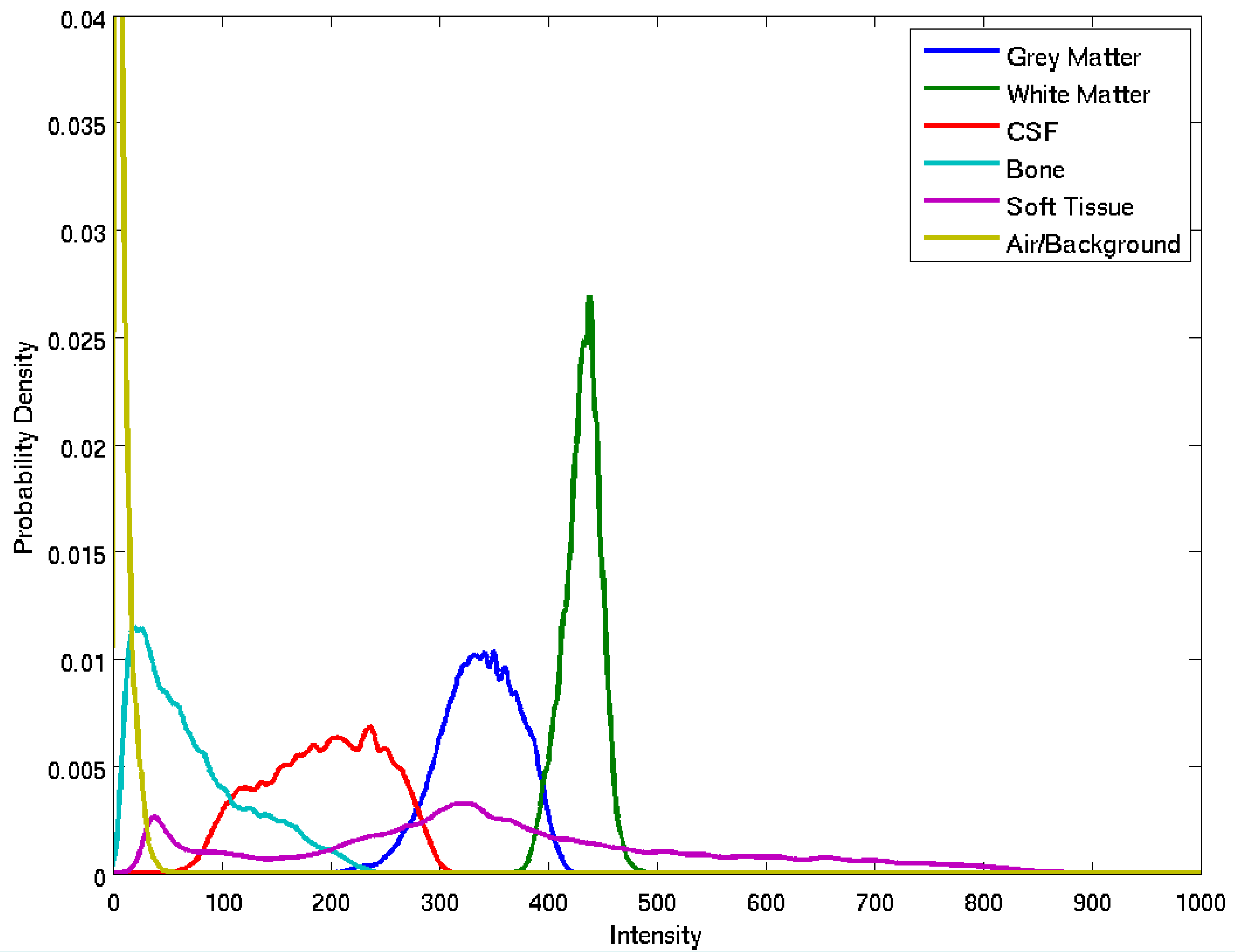
Segmentation results



Spatially normalised BrainWeb phantoms (T1, T2, PD)

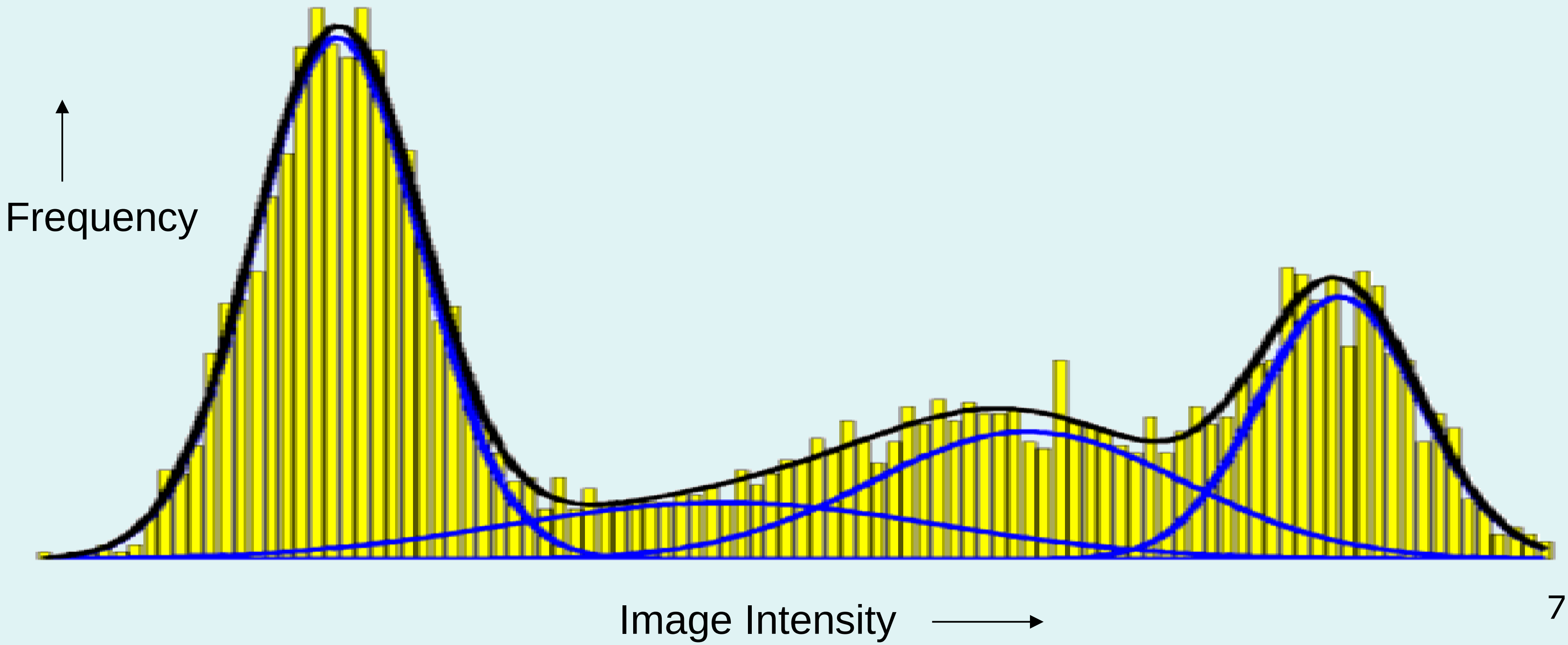
Tissue probability maps of GM and WM

Tissue intensity distributions (T1w-MRI)



Mixture of Gaussians (MoG)

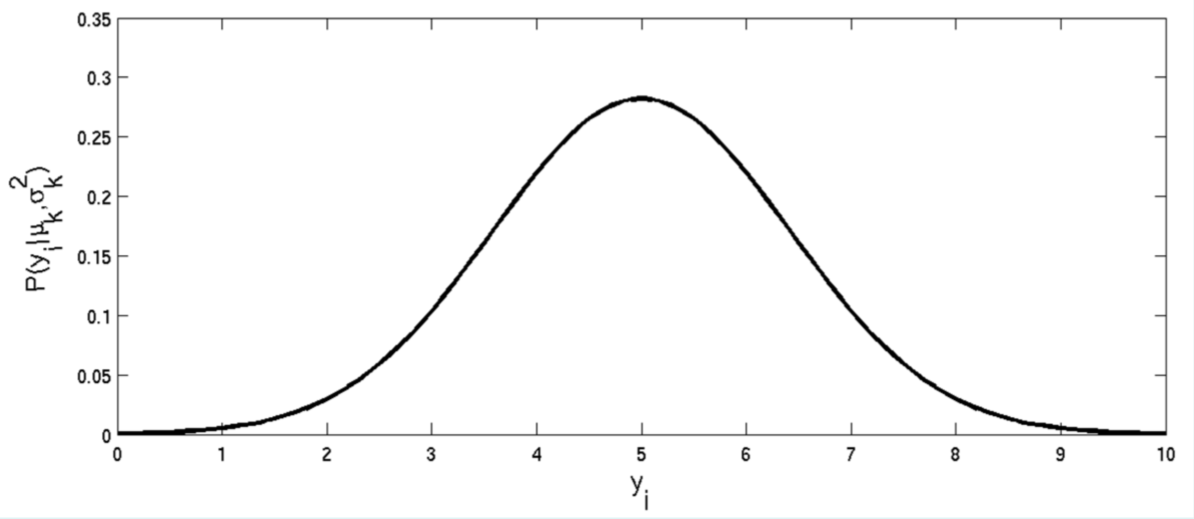
Classification is based on a Mixture of Gaussians model (MOG), which represents the intensity probability density by a number of Gaussian distributions.



