Extracting features from fMRI & other imaging/data modalities

Christophe Phillips

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Overview

fMRI data

- Introduction
- “Brain decoding” problem
- “Subject prediction” problem
- Conclusion

Other imaging & data modalities

- Introduction
- PET data
- Diffusion-weighted MRI
- MEG/EEG/electrophysiological data
- Behavioural & clinical scores
- Conclusion

Overview

fMRI data

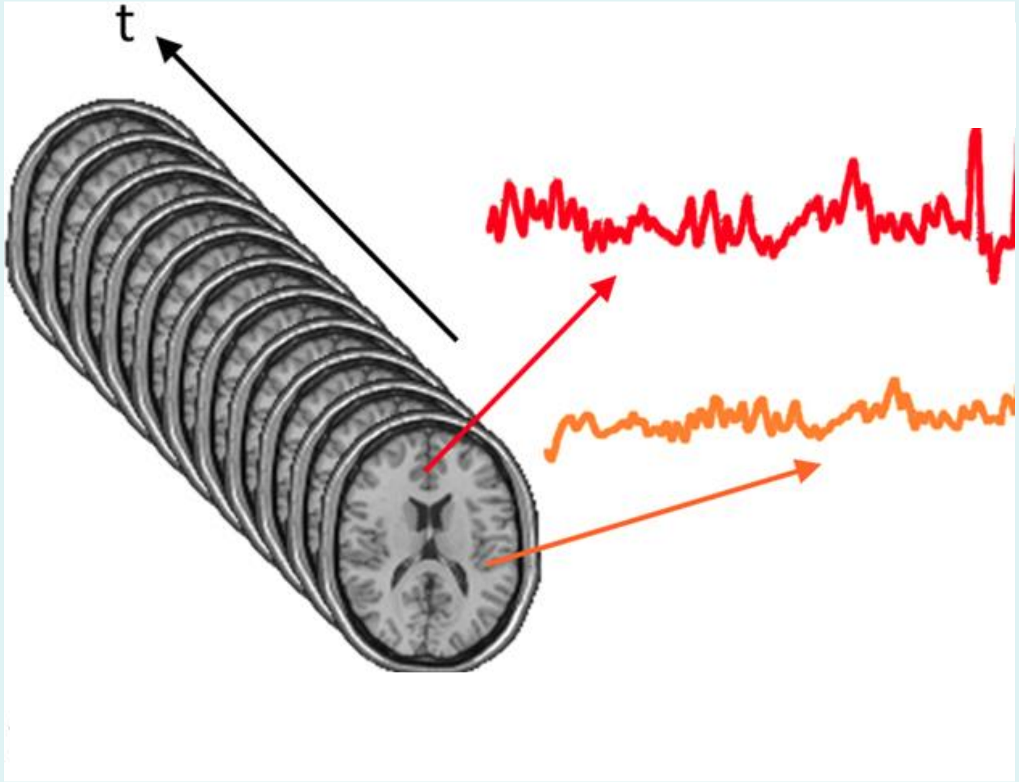
- Introduction
  - fMRI data & processing
  - GLM & BOLD response
  - classical univariate approach
  - levels of inference
- “Brain decoding” problem
- “Subject prediction” problem
- Conclusion

Other imaging & data modalities

fMRI data

fMRI time series

= 4D image
= 3D array of time series → voxel-based
= time series of 3D fMRI's → volume-based



Spatial pre-processing & SPM

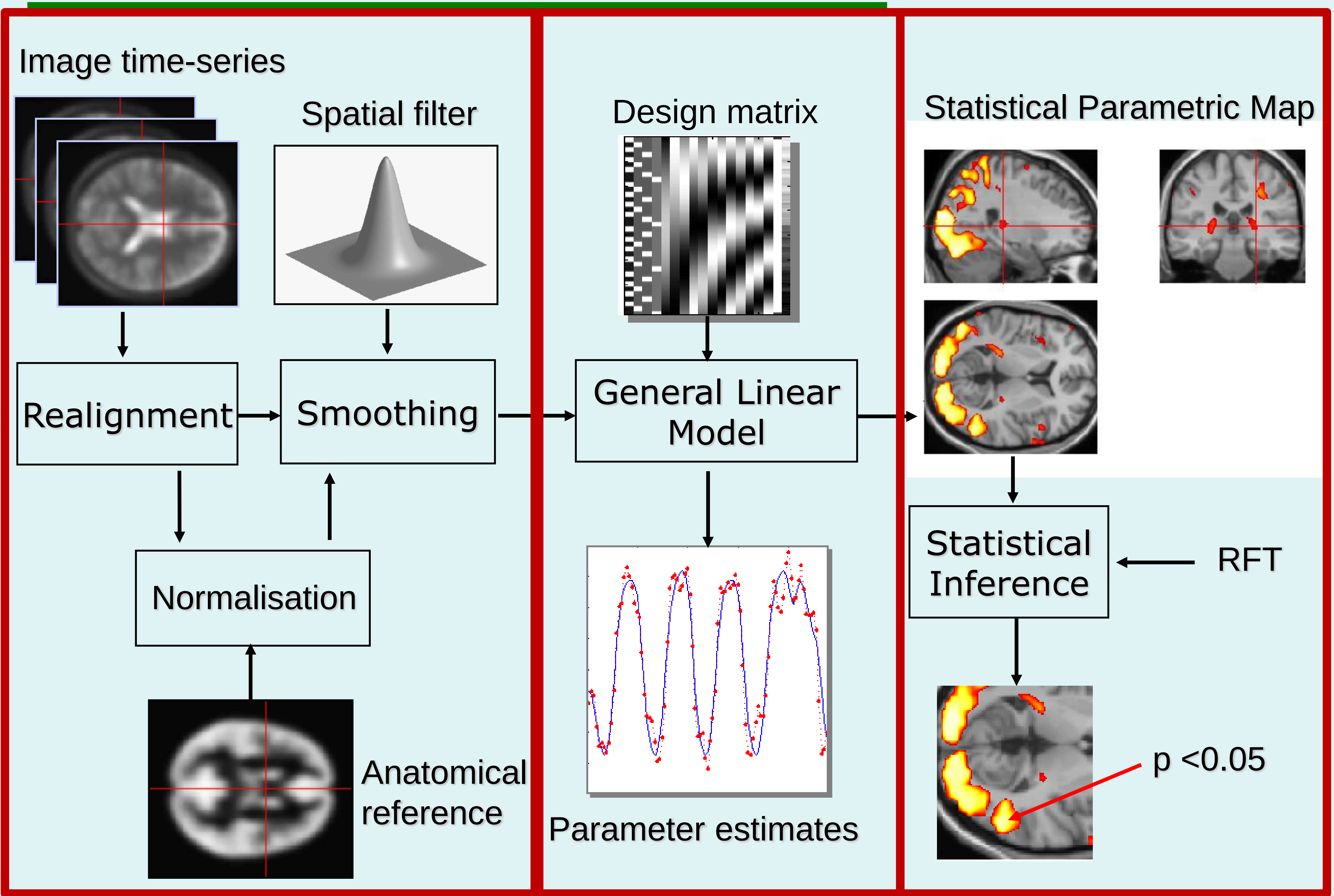


Image time-series

Spatial filter

Realignment

Smoothing

Normalisation

Anatomical reference

Design matrix

General Linear Model

Parameter estimates

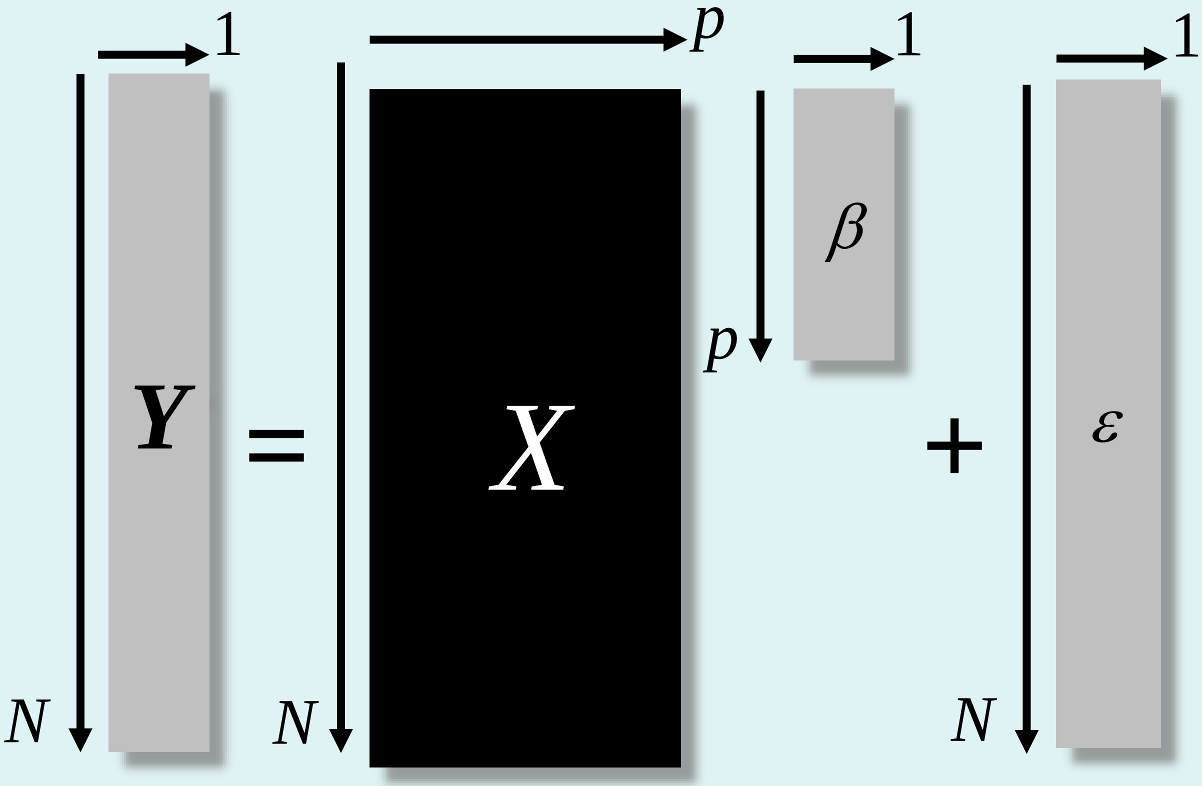
Statistical Parametric Map

Statistical Inference

RFT

$p < 0.05$

GLM *univariate* approach



$$\boxed{Y = X\beta + \varepsilon}$$

N: # images

p: # regressors

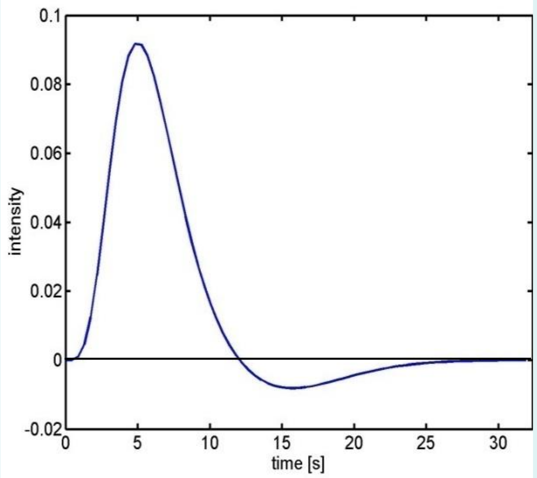
GLM defined by:

- design matrix X
- error term ε distribution, e.g.

$$\boxed{\varepsilon \sim N\left(0, \sigma V\right)}$$

BOLD response

Hemodynamic response function (HRF):



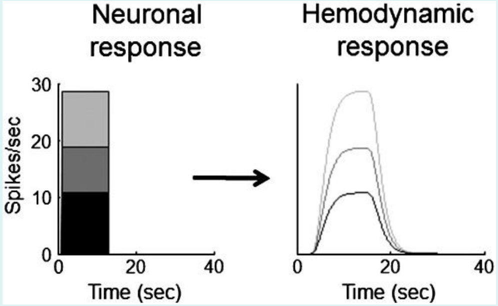
Linear time-invariant (LTI) system:

$$u(t) \longrightarrow \boxed{hrf(t)} \longrightarrow x(t)$$

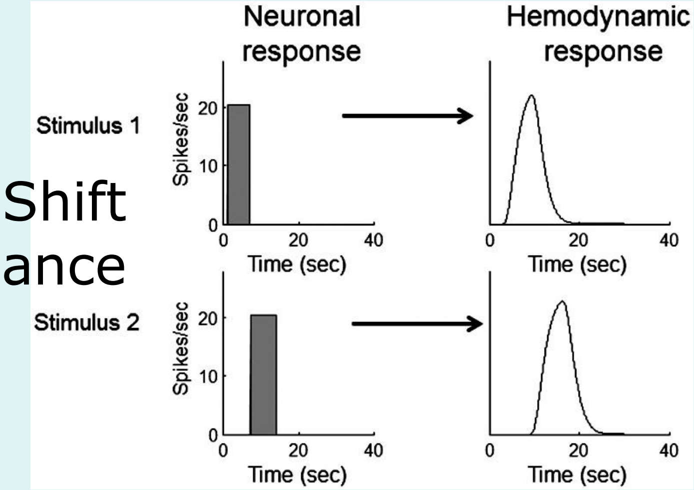
Convolution operator:

$$\begin{aligned} x(t) &= u(t) * hrf(t) \\ &= \int_{o}^{t} u(\tau) hrf(t-\tau) d\tau \end{aligned}$$

