Introduction to fMRI

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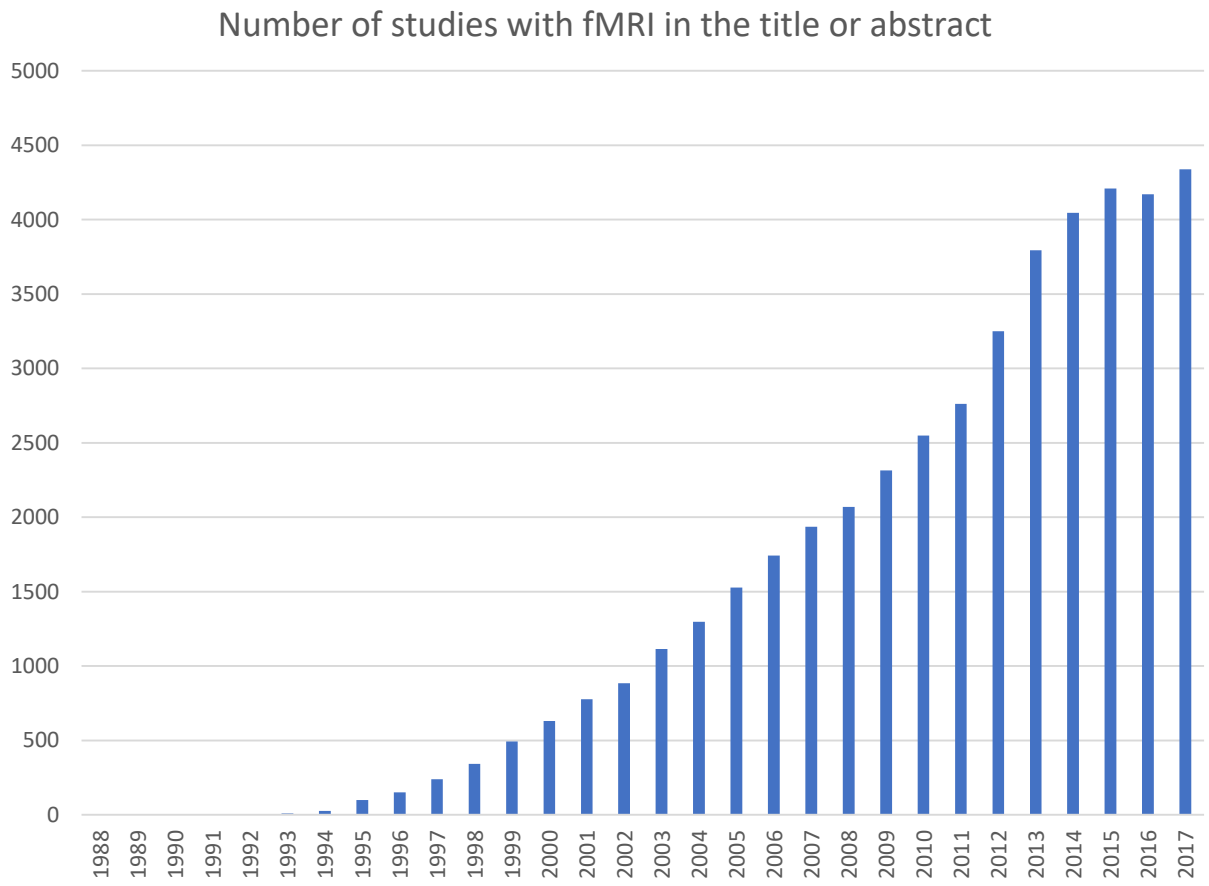
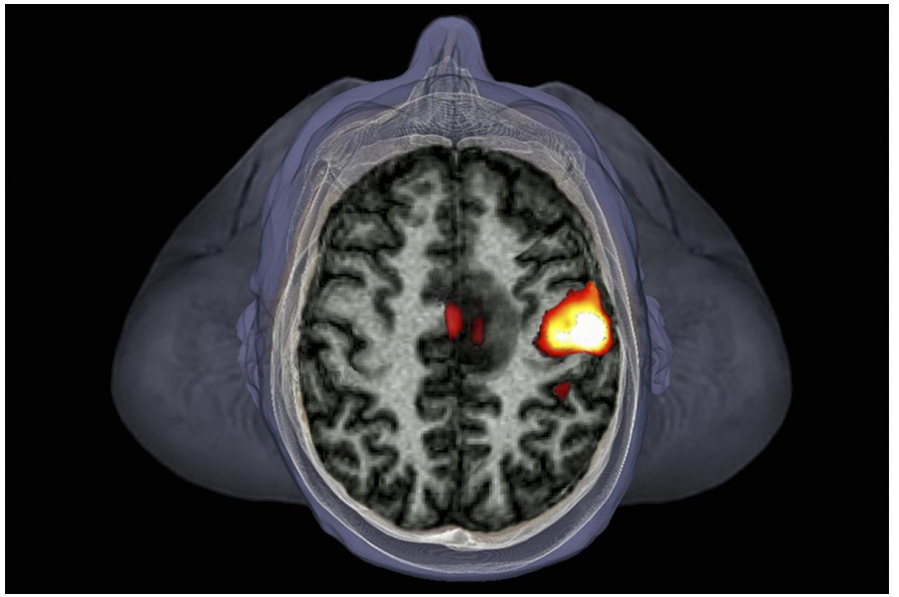
fMRI outline

- Advantages
- MRI vs. fMRI
- Basic neurophysiology
- fMRI experiment
- Analysis steps
- Connectivity
- Limitations

Why is it so cool?



Source: PubMed search

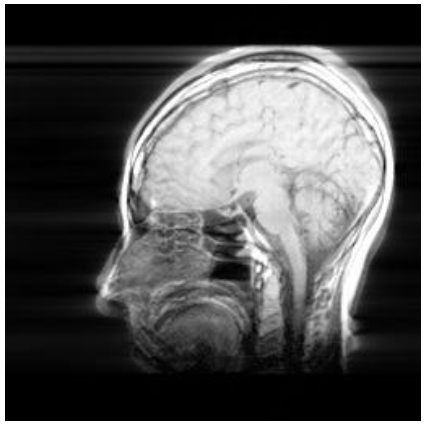


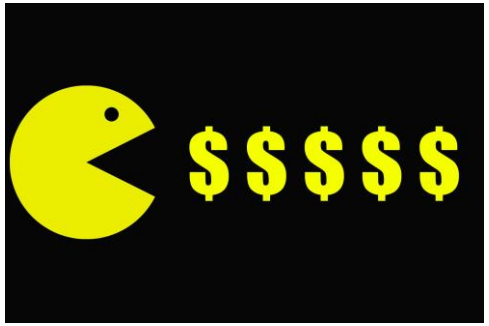
Zephyr/Science Photo Library

- Noninvasive and doesn't involve radiation
- Excelent spatial and good temporal resolution
- Tool for imaging entire network of brain regions engaged when performing particular tasks (cognitive/affective/motor functions)
- Broad application

Why it is not so cool?

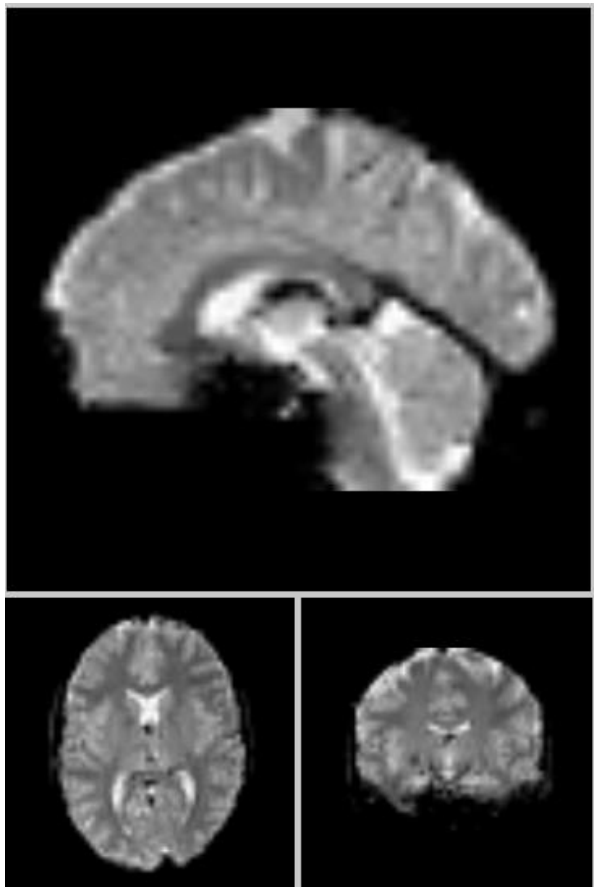
- Contraindications
- Motion artefacts
- Expensive
- Surrogate signal - indirect measurement of neuronal activity – hard to interpret





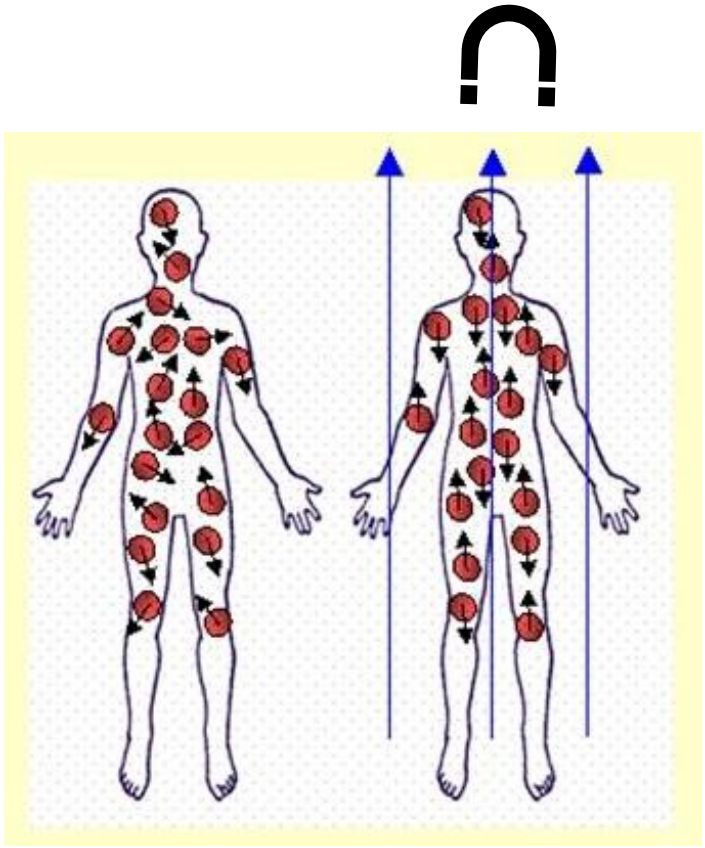
MRI vs. fMRI

- Anatomic structure
- High resolution (1 mm)
- One image (volume)

