PET Centre Neurocourse

fMRI preprocessing

(Fall 2017)

Enrico Glerean – twitter: @eglerean

fMRI preprocessing
outline

- **fMRI and BOLD**
- **Preprocessing:** the way it was and state of the art
- **Tools available**
- **Final remarks and take home messages**

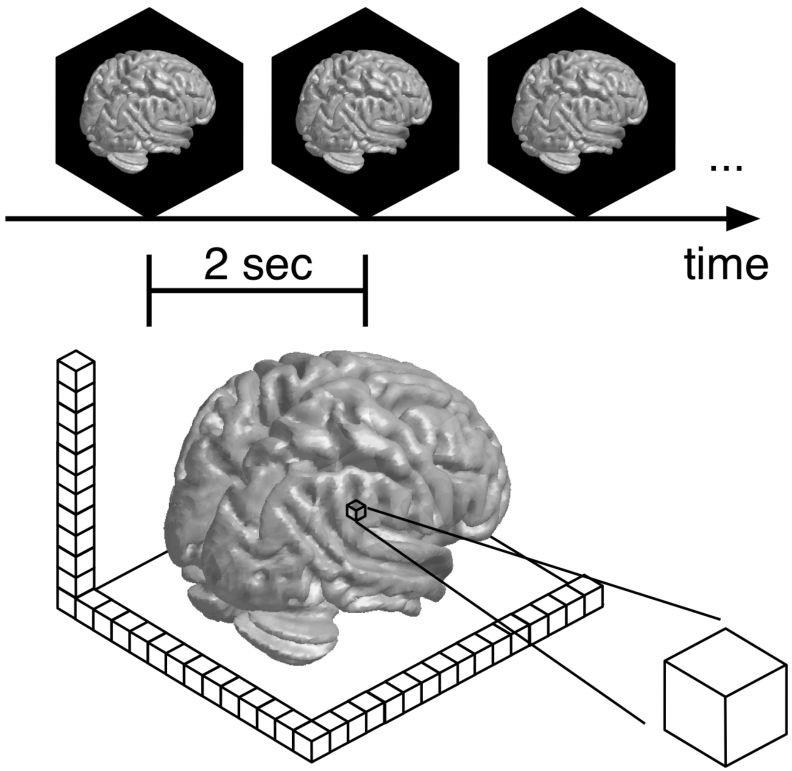
Feel free to interrupt with questions.

fMRI preprocessing
learning outcomes

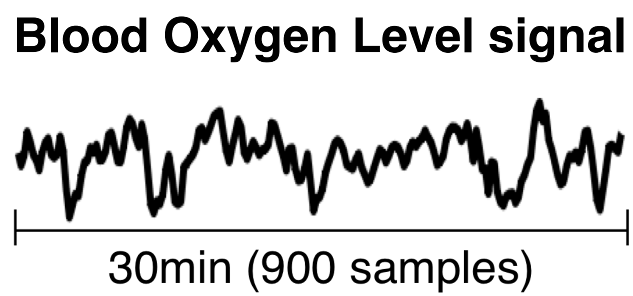
- **Gain knowledge on the issues with valuable references**
- **Understanding why we need and why we do preprocessing**
- **Being able to critically assess fMRI literature**

What is fMRI?

Functional magnetic resonance imaging (fMRI)



- We measure **multiple time series** at once
- **NOTE:** 1 voxel -> 5.5e6 neurons 4e10 synapses (density ~1/1000) [Logothetis 2008 Nature]



Optional reference: Sarty "Computing Brain Activity Maps from fMRI Time-Series Images" http://www.cambridge.org/catalogue/catalogue.asp?isbn=0511258380

What is BOLD?

What is BOLD?

- **Everybody should read this article**
- **BOLD as a population measure of energy consumption** (but … it's complicated)
- **BOLD is slow** so it's good if you want to measure neuromodulatory effects of arousal, attention, memory.

