



Signal, Noise and Preprocessing*

Methods and Models for fMRI Analysis

Sam Harrison

October 9th, 2018

Translational Neuromodeling Unit

Generous slide support:

Lars Kasper

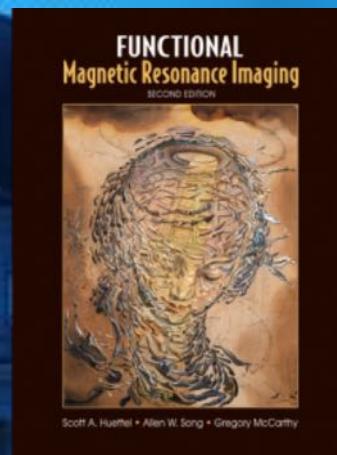
Guillaume Flandin

Ged Ridgway

Klaas Enno Stephan

John Ashburner

*Huettel et al.



Overview of SPM for fMRI



SNR & Preproc

Temporal

Spatial

General

Realign

Coreg

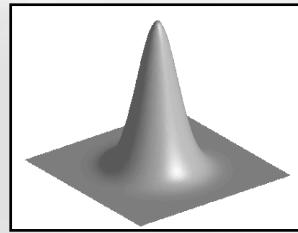
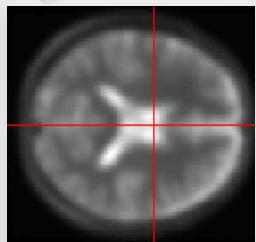
Normalise

Smooth

Preprocessing

Image time-series

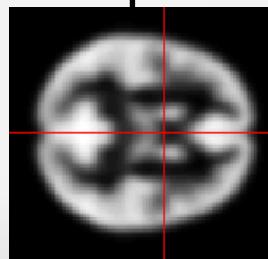
Kernel



Realignment

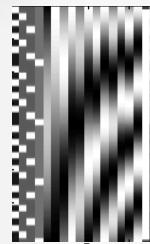
Smoothing

Normalisation

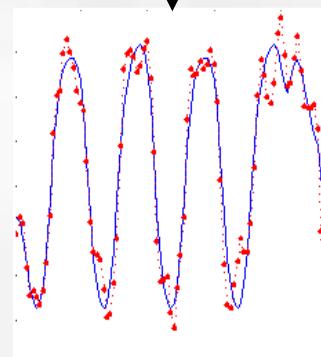


Template

Design matrix

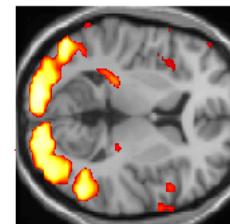
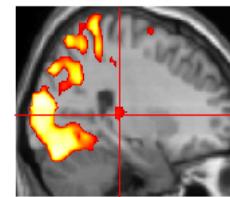


General linear model

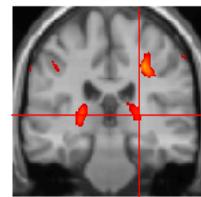


Parameter estimates

Statistical parametric map (SPM)



Statistical
inference



Random
field theory

$p < 0.05$

fMRI = Acquiring Movies



SNR & Preproc

Temporal

Spatial

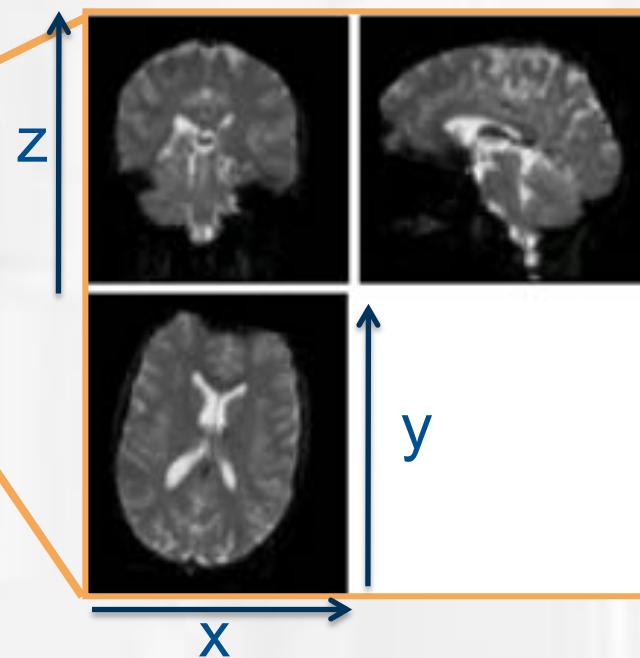
General

Realign

Coreg

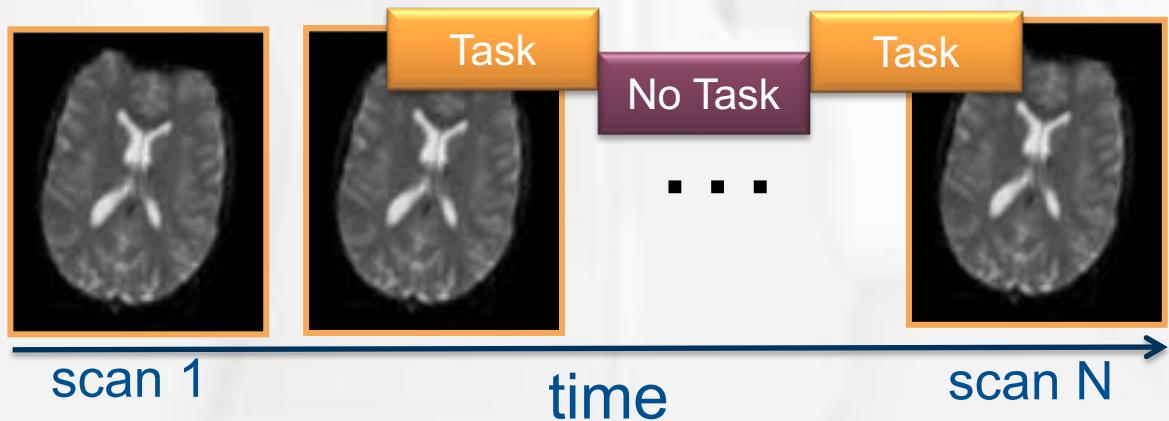
Normalise

Smooth



- ...of 3D Blood-Oxygen-Level Dependent (BOLD) contrast images
- typically Echo-Planar Images (EPI)

- Run/session:
time-series of
images



fMRI = Acquiring Movies



SNR & Preproc

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General

Realign

Coreg

Normalise

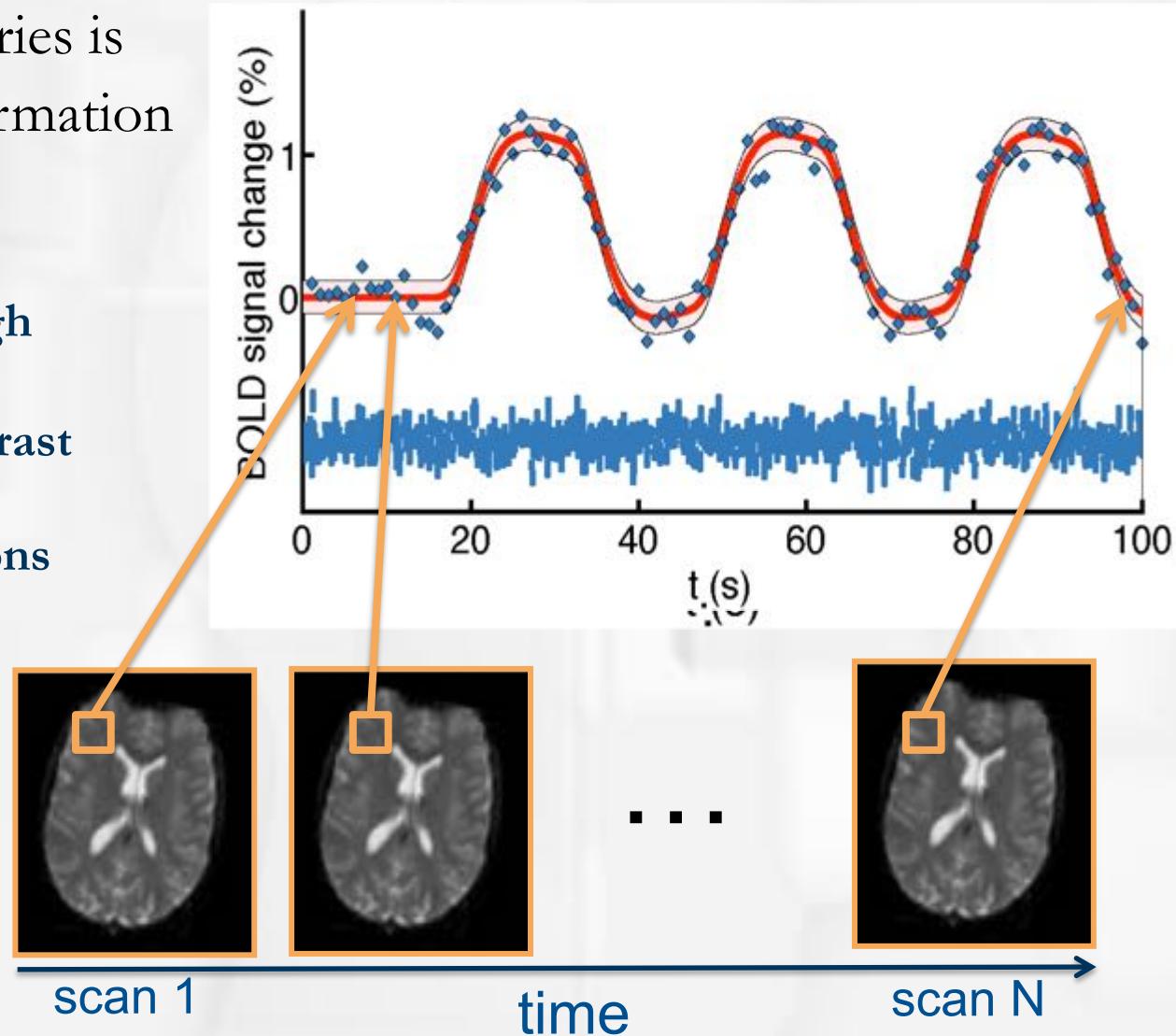
Smooth

- The localized time-series is the fundamental information unit of fMRI

Signal: fluctuation through Blood-Oxygen-Level Dependent (**BOLD**) contrast

Noise: all other fluctuations

- Run/session: time-series of images



fMRI Movie: An example



SNR & Preproc

Temporal

Spatial

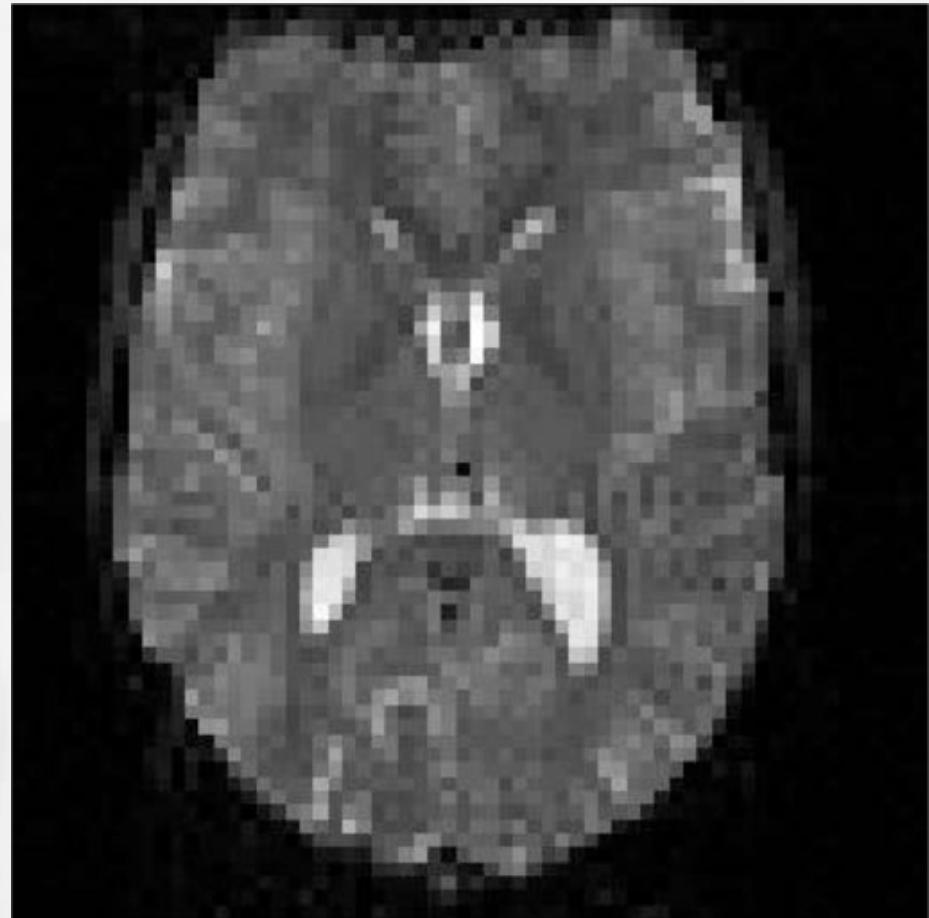
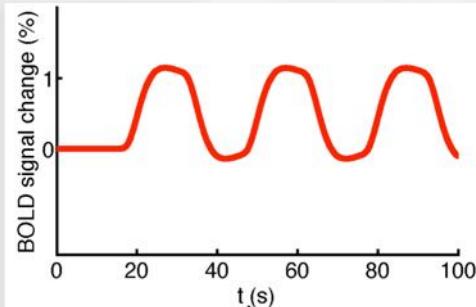
General

Realign

Coreg

Normalise

Smooth



fMRI Movie: Subtract the Mean



SNR & Preproc

Temporal

Spatial

General

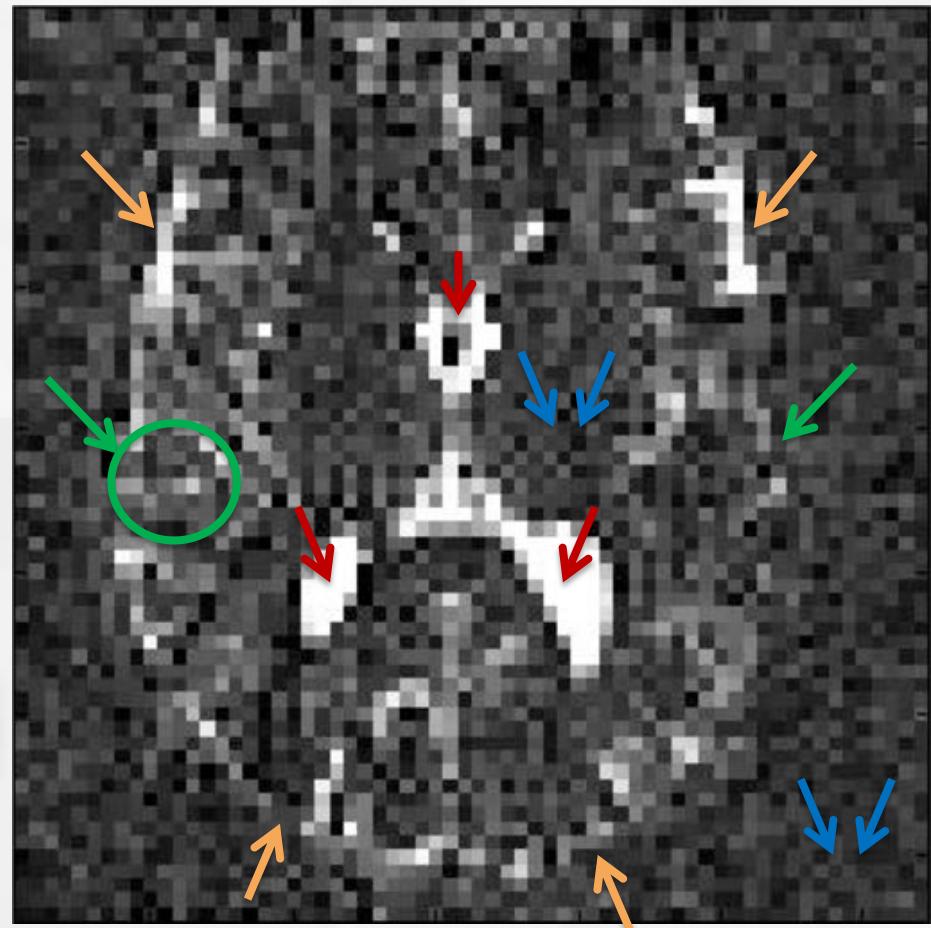
Realign

Coreg

Normalise

Smooth

- Interested in fluctuations only



The Goal of Preprocessing



SNR & Preproc

Temporal

Spatial

General

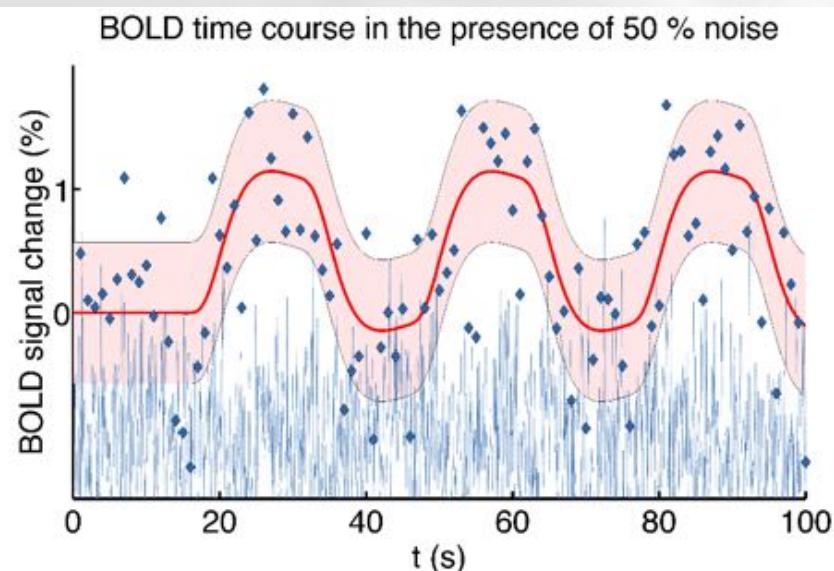
Realign

Coreg

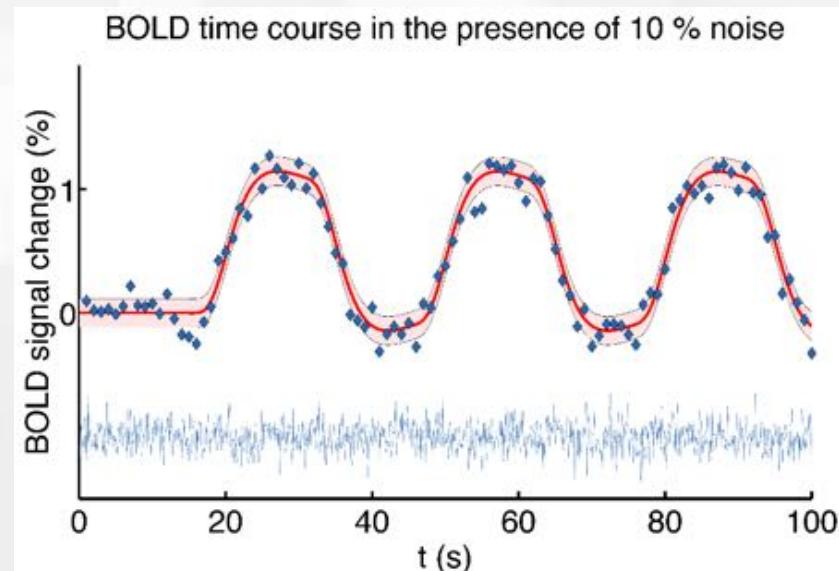
Normalise

Smooth

Before



After



Preprocessing

Sources of Noise in fMRI



SNR & Preproc

Temporal

Spatial

General

Realign

Coreg

Normalise

Smooth

- Acquisition Timing
- Subject Motion
- Anatomical Identity
- Inter-subject variability
- Thermal Noise
- Physiological Noise

