Signal, Noise and Preprocessing*

Zurich SPM Course 2015

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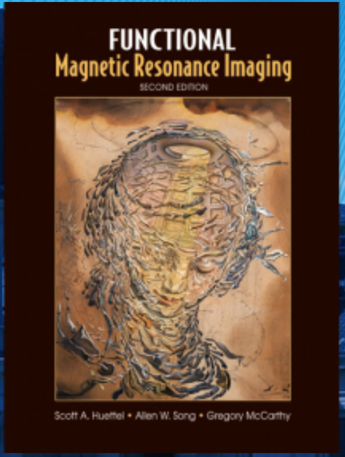
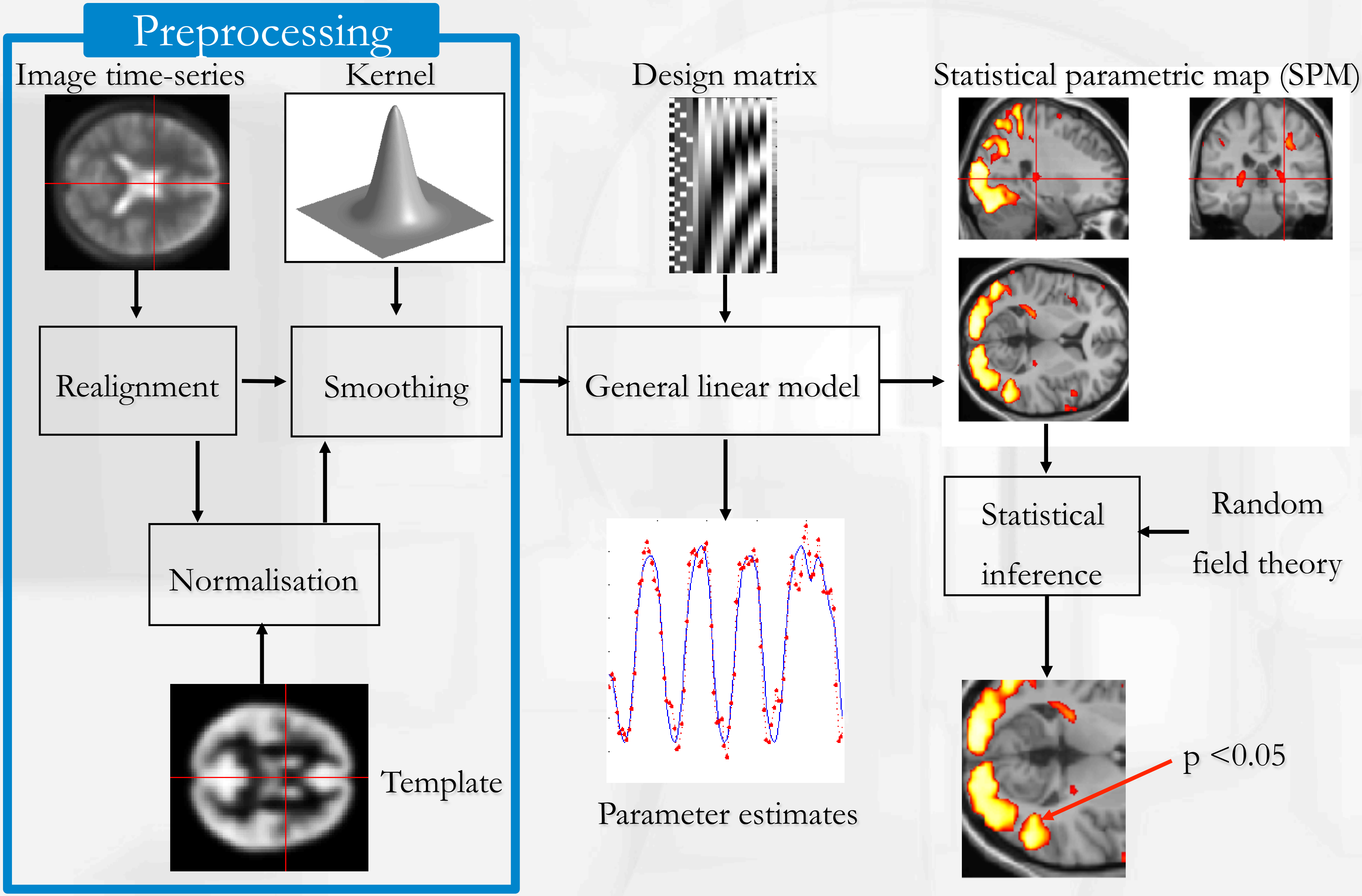
*Huettel et al.

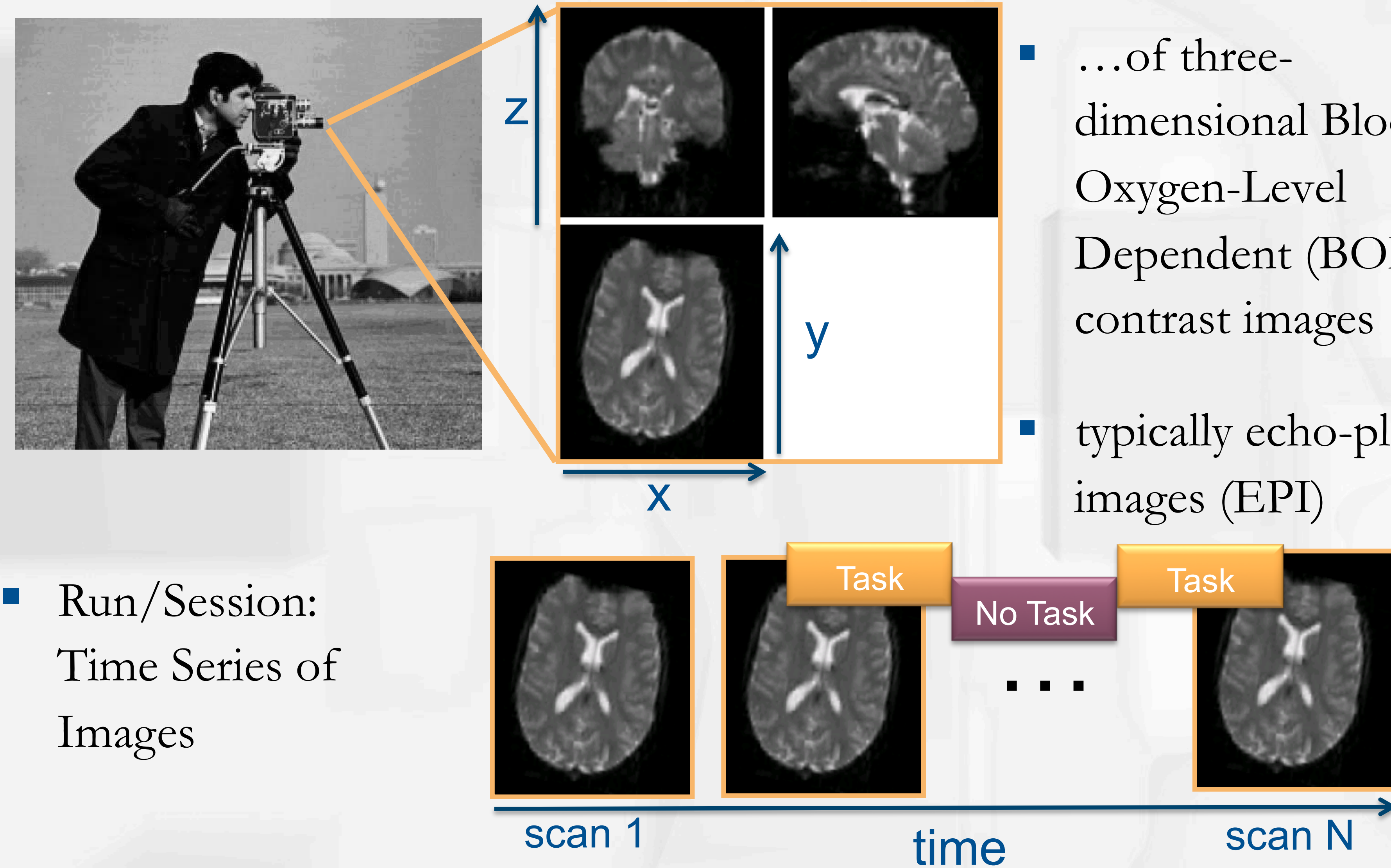


Overview of SPM for fMRI



fMRI = Acquiring Movies

Translational Neuromodeling Unit



- …of three-dimensional Blood Oxygen-Level Dependent (BOLD) contrast images
- typically echo-planar images (EPI)

- Run/Session: Time Series of Images

fMRI = Acquiring Movies

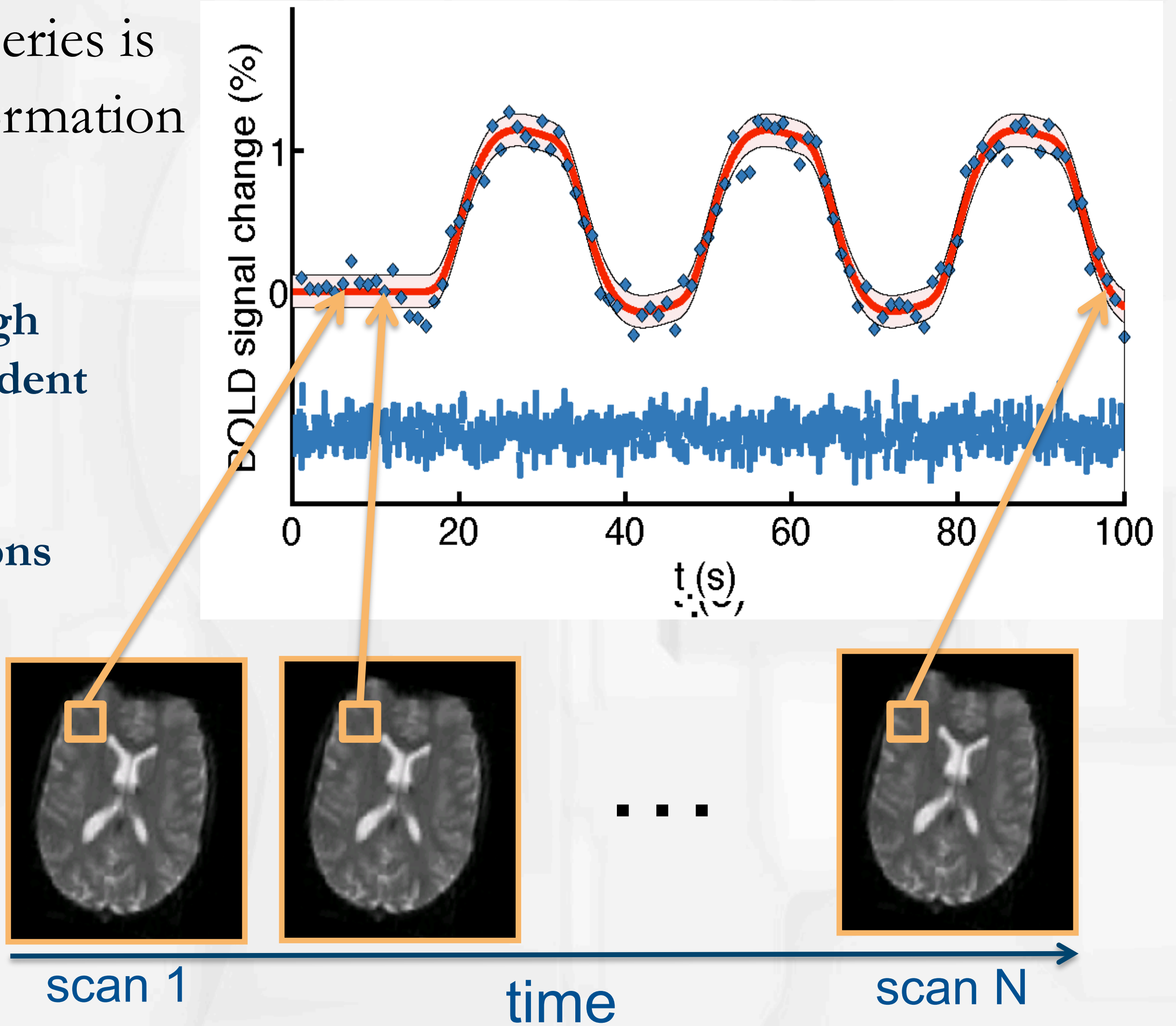
Translational Neuromodeling Unit

- The Localized Time-series is the Fundamental Information Unit of fMRI

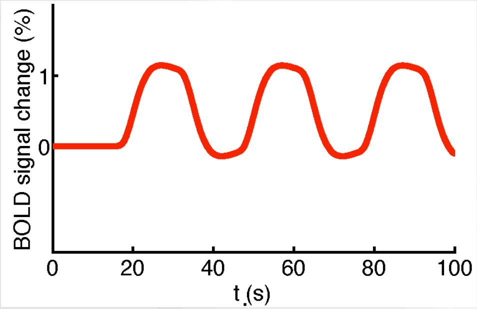
Signal: Fluctuation through Blood oxygen level dependent (BOLD) contrast

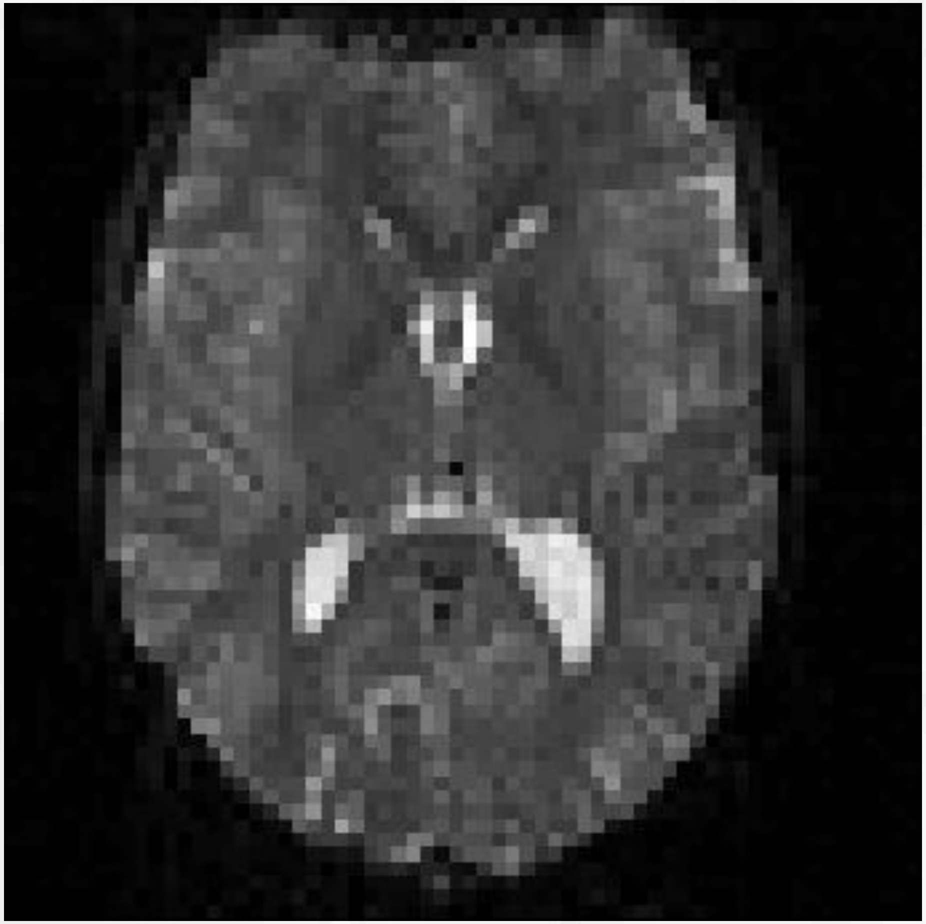
Noise: All other fluctuations

- Run/Session: Time Series of Images



fMRI Movie: An example

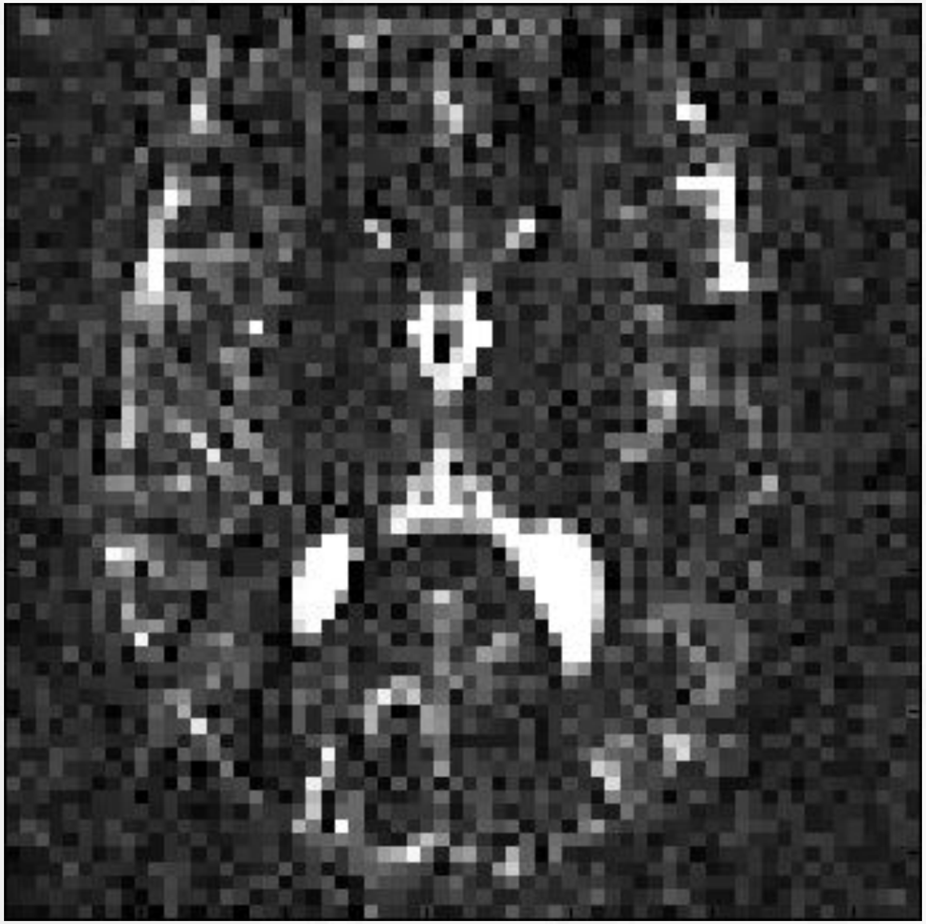




fMRI Movie: Subtracting the Mean

Translational Neuromodeling Unit

- interest in fluctuations only

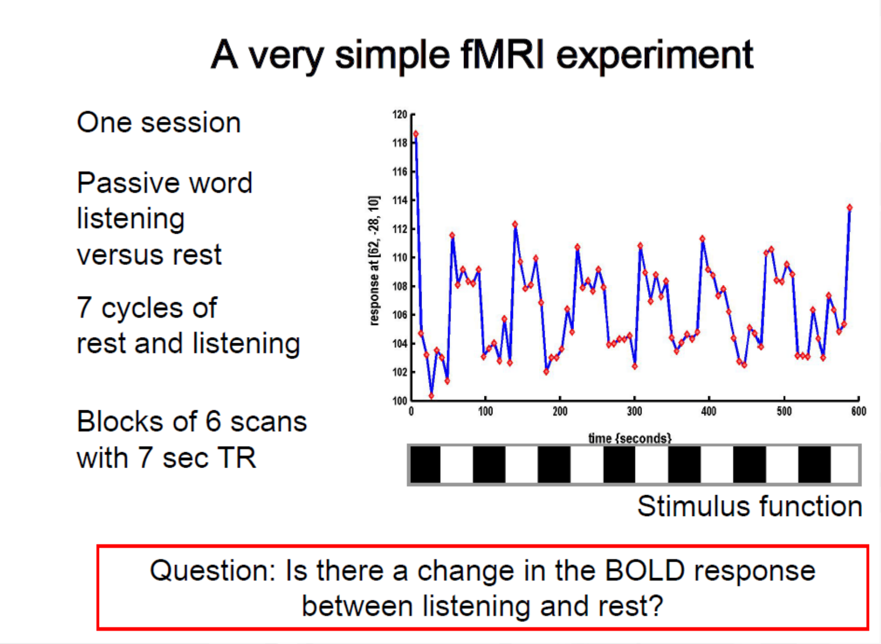


Introducing the Dataset (MoAE)

Translational Neuromodeling Unit

- Mother of All Experiments: Auditory Stimulation
  - TR 7 seconds
  - 6 TR rest
  - 6 TR binaural stimulation

  (1 bi-syllabic word per second)

