Introduction to fMRI analysis and classification

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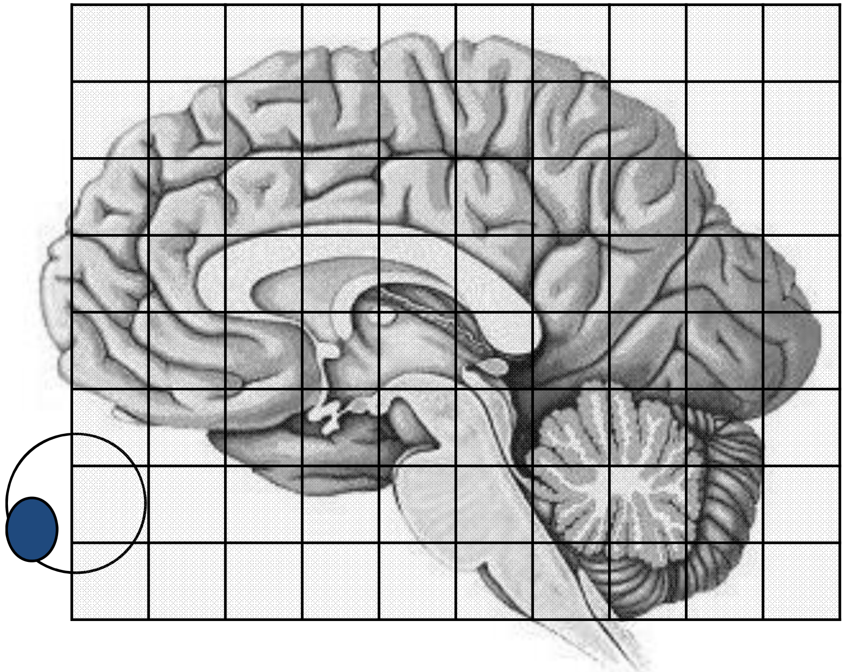
Overview

- Intro
- fMRI Physics and Physiology
- Analysis – Preprocessing
- Analysis – GLM
- Example – Retinotopy
- fMRI Classification
- Example – Decoding rotation
- Interpretation of Results
- Discussion, Wrap up etc.

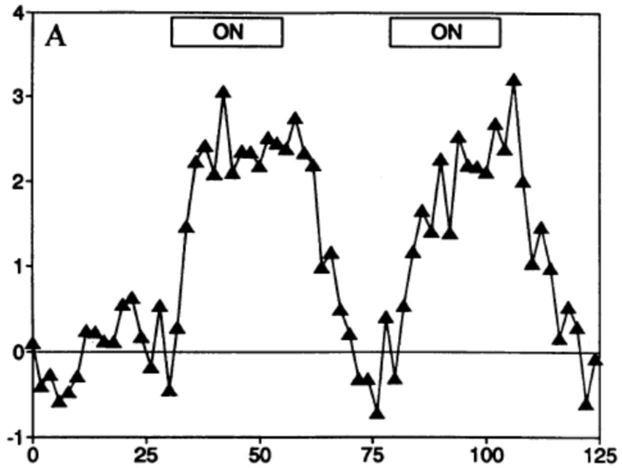
Visual fMRI in a nutshell

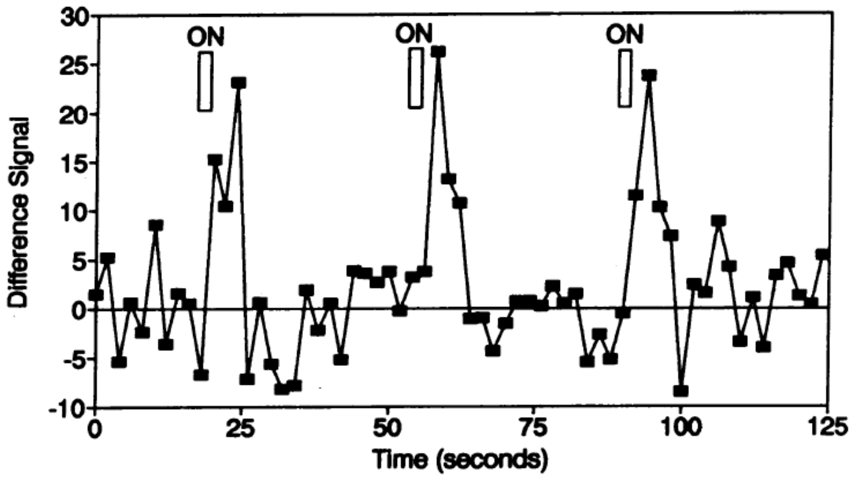


?

A bit of history – First visual fMRI

Is there fMRI activation in the visual cortex?

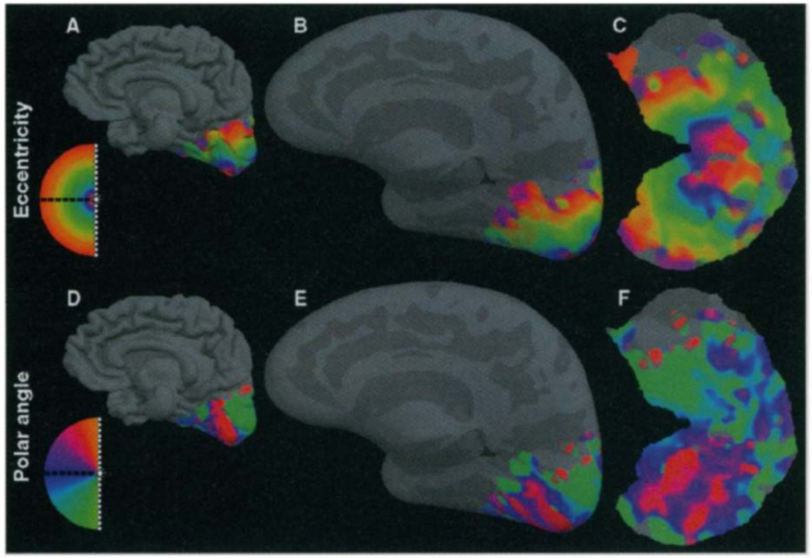




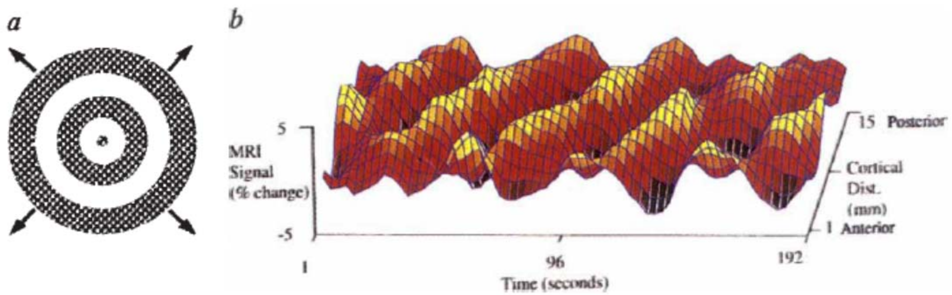
Source: Blamire et al, PNAS, 1992

A bit of history – Retinotopic Mapping

Can we see large scale organization in visual signals?



Sereno et al, Science, 1995



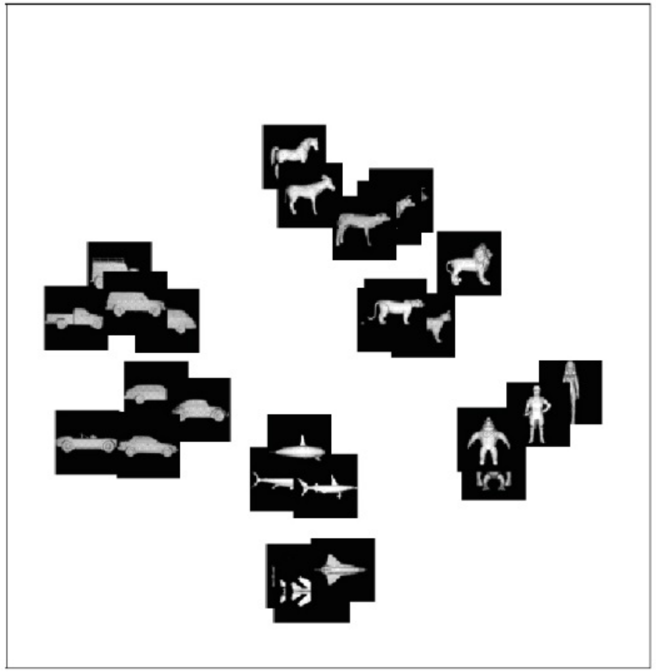
Engel et al, Nature, 1997

A bit of history – Content specific activation

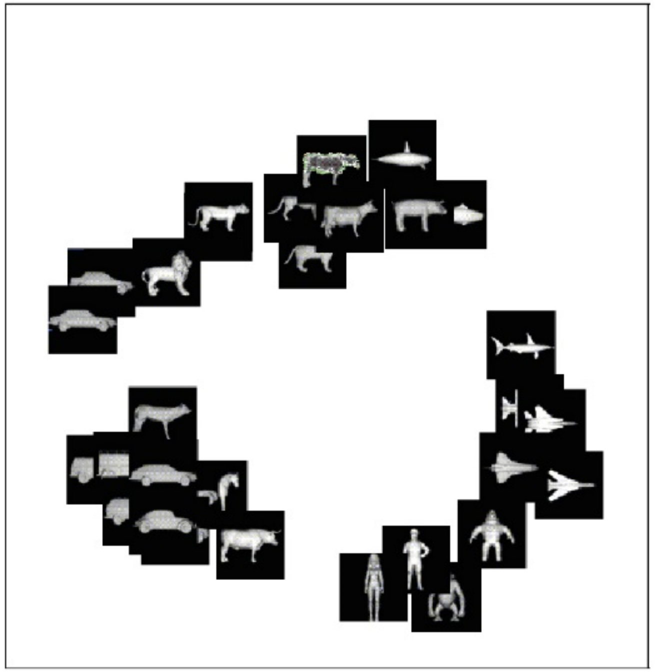
Can we see functional specialization of areas?

A bit of history – MVPA Studies

Psychophysical rating

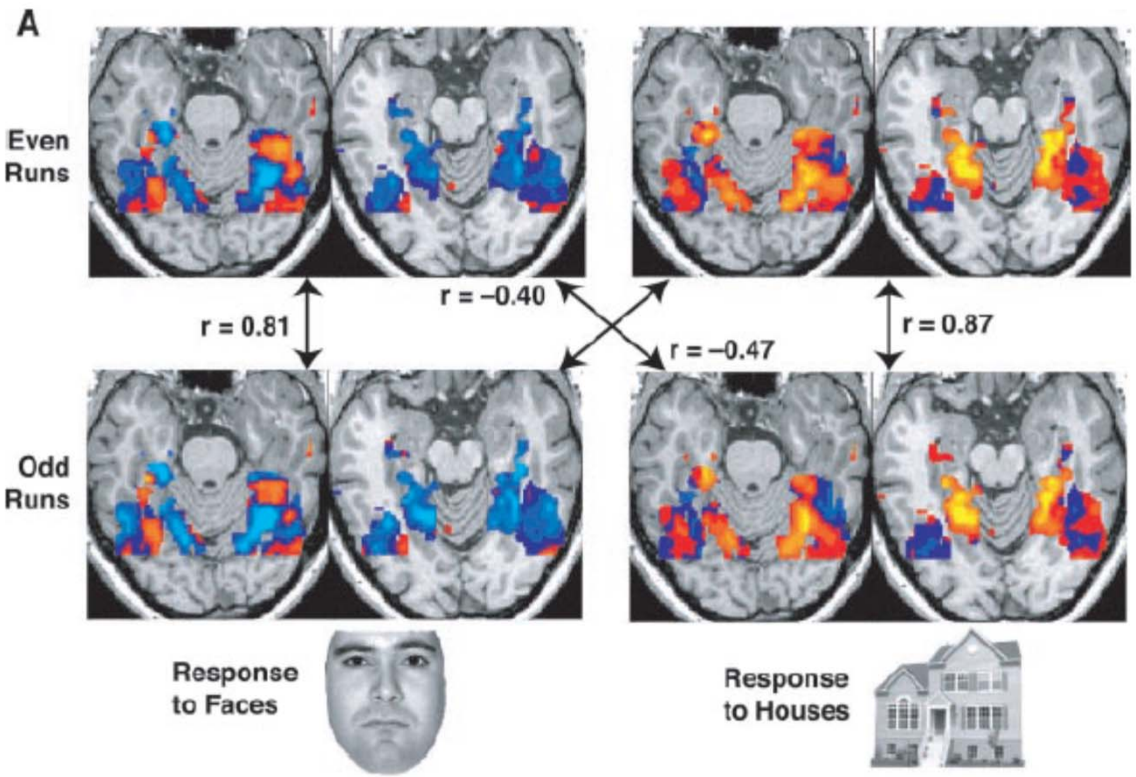


fMRI



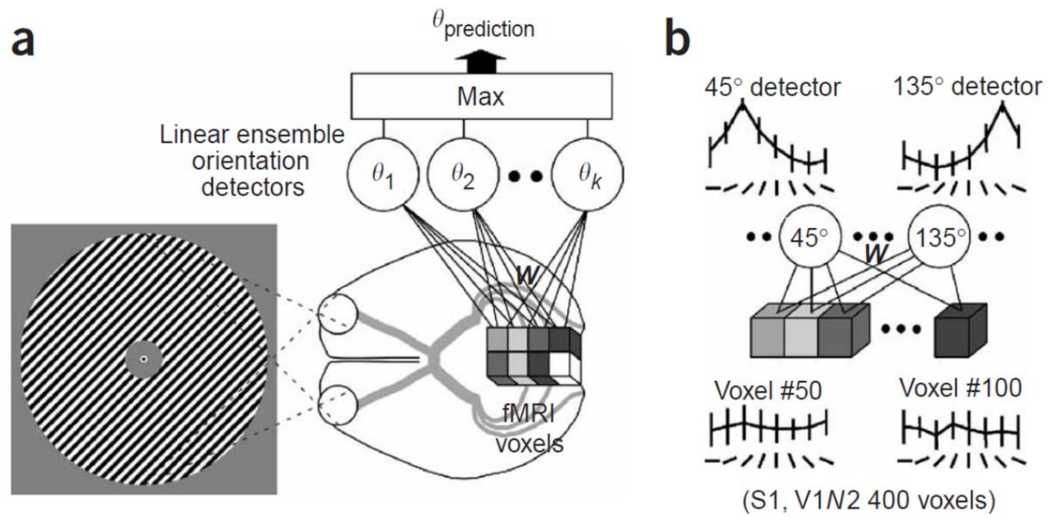
Edelman et al, Psychobiology, 1998

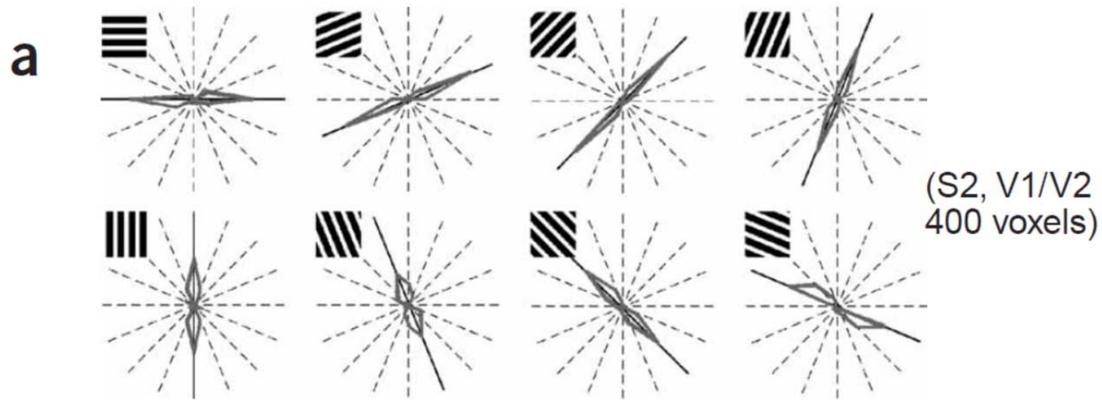
A bit of history – Classification Studies



Haxby et al, Science, 2001

A bit of history – Classification Studies





Kamitani and Tong, Nat Neurosci, 2005

Haynes and Rees, Nat Neurosci 2005

In this tutorial

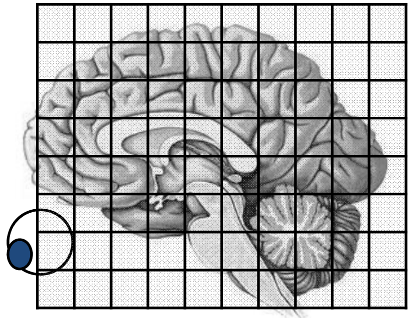
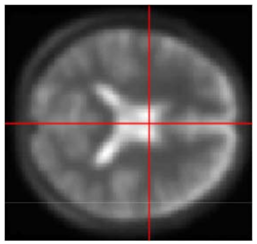