Temporal Preproc

Spatial Preproc

Spatial Preproc

Spatial Preproc

Spatial Preproc

Noise Modeling

- Slice-Timing
- Realignment
- Co-registration
- Segmentation
- Smoothing
- PhysIO Toolbox

fMRI Movie: Noise Sources



SNR & Preproc

Temporal

Spatial

General

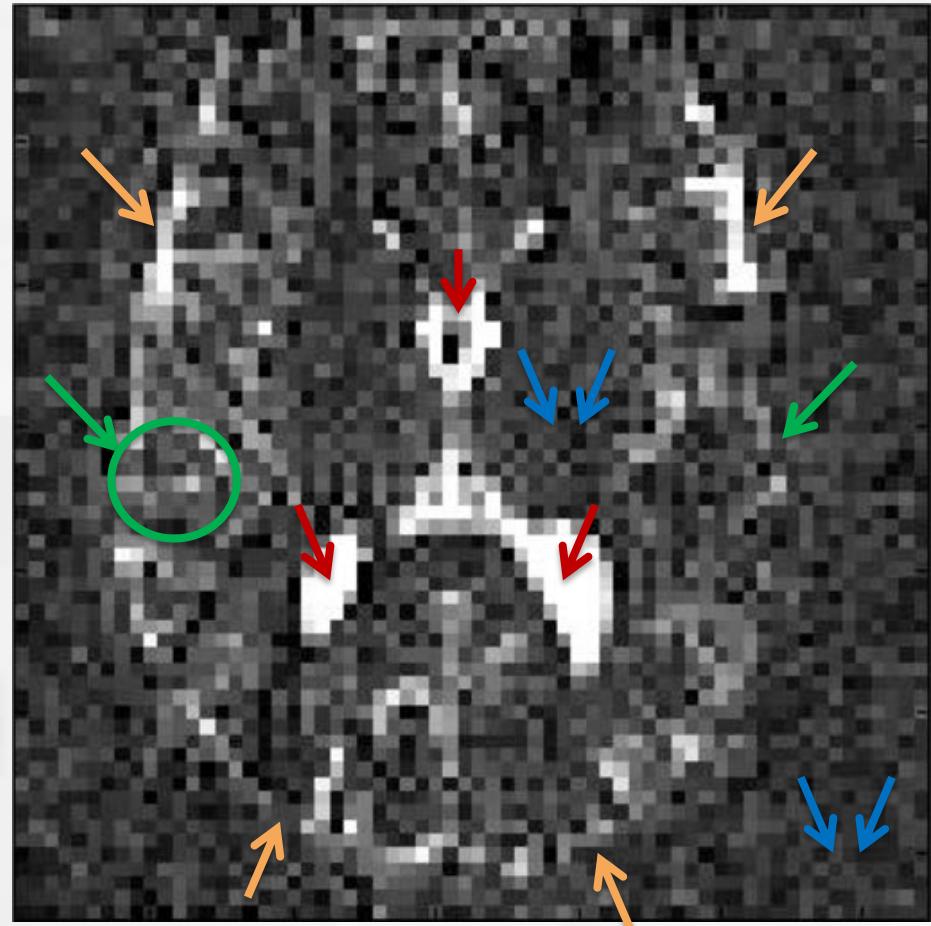
Realign

Coreg

Normalise

Smooth

- interest in fluctuations only



The SPM Graphical User Interface



SNR & Preproc

Temporal

Spatial

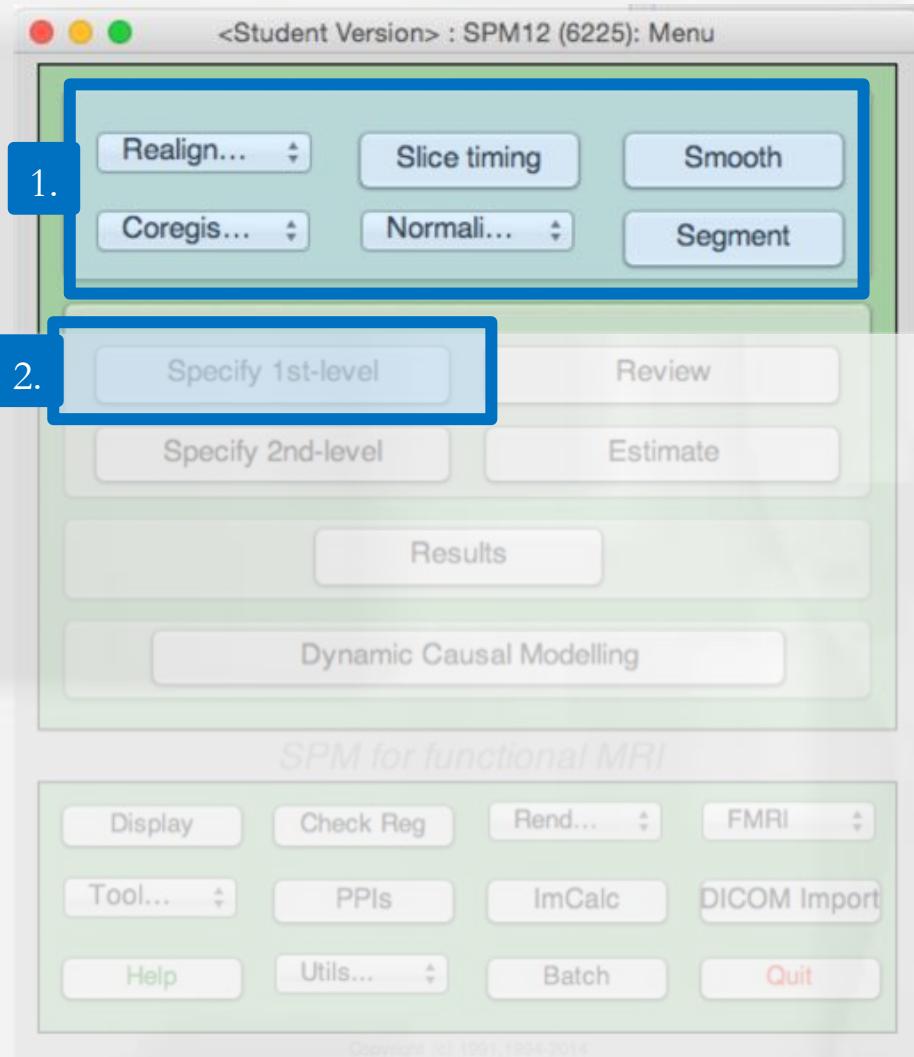
General

Realign

Coreg

Normalise

Smooth



■ Preprocessing

- Realignment
- Slice-Timing Correction
- Co-registration
- Unified Segmentation & Normalisation
- Smoothing...

■ Noise Modeling

- Physiological Confound Regressors

Sources of Noise in fMRI



SNR & Preproc

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Temporal Preproc

- Slice-Timing
- Realignment
- Co-registration
- Segmentation
- Smoothing
- PhysIO Toolbox

Slice-timing correction (STC)



SNR & Preproc

Temporal

Spatial

General

Realign

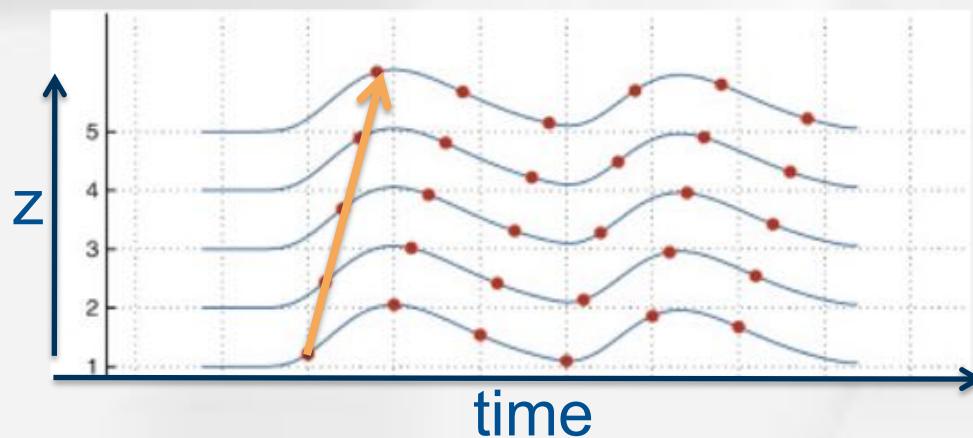
Coreg

Normalise

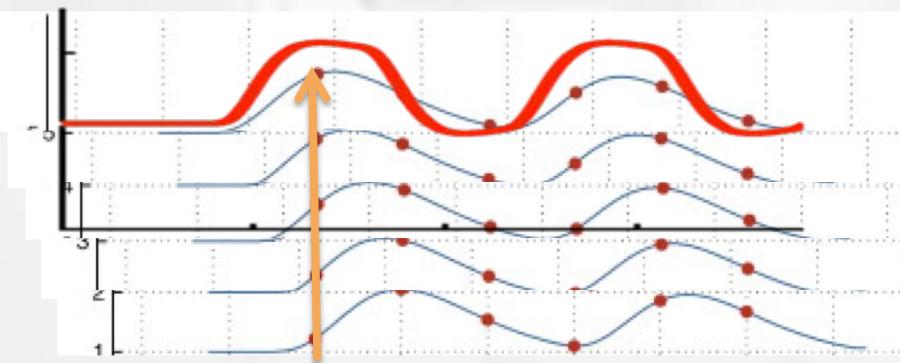
Smooth

- Slices of 1 scan volume are not acquired simultaneously (60 ms per slice)
- Creates shifts of up to 1 volume repetition time (TR), so typically several seconds
- This acquisition delay reduces sensitivity for time-locked effects (i.e. a smaller correlation with a temporally fixed model)

True 2D Acquisition



Same-Timepoint Assumption



Slice-timing correction (STC)



SNR & Preproc

Temporal

Spatial

General

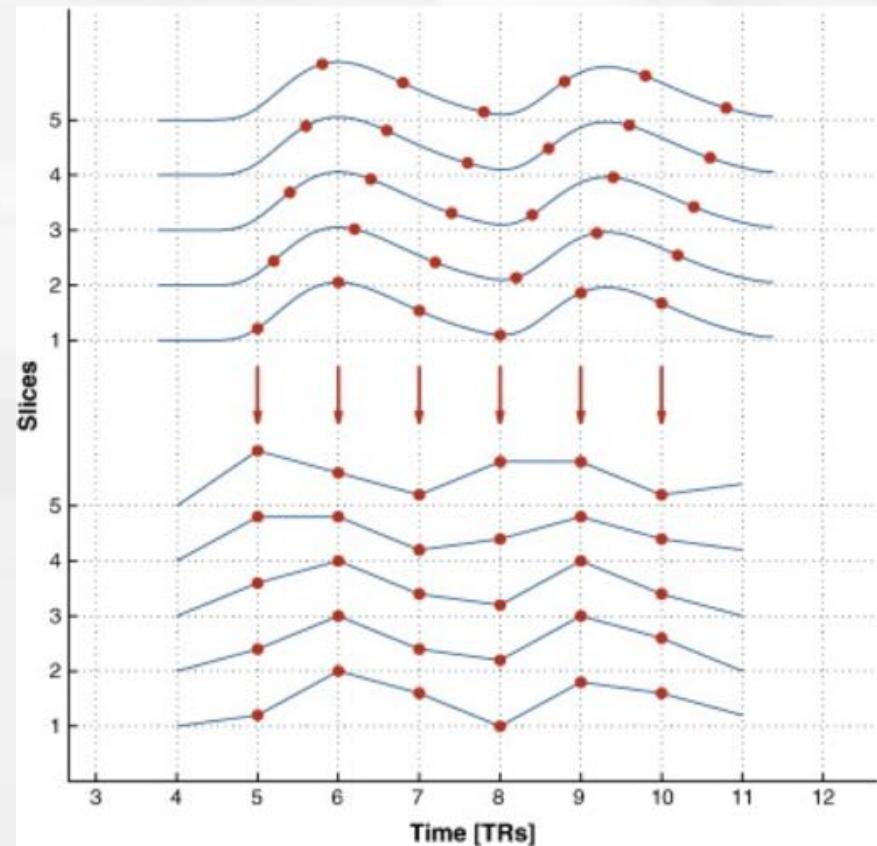
Realign

Coreg

Normalise

Smooth

- Slice-timing correction: all voxel time series are aligned to acquisition time of 1 slice
- Missing data is sinc-interpolated (band-limited signal)



Sladky et al, NeuroImage 2011

Interpolation



SNR & Preproc

Temporal

Spatial

General

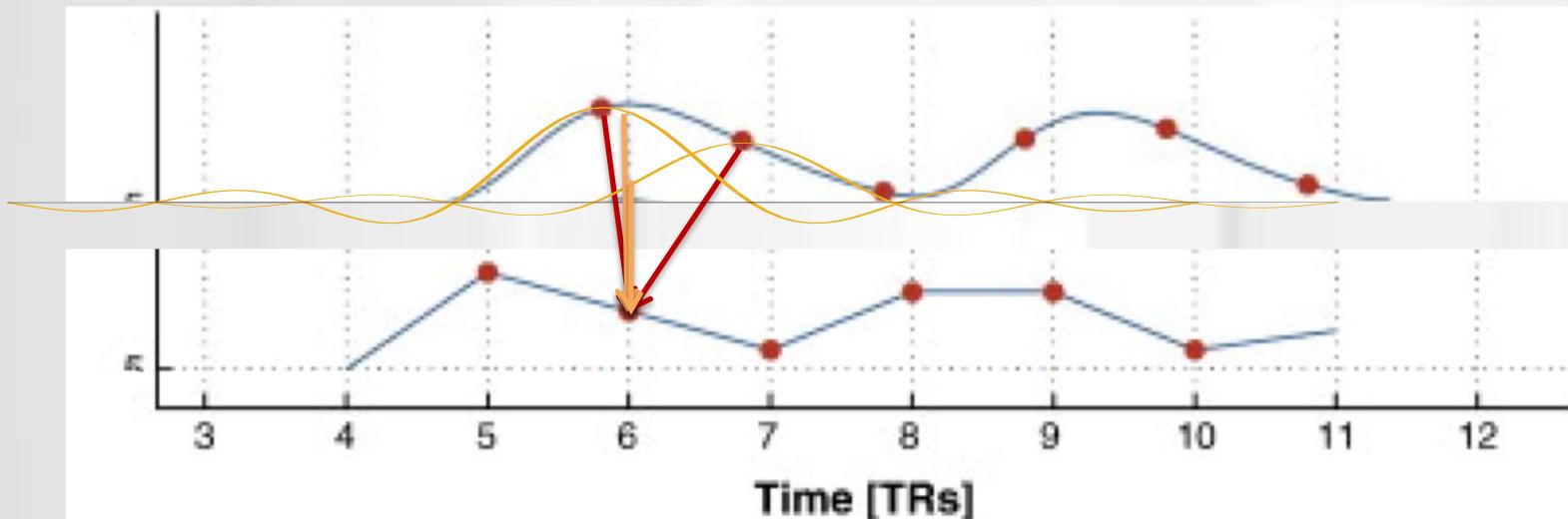
Realign

Coreg

Normalise

Smooth

- Interpolation: estimate missing data between existing data via certain regularity assumptions



- Signal at missing point is weighted average of neighbors
- Weighting function = interpolation “kernel”
- Here: assumption of limited frequency range of signal:
sinc-interpolation

Slice-timing correction (STC)



SNR & Preproc

Temporal

Spatial

General

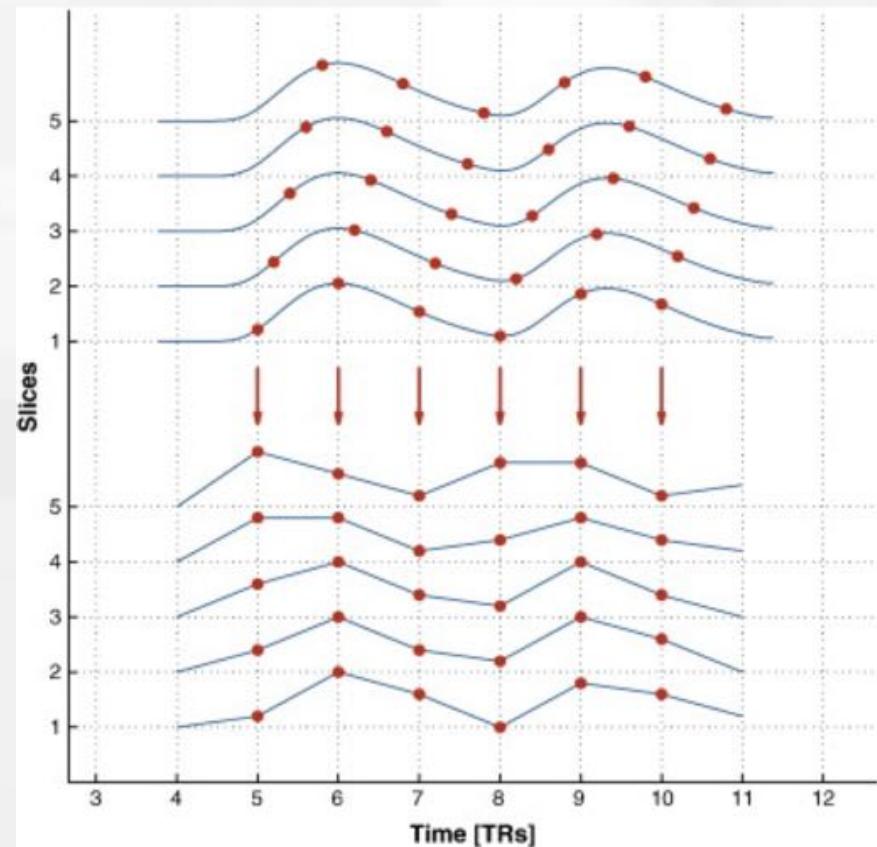
Realign

Coreg

Normalise

Smooth

- Slice-timing correction: all voxel time series are aligned to acquisition time of 1 slice
- Missing data is sinc-interpolated (band-limited signal)
- Before or after realignment?
 - before: dominant through-slice motion
 - after: dominant within-slice motion
- At all?



Sladky et al, NeuroImage 2011

STC Results: Simulation



SNR & Preproc

Temporal

Spatial

General

Realign

Coreg

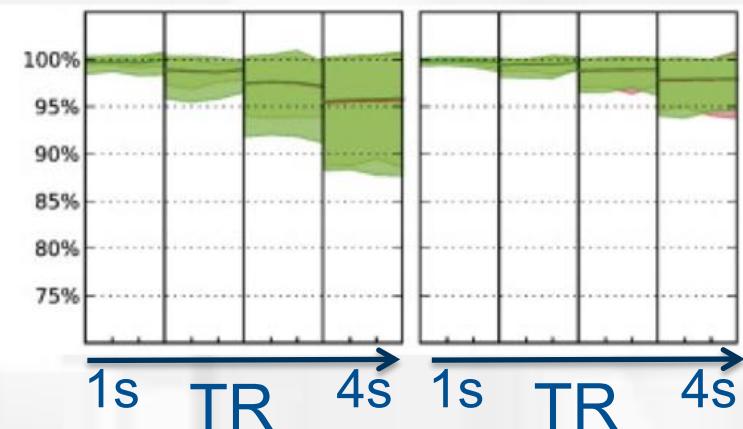
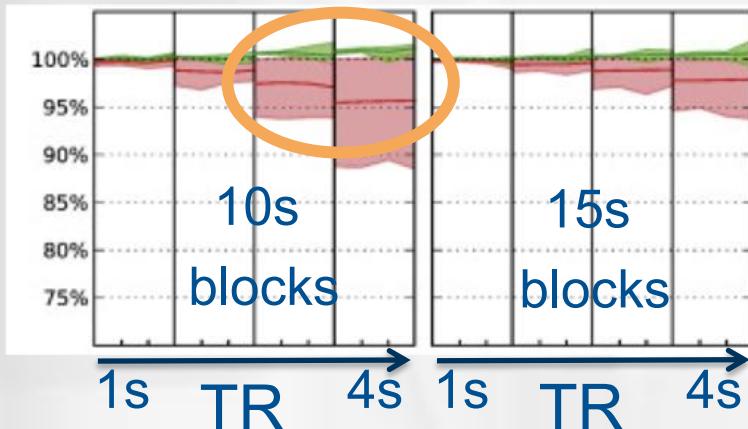
Normalise

Smooth

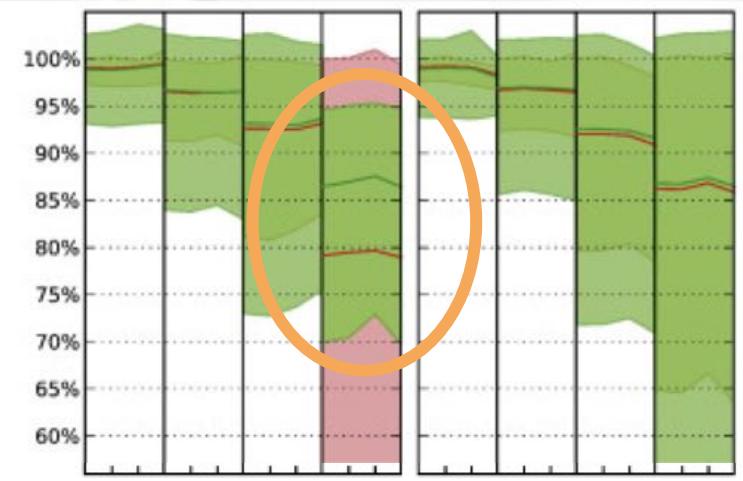
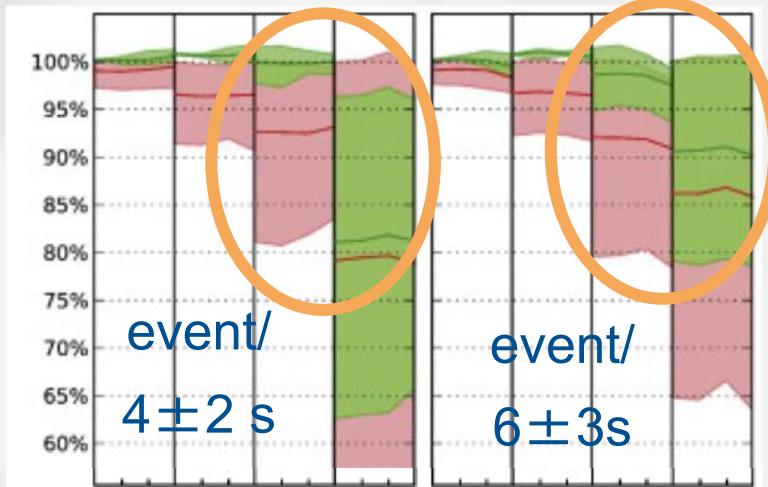
Slice-timing Correction