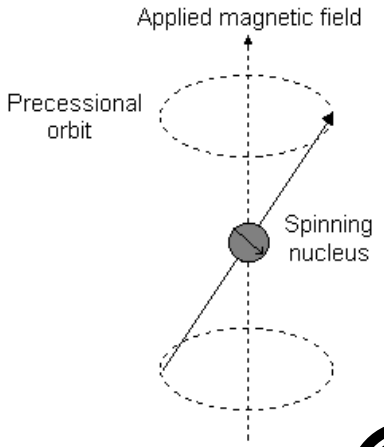


- function
- Low resolution (3 mm)
- Number of images (volumes) in succession

(N)MRI principle in a nutshell

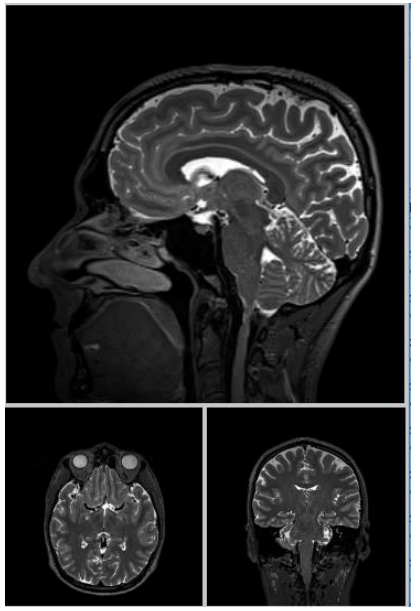


Hydrogen nucleus



T1

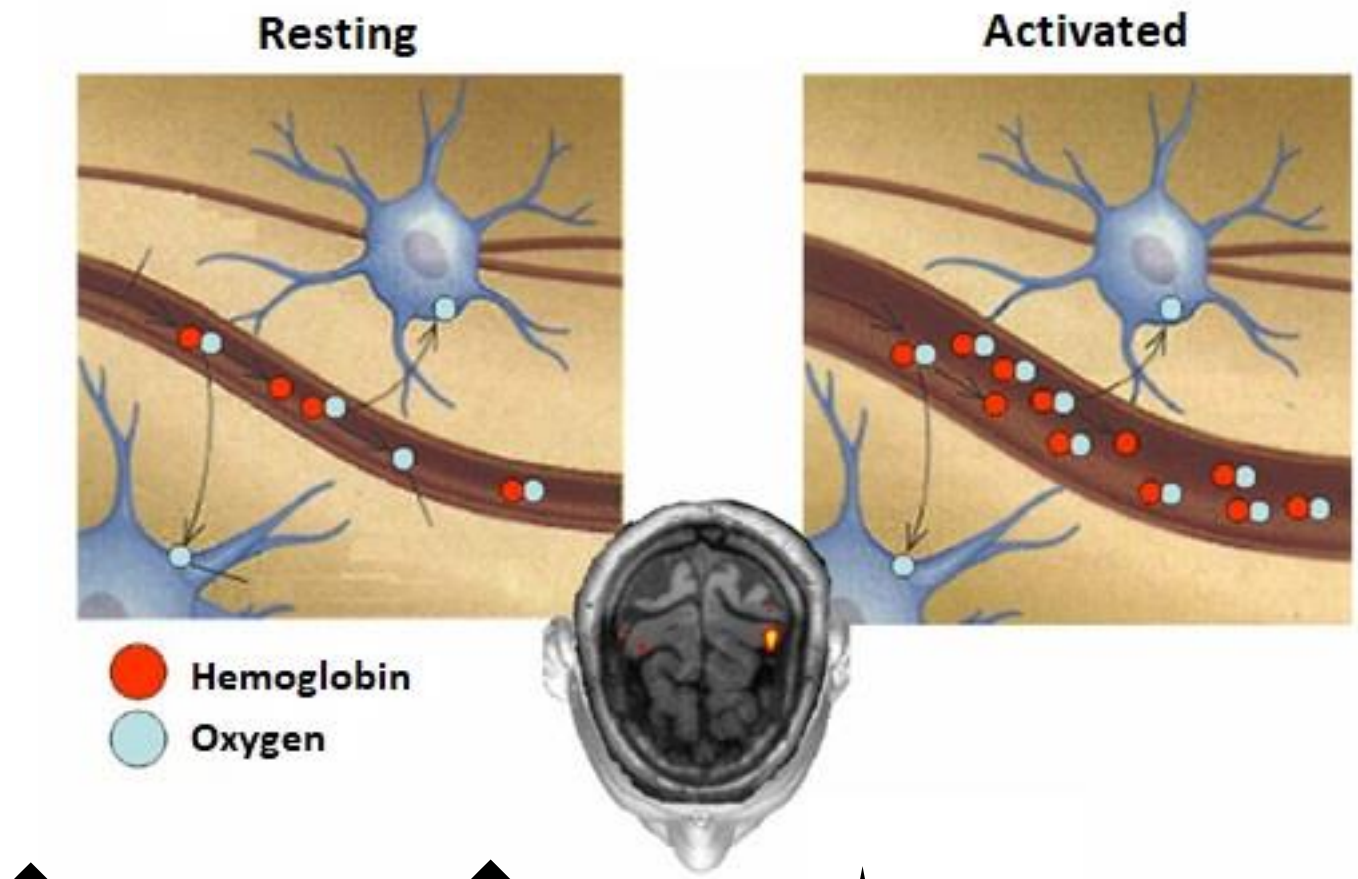
T2



1. Hydrogen nuclei (protons) are aligned by a strong magnetic field
2. Protons can be rotated using radio waves
3. Protons oscillate while returning to equilibrium
4. During realignment the nuclei lose energy and a measurable radio frequency (RF) signal
5. Detected signal is used for detailed images of body tissues

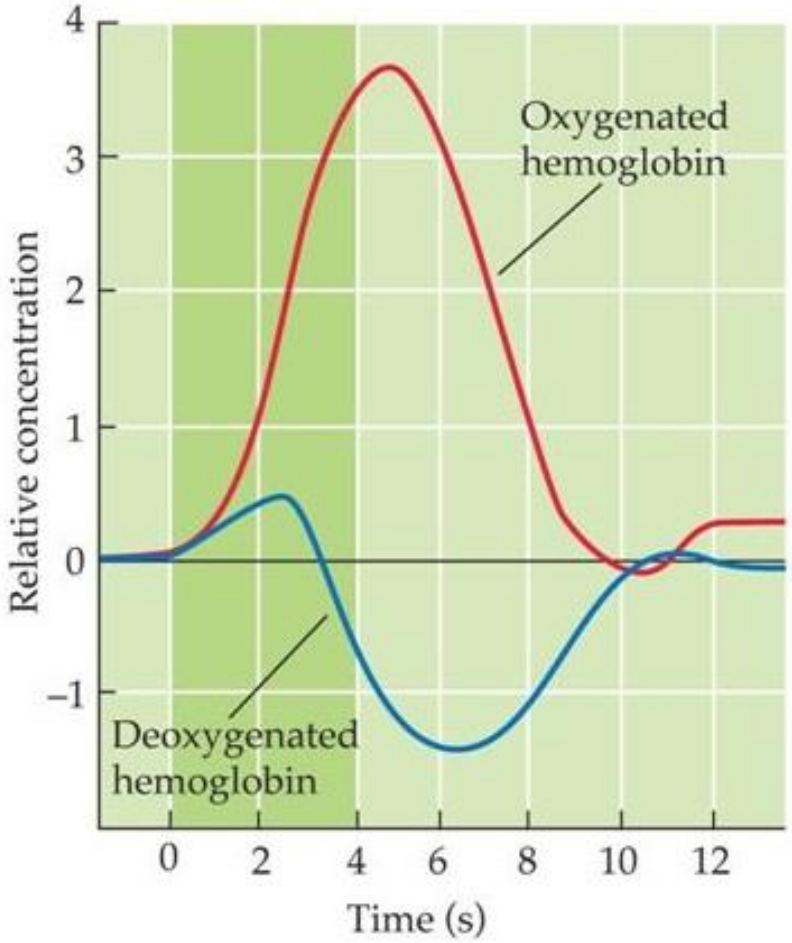
fMRI principle

Blood **O**xygen **L**evel **D**ependent - **BOLD** signal

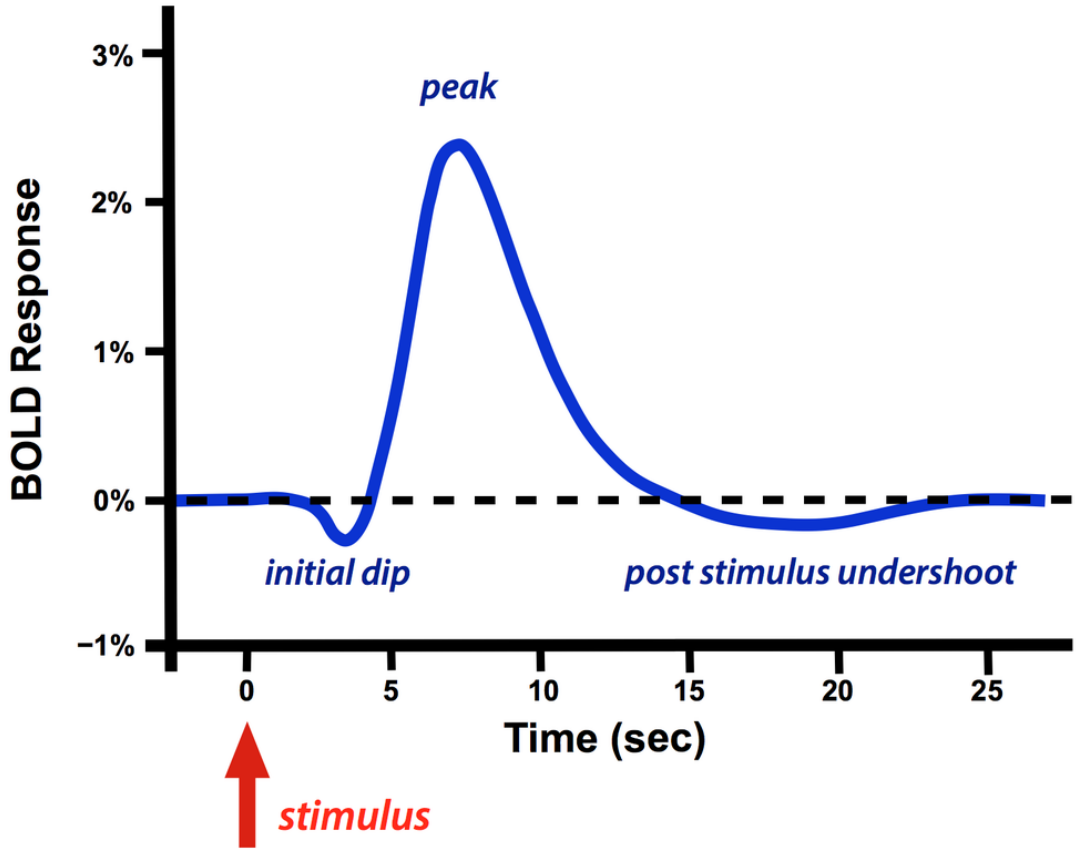


↑ neural activity → ↑ blood flow → ↓ deoxyhemoglobin → ↑ MR signal

Hemodynamic Response Function (HRF)



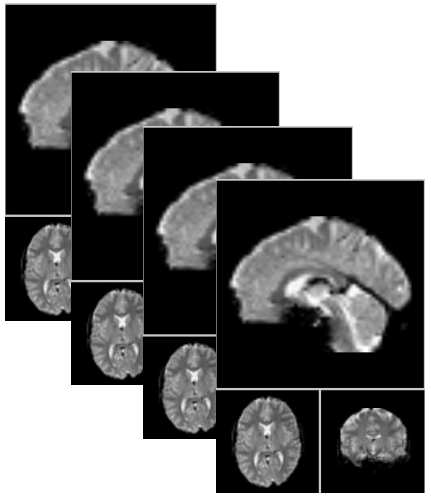
(Malonek and Grinvald, 1996)

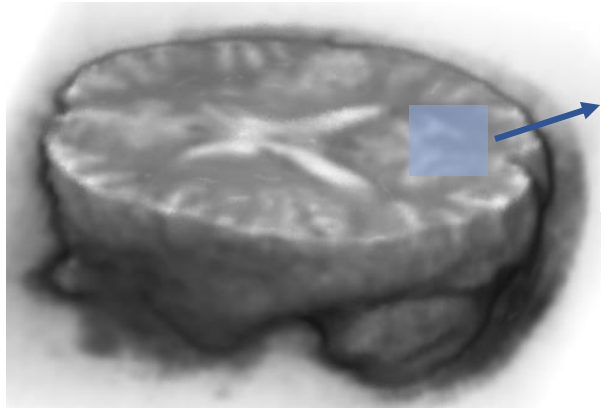


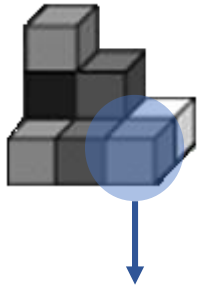
http://mriquestions.com

fMRI raw data

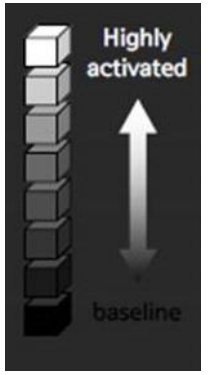
Slices (2D)