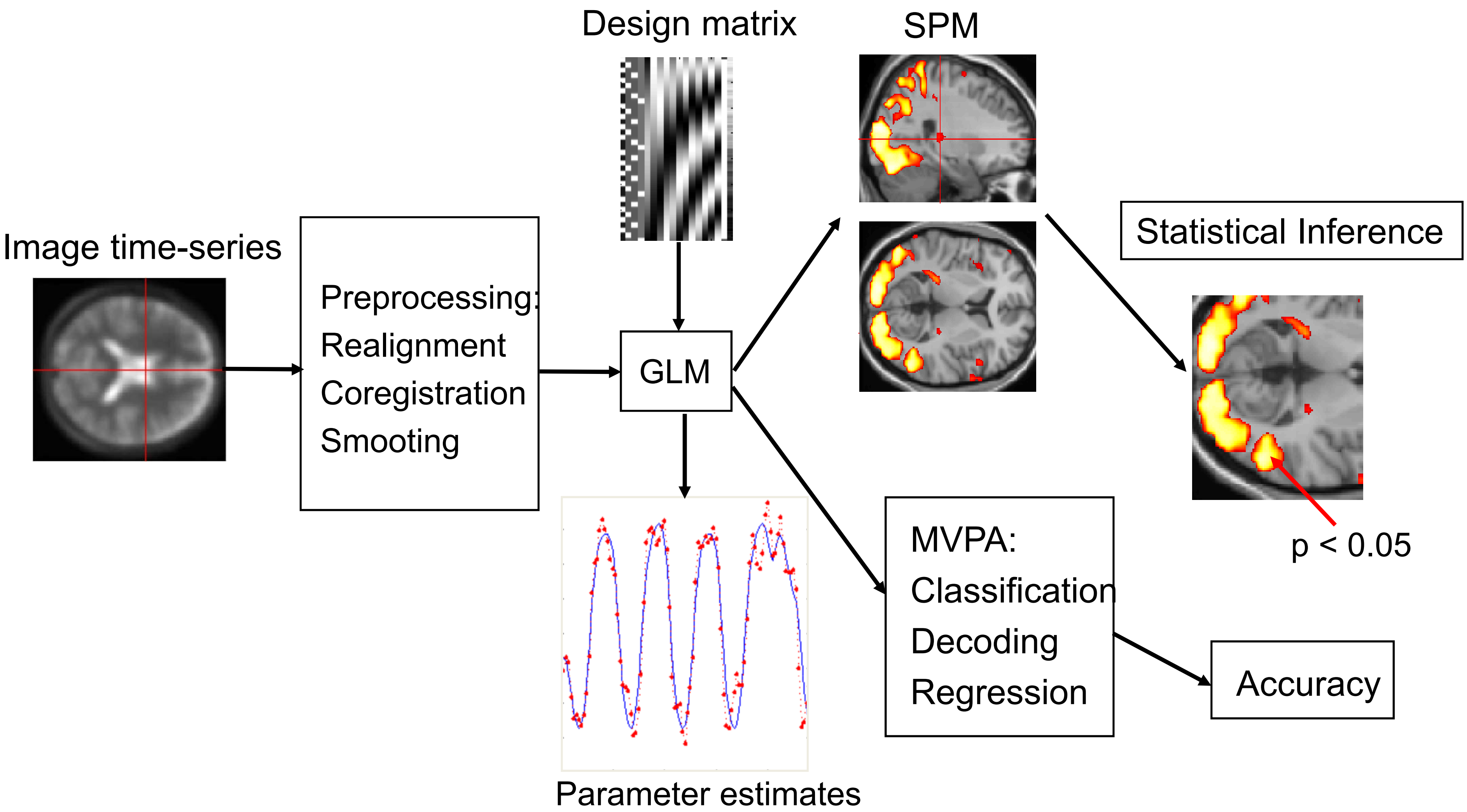
Image time-series



Statistics, Accuracy,
Answer to experimental question

Usually a several days long course …
… only a glance can be given here.

Overview analysis



SPM: Statistical Parametric Map, MVPA: Multivariate Pattern Analysis

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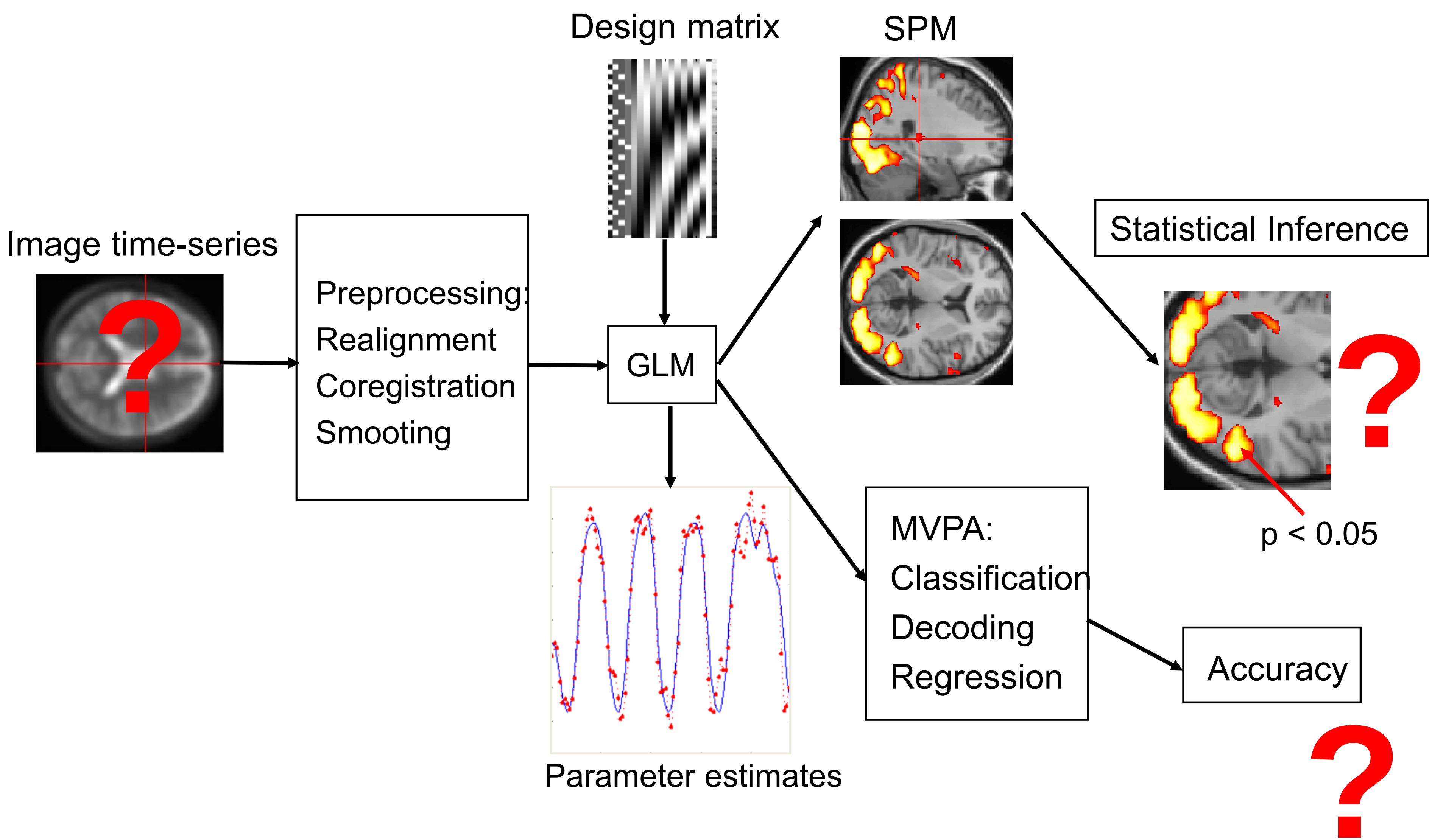

SPM: Statistical Parametric Map, MVPA: Multivariate Pattern Analysis

fMRI physics and physiology

Cognitive processes (Sensory, motor, etc.)

Control and measure

Information processing in ensembles of neurons, e.g. synaptic processes and neural spiking

Try to infer something about

Changes in blood flow, oxygen concentration, blood volume

3. How is the BOLD signal related to neural processing?

Changes in MRI contrasts due to changes in relative hemoglobin concentrations

2. What do we measure with fMRI?

Measured MRI signal

1. What do we measure with MRI?

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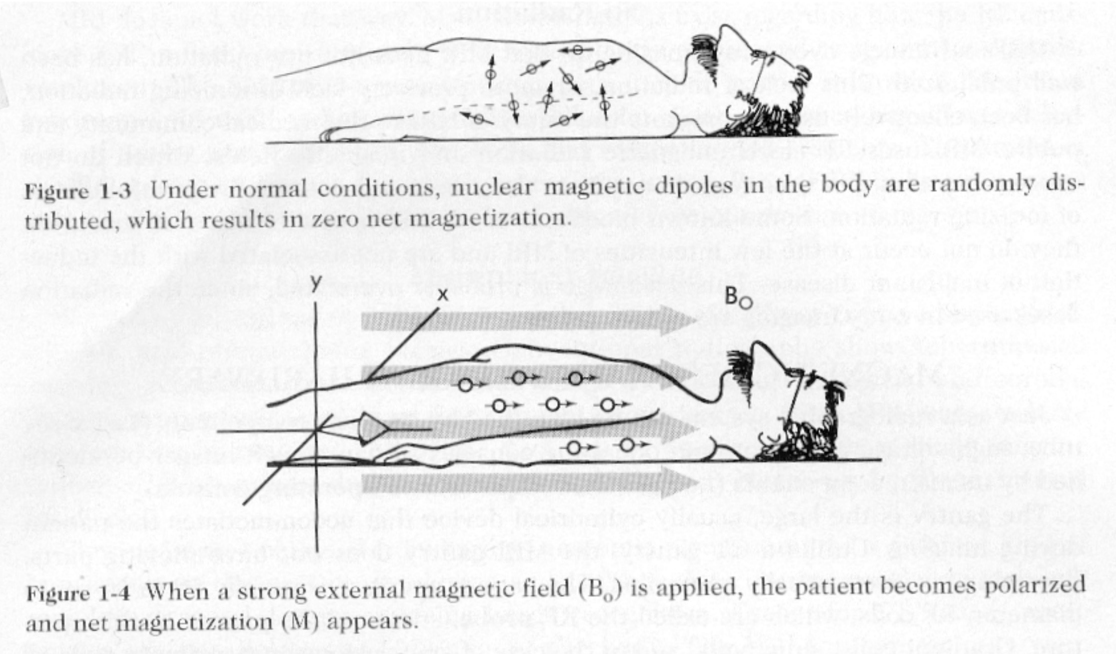
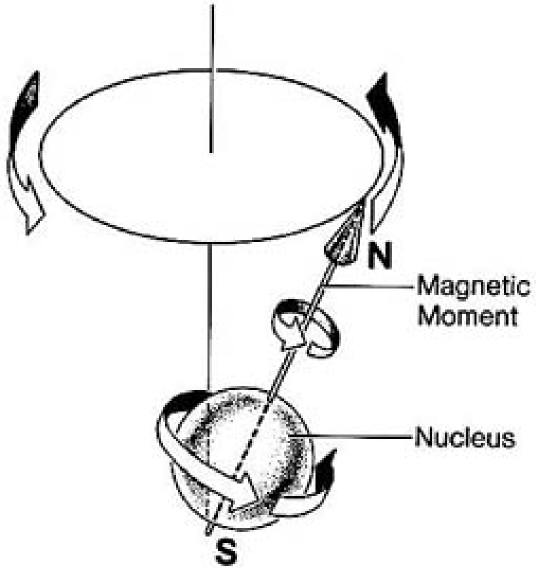


Figure 1-3 Under normal conditions, nuclear magnetic dipoles in the body are randomly distributed, which results in zero net magnetization.

Figure 1-4 When a strong external magnetic field (B_o) is applied, the patient becomes polarized and net magnetization (M) appears.

Protons align with the magnetic field.

We can measure the average magnetization.

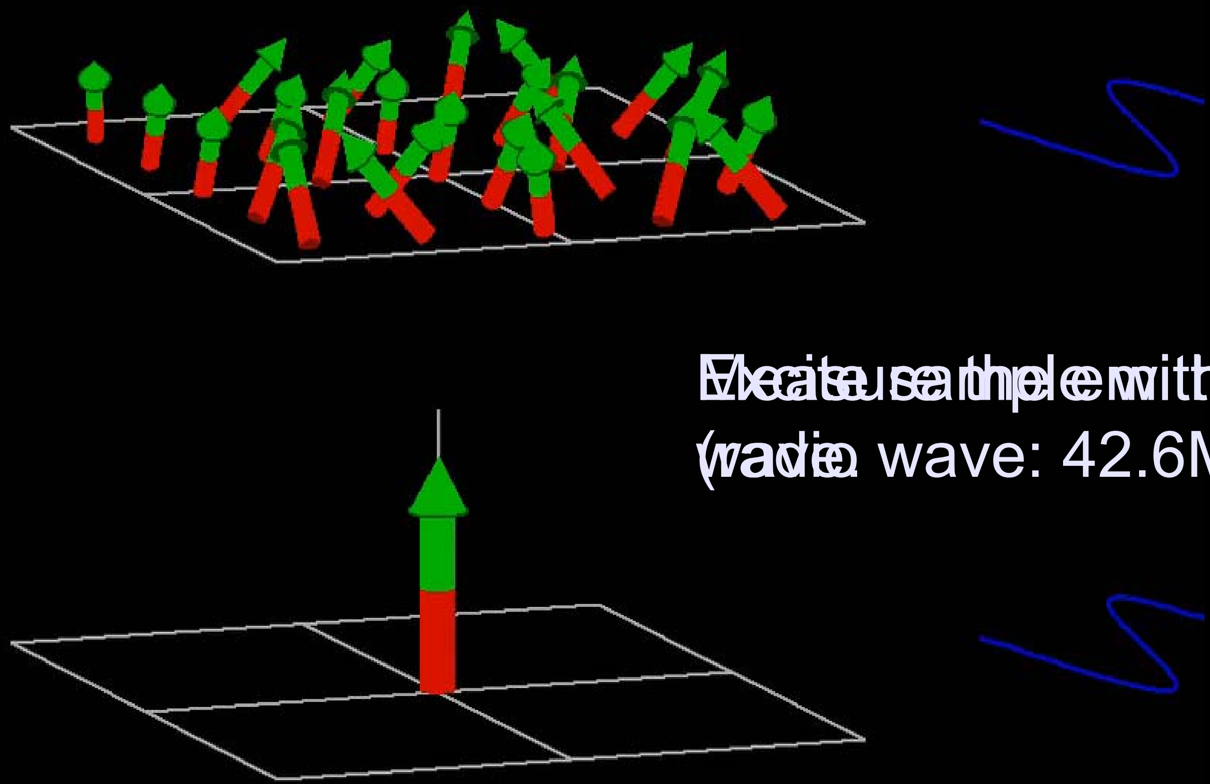


Spin = rotation of a proton around some axis

→ magnetic moment

Images: www.fmri4newbies.com

Excitation and relaxation of spins



Excite sample with RF pulse (radio wave: 42.6MHz/Tesla).

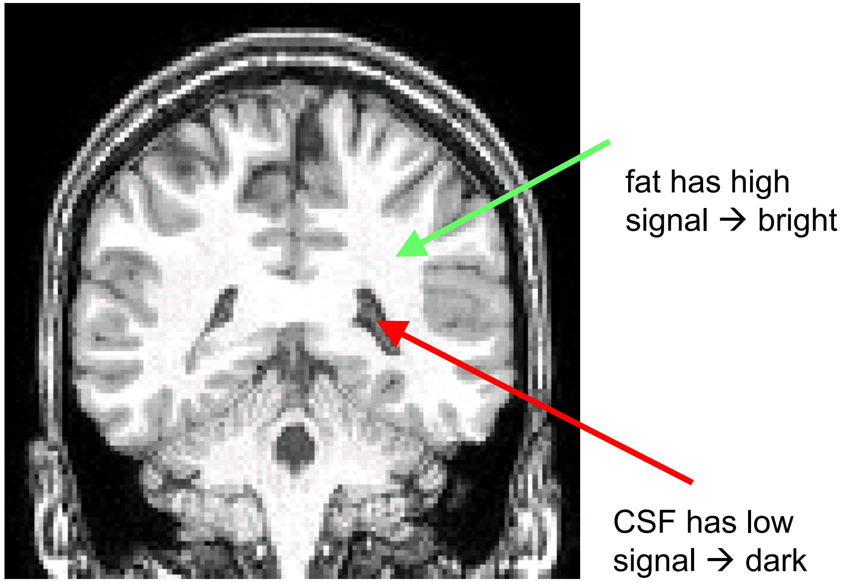
Measure the emitted radio wave.

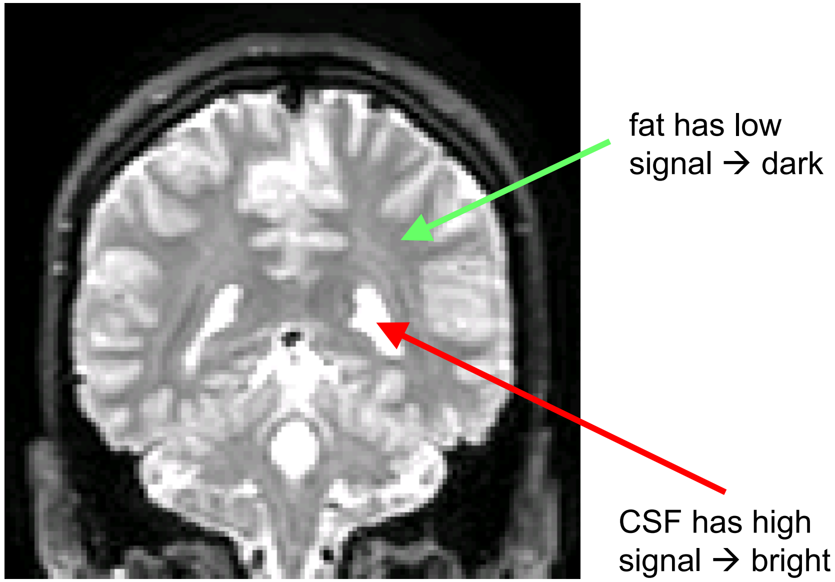
Movies:
K. Prüssmann

Signal decay depends on tissue

T1 = How quickly do protons realign with magnetic field?

T2 = How quickly do protons emit energy (phase out) when recovering to equilibrium?