Temporal-Derivative Modelling

Block
Stimulation



Event-Related
Stimulation



true beta = 100 %
uncorrected
corrected

Sladky et al, NeuroImage 2011

STC Issues: Motion



SNR & Preproc

Temporal

Spatial

General

Realign

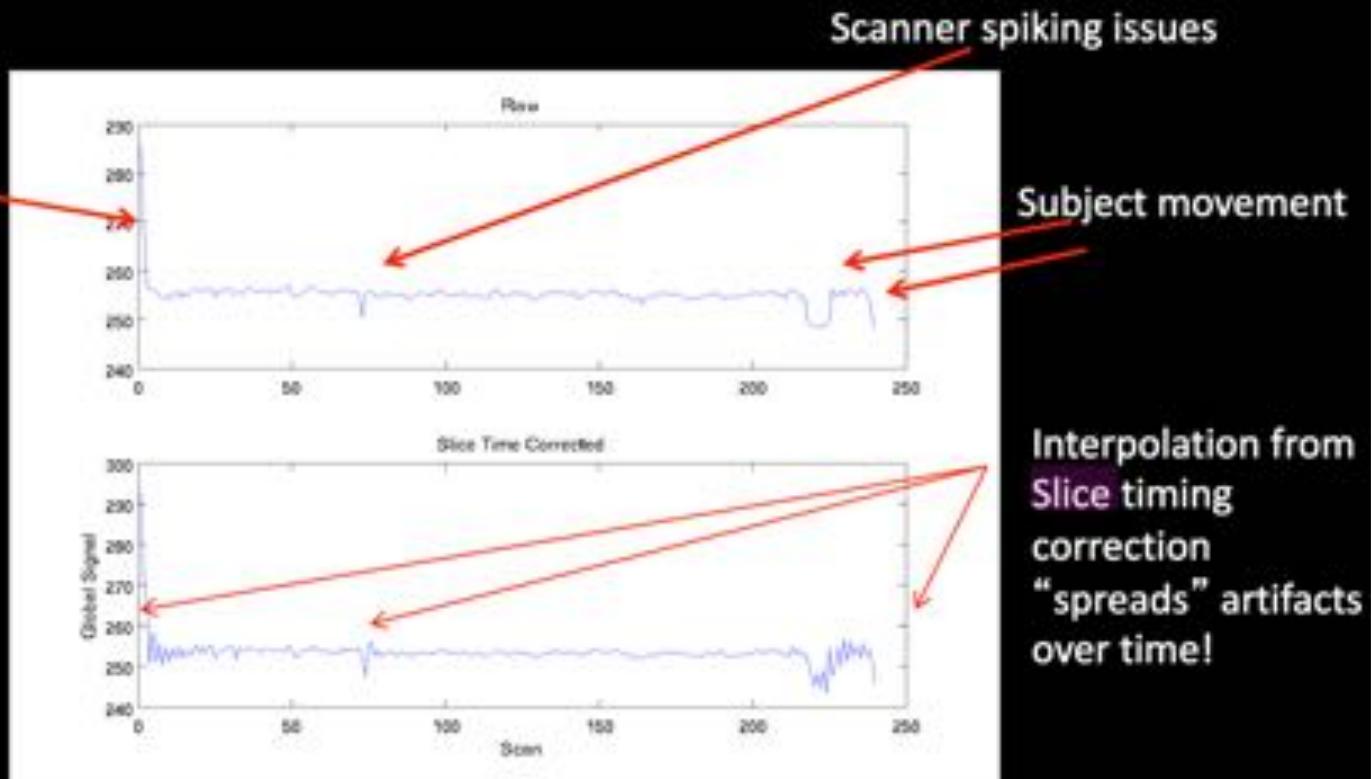
Coreg

Normalise

Smooth

T1 settling time

Global signal
(mean over space): a good indicator of large scale changes in signal



Courtesy of Derek Nec

Hernandez-Garcia, UM FMRI course

<http://imaging.mrc-cbu.cam.ac.uk/imaging/SliceTiming>

Slice-timing correction (STC)



SNR & Preproc

Temporal

Spatial

General

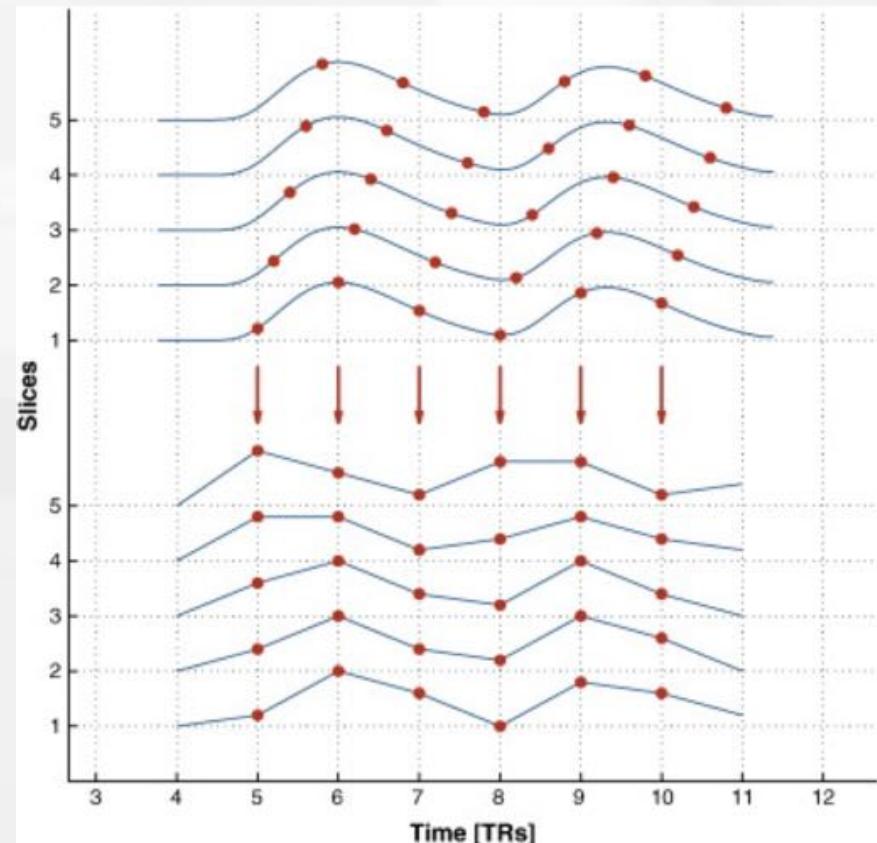
Realign

Coreg

Normalise

Smooth

- Slice-timing correction: all voxel time series are aligned to acquisition time of 1 slice
- Missing data is sinc-interpolated (band-limited signal)
- Before or after realignment?
 - before: dominant through-slice motion
 - after: dominant within-slice motion
- At all?
 - block design: for long TR (3s+) & short blocks (10s) improves estimates > 5 %
 - event-related: for normal TRs (2s+) improves estimates > 5 %



Sladky et al, NeuroImage 2011

STC Results: Experiment



SNR & Preproc

Temporal

Spatial

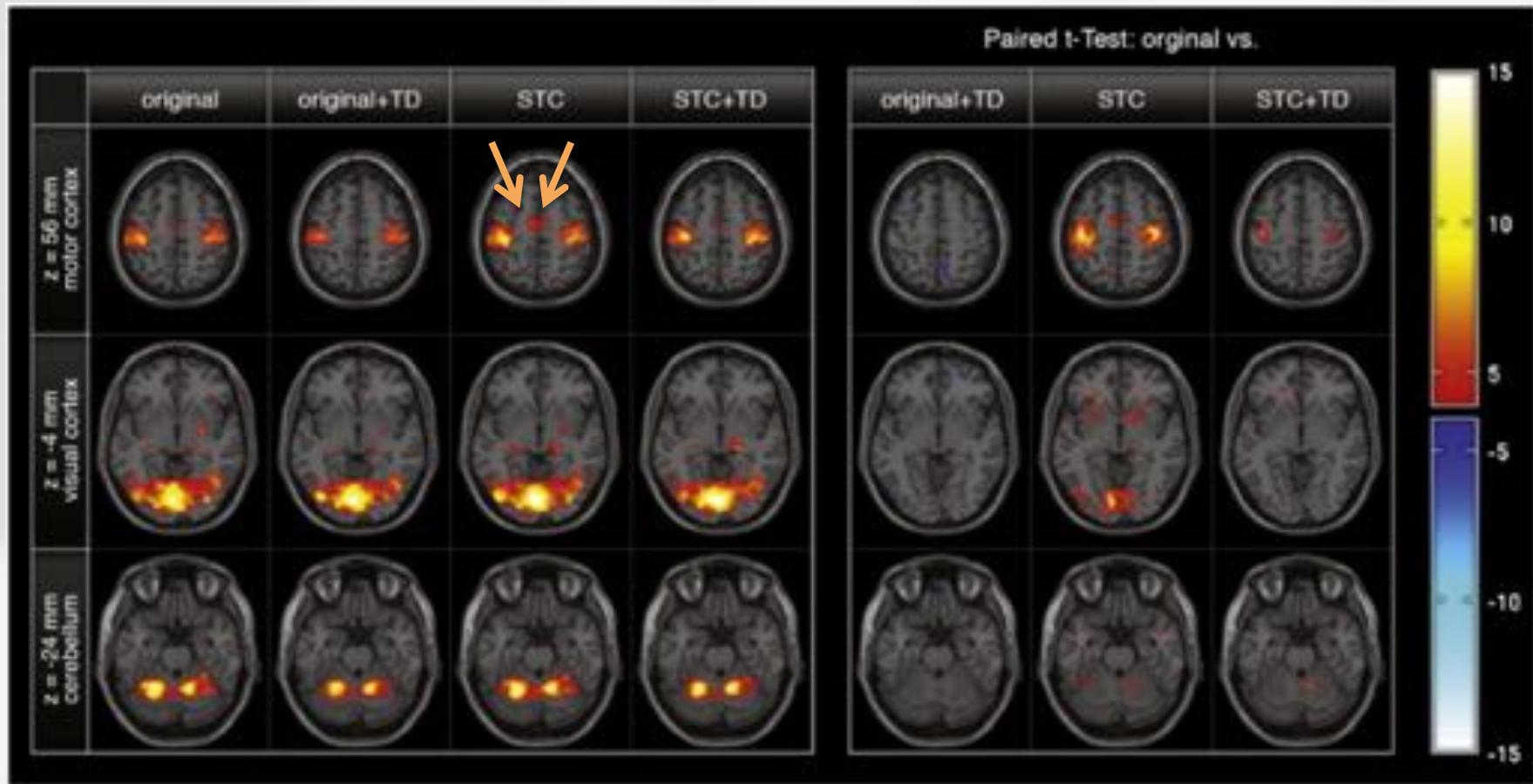
General

Realign

Coreg

Normalise

Smooth



Sladky et al, *NeuroImage* 2011



Sources of Noise in fMRI

SNR & Preproc

Temporal

Spatial

General

Realign

Coreg

Normalise

Smooth

- Acquisition Timing
- Subject Motion
- Anatomical Identity
- Inter-subject variability
- Thermal Noise
- Physiological Noise

Spatial Preproc

Spatial Preproc

Spatial Preproc

Spatial Preproc

- Slice-Timing
- Realignment
- Co-registration
- Segmentation
- Smoothing
- PhysIO Toolbox

Finite Resolution and Voxel Identity



SNR & Preproc

Temporal

Spatial

General

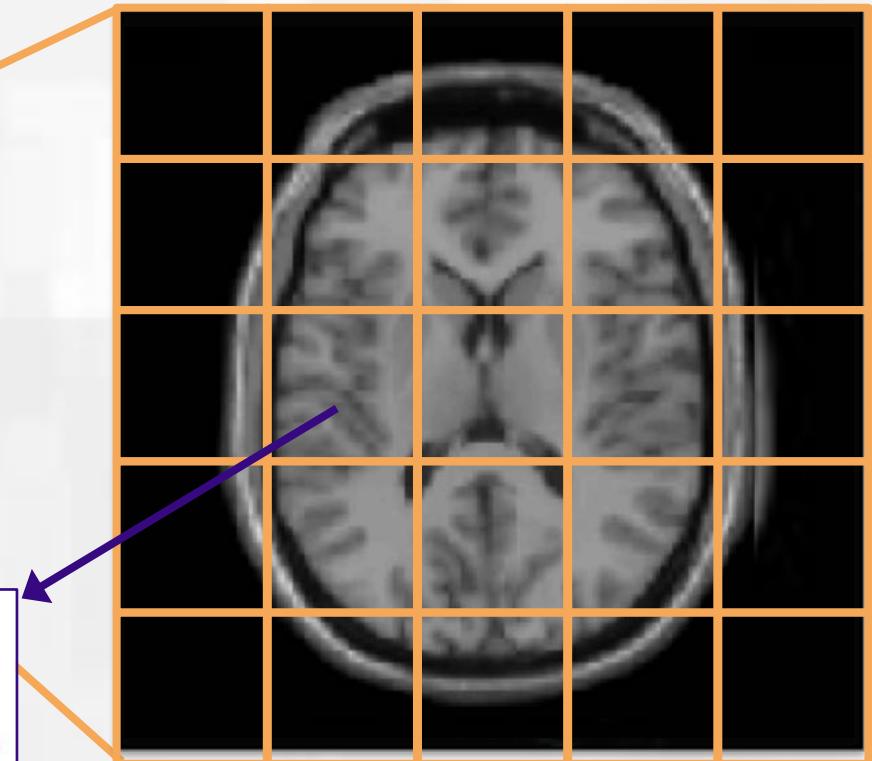
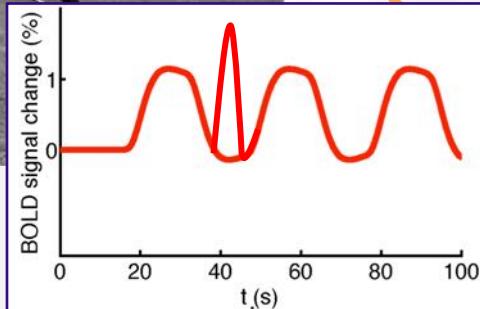
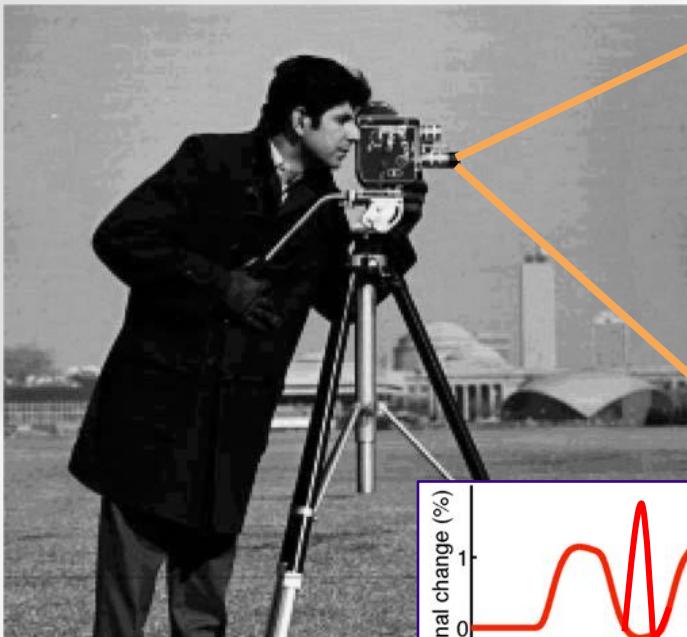
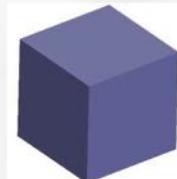
Realign

Coreg

Normalise

Smooth

- voxel = volume element (3D pixel)



Preproc = Correct Voxel Mismatch



SNR & Preproc

Temporal

Spatial

General

Realign

Coreg

Normalise

Smooth

Voxel Mismatch Between

Functional
Scans/Runs

Functional/Structural
Images

Subjects

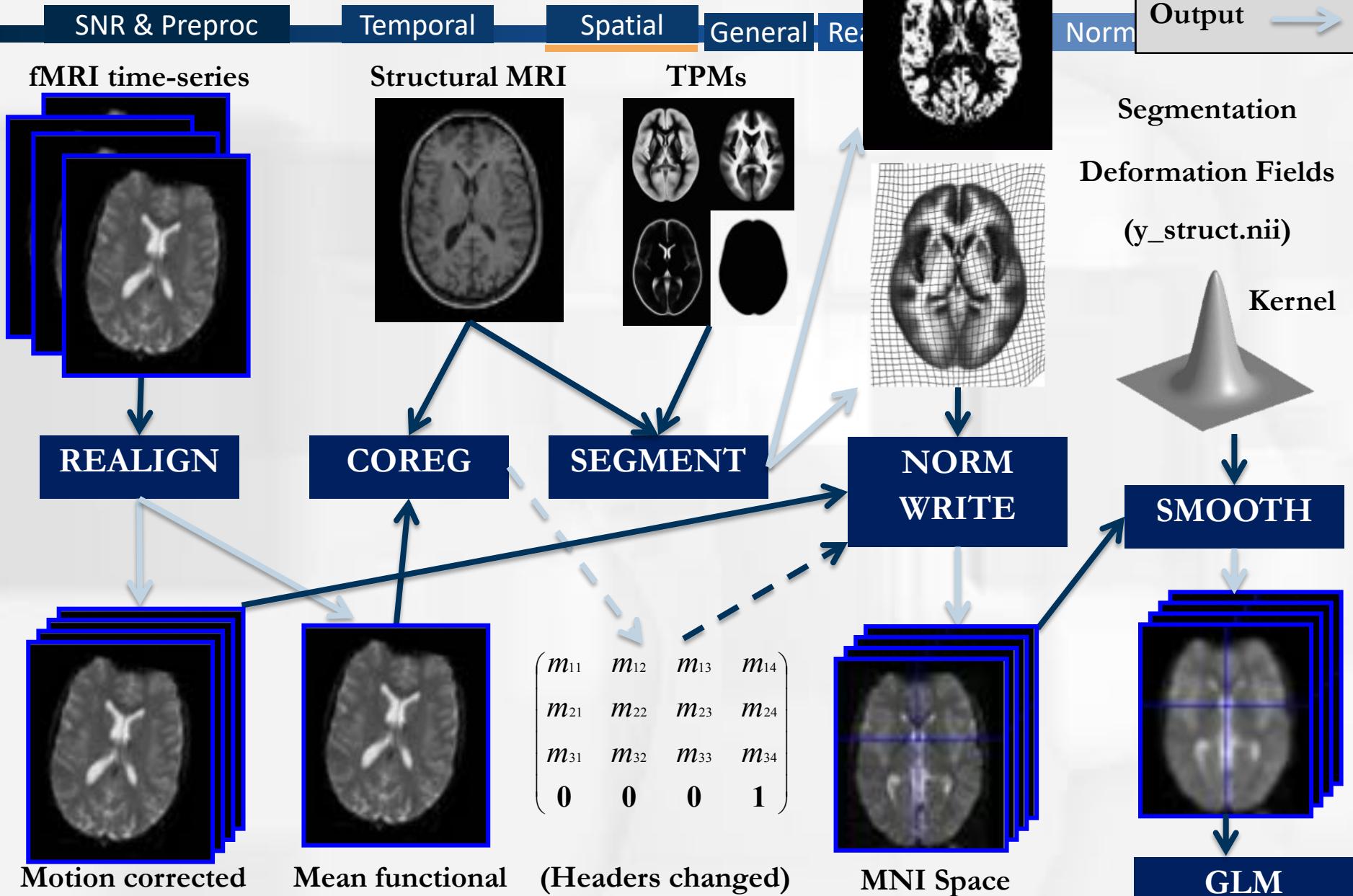
Realignment

Inter-Modal
Coregistration

Normalisation/
Segmentation

Smoothing

Spatial Preprocessing



General Remarks: Image Registration



SNR & Preproc

Temporal

Spatial

General

Realign

Coreg

Normalise

Smooth

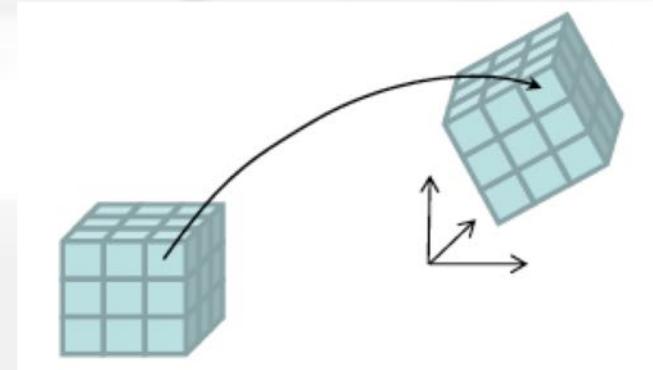
- Realignment, Co-Registration and Normalisation (via Unified Segmentation) are all *image registration methods*
- Goal: manipulate one set of images to arrive in same coordinate system as a reference image
- Key ingredients for image registration
 - A. Voxel-to-world mapping
 - B. Transformation
 - C. Similarity Measure
 - D. Optimisation
 - E. Interpolation