Gaussian probability density

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

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

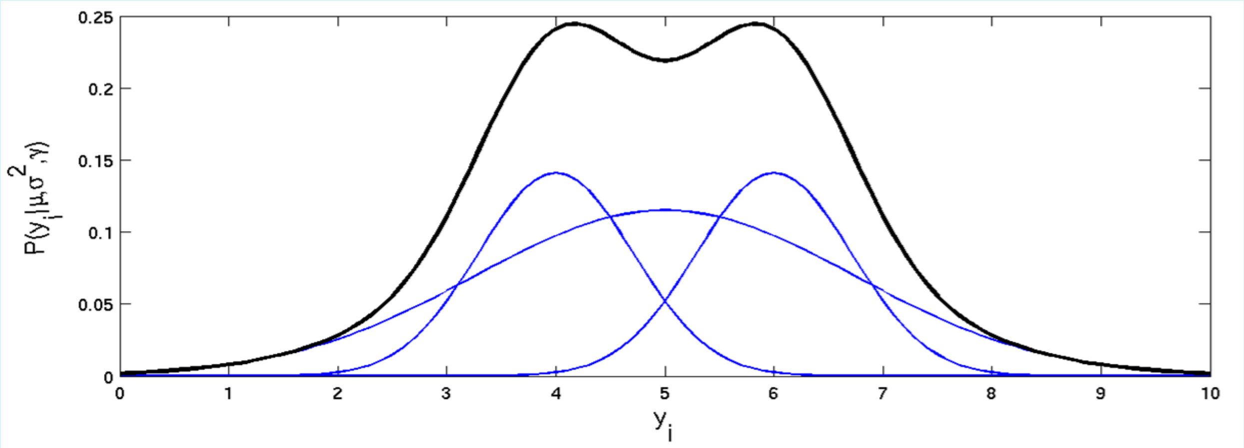


Non-Gaussian probability density

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

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

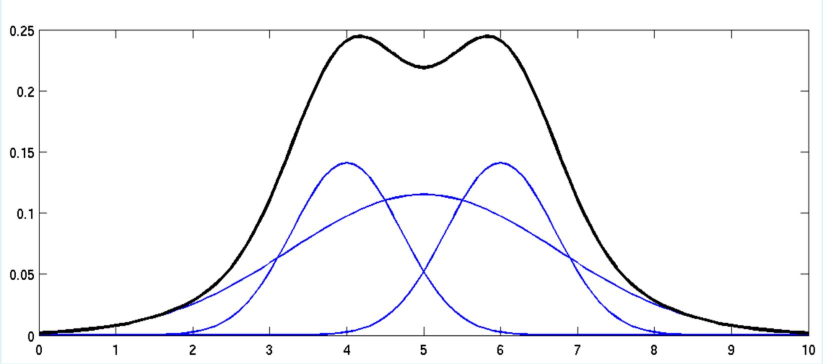
Mixing proportion - positive and sums to one



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:

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

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

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:

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

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

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

Modelling a bias field

- A bias field is included, such that the required scaling at voxel i, parameterised by $\boldsymbol{\beta}$, is $\rho_i(\boldsymbol{\beta})$.

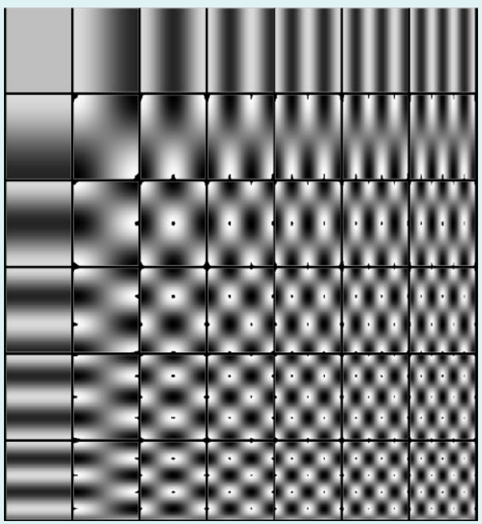
- Replace the means by $\mu_k/\rho_i(\boldsymbol{\beta})$
- Replace the variances by $(\sigma_k/\rho_i(\boldsymbol{\beta}))^2$

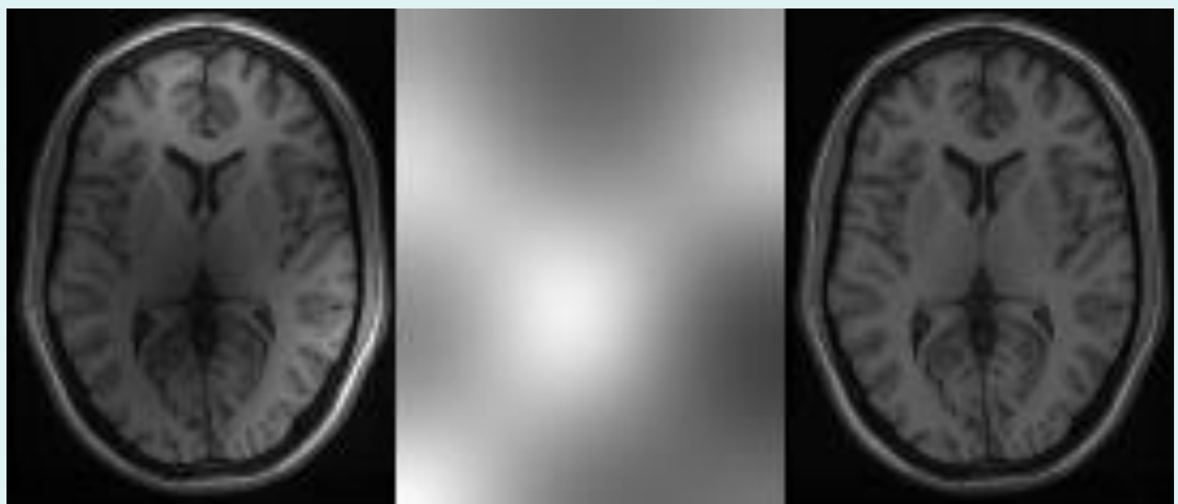
$$P(y_i \mid c_i = k, \mu, \sigma^2, \beta) = \frac{1}{\sqrt{2\pi(\sigma_k/\rho_i(\beta))^2}} \exp\left(-\frac{(y_i - \mu_k/\rho_i(\beta))^2}{2(\sigma_k/\rho_i(\beta))^2} \right)$$

Modelling a bias field

After rearranging:

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



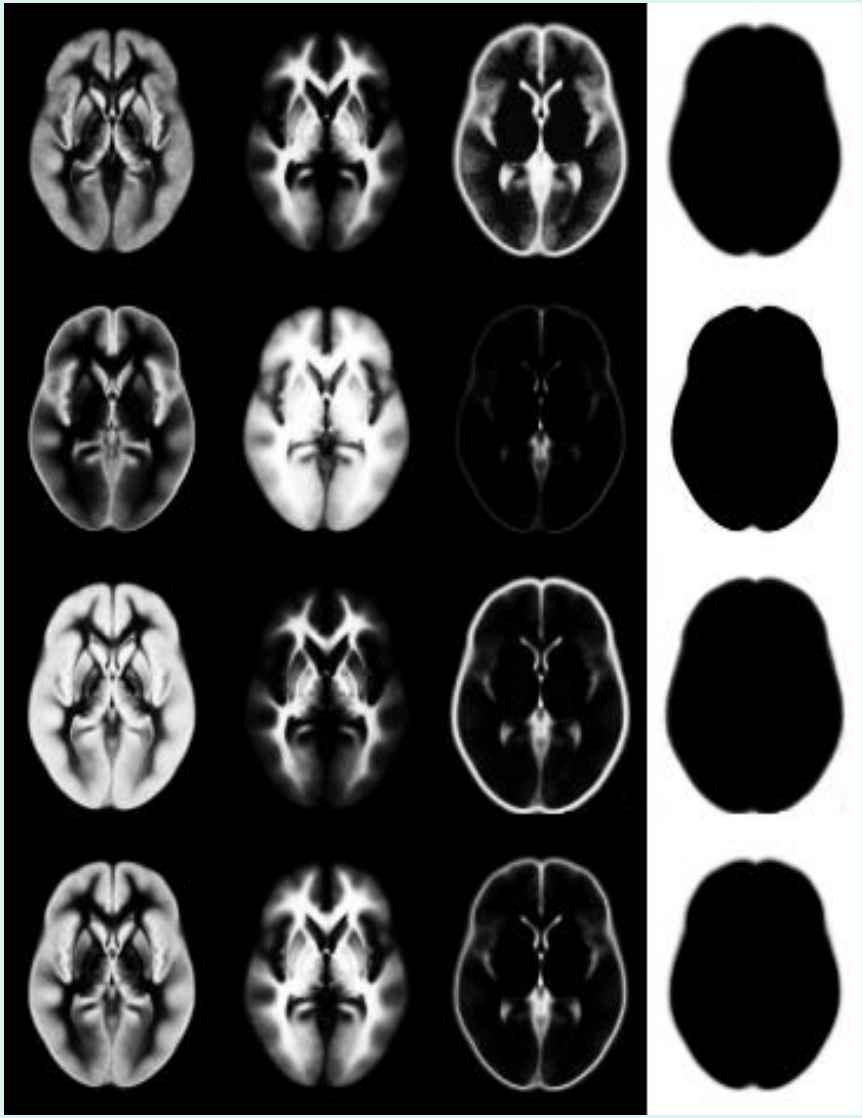


y $\rho(\beta)$ **y** $\rho(\beta)$

"Mixing proportions"