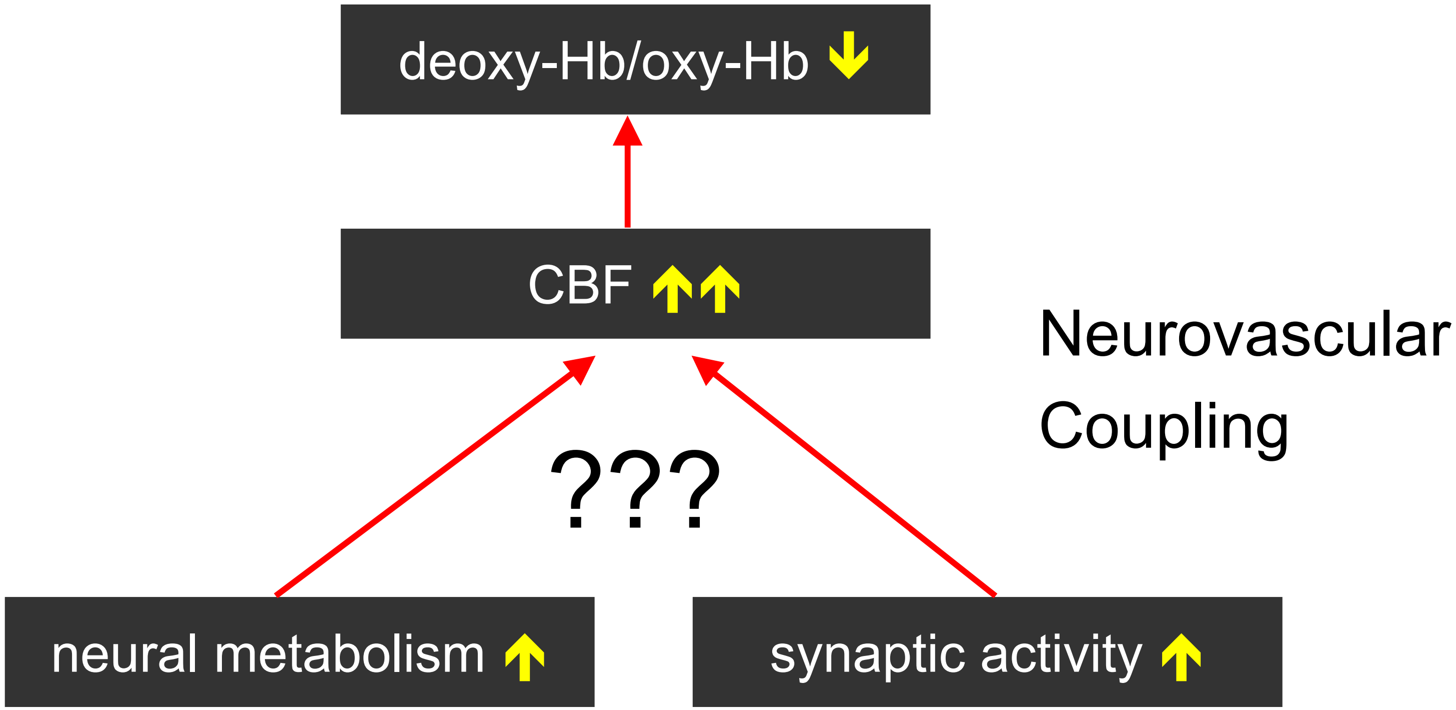
T2* magnetization decay

- Decay of transverse magnetization has two factors:
  1) molecular interactions (tissue properties) (T2)
  2) local inhomogeneities of the magnetic field
- The combined time constant is called T2*.

The general principle of MRI:

- excite spins in static field by RF pulses & detect the emitted RF
- use an acquisition technique that is sensitive to local differences in T1, T2 or T2*
- construct a spatial image

2. What do we measure with fMRI?



Increased neural activity leads to an over-compensatory increase of regional CBF, which decreases the relative amount of deoxy-Hb
→ higher T2* signal intensity

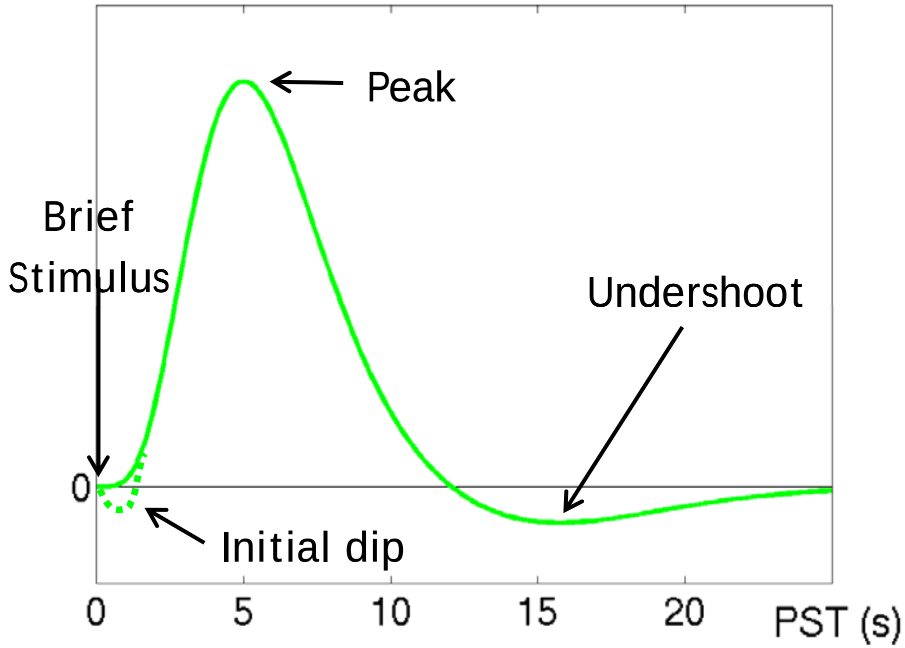
The hemodynamic response function (HRF)

sometimes shows initial undershoot → initial dip

peaks after 4-6 secs

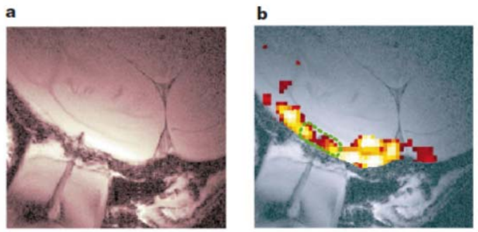
back to baseline after approx. 30 secs

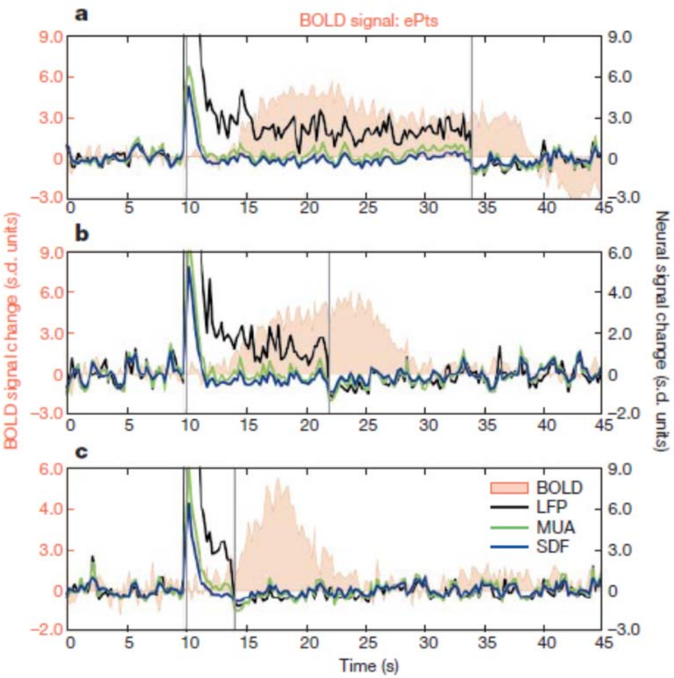
can vary between regions and subjects



Hemodynamic response function = BOLD response to a brief stimulus

3. How is the BOLD signal related to neural processing?





Local Field Potentials (LFP)

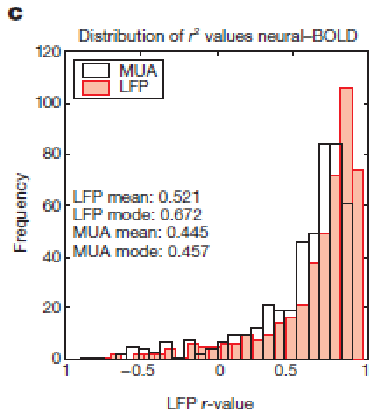
- reflect summation of post-synaptic potentials

Multi-Unit Activity (MUA)

- reflects action potentials/spiking

combined BOLD fMRI and electrophysiological recordings

→ found that BOLD activity is more closely related to LFPs than MUA



Source: Logothetis et al, Nature, 2001

3. How is the BOLD signal related to neural processing?

- The BOLD signal is best correlated to postsynaptic activity (as measured by LFPs)
  - In many cases action potentials and LFPs are themselves highly correlated.
  - rCBF-increase can be independent from spiking activity, but so far no case has been found where it was independent of LFPs.
- Present conclusion: BOLD more strongly reflects the **input to** a neuronal population as well as its **intrinsic processing**, rather than its spiking output.

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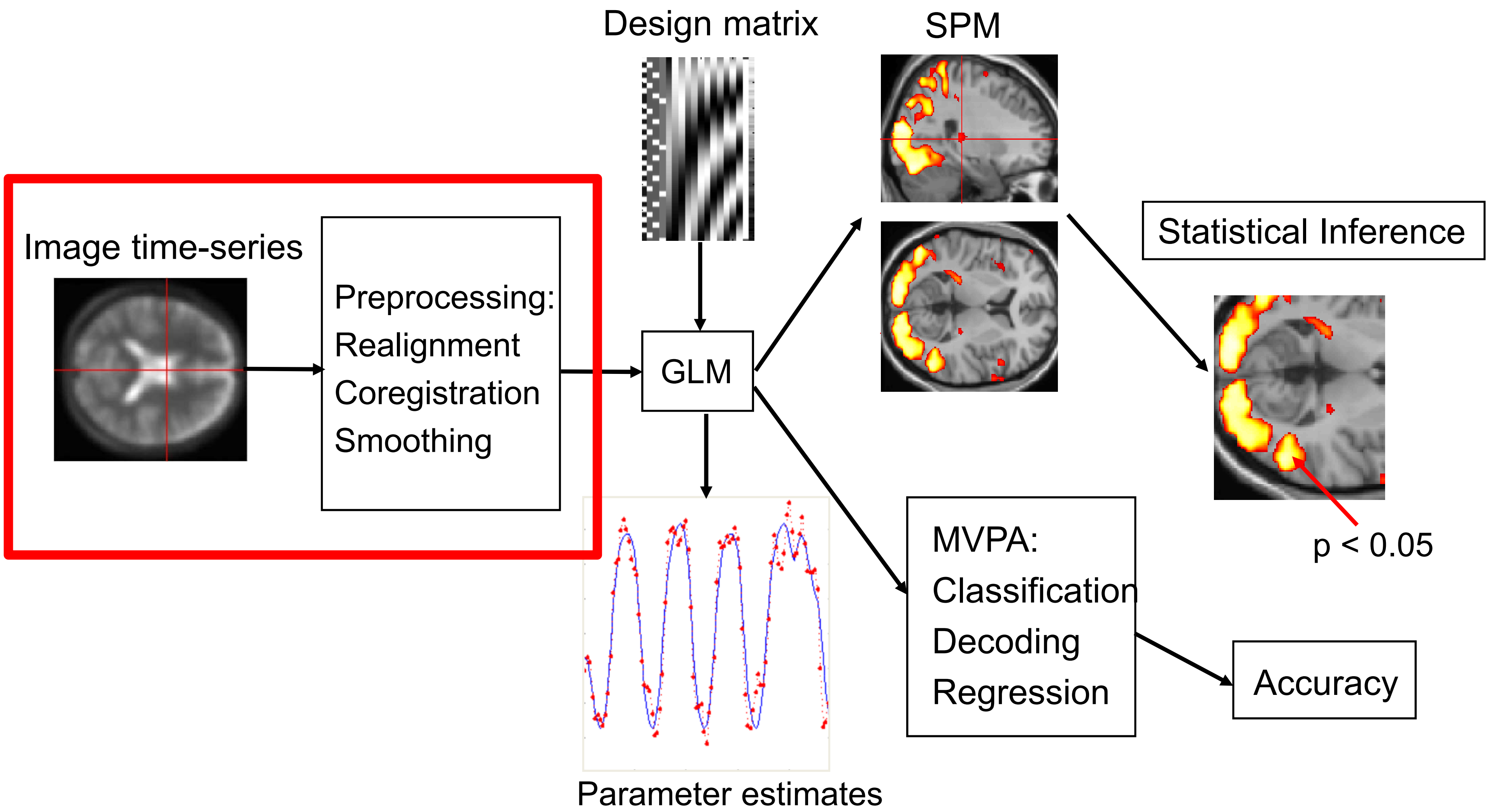


SPM: Statistical Parametric Map, MVPA: Multivariate Pattern Analysis

Terminology

Why does fMRI require spatial preprocessing?