A. Voxel-to-World Mapping



SNR & Preproc Temporal Spatial General **Realign** Coreg Normalise Smooth

- 3D images are made up of voxels.
- Voxel intensities are stored on disk as lists of numbers.
- Meta-information about the data:
 - image dimensions
 - conversion from list to 3D array
 - “voxel-to-world mapping”
 - Spatial transformation that maps
 - from: data coordinates (voxel column i, row j, slice k)
 - to: a real-world position (x,y,z mm) in a coordinate system e.g.:
 - Scanner coordinates
 - T&T/MNI coordinates



A. Voxel-to-World: Standard Spaces



SNR & Preproc

Temporal

Spatial

General

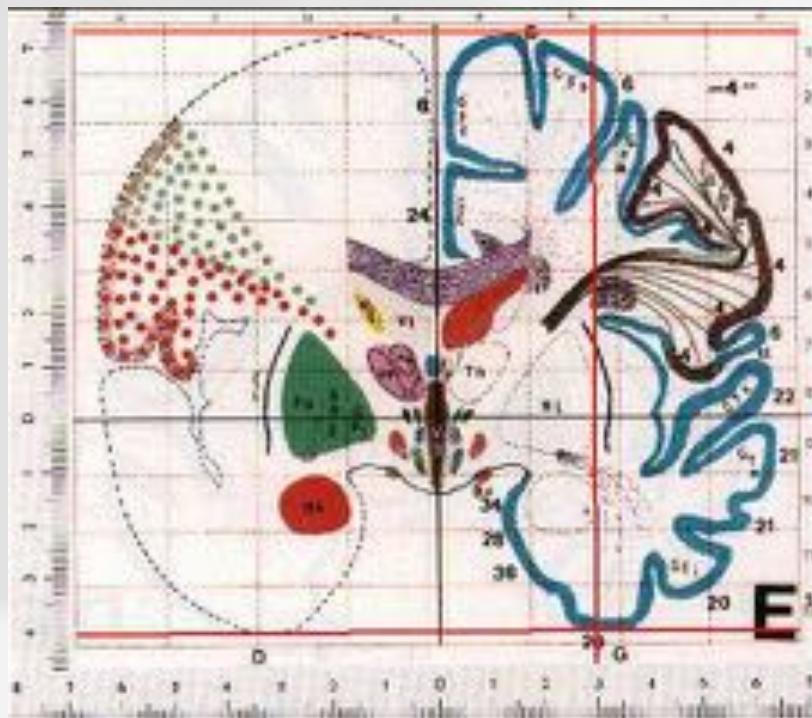
Realign

Coreg

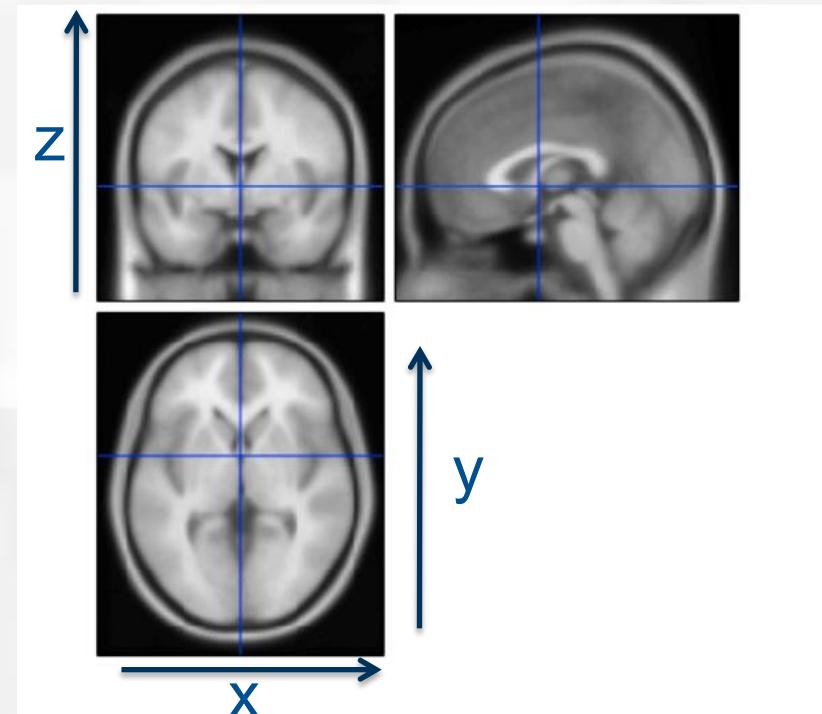
Normalise

Smooth

Talairach Atlas



MNI/ICBM AVG152 Template



- Definition of coordinate system:
 - Origin (0,0,0): anterior commissure
 - Right = +X; Anterior = +Y; Superior = +Z

- Actual brain dimensions
 - European brains,
a bit dilated (bug)

B. Transformations



SNR & Preproc

Temporal

Spatial

General

Realign

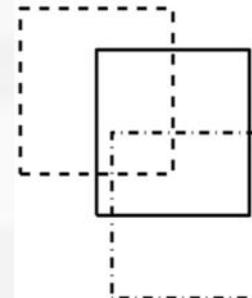
Coreg

Normalise

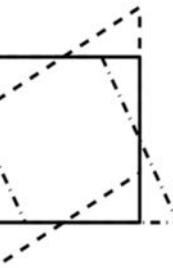
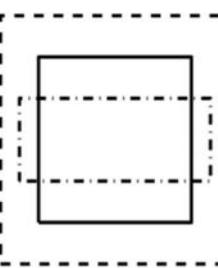
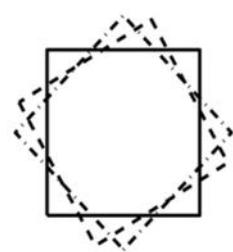
Smooth

- Transformations describe the mapping of all image voxels from one coordinate system into another
- Types of transformations
 - rigid body = translation + rotation
 - affine = rigid body + scaling + shear
 - non-linear = any mapping
 - (x,y,z) to new values (x',y', z')
 - described by deformation fields

Translation

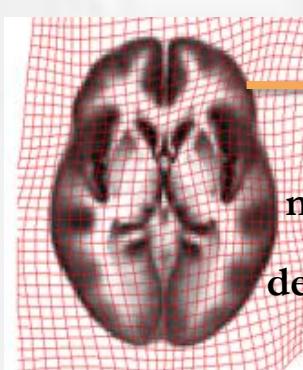


Rotation

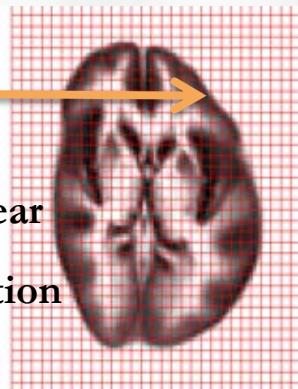


Scaling

Shear



non-linear
deformation



Spatial Preproc: SPM vocabulary



SNR & Preproc

Temporal

Spatial

General

Realign

Coreg

Normalise

Smooth

- SPM uses different names for different modes of image registration
- depending on input images and allowed transformations



- Intra-modal image registration
 - e.g. functional images
- rigid body transformations
 - translation/rotation
- Inter-modal registration
 - e.g. T1/T2 contrast
 - functional to structural image
- affine transformations
 - rigid body
 - stretching/shearing
- Multi-modal registration
 - e.g. T1 and/or T2
 - structural image(s) to template
- non-linear transformations
 - voxel-wise mapping (deformation fields)

C. Similarity & D. Optimisation



SNR & Preproc

Temporal

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General

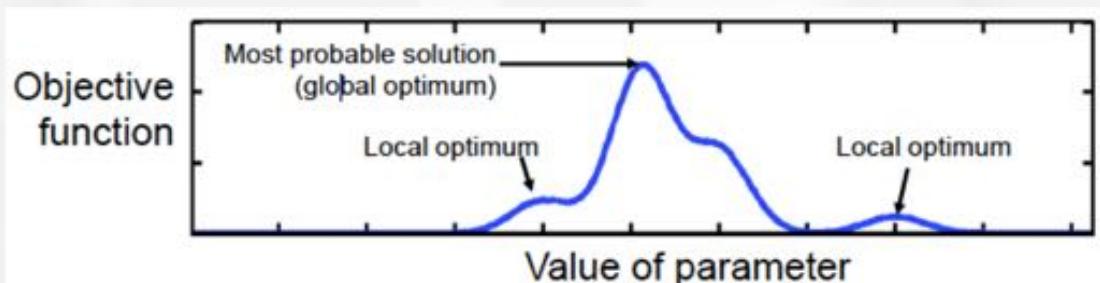
Realign

Coreg

Normalise

Smooth

- Similarity measure summarizes resemblance of (transformed) image and reference into 1 number
 - mean-squared difference
 - correlation-coefficient
 - mutual information
- Automatic image registration uses an optimisation algorithm to maximise/minimise an “objective function”
 - Similarity measure is part of objective function
 - Algorithm searches for transformation that maximises similarity of transformed image to reference
 - Also includes constraints on allowed transformations (priors)



Preprocessing Step Categorisation



SNR & Preproc

Temporal

Spatial

General

Realign

Coreg

Normalise

Smooth

B. Allowed Transformations

Rigid-Body

Affine

Non-linear

REALIGN

COREG

SEGMENT

NORM
WRITE

C. Similarity Measure

Mean-squared
Difference

Mutual
Information

Tissue Class
Probability

Exact Linearized
Solution

Conjugate Direction
Line Search

Iterated Conditional Modes
(EM/Levenberg-Marquardt)

E. Reslicing/Interpolation



SNR & Preproc

Temporal

Spatial

General

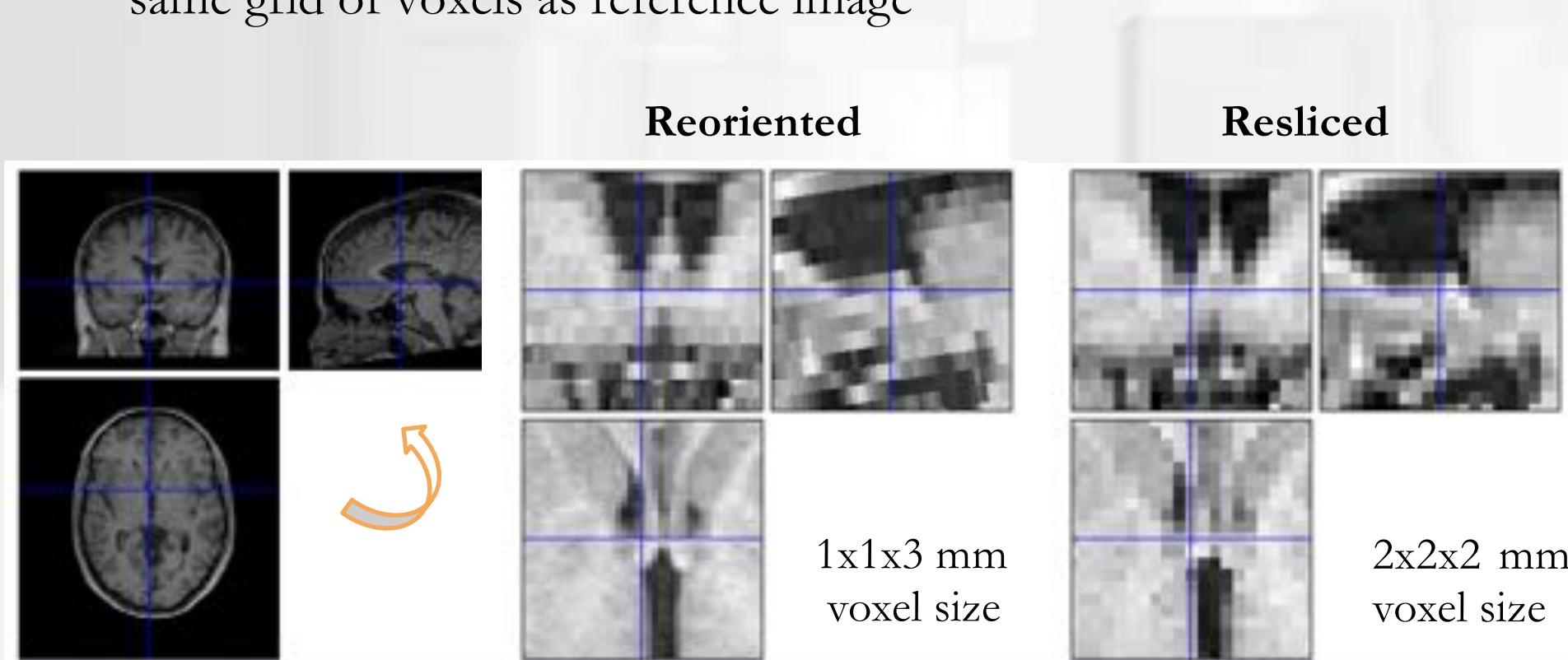
Realign

Coreg

Normalise

Smooth

- Finally, images have to be saved as voxel intensity list on disk again
- After applying transformation parameters, data is re-sampled onto same grid of voxels as reference image



E. B-spline Interpolation



SNR & Preproc

Temporal

Spatial

General

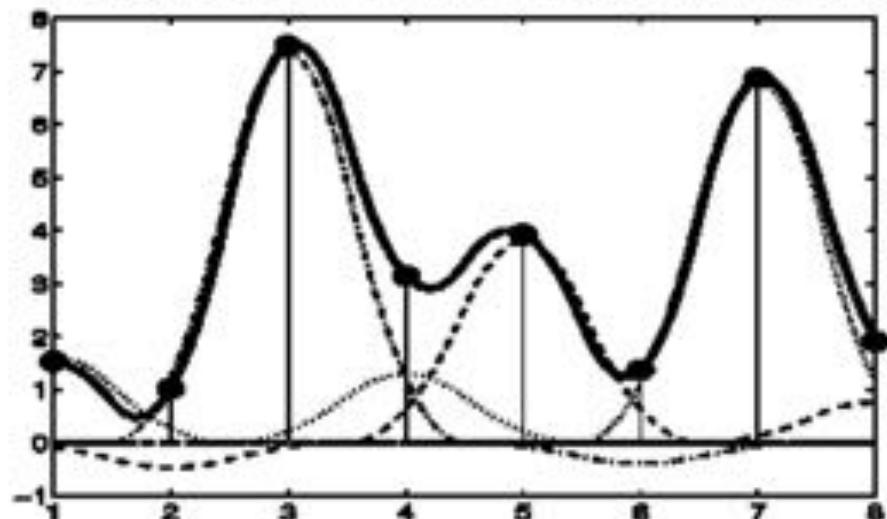
Realign

Coreg

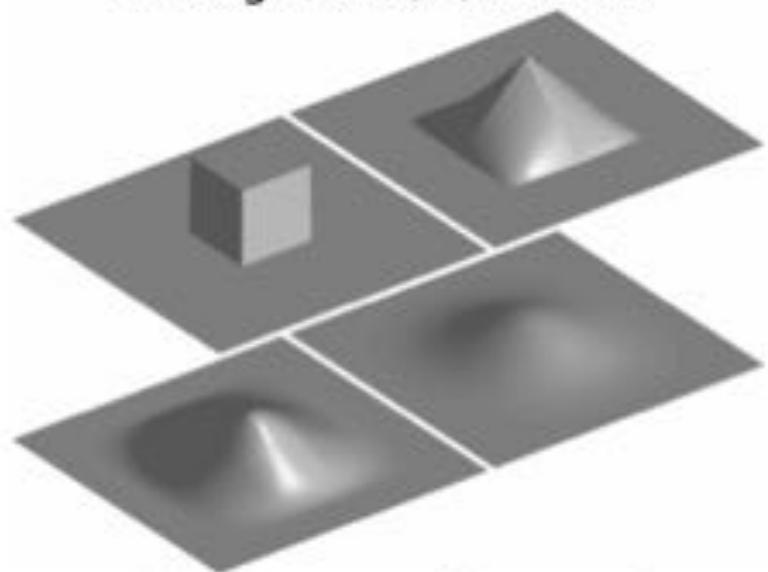
Normalise

Smooth

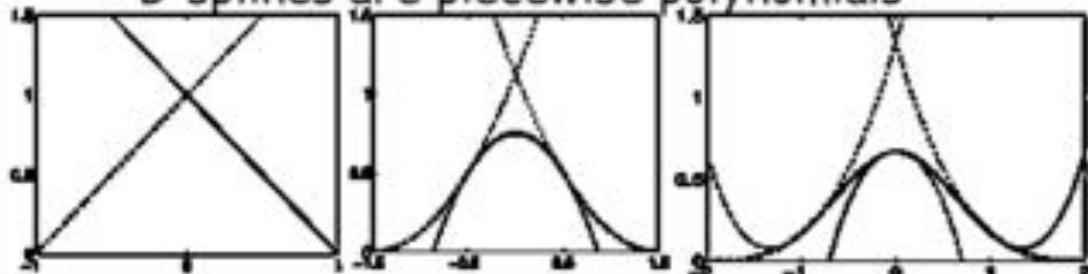
A continuous function is represented by a linear combination of basis functions



2D B-spline basis functions of degrees 0, 1, 2 and 3

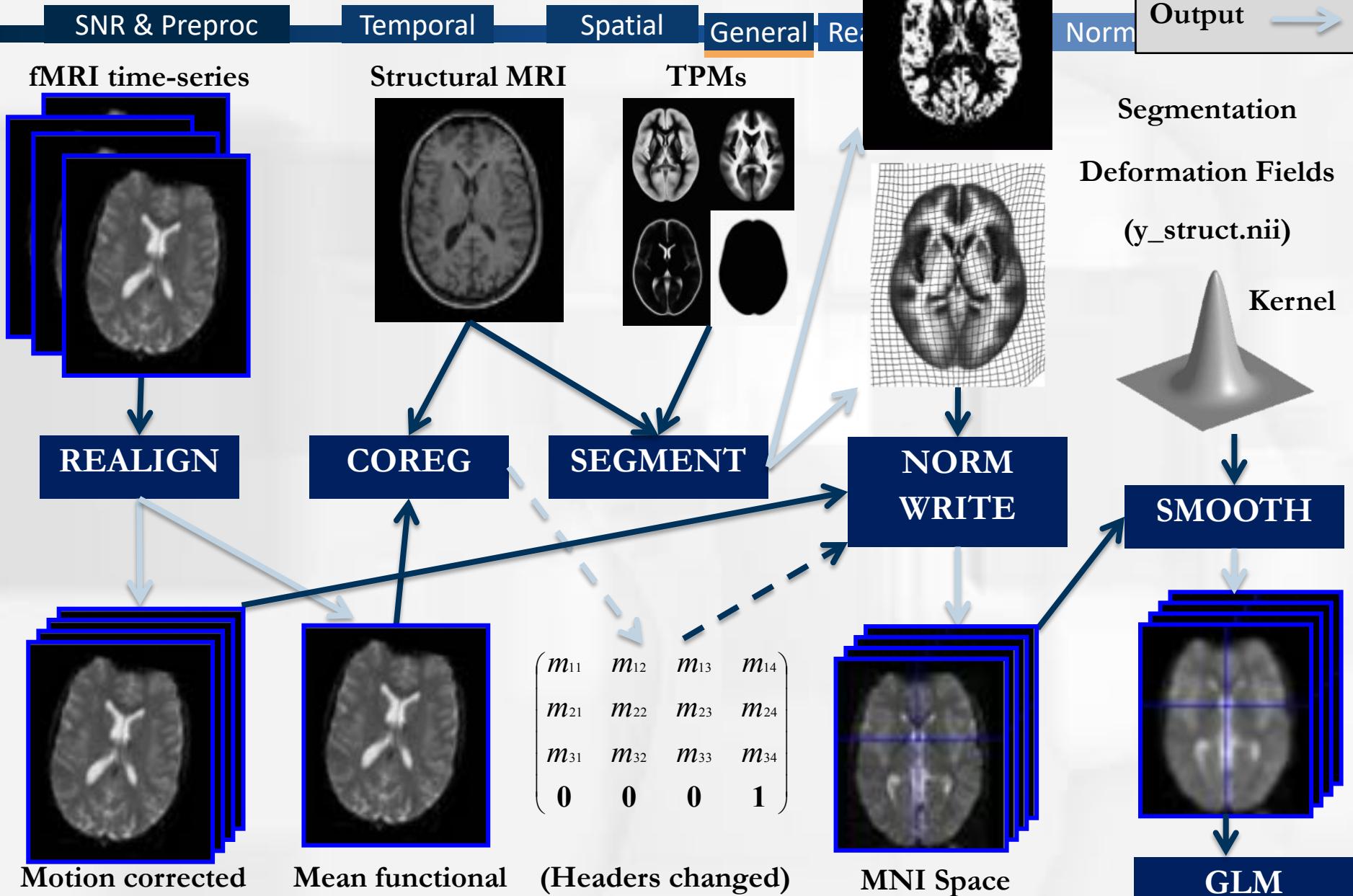


B-splines are piecewise polynomials



Nearest neighbour and trilinear interpolation are the same as B-spline interpolation with degrees 0 and 1.