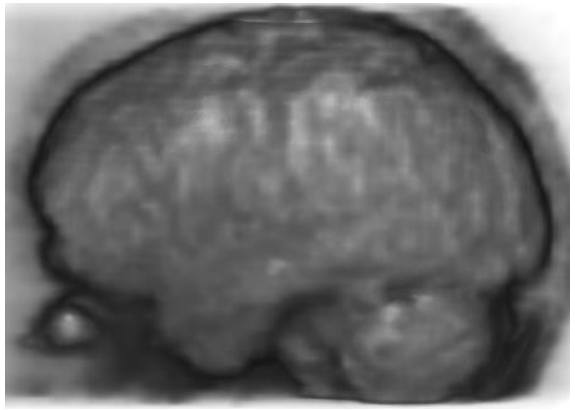




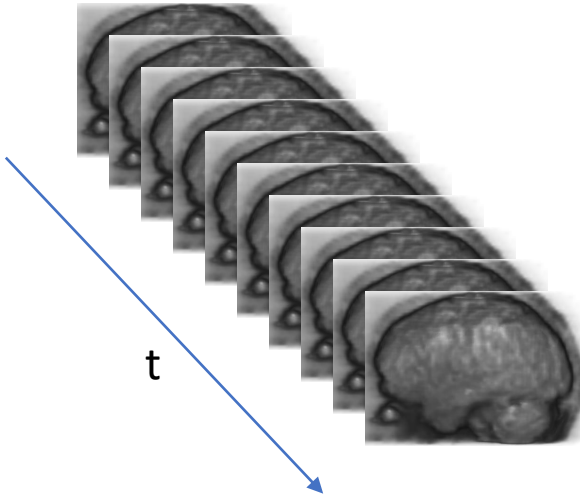
One voxel



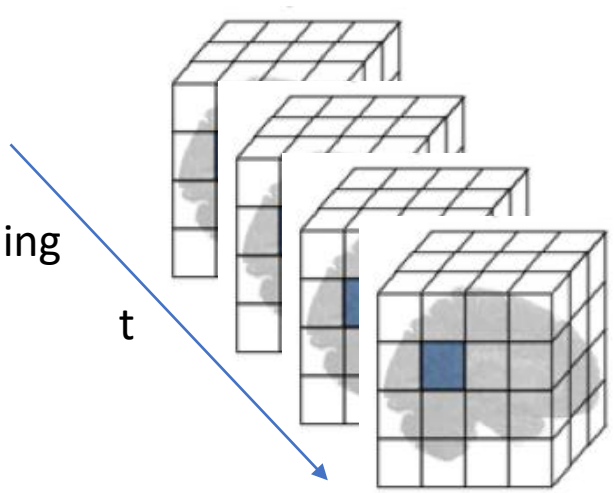
Volume (3D)



Acquisition time 1,5-3 s

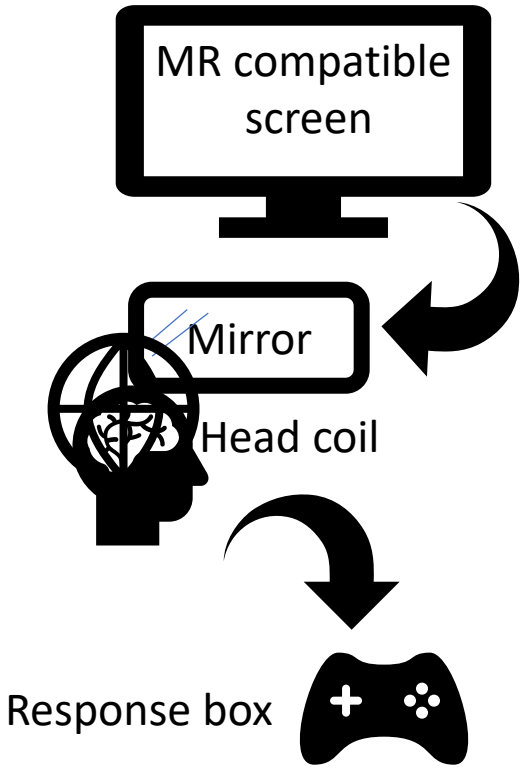


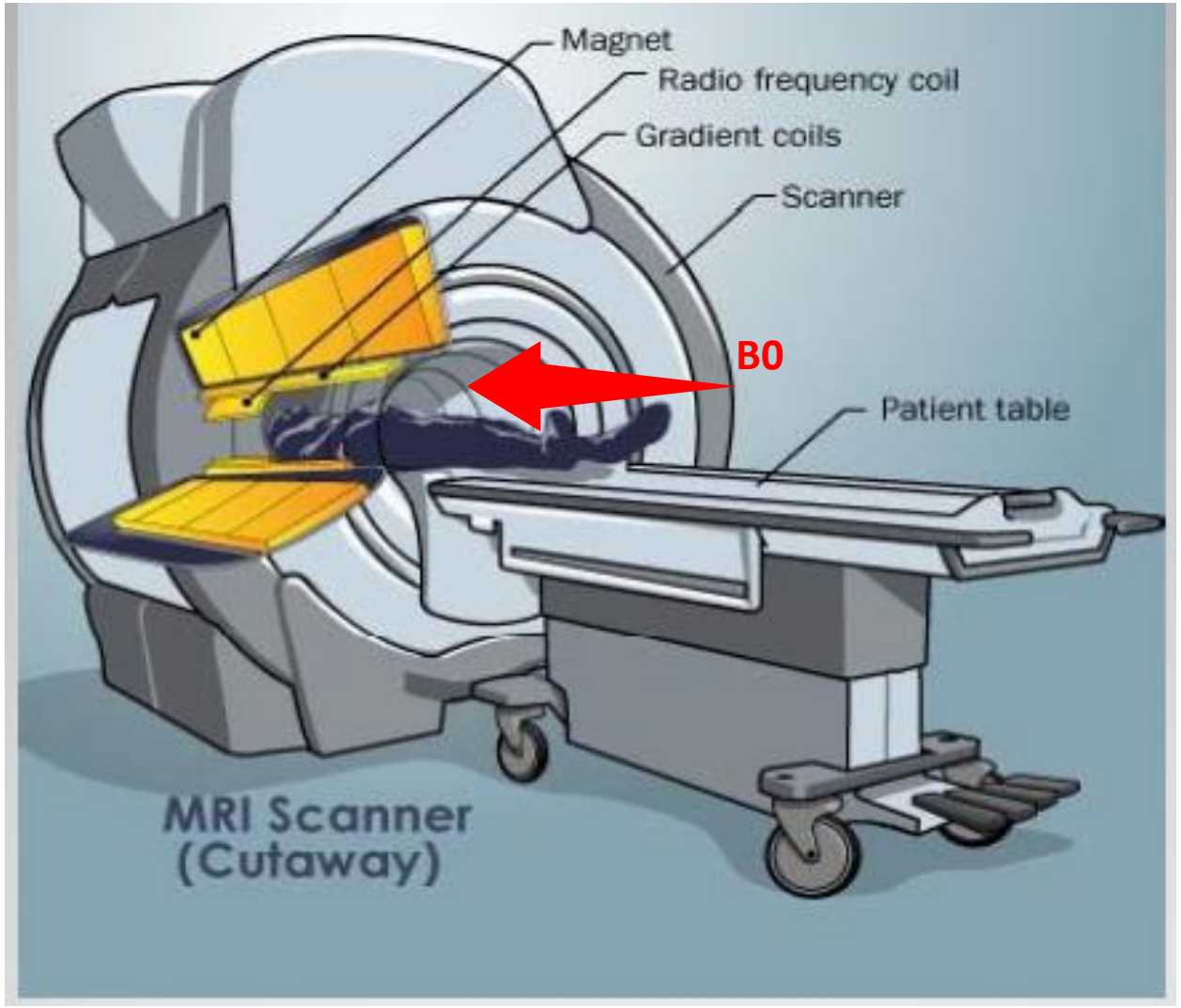
One measuring session
Number of images depending on measuring time