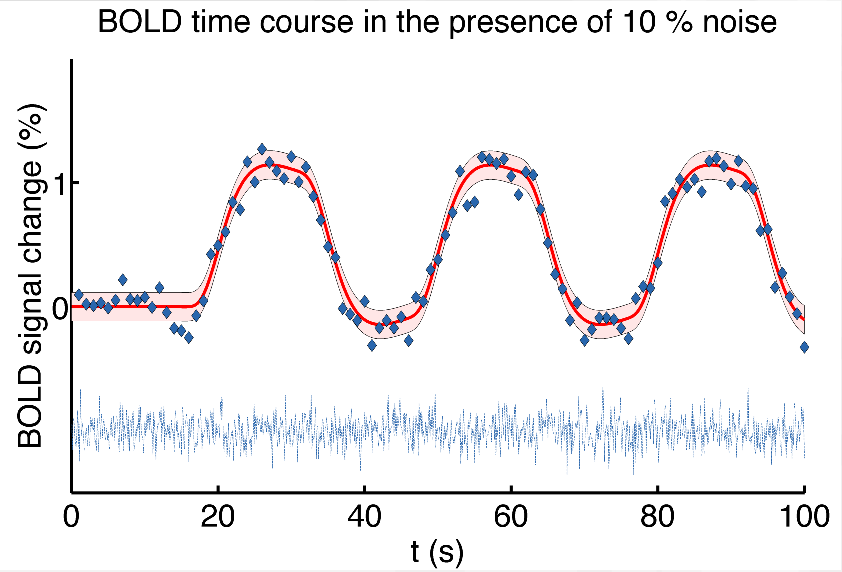


- Chapter 28 of SPM manual

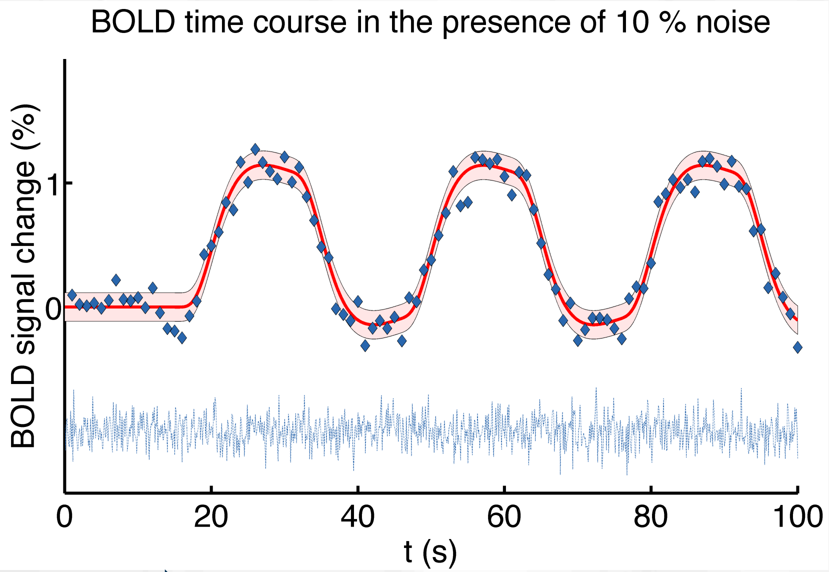
The Goal of Preprocessing

Translational
Neuromodeling
Unit

Before



After



Preprocessing

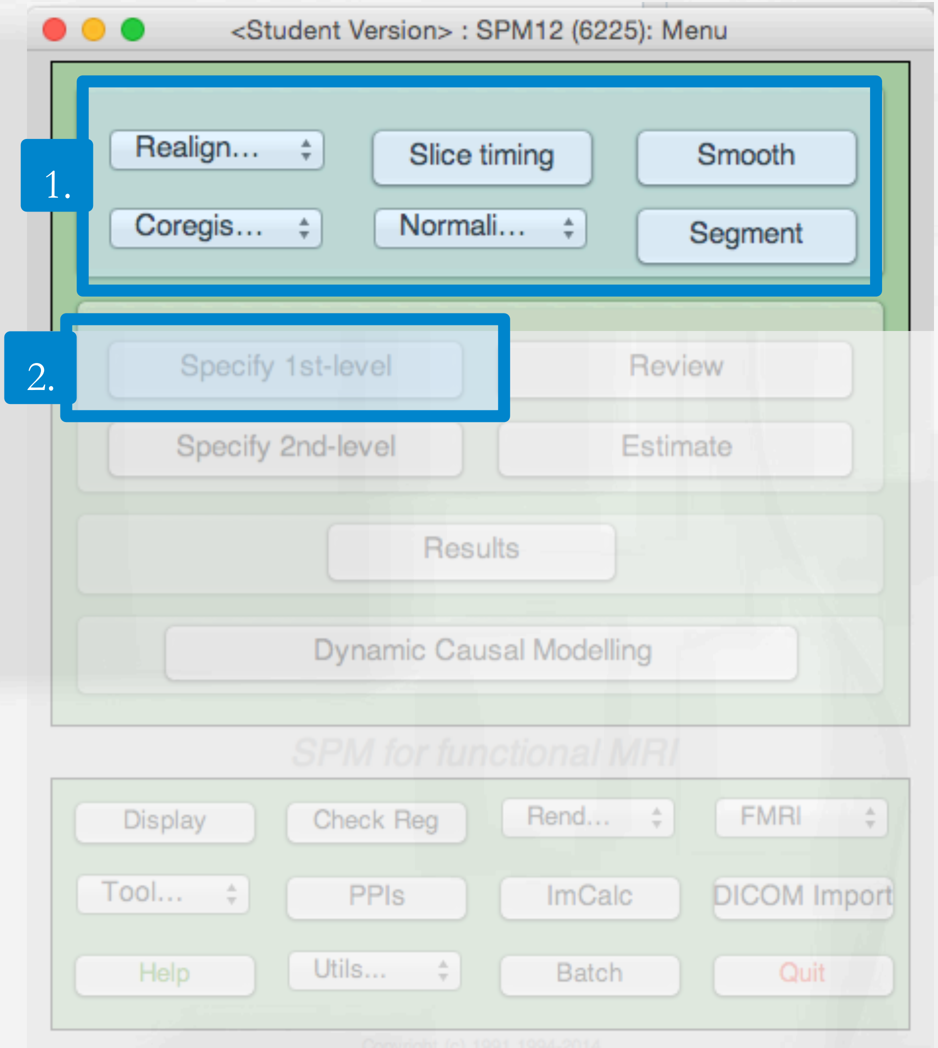
Sources of Noise in fMRI

Translational Neuromodeling Unit

Source	Preprocessing	Step
Subject Motion	Spatial Preproc	Realignment
Acquisition Timing	Temporal Preproc	Slice-Timing
Anatomical Identity	Spatial Preproc	Co-registration
Inter-subject variability	Spatial Preproc	Segmentation
Thermal Noise	Spatial Preproc	Smoothing
Physiological Noise	Noise Modelling	PhysIO Toolbox

The SPM Graphical User Interface (GUI)

Translational Neuromodeling Unit



- Preprocessing
  - Realignment
  - Slice-Timing Correction
  - Co-registration
  - Unified Segmentation & Normalisation
  - Smoothing . . .
- Noise Modelling
  - Physiological Confound Regressors

Sources of Noise in fMRI

Translational Neuromodeling Unit

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

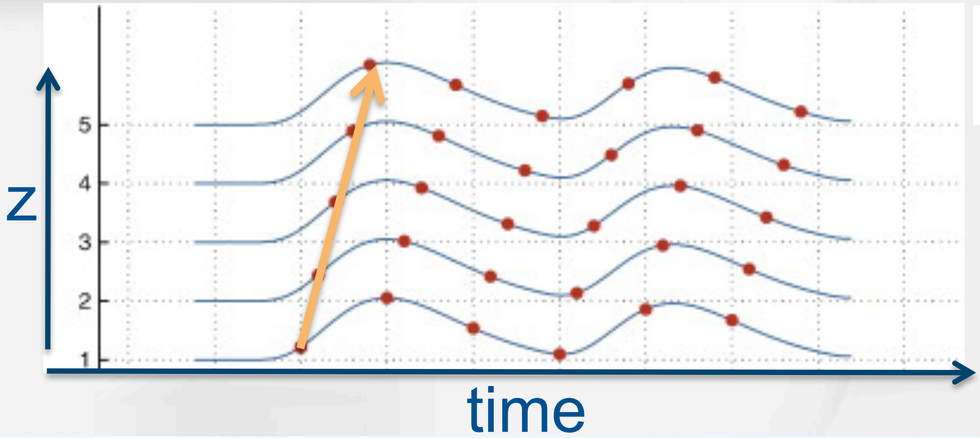
Temporal Preproc

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

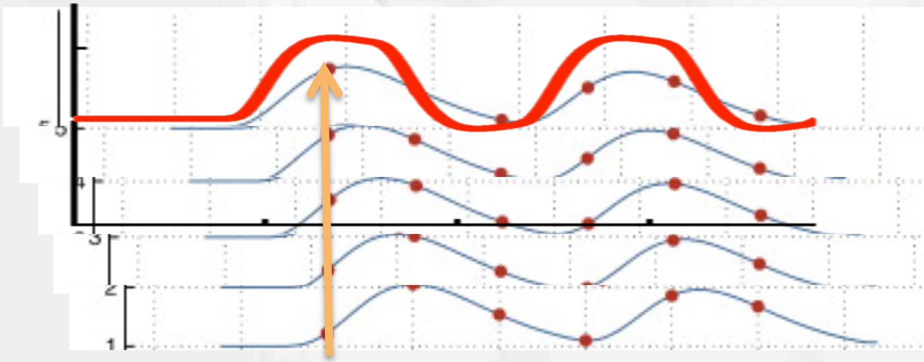
Slice-timing correction (STC)

- Slices of 1 scan volume are not acquired simultaneously (60 ms per slice)
- Creates shifts of up to 1 volume repetition time (TR), i.e. several seconds
- Reduces sensitivity for time-locked effects (smaller correlation)

True 2D Acquisition



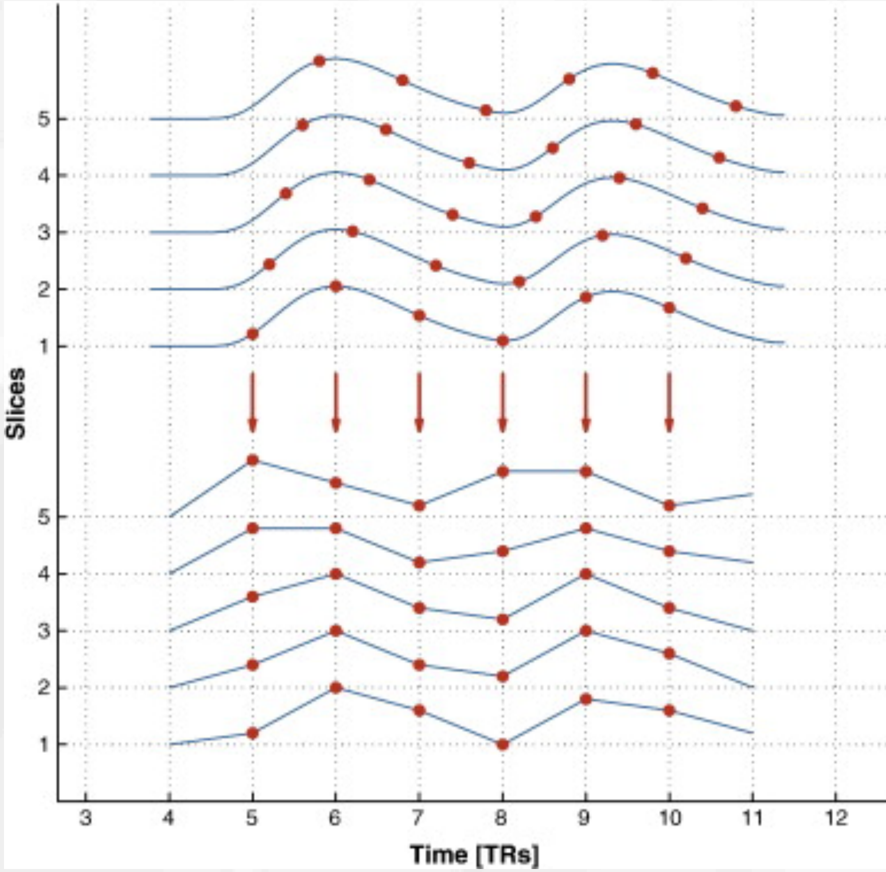
Same-Timepoint Assumption



Slice-timing correction (STC)

Translational Neuromodeling Unit

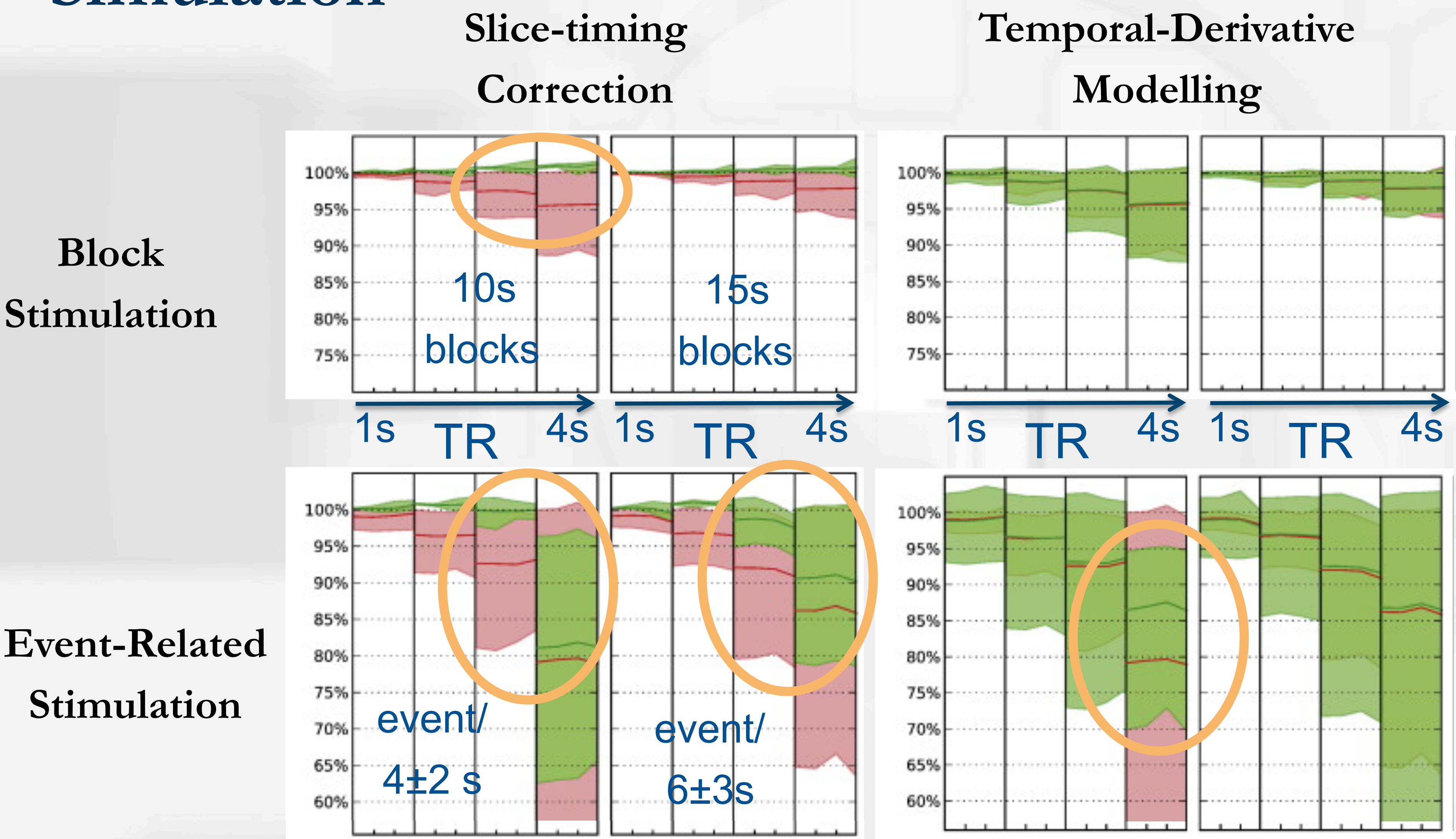
- Slice-timing correction: All voxel time series are aligned to acquisition time of 1 slice (e.g. centre slice)
- Missing data is interpolated via sinc-interpolation (band-limited signal)
- Before or after realignment?
  - before: dominant through-slice motion
  - after: dominant within-slice motion
- 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

Slice-timing correction (STC): Simulation

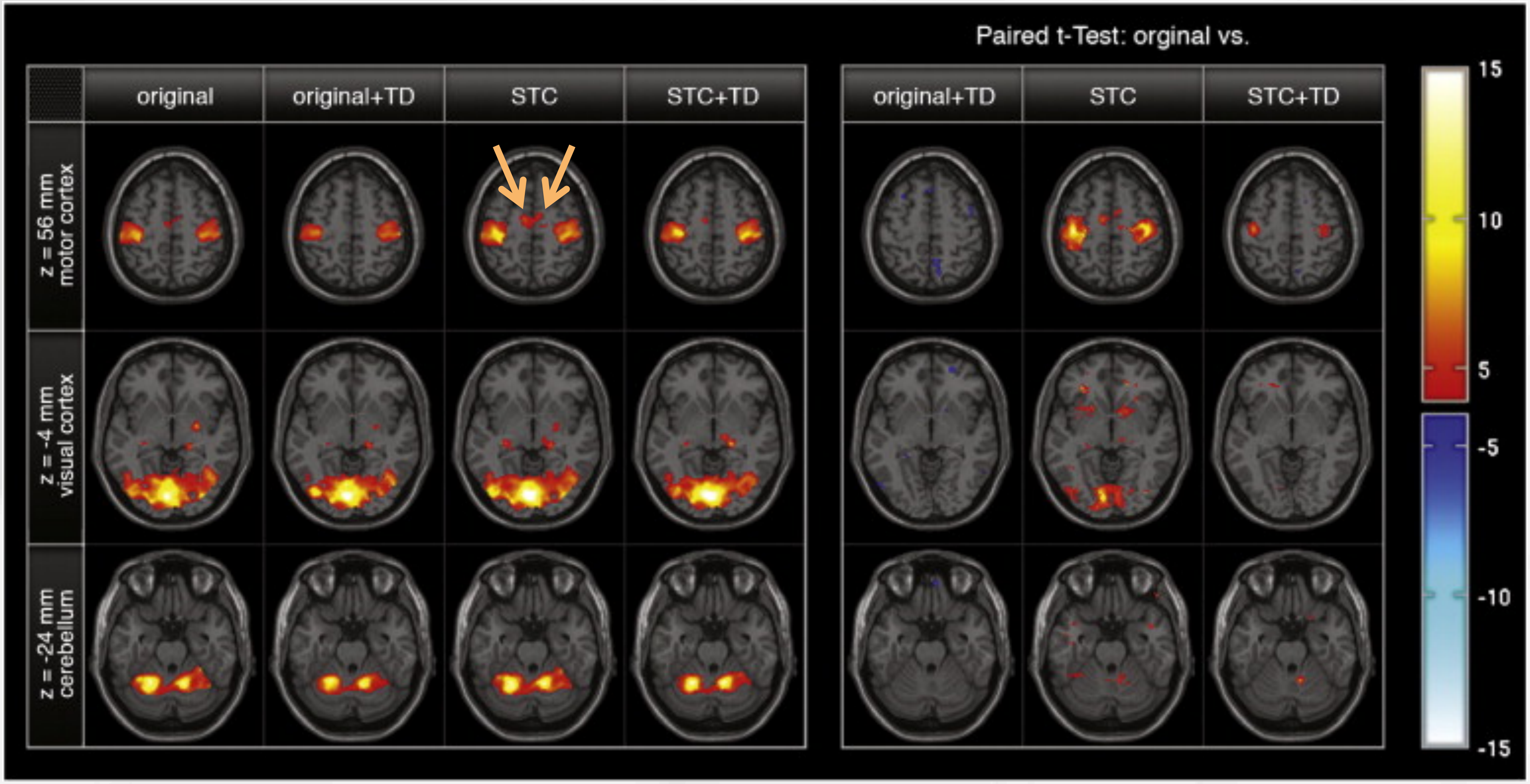
Translational Neuromodeling Unit



Sladky et al, NeuroImage 2011

Slice-timing correction (STC): Experiment

Translational Neuromodeling Unit



Sladky et al, NeuroImage 2011

Sources of Noise in fMRI

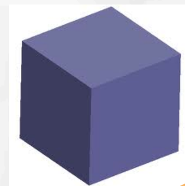
Translational Neuromodeling Unit

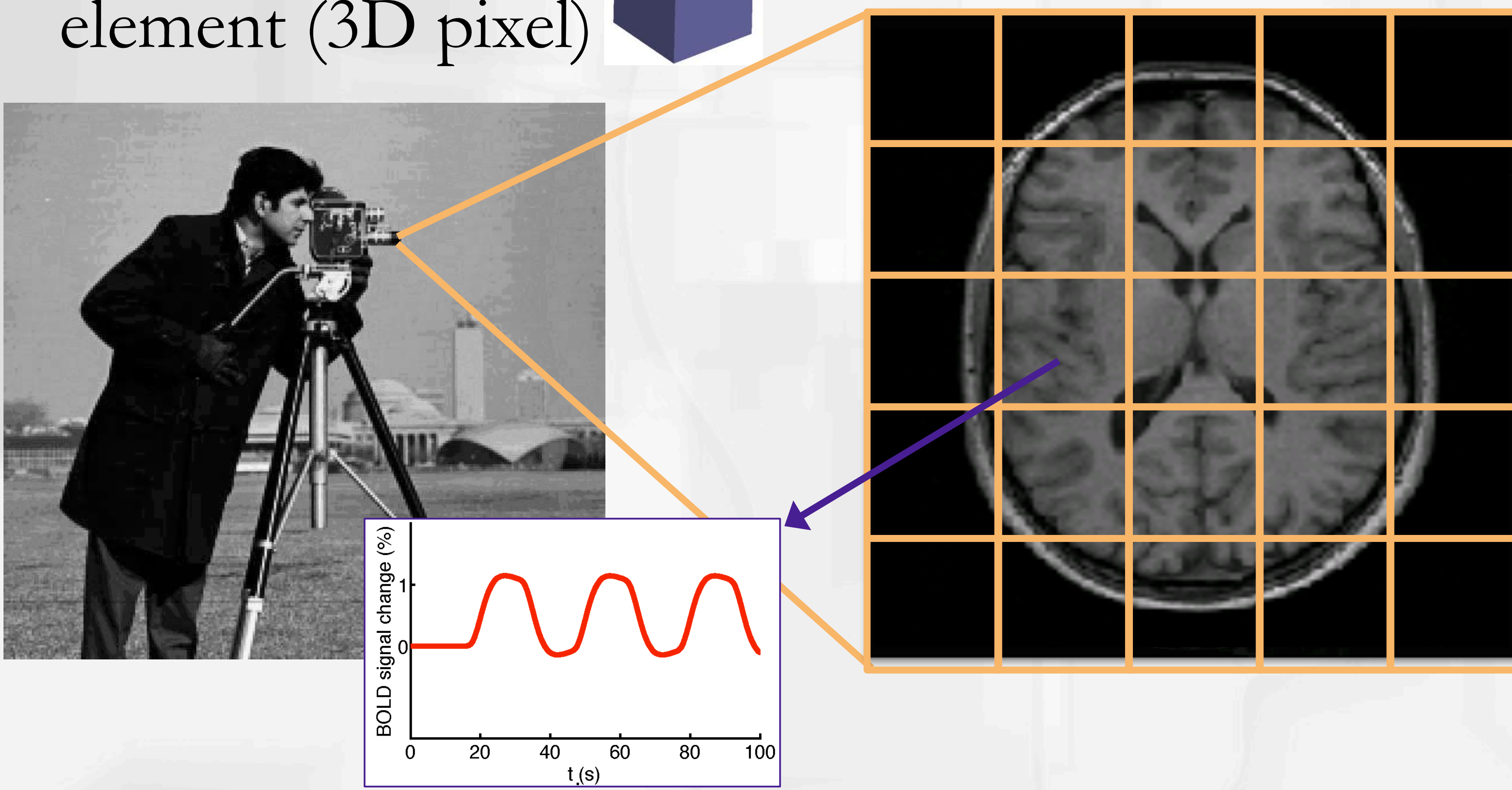
Source of noise		Preprocessing
Subject Motion	Spatial Preproc	Realignment
Acquisition Timing		Slice-Timing
Anatomical Identity	Spatial Preproc	Co-registration
Inter-subject variability	Spatial Preproc	Segmentation
Thermal Noise	Spatial Preproc	Smoothing
Physiological Noise		PhysIO Toolbox