Spatial Preprocessing



Realignment



SNR & Preproc

Temporal

Spatial

General

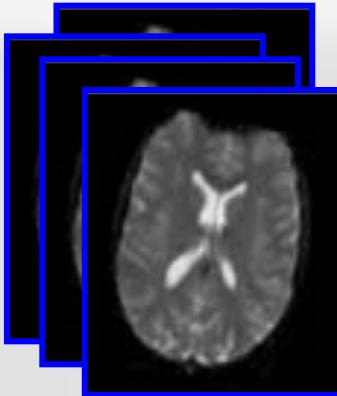
Realign

Coreg

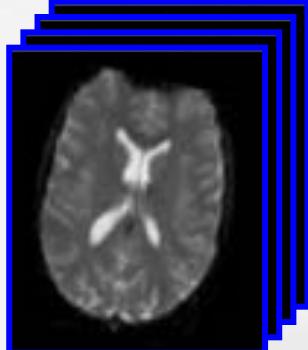
Normalise

Smooth

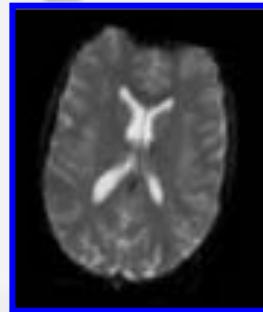
fMRI time-series



REALIGN



Motion corrected



Mean functional

- Aligns all volumes of all runs spatially
- Rigid-body transformation: three translations, three rotations
- Objective function: mean squared error of corresponding voxel intensities
- Voxel correspondence via interpolation

Realignment Output: Parameters



SNR & Preproc

Temporal

Spatial

General

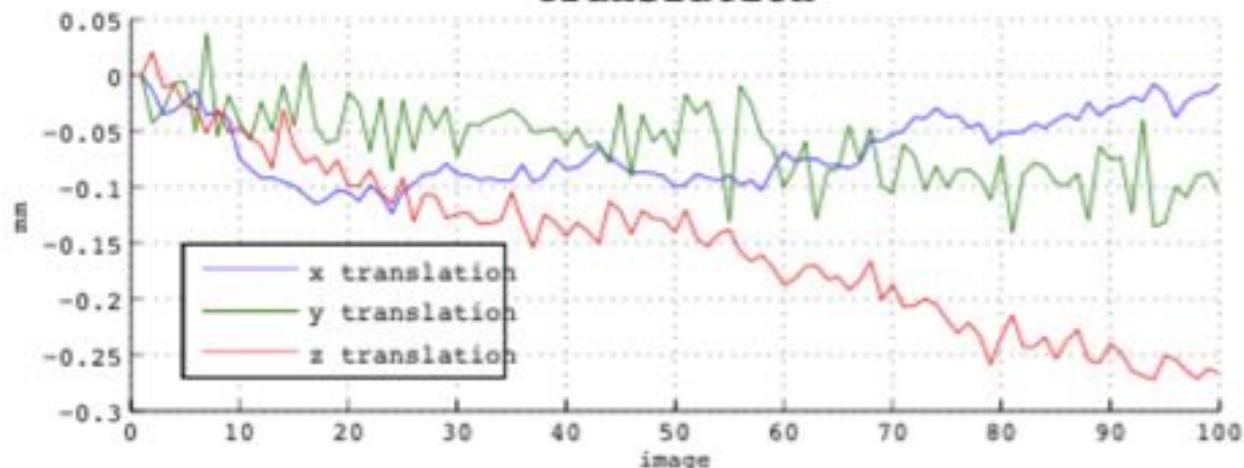
Realign

Coreg

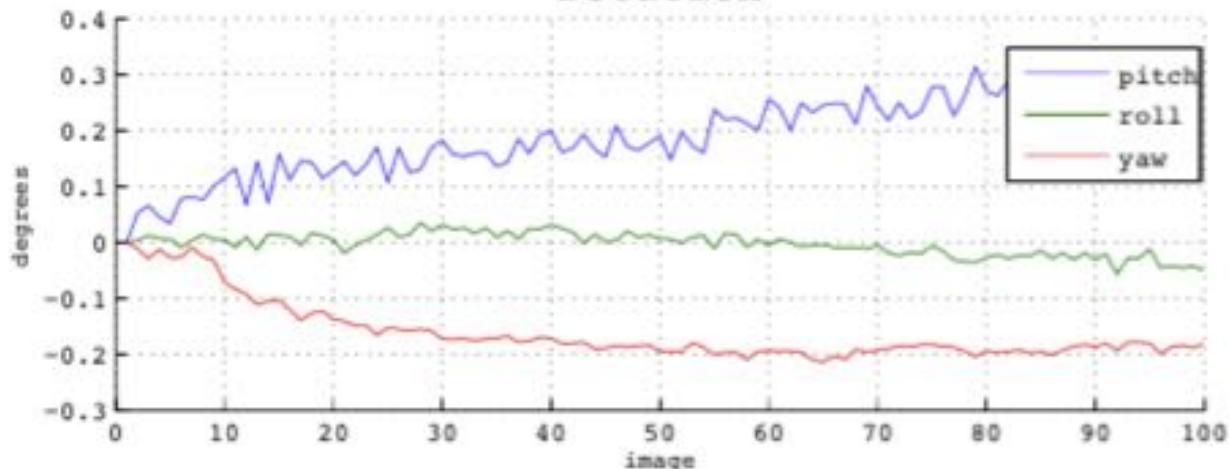
Normalise

Smooth

translation



rotation



fMRI Run after Realignment



SNR & Preproc

Temporal

Spatial

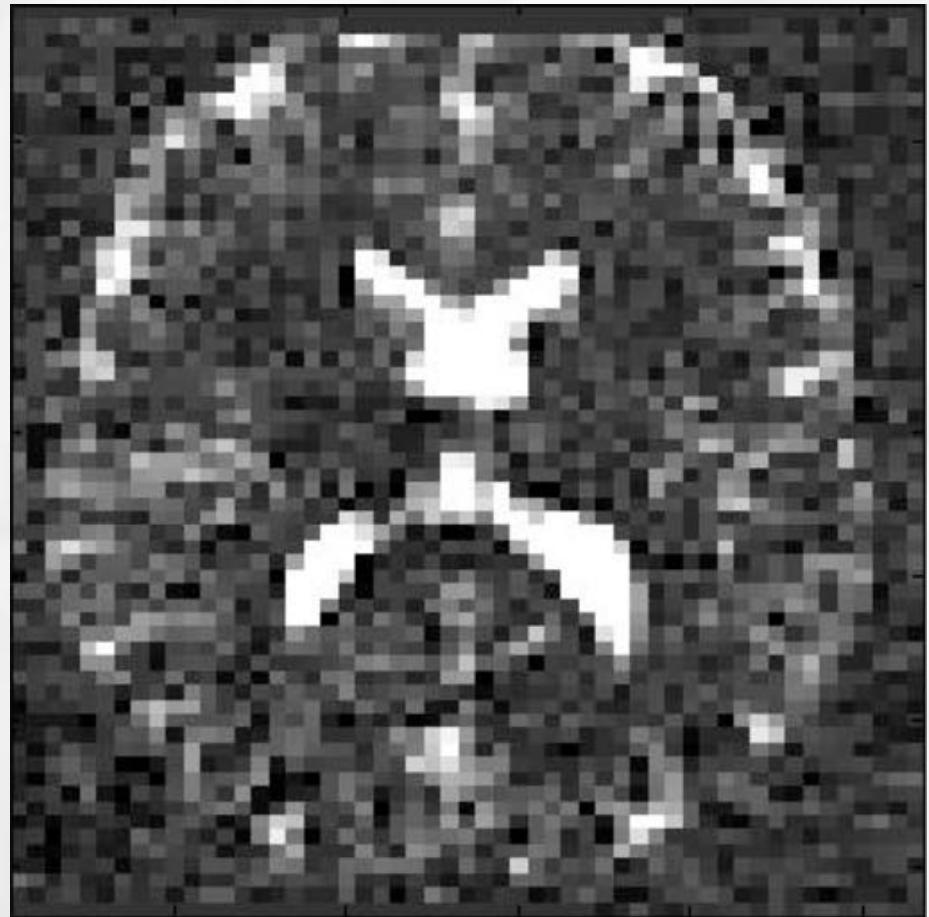
General

Realign

Coreg

Normalise

Smooth



Co-Registration



SNR & Preproc

Temporal

Spatial

General

Realign

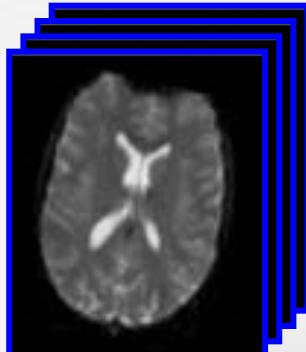
Coreg

Normalise

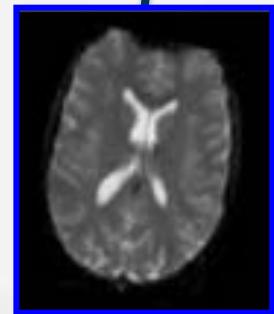
Smooth



COREG



Motion corrected



Mean functional

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

(Headers changed)

- Aligns structural image to mean functional image
- Affine transformation: translations, rotations, scaling, shearing
- Objective function: mutual information (diff. contrast!)
 - Optimisation via Powell's method: conjugate directions, line search along parameters
- Typically only trafo matrix ("header") changed

Co-Registration: Mutual Information



SNR & Preproc

Temporal

Spatial

General

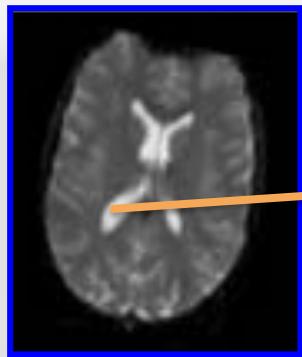
Realign

Coreg

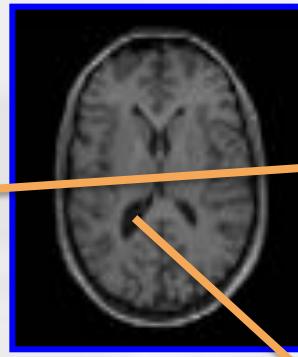
Normalise

Smooth

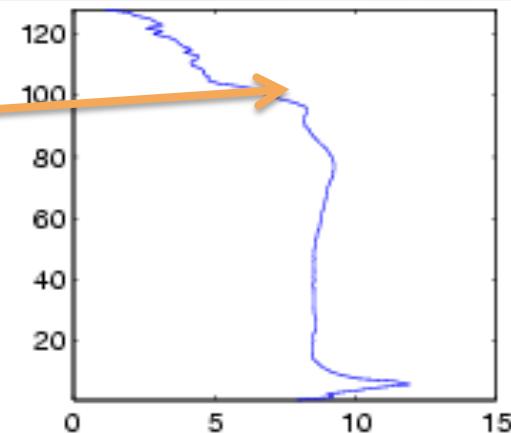
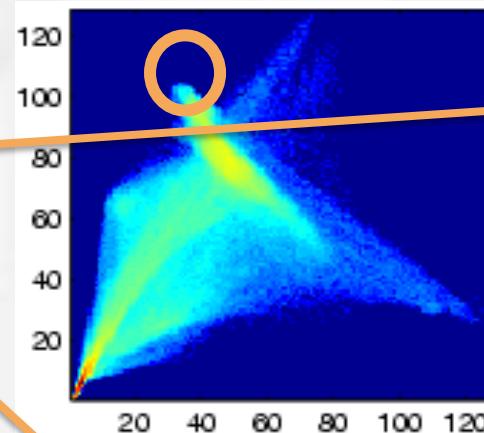
Joint Histogram



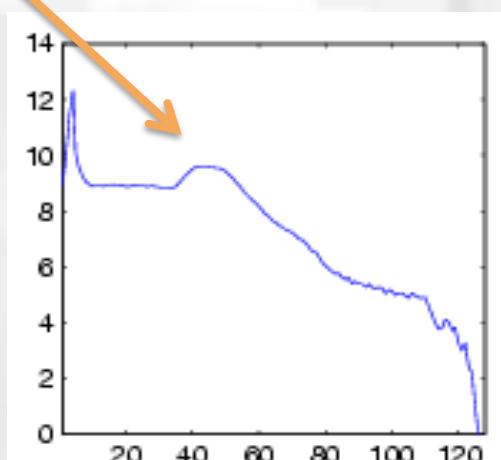
Mean functional



Anatomical MRI



- Voxels of same tissue identity have same intensity in an MR-contrast
- In a 2nd MR contrast, intensity might be different, but still the same among all voxels of the same tissue type
- Therefore, aligned voxels in 2 images induce crisp peaks in joint histogram



intensity bins
structural

intensity bins
functional

Joint Histogram:
 $h(i_f, i_s)$

Count of voxels who have intensity i_f in functional and i_s in structural image

Co-Registration: Mutual Information



SNR & Preproc

Temporal

Spatial

General

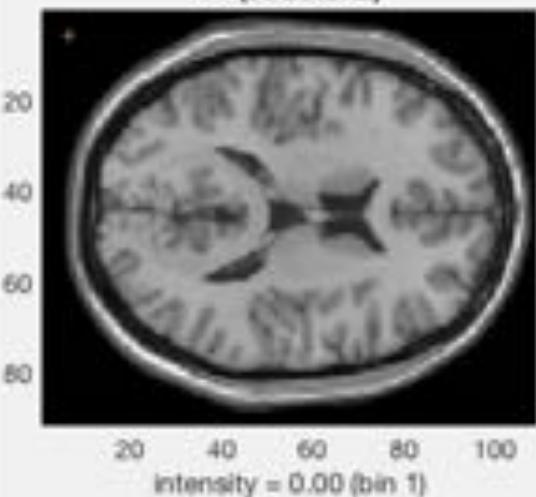
Realign

Coreg

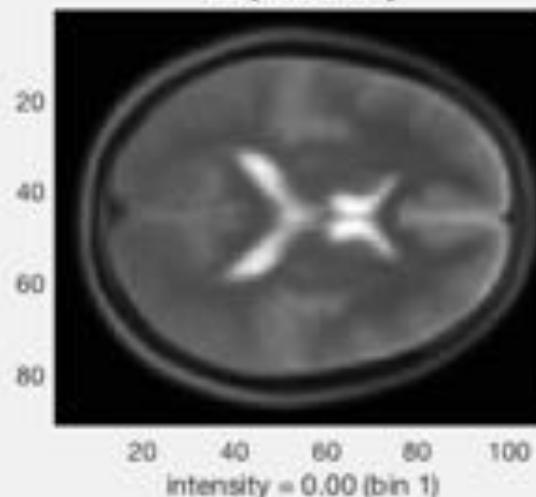
Normalise

Smooth

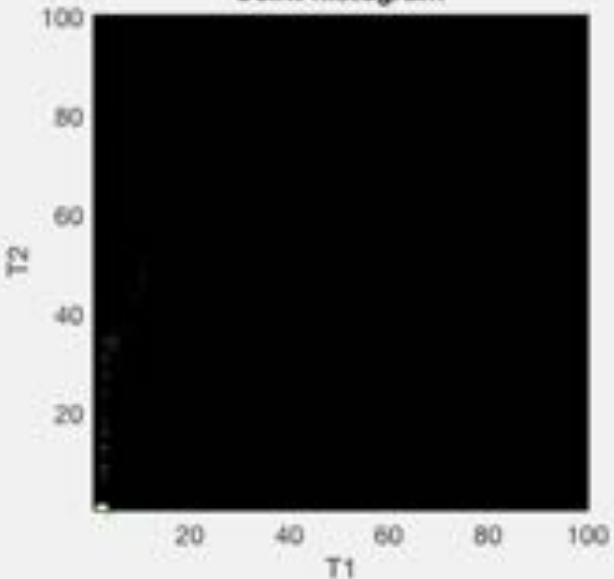
T1 (structural)



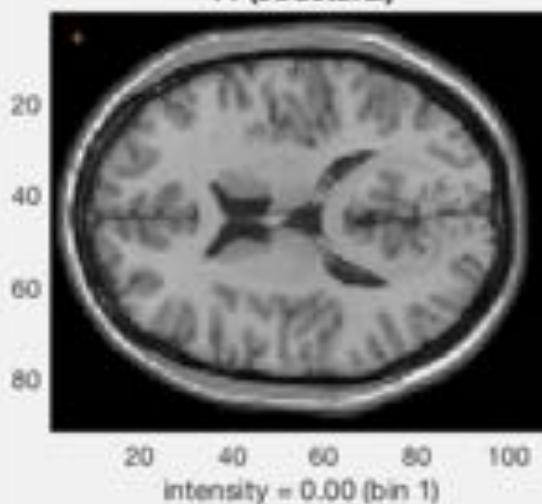
T2 (functional)



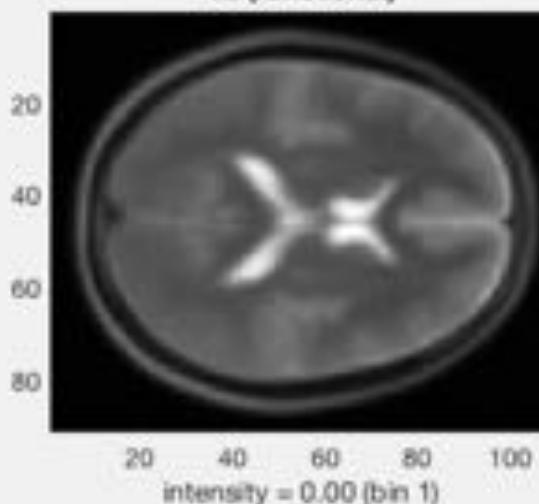
Joint histogram



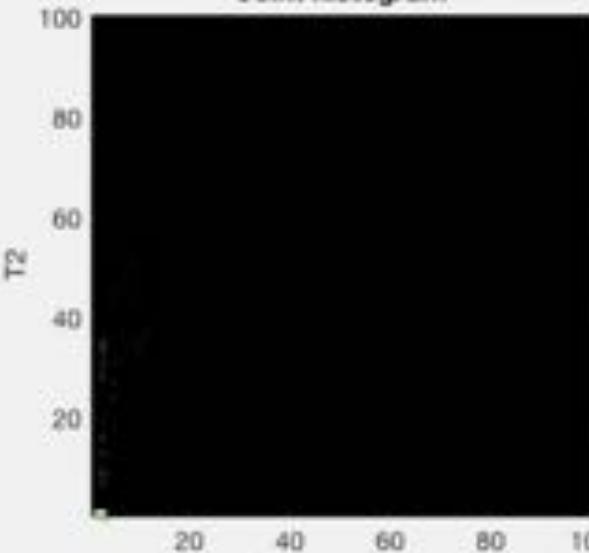
T1 (structural)



T2 (functional)