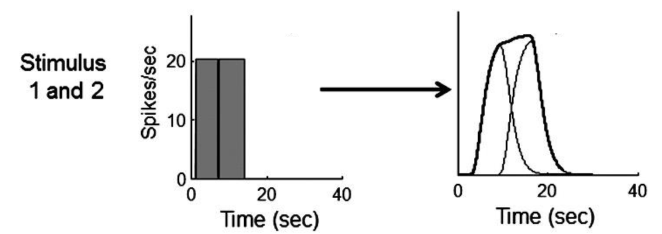
Scaling



Shift invariance



Additivity

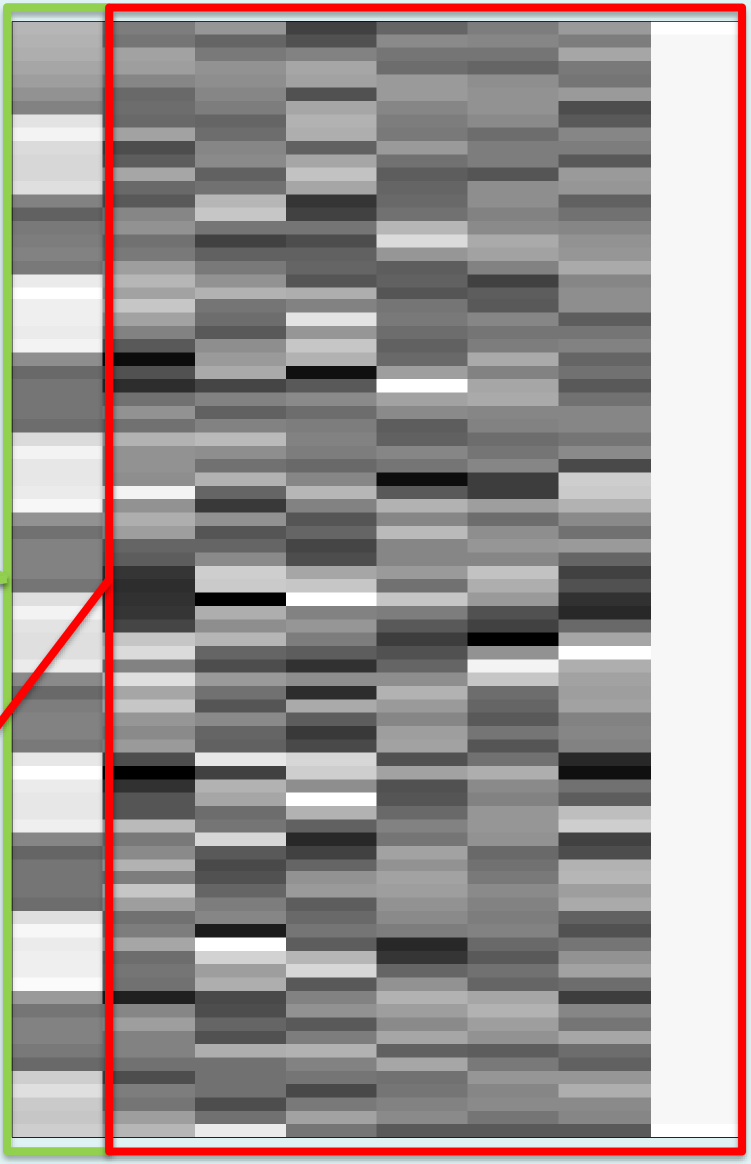


Boynton et al, NeuroImage, 2012.

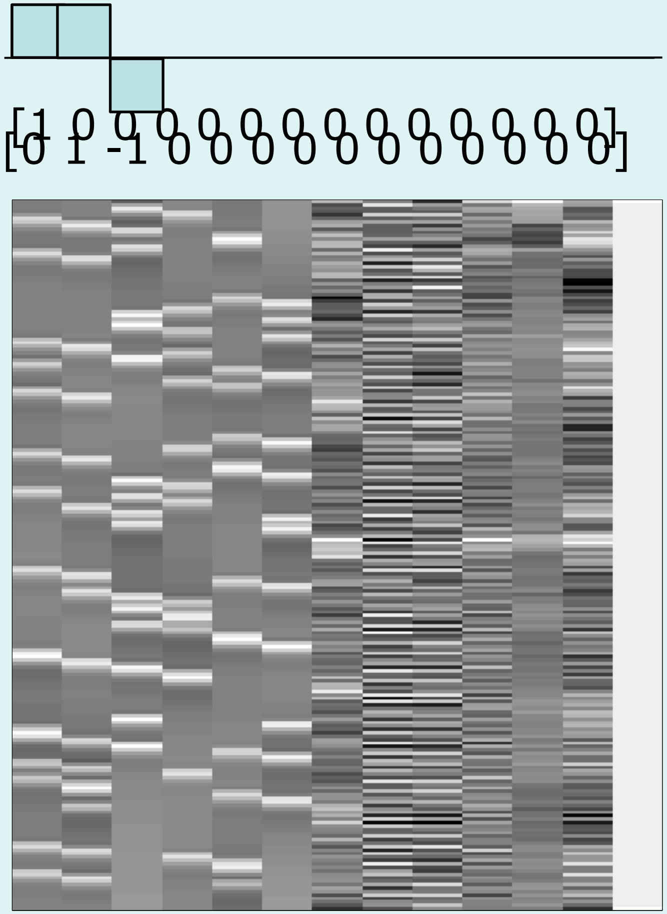
Confounds modelling

Model

- condition(s) of interest, i.e. "activation"
- "confounds":
  - BOLD hrf
  - Nuisance regressors, e.g. estimated movement parameters + constant



Contrast & inference



A contrast selects a **specific effect of interest**.

- ⇨ A contrast c is a vector of length p.
- ⇨ $c^T\beta$ is a linear combination of regression coefficients β.

$$c = [1\ 0\ 0\ 0\ \ \ldots]^T$$

$$c^T\beta = \mathbf{1} \times \beta_1 + \mathbf{0} \times \beta_2 + \mathbf{0} \times \beta_3 + \mathbf{0} \times \beta_4 + \cdots$$

$$= \boldsymbol{\beta_1}$$

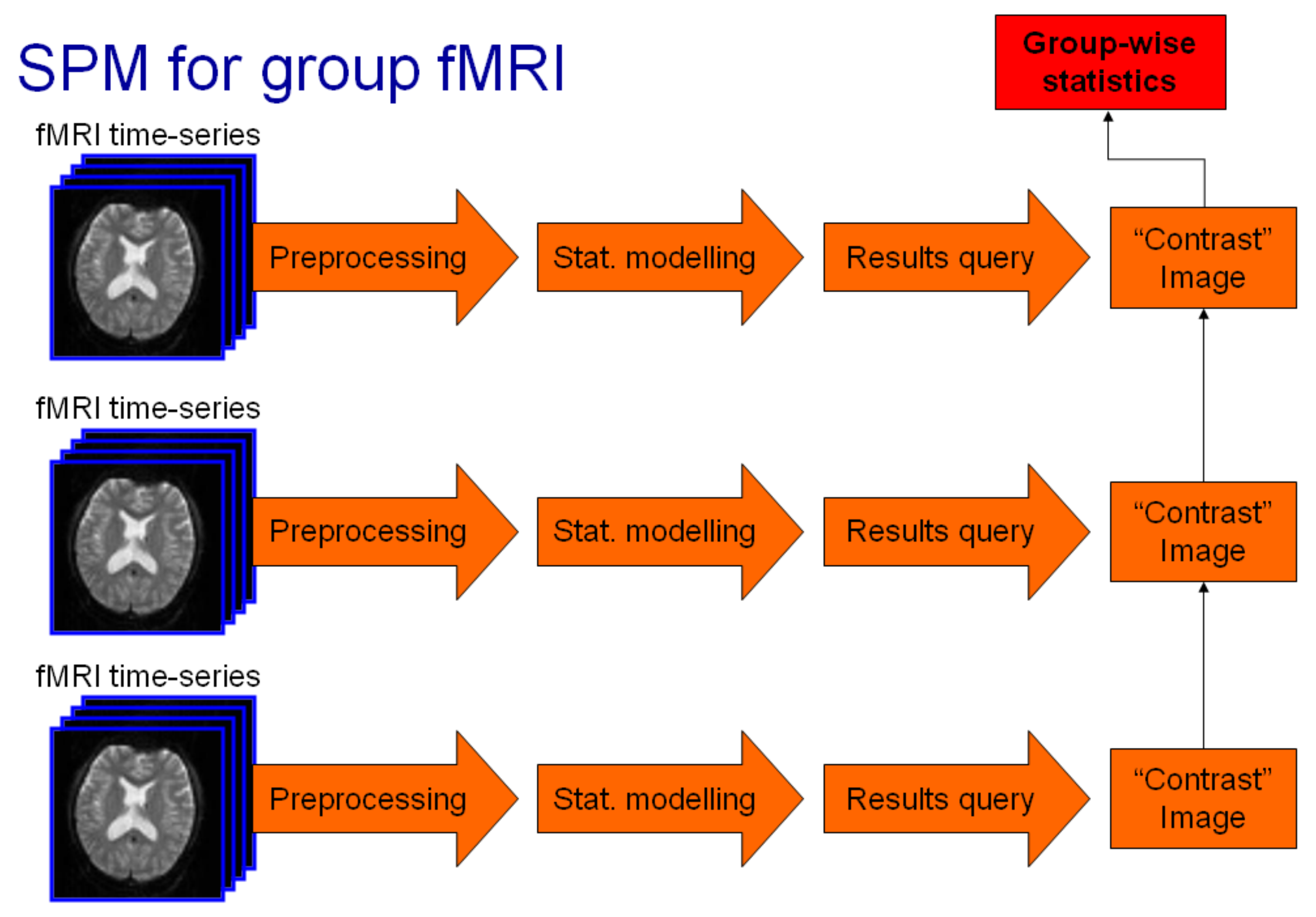
$$c = [0\ 1\ \ -1\ 0\ \ \ldots]^T$$

$$c^T\beta = \mathbf{0} \times \beta_1 + \mathbf{1} \times \beta_2 + \mathbf{-1} \times \beta_3 + \mathbf{0} \times \beta_4 + \cdots$$

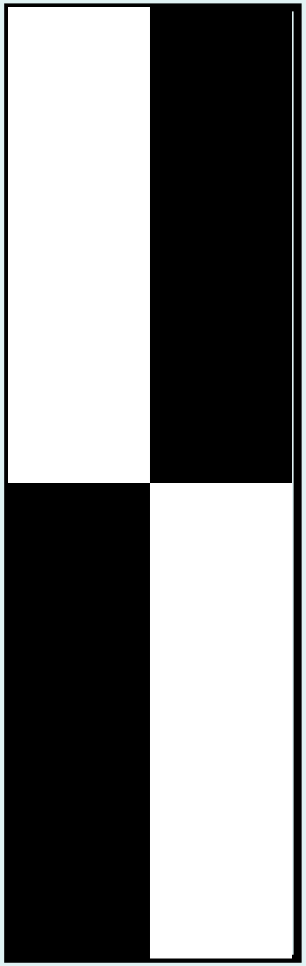
$$= \boldsymbol{\beta_2 - \beta_3}$$

$$\boxed{c^T\hat{\beta} \sim N(c^T\beta, \sigma^2 c^T (X^T X)^{-1} c)}$$

Group-level analysis

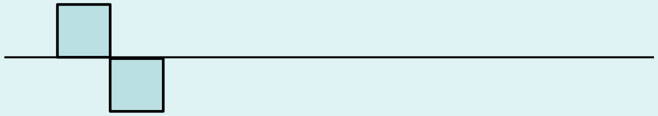


Group A vs. Group B design

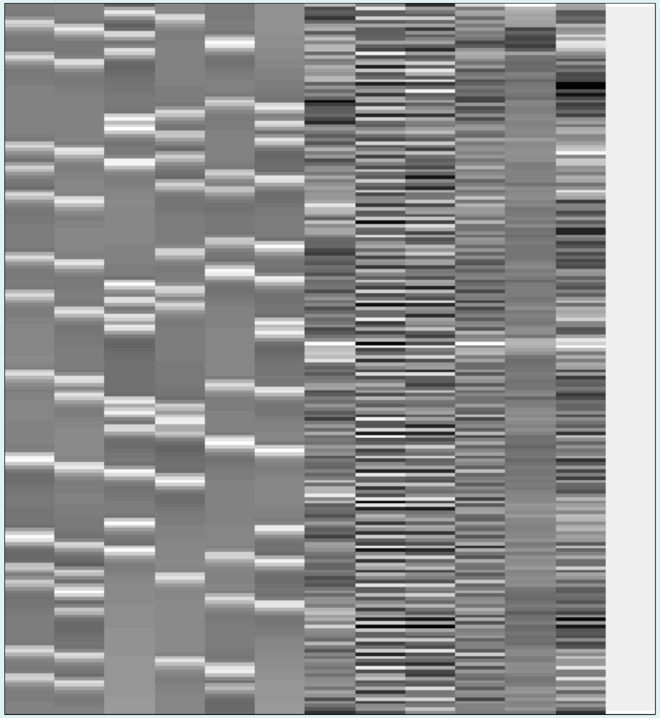


"Summary statistics" approach.