Vol 453|12 June 2008|doi:10.1038/nature06976

nature

REVIEWS

What we can do and what we cannot do with fMRI

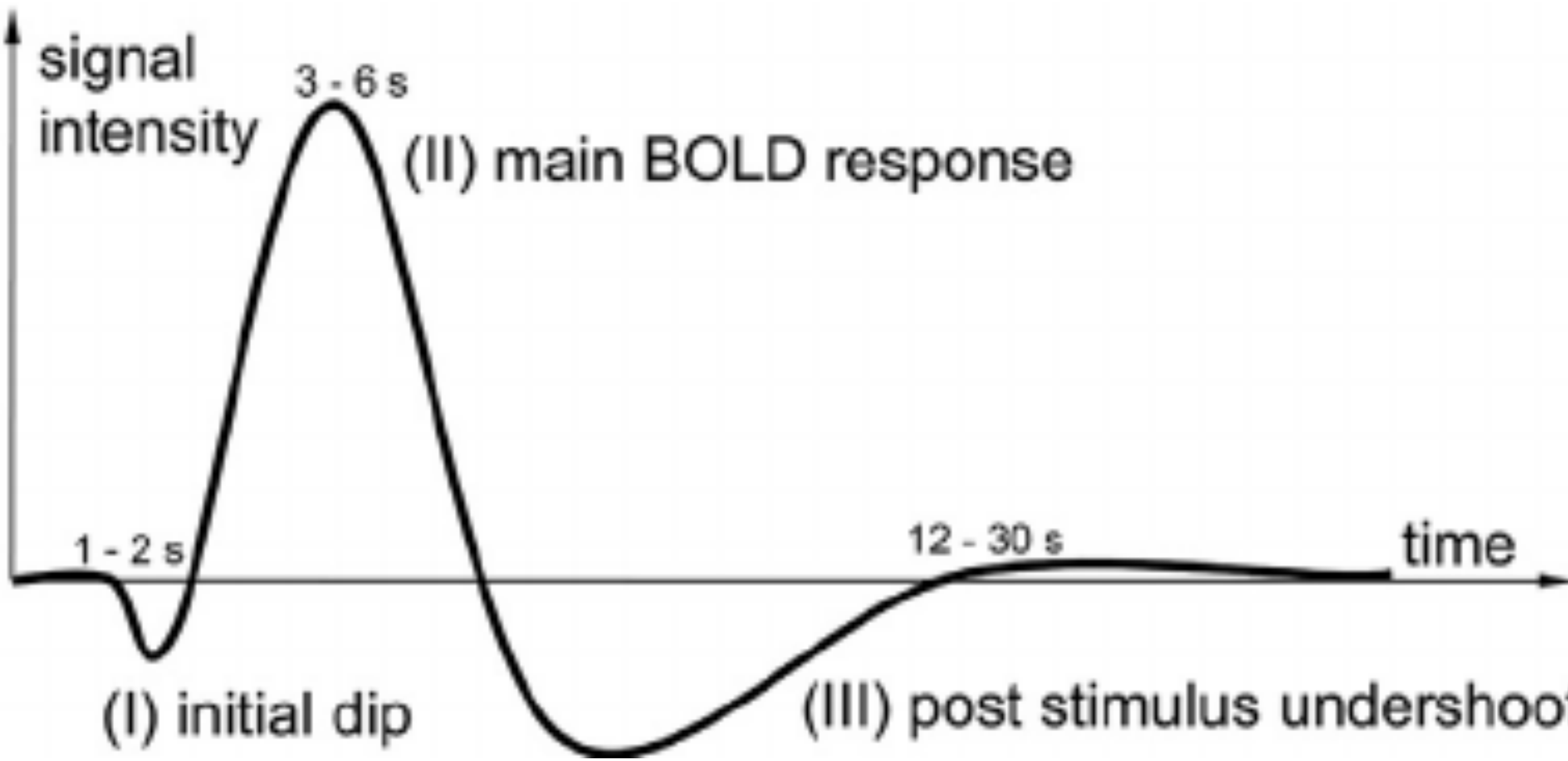
Nikos K. Logothetis[1]