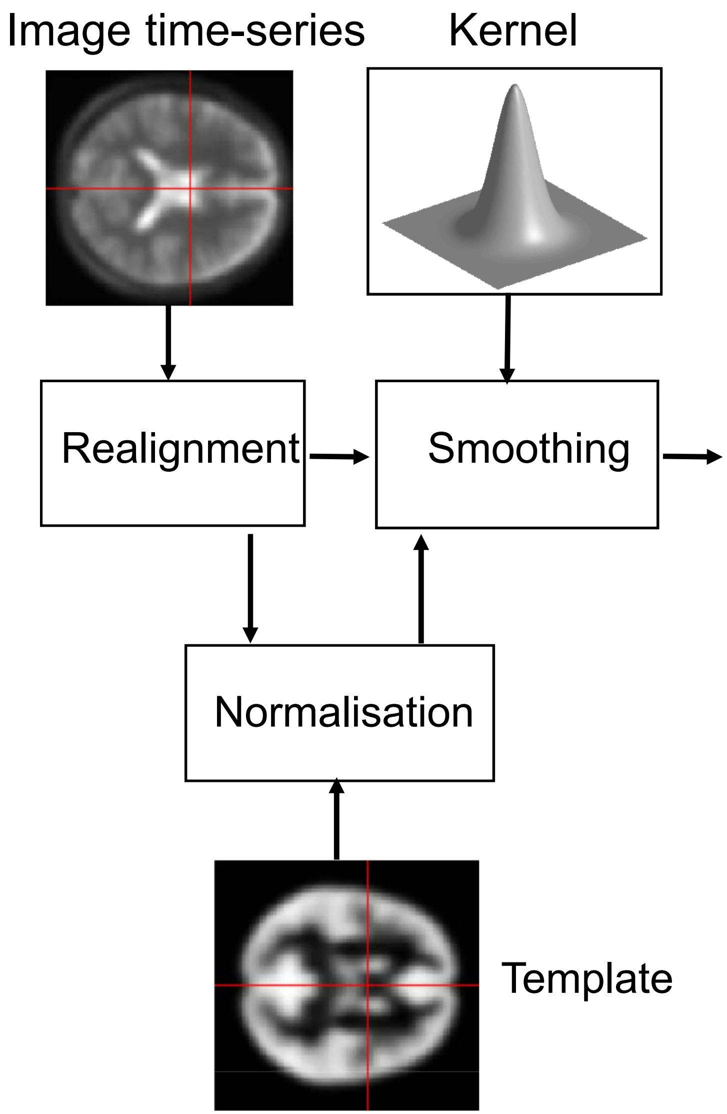
- Head motion artefacts during scanning

  → Realignment

- Brains are quite different across subjects

  → Normalisation (“Warping”)
  → Smoothing

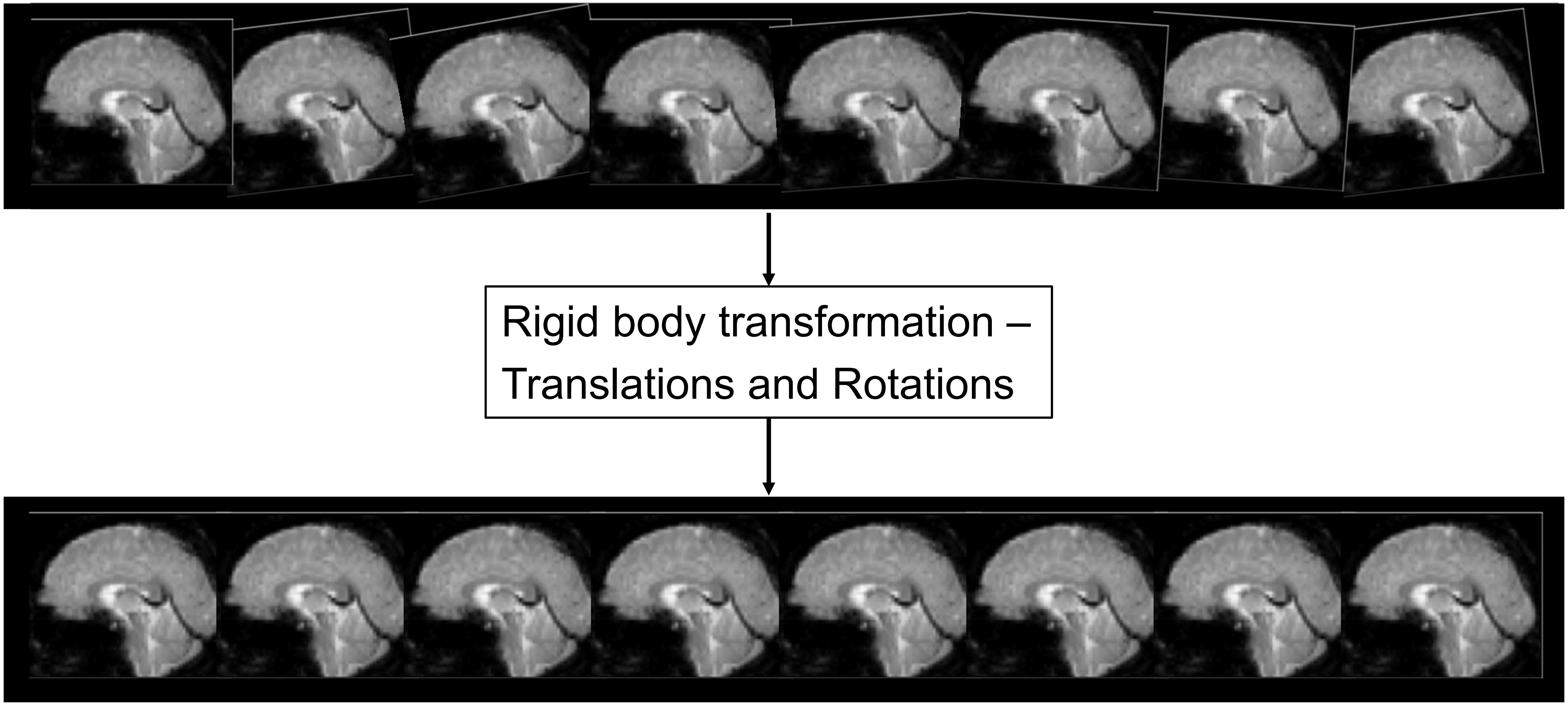
Preprocessing



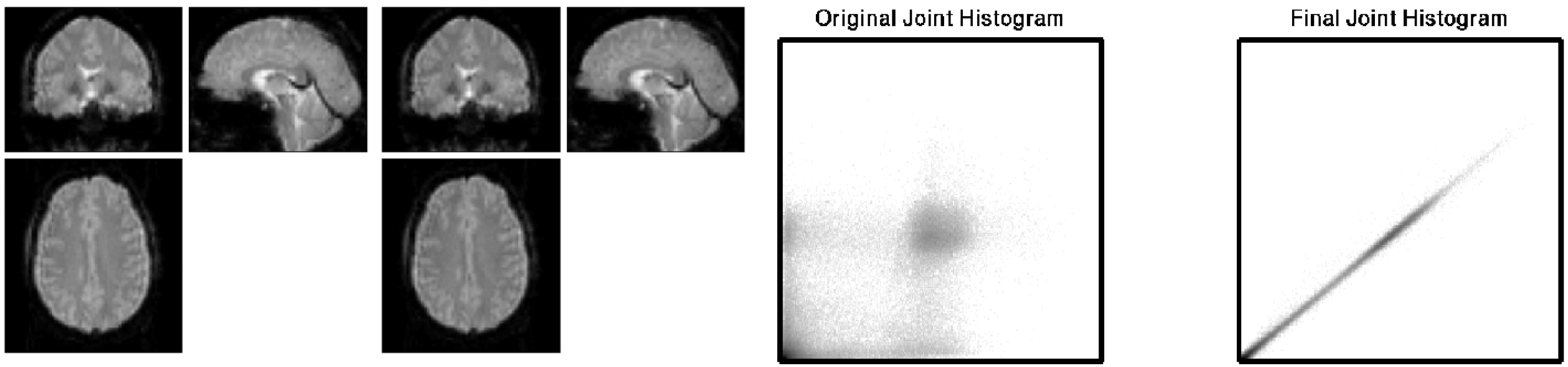
Realignment and coregistration to anatomy in all cases.

Smoothing and normalisation possibly later, depending on analysis

Realignment (Motion correction)



Realignment

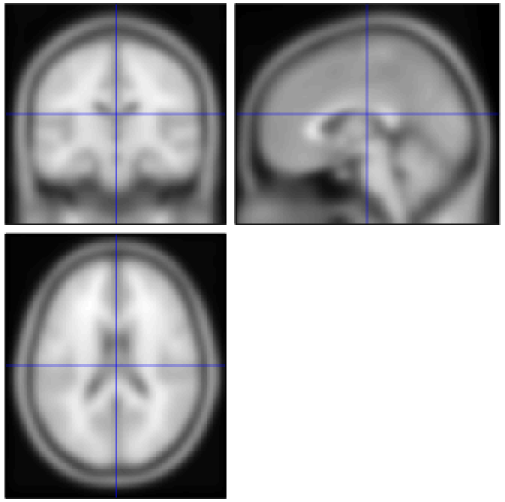


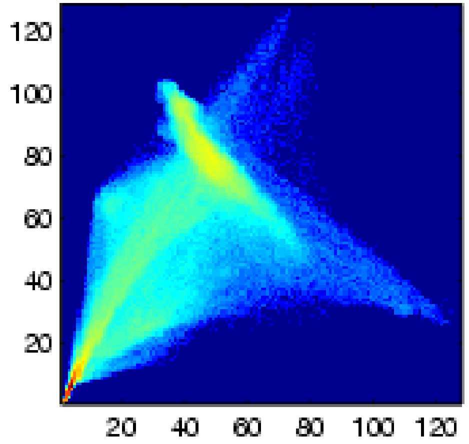
- Goal: minimise squared differences between source and reference image
- Other methods available (e.g. mutual information)

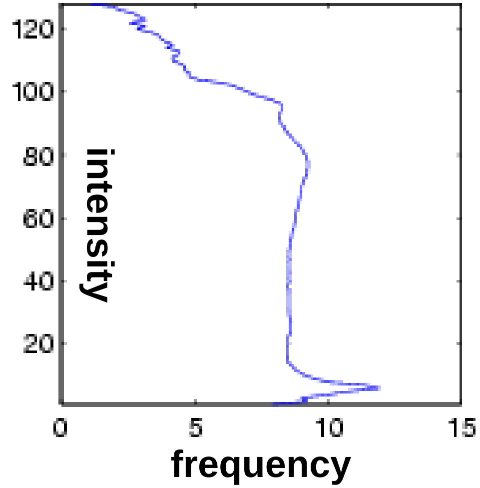
Coregistration

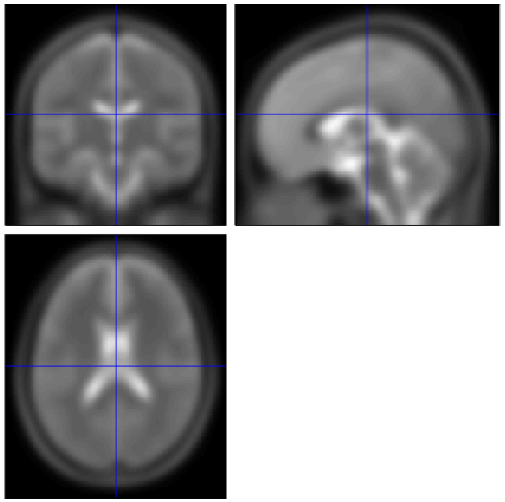
- also affine registration (like realignment)
- used to register a structural image to a (mean) functional one
  - allows more accurate anatomical localisation of activations
  - must be done before spatial normalisation (if warping parameters are estimated from the T1 image)
- examples in SPM8 Manual, Chapters 28, 29

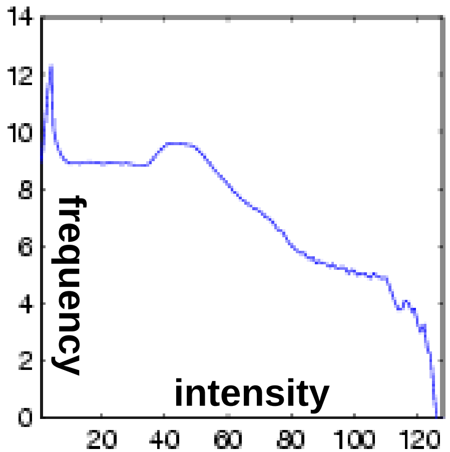
Joint and marginal histograms



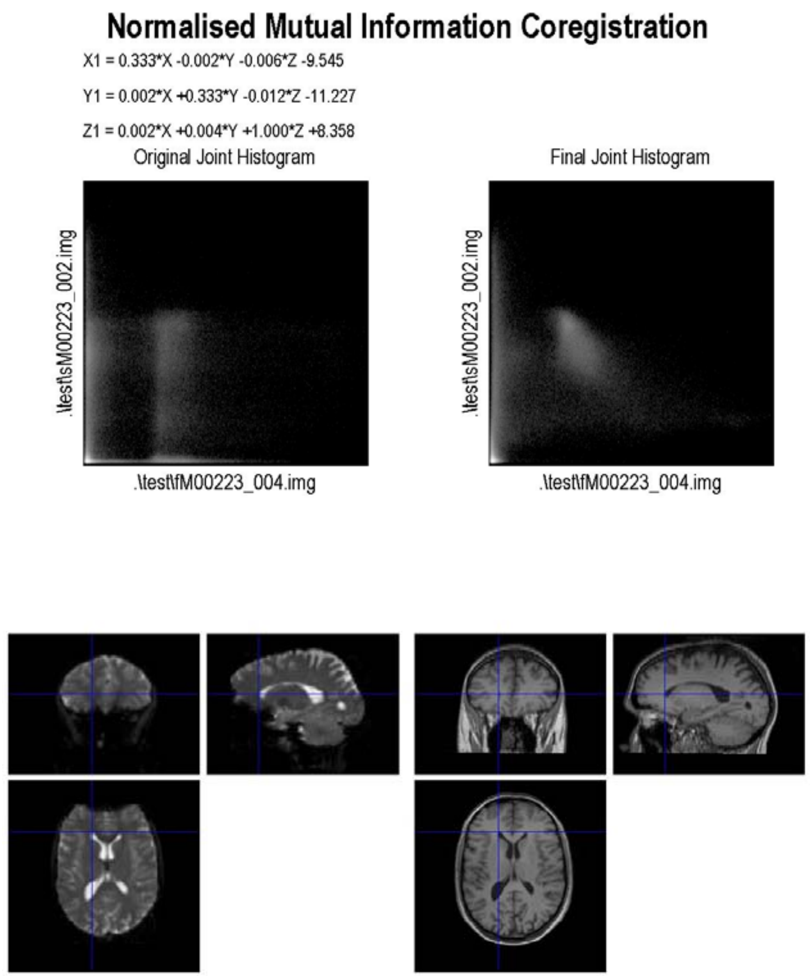




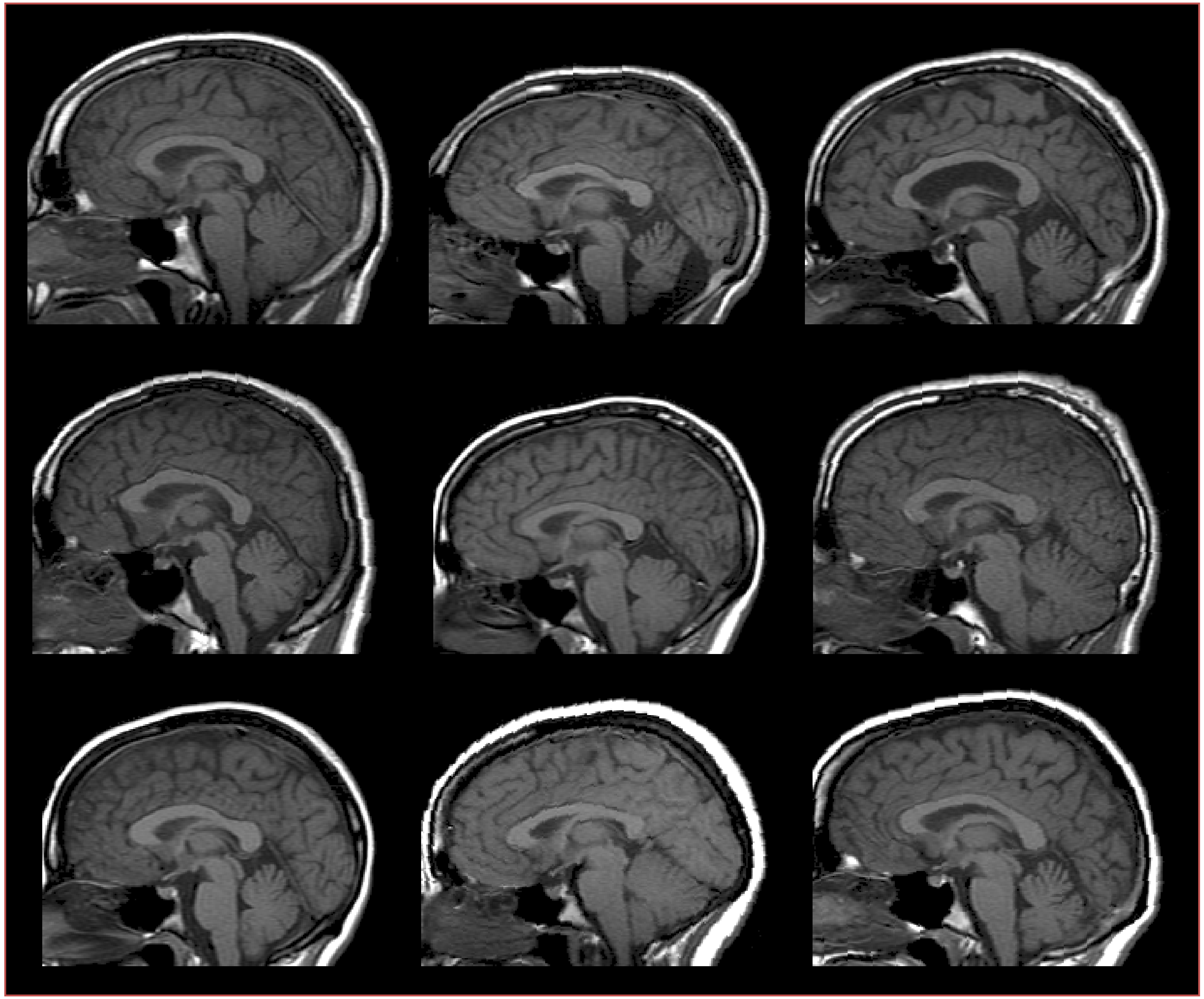




Normalised MI coregistration



Brains differ in size, shape and folding

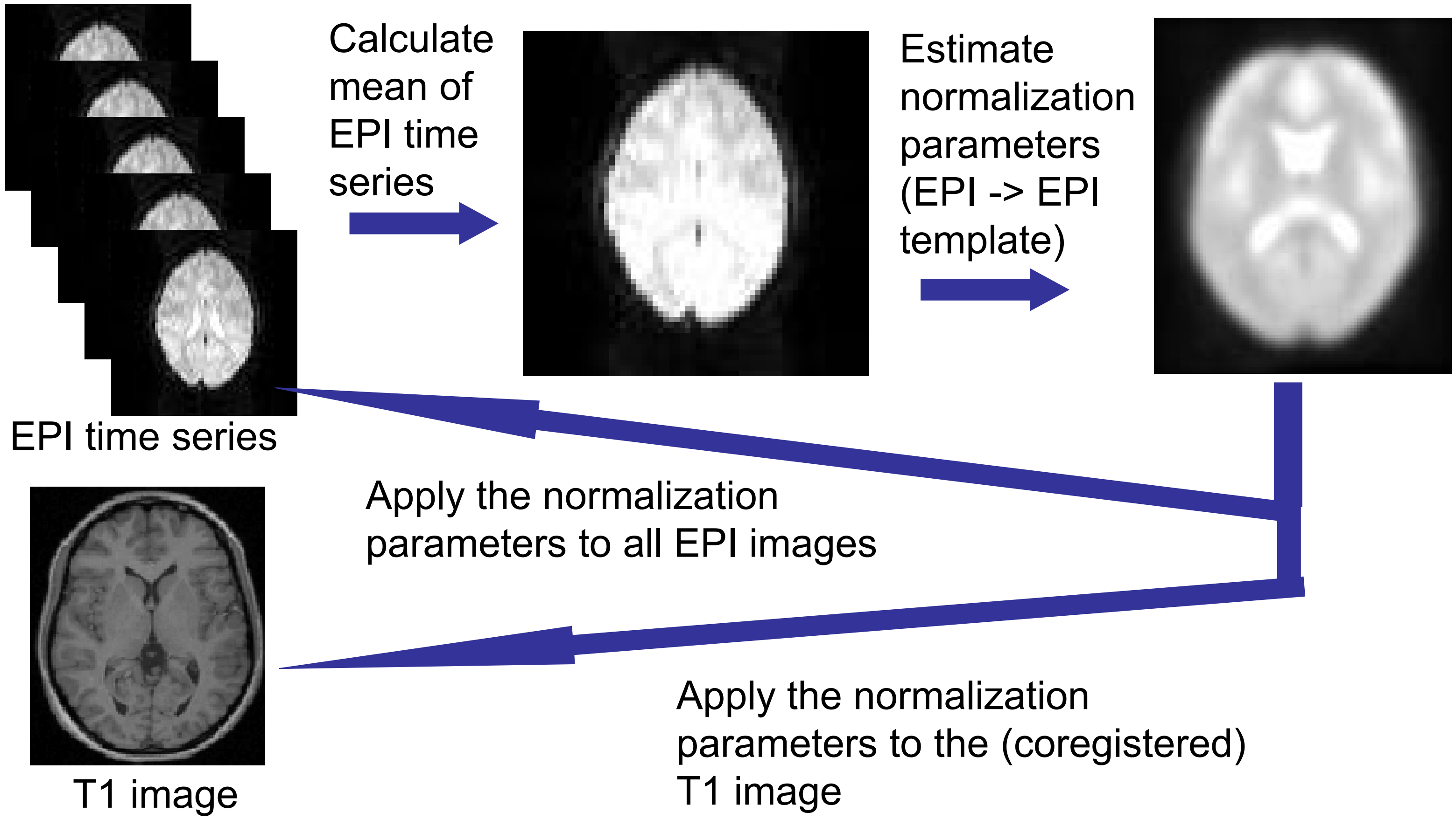


Spatial normalisation: why necessary?