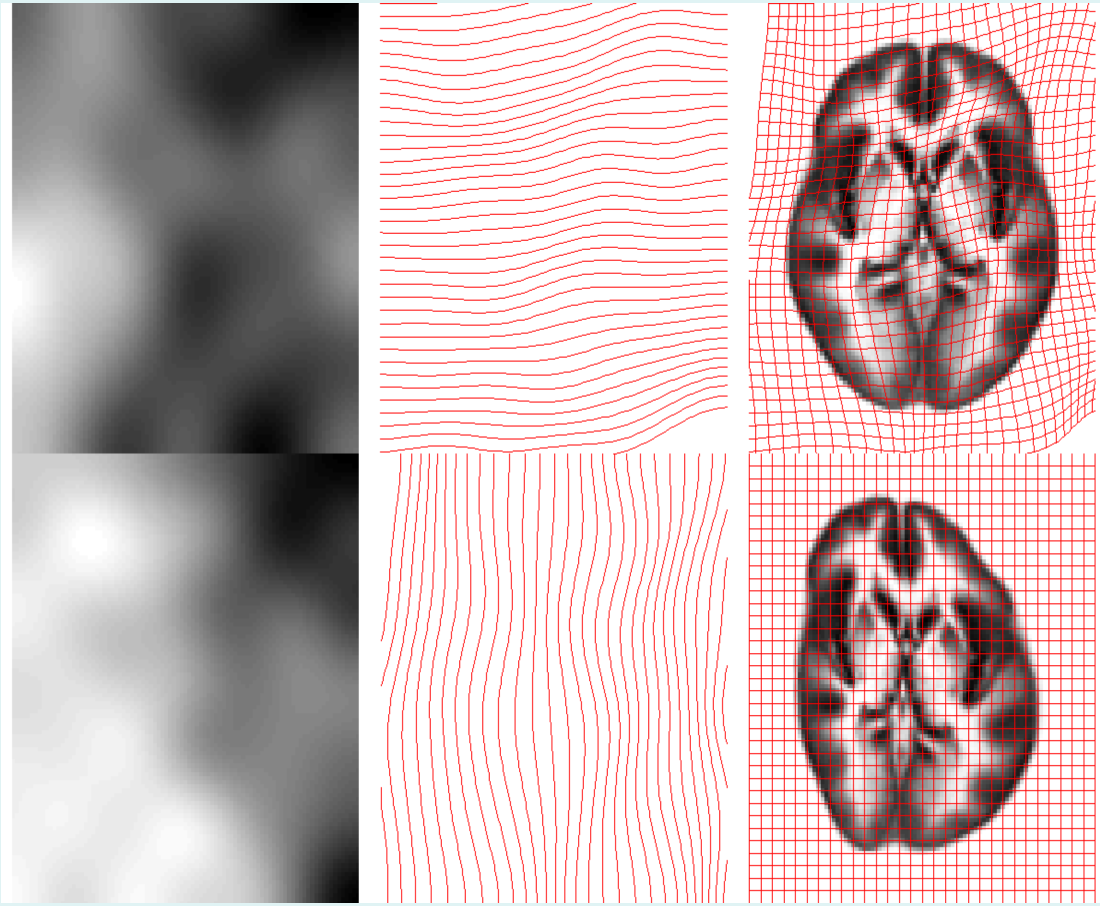
- Tissue probability maps for each class are included.
- The probability of obtaining class k at voxel i, given weights γ is then:

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



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:

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

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

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.

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

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

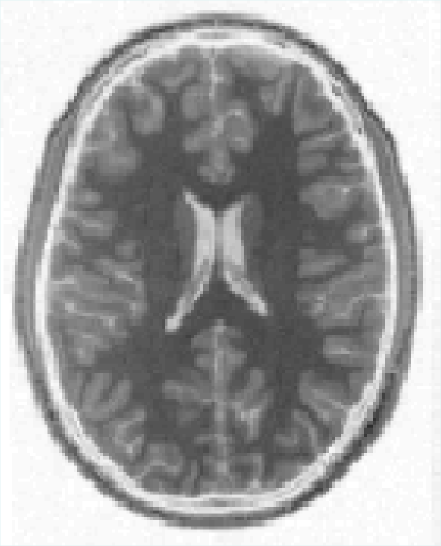
  Use an Expectation Maximisation (EM) strategy.

end

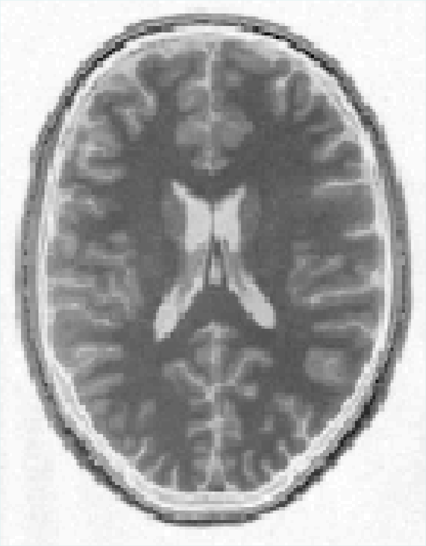
Spatial normalisation, overfitting

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

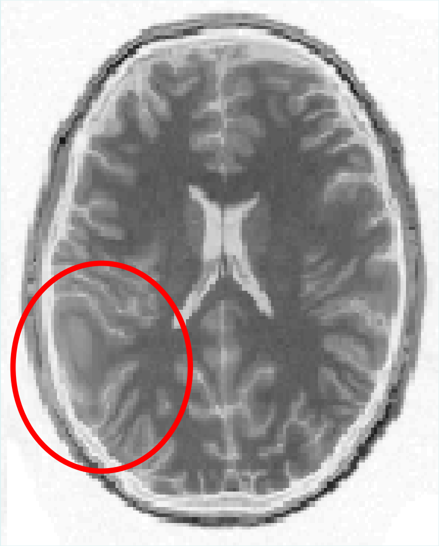
Template image



Affine registration.



Non-linear registration without regularisation.



Linear regularisation

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

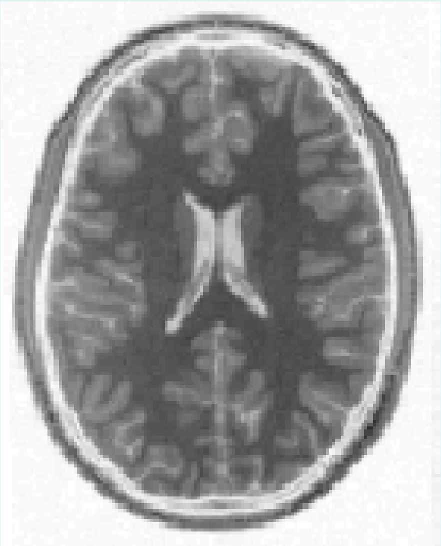
$$-\log\left[P(\theta,\mathbf{y})\right] = -\log\left[P(\mathbf{y}|\theta)\right] - \log\left[P(\theta)\right]$$

- Prior probability distributions can be modelled by a multivariate normal distribution.
  - Mean vector $\mu_{\mathbf{a}}$ and $\mu_{\mathbf{b}}$
  - Covariance matrix $\Sigma_{\mathbf{a}}$ and $\Sigma_{\mathbf{b}}$
  - $-\log[P(\mathbf{a})] = (\mathbf{a}-\mathbf{m_a})^T \mathbf{S_a}^{-1}(\mathbf{a}-\mathbf{m_a}) + \text{const}$