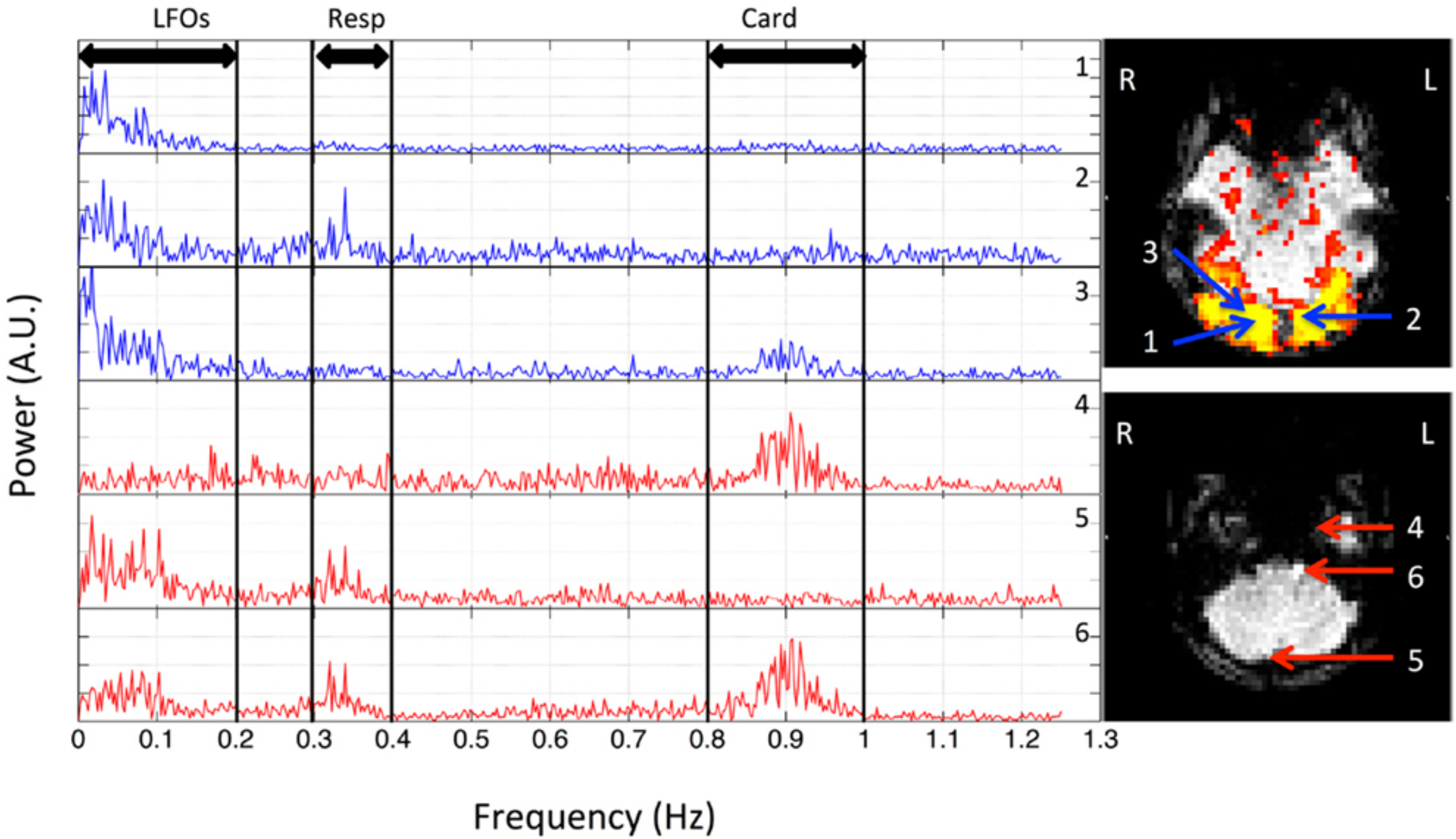
Functional magnetic resonance imaging (fMRI) is currently the mainstay of neuroimaging in cognitive neuroscience. Advances in scanner technology, image acquisition protocols, experimental design, and analysis methods promise to push forward fMRI from mere cartography to the true study of brain organization. However, fundamental questions concerning the interpretation of fMRI data abound, as the conclusions drawn often ignore the actual limitations of the methodology. Here I give an overview of the current state of fMRI, and draw on neuroimaging and physiological data to present the current understanding of the haemodynamic signals and the constraints they impose on neuroimaging data interpretation.

Magnetic resonance imaging (MRI) is the most important imaging advance since the introduction of X-rays by Conrad Röntgen in 1895. Since its introduction in the clinic in the 1980s, it has assumed a role of unparalleled importance in diagnostic medicine and more recently in basic research. In medicine, MRI is primarily used to produce structural images of organs, including the central nervous system, but it can also provide information on the physico-chemical state of tissues, their vascularization, and perfusion. Although all of these capacities have long been widely appreciated, it was the emergence of functional MRI (fMRI)—a technique for measuring haemodynamic changes after enhanced neural activity—in the early 1990s that had a real impact on basic cognitive neuroscience research. A recent database (ISI/Web of Science) query using the keywords 'fMRI' or 'functional MRI' or 'functional magnetic resonance imaging' returned over 19,000 peer-reviewed articles. Given that the first fMRI study without exogenous contrast agents was published in 1991, this corresponds to approxi-