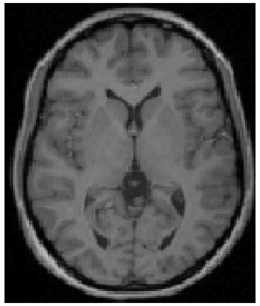
- Inter-subject averaging/analysis
  - Increase sensitivity with more subjects
    - Fixed-effects analysis
  - Extrapolate findings to the population as a whole
    - Random / mixed-effects analysis

- Make results from different studies comparable by bringing them into a standard coordinate system
  - e.g. MNI space

Normalising EPI images to EPI template



Normalising structural image to T1 template

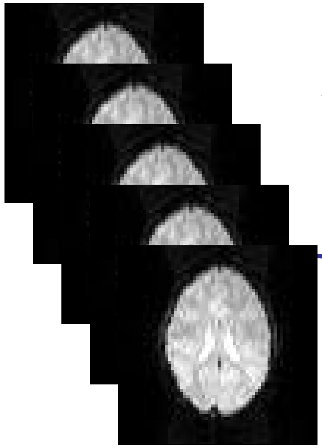


T1 image

Estimate normalization parameters
(T1 -> T1 template)

using conventional BF method or
unified segmentation approach

Apply the normalization
parameters to the T1 image



EPI time series

And apply the normalization parameters to the
(coregistered) functional images

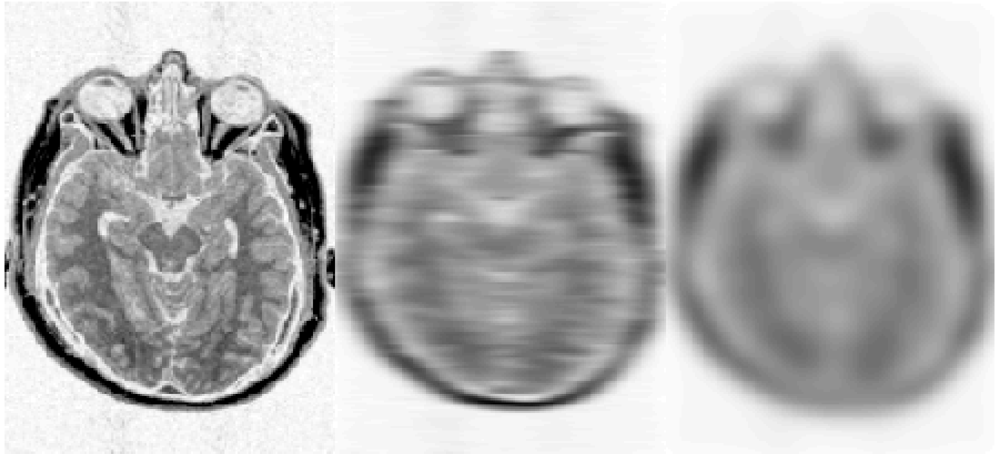
NB: this requires that the structural is initially coregistered
to the mean functional image!

Back to main

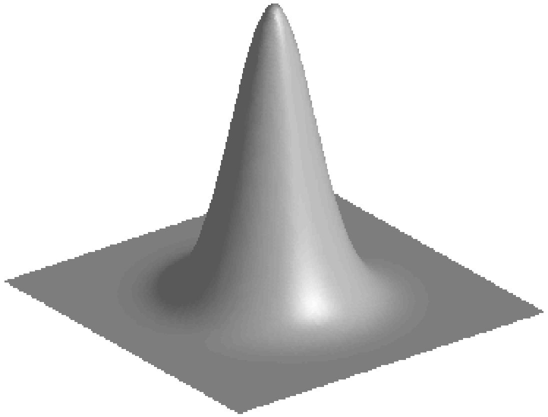
Smoothing

- Why smooth?
  - increase signal to noise
  - inter-subject averaging
  - increase validity of Gaussian Random Field theory
- In SPM, smoothing is a convolution with a Gaussian kernel.
- Kernel defined in terms of FWHM (full width at half maximum).

Gaussian convolution is separable



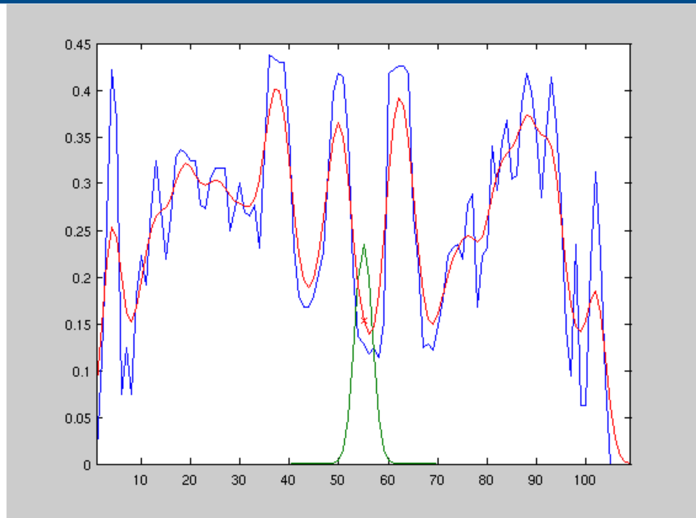
Gaussian smoothing kernel



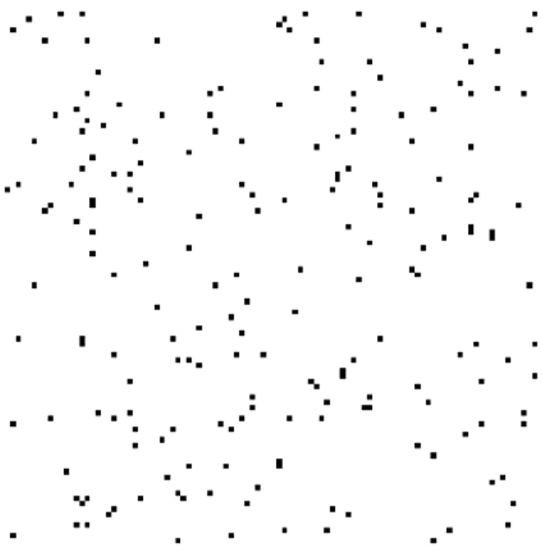
Smoothing

Smoothing is done by convolving with a 3D Gaussian which is defined by its full width at half maximum (FWHM).

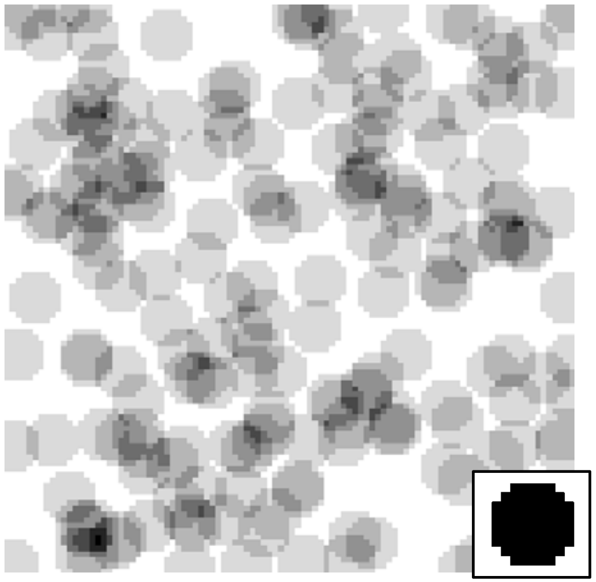
Each voxel after smoothing effectively becomes the result of applying a weighted region of interest.



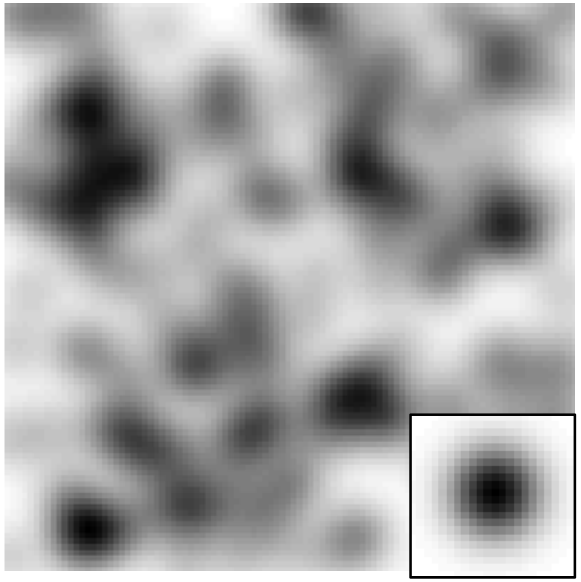
Before convolution



Convolved with a circle



Convolved with a Gaussian



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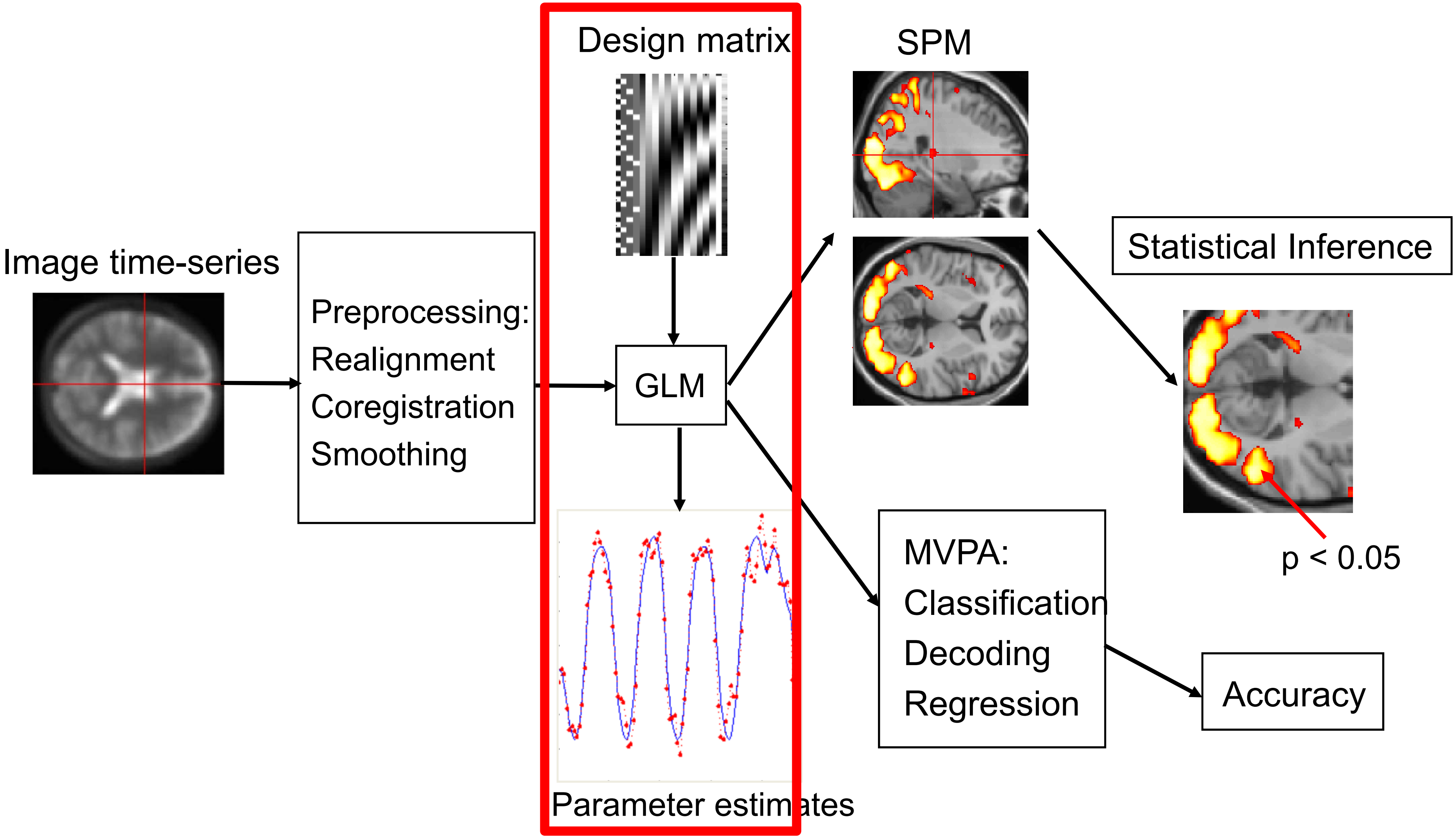


SPM: Statistical Parametric Map, MVPA: Multivariate Pattern Analysis

Terminology

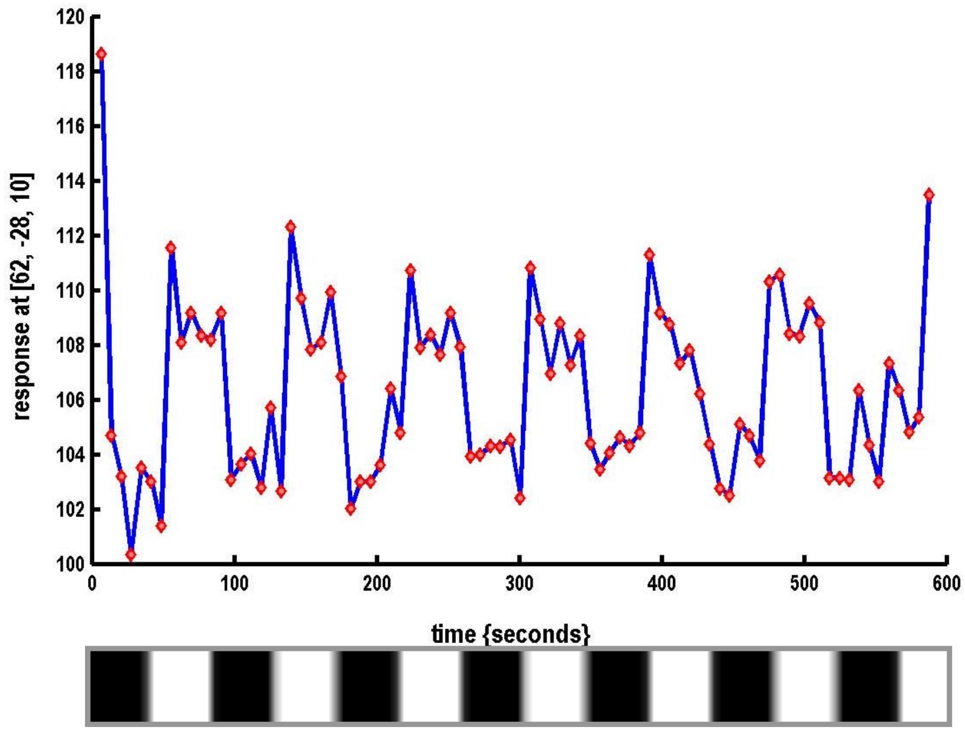
A very simple fMRI experiment

One session

Visual stimulation versus rest

7 cycles of rest and stimulation

Blocks of 6 scans with 7 sec TR



Stimulus function

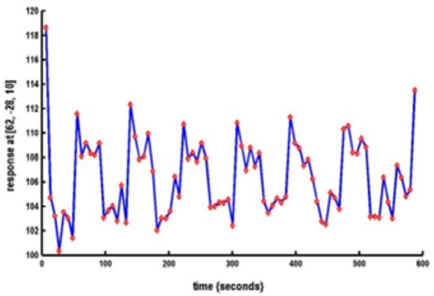
Question: Is there a change in the BOLD response between visual input and rest?