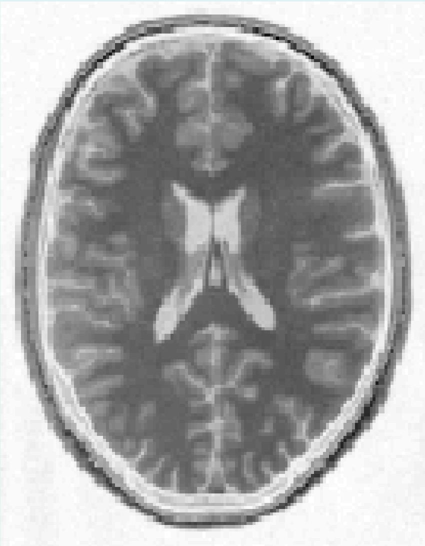
Spatial normalisation, overfitting

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

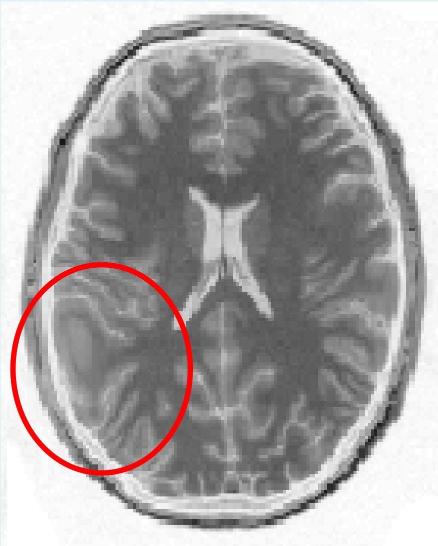
Template image



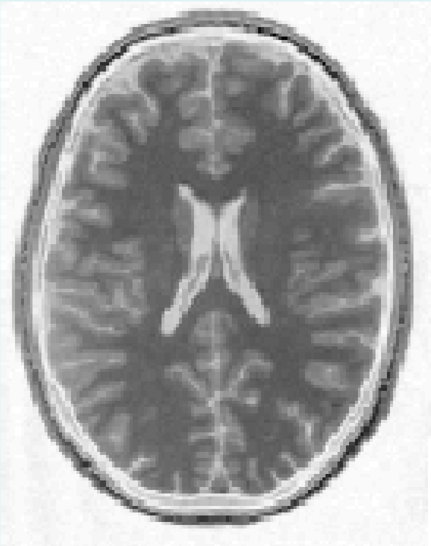
Affine registration.



Non-linear registration without regularisation.

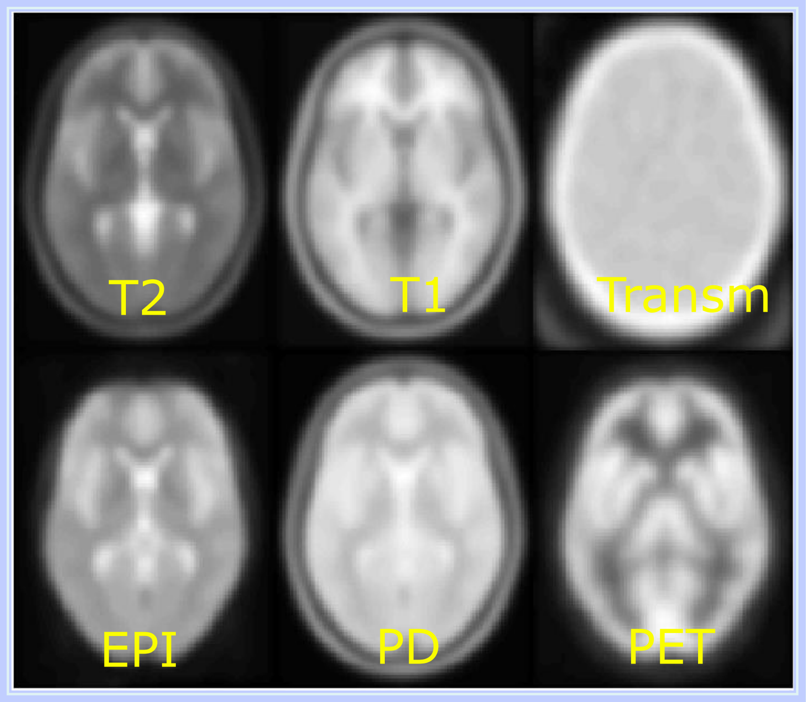


Non-linear registration using regularisation.

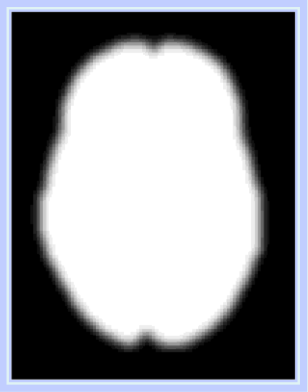


Old fashioned template matching

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.

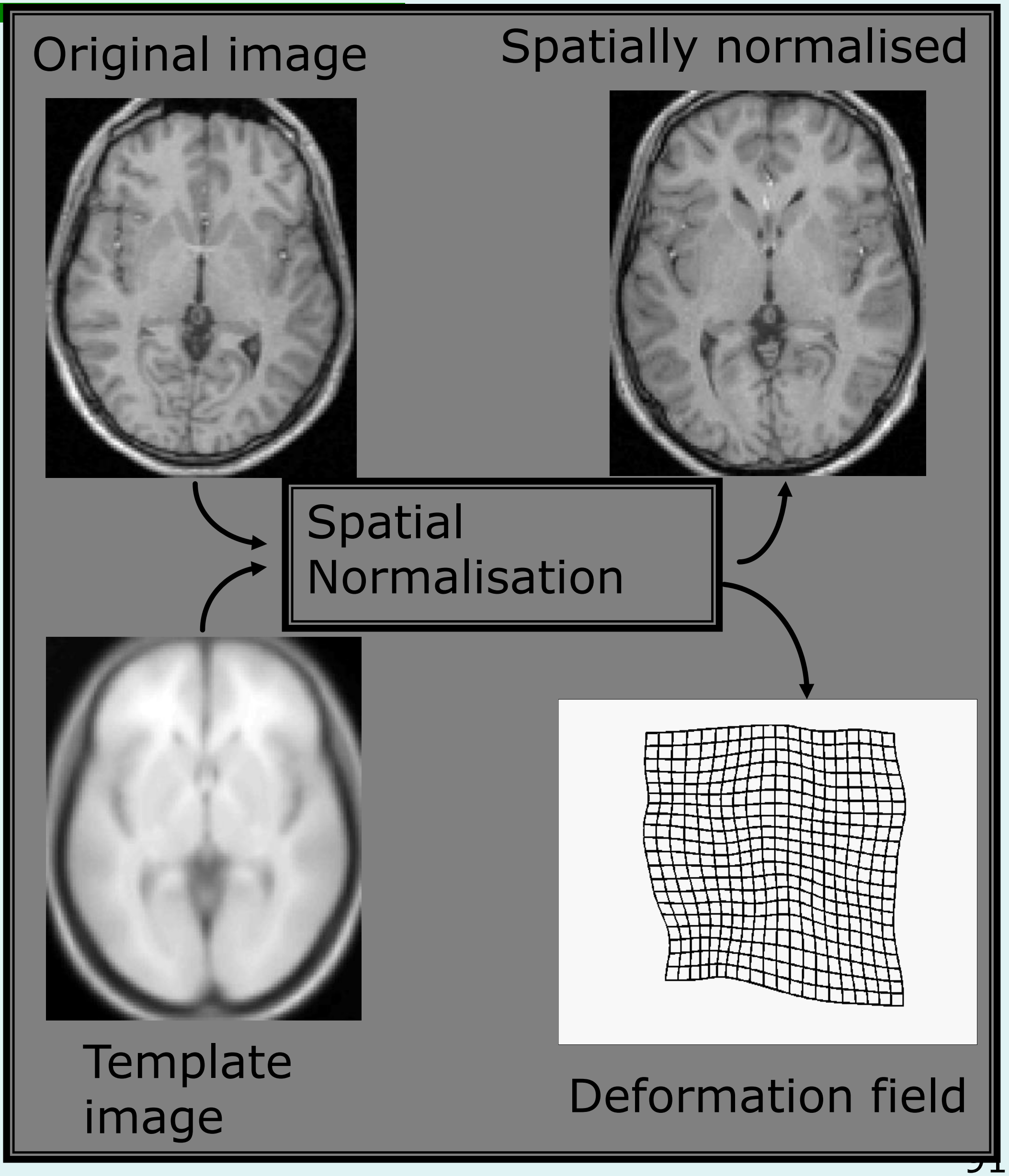
Old fashioned template matching

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.