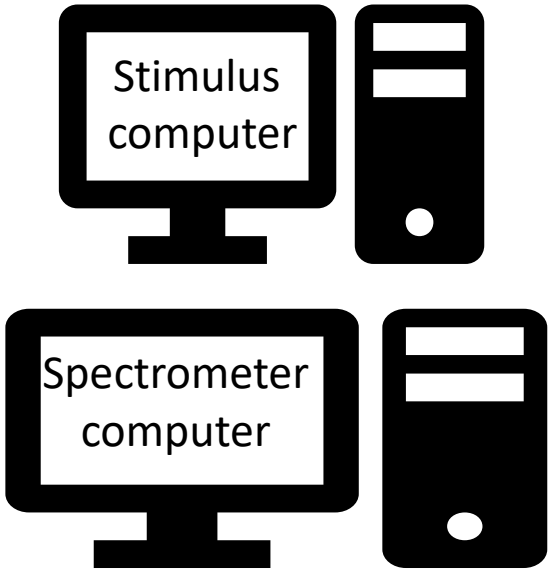


4D matrix

fMRI setup

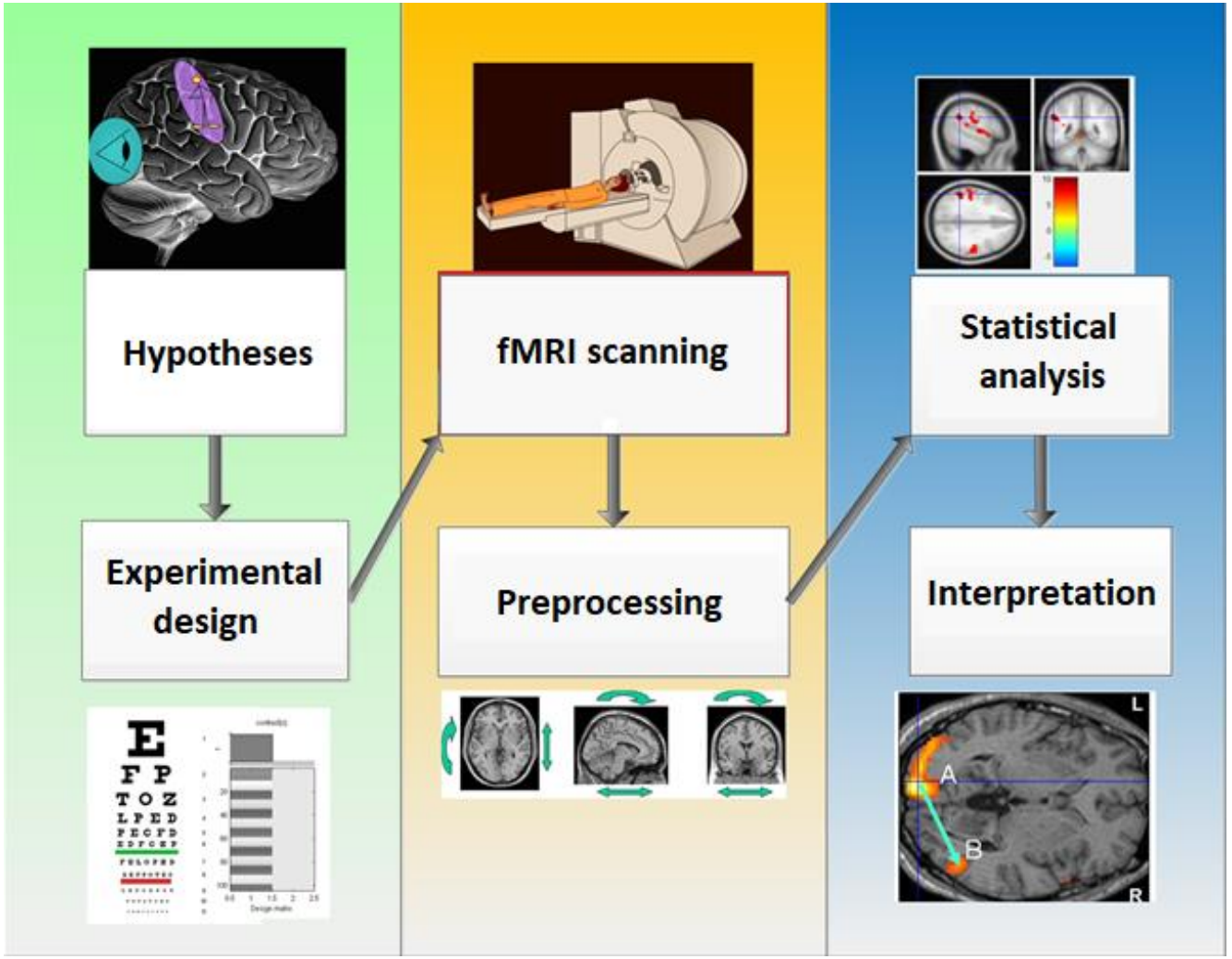






http://www.howstuffworks.com/

fMRI experiment



fMRI experiment issues

We don’t know the baseline BOLD signal level

→ measurement of resting state or other control condition

Very small signal change

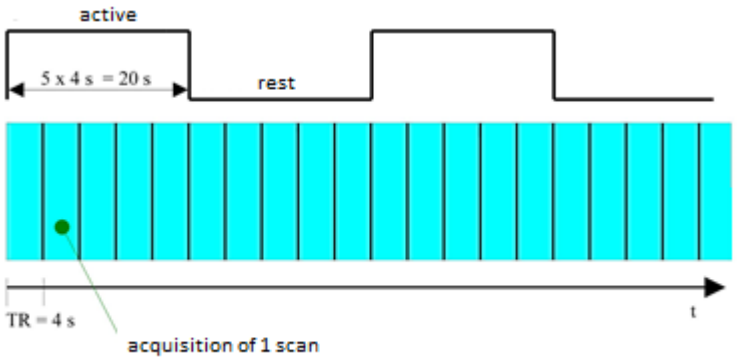
→ repetition of conditions many times, acquisition of lot of data to detect the difference

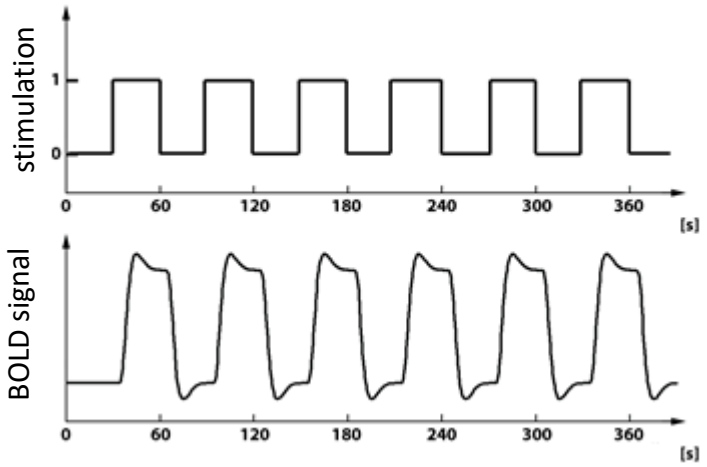
Low-frequency fluctuations and BOLD signal drift

→ alternations of experimental states during stimulation

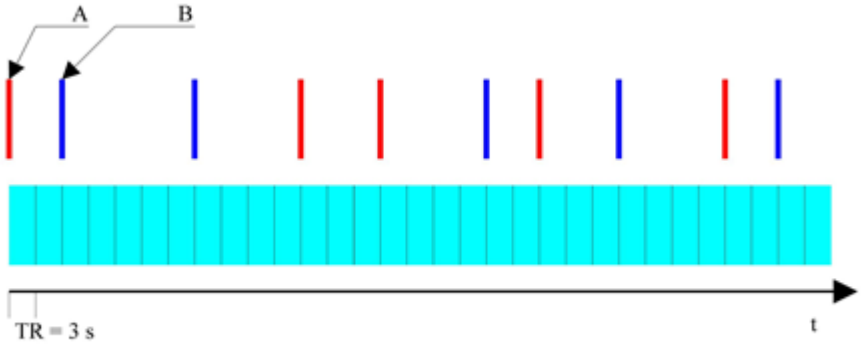
fMRI experiments - design

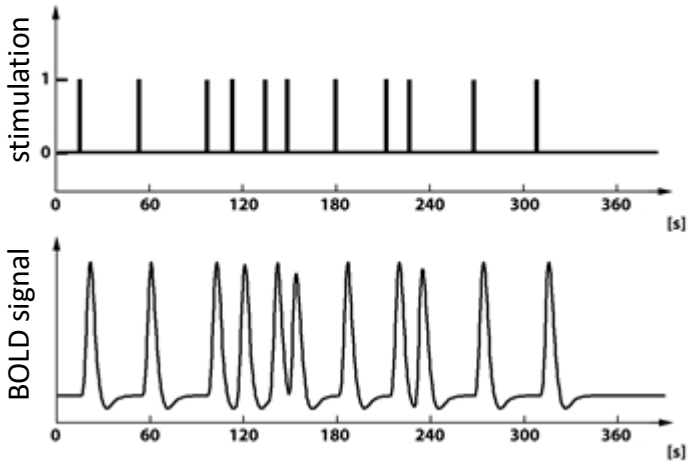
Blocked





Event-related





Experimental design – advantages/disadvantages

Blocked

- Series of stimuli during time epoch(16-60s)
- Simple and powerful
- Easy to analyze
- Very good detection power
- Longer blocks may evoke heterogenous neuronal activity
- Estimating relative changes between tasks

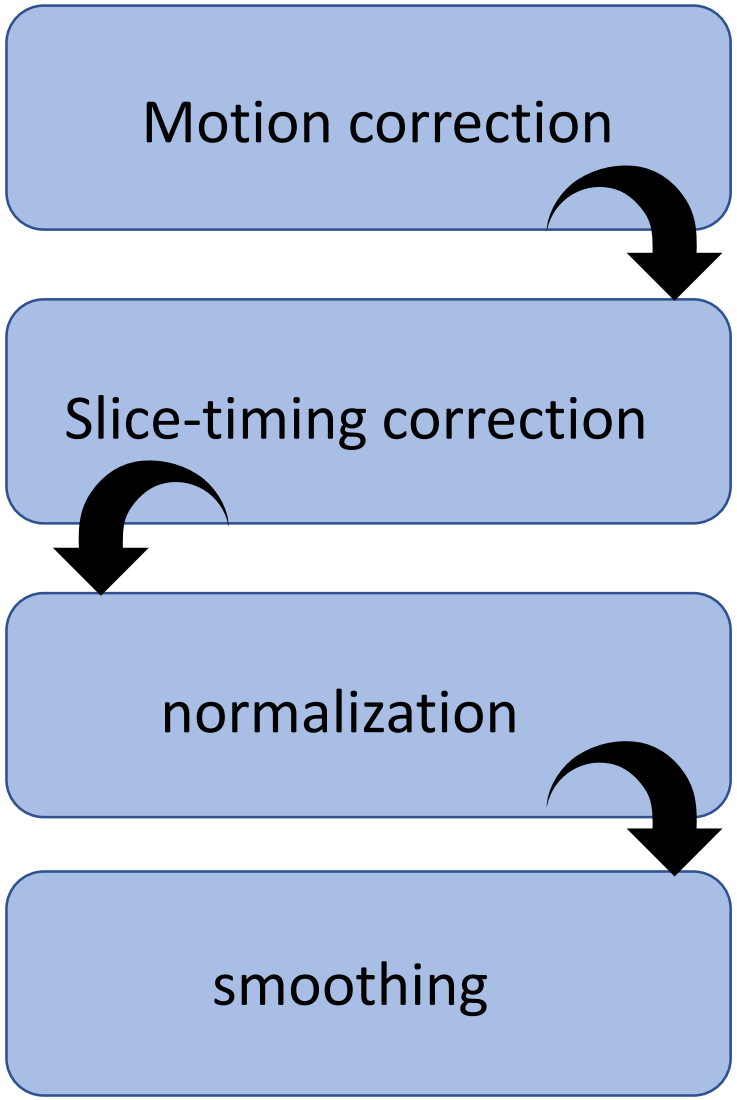
Event related

- Reactions to single stimuli
- Lower statistic power
- Estimation of HRF possible
- Longer measurement necessary
- More complicated data analysis

Sequence parametres

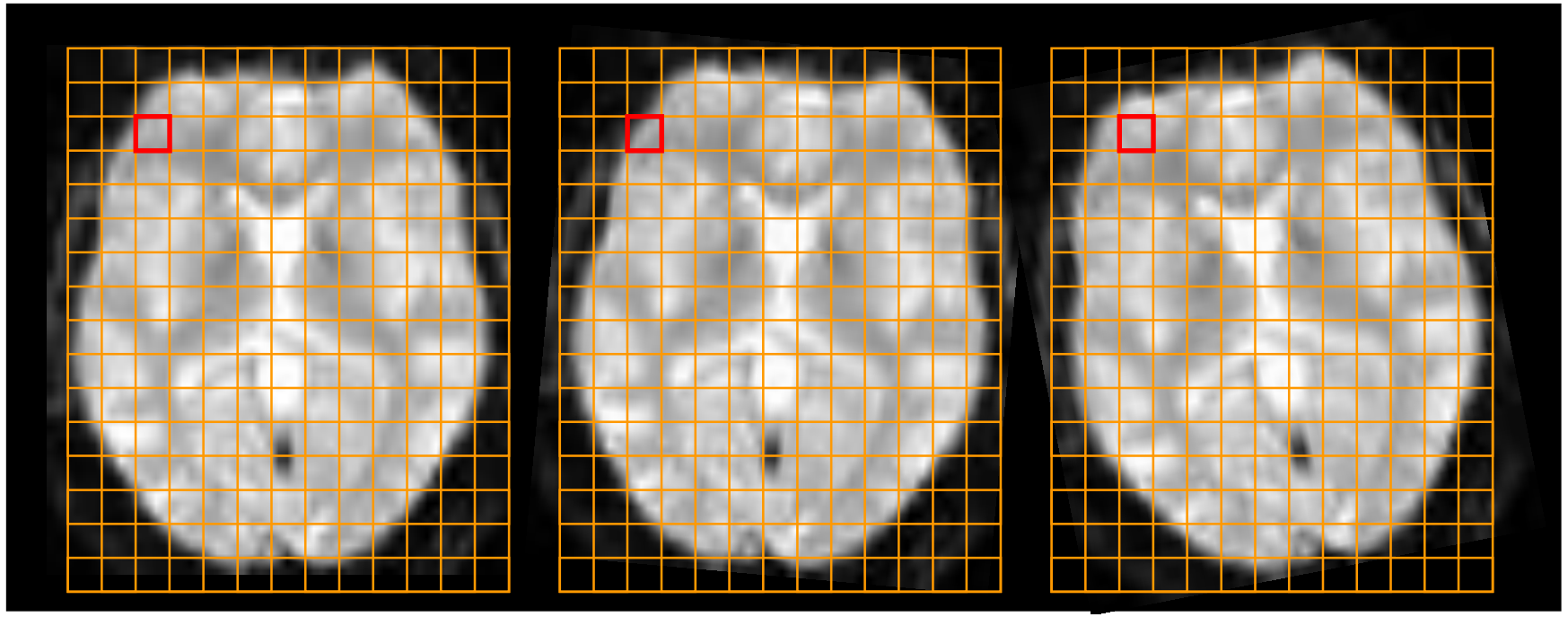
- T2* weighted, echo-planar BOLD images
- Typical parametres on 1,5 T MR:
  - resolution: 64x64 (128x128)
    - FOV = 220 mm $\Rightarrow$ 3,4375 x 3,4375 mm^2
  - Slice thickness: 3 - 7 mm
    - Bigger thickness – better SNR
  - Number of slices: 16 - 32
  - Volume acquisition time
    - Repetition time (TR)
    - 1,5 – 4 s
- Stronger fields possible
  - 3T, 7T, (9T, 11T, ...)
  - Stronger field $\Rightarrow$ better SNR X worse susceptibility to artefacts