Finite Resolution and Voxel Identity

Translational Neuromodeling Unit

- voxel = volume element (3D pixel)





Spatial Preprocessing = Correcting Voxel Mismatches

Translational Neuromodeling Unit

Voxel Mismatch Between

- Functional Scans/Runs
- Functional/Structural Images
- Subjects

Realignment	Inter-Modal Coregistration	Normalisation/ Segmentation

Smoothing

Spatial Preprocessing

Translational Neuromodeling Unit

REALIGN

COREG

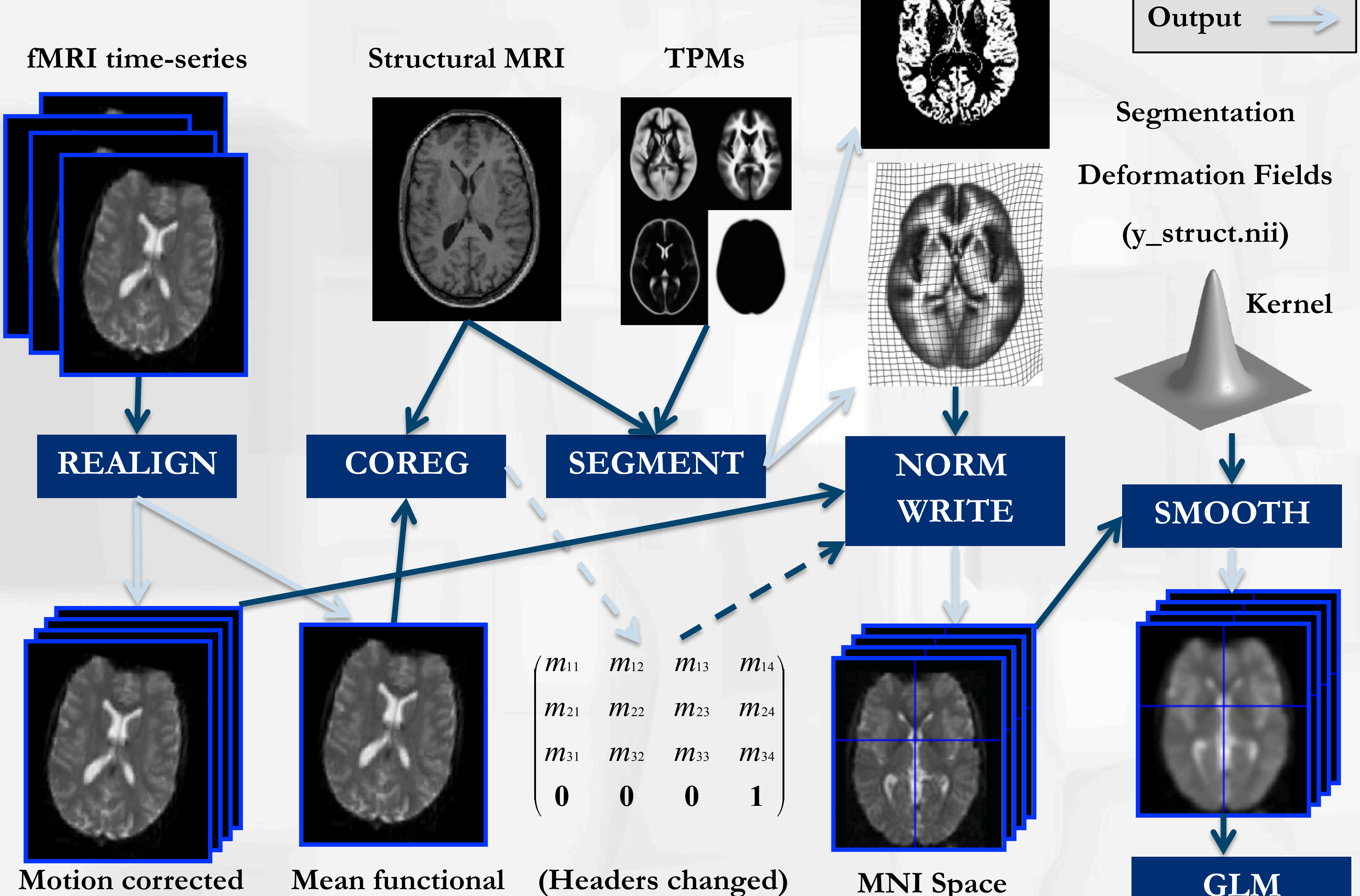
SEGMENT

NORM WRITE

SMOOTH

GLM

Spatial Preprocessing



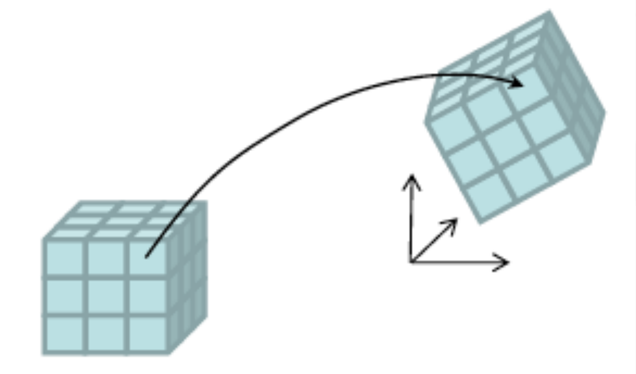
General Remarks on Image Registration

Translational Neuromodeling Unit

- 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

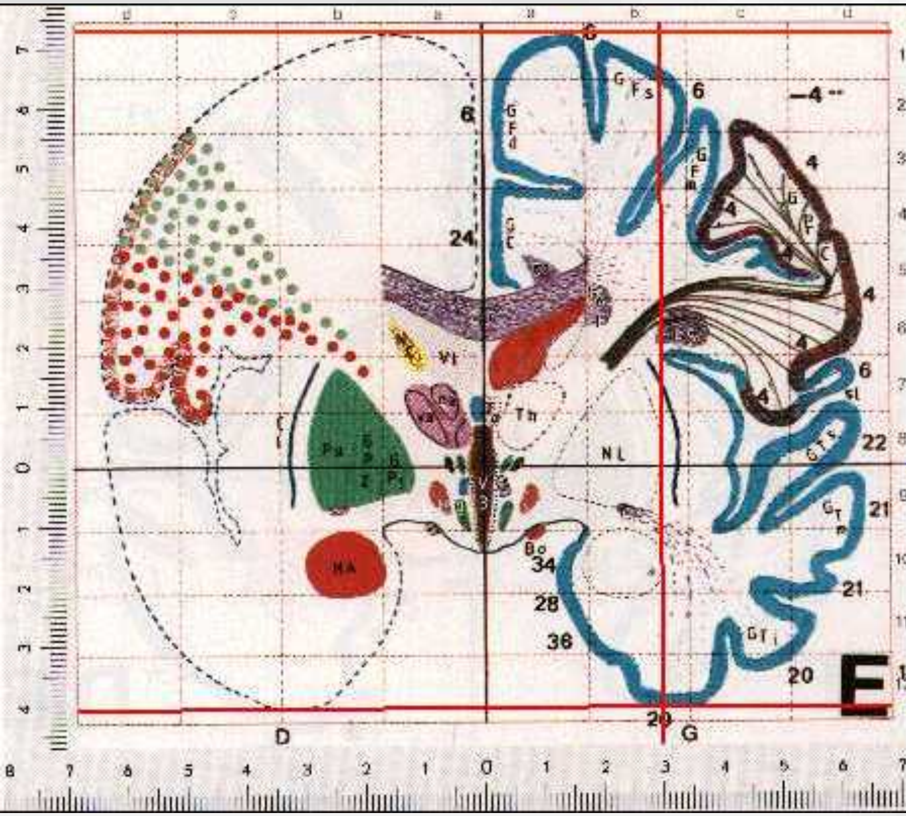
- 3D images are made up of voxels.
- Voxel intensities are stored on disk as lists of numbers.
- Meta-information about the data:
  - image dimensions
    - conversion from list to 3D array
  - "voxel-to-world mapping"
    - Spatial transformation that maps
      - from: data coordinates (voxel column 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



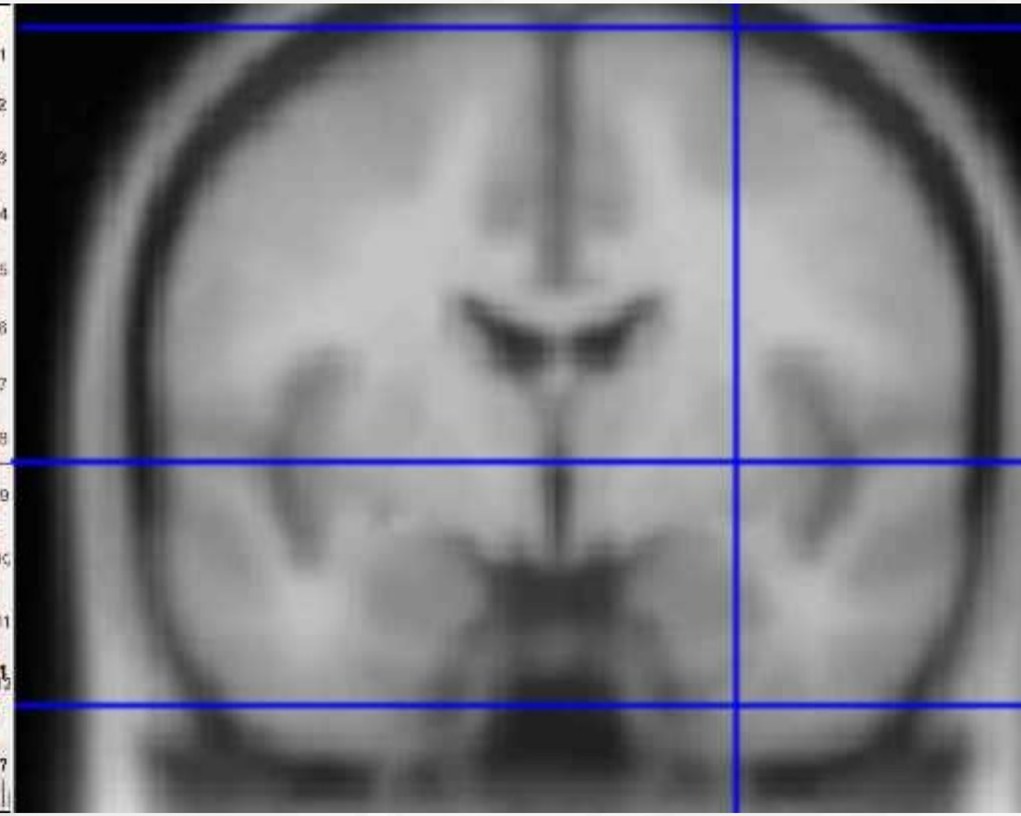
A. Voxel-to-World: Standard Spaces

Translational Neuromodeling Unit

The Talairach Atlas



The MNI/ICBM AVG152 Template



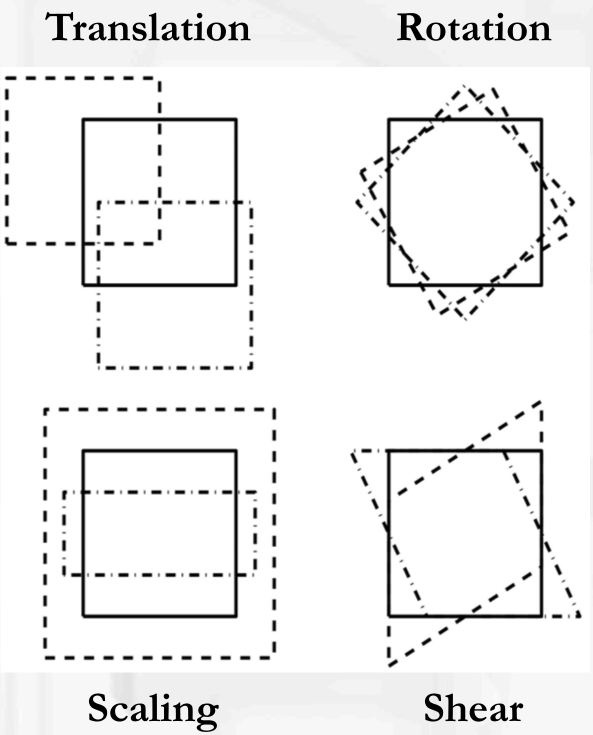
The MNI template follows the convention of T&T, but doesn't match the particular brain

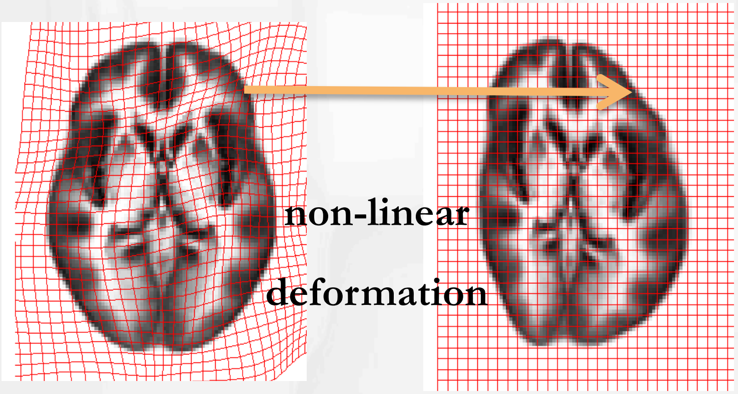
Recommended reading: http://imaging.mrc-cbu.cam.ac.uk/imaging/MniTalairach

B. Transformations

- Transformations describe the mapping of all image voxels from one coordinate system into another

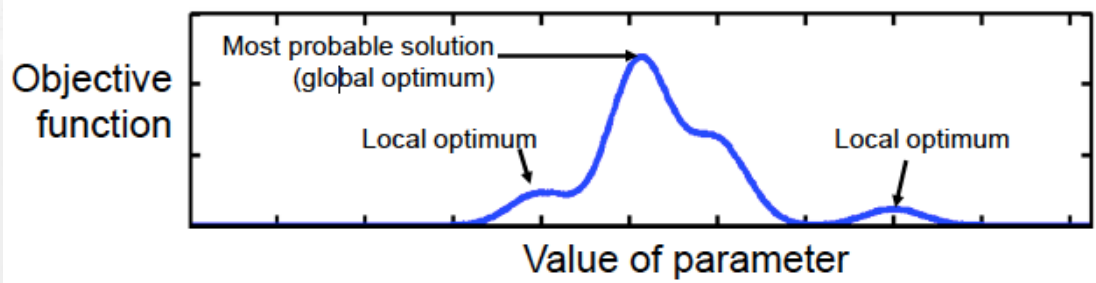
- Types of transformations
  - rigid body = translation + rotation
  - affine = rigid body + scaling + shear
  - non-linear = any mapping
    - (x,y,z) to new values (x',y', z')
    - described by deformation fields





C. Similarity Measures & D. Optimisation

- 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)

Spatial Preprocessing & Image Registration Contents

Translational Neuromodeling Unit

B. Allowed Transformations

Rigid-Body	Affine	Non-linear	
REALIGN	COREG	SEGMENT	NORM WRITE

C. Similarity Measure

Mean-squared Difference	Mutual Information	Tissue Class Probability

D. Optimisation

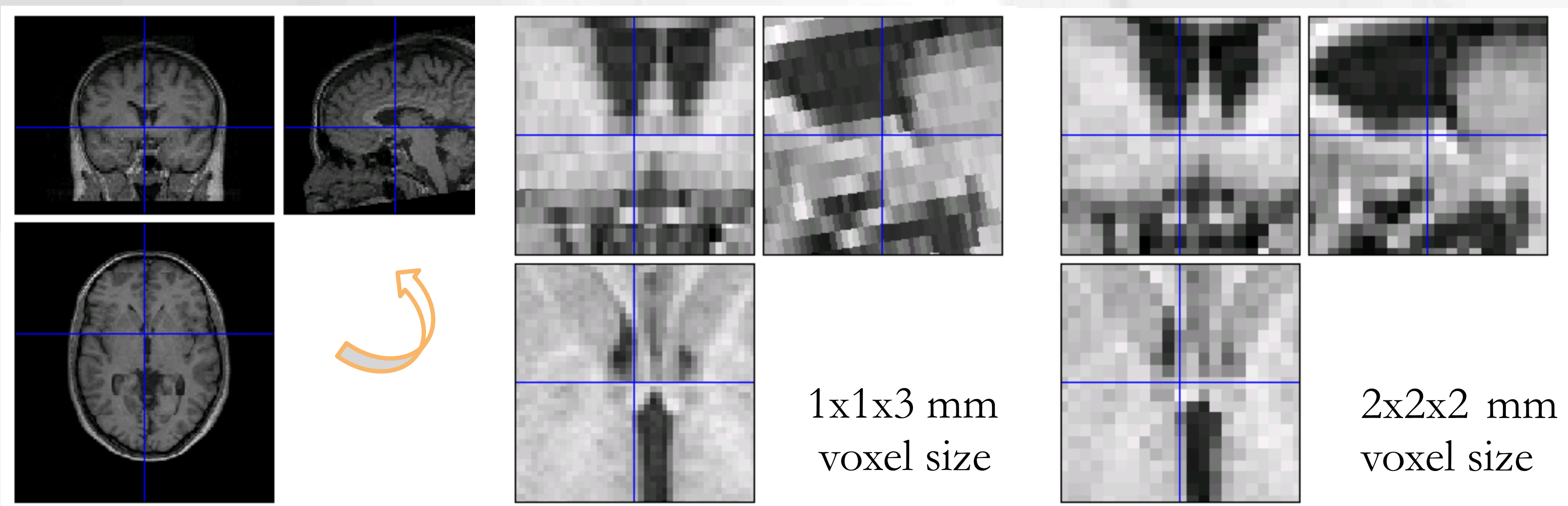
Exact Linearized Solution	Conjugate Direction Line Search	Iterated Conditional Modes (EM/Levenberg-Marquardt)

E. Reslicing/Interpolation

Translational Neuromodeling Unit

- 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

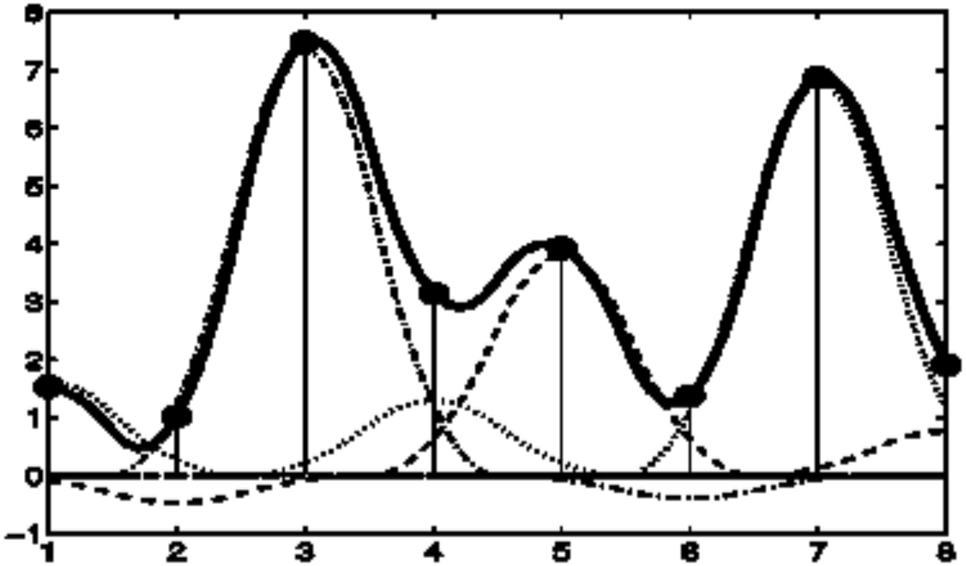
Reoriented **Resliced**



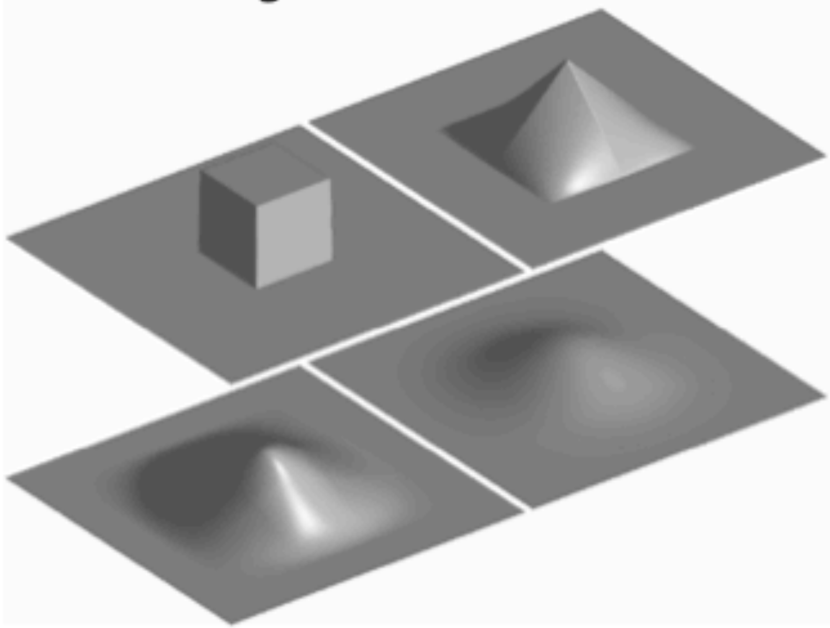
E. B-spline Interpolation

Translational Neuromodeling Unit

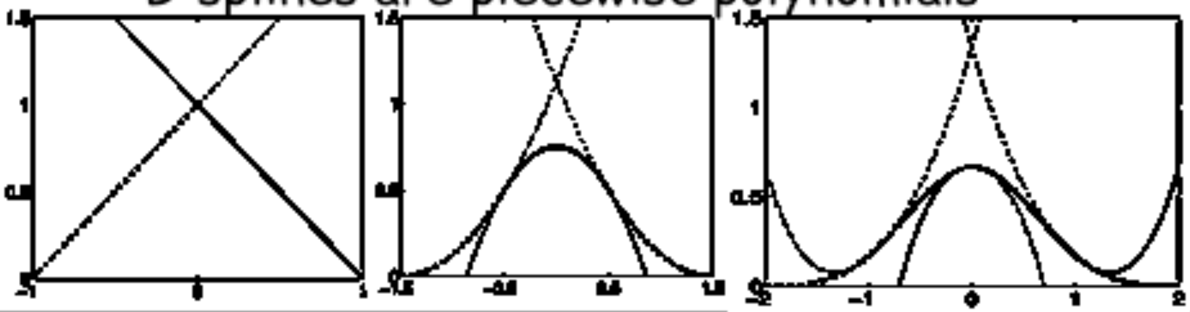
A continuous function is represented by a linear combination of basis functions