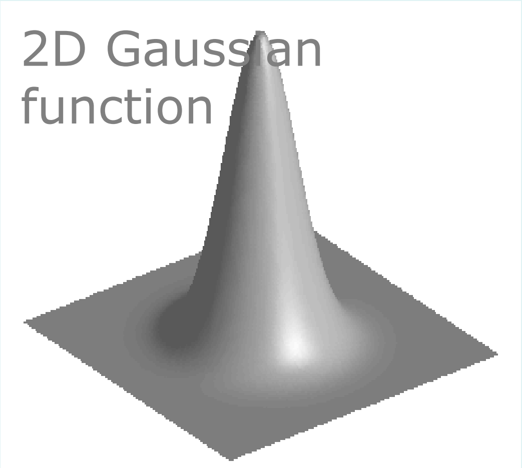


Content

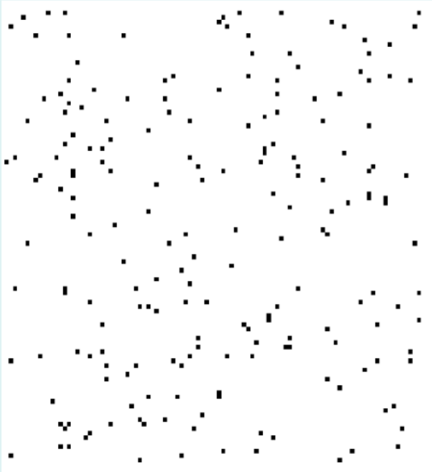
- **Preliminaries**
- **Within-subject**
- **Between-subject**
- **Smoothing**
- **Conclusion**

Smoothing, principle

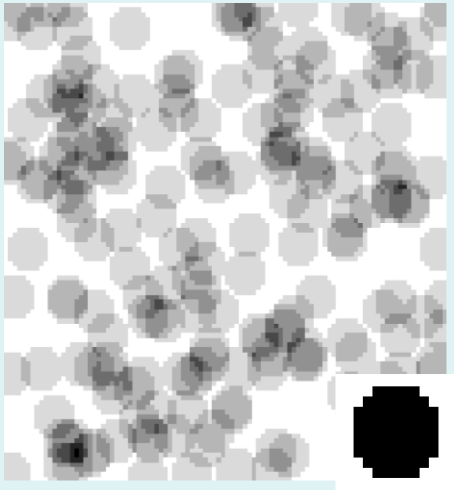
- Smoothing is done by convolution.
- Each voxel after smoothing effectively becomes the result of applying a weighted region of interest (ROI).
- Gaussian function, defined by its "*full width at half maximum*" (FWHM)



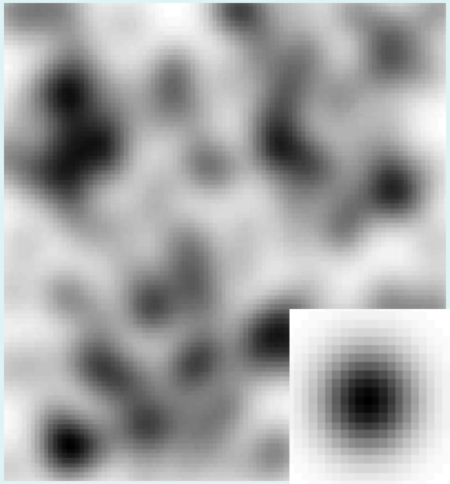
Before convolution



Convolved with a circle



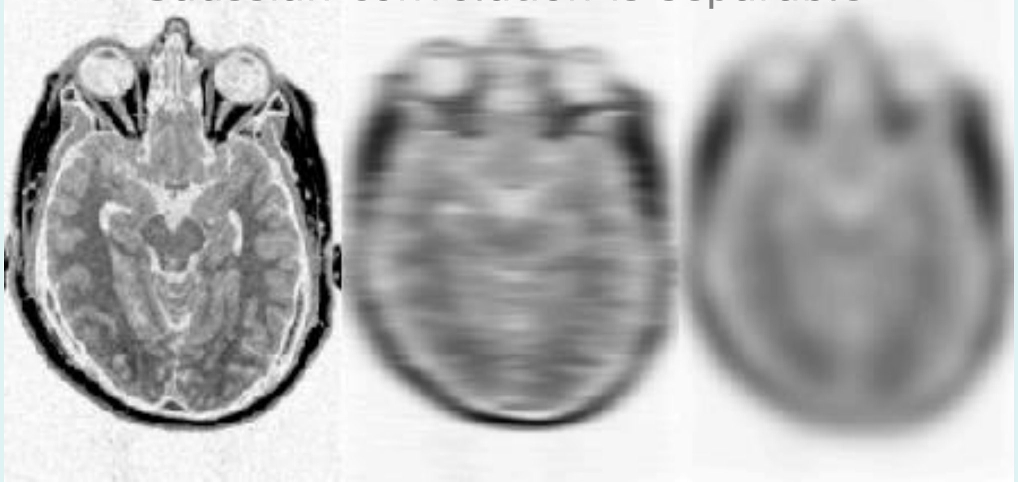
Convolved with a Gaussian

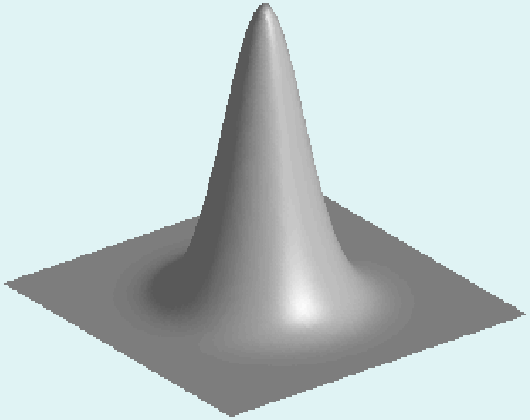


Smoothing, why blur the data?

- 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

Gaussian convolution is separable

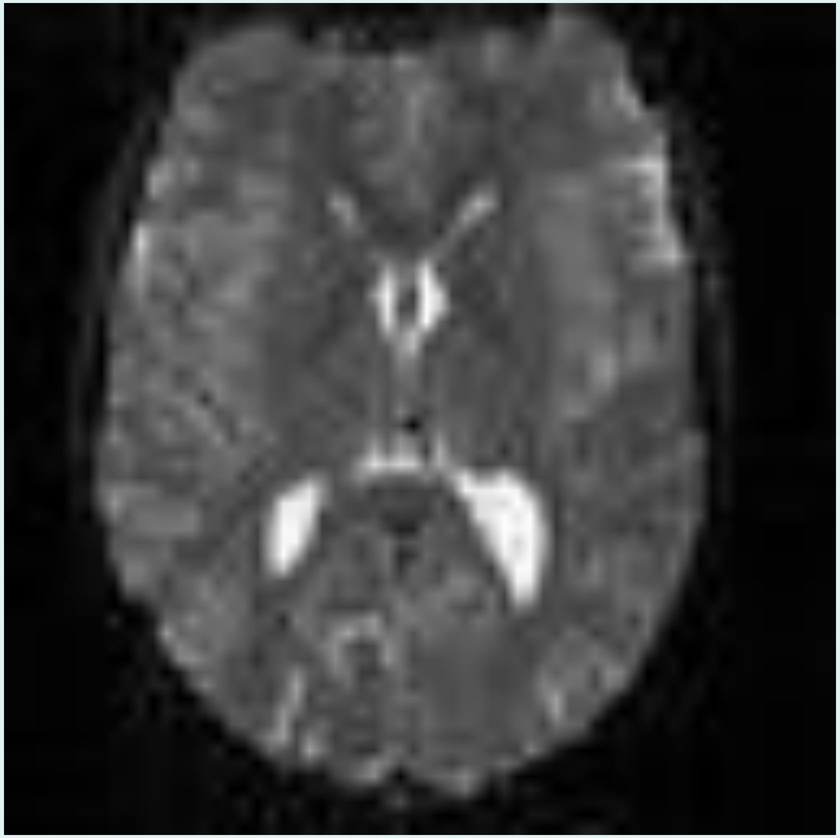


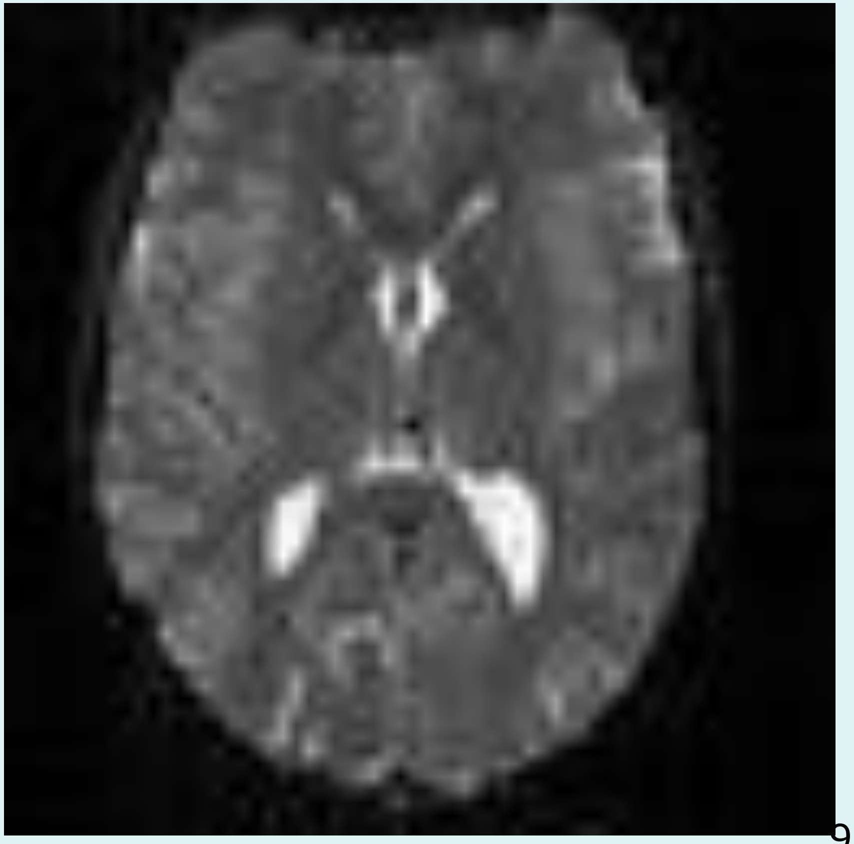


Smoothing, kernel size

Decide *a priori*, based on:

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





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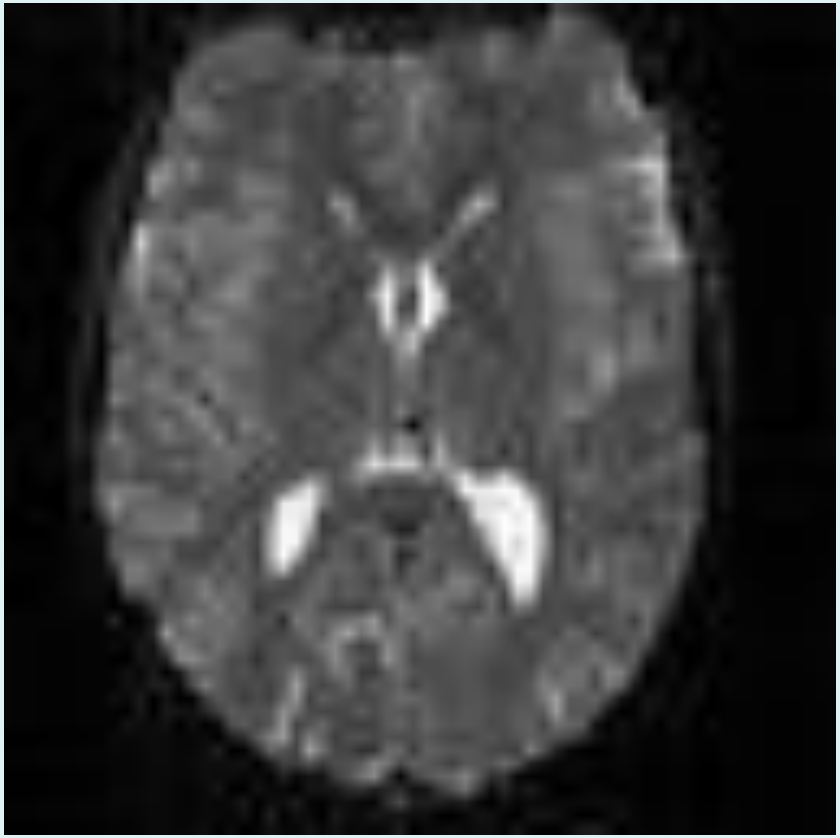

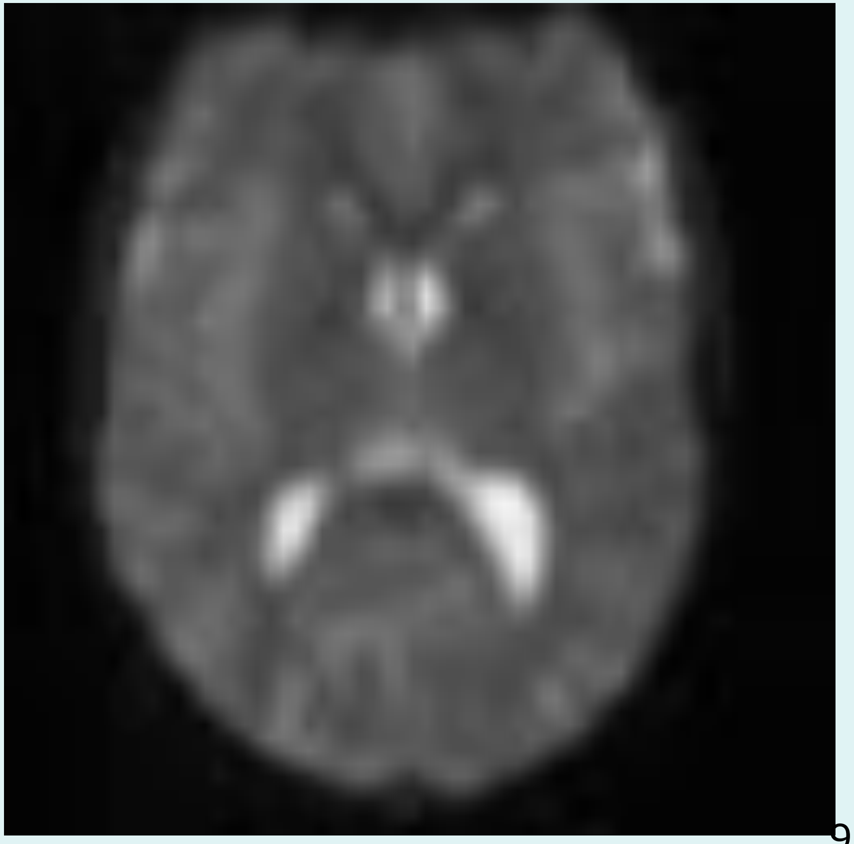

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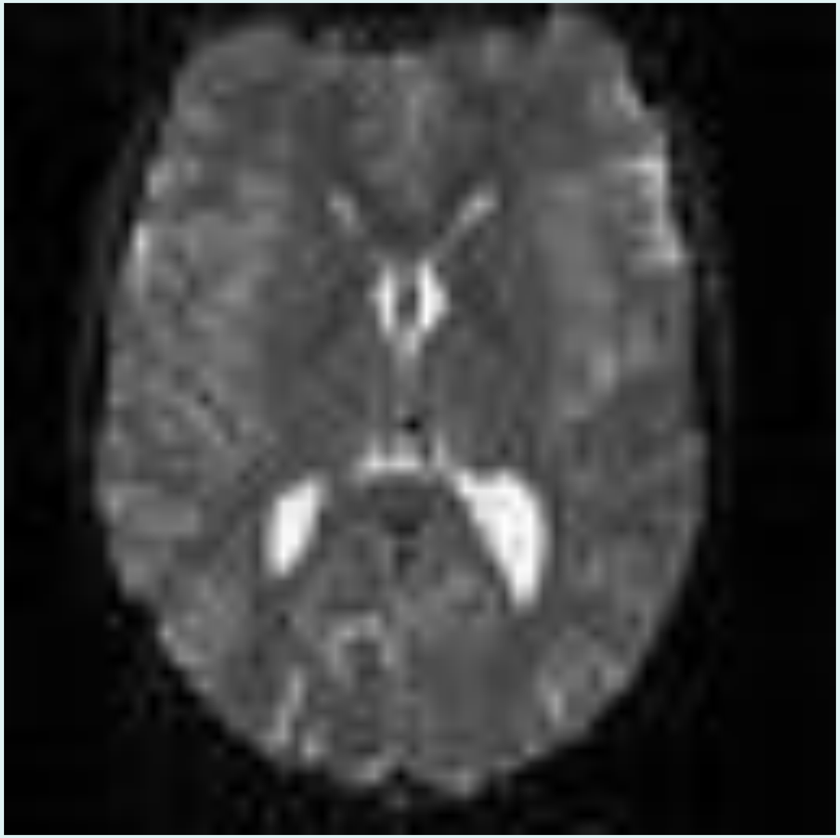