Joint histogram



Co-Registration: Output



SNR & Preproc

Temporal

Spatial

General

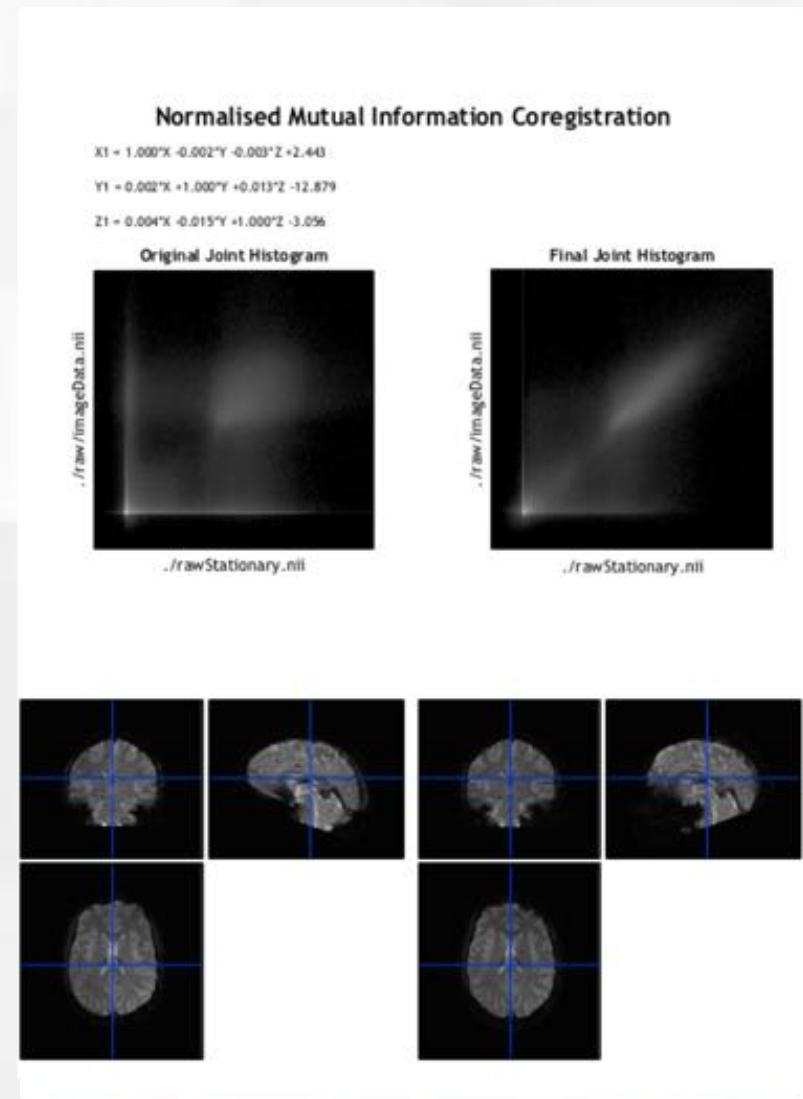
Realign

Coreg

Normalise

Smooth

- Aligned voxels in 2 images induce crisp peaks in joint histogram
- Optimization criterion:
 - Joint histogram: quantify how well voxel intensity in one image predicts the intensity in the other
 - how much shared (=mutual) information
 - Joint histogram: proxy to joint probability distribution





Sources of Noise in fMRI

SNR & Preproc

Temporal

Spatial

General

Realign

Coreg

Normalise

Smooth

- Acquisition Timing
- Subject Motion
- Anatomical Identity
- Inter-subject variability
- Thermal Noise
- Physiological Noise
- Slice-Timing
- Realignment
- Co-registration
- Segmentation
- Smoothing
- PhysIO Toolbox

Spatial Preproc

Spatial Normalisation: Reasons



SNR & Preproc

Temporal

Spatial

General

Realign

Coreg

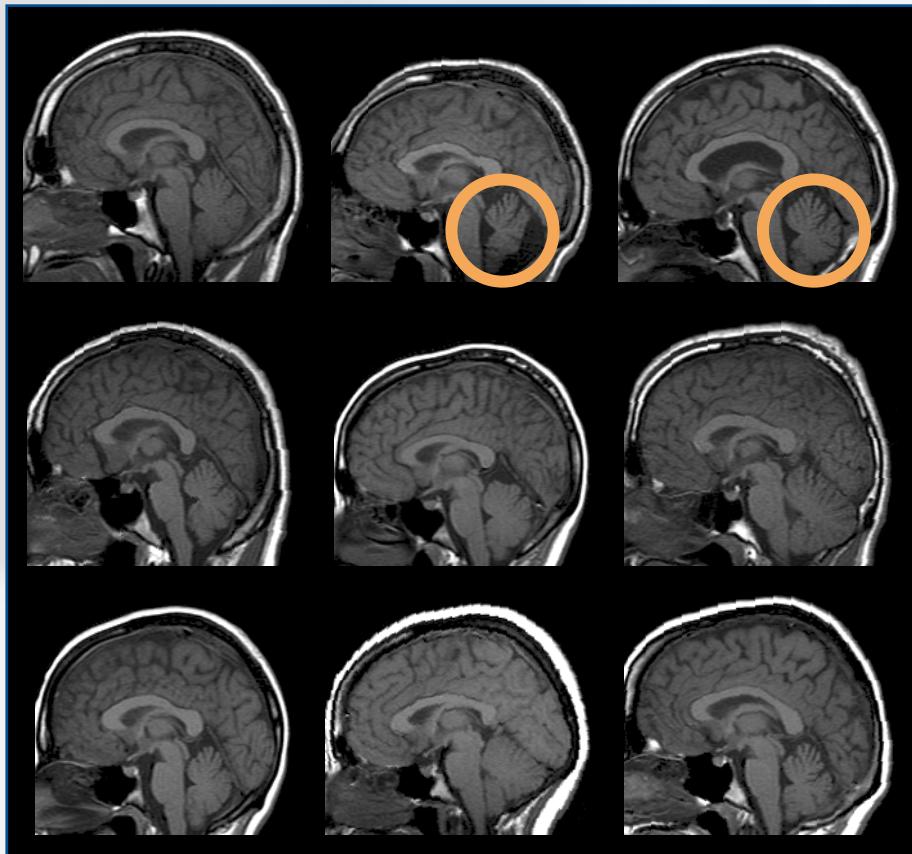
Normalise

Smooth

- Inter-Subject Variability



- Inter-Subject Averaging



- Increase sensitivity with more subjects (fixed-effects)
- Generalise findings to population as a whole (mixed-effects)
- Ensure Comparability between studies (alignment to standard space)
 - Talairach and Tournoux (T&T) convention using the Montreal Neurological Institute (MNI) space
 - Templates from 152/305 subjects

Unified Segmentation



SNR & Preproc

Temporal

Spatial

General

Realign

Coreg

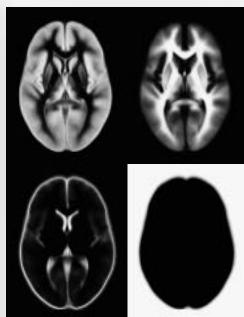
Normalise

Smooth

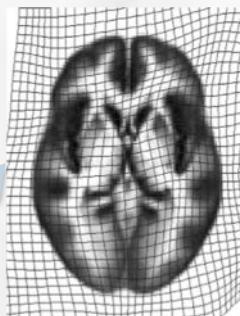
Structural MRI



TPMs



Deformation
Fields

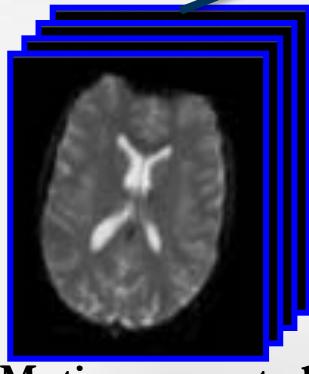


Segmented
Images



SEGMENT

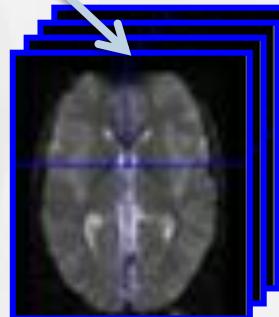
NORM
WRITE



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

Motion corrected

(Headers changed)



MNI Space

- Warp structural image to standard space (MNI)
- Non-linear transformation: discrete cosine transforms (~1000)
- Objective function: Bayes probability of voxel intensity

Theory: Segmentation/Normalisation



SNR & Preproc

Temporal

Spatial

General

Realign

Coreg

Normalise

Smooth

- Why is normalisation difficult?
 - No simple similarity measure, a lot of possible transformations...
 - Different imaging sequences (contrasts, geometry distortion)
 - Noise, artefacts, partial volume effects
 - Intensity inhomogeneity (bias field)
- **Normalisation** of segmented tissues is more robust and precise than of original image
- Tissue **segmentation** benefits from spatially aligned tissue probability maps (of prior segmentation data)
→ Motivates a unified model of segmentation/normalisation

Summary of the unified model



SNR & Preproc

Temporal

Spatial

General

Realign

Coreg

Normalise

Smooth

- SPM12 implements a generative model of voxel intensity from tissue class probabilities
 - Principled Bayesian probabilistic formulation
 - Gaussian mixture model: segmentation by tissue-class dependent Gaussian intensity distributions
 - Voxel-wise prior mixture proportions given by tissue probability maps
- Deformations of prior tissue probability maps also modelled
 - Non-linear deformations are constrained by regularisation factors
 - Inverse of estimated transformation for TPMs normalises the original image
- Bias field correction is included within the model

Theory: Unified Model Segmentation



SNR & Preproc

Temporal

Spatial

General

Realign

Coreg

Normalise

Smooth

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

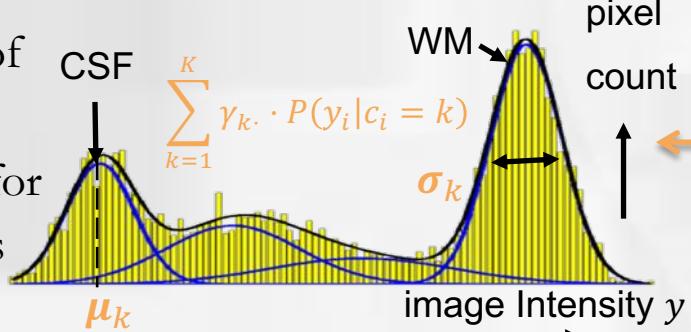
(2005), Neuroimage

- Objective function: log joint probability of all voxel intensities \mathbf{y}

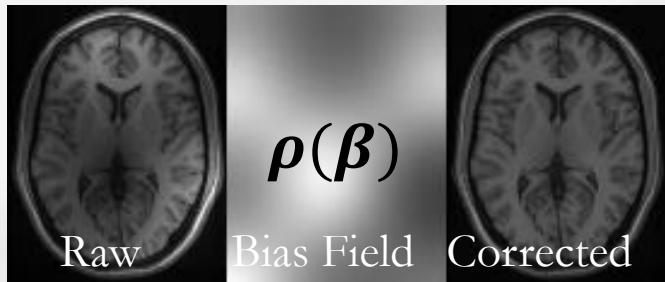
$$\mathcal{E} = \log P(\mathbf{y}|\boldsymbol{\mu}, \boldsymbol{\sigma}, \boldsymbol{\gamma}, \mathbf{b}_{1..K}, \boldsymbol{\alpha}, \boldsymbol{\beta})$$

Gaussian Mixture Model

probability of
intensity in
given voxel for
tissue class

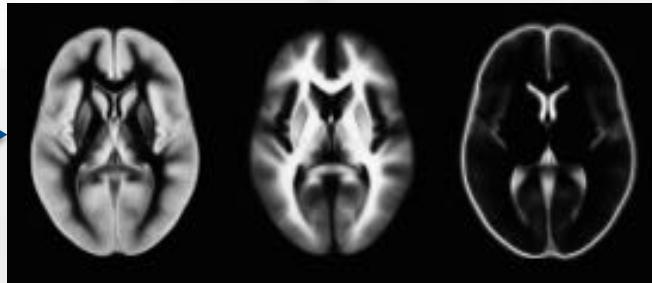


Bias Field



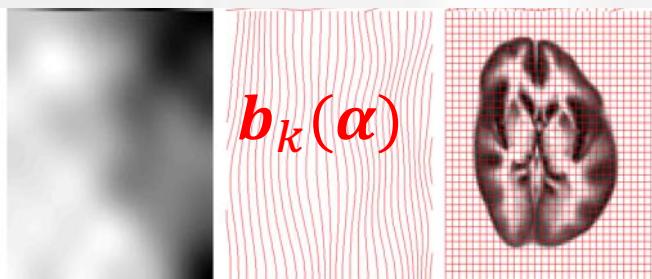
coil
inhomo-
geneities

Prior: Tissue probability maps



TPMs
in MNI
space

Deformation Fields



~1000
discrete
cosine
transforms

Segmentation results

SNR & Preproc

Temporal

Spatial

General

Realign

Coreg

Normalise

Smooth

- Segmentation works irrespective of image contrast

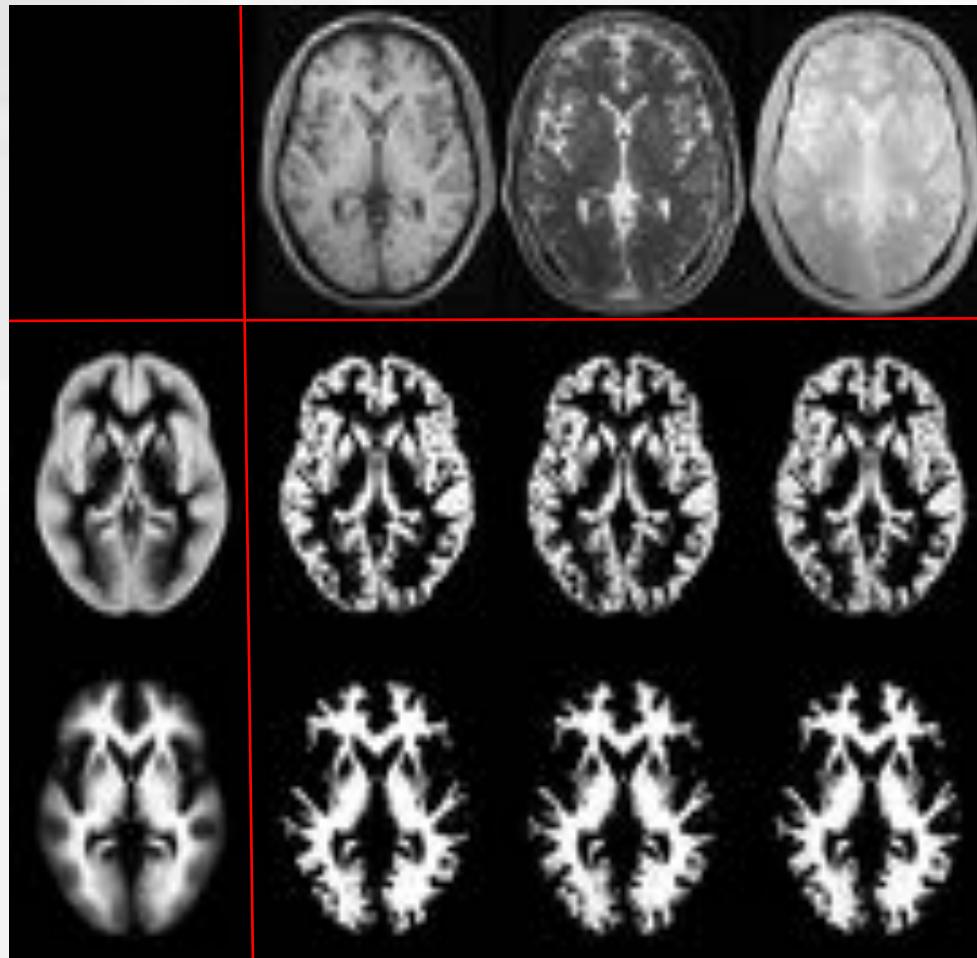
Spatially
normalised
BrainWeb
phantoms

T1

T2

PD

Estimated
Tissue
Probability
Maps (TPMs)



Cocosco, Kollokian, Kwan &
Evans. "BrainWeb: Online Interface
to a 3D MRI Simulated Brain
Database". NeuroImage
5(4):S425 (1997)

Benefits of Unified Segmentation



SNR & Preproc

Temporal

Spatial

General

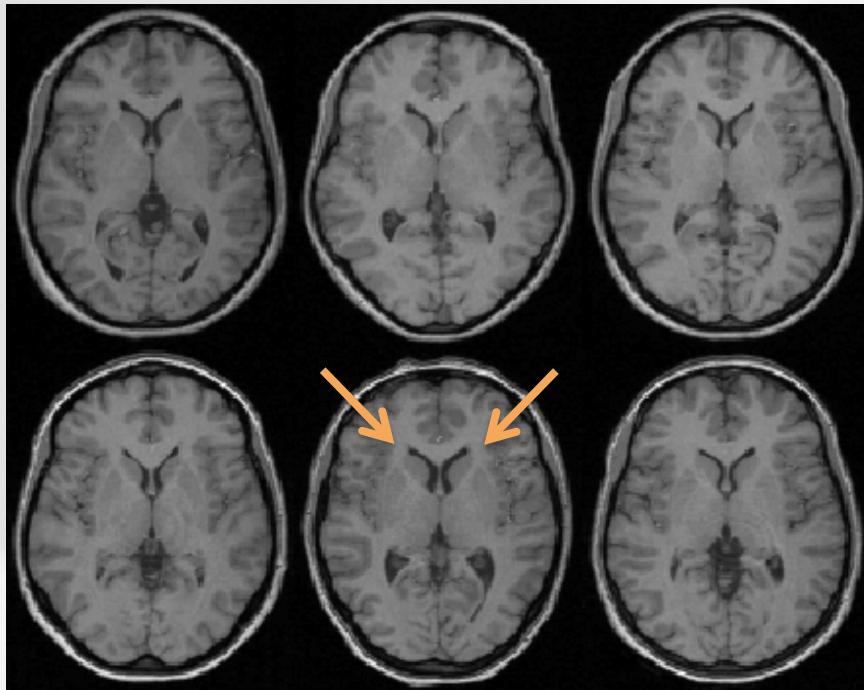
Realign

Coreg

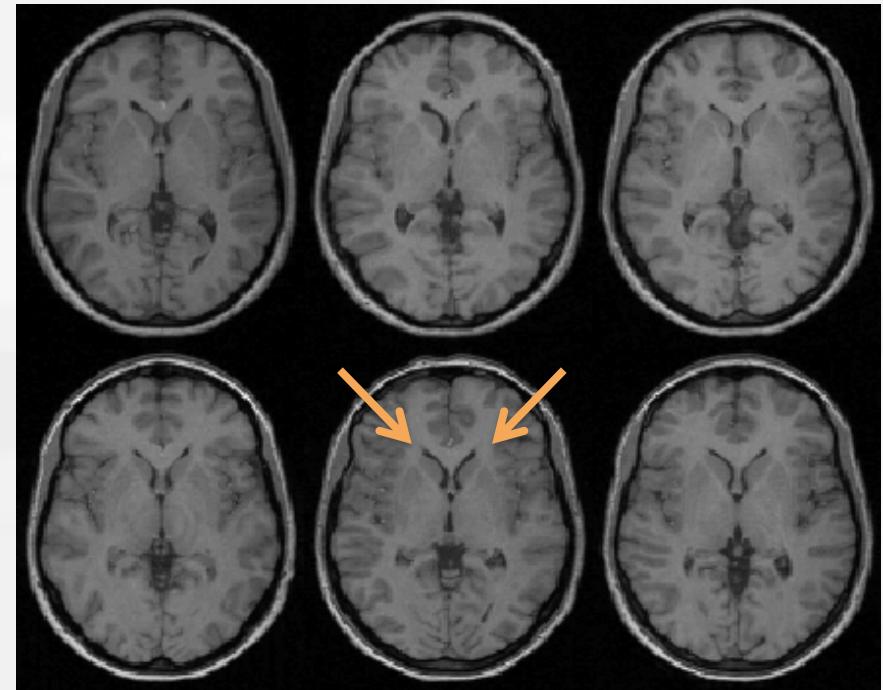
Normalise

Smooth

Affine registration



Non-linear registration



Spatial normalisation – Limitations



SNR & Preproc

Temporal

Spatial

General

Realign

Coreg

Normalise

Smooth

- Seek to match functionally homologous regions, but...
 - Challenging high-dimensional optimisation
 - many local optima
 - Different cortices **can** have different folding patterns
 - No exact match between structure and function
 - See e.g. Amiez et al. (2013), PMID:23365257