Contrast & inference



[0 1 -1 0 0 0 0 0 0 0 0 0 0]



Question: β_2 larger than β_3 ?

=

$\beta_2 - \beta_3 = c^T\beta > 0$?

Null hypothesis: $H_0: c^T\beta = 0$

Test statistic: $T = \dfrac{\textbf{\textit{contrast} of estimated parameters}}{\sqrt{\textbf{variance estimate}}}$

$$T = \frac{c^T\hat{\beta}}{\sqrt{\mathrm{var}(c^T\hat{\beta})}} = \frac{c^T\hat{\beta}}{\sqrt{\hat{\sigma}^2 c^T\left(X^TX\right)^{-1}c}} \sim t_{N-p}$$

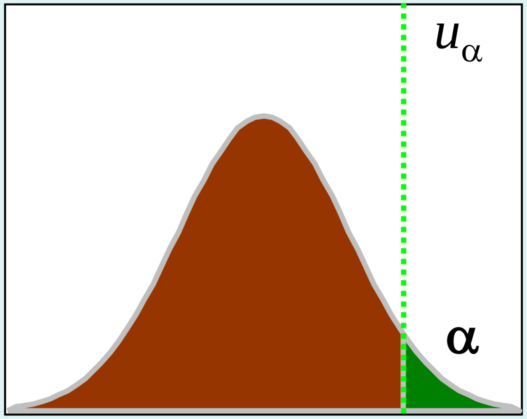
Classical inference

The Null Hypothesis H_0

= what we want to disprove (no effect).

⇨ The Alternative Hypothesis H_A

= outcome of interest.



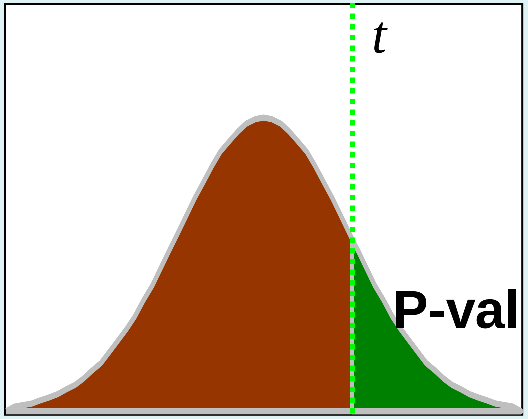
Null Distribution of T

Significance level α:

Acceptable *false positive rate α*.

⇨ threshold u_α

$$\alpha = p(T > u_\alpha \mid H_0)$$



Null Distribution of T

Observation of test statistic t

= a realisation of T

⇨ Reject H_0 in favour of H_A if $t > u_\alpha$

p-value = evidence against H_0

$$\boxed{p(T > t \mid H_0)}$$

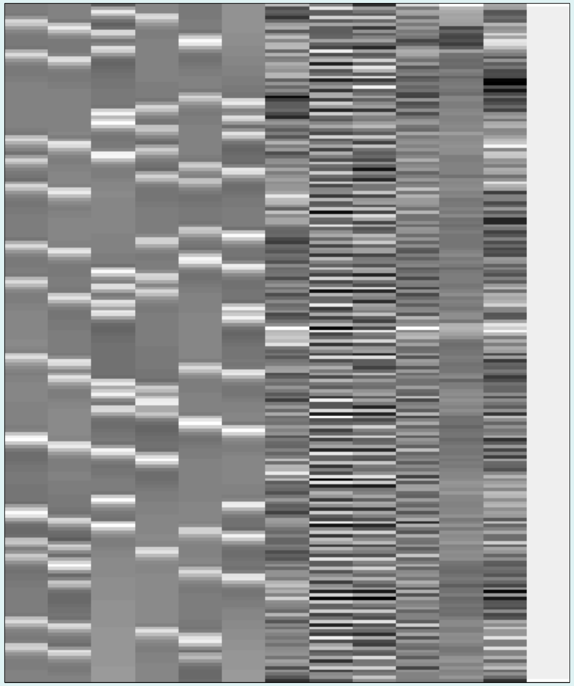
Overview

fMRI data

- Introduction
- “Brain decoding” problem
  - BOLD signal & HRF
  - Raw signal
  - Beta images
- “Subject prediction” problem
- Conclusion

Other imaging & data modalities

Brain decoding



Data:

fMRI volumes time series from 1 (or a few) subject(s)

Goal:

Find temporary mental state, from fixed set, of a subject based on pattern of brain activity.

➔ decode BOLD signal over 1 or few images

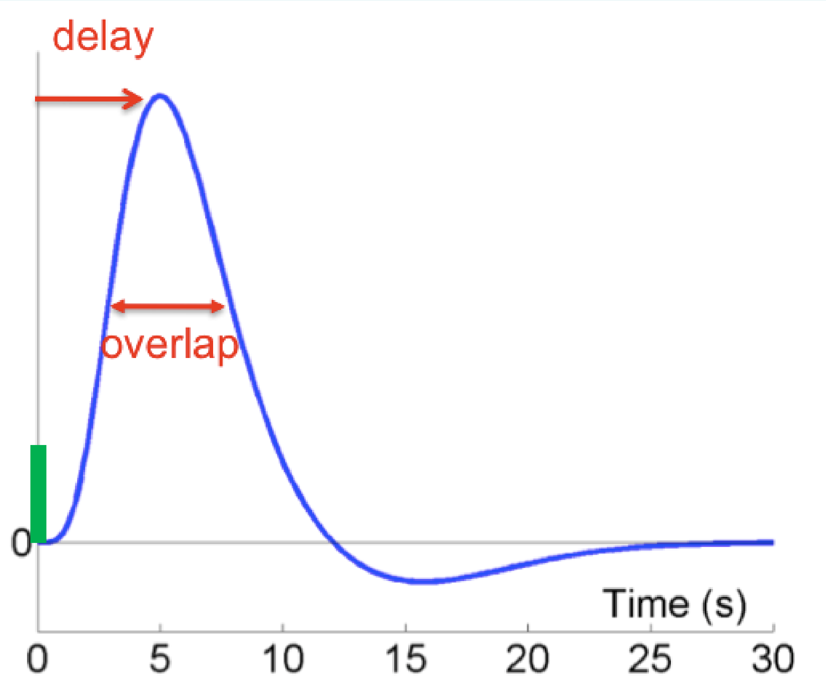
Similar to FFX analysis

Brain decoding: signal

Use the raw BOLD signal but

- Block or event-related design?
- How to account for haemodynamic function?

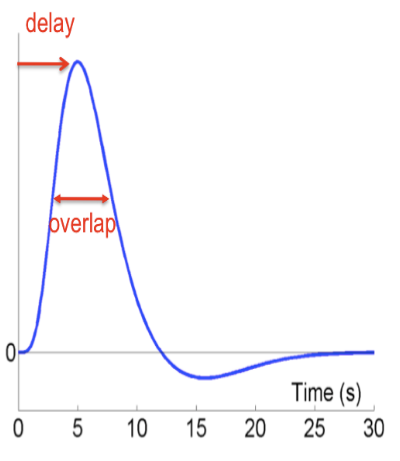
Standard impulse response function ➔

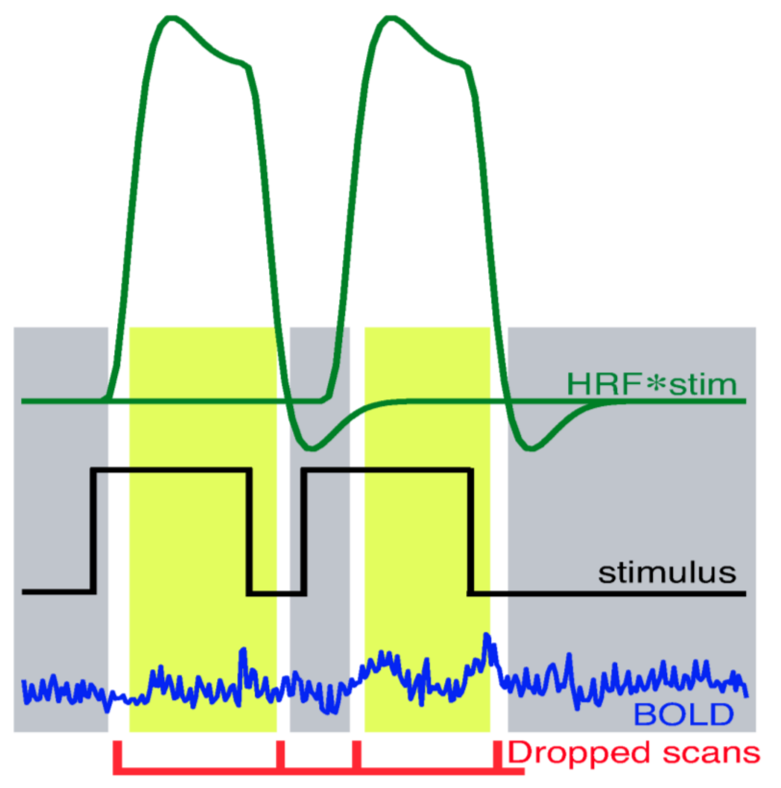


Brain decoding: raw BOLD

Design:

- Block or event-related design
- Accounting for haemodynamic function, with HRF ‘*delay*’ & ‘*overlap*’

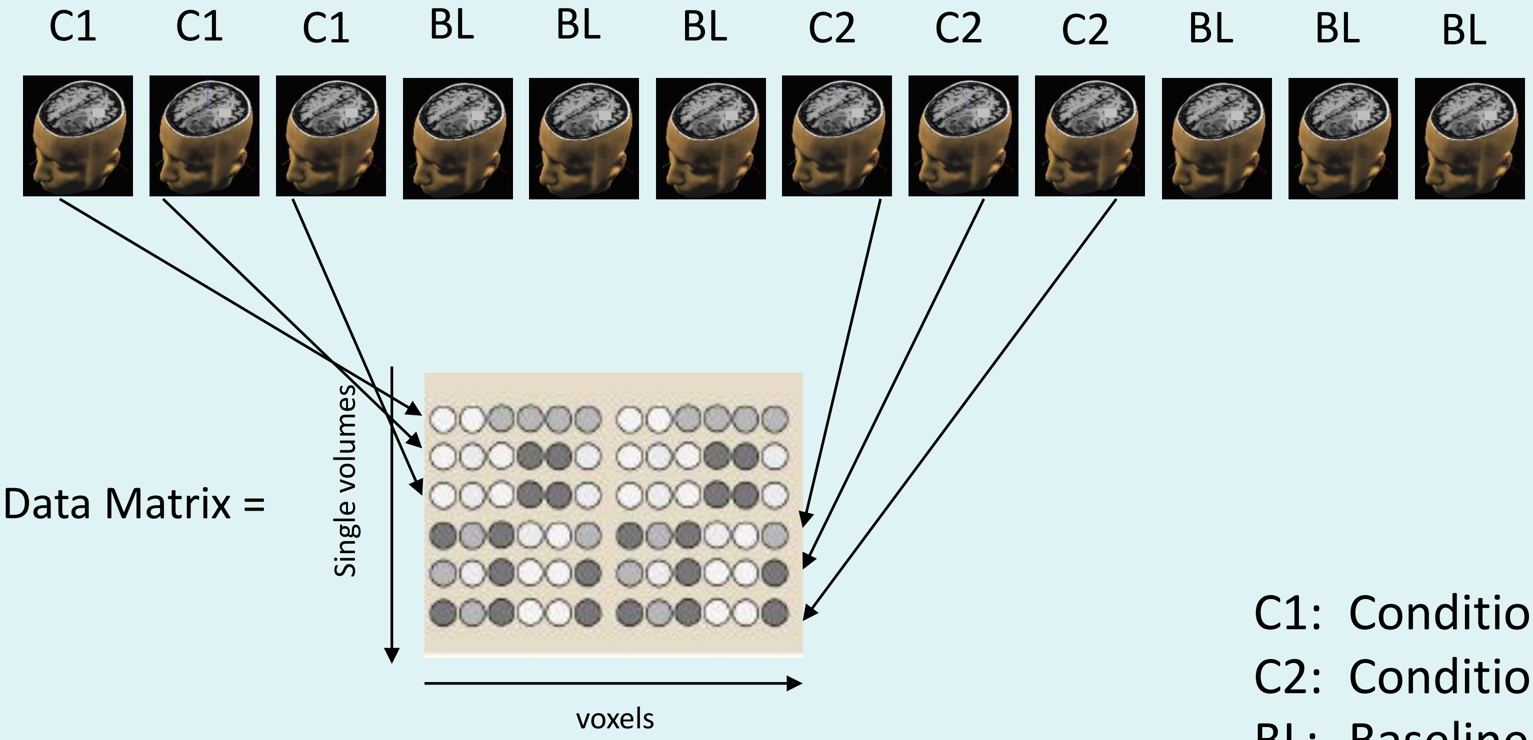




Brain decoding: raw BOLD

Design:

- Block design
- Use single scans



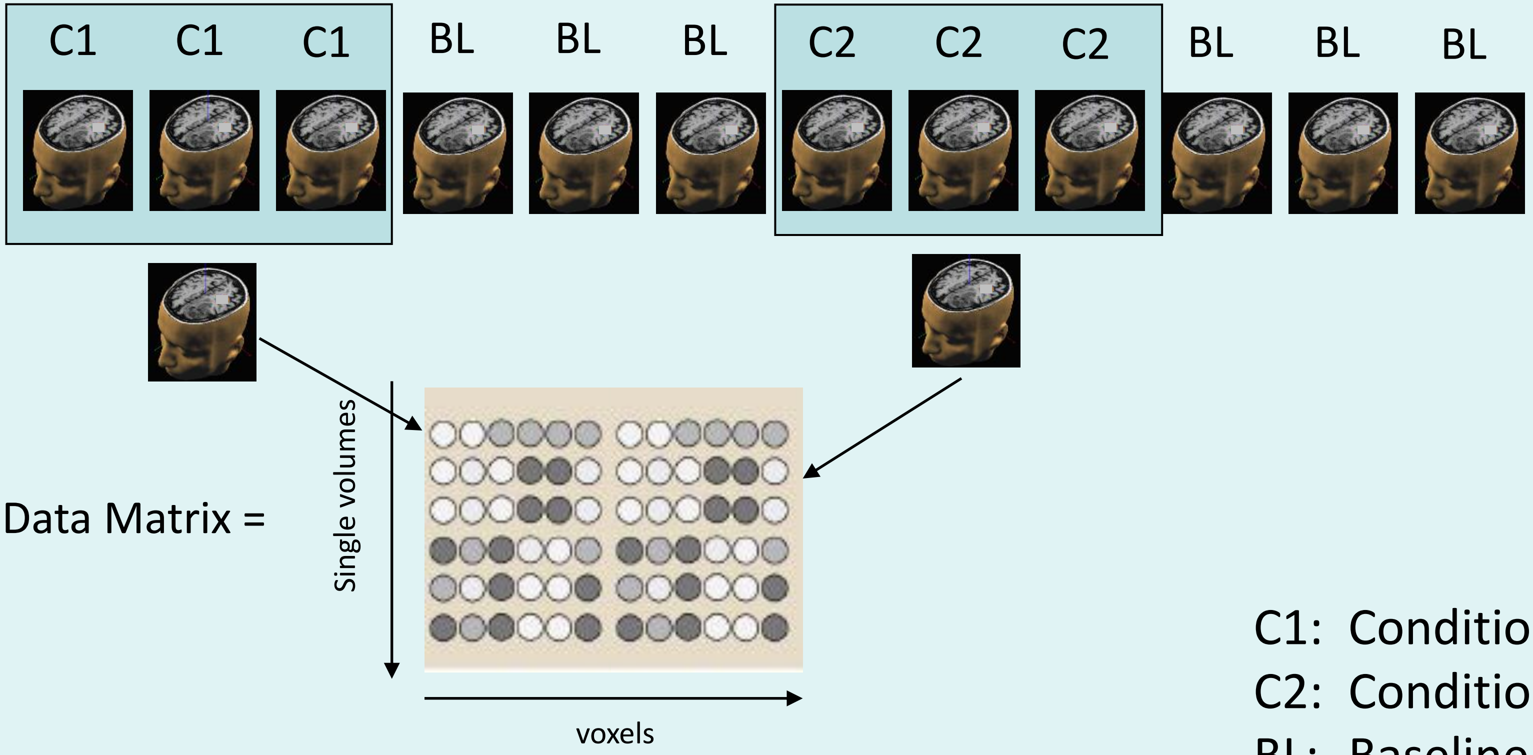
C1: Condition 1
C2: Condition 2
BL: Baseline

Brain decoding: raw BOLD

Design:

- Block design
- Use single scans

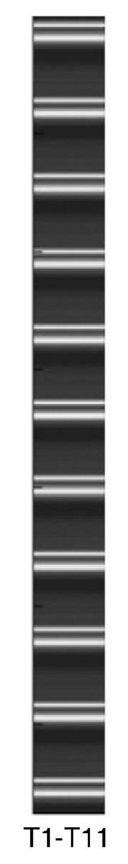
➔ **Average scans** over blocks/events



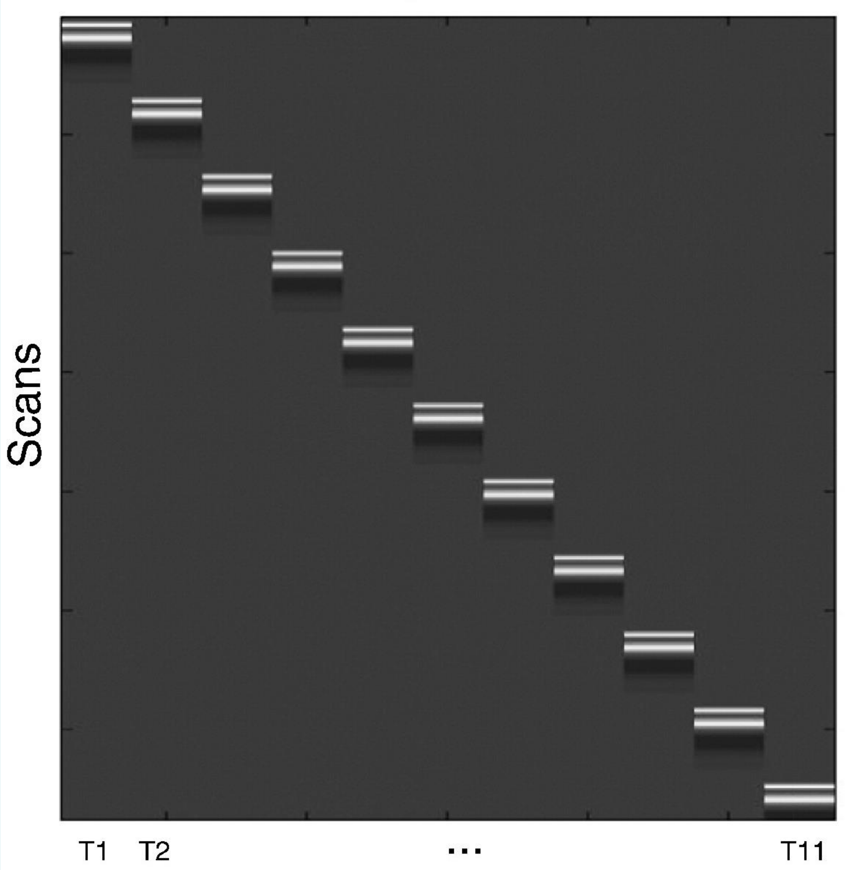
C1: Condition 1
C2: Condition 2
BL: Baseline

Brain decoding: beta image

GLM with each event/block as a different "condition"
⇒ 1 beta per event/block



LSA



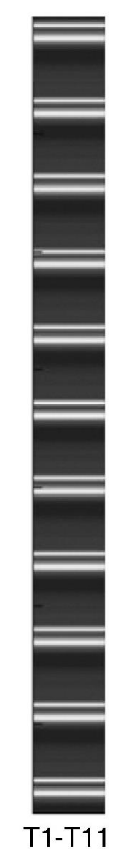
LSU

"Least Squares All" (LSA) and
"Least Squares Unitary" (LSU)

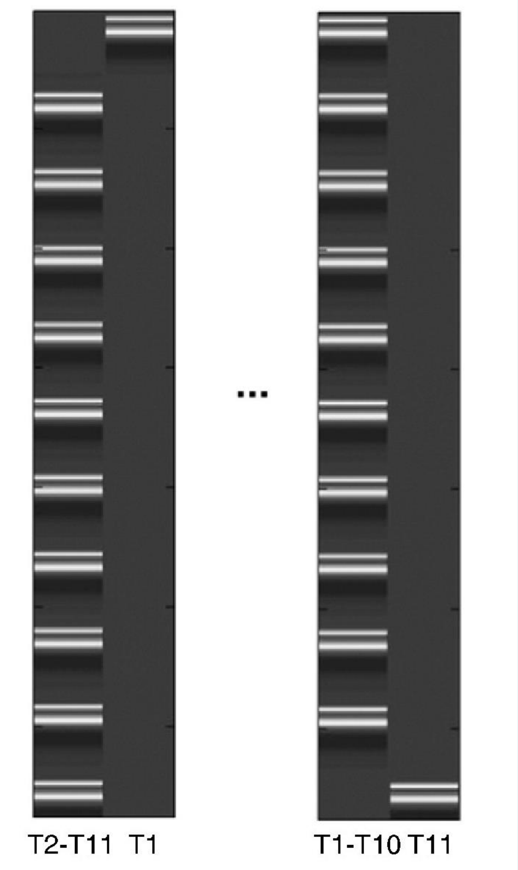
Abdulrahman & Henson, Neuroimage, 2016

Brain decoding: beta image

1 GLM per “targeted” event/block
⇒ 1 beta per event/block



LSA



LSS

“Least Squares All” (LSA) and
“Least Squares Separate” (LSS)

Abdulrahman & Henson, Neuroimage, 2016

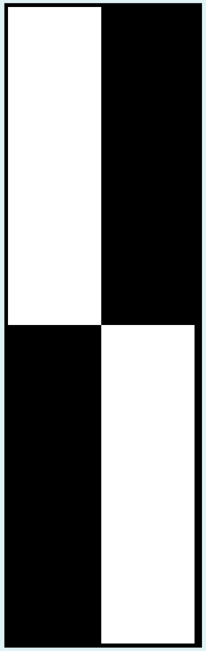
Overview

fMRI data

- Introduction
- "Brain decoding" problem
- "Subject prediction" problem
  - Definition & summary approach
  - Event/block design
  - Resting state design
- Conclusion

Other imaging & data modalities

Subject prediction



Data:

N subjects 1 (or a few) image(s) per subject

Goal:

Find target value (class or score) of a subject based on pattern from many subjects.

➔ decode "summary" image(s) per subject

Similar to RFX analysis

Subject prediction: summary image

fMRI time series

➔ summary image

Event/block design

➔ build contrast image(s)

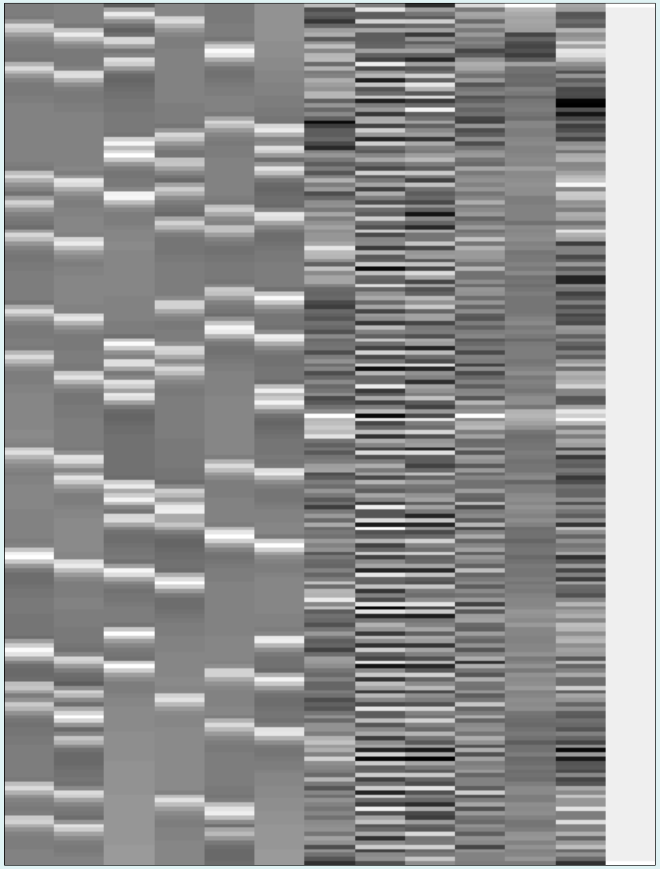
e.g.