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

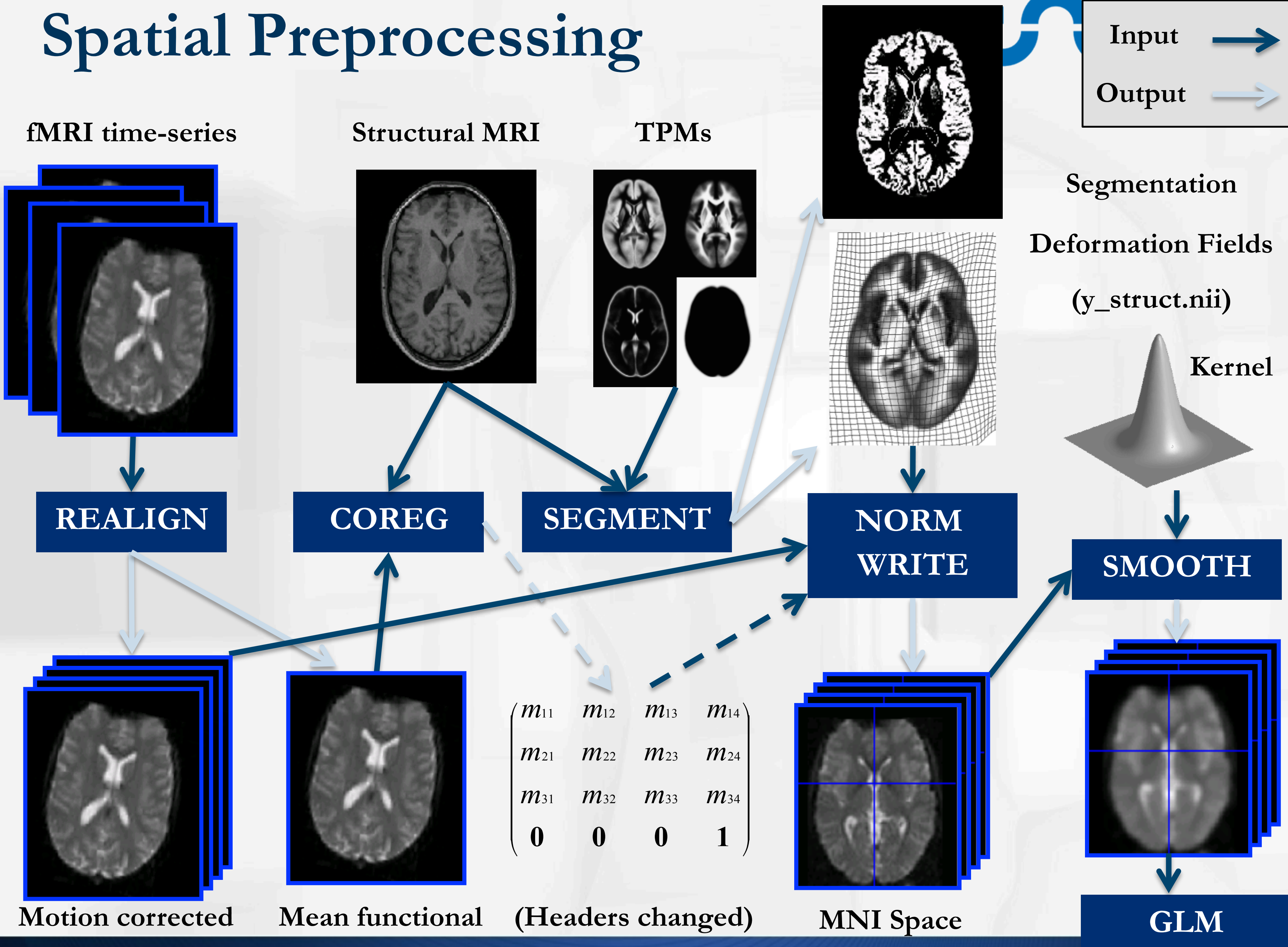


B-splines are piecewise polynomials

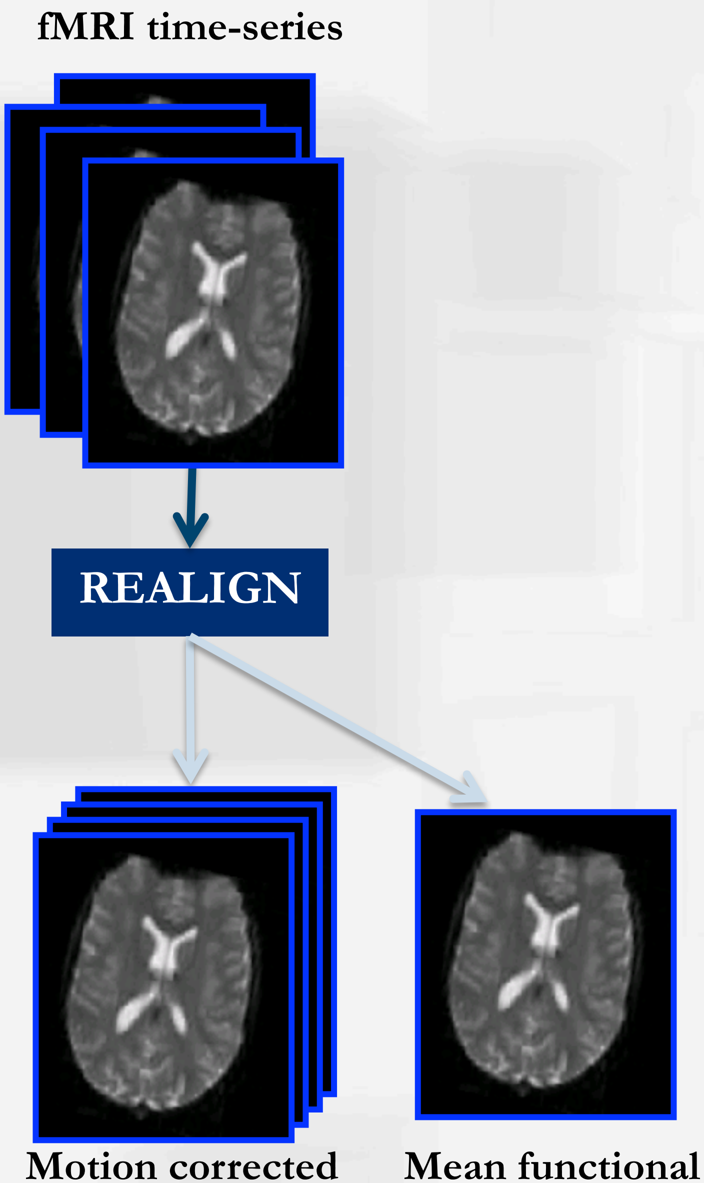


Nearest neighbour and trilinear interpolation are the same as B-spline interpolation with degrees 0 and 1.

Spatial Preprocessing

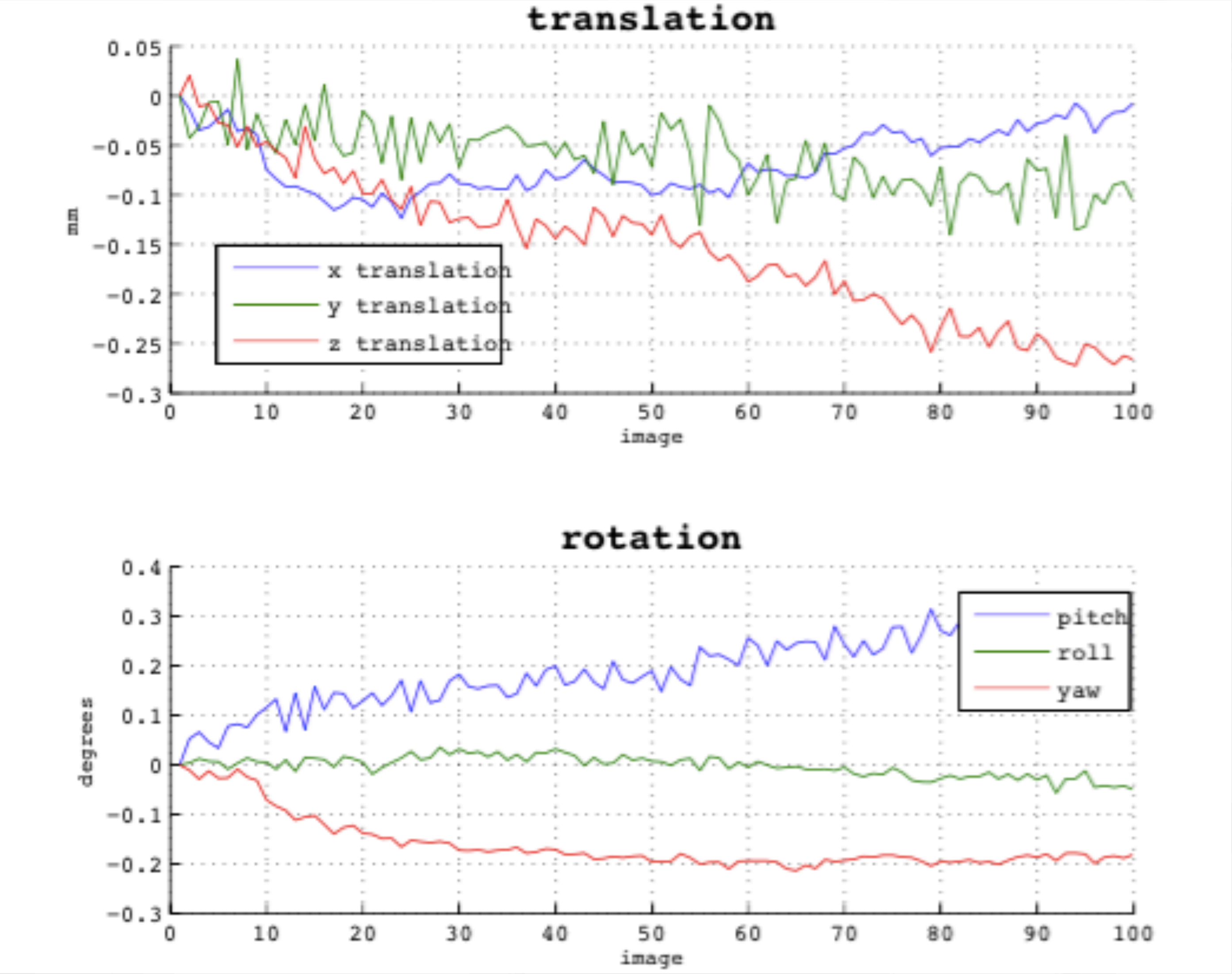


Realignment



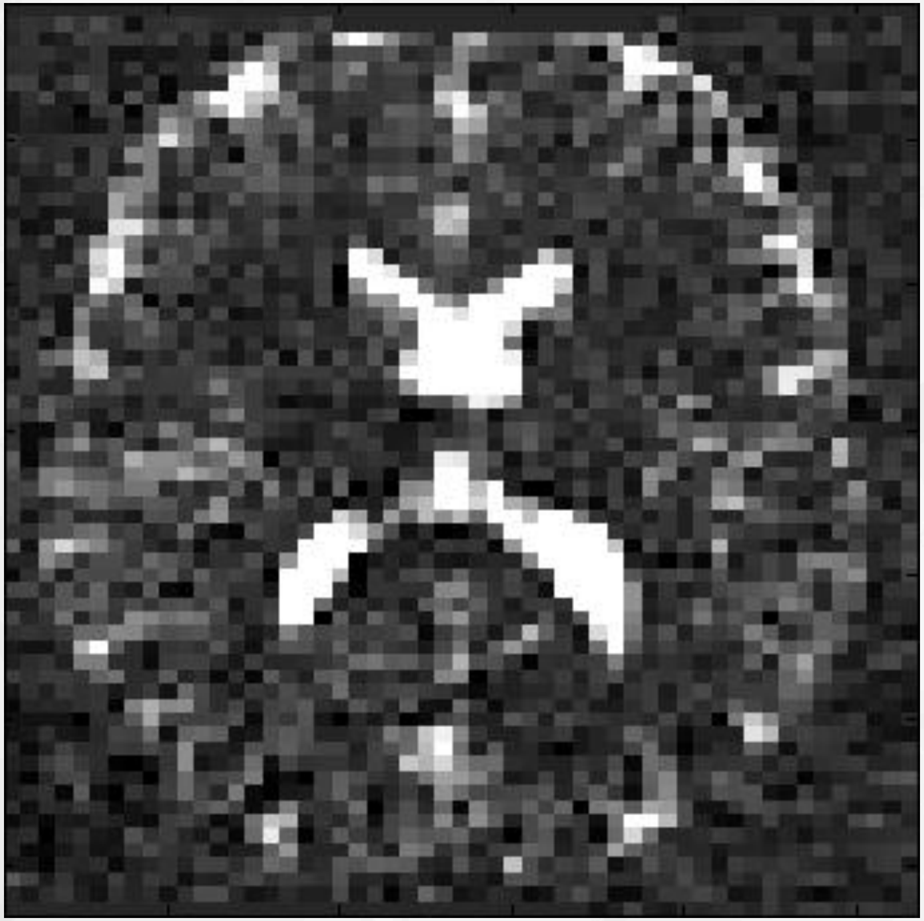
- Aligns all volumes of all runs spatially
- Rigid-body transformation: three translations, three rotations
- Objective function: mean squared error of corresponding voxel intensities
- Voxel correspondence via Interpolation

Realignment Output: Parameters



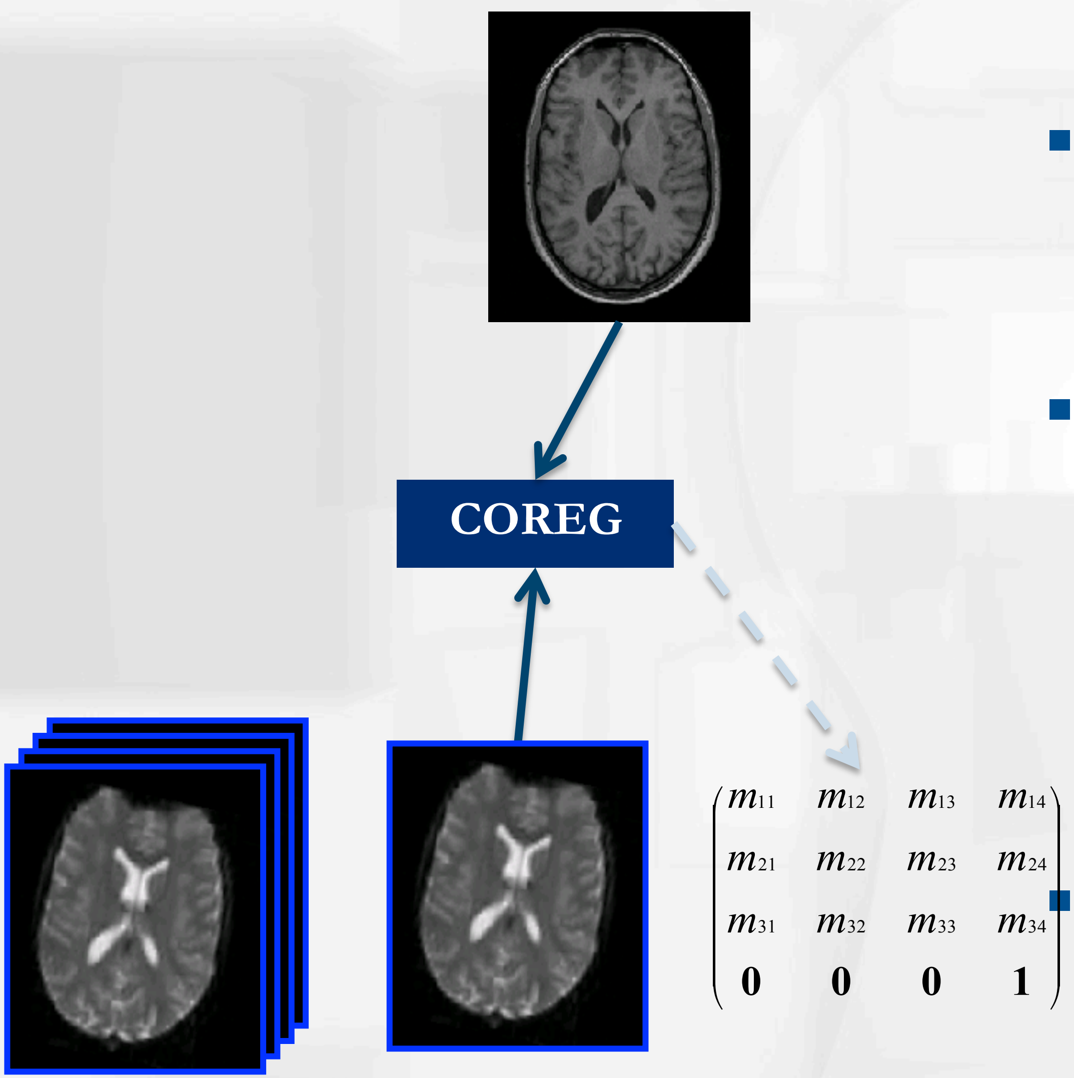
fMRI Run after Realignment

Translational Neuromodeling Unit



Co-Registration

Translational Neuromodeling Unit

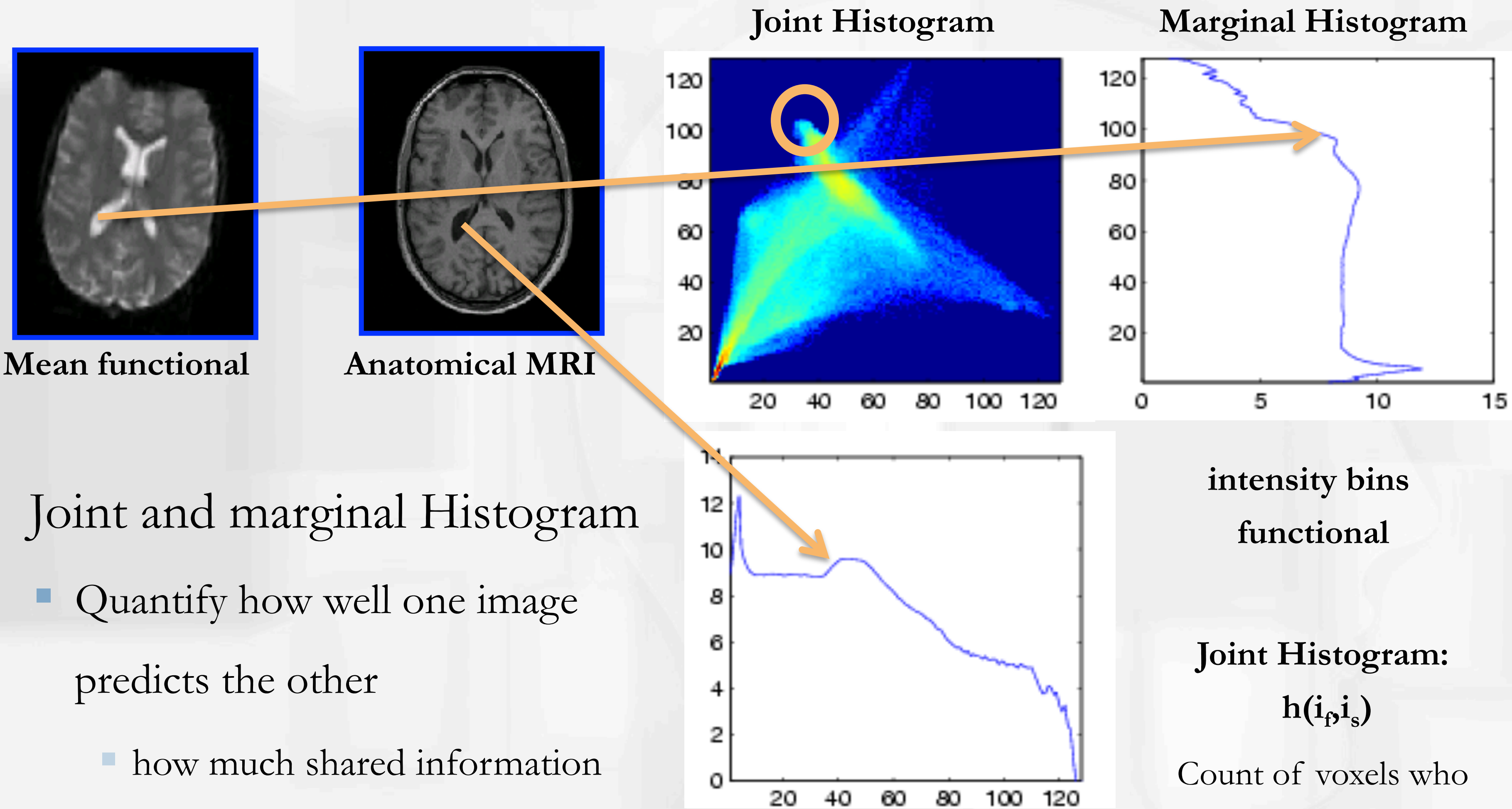


$$\begin{pmatrix} m_{11} & m_{12} & m_{13} & m_{14} \\ m_{21} & m_{22} & m_{23} & m_{24} \\ m_{31} & m_{32} & m_{33} & m_{34} \\ \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{1} \end{pmatrix}$$

- Aligns structural image to mean functional image
- Affine transformation: translations, rotations, scaling, shearing
- Objective function: mutual information, since contrast different
  - Optimisation via Powell's method: conjugate directions, line seach along parameters
- Typically only transformation matrix ("header") changed (no reslicing)