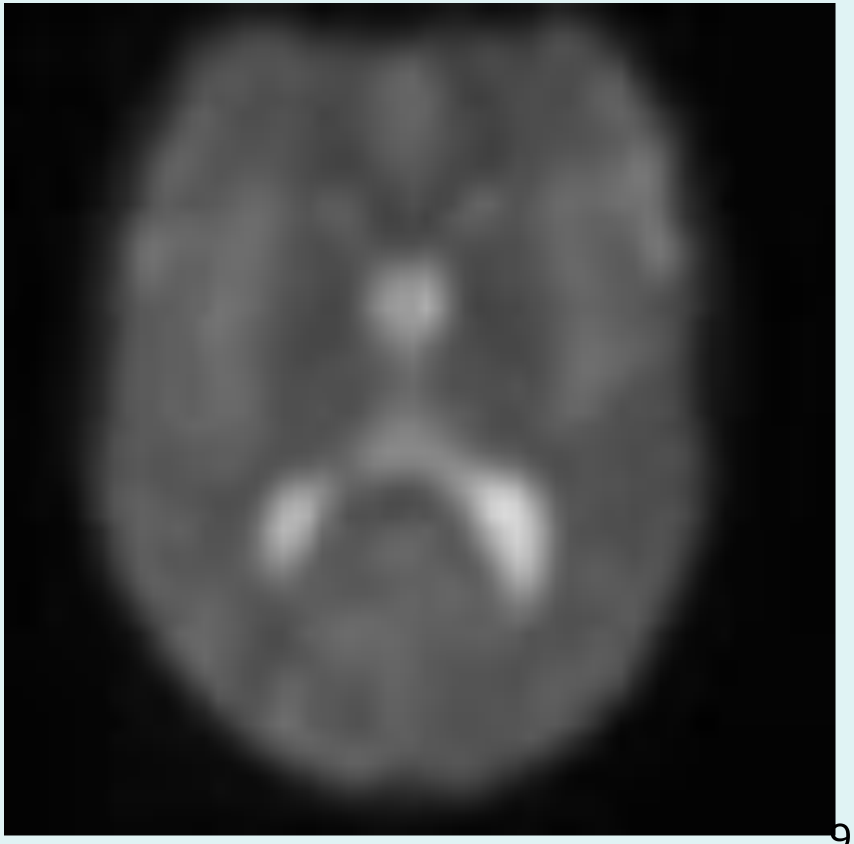

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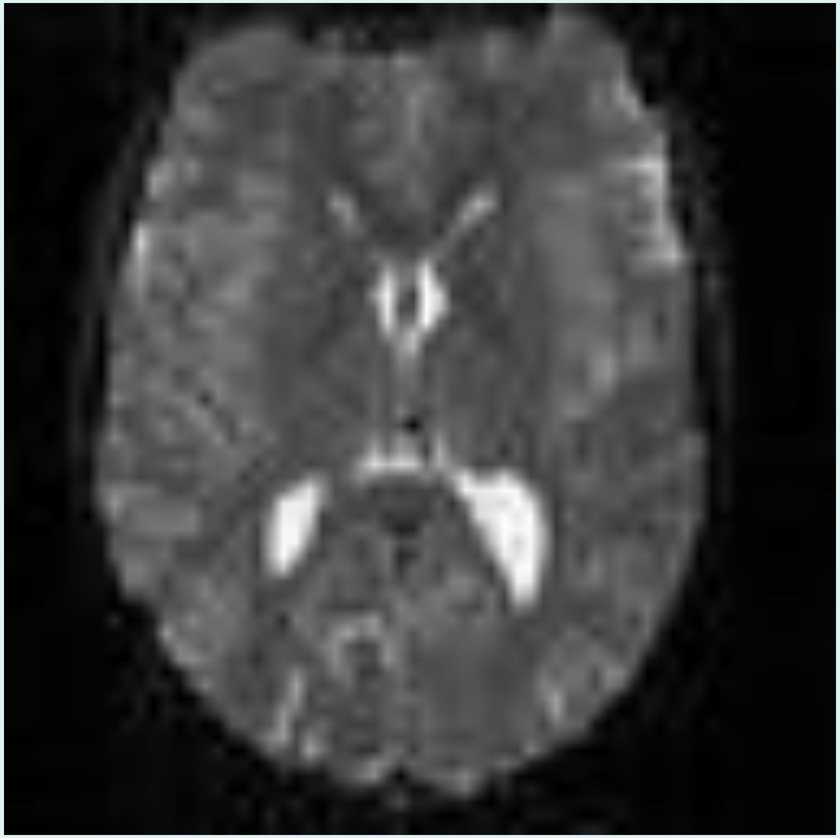

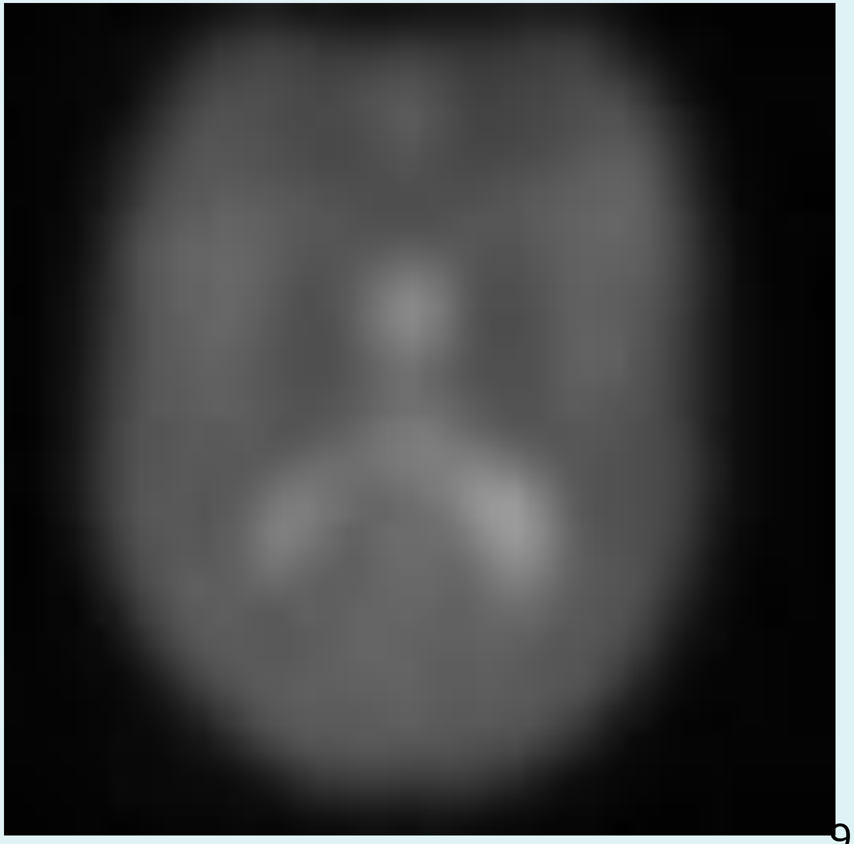

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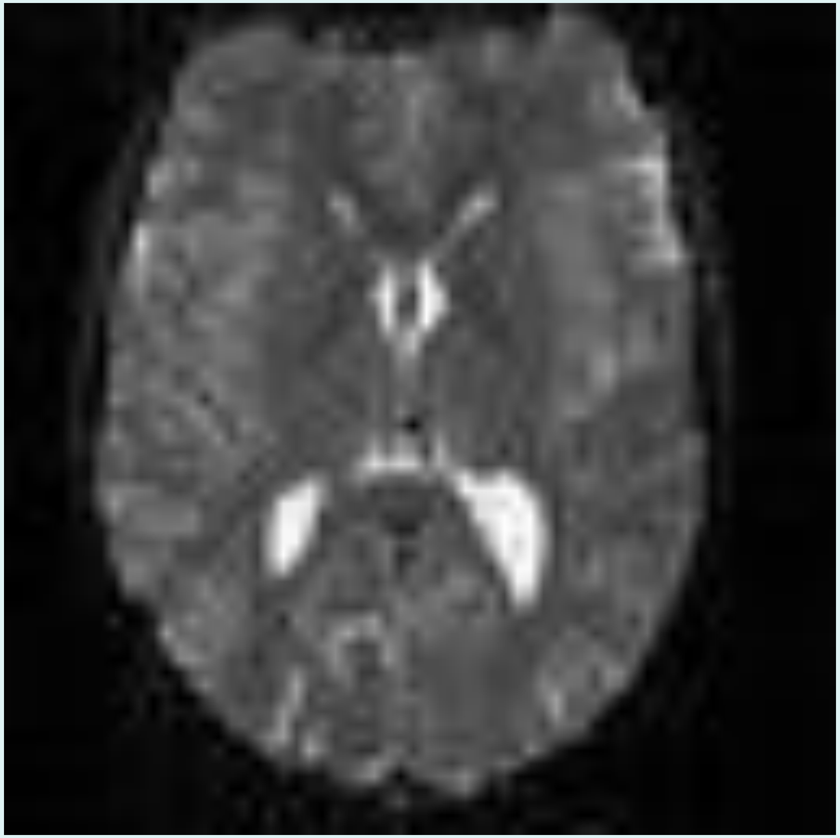