Spatial normalisation – Limitations



SNR & Preproc

Temporal

Spatial

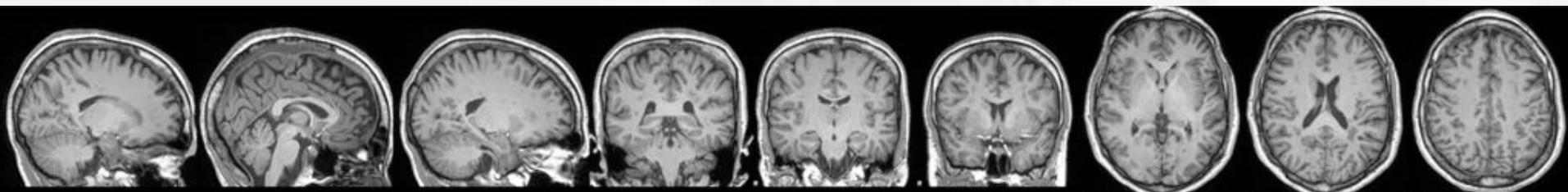
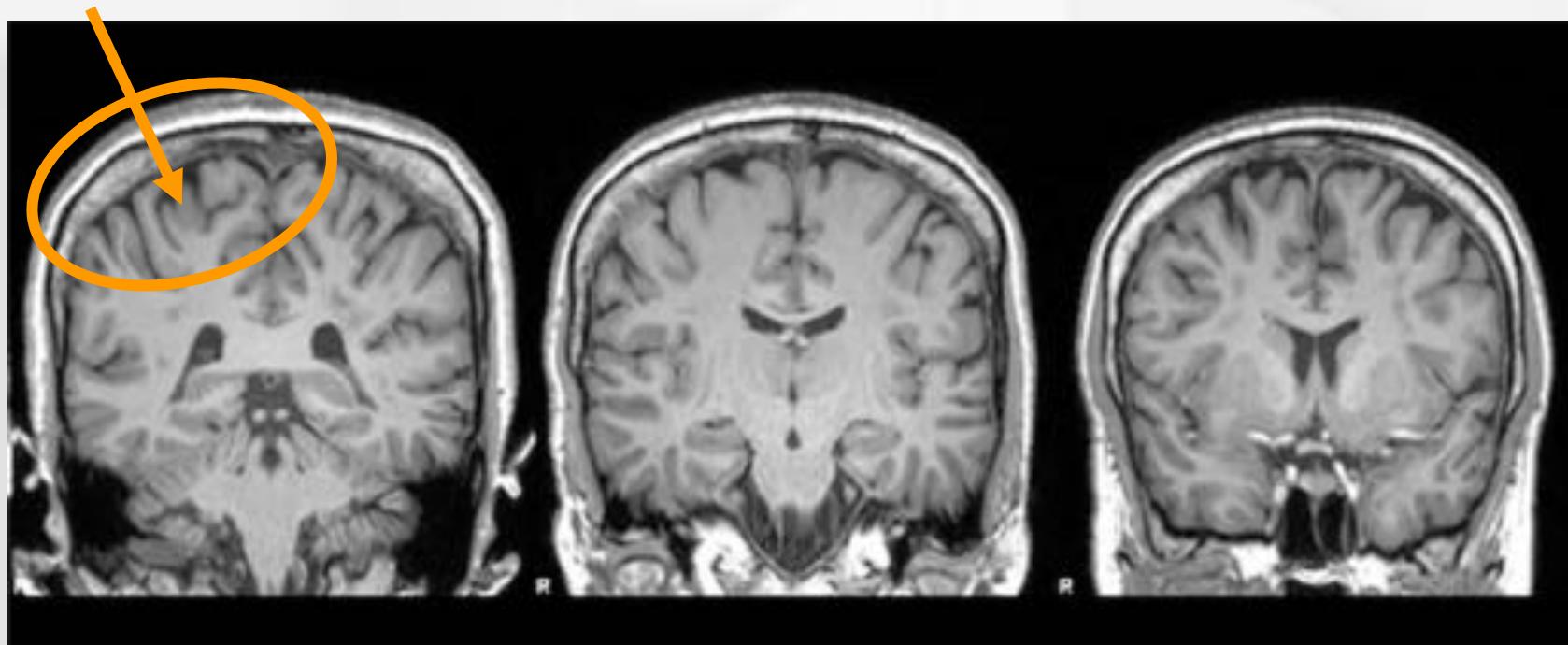
General

Realign

Coreg

Normalise

Smooth



UK Biobank data: eventually, 100,000 subjects and 80 mins!

Spatial normalisation – Limitations



SNR & Preproc Temporal Spatial General Realign Coreg **Normalise** Smooth

- Seek to match functionally homologous regions, but...
 - Challenging high-dimensional optimisation
 - many local optima
 - Different cortices **can** have different folding patterns
 - No exact match between structure and function
 - See e.g. Amiez et al. (2013), PMID:23365257
- Compromise
 - Correct relatively large-scale variability
 - Smooth over finer-scale residual differences

Smoothing – Why blurring the data?



SNR & Preproc

Temporal

Spatial

General

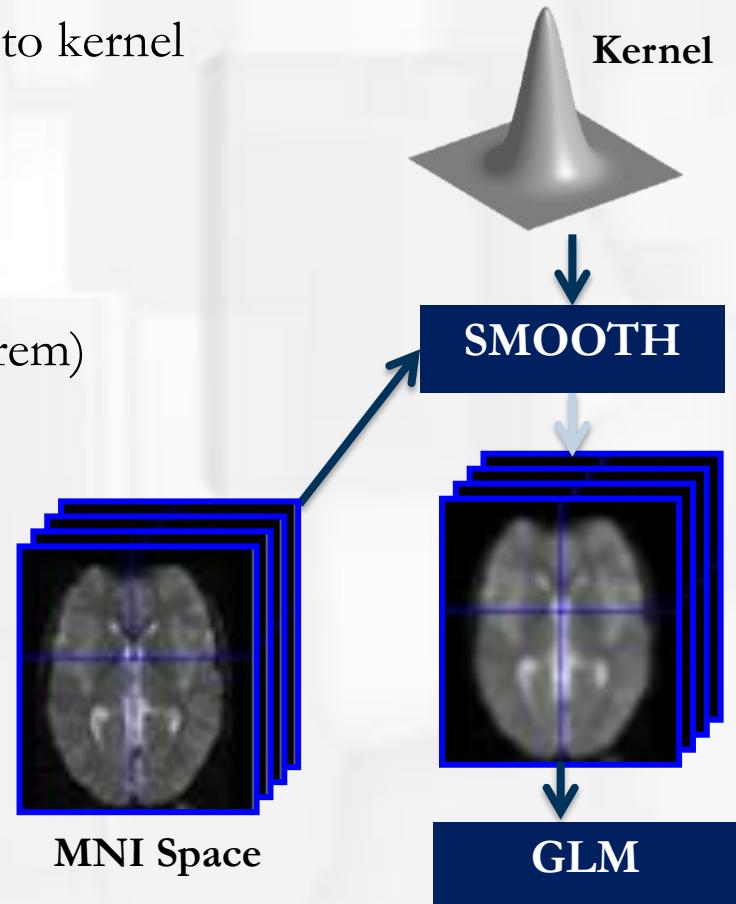
Realign

Coreg

Normalise

Smooth

- Intra-subject signal quality
 - Suppresses thermal noise (averaging)
 - Increases sensitivity to effects of similar scale to kernel (matched filter theorem)
- Single-subject statistical analysis
 - Makes data more Gaussian (central limit theorem)
 - Reduces the number of multiple comparisons
- Second-level statistical analysis
 - Improves spatial overlap by blurring anatomical differences



Smoothing – How is it implemented?



SNR & Preproc

Temporal

Spatial

General

Realign

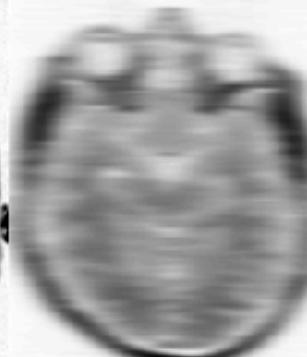
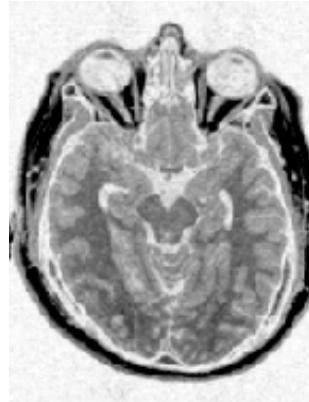
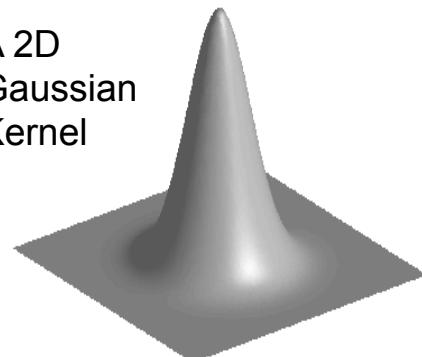
Coreg

Normalise

Smooth

- Convolution with a 3D Gaussian kernel, of specified full-width at half-maximum (FWHM) in mm
 - Mathematically equivalent to slice-timing operation or reslicing, but different kernels there (sinc, b-spline)
- Gaussian kernel is separable, and we can smooth 2D data with 2 separate 1D convolutions

A 2D Gaussian Kernel



fMRI Run after Smoothing



SNR & Preproc

Temporal

Spatial

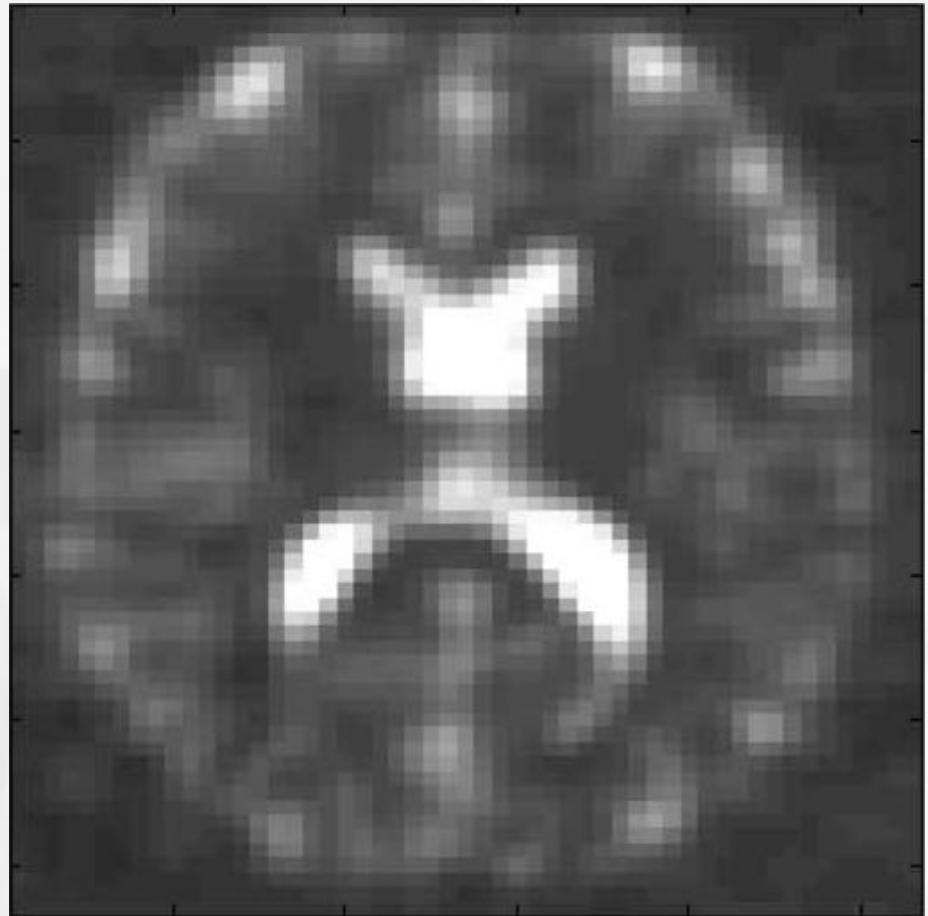
General

Realign

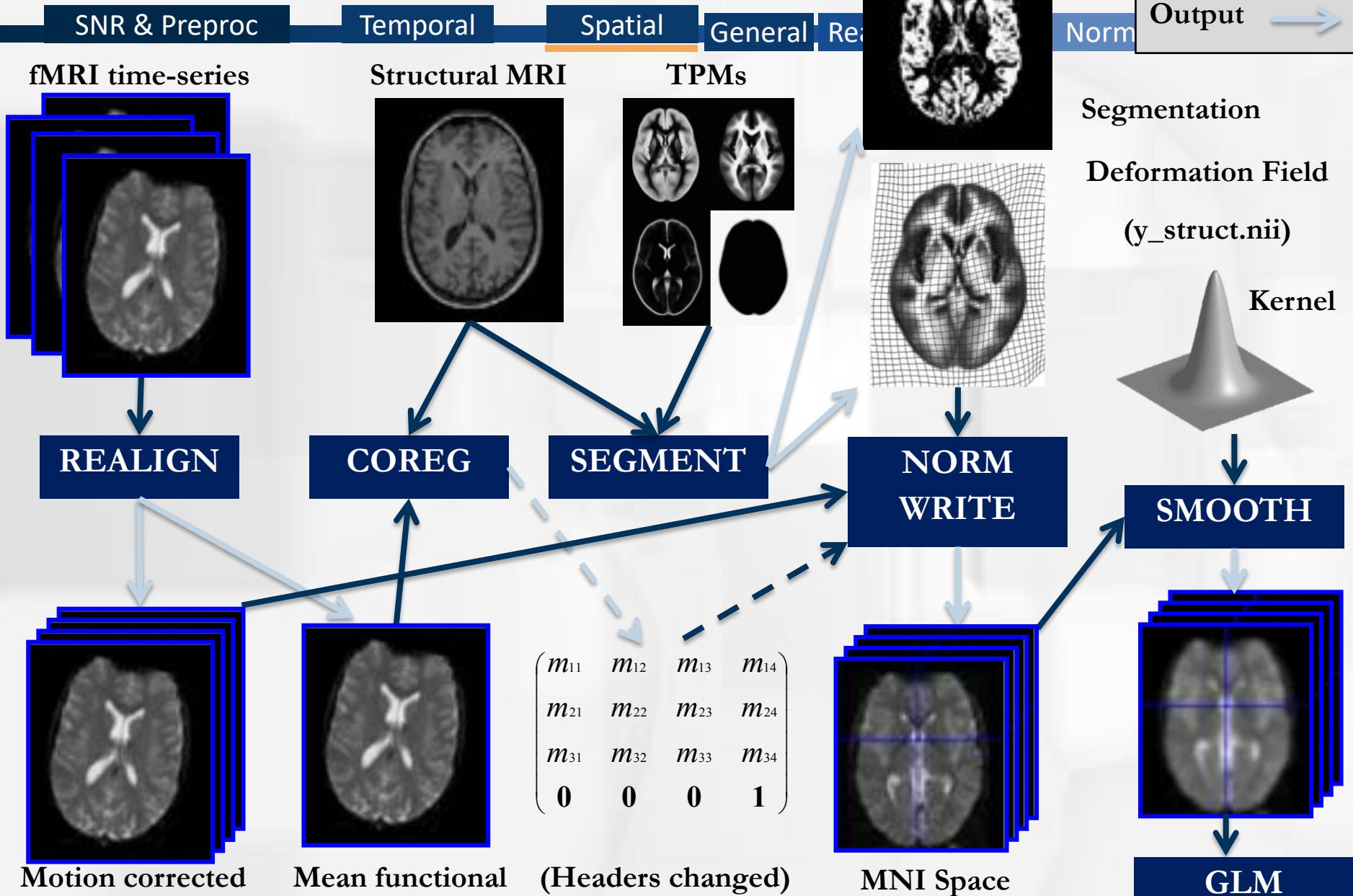
Coreg

Normalise

Smooth



Spatial Preprocessing



Sources of Noise in fMRI



SNR & Preproc

Temporal

Spatial

General

Realign

Coreg

Normalise

Smooth

- Acquisition Timing
- Subject Motion
- Anatomical Identity
- Inter-subject variability
- Thermal Noise
- Physiological Noise

Temporal Preproc

Spatial Preproc

Spatial Preproc

Spatial Preproc

Spatial Preproc

Noise Modeling

- Slice-Timing
- Realignment
- Co-registration
- Segmentation
- Smoothing
- PhysIO Toolbox

Teaser: PhysIO Noise Modelling



SNR & Preproc

Temporal

Spatial

General

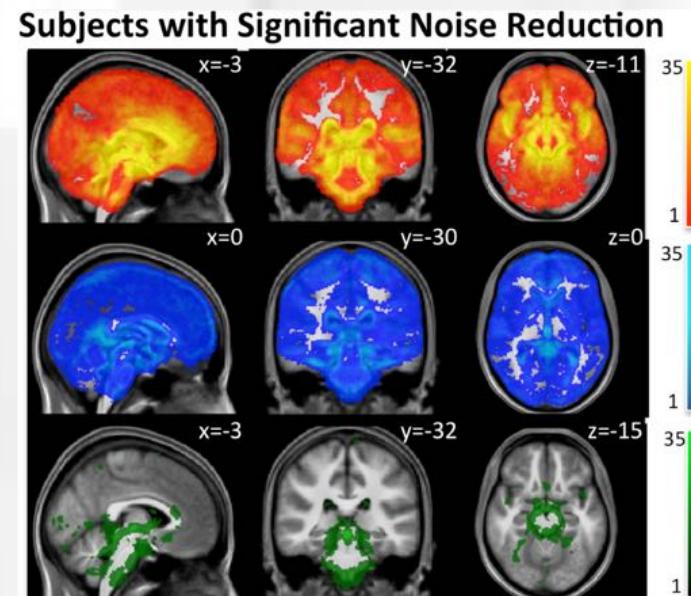
Realign

Coreg

Normalise

Smooth

- We can model time series of non-BOLD physiological fluctuations from prior knowledge (locations, dominant frequencies) or peripheral recordings (ECG, breathing belt)
- “Filter” these out via incorporation into general linear model
 - See Frederike’s talk!
- Result:
 - Cardiac (red), respiratory (blue) physiological time courses, and their interaction (green) contribute severely to remaining non-Gaussian voxel fluctuations
- For more details: See Lars’ talk on **20th November...**



Thank you...



SNR & Preproc

Temporal

Spatial

General

Realign

Coreg

Normalise

Smooth

- ...and:
 - TNU
 - Lars Kasper
 - Everyone Lars borrowed slides from ☺



Further Reading



SNR & Preproc

Temporal

Spatial

General

Realign

Coreg

Normalise

Smooth

- Good Textbook: Karl Friston, J.A., William Penny (Eds.), *Statistical Parametric Mapping*, Academic Press, London, in particular
 - Ashburner, J., Friston, K., 2007a. Chapter 4 - Rigid Body Registration, pp. 49–62.
 - Ashburner, J., Friston, K., 2007b. Chapter 5 - Non-linear Registration, pp. 63–80.
 - Ashburner, J., Friston, K., 2007c. Chapter 6 - Segmentation, pp. 81–91.
- For mathematical/engineering connoisseurs: (see also extra slides here):
 - Ashburner, J., Friston, K.J., 2005. Unified segmentation. *NeuroImage* 26, 839–851. doi:10.1016/j.neuroimage.2005.02.018

Mixture of Gaussians



SNR & Preproc

Temporal

Spatial

General

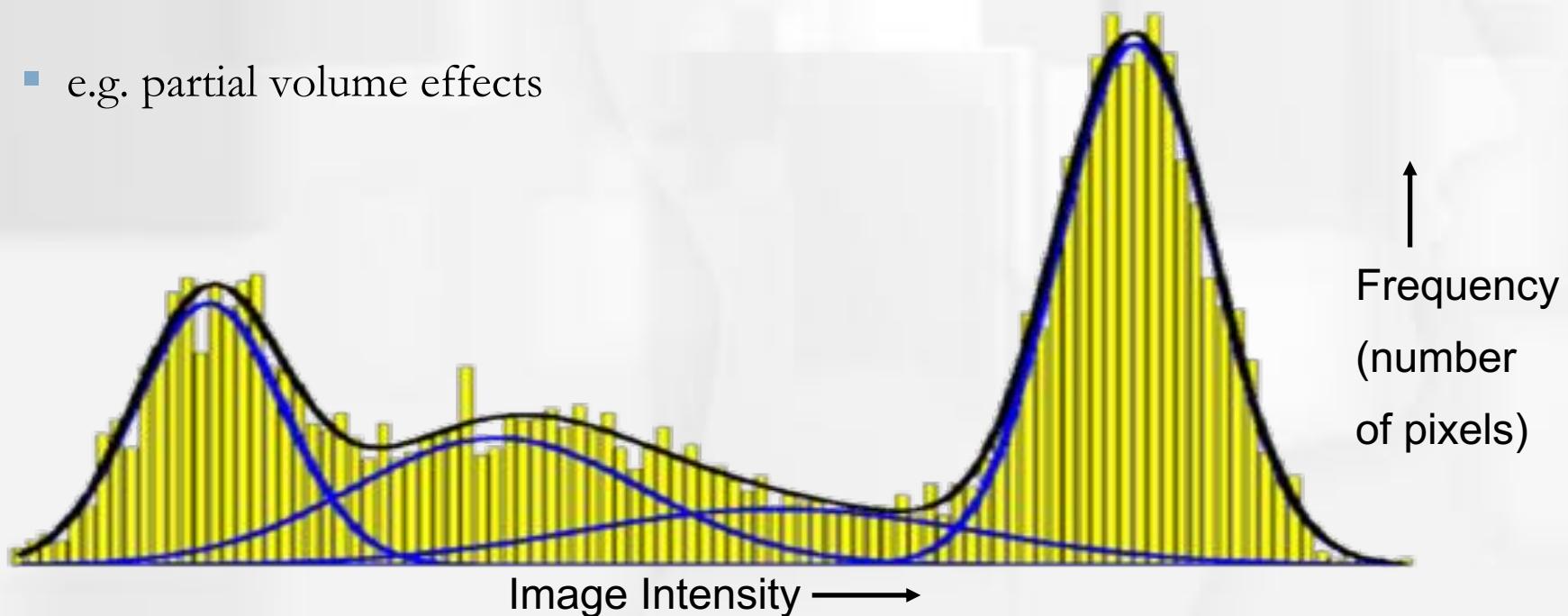
Realign

Coreg

Normalise

Smooth

- Classification is based on a Mixture of Gaussians model, which represents the intensity probability density by a number of Gaussian distributions.
- Multiple Gaussians per tissue class allow non-Gaussian intensity distributions to be modelled
 - e.g. partial volume effects