Co-Registration: Output

Translational Neuromodeling Unit



- Joint and marginal Histogram
  - Quantify how well one image predicts the other
    - how much shared information
  - Joint probability distribution estimated from joint histogram

intensity bins functional

intensity bins structural

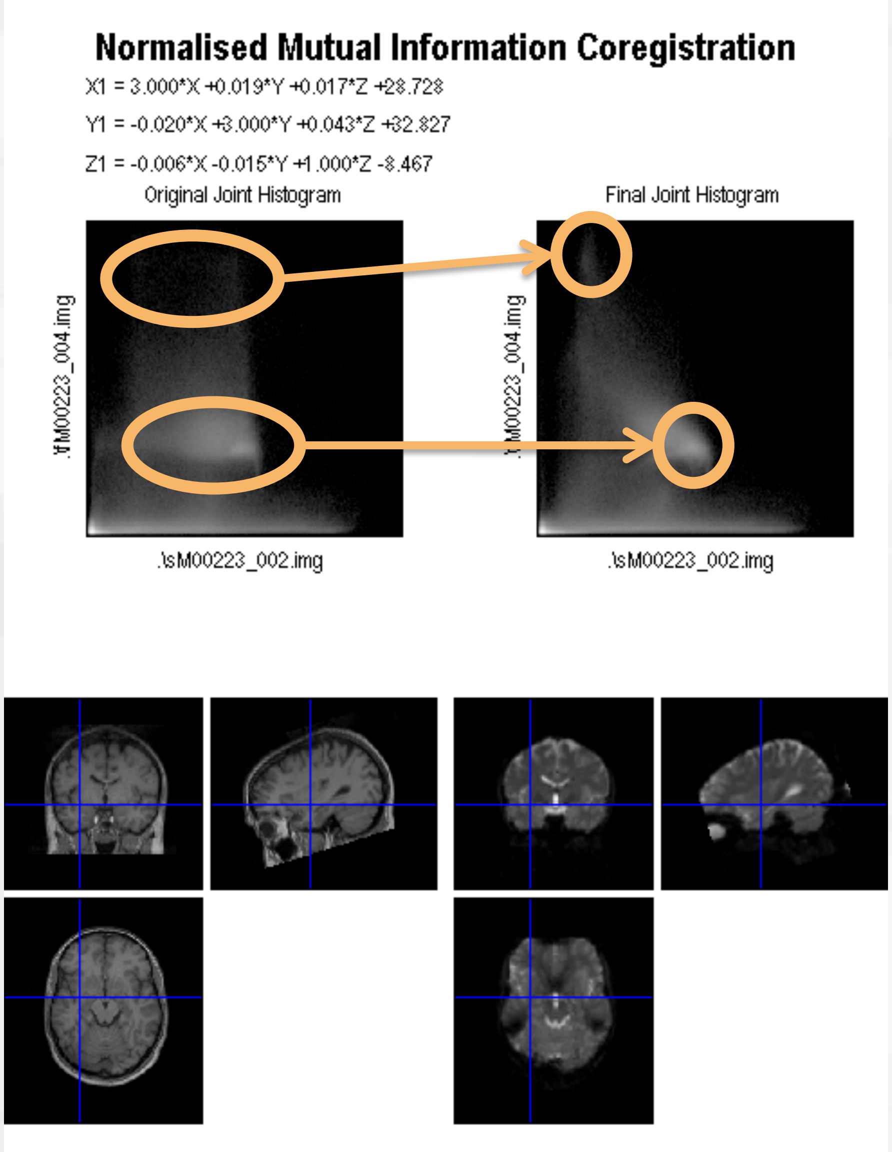
Joint Histogram: $h(i_f,i_s)$

Count of voxels who have intensity $\mathbf{i_f}$ in functional and $\mathbf{i_s}$ in structural image

Co-Registration: Output

Translational
Neuromodeling
Unit

- Voxels of same tissue identity should have same intensity in an MR-contrast
- In a second MR contrast, this 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



Sources of Noise in fMRI

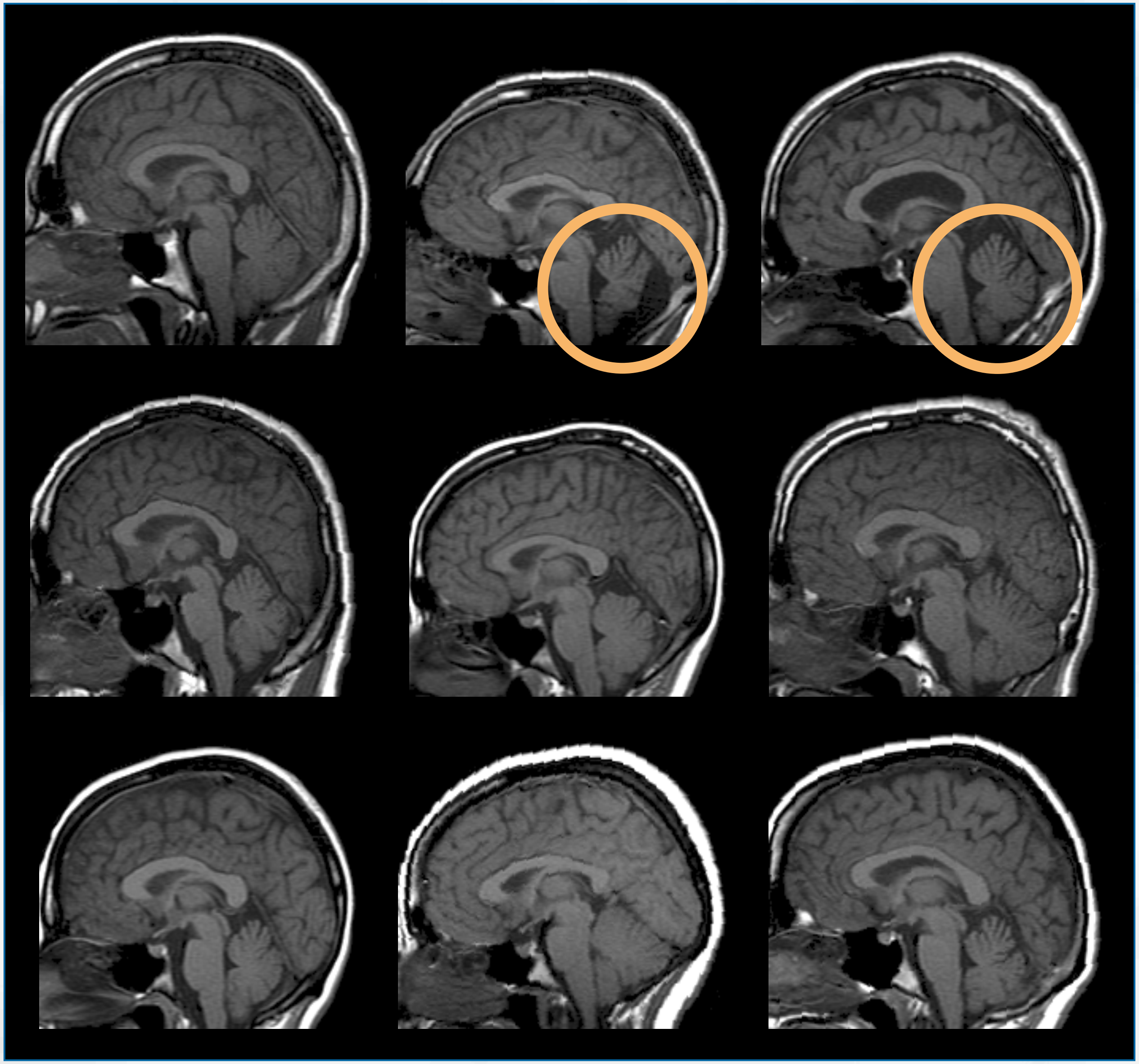
Translational Neuromodeling Unit

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

Spatial Preproc

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

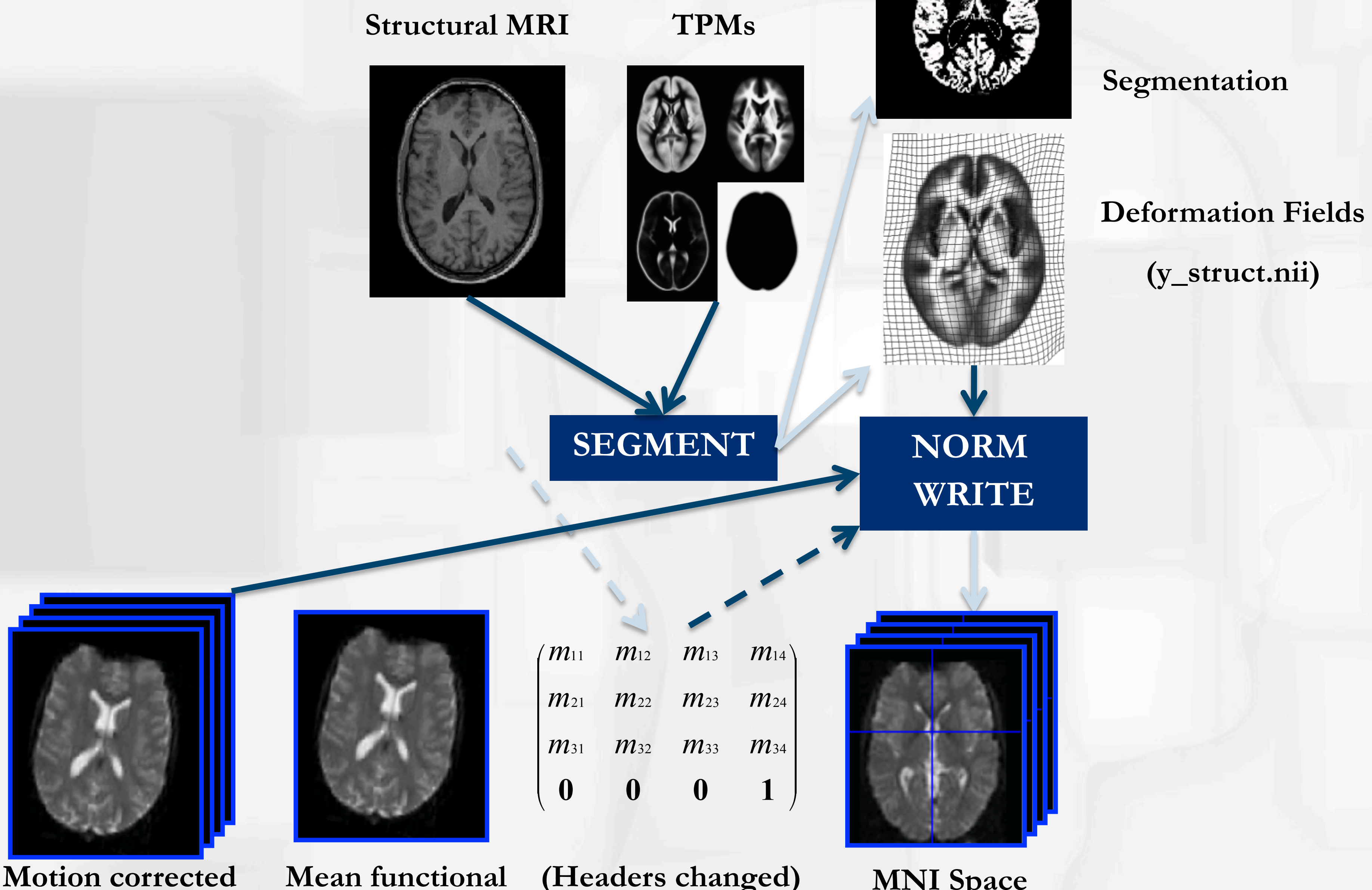
Inter-subject Variability



Spatial Normalisation - Reasons

- 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



Normalisation via Unified Segmentation

- MRI imperfections: No simple similarity measure, a lot of possible transformations…
  - Noise, artefacts, partial volume effects
  - Intensity inhomogeneity (bias field)
  - Geometric/Contrast differences between sequences
- **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)
- This *circularity* motivates simultaneous segmentation and normalisation in a unified model

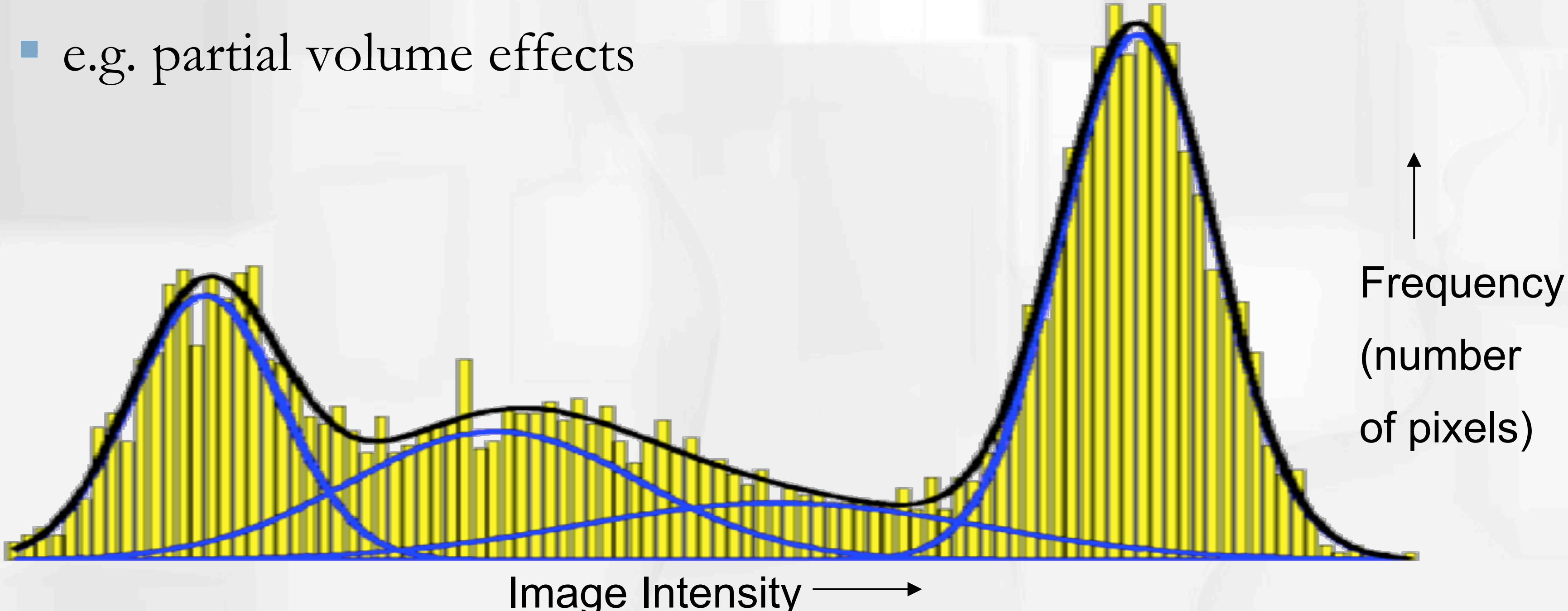
Summary of the unified model

Translational Neuromodeling Unit

- SPM12 implements a generative model of voxel intensity from tissue class probabilities
  - Principled Bayesian probabilistic formulation
  - Segmentation by inverting a Gaussian mixture model
- Deformations of prior tissue probability maps (TPMs, priors) are also part of the model
  - The inverse of the transformation that aligns the TPMs can be used to normalise the original image
  - Non-linear deformations are constrained by regularisation factors
- Bias correction is included within the model

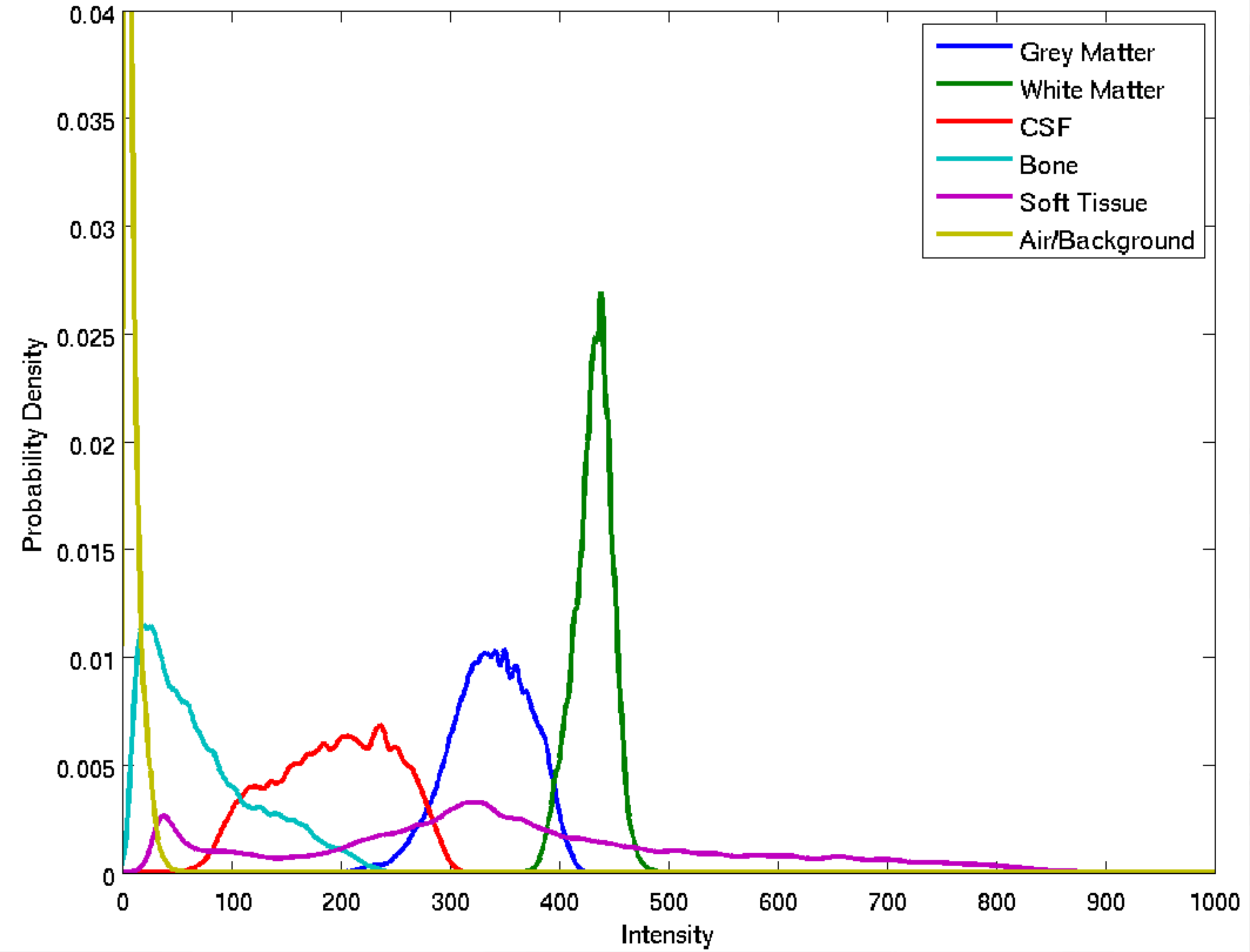
Mixture of Gaussians

- 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



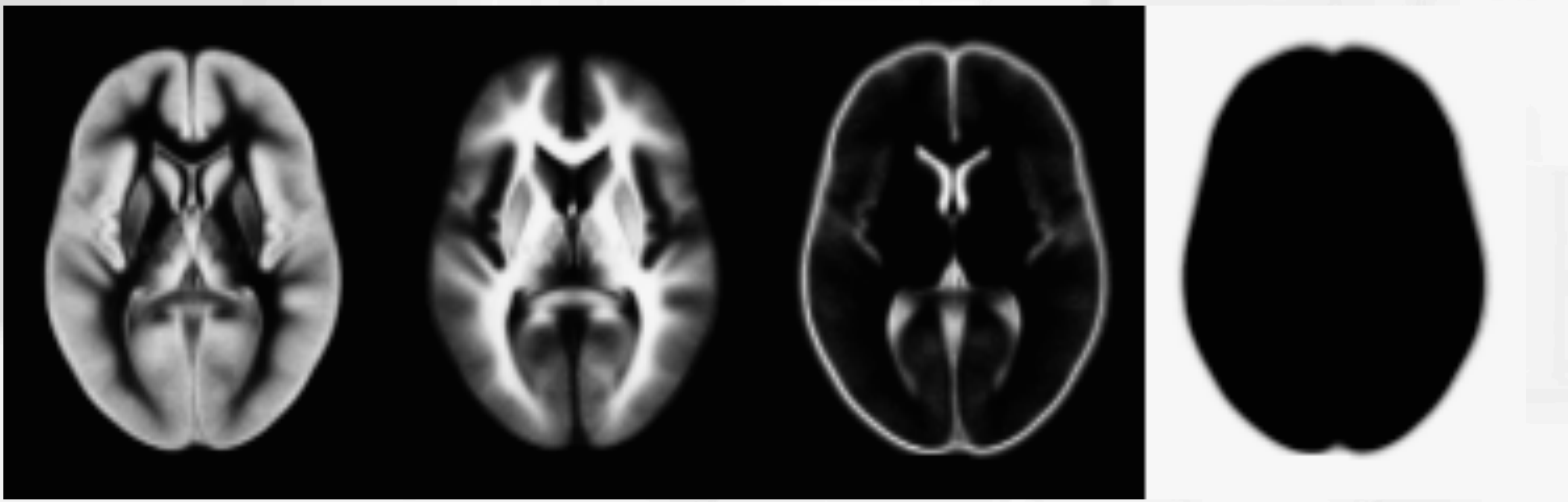
Tissue intensity distributions (T1-weighted MRI)