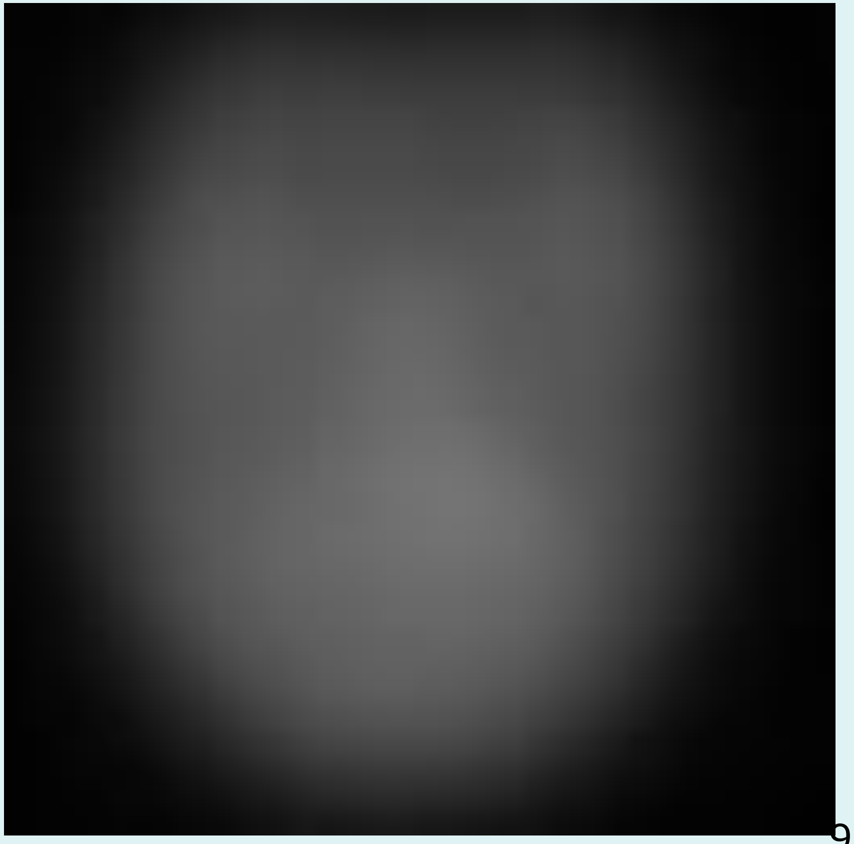

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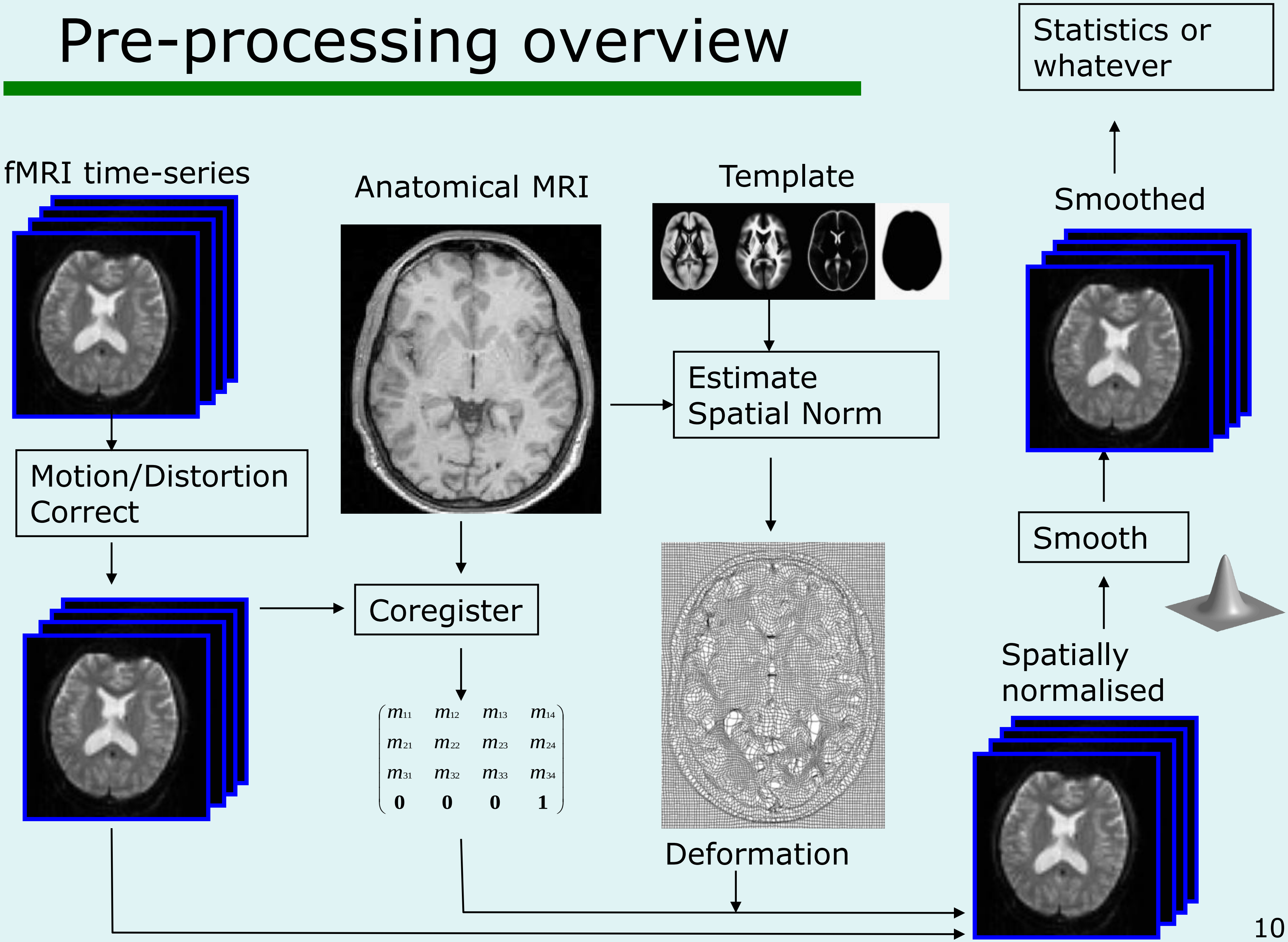
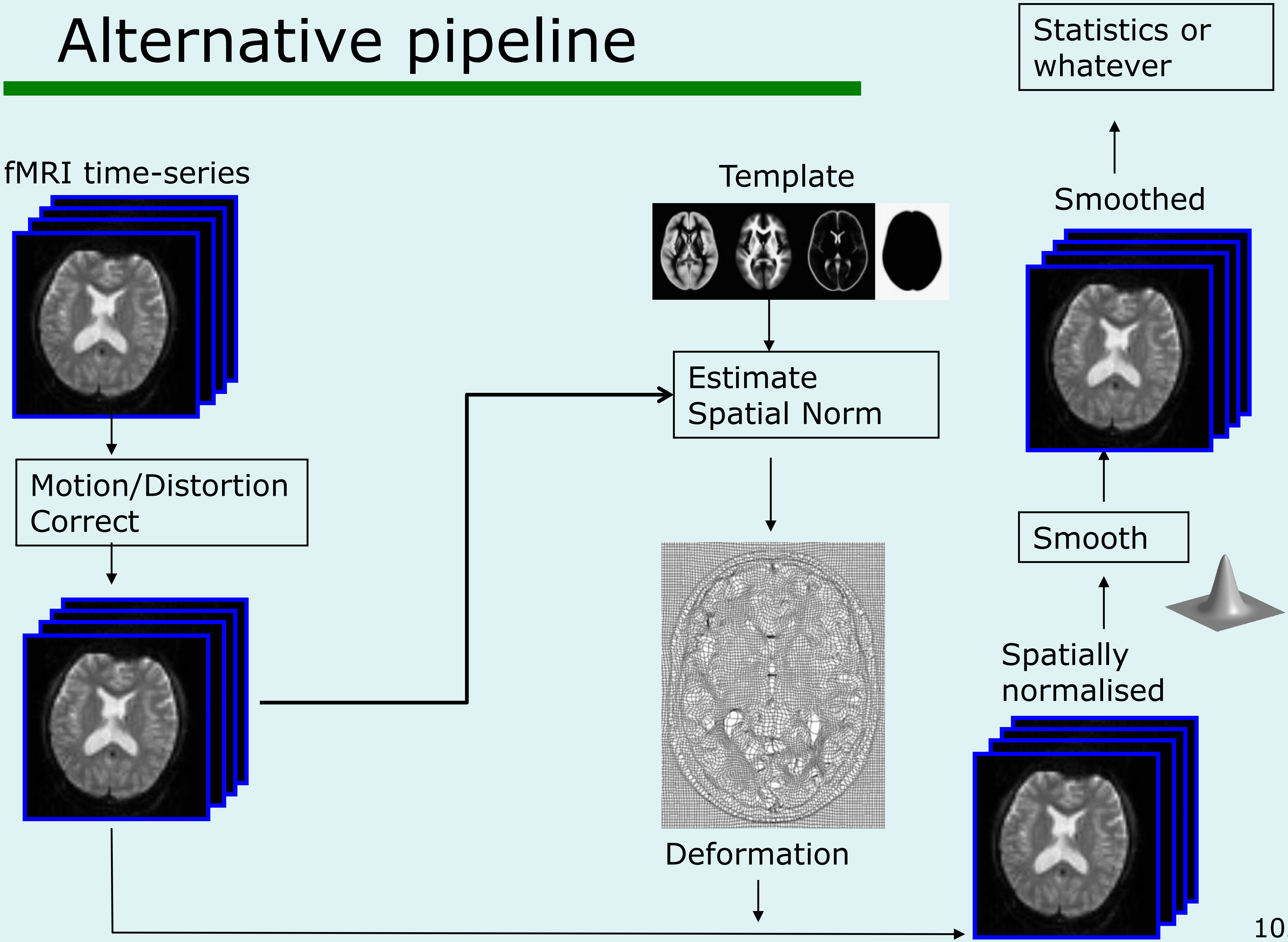
Pre-processing overview



Alternative pipeline



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