Perhaps the extreme positions on both sides result from a poor understanding of the actual capacities and limitations of this technology, as well as, frequently, a confusion between fMRI shortcomings and potential flaws in modelling the organizational principles of the faculties under investigation. For example, a frequently made assumption is that the mind can be subdivided into modules or parts whose activity can then be studied with fMRI. If this assumption is false, then even if the brain's architecture is modular, we would never be able to map mind modules onto brain structures, because a unified mind has no components to speak of. Even if true, the challenge remains in coming up with the correct recursive decompositions—in each of which any given cognitive capacity, however abstract, is divided into increasingly smaller functional units that are localized to specific brain parts, which in turn can be detected and studied with fMRI. This is not a neuroimaging problem but a cognitive one. Hierarchical decompositions are clearly possible within different sensory modalities and motor systems. Their mapping, which reflects

Mandatory reference: Logothetis "What we can do and what we cannot do with fMRI" http://kyb.mpg.de/fileadmin/user_upload/files/publications/attachments/NikosNatureJune2008_%5b0%5d.pdf


signal
intensity
3 - 6 s
(II) main BOLD response
1 - 2 s
12 - 30 s
time
(I) initial dip
(III) post stimulus undershoot

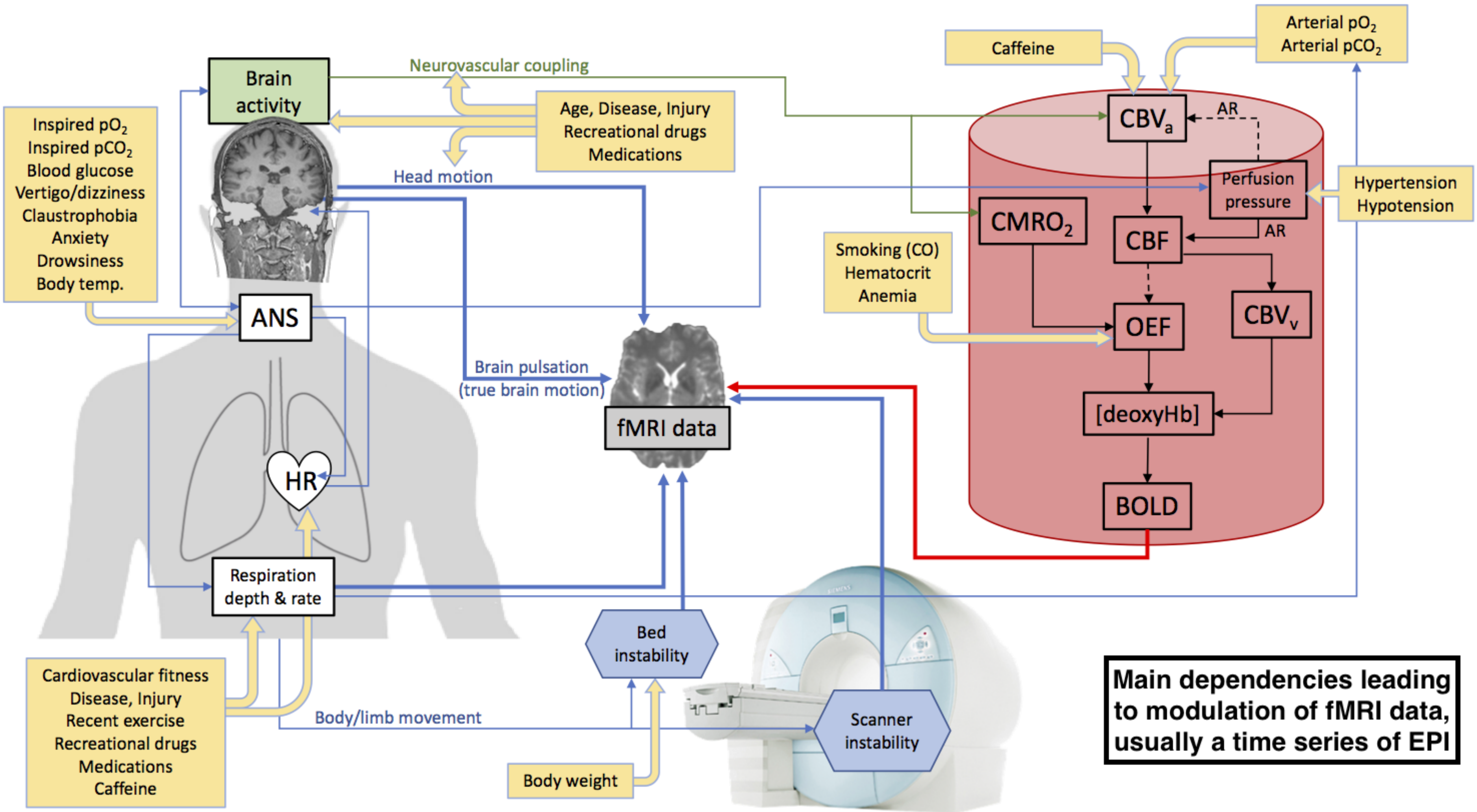


Reference: Tong 2014 "Studying the spatial distribution of physiological effects on BOLD signals using ultrafast fMRI" https://www.frontiersin.org/articles/10.3389/fnhum.2014.00196/full

All that glitter is not BOLD

How bad is the BOLD signal?