Translational Neuromodeling Unit



Tissue Probability Maps

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

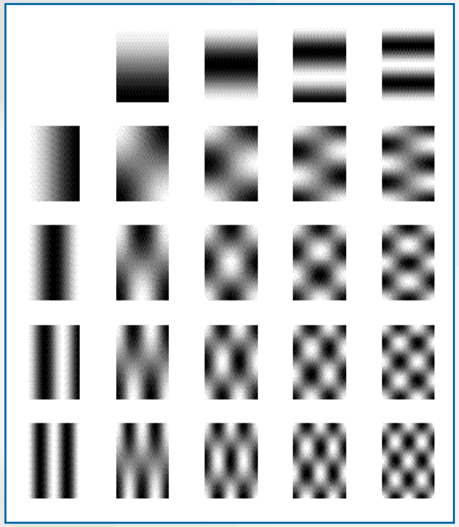


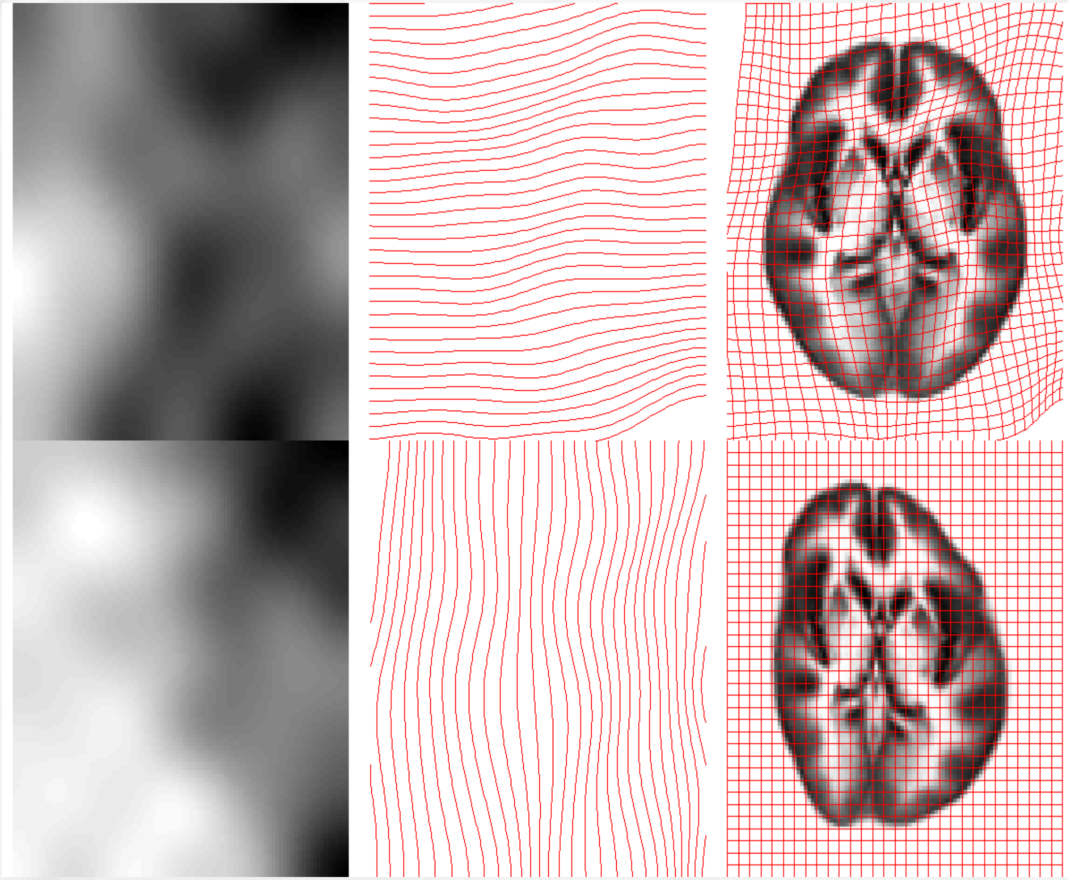
ICBM Tissue Probabilistic Atlases. These tissue probability maps were kindly provided by the **International Consortium for Brain Mapping**

Deforming the Tissue Probability Maps

- Tissue probability maps images are warped to match the subject

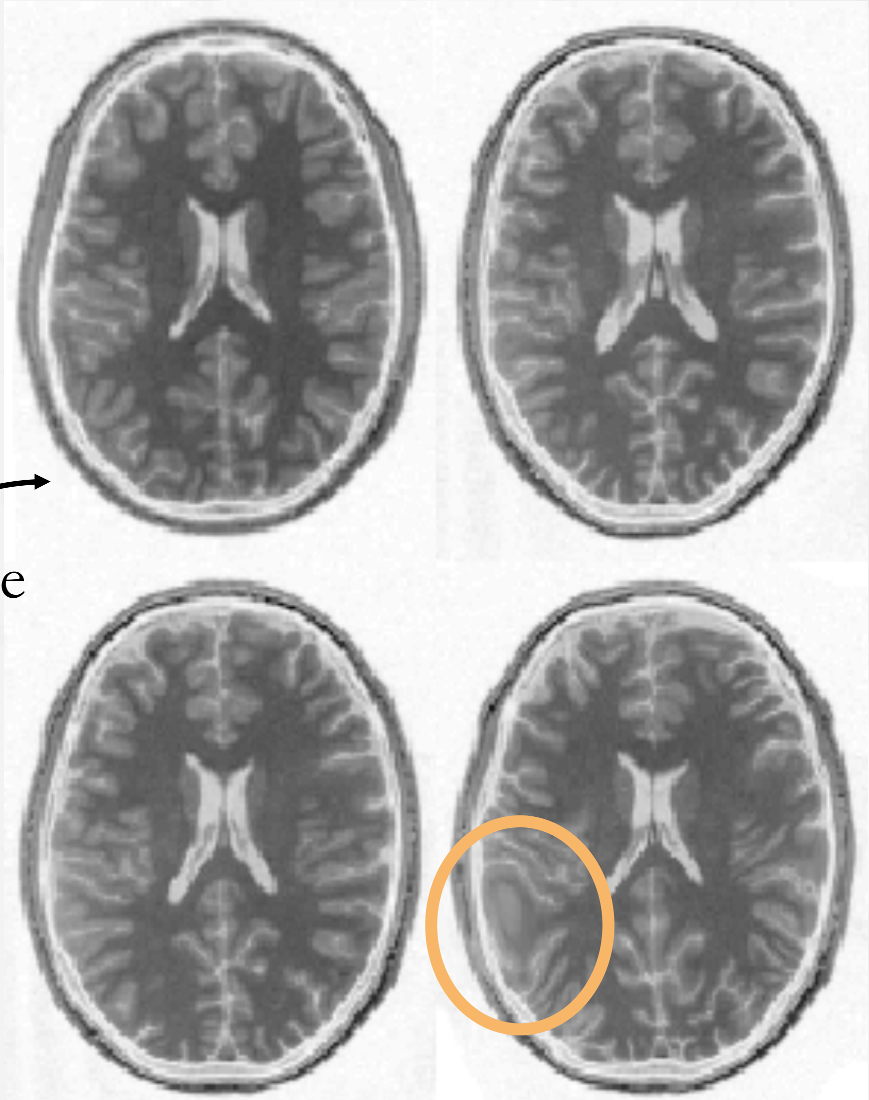
- The inverse transform warps to the TPMs



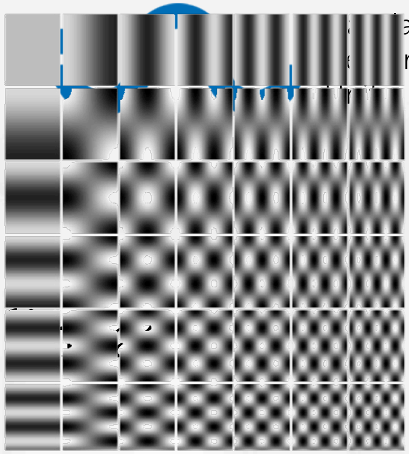


Why regularisation? – Overfitting

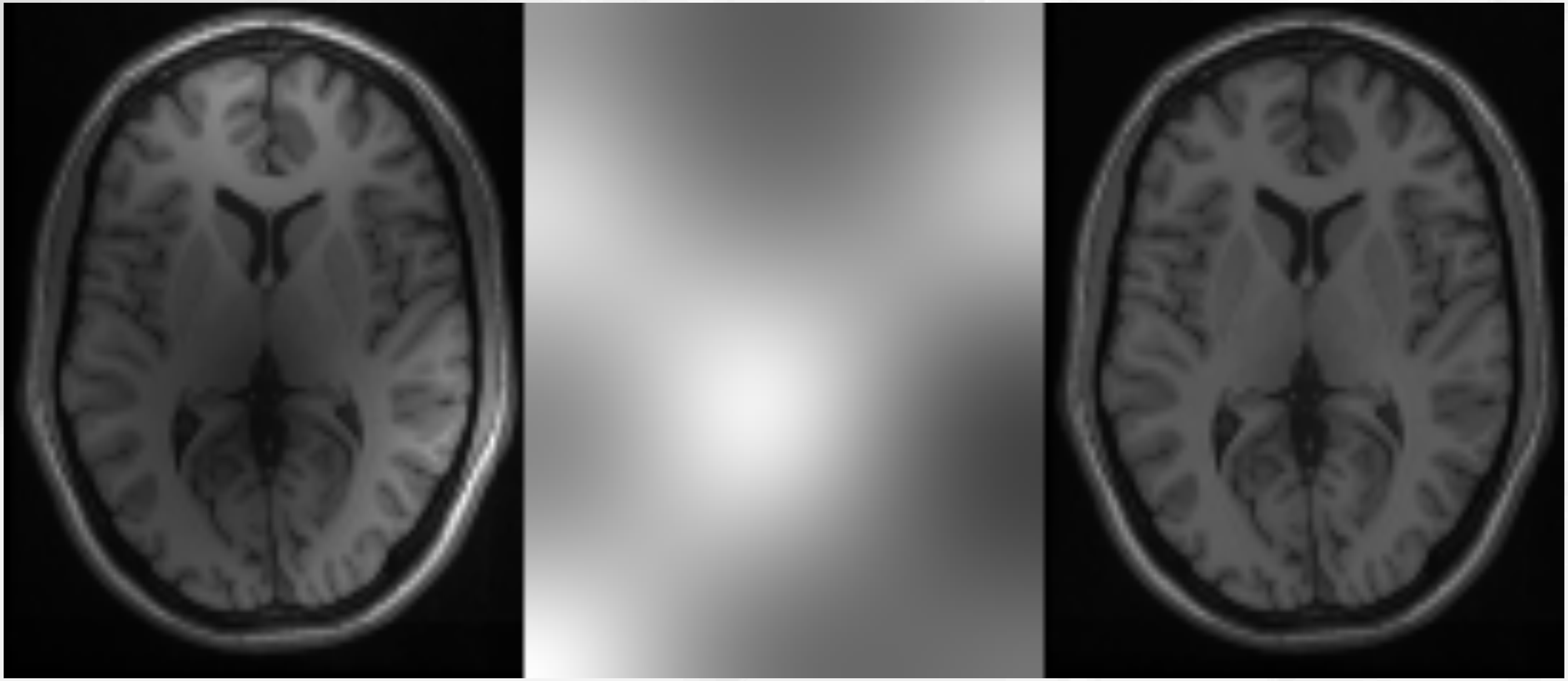
- Regularisation constrains deformations to realistic range (implemented as priors)



Modelling inhomogeneity



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

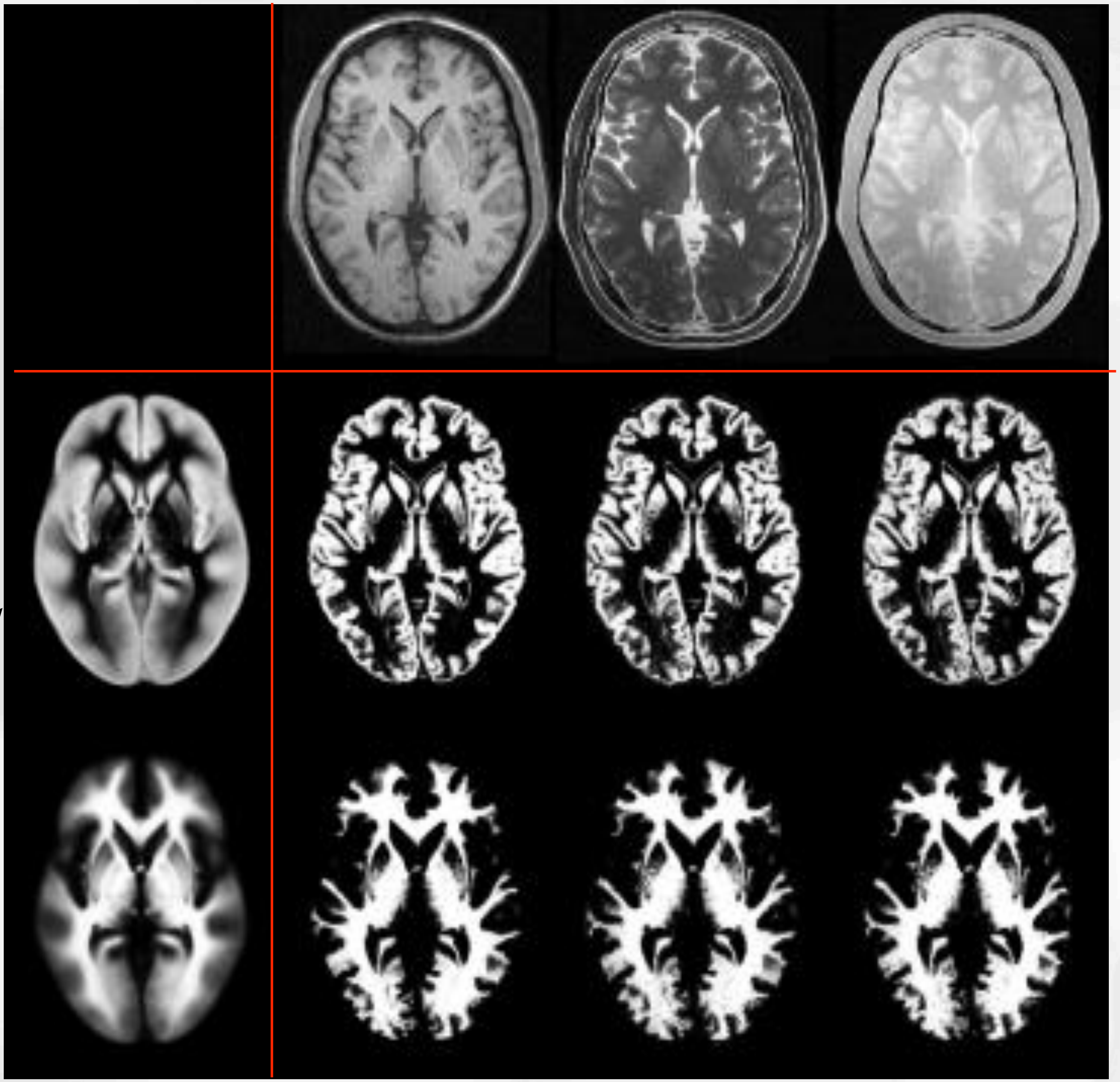


Corrupted image **Bias Field** **Corrected image**

Segmentation results

Translational Neuromodeling Unit

Tissue probability maps of GM and WM



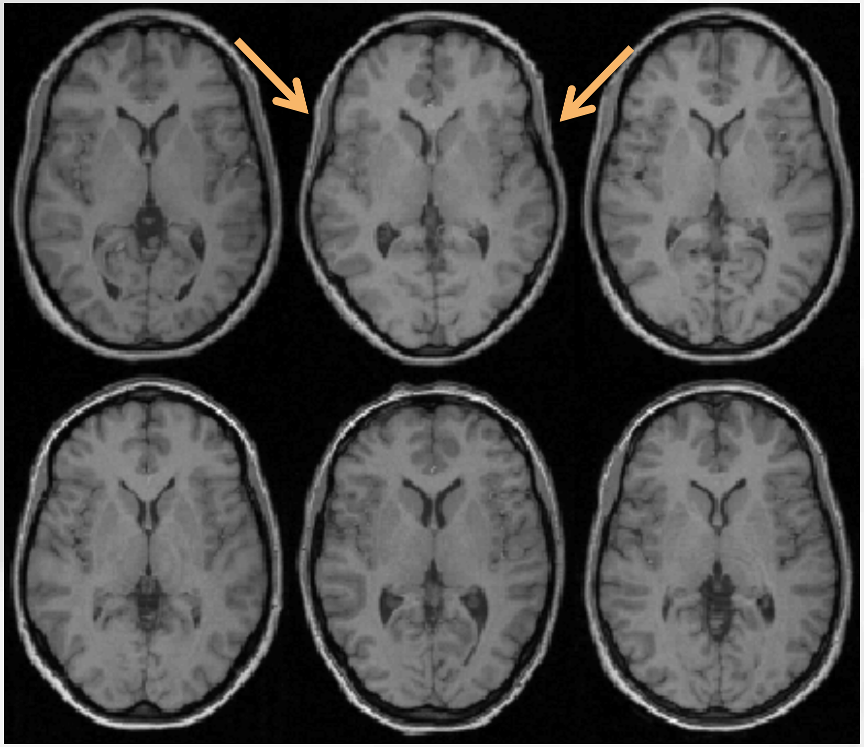
Spatially normalised BrainWeb phantoms (T1, T2, PD)

- segmentation works irrespective of image contrast

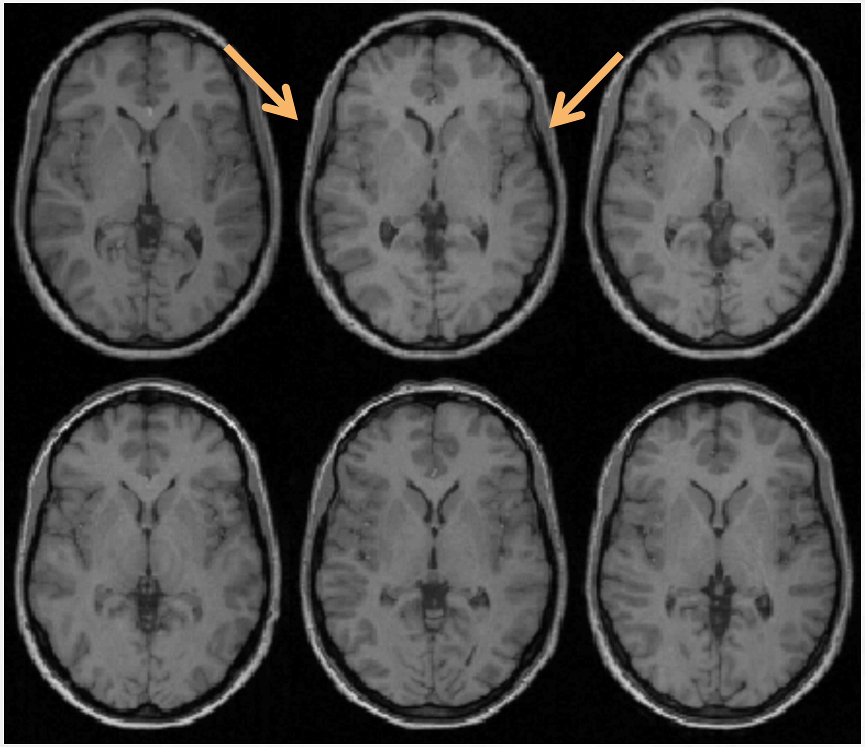
Cocosco, Kollokian, Kwan & Evans. "*BrainWeb: Online Interface to a 3D MRI Simulated Brain Database*". NeuroImage 5(4):S425 (1997)

Benefits of Unified Segmentation

Translational Neuromodeling Unit



Affine registration



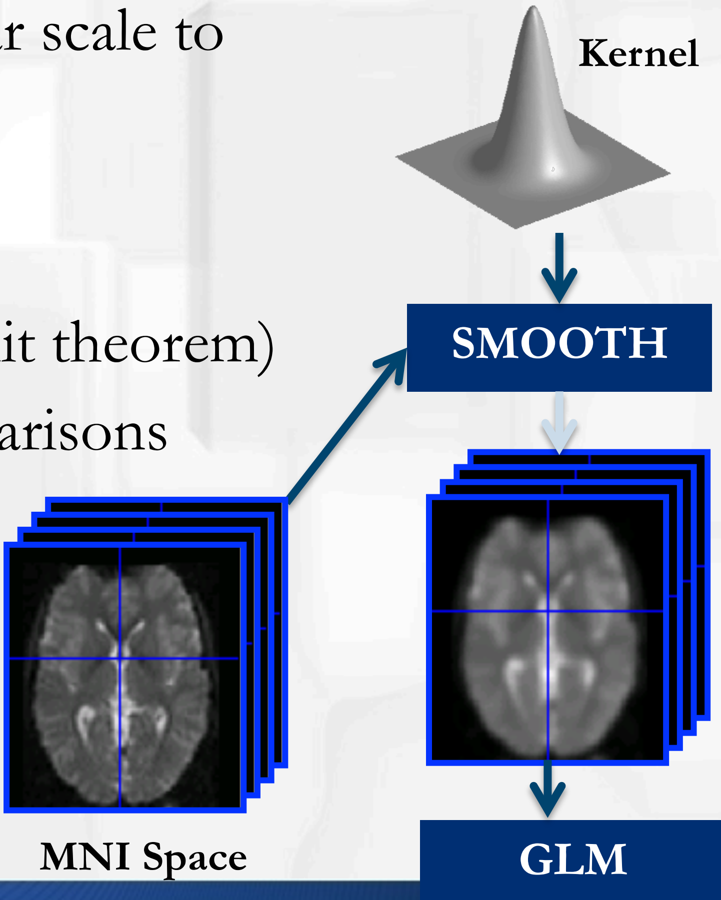
Non-linear registration

Spatial normalisation – Limitations

- 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
    - Interesting recent paper Amiez et al. (2013), PMID:23365257
- Compromise
  - Correct relatively large-scale variability
  - Smooth over finer-scale residual differences

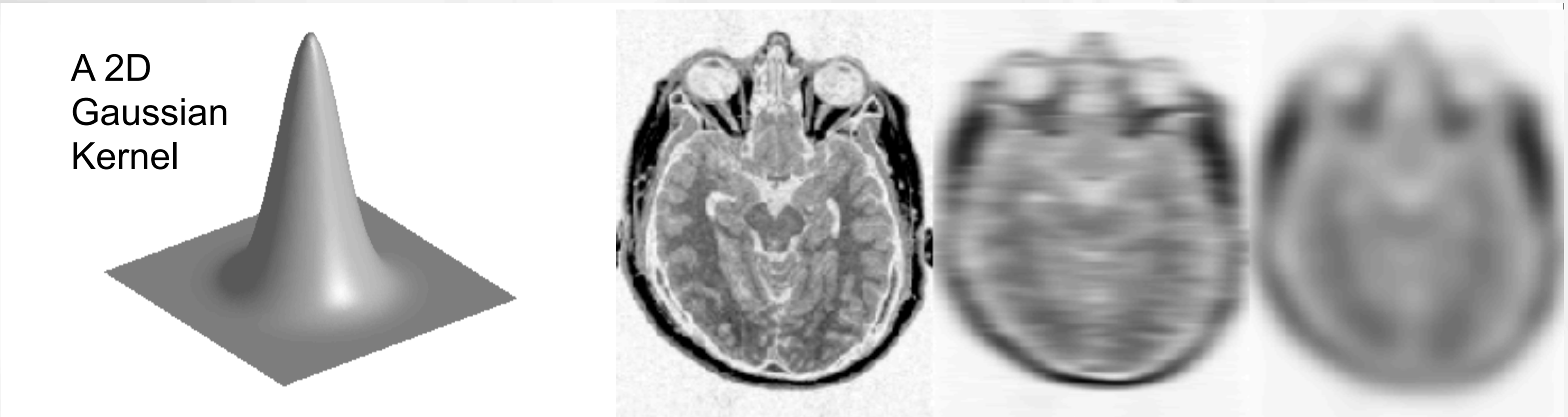
Smoothing – Why blurring the data?