- main/average effect,
  `[1 0 0…]` or `[0 1 1 0…]/2`
- difference between 2 conditions
  `[1 0 -1 0…]`
- …

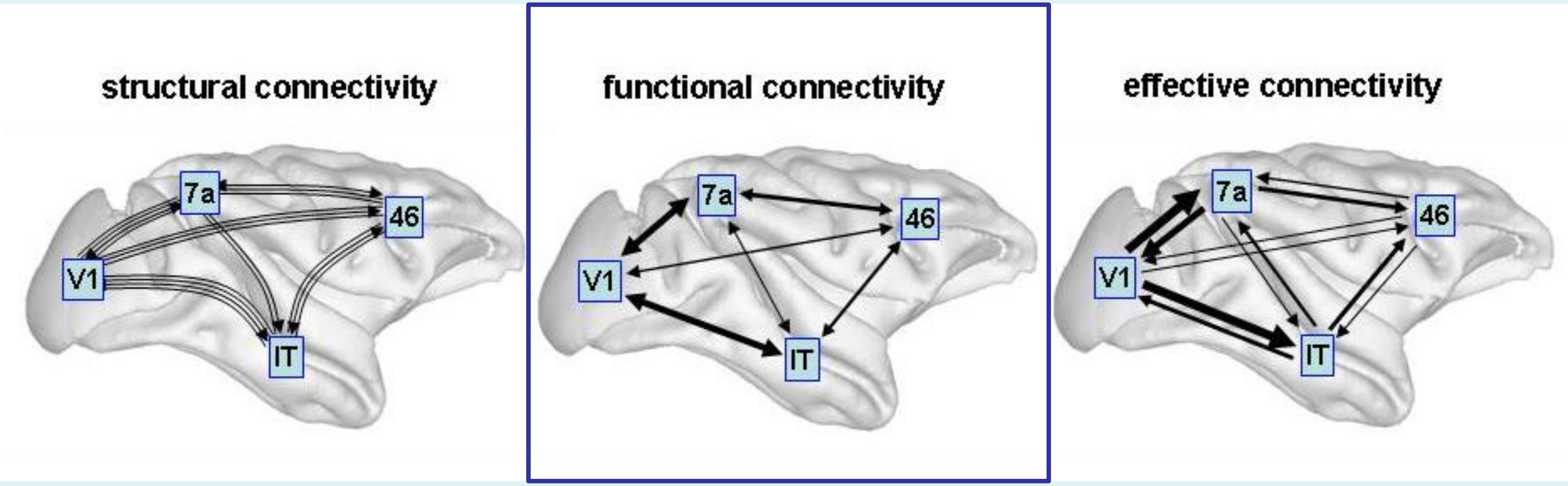
`[1 0 -1 0…]`

`[1 0 0…]`

`[0 1 1 0…]/2`



Brain connectivity



Functional connectivity = statistical concept

Statistical dependence estimated by measuring *correlation* or *covariance*

http://www.scholarpedia.org/article/Brain_connectivity

Resting state fMRI

Resting state functional MRI […] is a […] method for evaluating regional interactions that occur when a subject is not performing an explicit task.

Paradigm shift:

- Activation ➔ functional segregation
- Spontaneous ➔ functional integration

Goal:

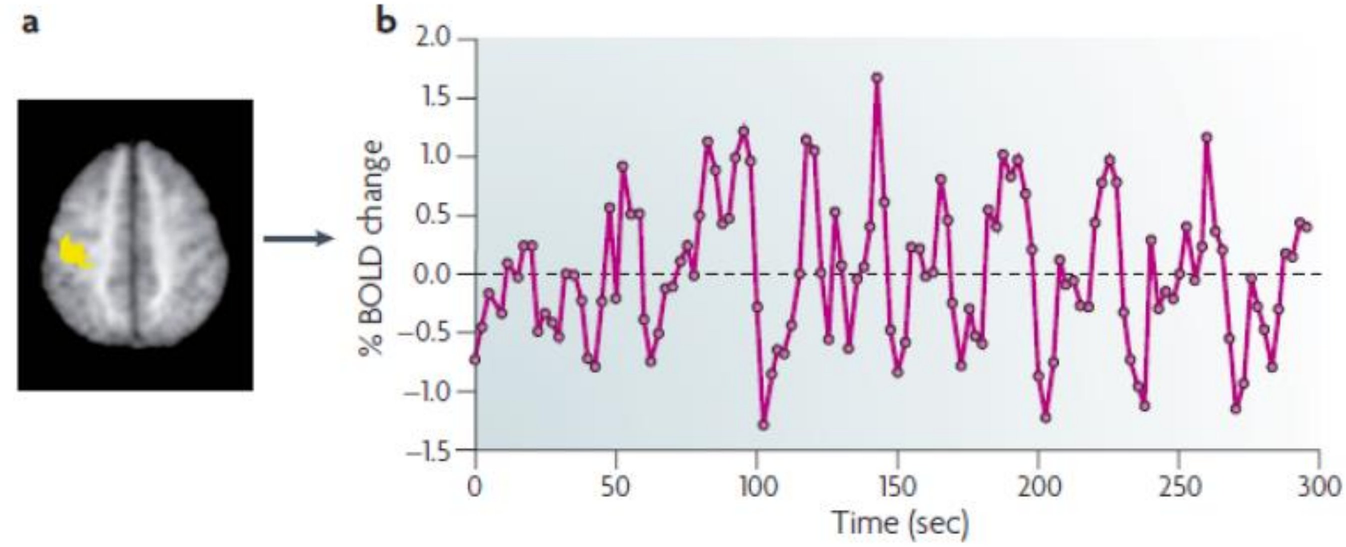
Summarize rs-fMRI time series into 1 (few) map(s).

https://www.humanconnectome.org/study/hcp-young-adult/project-protocol/resting-state-fmri

Rs-fMRI: model based approach

Pick one (few) region(s) of interest:

- Extract BOLD signal time-series



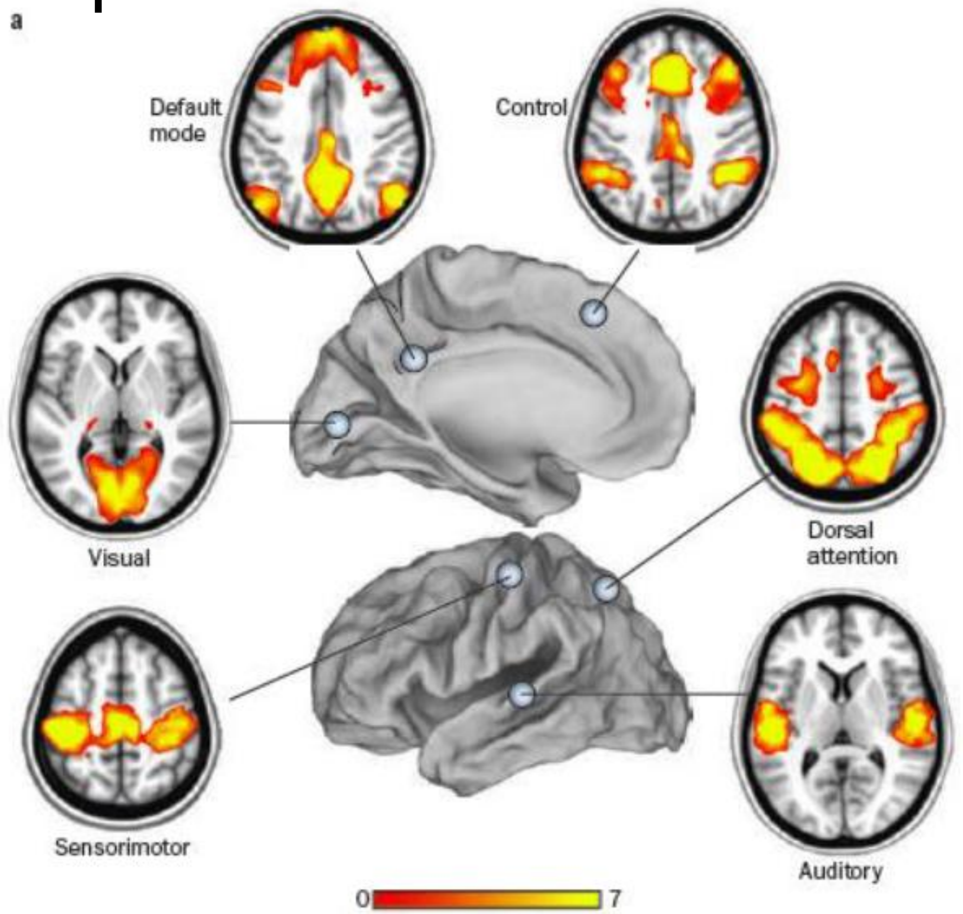
Fox & Raichle, 2007, *Nature Reviews, Neuroscience*

- Enter time series (+confounds) as regressor in a GLM & find correlation map

Rs-fMRI: model based approach

Multiple/different region of interest

➔ multiple/different maps



Zhang & Raichle, 2010, *Nature Reviews, Neurology*

Rs-fMRI: model free approach

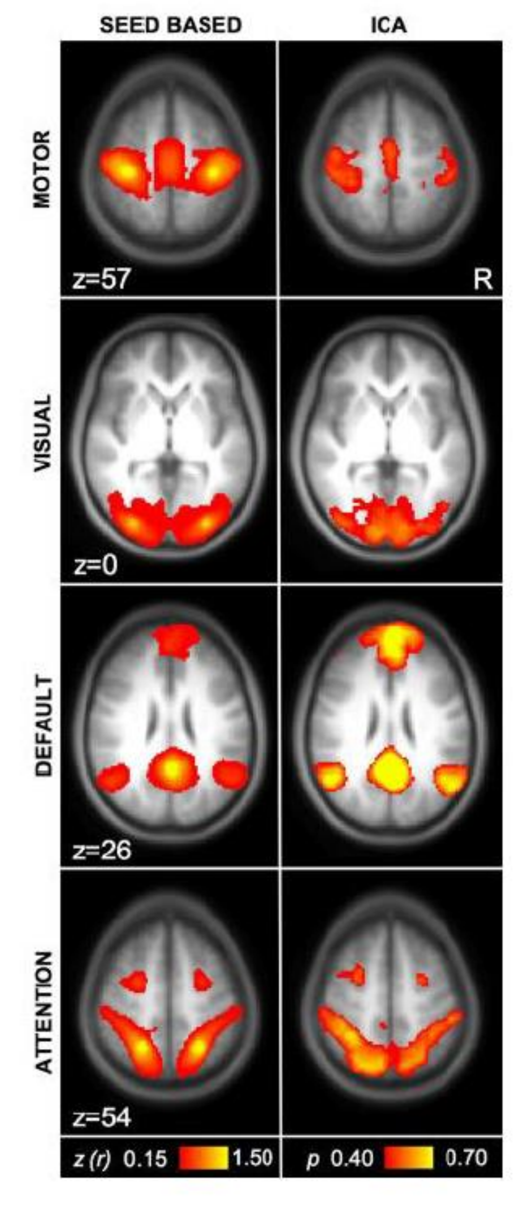
Decompose original fMRI time series into linear combination of

- basis vectors, PCA
- independent components, ICA

i.e. data driven approach.

➔ A few basis/component maps per subject

Rs-fMRI: model free approach



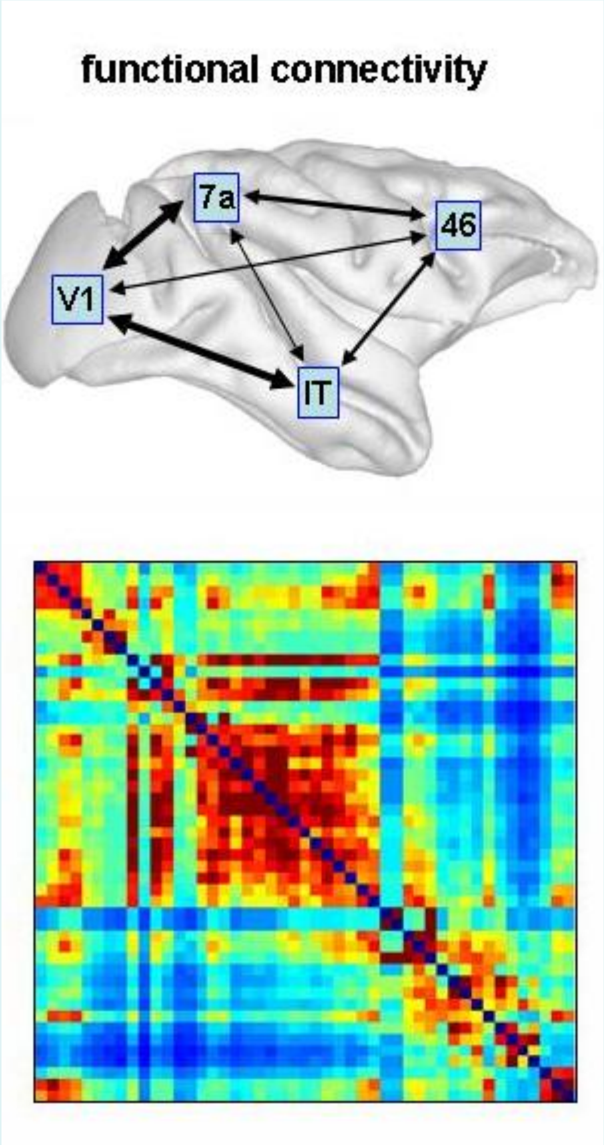
Van Dijk, 2010, *J Neurophysiol*

Connectomics

Typically

- atlas based with `N` ROIs
- extract `N` time series (cleaning?)
- estimate a `N x N` correlation matrix per subject

➔ create one `.mat` data file per subject



Overview

fMRI data

- Introduction
- “Brain decoding” problem
- “Subject prediction” problem
- **Conclusion**

Other imaging & data modalities

Conclusion

1 sample = 1 image or `.mat` file

- account for BOLD haemodynamic response for "brain decoding"
- summary image for "subject prediction"

Key questions:

- What is your question of interest?
- At what level of inference ?
- What is the experimental design?
- How much data is be available?