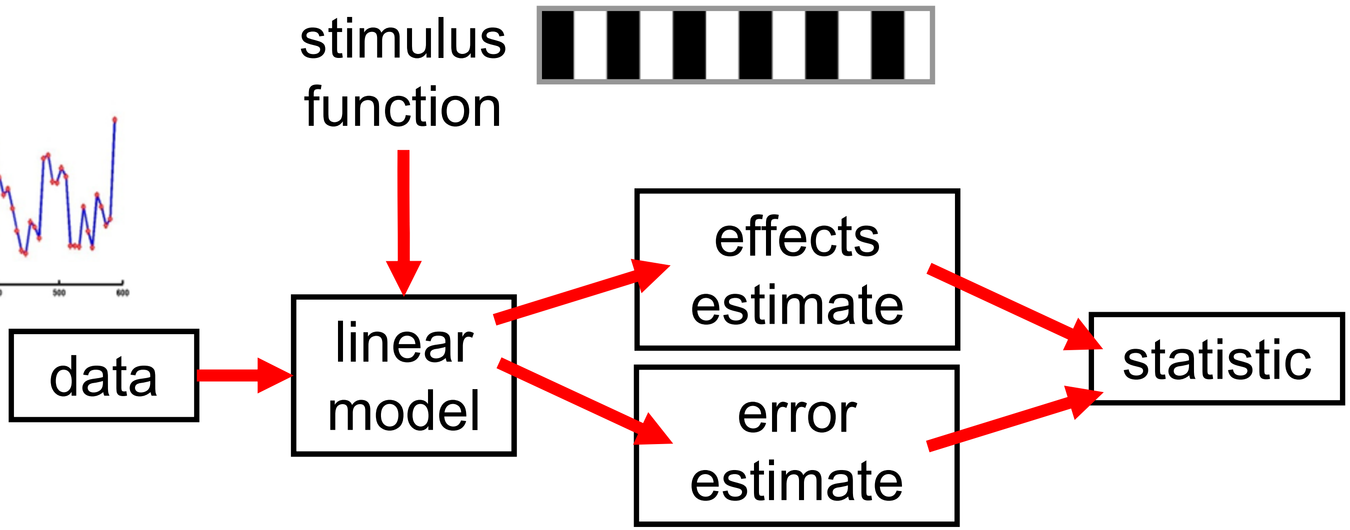
Modeling the measured data

Why? Make inferences about effects of interest

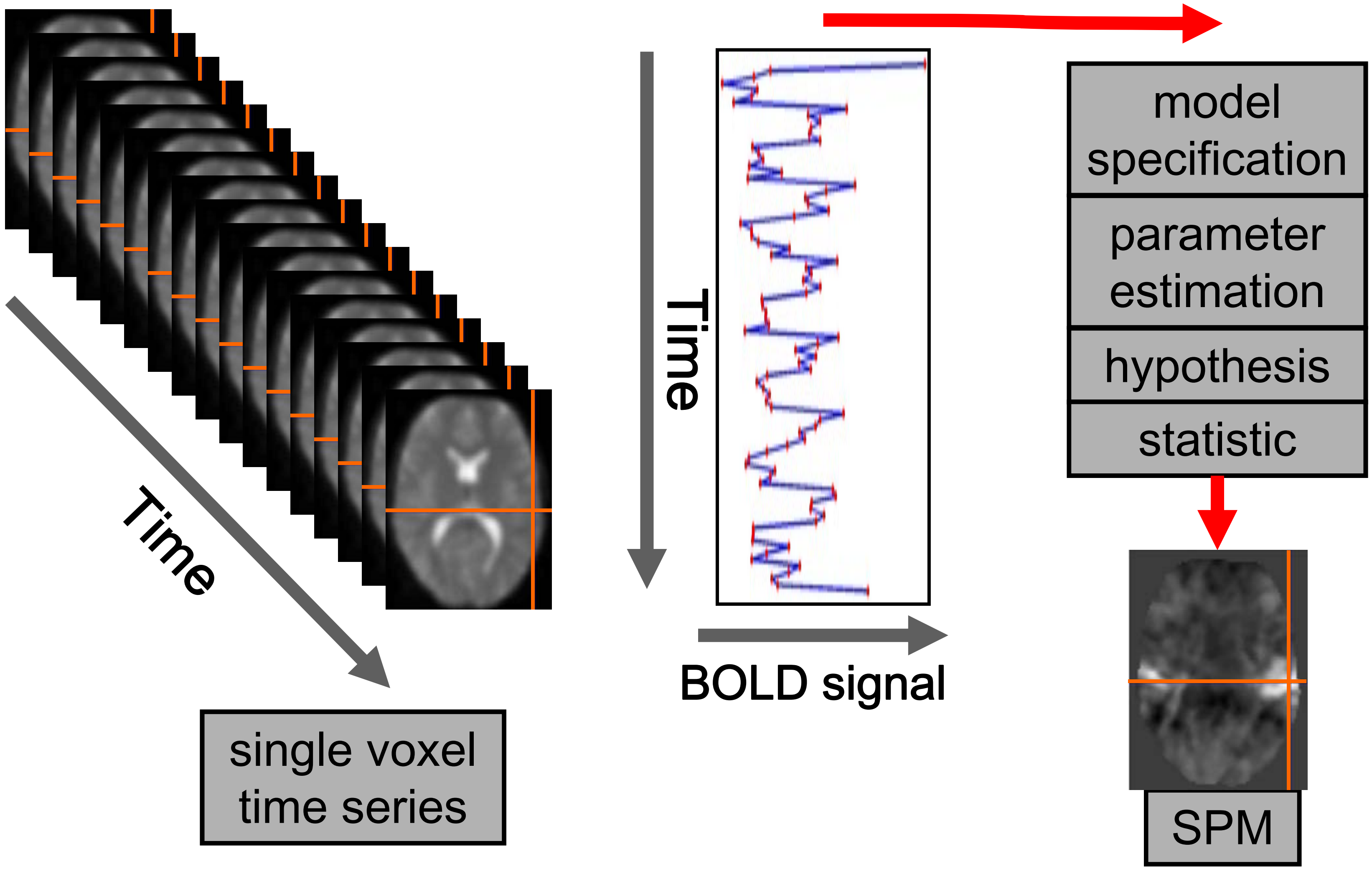
How?

1. Decompose data into effects and error
2. Form statistic using estimates of effects and error

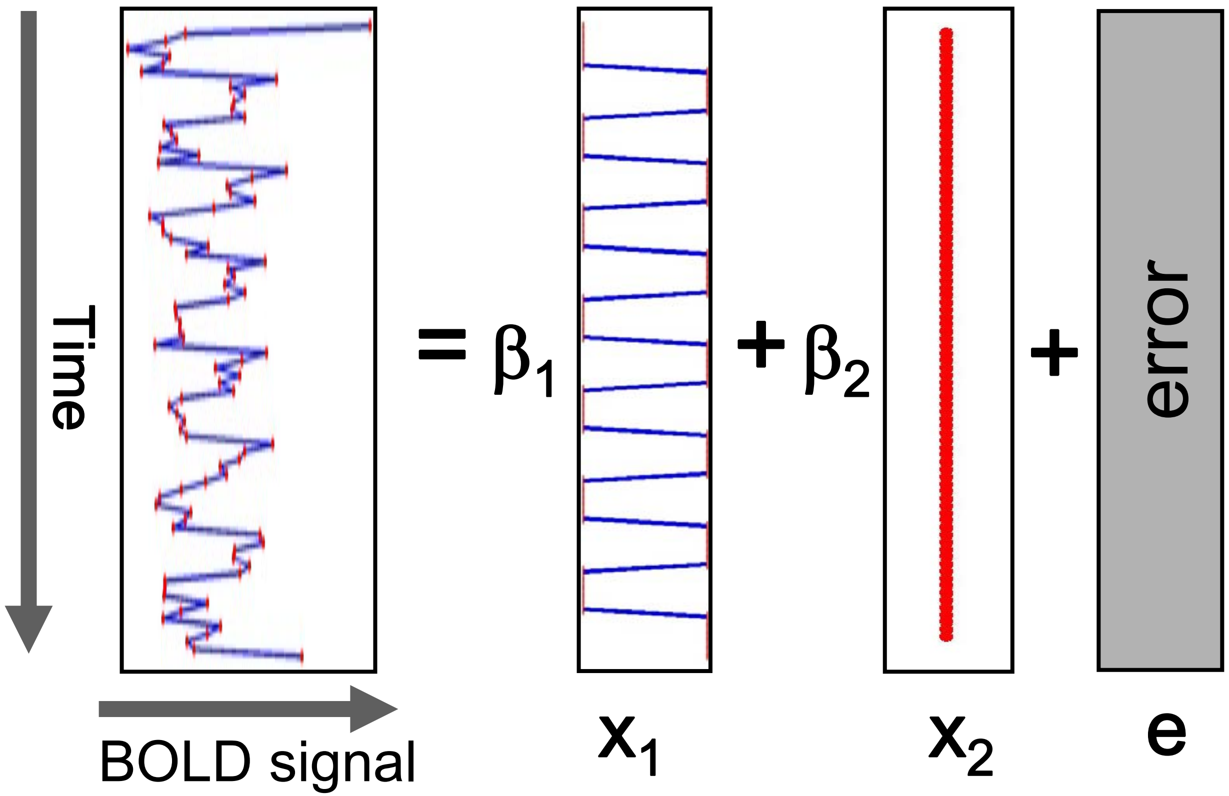




Voxel-wise time series analysis

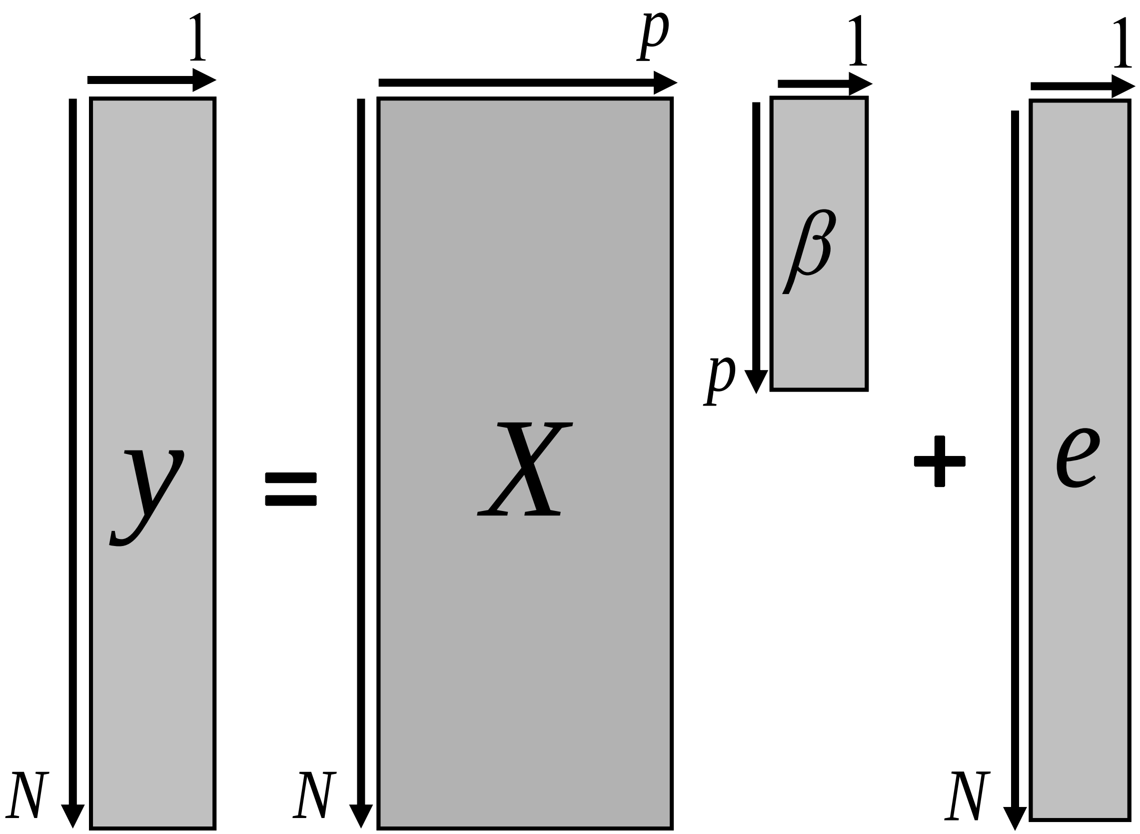


Single voxel regression model



$$y = x_1\beta_1 + x_2\beta_2 + e$$

Mass-univariate analysis: voxel-wise GLM



$$y = X\beta + e$$

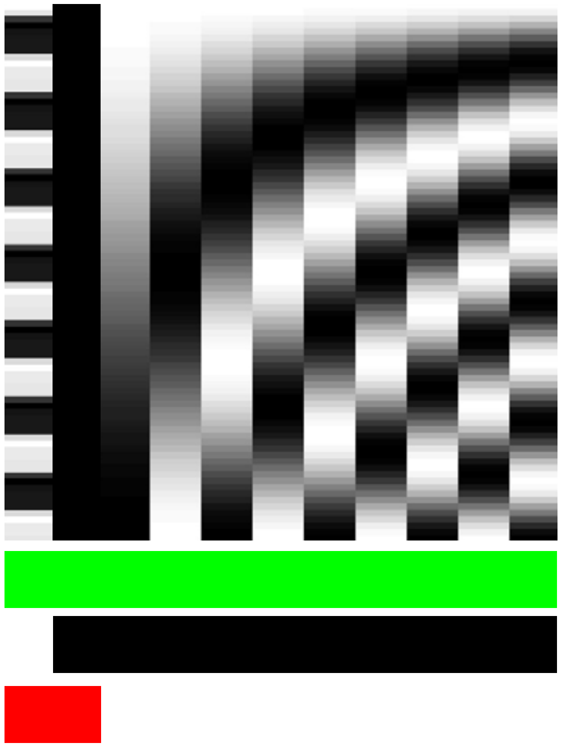
$$e \sim N(0, \sigma^2 I)$$

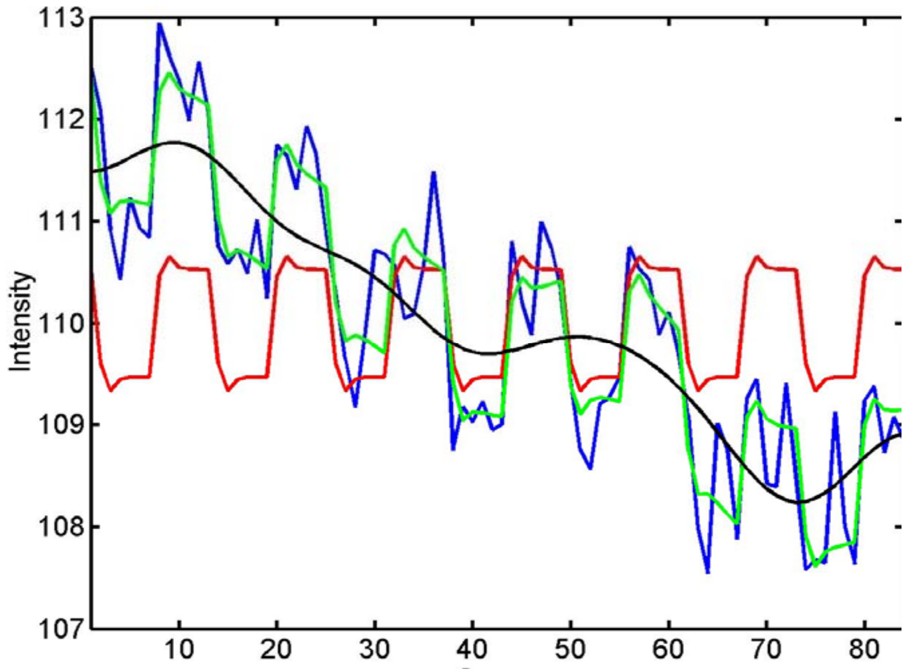
Model is specified by
1. Design matrix X
2. Assumptions about e

N: number of scans
p: number of regressors

The design matrix embodies all available knowledge about experimentally controlled factors and potential confounds.

Including "noise" in the model





blue = data

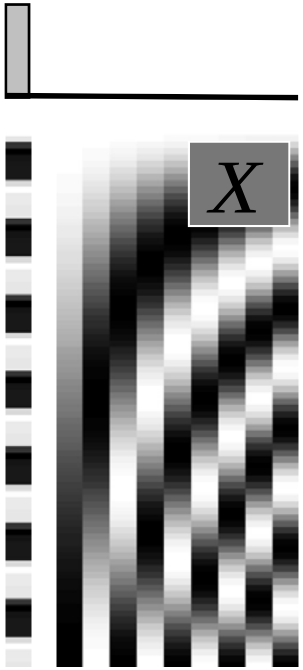
black = mean + low-frequency drift

green = predicted response, taking into account low-frequency drift

red = predicted response, NOT taking into account low-frequency drift

Contrasts & statistical parametric maps

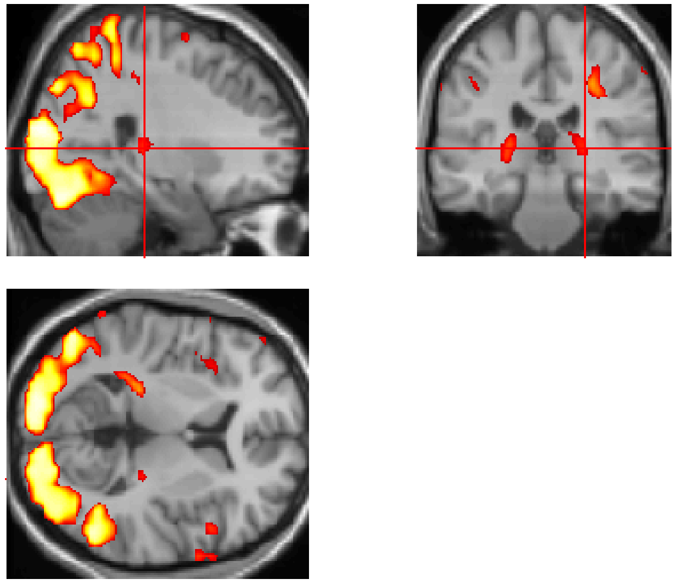
c = 1 0 0 0 0 0 0 0 0 0 0 0



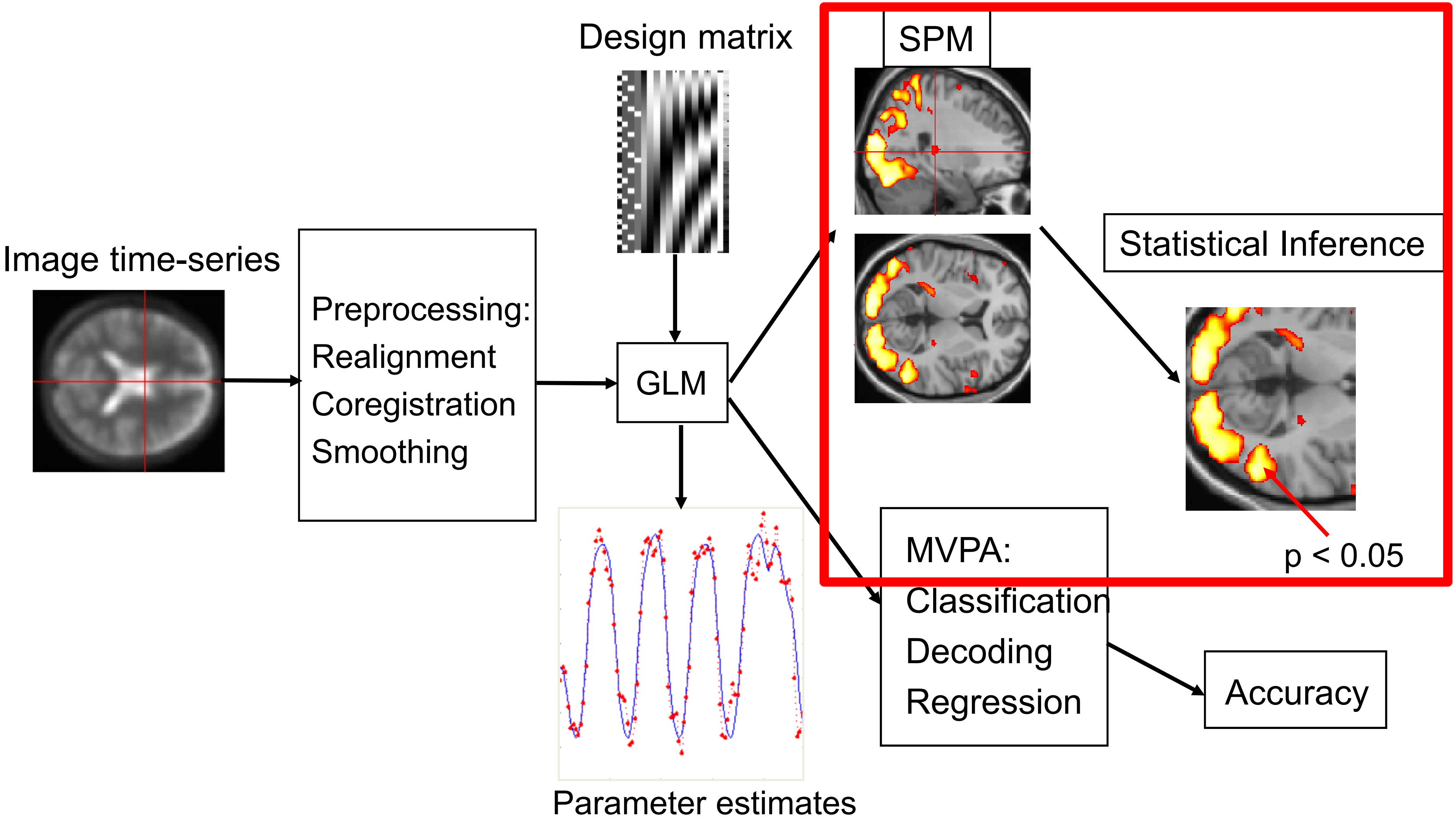
Q: activation during listening ?