Preprocessing of the data



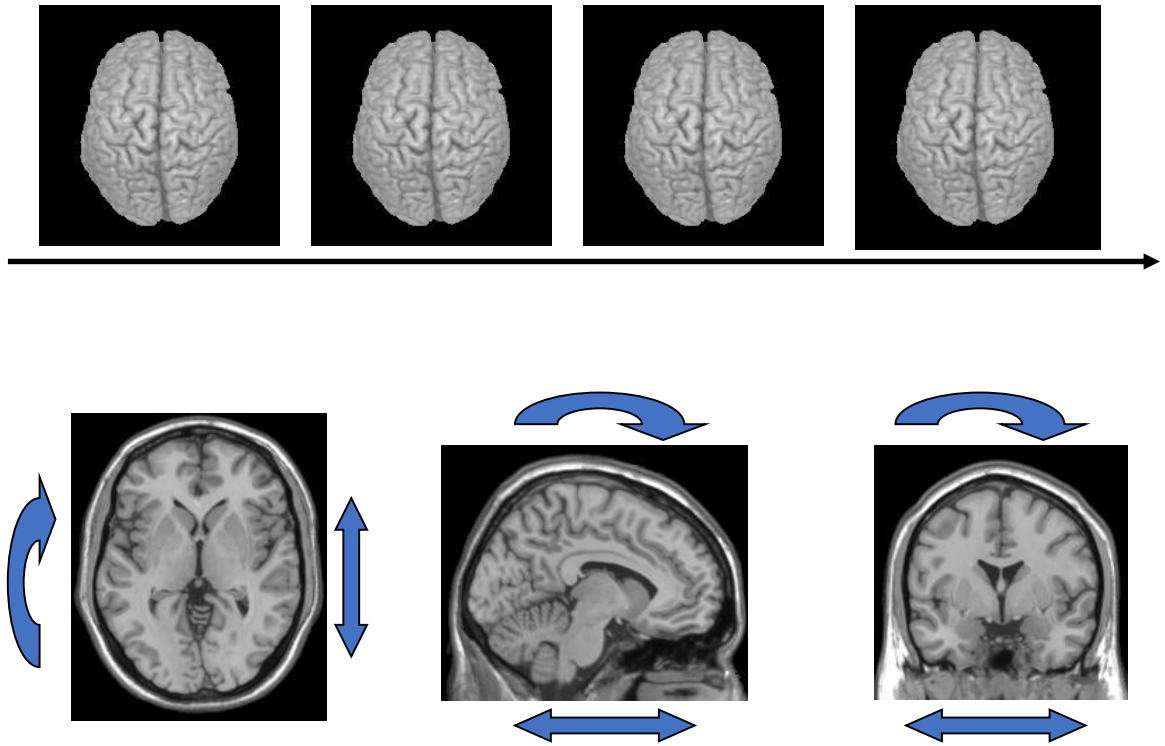
Motion correction

- Motion artefacts are the most problematic in fMRI
- Statistical parametric mapping methods work with single voxels independently
- The same voxel must correspond with the same spot in the brain



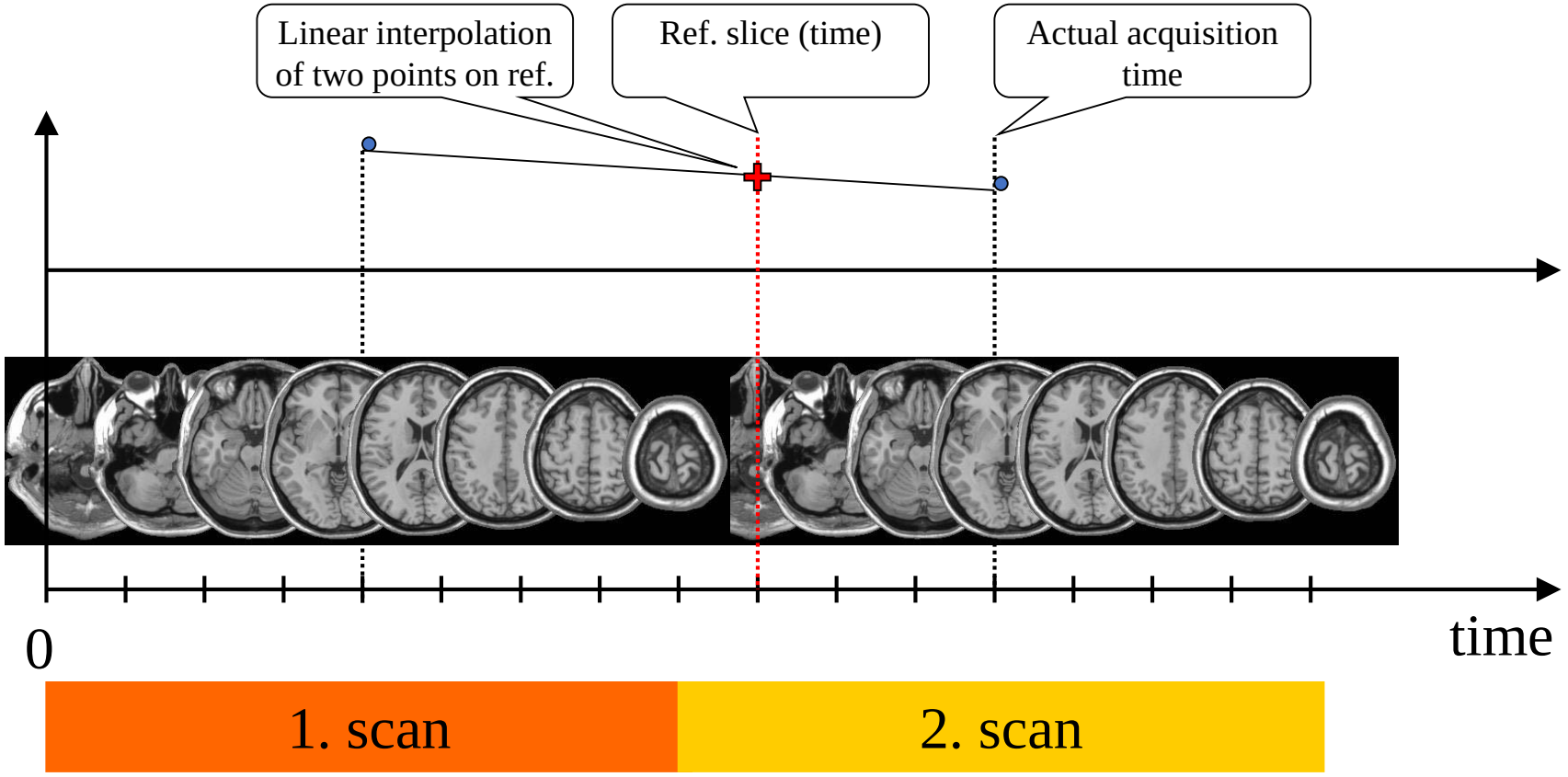
Motion correction

- Realignment to the first (referential) image
- Searching for optimal parameters (translation, rotation)



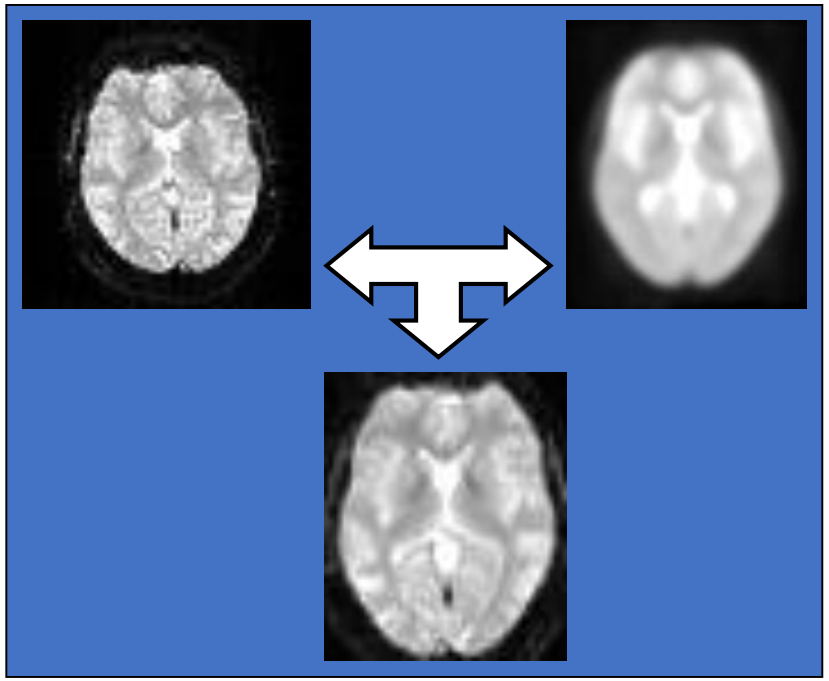
Slice timing correction

- Ideal case – acquisition of the whole brain volume in an infinitely short time
- Scanning of individual slices between 100 and 500 ms
- First and last layer from 2 to 4s apart
- Different slices different HRF
- Can be corrected by weighted distance from referential slice and referential time



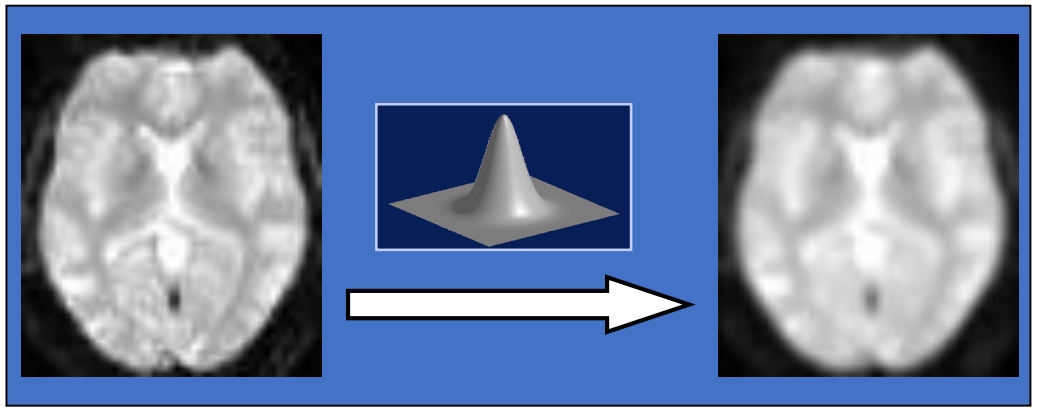
Normalization

- Neuroscience research X clinical application
- Transformation into standardized template (MNI, Talairach)
- Linear transformations
  - Translation
  - Rotation
  - Size change
- Nonlinear deformations



Spatial smoothing

- Filtration of rapid changes in signal intensity
- Various filter shapes – most frequent Gaussian kernel