Overview

fMRI data

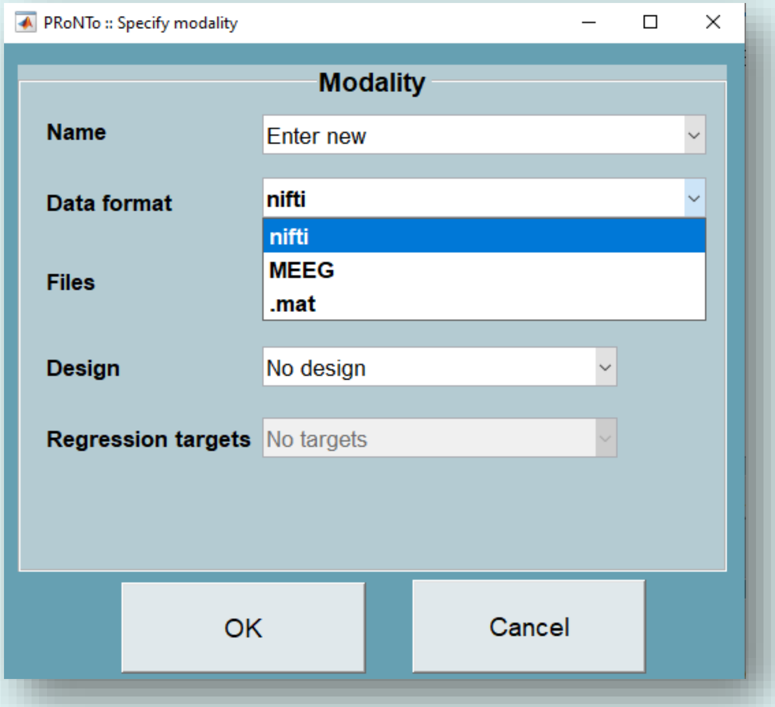
Other imaging & data modalities

- Introduction
- PET data
- Diffusion-weighted MRI
- MEG/EEG/electrophysiological data
- Behavioural & clinical scores
- Conclusion

Data format

Data input format for PRoNTo:

- any data in (2D or 3D) NIfTI image format
- SPM's `@meeg` data format for EEG/MEG/…
- Matlab array in a `.mat` file



Goal:

Make sure data are in appropriate format for your data!

https://nifti.nimh.nih.gov/

Overview

fMRI data

Other imaging & data modalities

- Introduction
- PET data
- Diffusion-weighted MRI
- MEG/EEG/electrophysiological data
- Behavioural & clinical scores
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PET imaging

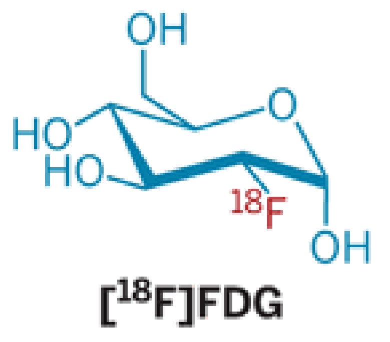
- Based on radioactive decay of radiotracer
- Radiotracer tracks a specific physiological process in the brain
- Typically clinical applications, e.g. Alzheimer or Parkinson diseases (AD or PD)
- Qualitative or quantitative values
- 1 (or few) scan(s) per subject

➔ “Subject prediction” problem

FDG-PET image

Example:

fluorodeoxyglucose (FDG)
PET image
➔ local glucose in-take



[^{18}F]FDG

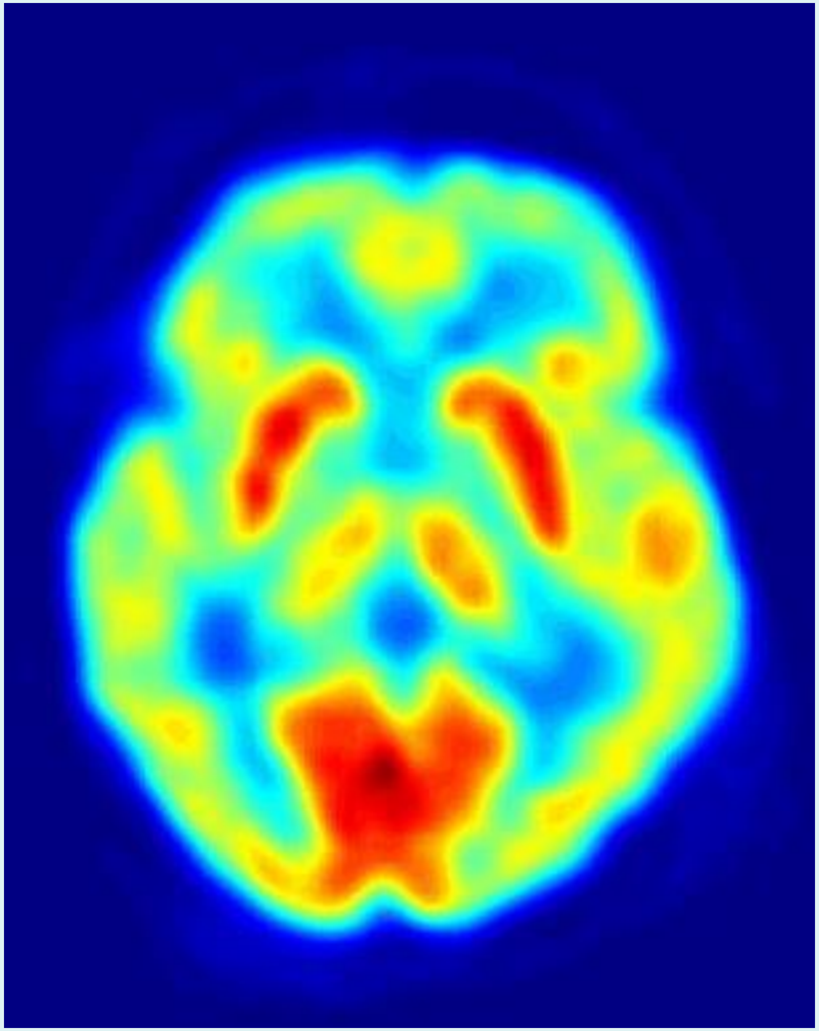


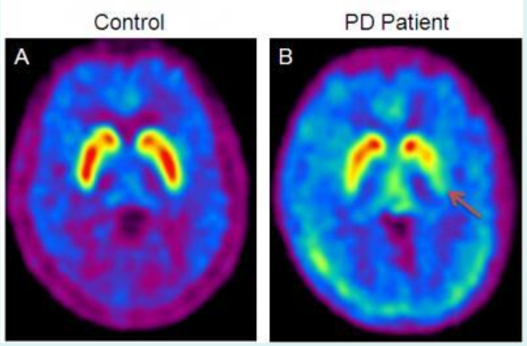
Image characteristics:

- physiological information
- blurry, i.e. limited anatomical information

PET imaging specificities

Things to worry about:

- Spatial alignment, i.e. normalization
  - ➔ easier with sMRI (dealt with in SPM)
- Intensity scaling if not quantitative values
  - ➔ local/extended disease effect ?
- Region of interest
  - ➔ limited "activated" area, still an "image"?



Fallypride antagonist to
dopamine receptors D2/D3
➔ Parkinson disease marker

Overview

fMRI data

Other imaging & data modalities

- Introduction
- PET data
- Diffusion-weighted MRI
  - basics
  - DTI & NODDI
  - connectomics
- MEG/EEG/electrophysiological data
- Behavioural & clinical scores
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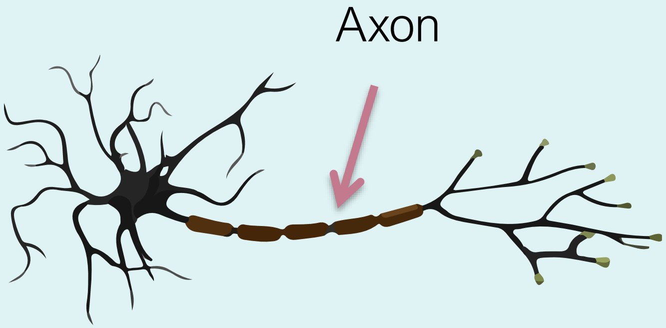
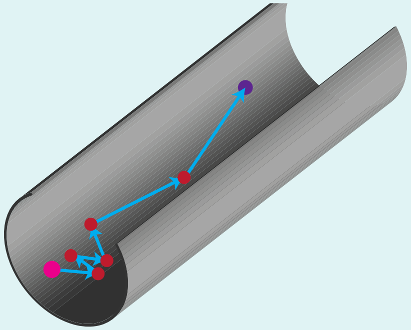
DW-MRI

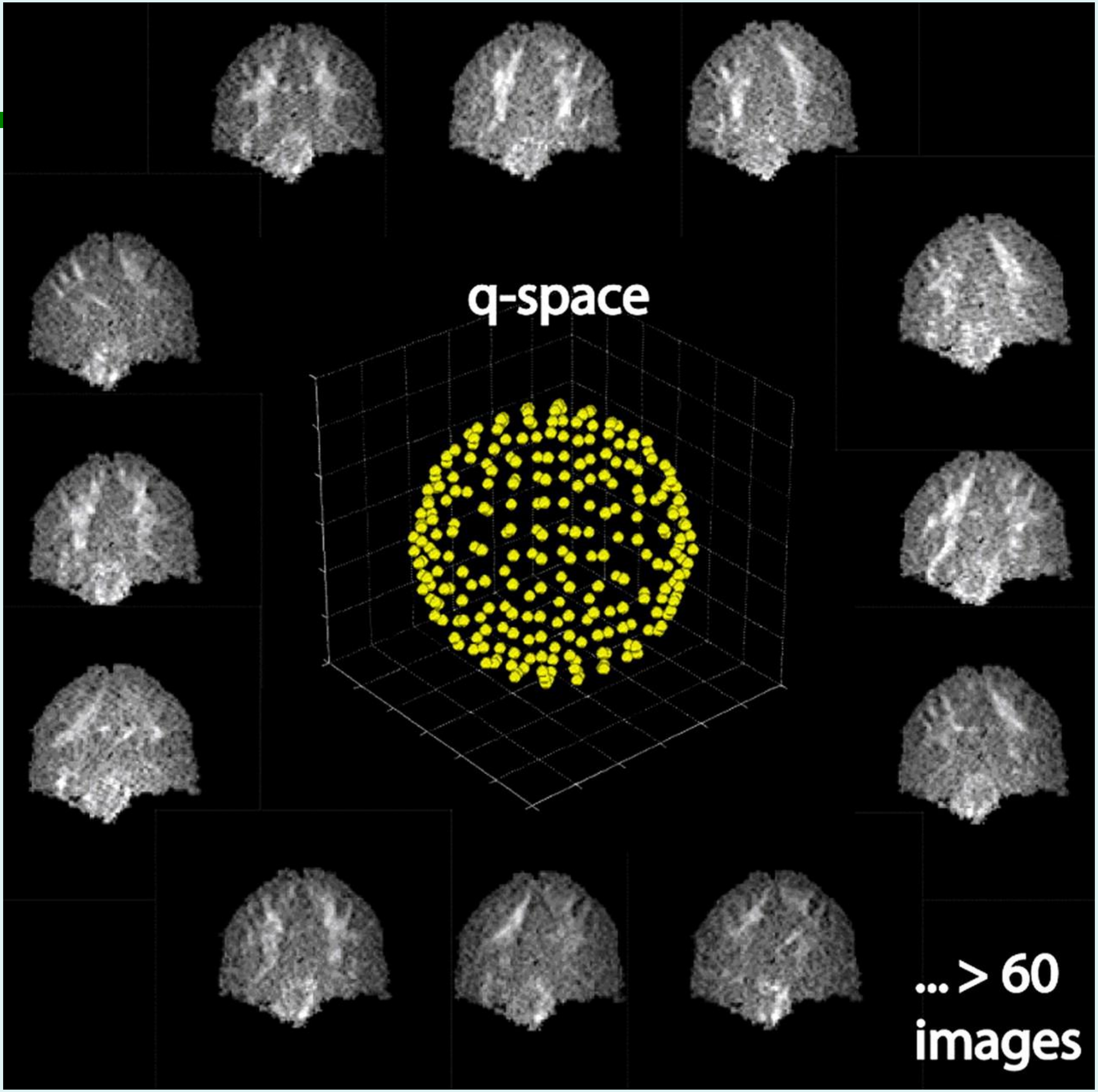
Signal $\propto$ 1/(water diffusion in brain tissue)

<u>Raw data:</u>

- N (>20) images
- 1 image = signal attenuation due to water-diffusion in 1 direction
- some images without diffusion (ref. signal)






q-space
... > 60 images

DW-MRI

Signal $\propto$ 1/(water diffusion in brain tissue)

<u>Raw data:</u>

- N (>20) images
- 1 image = signal attenuation due to water-diffusion in 1 direction
- some images without diffusion (ref. signal)

➔ Fit a model to the data

➔ One (or few) parametric image(s)

➔ “subject prediction” problem

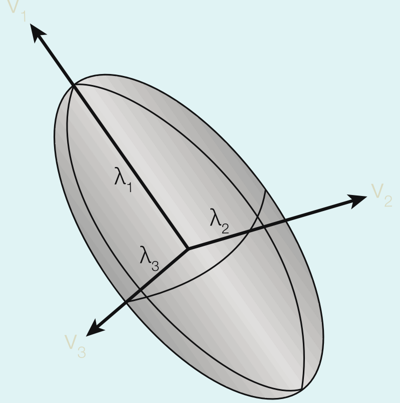
Diffusion Tensor Imaging

- Fit a tensor model at each voxel
- Derive scalar map(s)