- 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

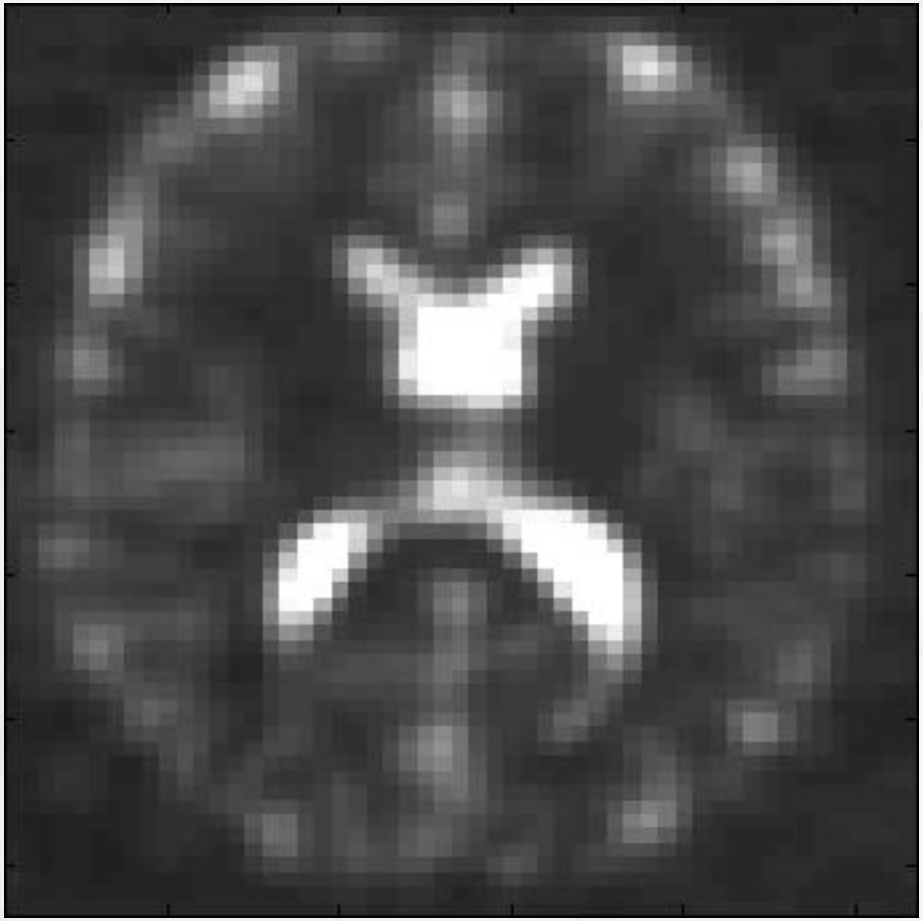


Smoothing – How is it implemented?

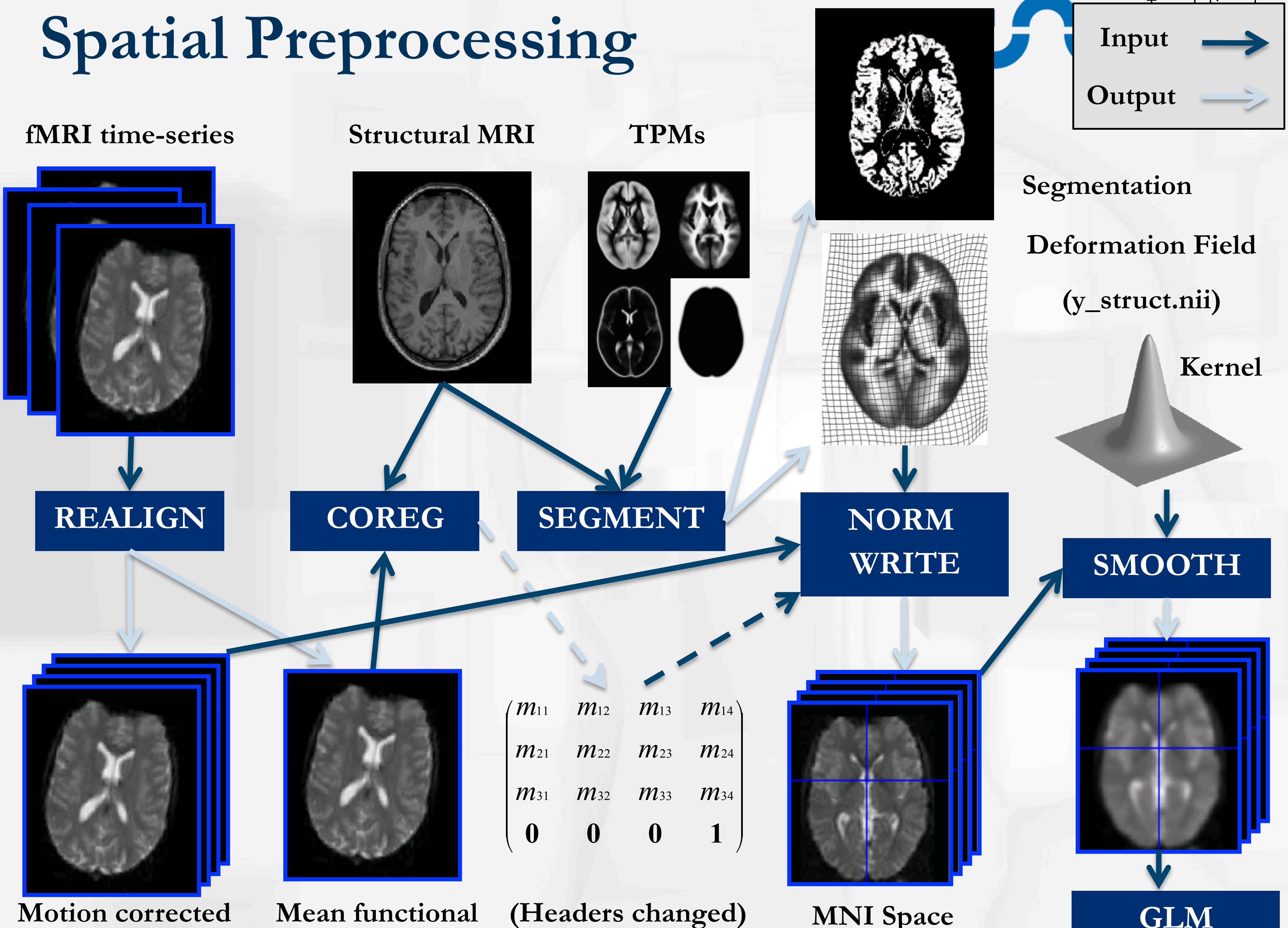
- Convolution with a 3D Gaussian kernel, of specified full-width at half-maximum (FWHM) in mm
  - mathematically equivalent to slice-timing operation or reslicing, but different kernels there (Sinc, b-spline)
- Gaussian kernel is separable, and we can smooth 2D data with 2 separate 1D convolutions



fMRI Run after Smoothing



Spatial Preprocessing



Sources of Noise in fMRI

Translational
Neuromodeling
Unit

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

Noise Modelling

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

The Problem: Physiological Noise

- Cardiac effects
- Respiratory effects

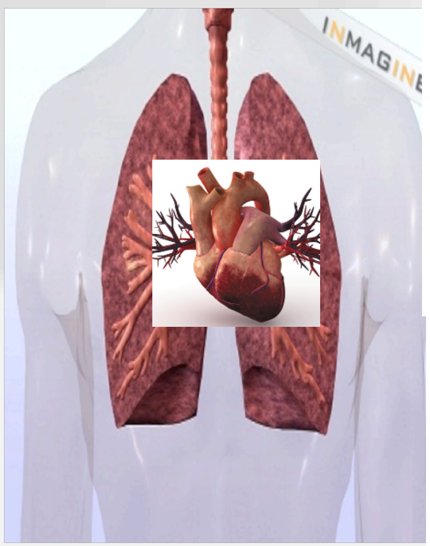
The Problem: Physiological Noise

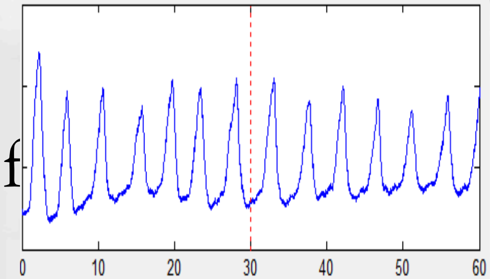
- Cardiac effects
  - Systole:
    - Blood pumped into brain, vessel volume increases: pulsatile vessels
    - CSF pushed down: pulsatile CSF
  - Diastole:
    - Vessel volume decreases
    - CSF flows back into “void” brain volume

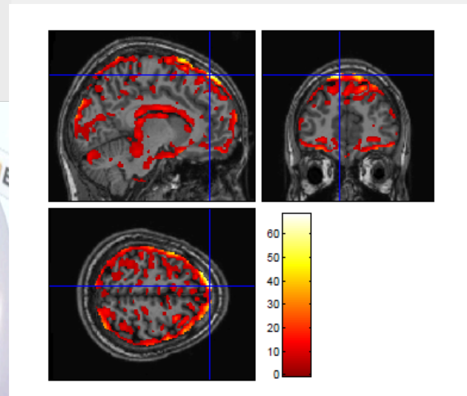
A Cardiac Cycle in the Brain

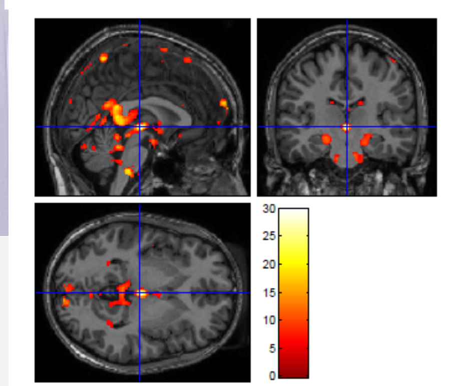
The Problem: Physiological Noise

- Cardiac ef





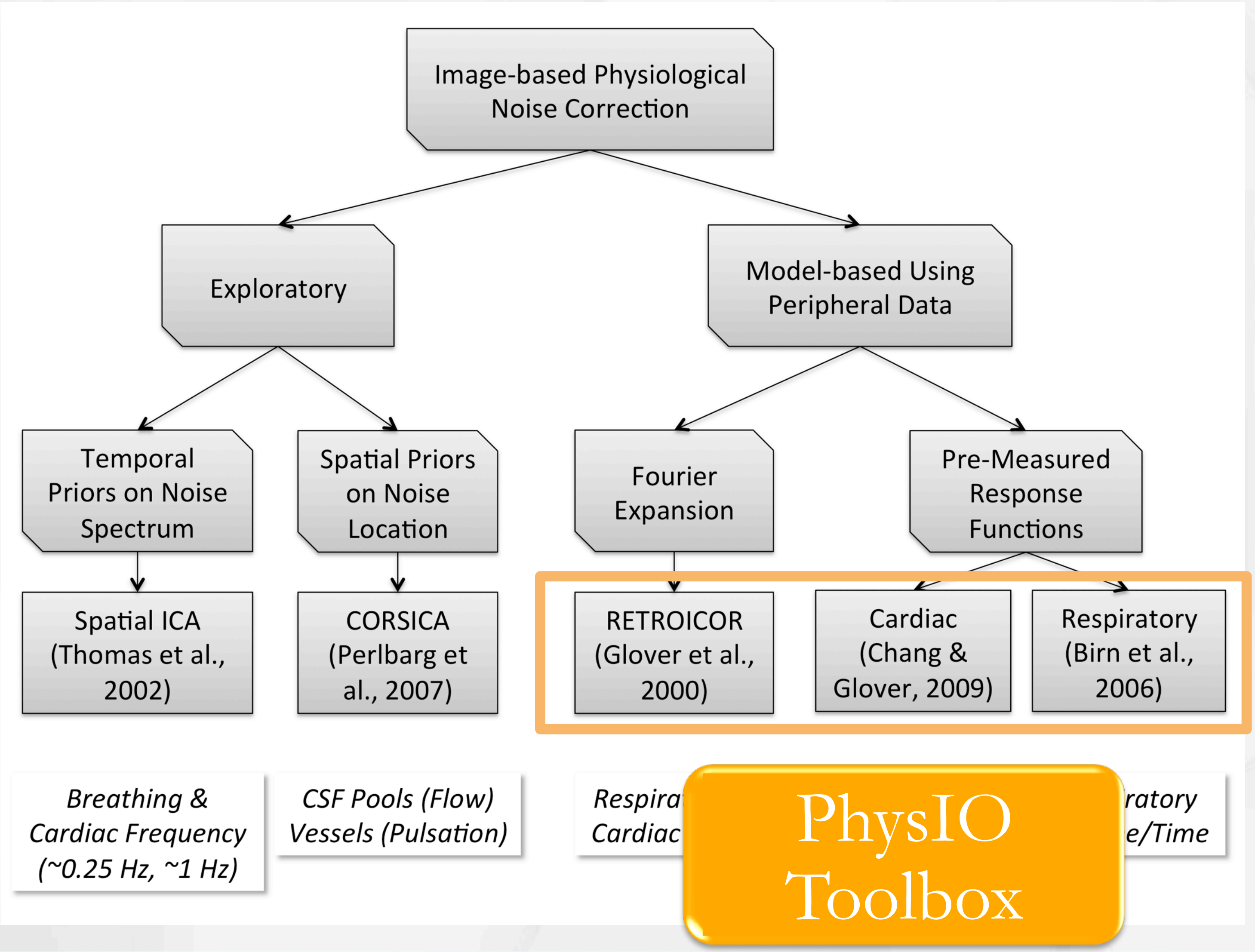




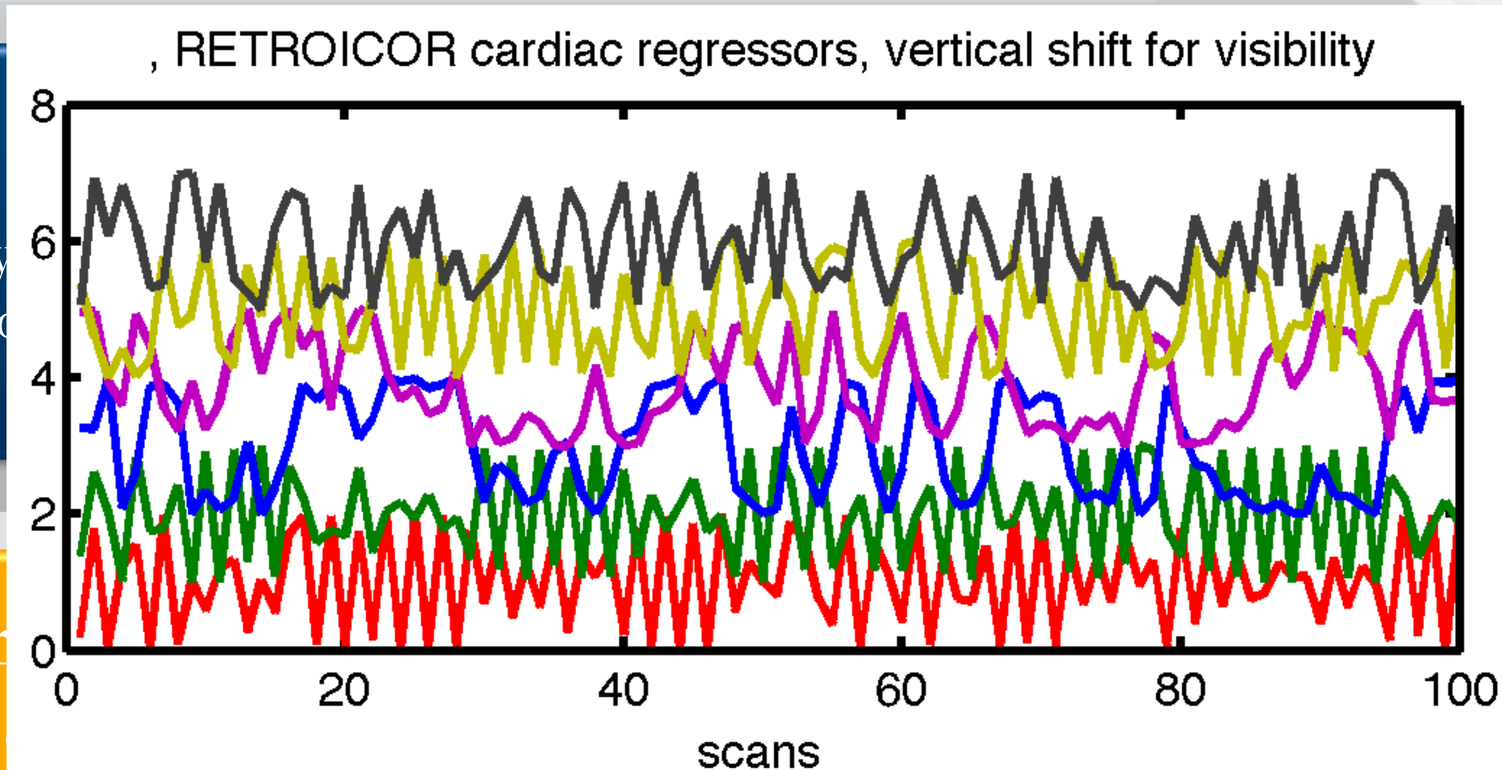
- Respiratory effects
  - Chest (&head) moves with respiratory cycle
  - Changes in lung volume change encoding magnetic field for MR
    - Geometric distortion/scaling
  - Respiratory-sinus arrythmia
    - Heart beats faster during inhalation