Null hypothesis: $\beta_1 = 0$

$$t = \frac{c^T \hat{\beta}}{Std(c^T \hat{\beta})}$$



Overview analysis



SPM: Statistical Parametric Map, MVPA: Multivariate Pattern Analysis

Overview

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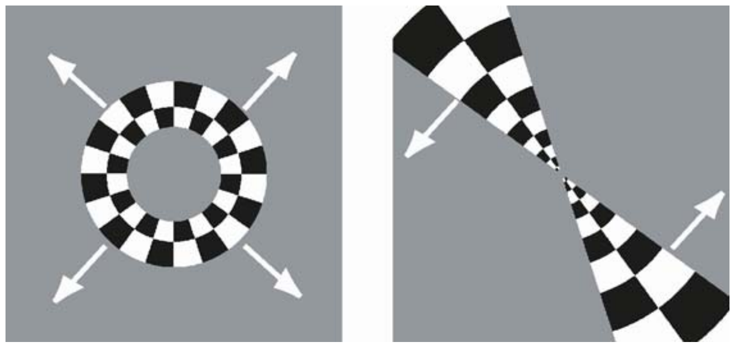
Travelling wave method

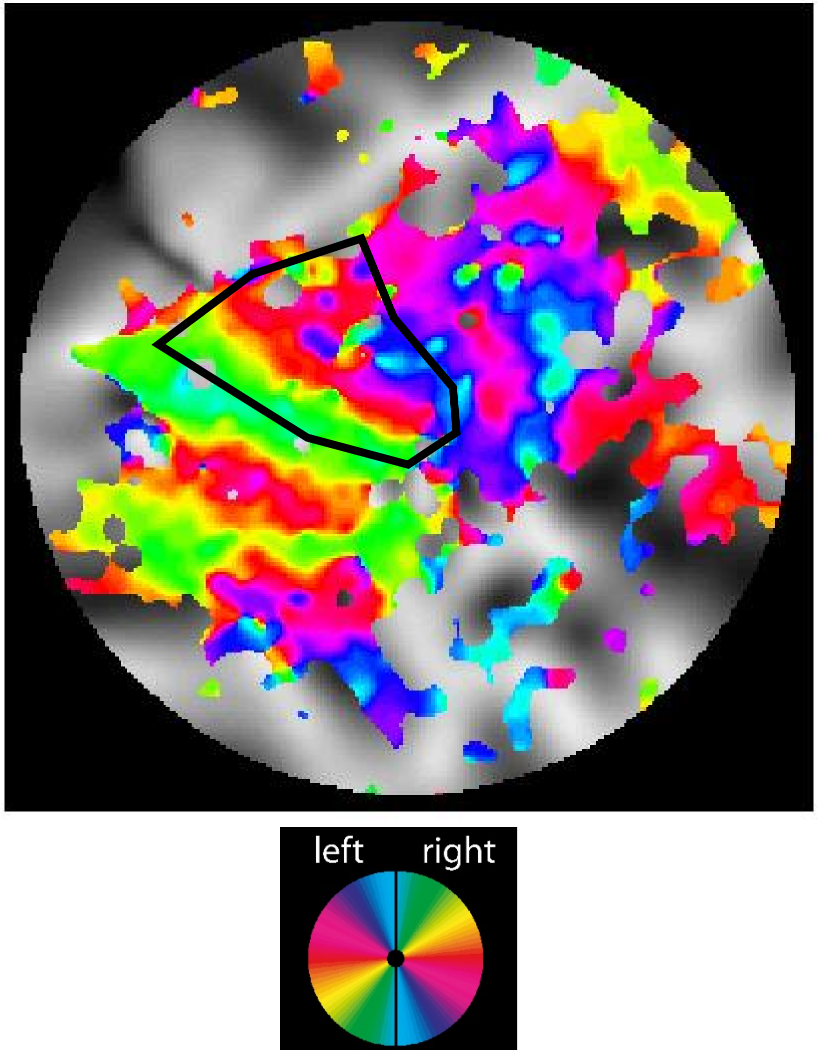
Rotating wedges and expanding rings cause activity «travelling along the cortical surface».

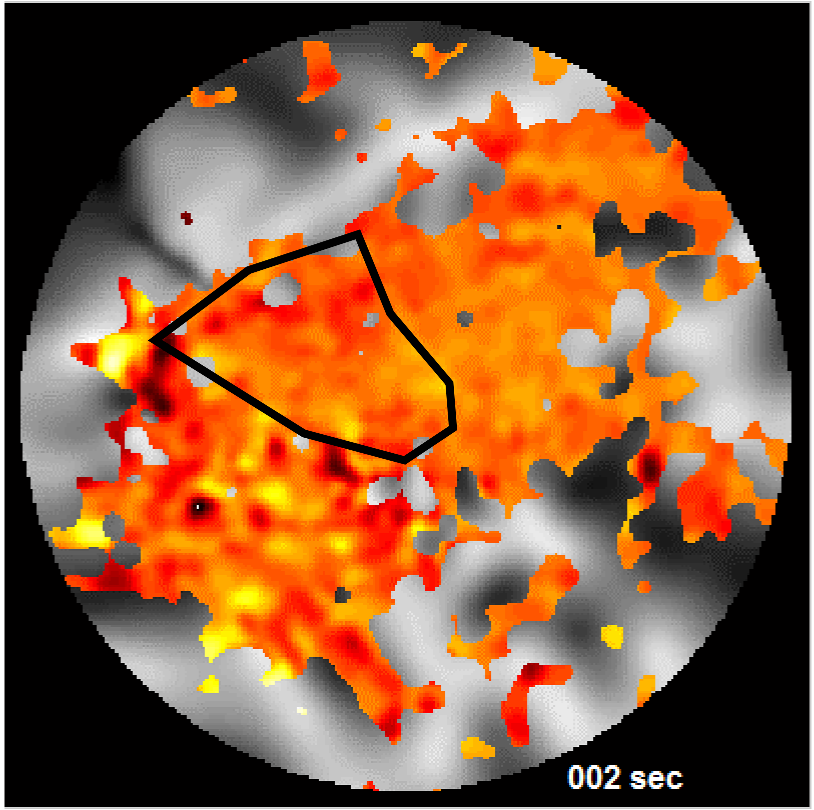


Comparing the phase of different voxels allows to assess the position they represent in the visual field.

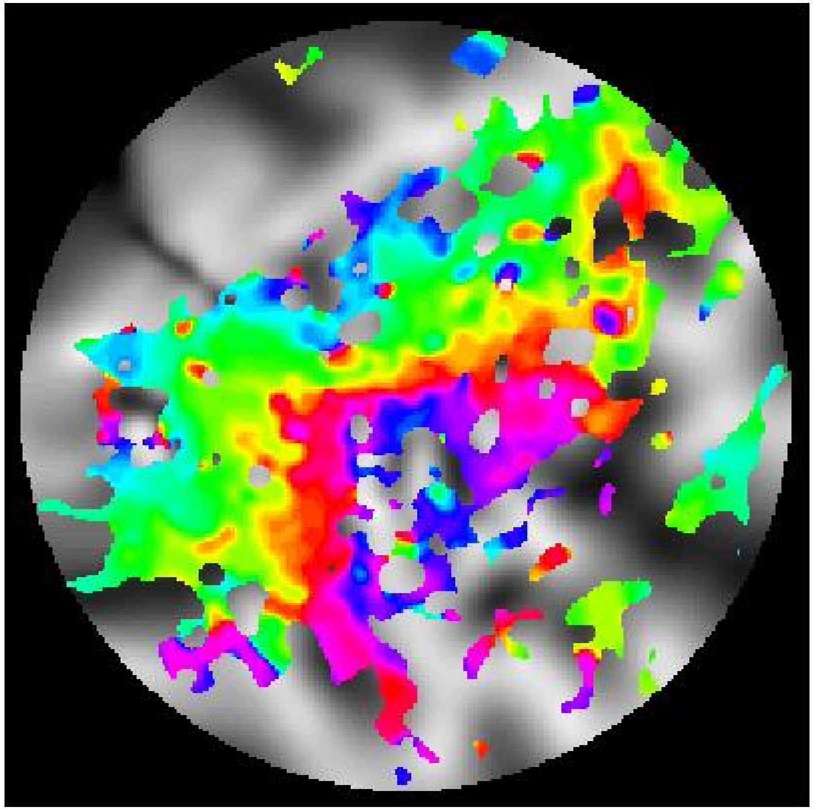
Short retinotopy demo

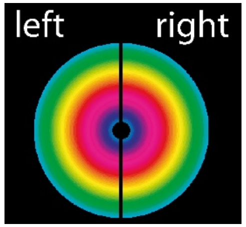
Movie: Rotating wedge

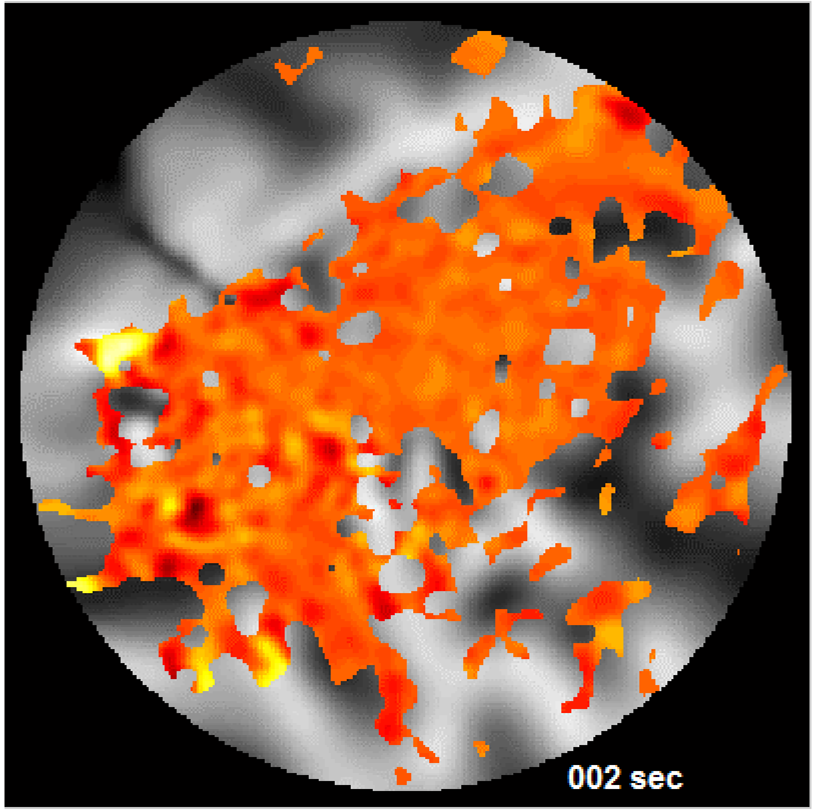




Movie: Expanding ring







Other retinotopy approaches

- Population receptive field estimation (Dumoulin and Wandell, 2008; Lee et al, 2013)
- Multifocal mapping (Vanni et al., 2008)
- Decoding using retinotopy (Kay et al., 2008, Thirion et al., 2006)

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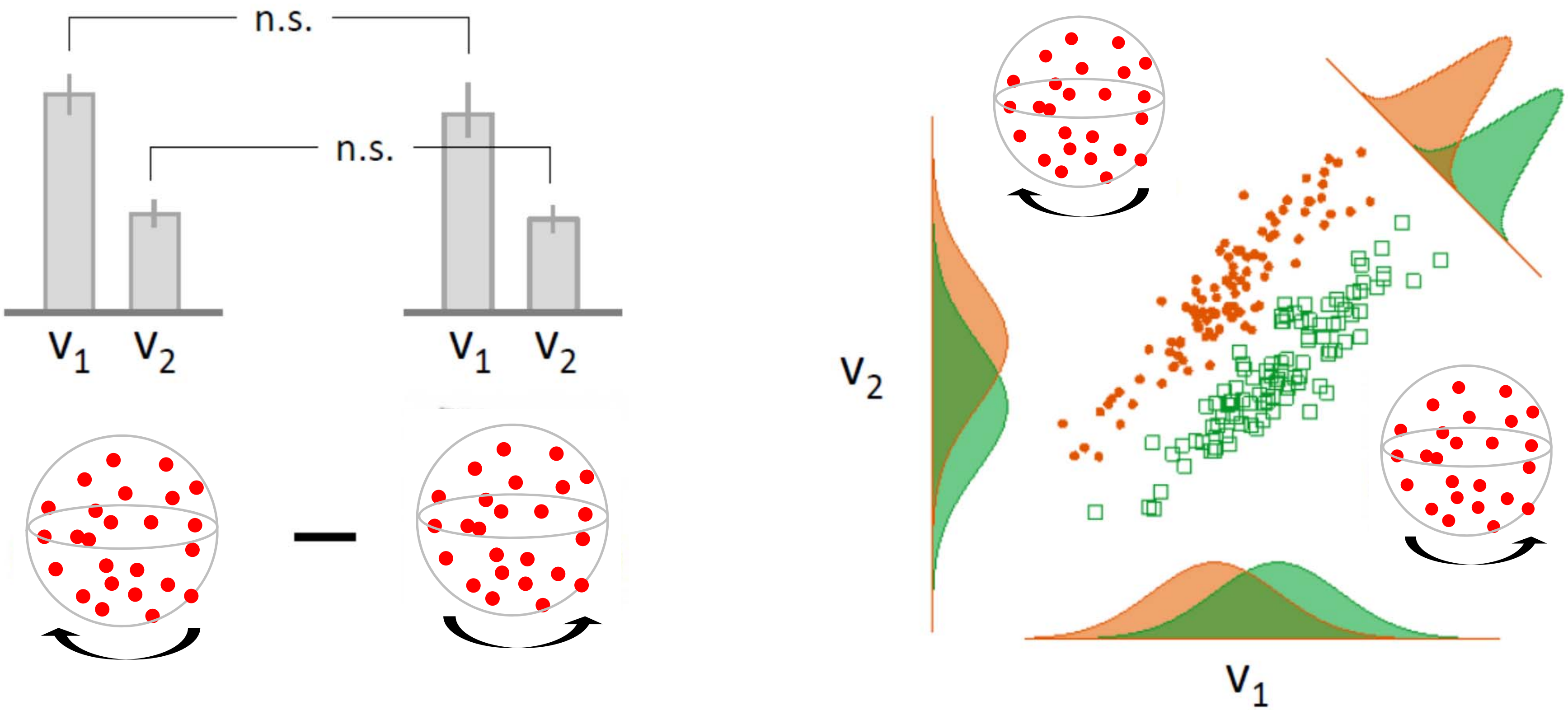
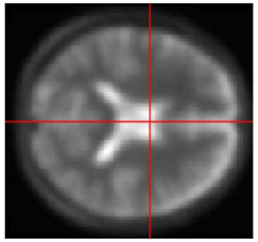
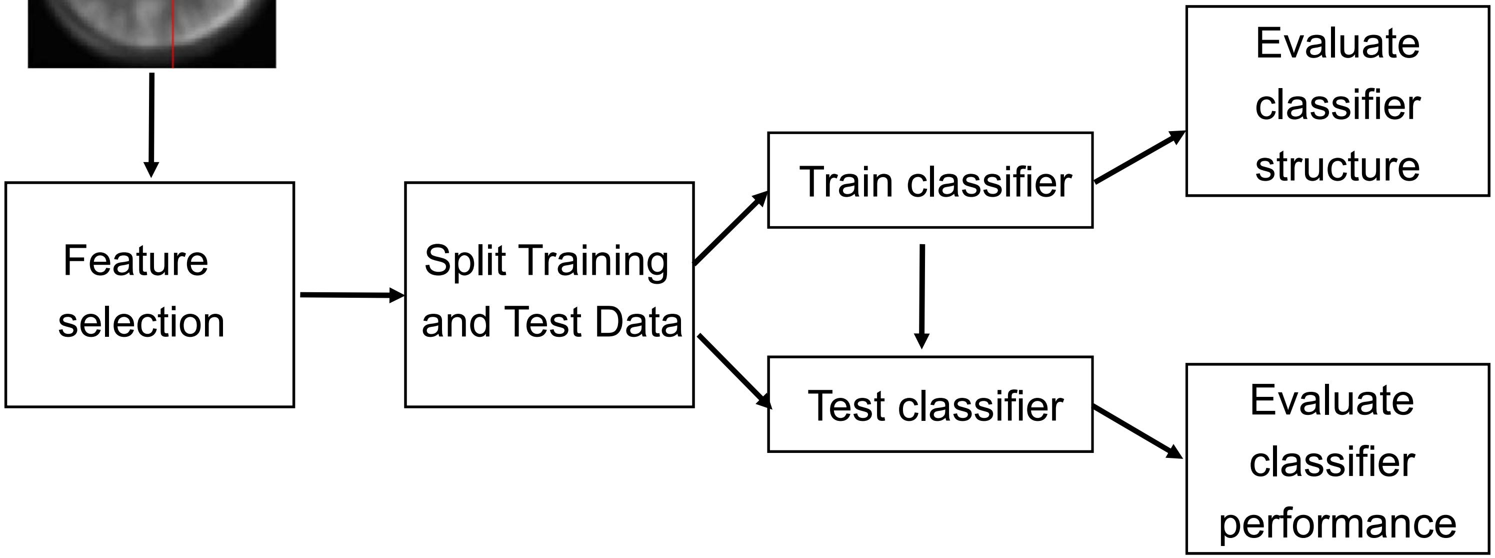
Why multivariate?