➔ “interpretable” values,

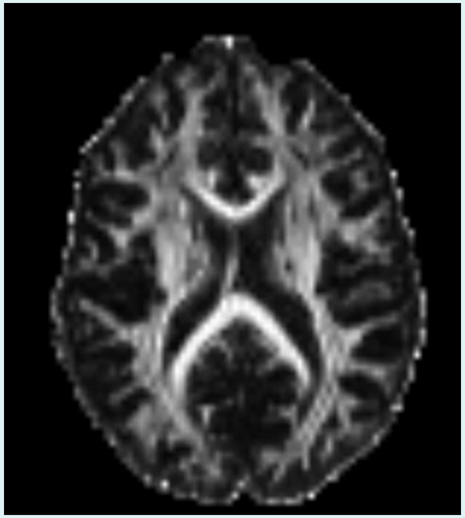
e.g. FA and MD

$$\begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{bmatrix}$$



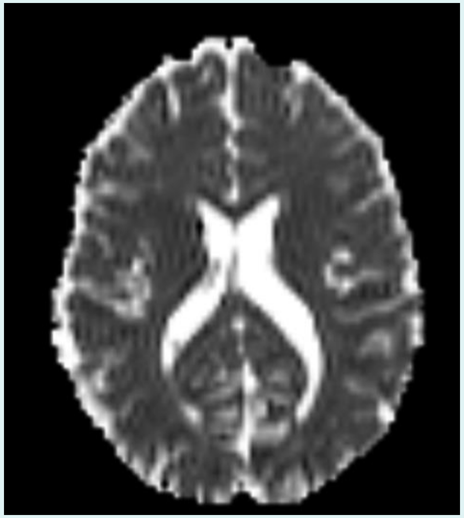
Tensor ellipsoid

Fractional anisotropy



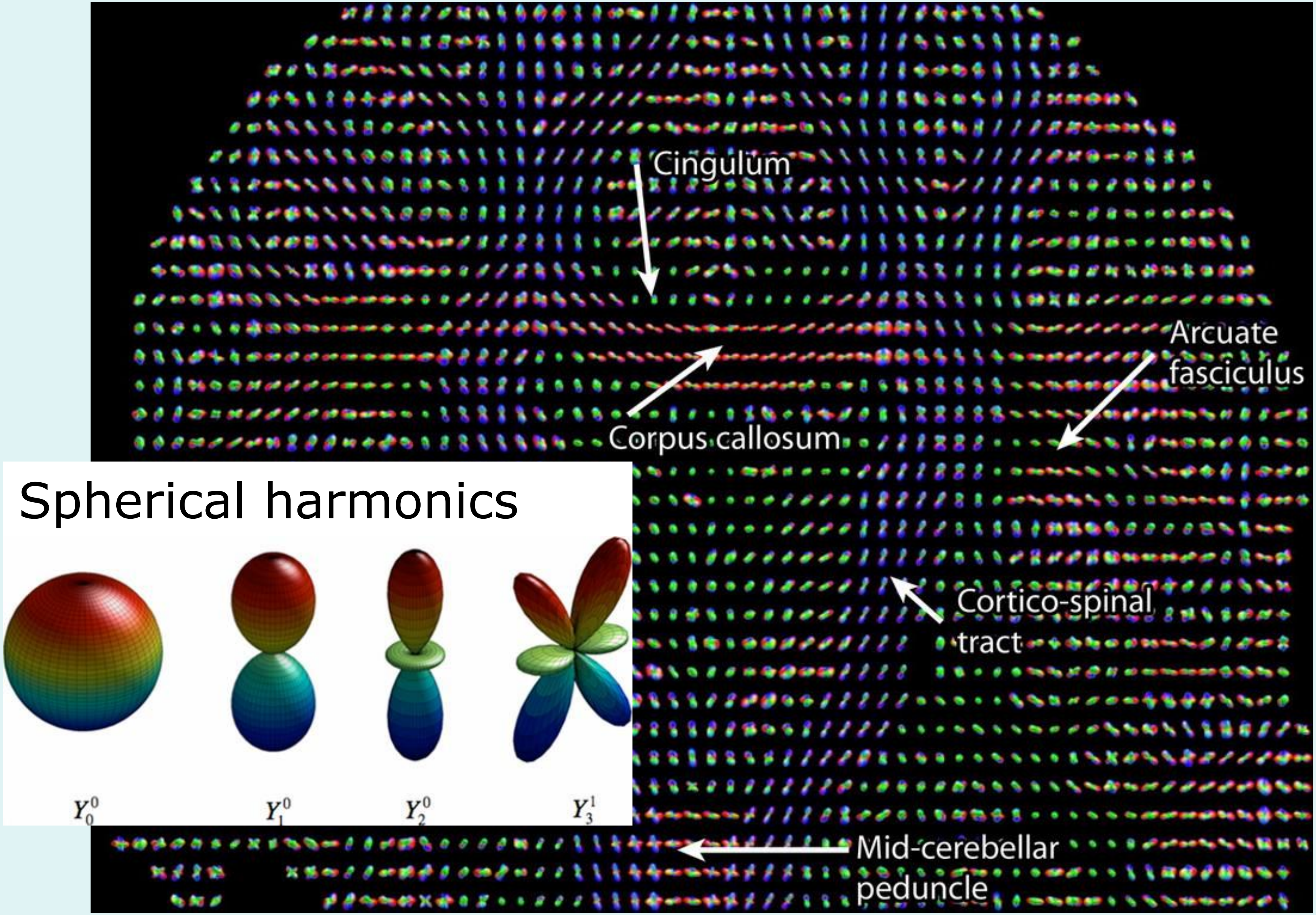
Reflects directionality of diffusion

Mean diffusivity



Reflects strength of diffusion

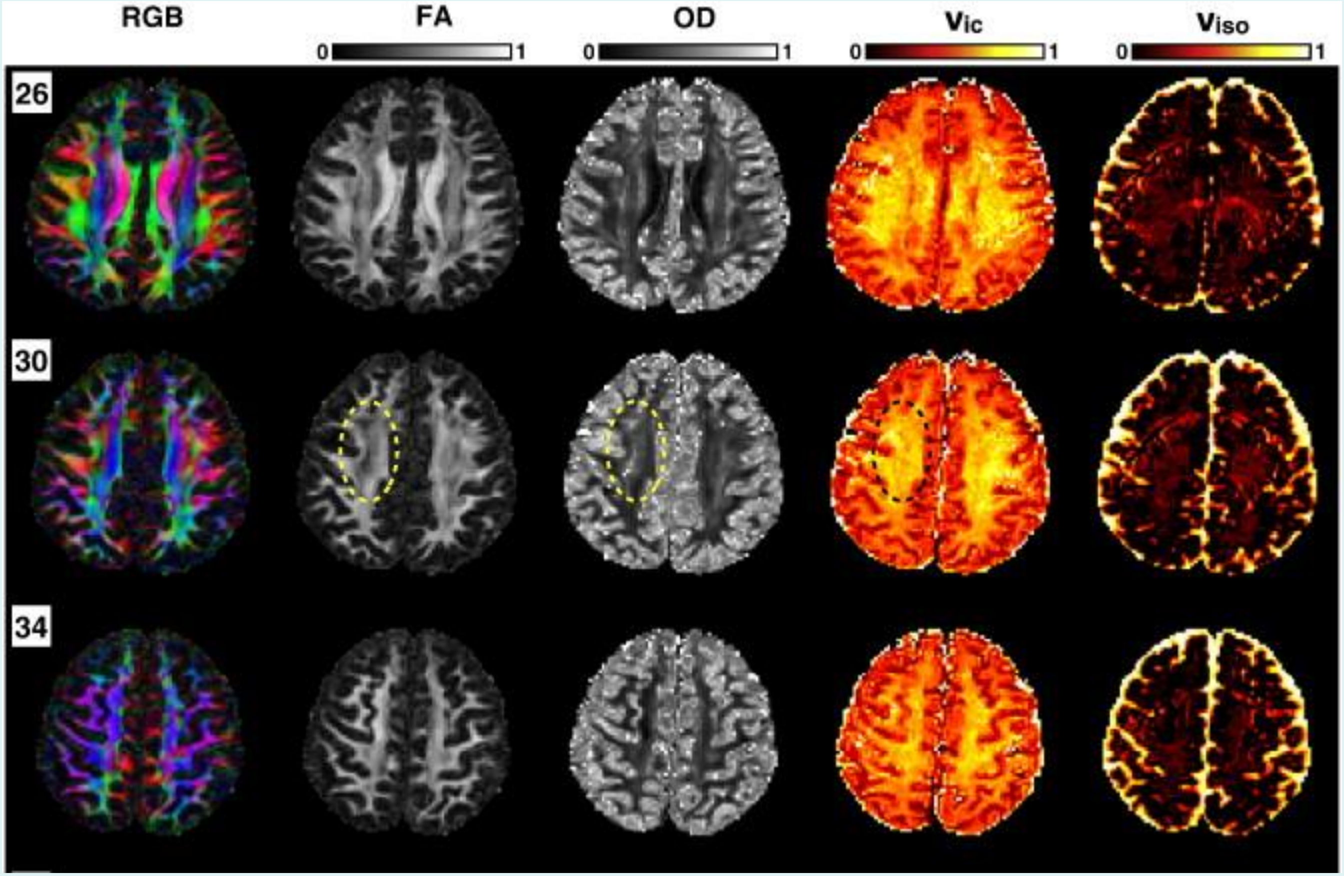
Other models…



Spherical harmonics

Neurite orientation dispersion and density imaging (NODDI)

RGB-encoded principal direction $\boldsymbol{\mu}$, FA, orientation dispersion index OD, intra-cellular volume fraction v_{ic}, and isotropic (CSF) volume fraction v_{iso}



G. Zhang et al., Neuroimage, 2012

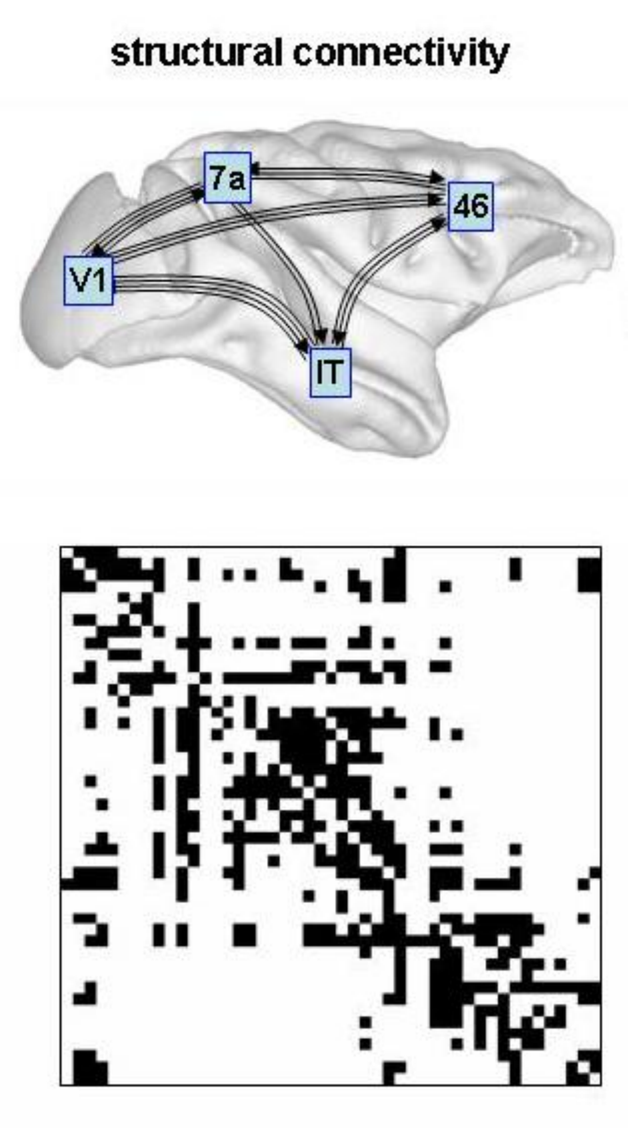
Connectomics

About the same as functional connectivity in fMRI…

Typically

- atlas based with `N` ROIs
- build a `N x N` (weighted) connectivity matrix per subject

➔ use one `.mat` data file per subject (or 2D NIfTI image)



DWI data

- Requires specific
  - pre-processing (movement, distortion, normalization…)
  - parameter map or tractography reconstruction
- Use 1 (or few) images(s) or `.mat` file(s) per subject
- Typically group comparison or parametric regression.