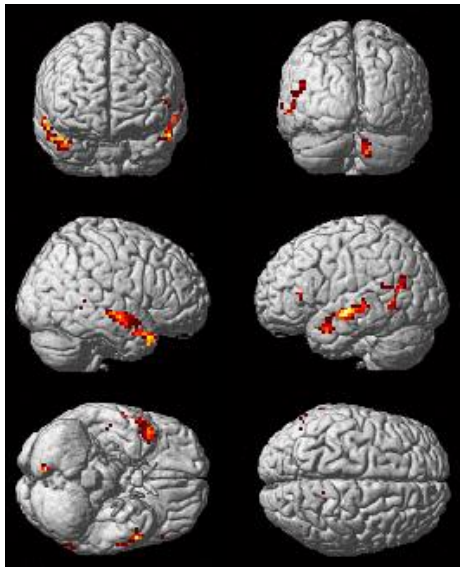


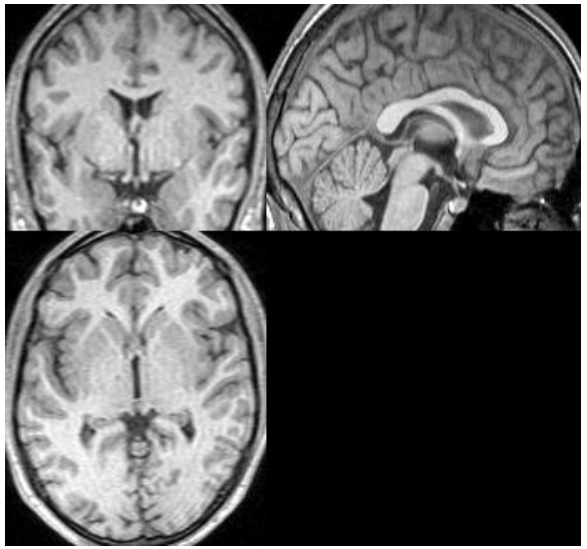
- reduces noise in the image (increase signal to noise ration - SNR)
- improves spatial distribution of the data
- better fit in group comparison

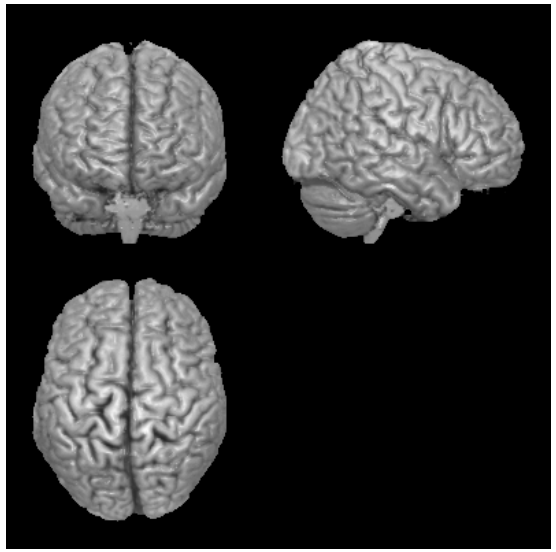
- Risk of loosing activated regions
- data transformation – not working with the raw data

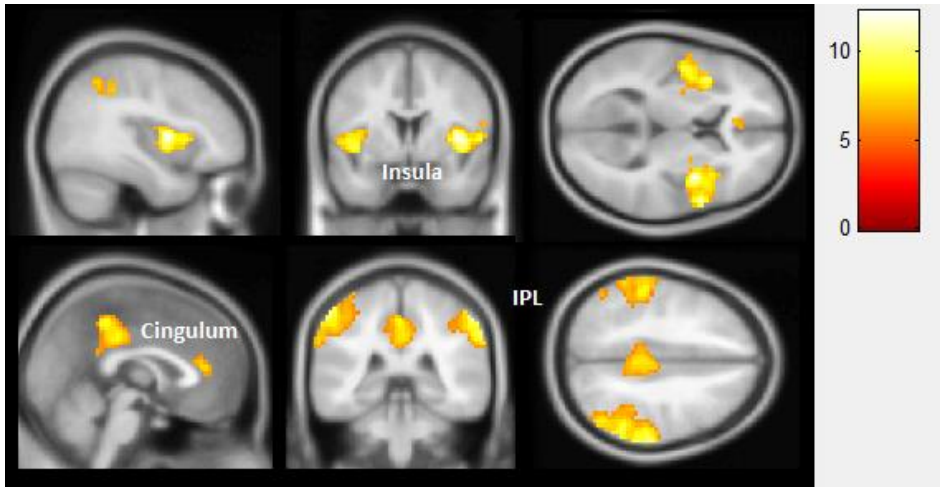
Anatomical images

- Normalization and co-registration with functional scans
- Segmentation and rendering (3D view)
- Used for display of activation maps



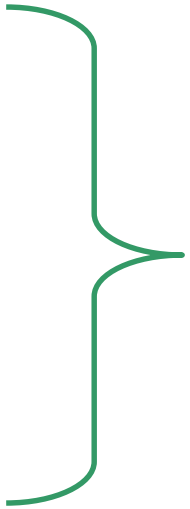






Statistical analysis

- Methods without model
  - ICA/PCA
- Methods with model (hypothesis about the shape of the BOLD signal)
  - Correlation
  - T-test
  - ANOVA
  - AnCova
  - Linear regression
  - Multiple regression
  - F-test
  - etc..



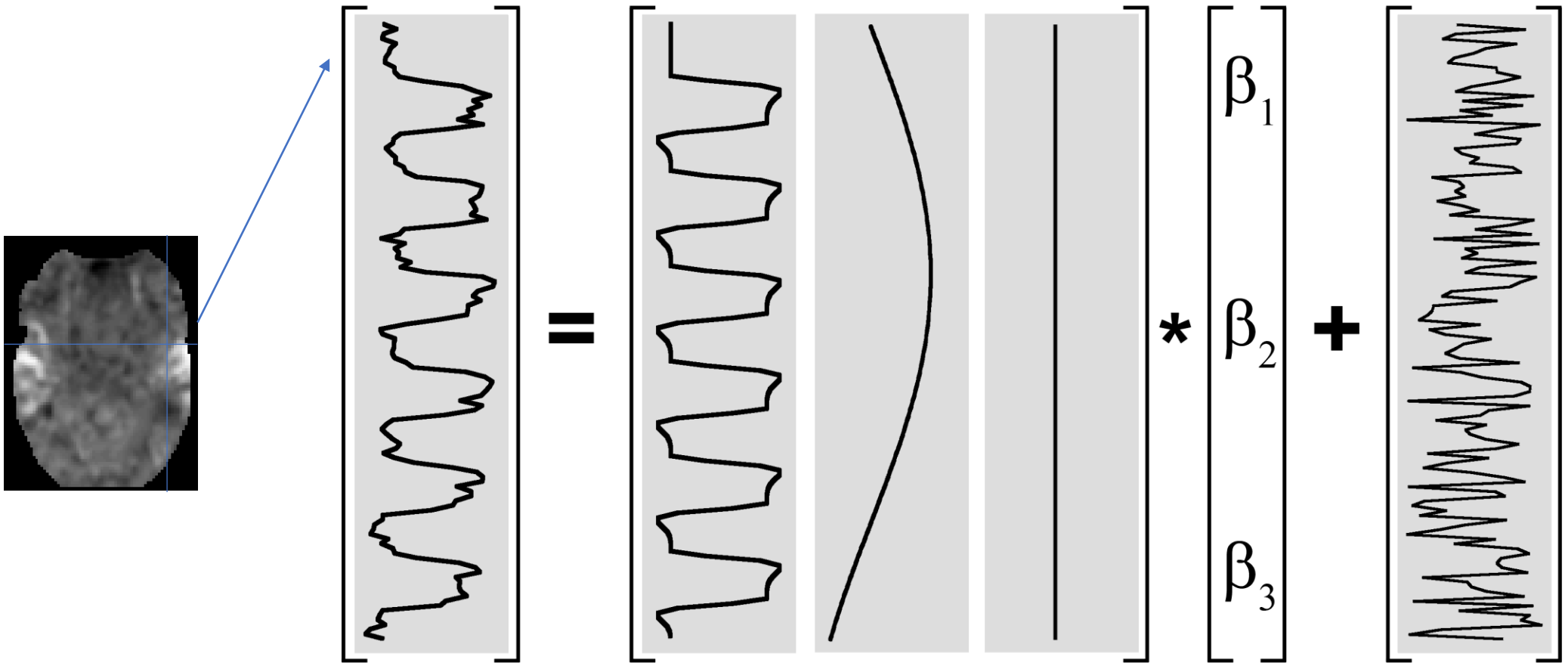
Cases of

GLM

(general linear model)

GLM

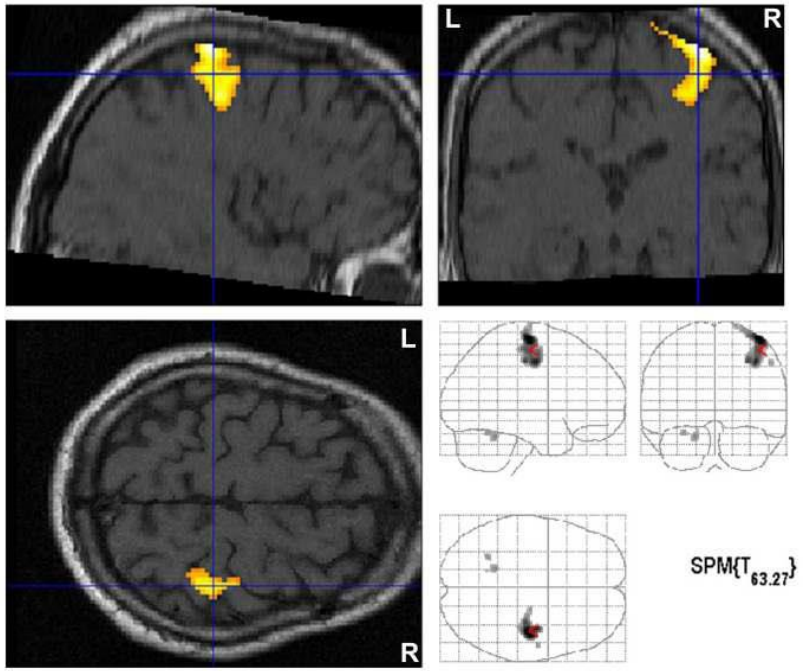
$$Y = X*\beta + \varepsilon$$



Measured signal | Regressors/modeled signals | parameters | residuals

Hypotheses testing

- T-test about β parametres
- T-test is run on every voxel across the brain
- Supratreshold voxels mark regions where tested effect was significant

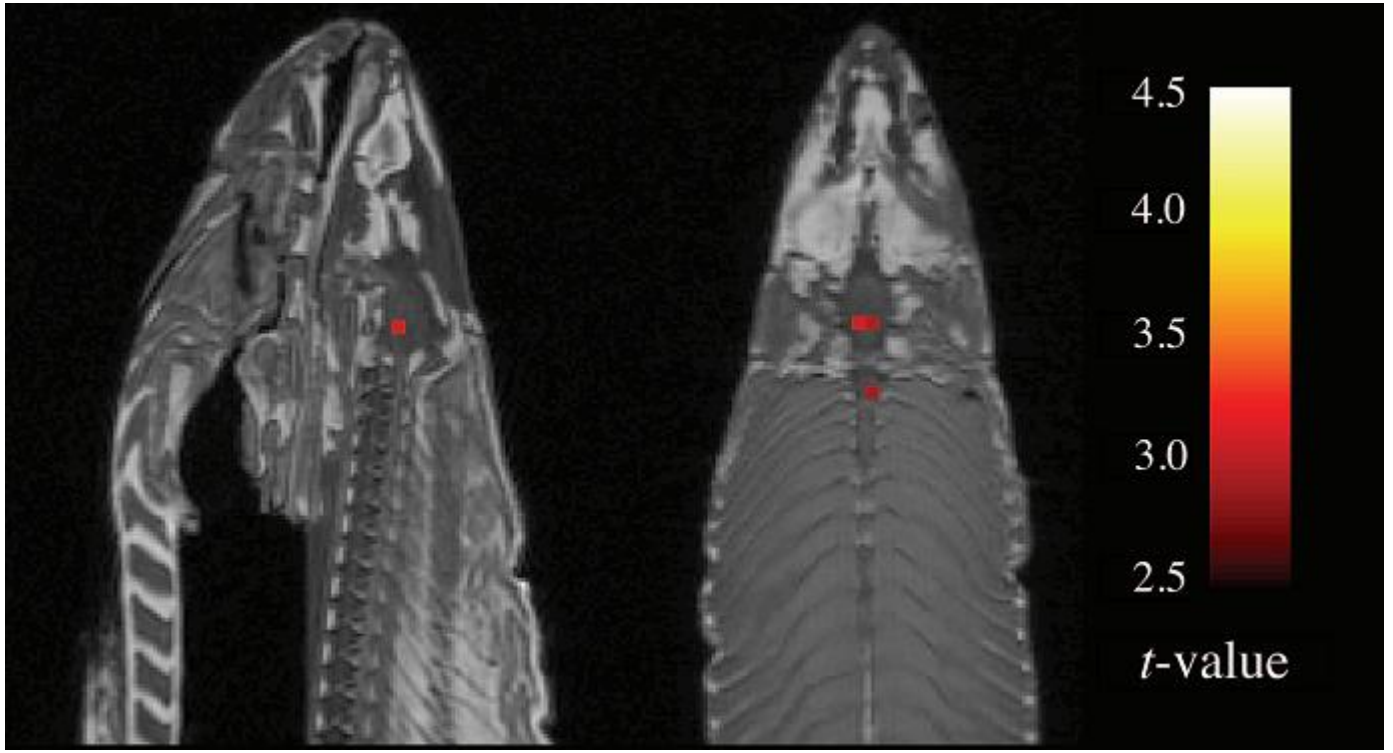


Movement of left hand

P < 0.001
T=3.1

Multiple comparisons problem

Neural correlates of interspecies perspective taking in the post-mortem Atlantic Salmon: An argument for multiple comparisons correction (Bennett et al., 2009)