Tissue Probability Maps



SNR & Preproc

Temporal

Spatial

General

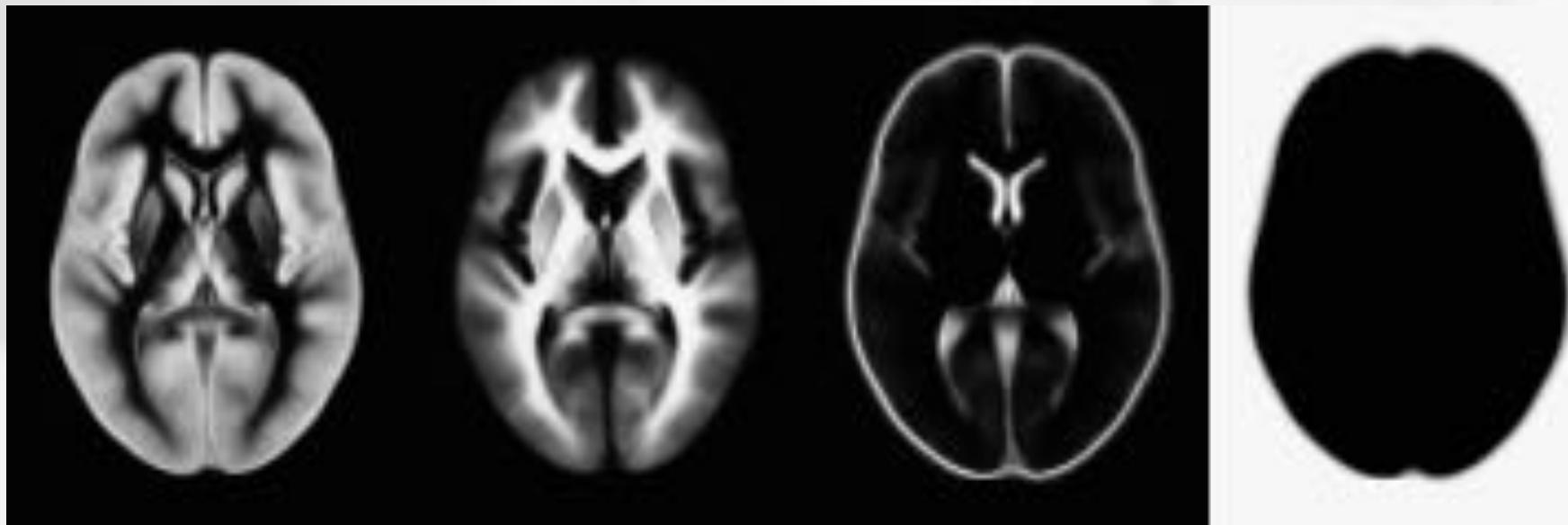
Realign

Coreg

Normalise

Smooth

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



ICBM Tissue Probabilistic Atlases. These tissue probability maps were kindly provided by the **International Consortium for Brain Mapping**

Deforming the Tissue Probability Maps



SNR & Preproc

Temporal

Spatial

General

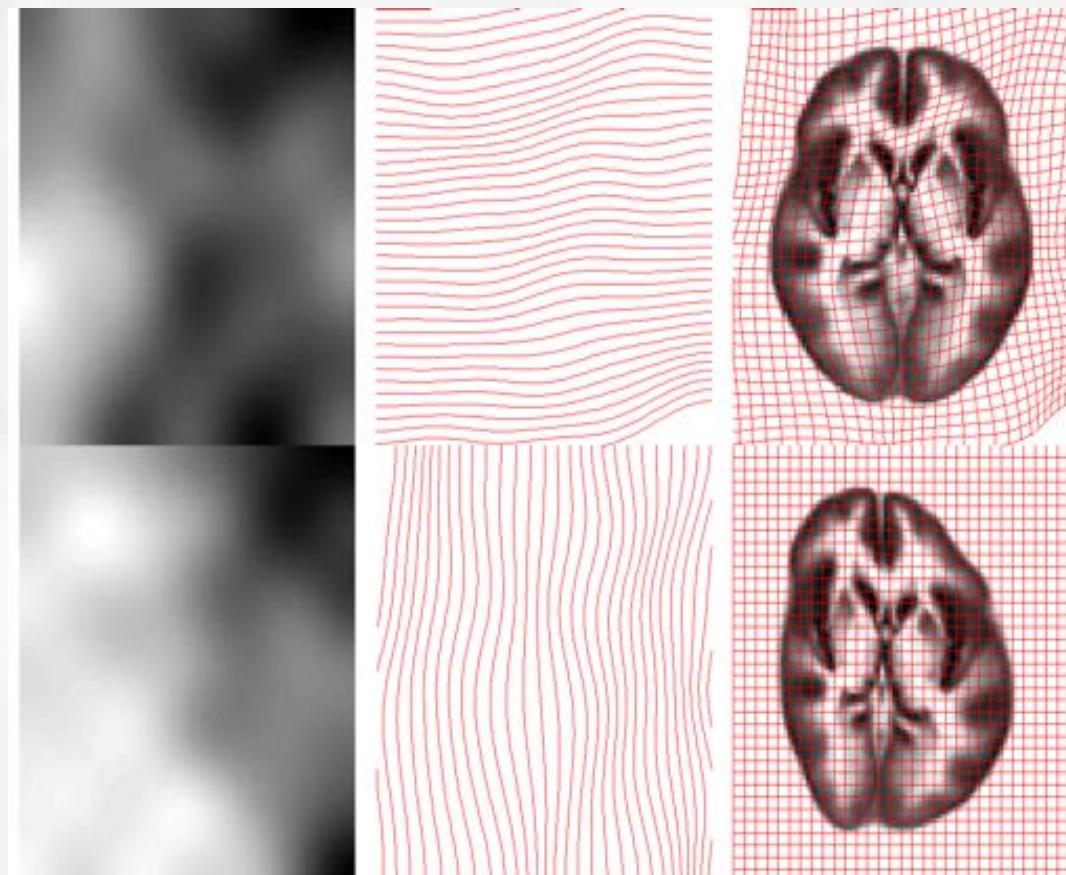
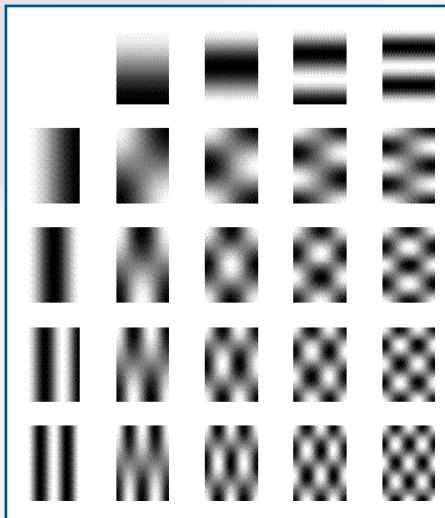
Realign

Coreg

Normalise

Smooth

- Tissue probability maps images are warped to match the subject
- The inverse transform warps to the TPMs



Why regularisation? – Overfitting



SNR & Preproc

Temporal

Spatial

General

Realign

Coreg

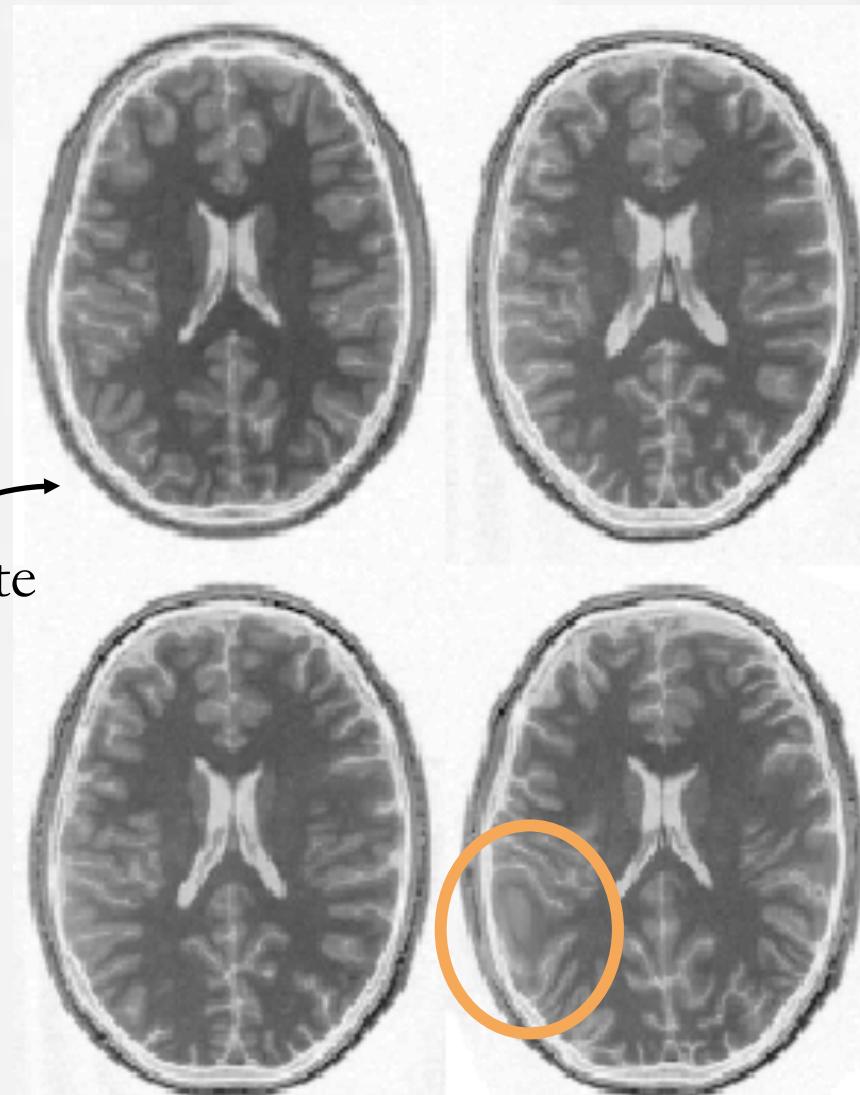
Normalise

Smooth

- Regularisation constrains deformations to realistic range (implemented as priors)

Non-linear registration using regularisation (error = 302.7)

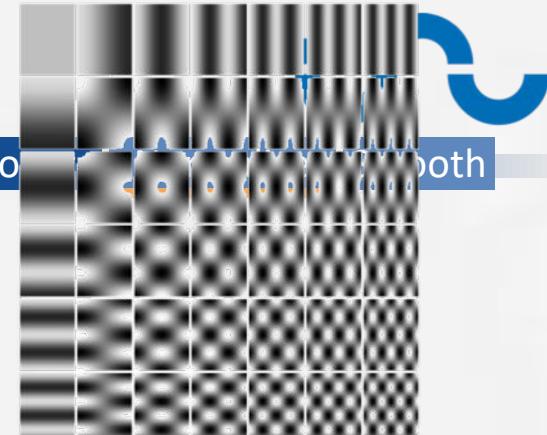
Template image



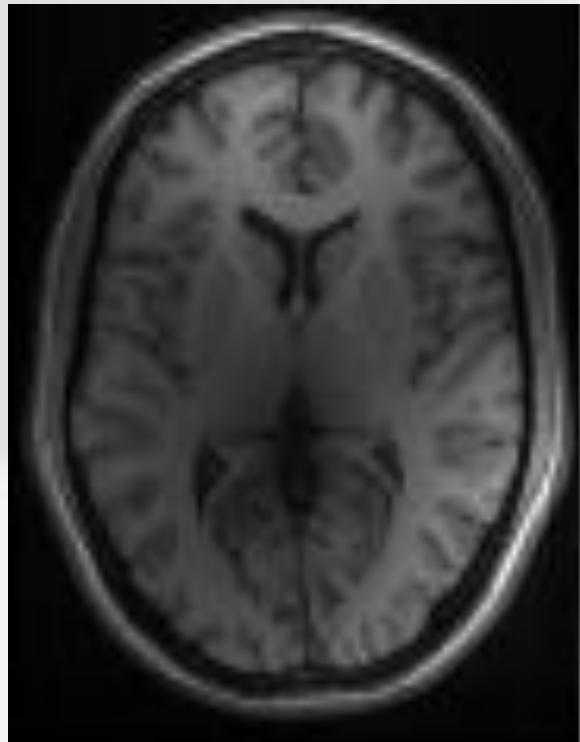
Affine registration (error = 472.1)

Non-linear registration without regularisation (error = 287.3)

Modelling inhomogeneity



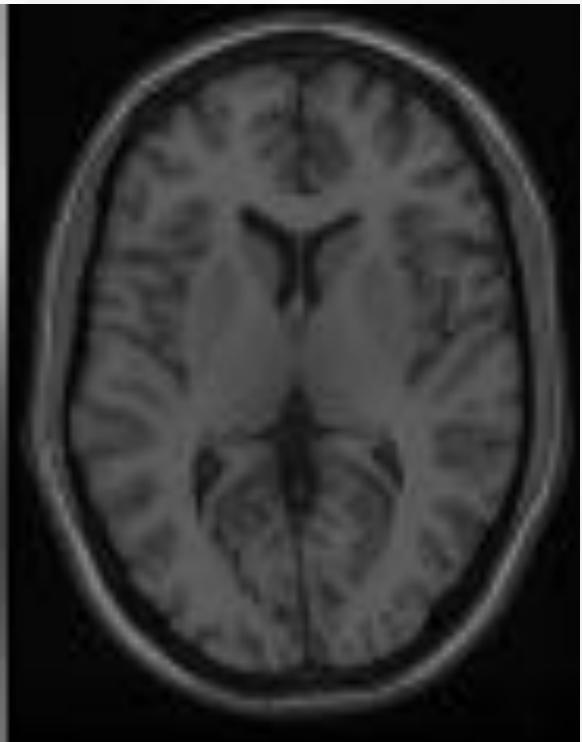
- A multiplicative bias field is modelled as a linear combination of basis functions.



Corrupted image



Bias Field



Corrected image

Unified segmentation: The maths



SNR & Preproc

Temporal

Spatial

General

Realign

Coreg

Normalise

Smooth

- Mixture of Gaussians: probability of voxel i having intensity y_i , given it is from a specific cluster k (e.g. tissue class gray matter)

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

- Prior probability of voxel's tissue class (e.g. voxel proportion) γ_k

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

- Joint Probability: $P(y_i, c_i = k|\mu_k, \sigma_k, \gamma_k) = P(y_i|c_i = k, \mu_k, \sigma_k)P(c_i = k|\gamma_k)$
- Marginal probability of voxel intensity:

$$P(y_i|\mu, \sigma, \gamma) = \sum_{k=1}^K P(y_i, c_i = k|\mu_k, \sigma_k, \gamma_k)$$

- Joint probability all voxels' intensity:

$$P(\mathbf{y}|\mu, \sigma, \gamma) = \prod_{i=1}^I P(y_i|\mu, \sigma, \gamma) = \prod_{i=1}^I \left(\sum_{k=1}^K \frac{\gamma_k}{(2\pi\sigma_k^2)^{\frac{1}{2}}} \exp\left(-\frac{(y_i - \mu_k)^2}{2\sigma_k^2}\right) \right) \quad (5)$$

US Maths: Bias Field

SNR & Preproc

Temporal

Spatial

General

Realign

Coreg

Normalise

Smooth

- Implemented by adjusting the Means and Variances of the Gaussians on a pixel-by-pixel basis by a function smoothly varying in space, $\rho_i(\beta)$:
- $\mu_k \mapsto \frac{\mu_k}{\rho_i(\beta)}$, $\sigma_k^2 \mapsto \left(\frac{\sigma_k}{\rho_i(\beta)}\right)^2$
- ρ_i is the exponential of a linear combination of low frequency basis functions
- Parameters to be estimated: vector β
- intensity probability conditioned on cluster identity:

$$P(y_i|c_i = k, \mu_k, \sigma_k, \beta)$$

$$= \frac{1}{(2\pi(\sigma_k/\rho_i(\beta))^2)^{\frac{1}{2}}} \exp\left(-\frac{(y_i - \mu_k/\rho_i(\beta))^2}{2(\sigma_k/\rho_i(\beta))^2}\right)$$

$$= \rho_i(\beta) \frac{1}{(2\pi\sigma_k^2)^{\frac{1}{2}}} \exp\left(-\frac{(\rho_i(\beta)y_i - \mu_k)^2}{2\sigma_k^2}\right)$$

US Maths: Spatial Priors by TPMs



SNR & Preproc

Temporal

Spatial

General

Realign

Coreg

Normalise

Smooth

- Replacing stationary mixing proportions γ_k by voxel-dependent proportions which are informed by the prior tissue probabilities b_{ik} for this voxel i and different tissue types k
- $$\gamma_k \mapsto \gamma_k(i) = \gamma_k \cdot \frac{b_{ik}}{\sum_{j=1}^K \gamma_j b_{ij}}$$
- Note: K can be larger than the number of tissue classes, since each class can be reflected by a mixture of Gaussians, e.g. 3 Gaussians for gray matter (to allow for non-Gaussian distributions per tissue class)
 - E.g. partial volume effects

US Maths: Deformation Fields



SNR & Preproc

Temporal

Spatial

General

Realign

Coreg

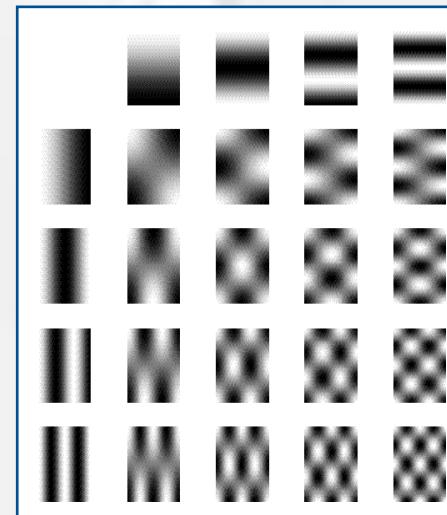
Normalise

Smooth

- Deformation (and thereby normalisation) is implemented by allowing the prior TPMs (which are in MNI-space) to be spatially transformed by a parameterised mapping

- $b_{ik} \mapsto b_{ik}(\alpha) \Rightarrow P(c_i = k | \gamma, \alpha) = \frac{\gamma_k b_{ik}(\alpha)}{\sum_{j=0}^K \gamma_j b_{ij}(\alpha)}$

- Parameter vector to be estimated: α
- about 1000 discrete cosine transforms



US Maths: Regularisation



SNR & Preproc

Temporal

Spatial

General

Realign

Coreg

Normalise

Smooth

- Linear Regularisation of Bias Field and Deformation Field Estimates
 - By including prior distributions for α and β as zero-mean multivariate Gaussians
 - Covariance: $\alpha^T C_\alpha \alpha = \text{bending energy}$; $\rho(\beta) = \exp(K_{70mm} * N(0, \beta))$
- Thus, the final objective function to be maximised is the log-joint probability of intensity, bias and deformation field parameters:

$$P(\mathbf{y}, \boldsymbol{\beta}, \boldsymbol{\alpha} | \boldsymbol{\gamma}, \mu, \sigma^2) = P(\mathbf{y} | \boldsymbol{\beta}, \boldsymbol{\alpha}, \boldsymbol{\gamma}, \mu, \sigma^2) P(\boldsymbol{\beta}) P(\boldsymbol{\alpha})$$

- Equivalently, the negative free energy is minimised:

$$\mathcal{F} = -\log P(\mathbf{y}, \boldsymbol{\beta}, \boldsymbol{\alpha} | \boldsymbol{\gamma}, \mu, \sigma^2) = \mathcal{E} - \log P(\boldsymbol{\beta}) - \log P(\boldsymbol{\alpha})$$

$$\begin{aligned} \mathcal{E} = & - \sum_{i=1}^I \log \left(\frac{\rho_i(\boldsymbol{\beta})}{\sum_{k=1}^K \gamma_k b_{ik}(\boldsymbol{\alpha})} \sum_{k=1}^K \gamma_k b_{ik}(\boldsymbol{\alpha}) (2\pi\sigma_k^2)^{-\frac{1}{2}} \right. \\ & \times \exp \left. \left(-\frac{(\rho_i(\boldsymbol{\beta})y_i - \mu_k)^2}{2\sigma_k^2} \right) \right) \end{aligned}$$