The Solution: Image-based Physiological Noise Correction

Translational Neuromodeling Unit



The Solution: Physiological Noise Correction



ECG, PPU → Cardiac cycle

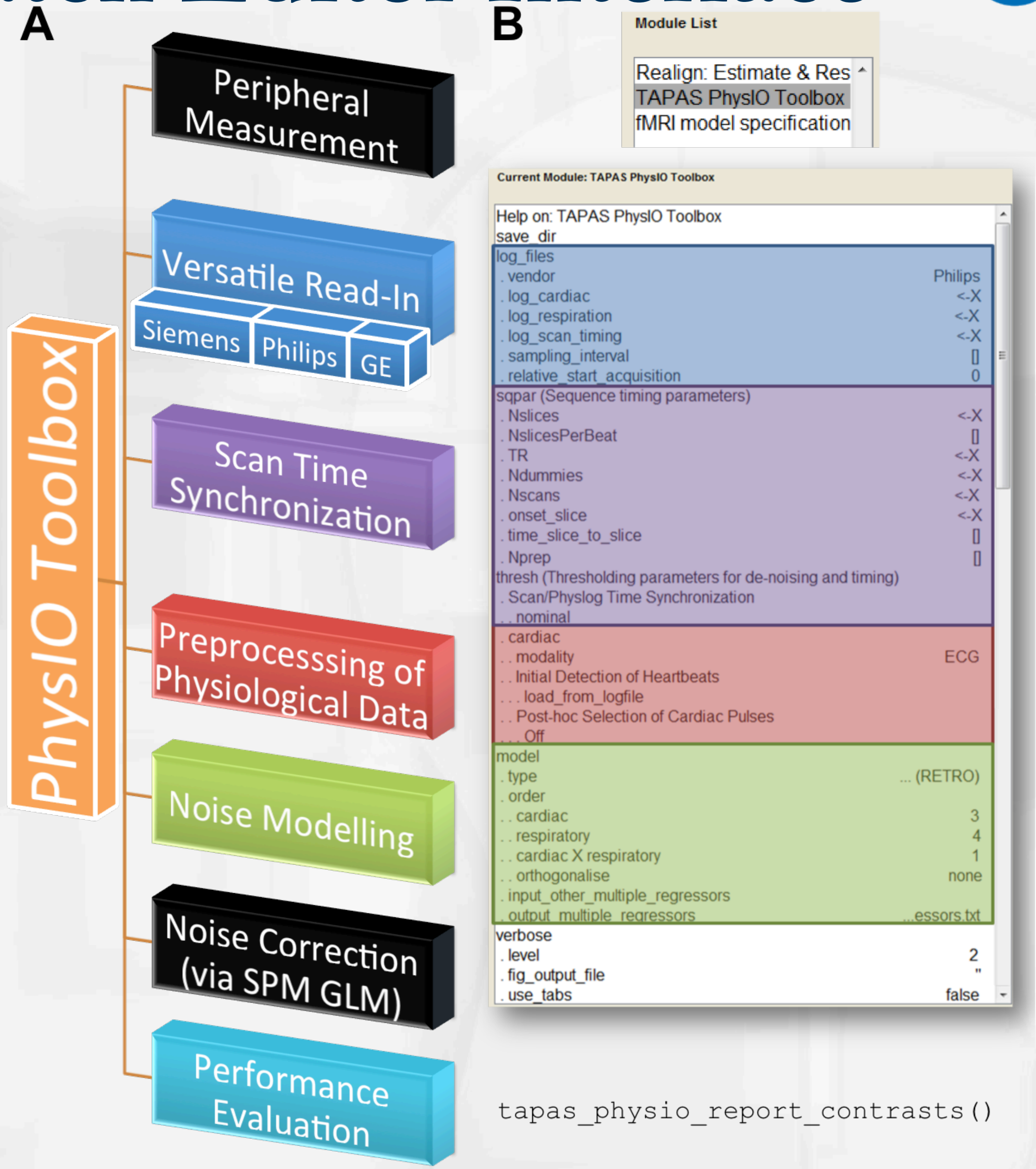
Breathing belt → Respiratory cycle

Capnograph → CO_2 concentration

Confound regressors

SPM Batch Editor Interface

Translational Neuromodeling Unit

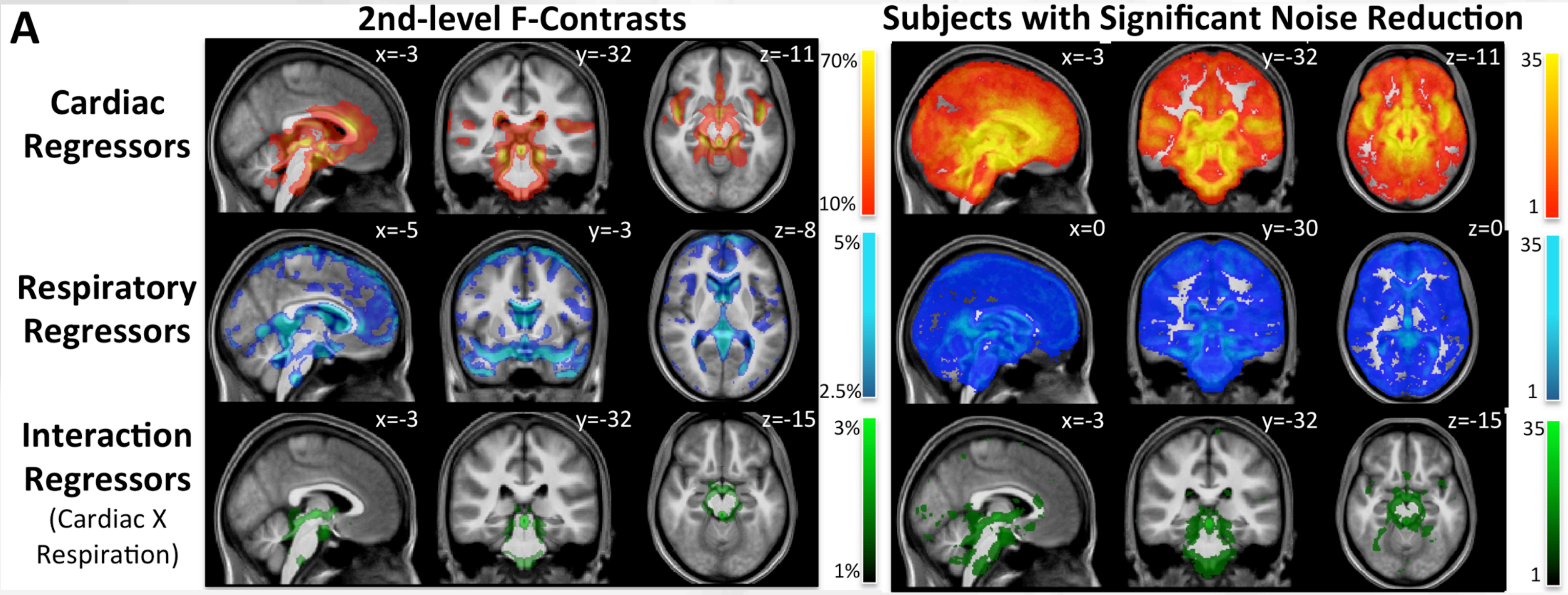


`tapas_physio_report_contrasts()`

When? – PhysIO experience

Translational Neuromodeling Unit

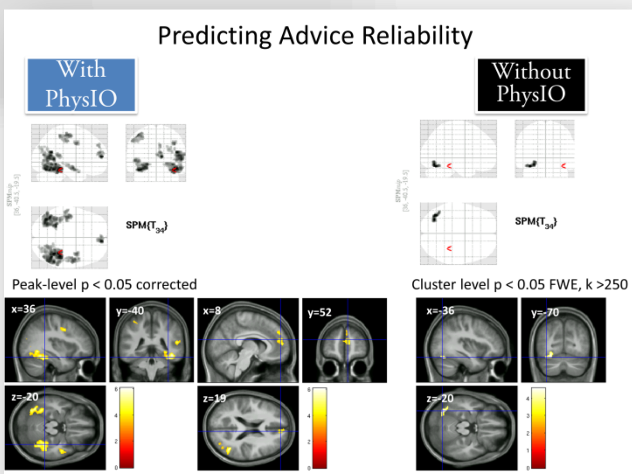
- Andreea Diaconescu (TNU): Social Learning Experiment, “Inferring on the Intentions of Others”

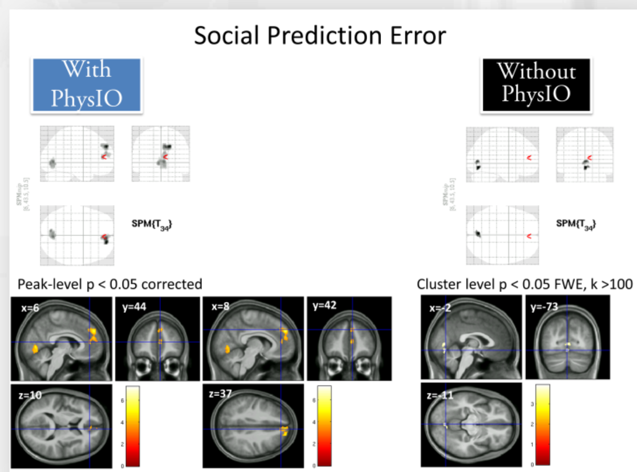


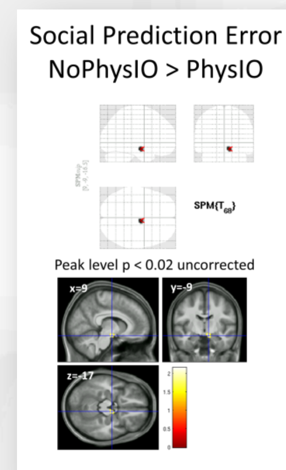
Diaconescu, et al., 2014. PLoS Comput Biol 10

When? – PhysIO experience

- Andreea Diaconescu (TNU): Social Learning
  - Higher sensitivity for group effects (N=35)
    - Prediction of advice reliability: dmPFC, bilateral FFA
    - Prediction error: dmPFC
  - Less false/ambiguous positives:
    - Brainstem (Substantia Nigra)

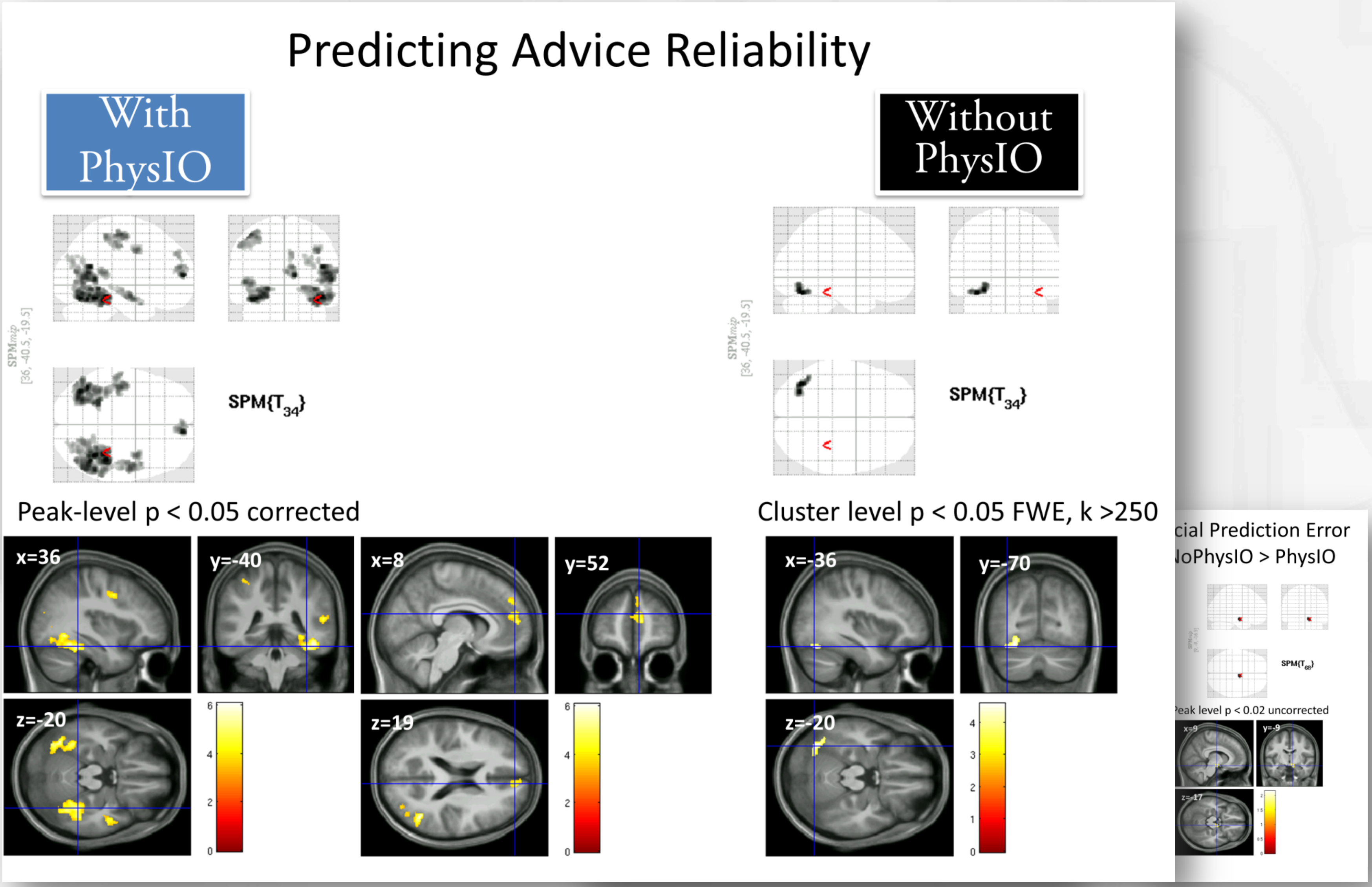






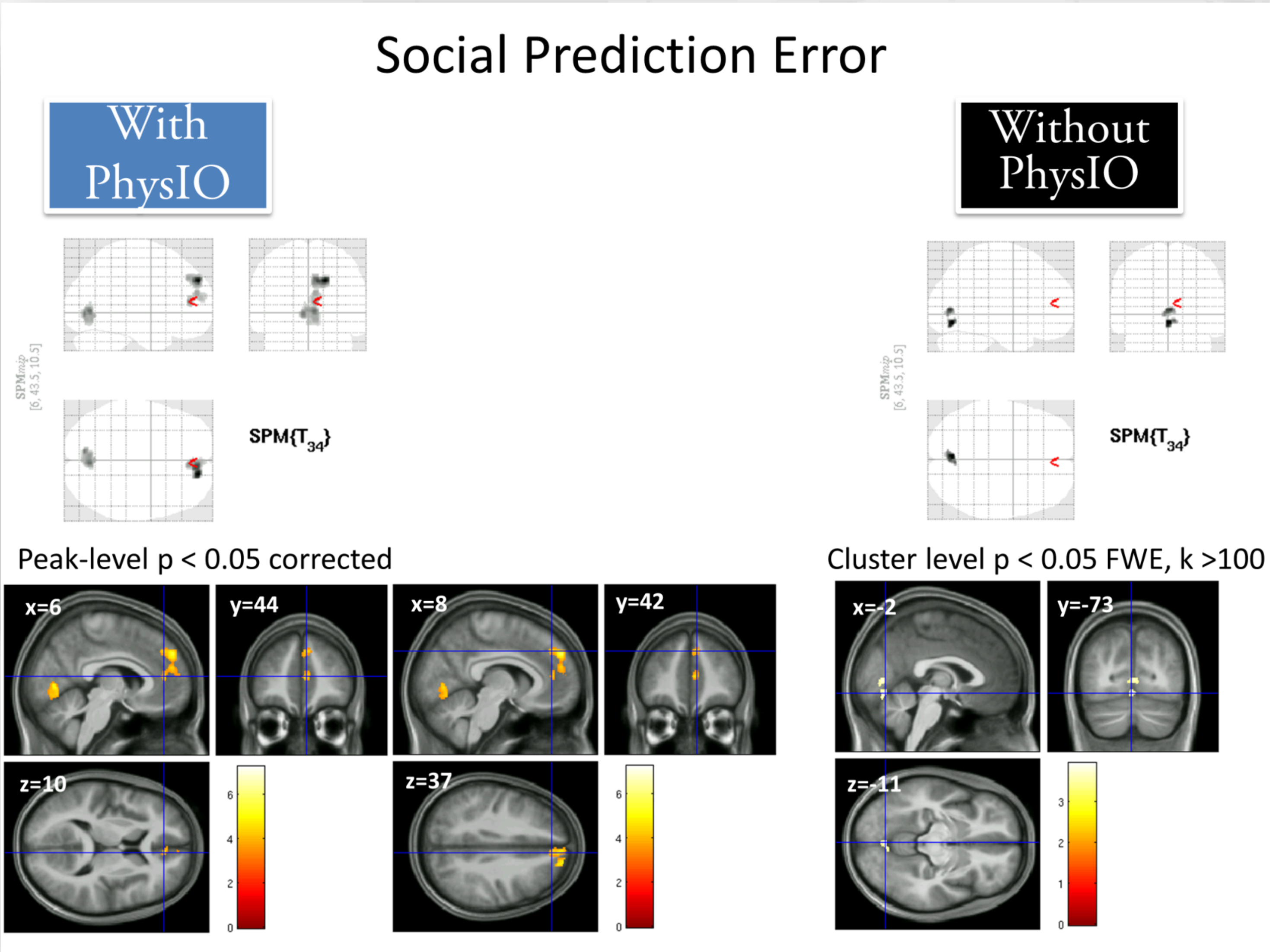
When? – PhysIO experience

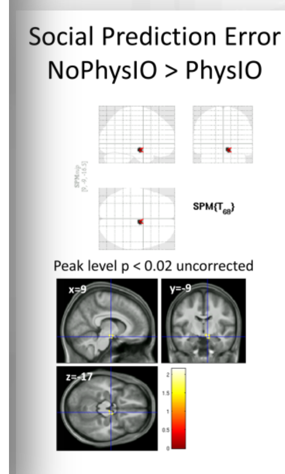
Translational Neuromodeling Unit



When? – PhysIO experience

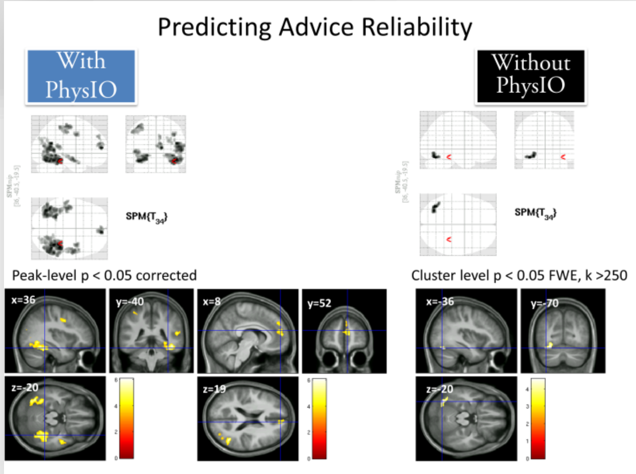
Translational
Neuromodeling
Unit

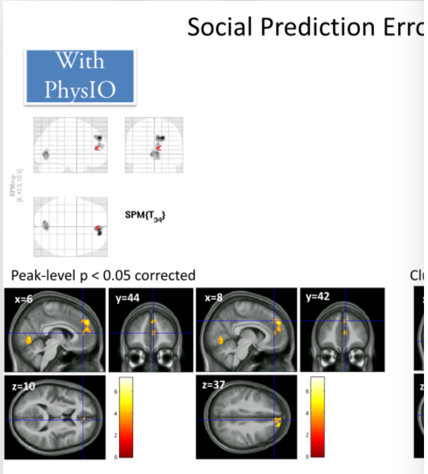


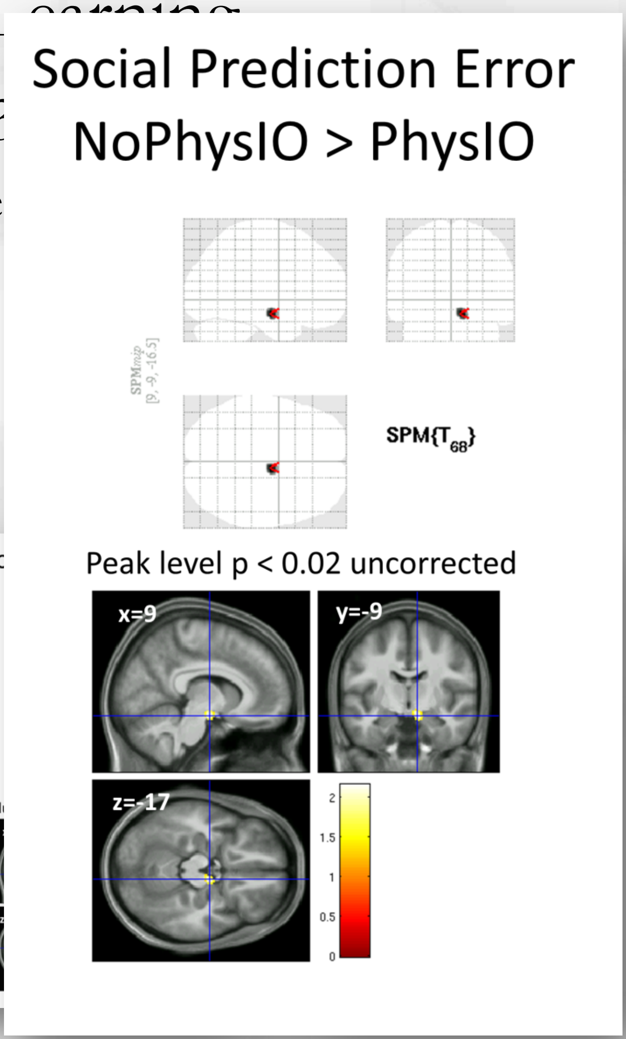


When? – PhysIO experience

- Andreea Diaconescu (TNU): Social L[earning]
  - Higher sensitivity for group effects (N=3
    - Prediction of advice reliability: dmPFC, bilate
    - Prediction error: dmPFC
  - Less false/ambiguous positives:
    - Brainstem (Substantia Nigra)







Sources of Noise in fMRI

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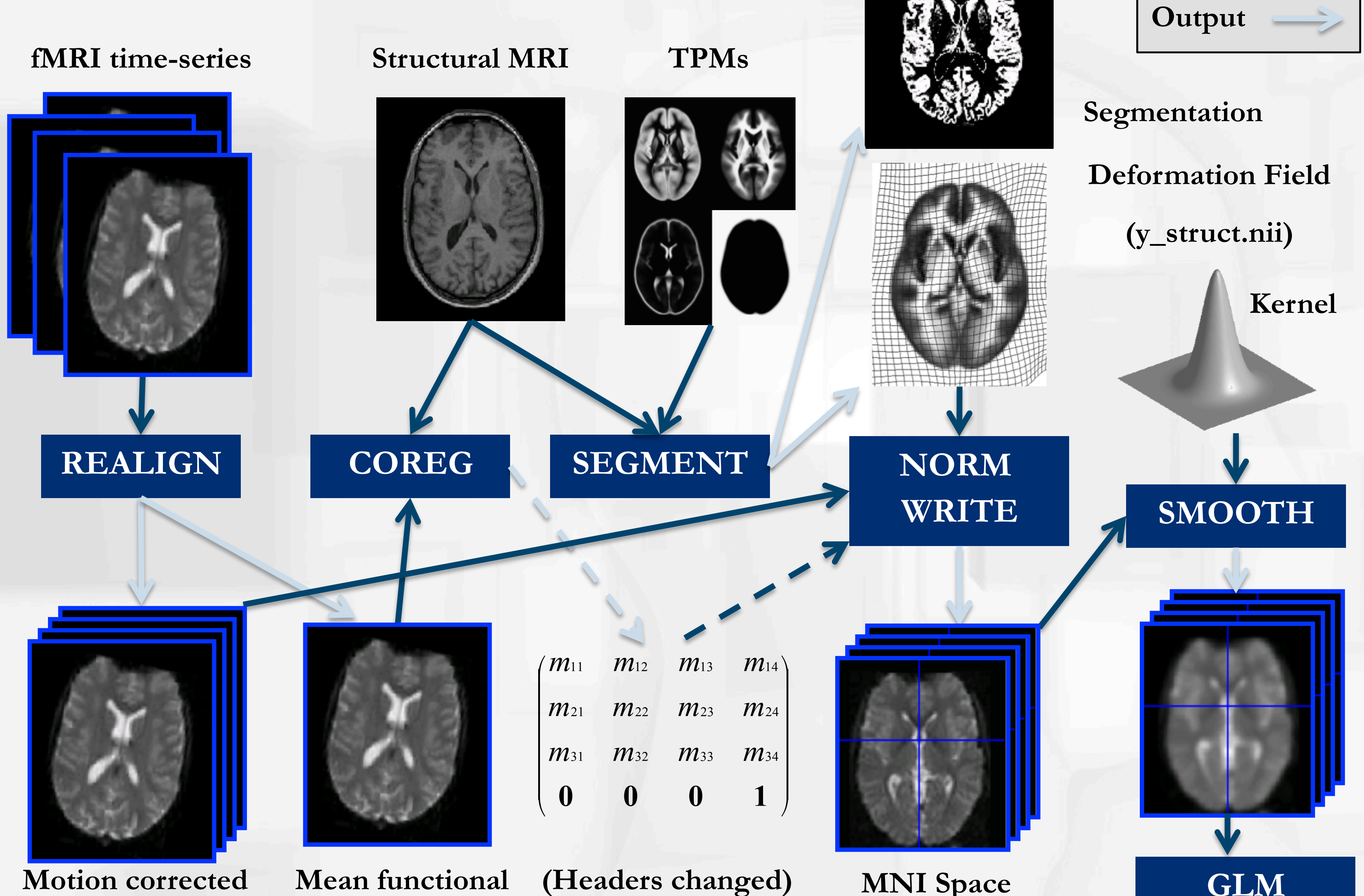
Subject Motion	Spatial Preproc	Realignment
Acquisition Timing	Temporal Preproc	Slice-Timing
Anatomical Identity	Spatial Preproc	Co-registration
Inter-subject variability	Spatial Preproc	Segmentation
Thermal Noise	Spatial Preproc	Smoothing
Physiological Noise	Noise Modelling	PhysIO Toolbox

Spatial Preprocessing



Thank you…

- …and:
  - TNU Zurich,
    in particular: Klaas
  - MR-technology Group IBT,
    in particular: Klaas
  - Everyone I borrowed slides from ☺