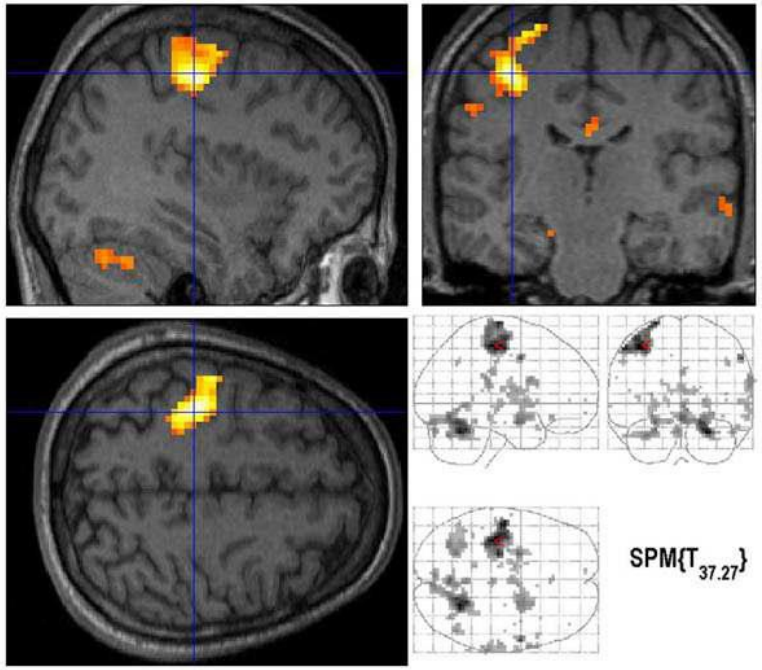


Uncorrected results

Correction for multiple testing

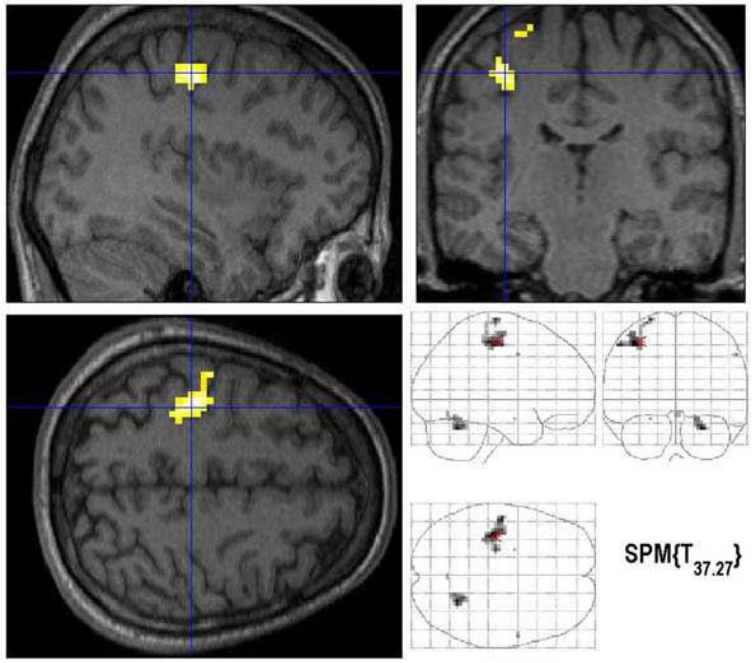
Without correction

- Sig. level for one voxel
  - When ***n*** results displayed, probability od false positive results increases ***n***-times!
  - $p < 0.001$



With correction

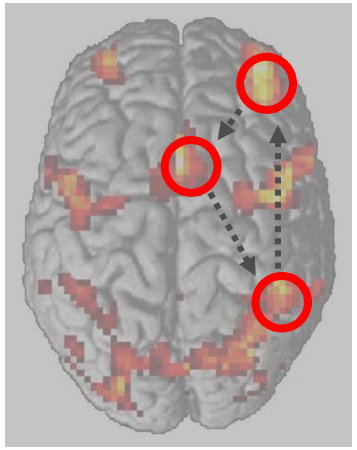
- Sig. level for whole sample
  - FEW – family wise error
  - FDR – false discovery rate
  - $p < 0.05$



Functional organization in the brain

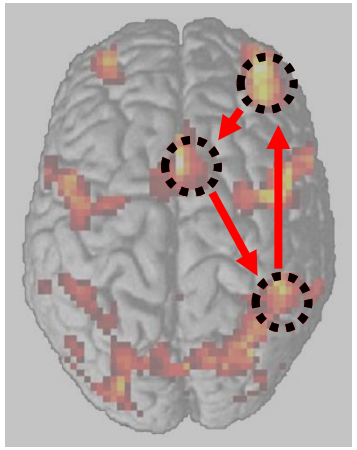
Functional specialization

- Specialized and spatially separated modules
- Regions of interest



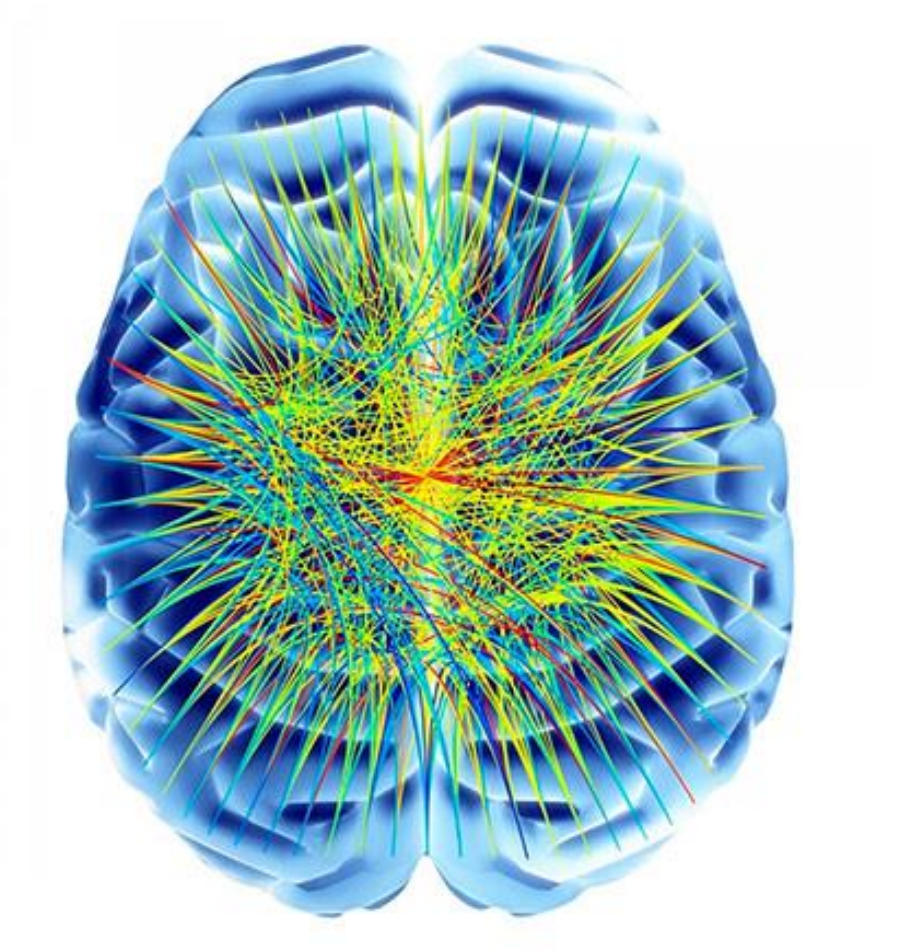
Functional integration

- Specific function is characterized by interconnection of relevant regions
- Large-scale neuroimaging
- networks