A general decoding fMRI pipeline

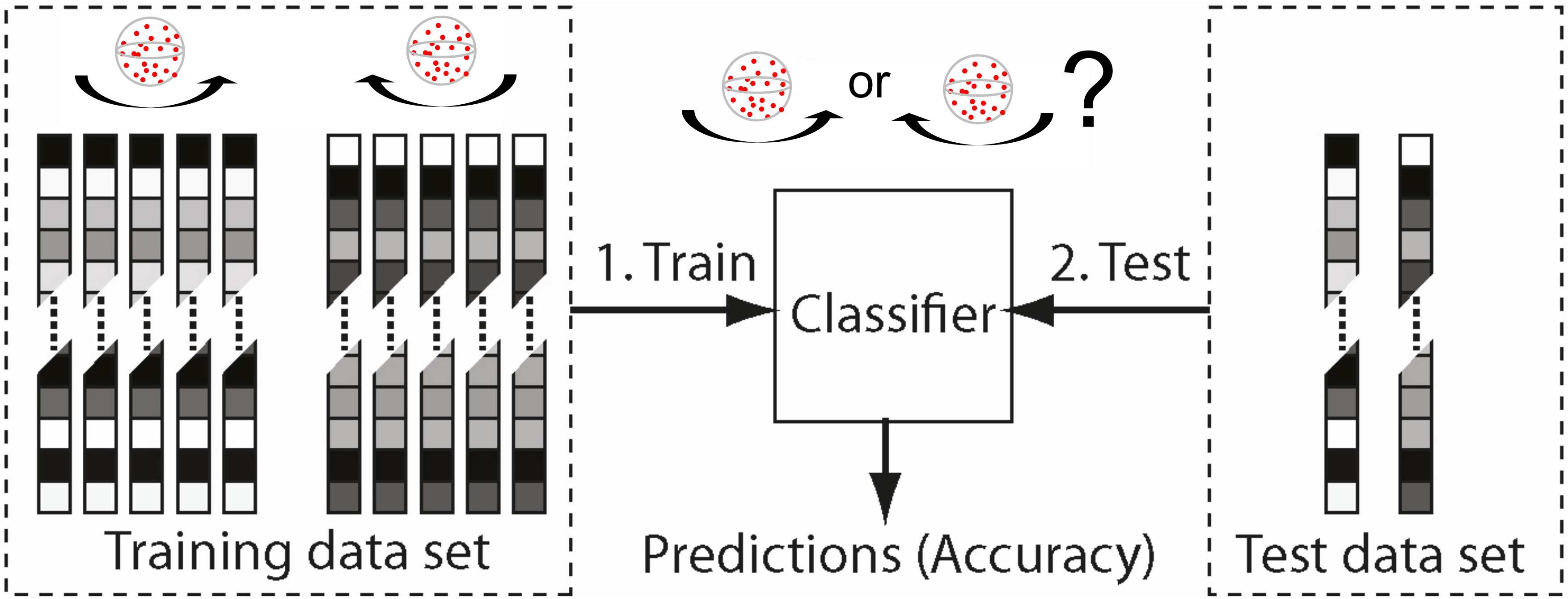
Can we say something about how this information is «stored»?



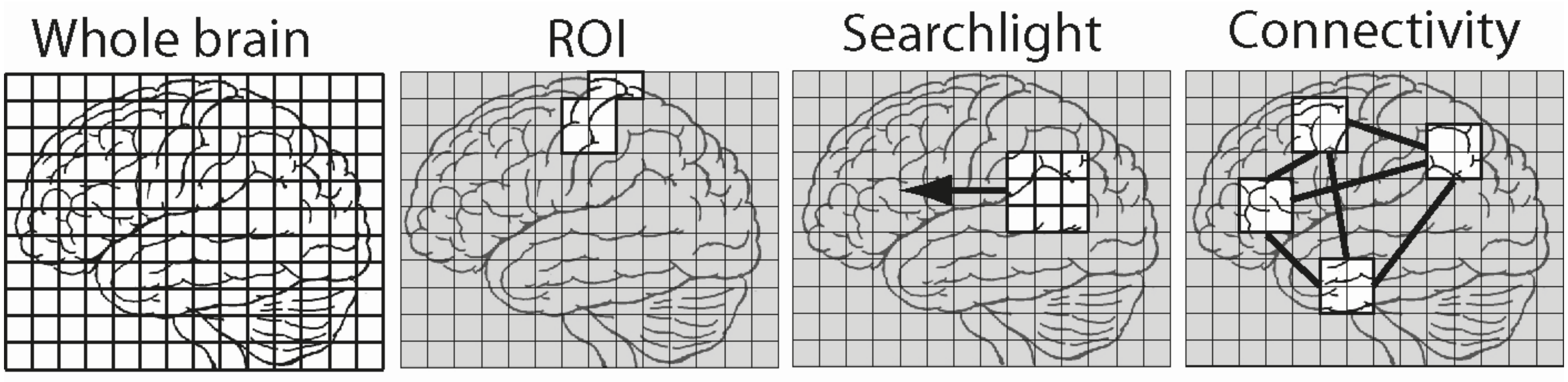


Does the data (features) contain Information about the labels?

Training and test data sets



Feature selection for fMRI



Other approaches

- Encoding models (Kay et al., 2008; Thirion et al., 2006; review in Naselaris et al, 2011, Kamitani)

- Representational similarity analysis (review Kriegeskorte, 2011)

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Short classification demo

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Statistical testing with classification

- Within subjects:
  - Permutation statistics always work
  - Parametric tests can be tricky (assumptions not met), e.g. Biomial- or t-test (c.f.
  - Krekelberg, 2013).
- Across subjects:
  - Permutation statistics always work
  - t-tests are not really valid in many cases
  - Full Bayesian model (correct, but assumptions might not be met for CV)

Be careful

- Use balanced accuracy.
- Always ***strictly separate*** test-data from training data.
- Use correct statistics, e.g. permutation tests.

Interpretation of MVPA

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Selective list of software

- SPM: http://www.fil.ion.ucl.ac.uk/spm/
  - Standard GLM analysis
- FSL: http://fsl.fmrib.ox.ac.uk/
  - Standard GLM analysis
- VISTA: http://white.stanford.edu/newlm/index.php/Software
  - Retinotopic mapping, surface analysis, population receptive fields
- Freesurfer: http://surfer.nmr.mgh.harvard.edu/
  - Segmentation, surface based analysis
- LibSVM: http://www.csie.ntu.edu.tw/~cjlin/libsvm/
  - Classification

Many other packages are available …

Some textbooks and manuals

- fMRI in general and MR-Physics
  - Functional magnetic resonance imaging (Huettel, Song, McCarthy)
  - MRI: From Picture to Proton (McRobbie, Moore, Graves, Prince)
- Analysis: Preprocessing, GLM etc.
  - SPM-manual: http://www.fil.ion.ucl.ac.uk/spm/
  - Statistical Parametric Mapping (Friston et al.)
- Machine Learning, Classification
  - Pattern Recognition and Machine Learning (Bishop)
  - Pattern Classification (Duda, Hart, Stork)

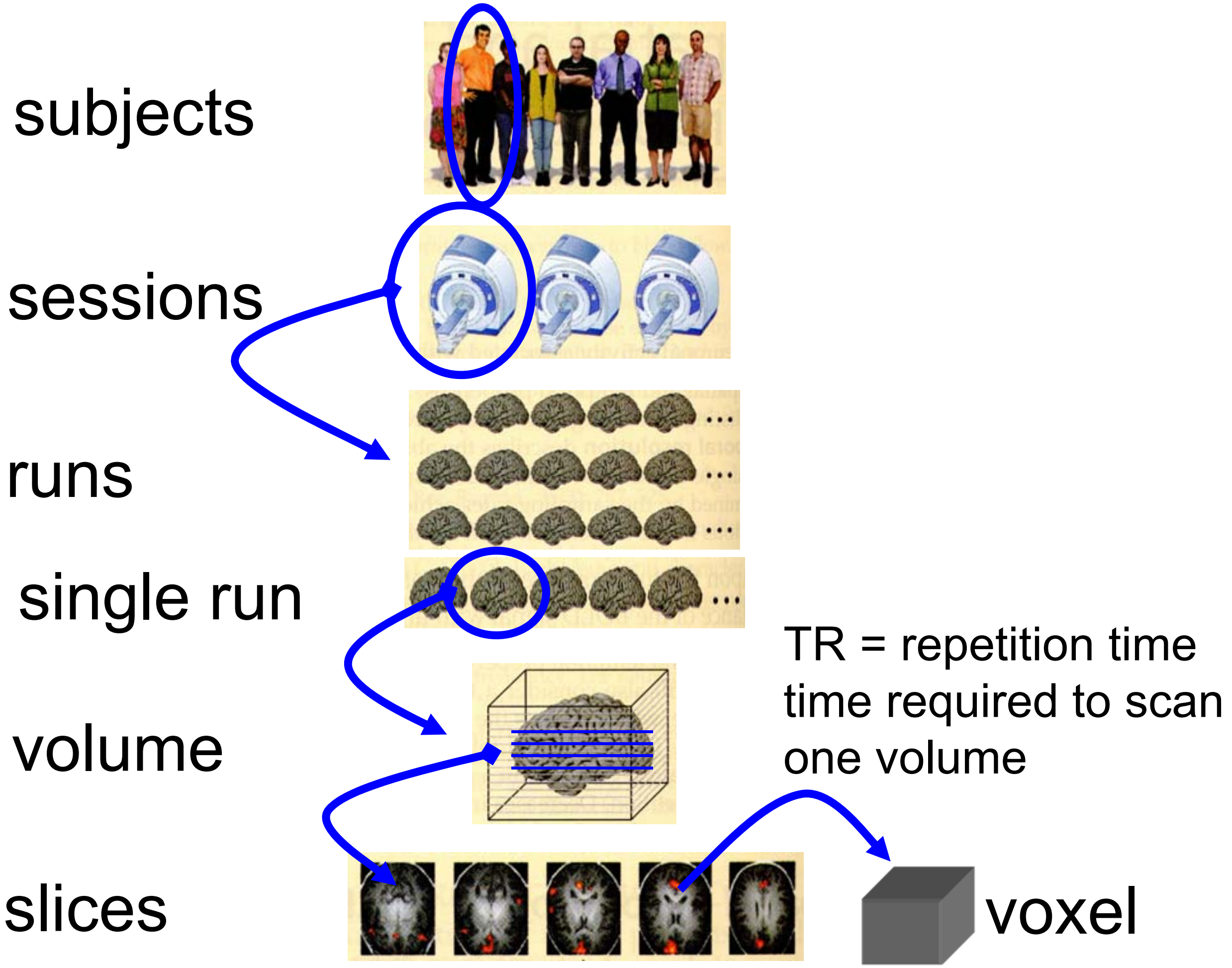
And many more …

References

Acknowledgments

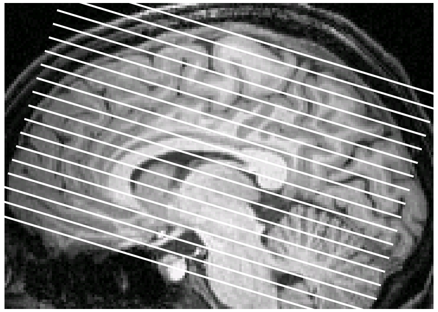
Many thanks to K.E. Stephan and K. Brodersen for sharing their teaching material.
Many thanks to T. Kahnt for providing the data for the classification demo.

Terminology of fMRI

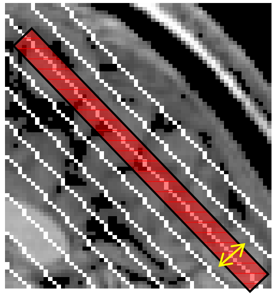


Volumes, Slices and Voxels

Scan Volume:
Field of View
(FOV),
e.g. 192 mm



Axial slices



Slice thickness
e.g., 3 mm

Matrix Size
e.g., 64 x 64

In-plane resolution
192 mm / 64
= 3 mm

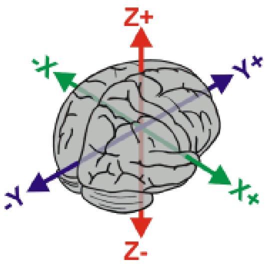
3 mm

3 mm

3 mm

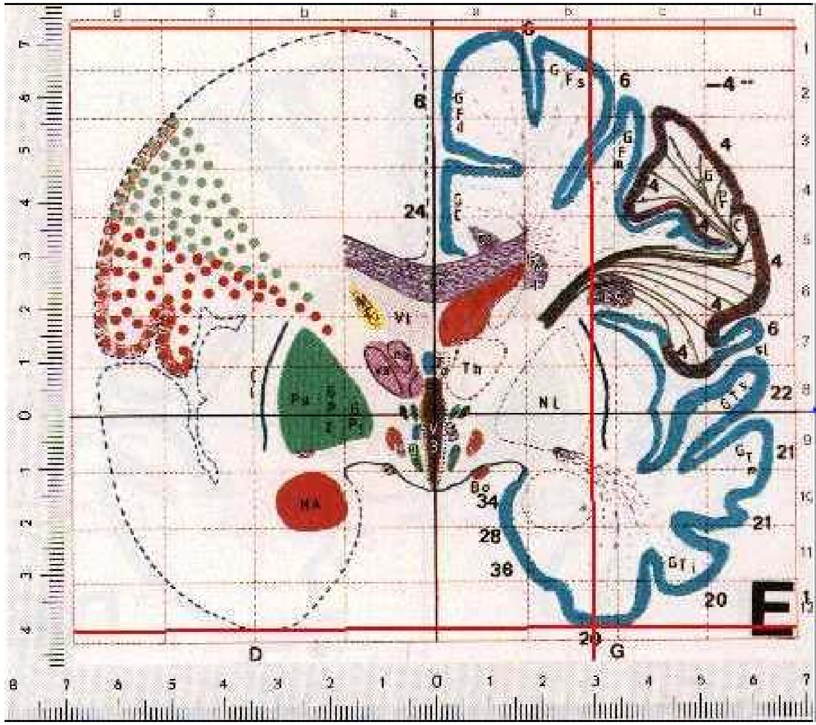
Voxel size
(volumetric pixel)

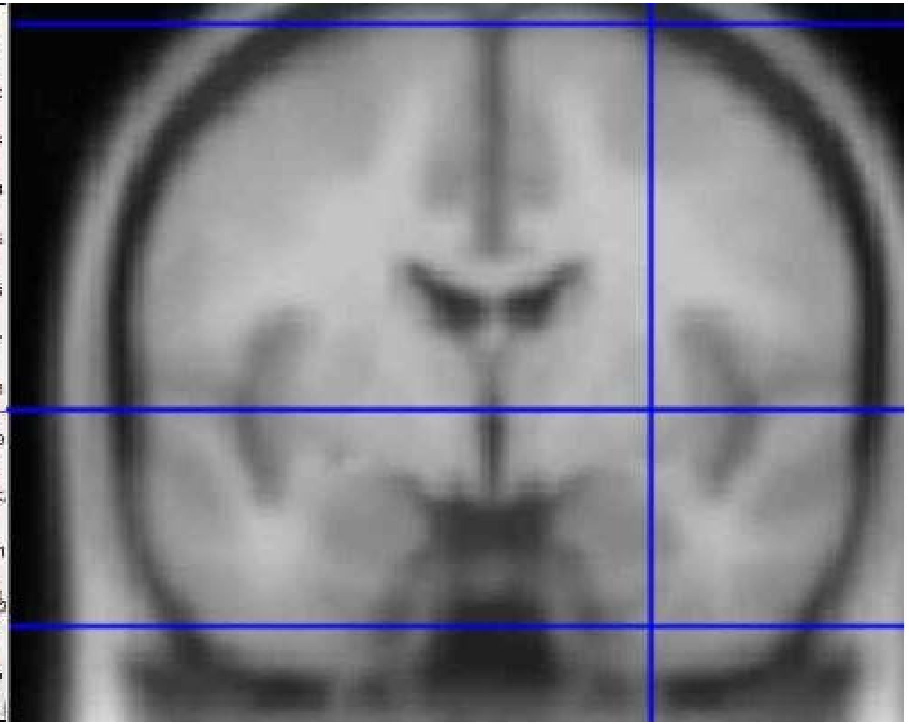
Standard space



The Talairach Atlas

The MNI/ICBM AVG152 Template





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