➔ “Subject prediction” problem

Overview

fMRI data

Other imaging & data modalities

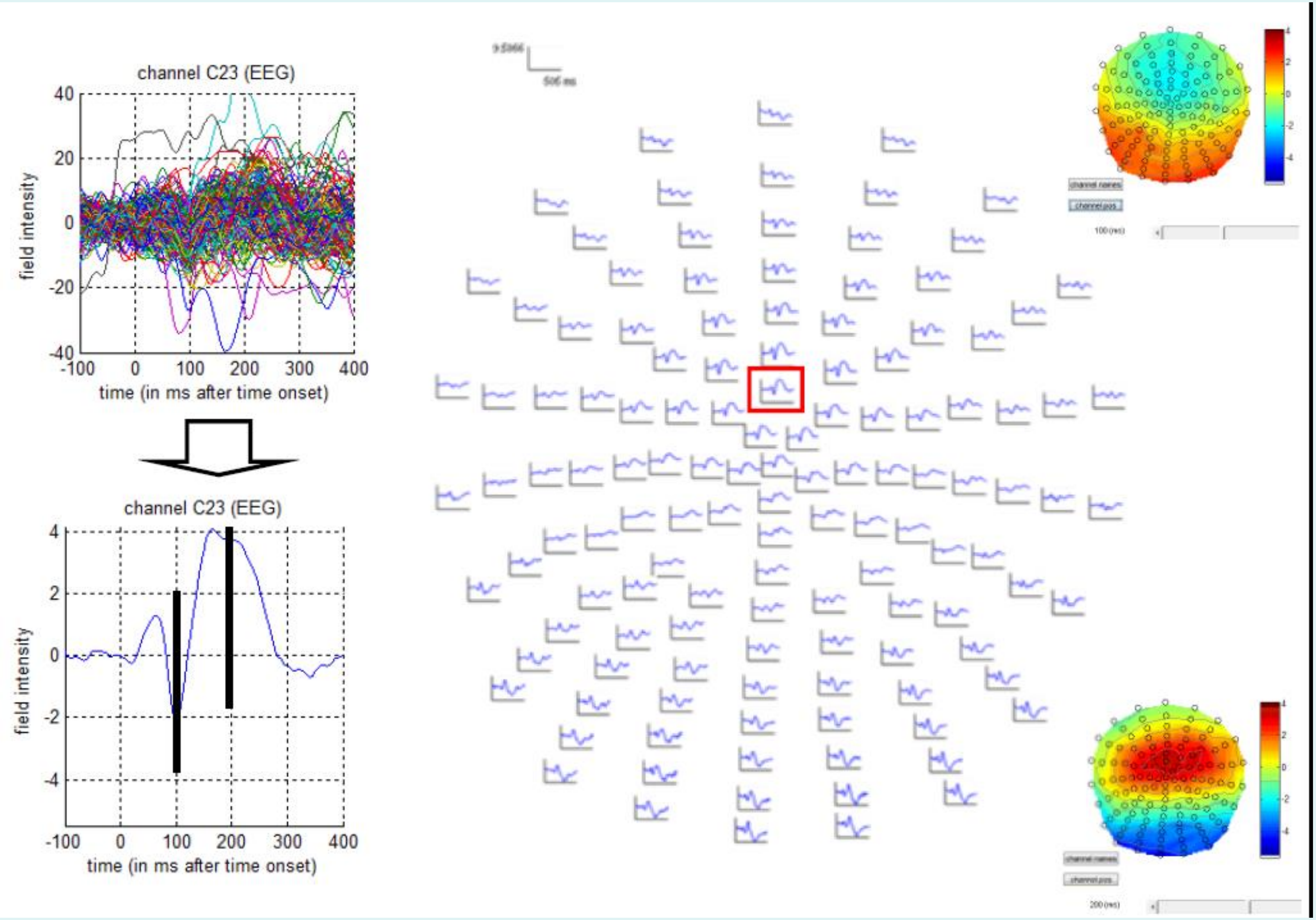
- Introduction
- PET data
- Diffusion-weighted MRI
- MEG/EEG/electrophysiological data
  - Data representation
  - Experimental considerations
- Behavioural & clinical scores
- Conclusion

MEG/EEG/ECoG/… data

Similar to fMRI:

- time series over set of channels
- “brain decoding” question,
  ➔ based on individual event response
- “subject prediction” question,
  ➔ based on summary maps

EEG data example



MEG/EEG/ECoG/… data

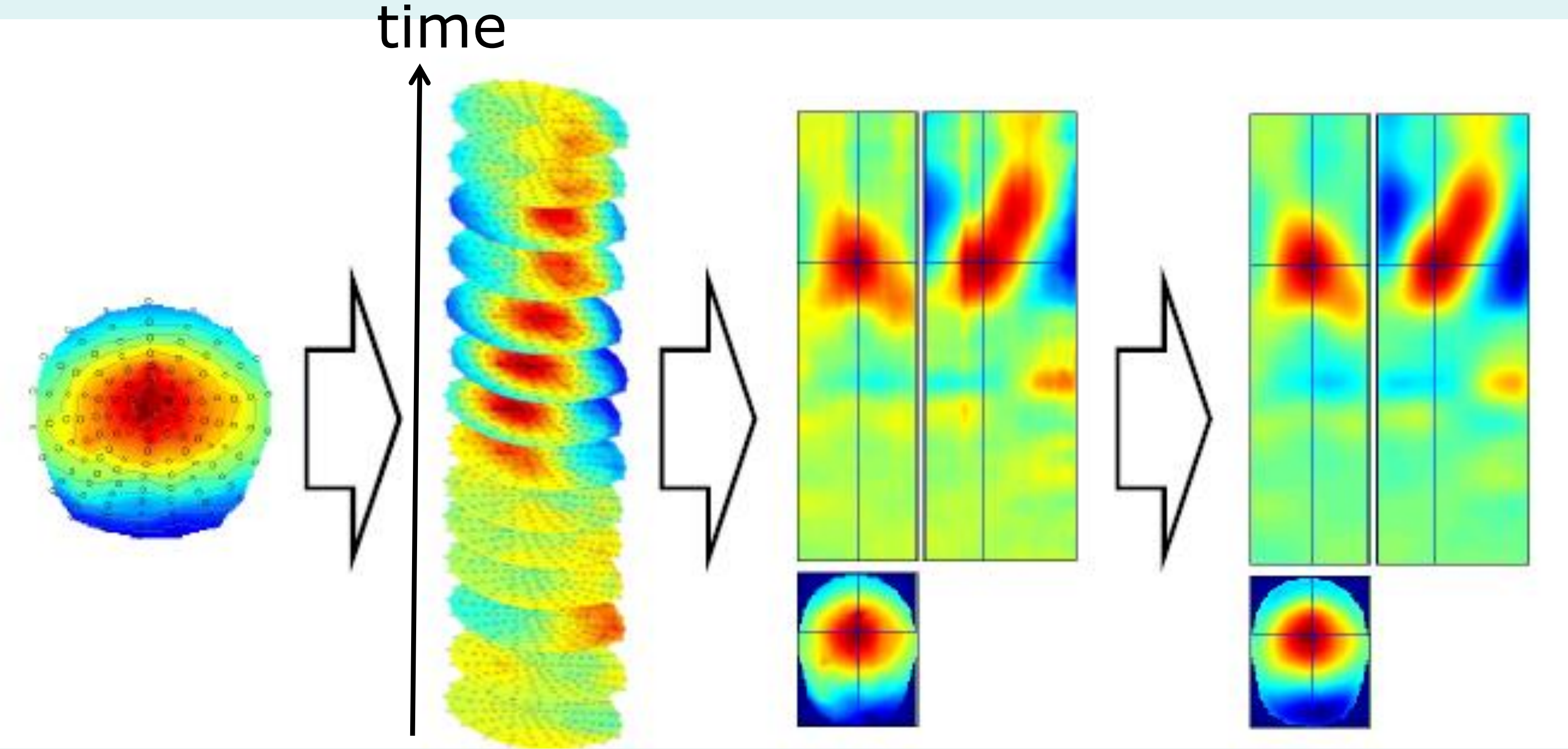
Similar to fMRI:

- time series over set of channels
- “brain decoding” question,
  ➔ based on individual event response
- “subject prediction” question,
  ➔ based on summary maps

Data representation:

- turn MEG/EEG data into NIfTI images
  ➔ as required for standard SPM M/EEG GLM analysis

`Time x scalp` 3D NIfTI image



(SPM does it for you…)

MEG/EEG/ECoG/… data

Similar to fMRI:

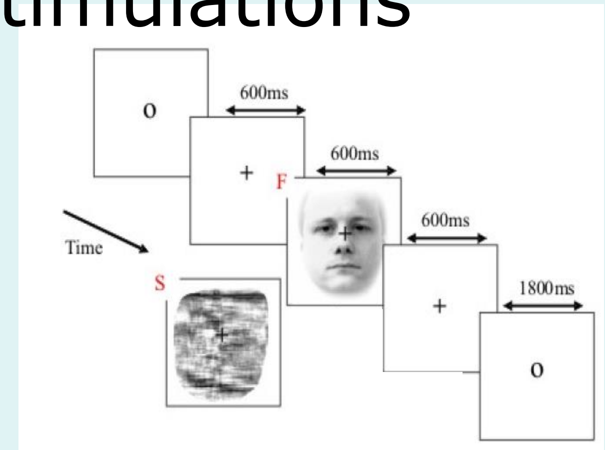
- time series over set of channels
- “brain decoding” question,
  ➔ based on individual event response
- “subject prediction” question,
  ➔ based on summary maps

Data representation:

- turn MEG/EEG data into NIfTI images
  ➔ as required for standard SPM M/EEG GLM analysis
- use SPM’s `@meeg` data format directly
  ➔ stay at channel level

Example of experiment

ERP, 2 conditions with visual stimulations “scrambled vs. faces”.



Single subject:

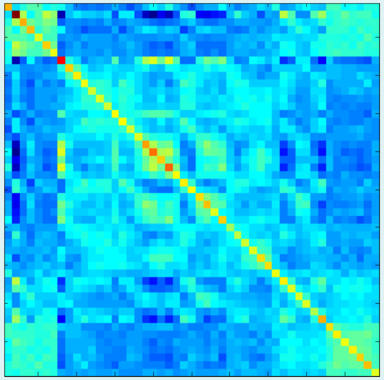
- ➔ for each stimulus, “was the subject seeing a face or a scrambled image ?”

Multiple subjects:

- ➔ with average ERP per subject, “was the subject in group A or group B?”

Other ideas…

- Contrast conditions
  - ➔ Specific effect of interest
- Use time-frequency decomposition
  - ➔ 3D image `channel x time x frequency`
- For resting/spontaneous signal, use synchrony measure over `channel x time` or a `channel x channel` correlation matrix
  - ➔ 2D/3D image or `.mat` file
- …



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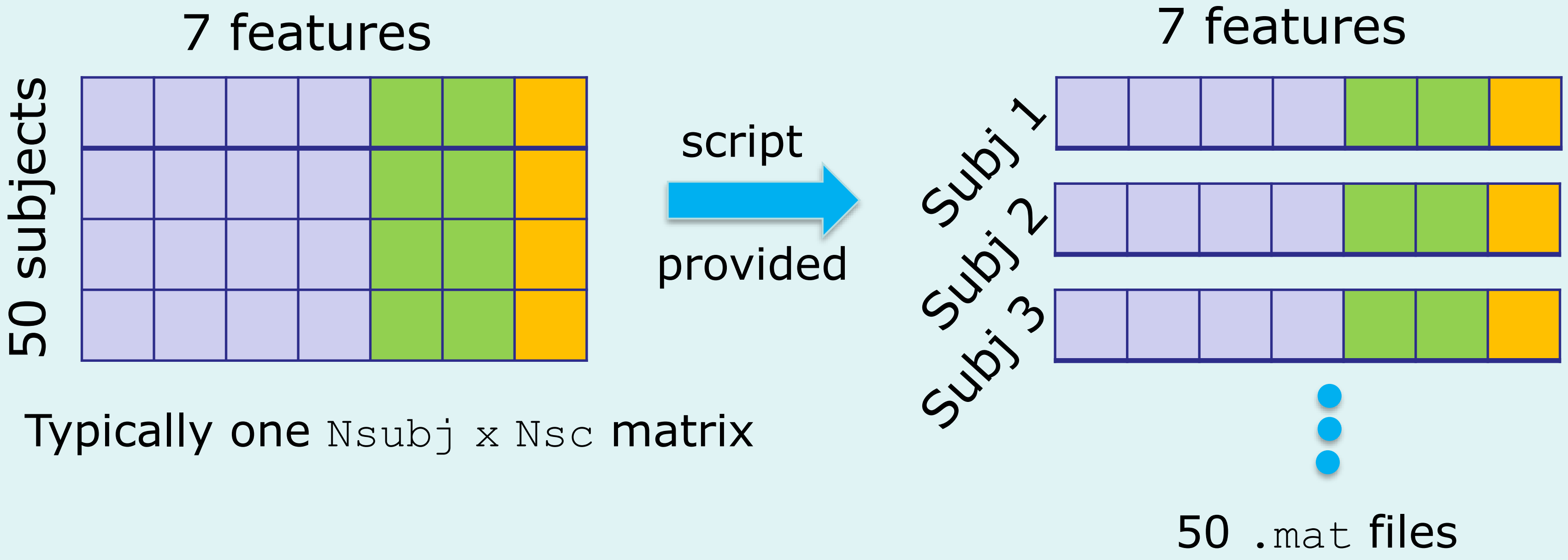
Behavioural & clinical scores

Like correlation/connectivity matrices!

…but

- 1D vector per subject
- with psychometric data or any numeral values



Typically one `Nsubj x Nsc` matrix

50 `.mat` files

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Conclusion

Data per modality

= `.nii` images, `.mat` files,
or `@meeg` object

➔ Data preparation!

Key questions:

- What is your question of interest?
- At what level of inference ?
- What is the experimental design?
- How much data is available?

Thank you for your attention!

Any question?

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FREEDOM TO RESEARCH

“Univariate vs. multivariate” concepts

Univariate	Multivariate
1 voxel	1 volume
target → data	data → target
look for difference or correlation	look for similarity or score
General Linear Model	Specific machine (SVM, GP,...)
GLM inversion	training & testing cross-validation
calculate contrast of interest & inference	estimate accuracy of prediction & inference