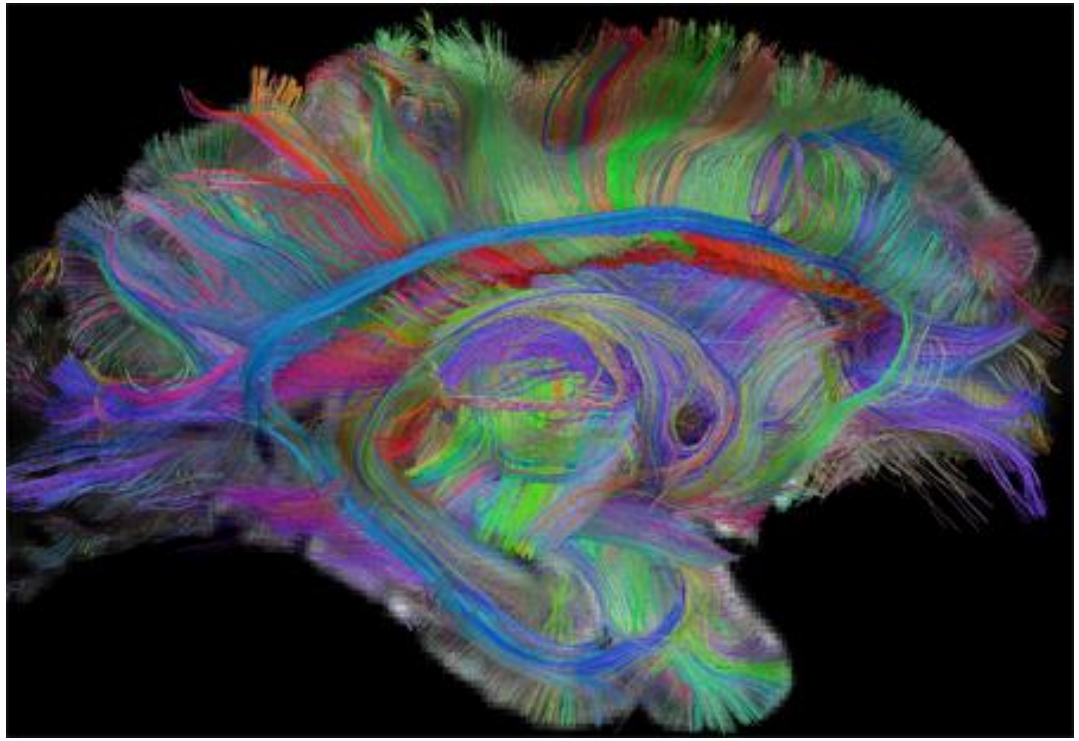
Connectivity

- Structural
- Functional
- Effective



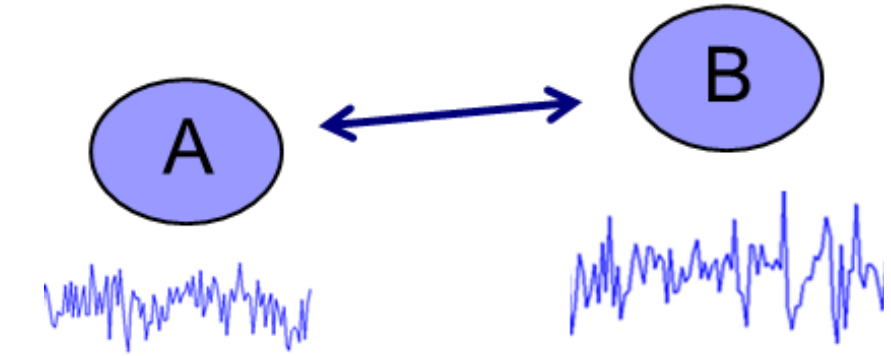
Structural connectivity

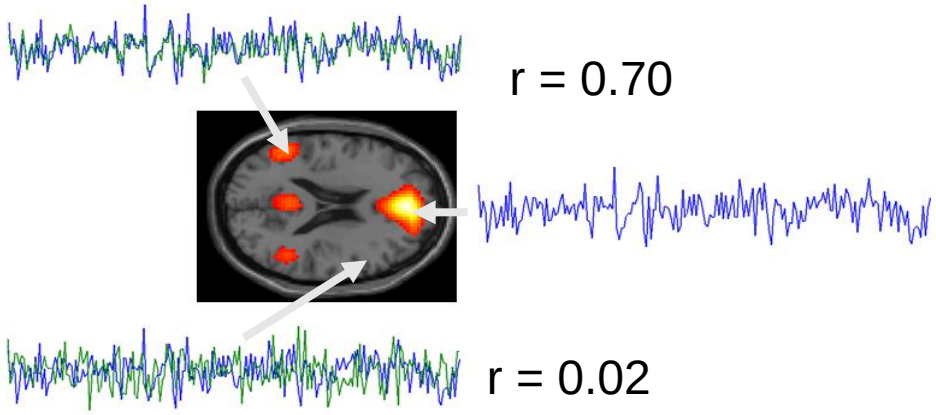
- Mapping of anatomical connections between cortical region
- white matter organization
- Diffusion tensor imaging (DTI)
- Static description of the system



Functional connectivity

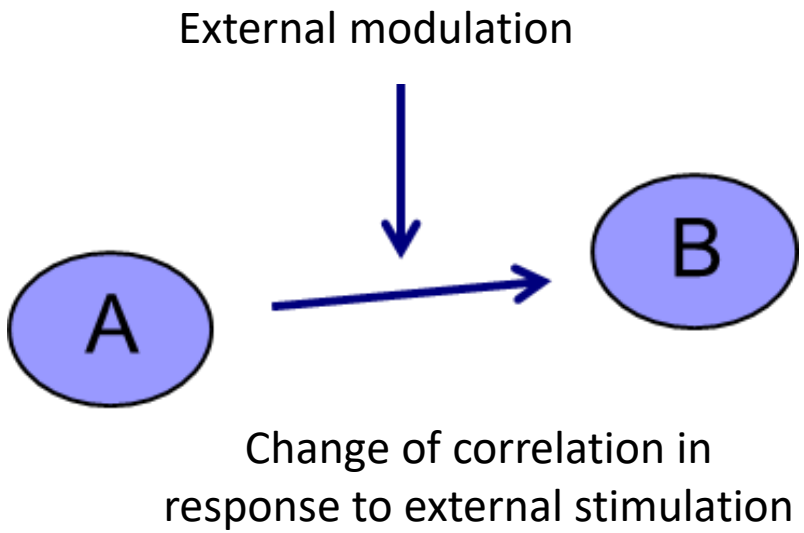
- Correlation between large distance neurophysiological events
- Indirect assumption about relationship between the regions
- Seed analysis, ICA





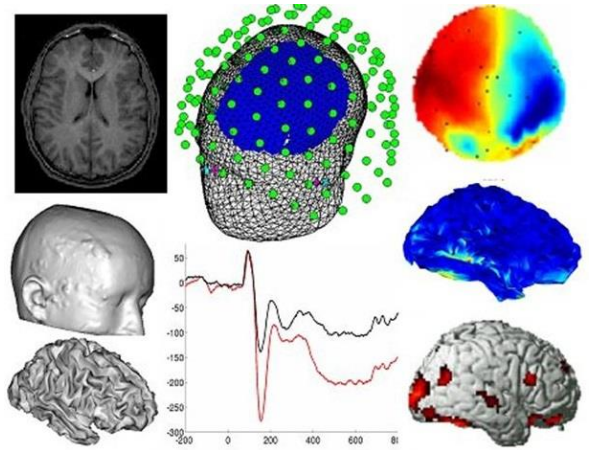
Effective connectivity

- Causal directed influences between neurons or neuronal populations
- Indirect assumption of connection between regions and how these are modulated by external stimulation
- PPI, DCM

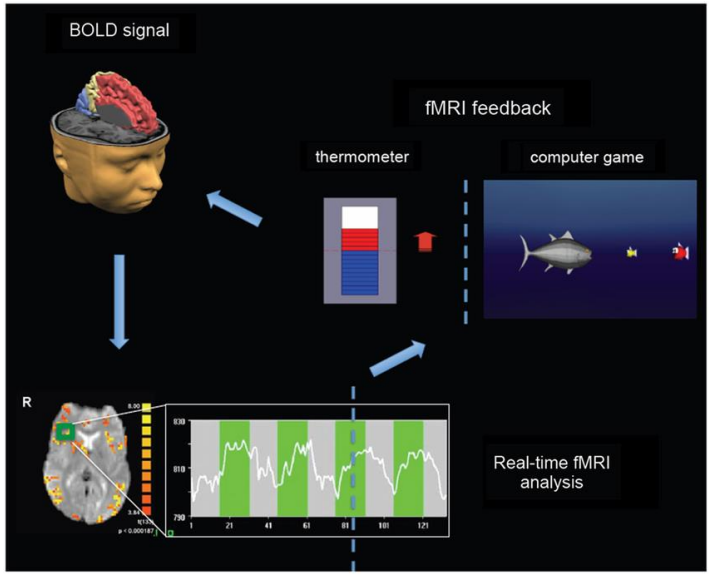


More examples of fMRI applications

- Resting state fMRI – large scale networks
- Real time fmri - neurofeedback
- multimodal imaging EEG-fMRI
- Hyperscanning
- Physiological mesurment ECG, breathing, galvanic response…



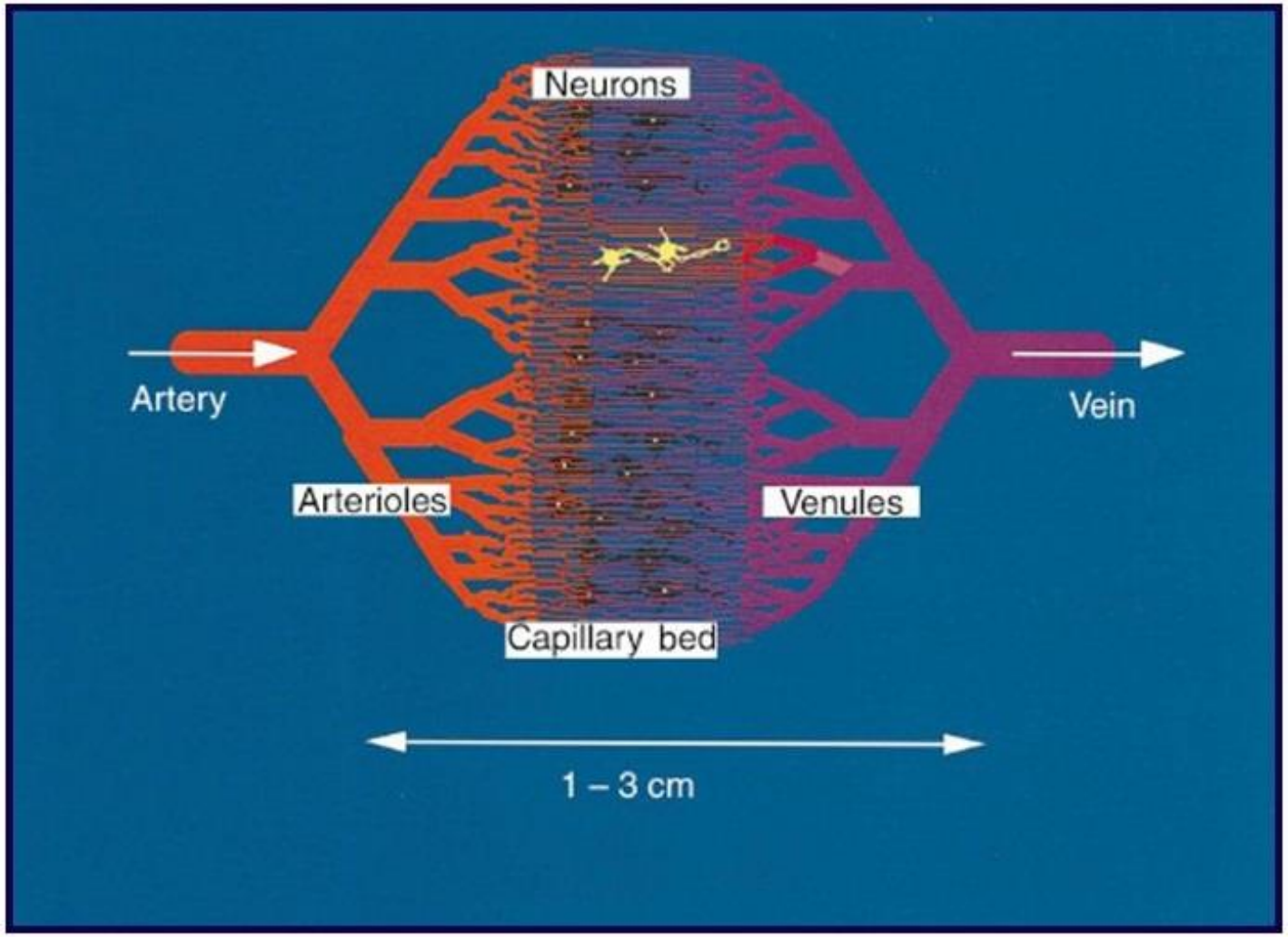
http://www.neuroscience.cam.ac.uk/directory/profile.php?RikHenson



(Carie and de Falco, 2015)

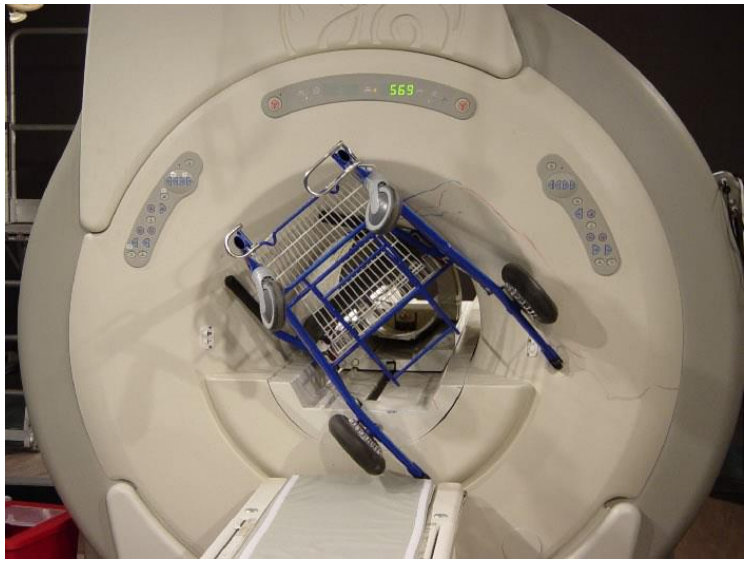
fMRI limitations

- **Artifacts** - misleading BOLD signal changes (head motion, ECG, respiration)
- BOLD response to a stimulus is delayed, which restricts maximum **temporal resolution** achievable
- Vasculature – implications for **spatial resolution**
- **Conceptual limitations**



(Menon and Kim, 1997)

Beware – the main magnetic field is always ON!



Thank you for attention…