- BOLD is a **qualitative** measure (Hoge 2012, Neuroimage)
- BOLD response on same subject has **different lags in different days** (Aguirre, 1998, Neuroimage)
- BOLD measures also **non-neuronal signals** (breathing, heart, cerebral blood flow) (Tong 2014, Frontiers)
- **Caffeine** changes BOLD (multiple ref., see next)
- **Eating salad** (NO3- nitrate intake), changes lag and amplitude of BOLD (Aamand et al 2013, Neuroimage)
- **Time of day** changes BOLD (multiple ref. see next)
- **BOLD response does not have the same lag/amplitude across all voxels**
- I am glad I asked this blogger to collect all the sources of confounds with BOLD https://thewinnower.com/papers/concomitant-physiologic-changes-as-potential-confounds-for-bold-based-fmri-a-checklist



Main dependencies leading to modulation of fMRI data, usually a time series of EPI

Reference: practiCalfMRI "Fluctuations and biases in fMRI data" (Aug/2017)
https://practicalfmri.blogspot.fi/2017/08/fluctuations-and-biases-in-fmri-data.html

Why do we do preprocessing?

Preprocessing can control for systematic and subject-related confounds

- **Systematic**: related to the scanner (magnetic field instability, heating up of scanner components with time) or related to the sequence used to measure fMRI
- **Subject-related:** all previously mentioned plus head motion

Note: It's actually a bit more complicated since they are not fully separable (e.g. subject lung movements and head motion causes magnetic field instability)

How do we collect fMRI data?

Most commonly used sequence is the Echo-Planar Imaging (EPI)

- fMRI time series usually done with **EPI sequence**
- Data are collected in **slices, one at a time,** forming a volume.
- Usually it takes **2 seconds** to cover the whole brain, so 2/NumOfSlices seconds per slice
- Interleaved acquisition usually preferred (mekes it easier to stabilize head motion)

Slice ordering

Sequential Ascending 1,2,3,4,5,6

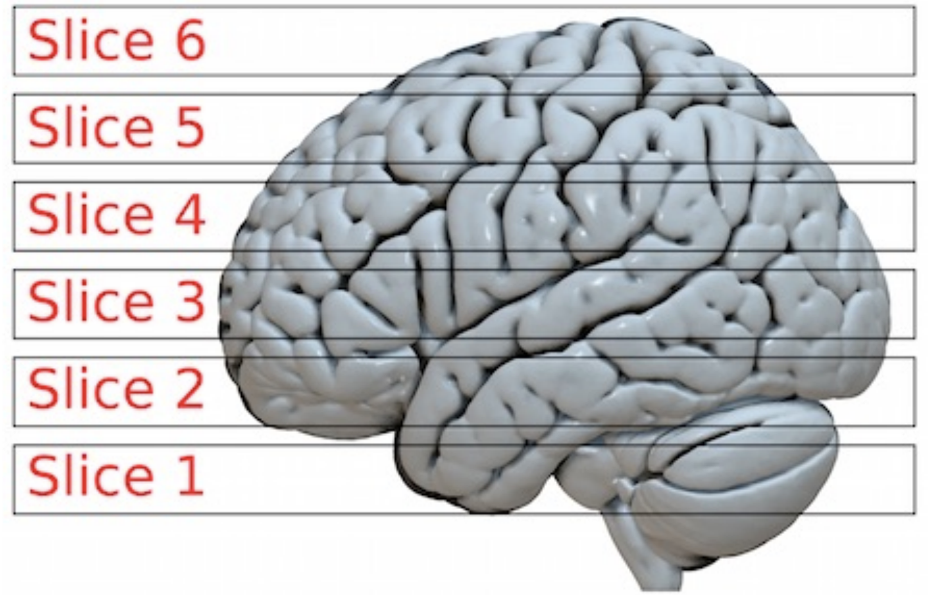
Sequential Descending 6,5,4,3,2,1

Interleaved Ascending 1,3,5,2,4,6

Interleaved Descending 6,4,2,5,3,1

Interleaved Ascending * 2,4,6,1,3,5

Interleaved Descending * 5,3,1,6,4,2



From: http://www.mccauslandcenter.sc.edu/crnl/tools/stc

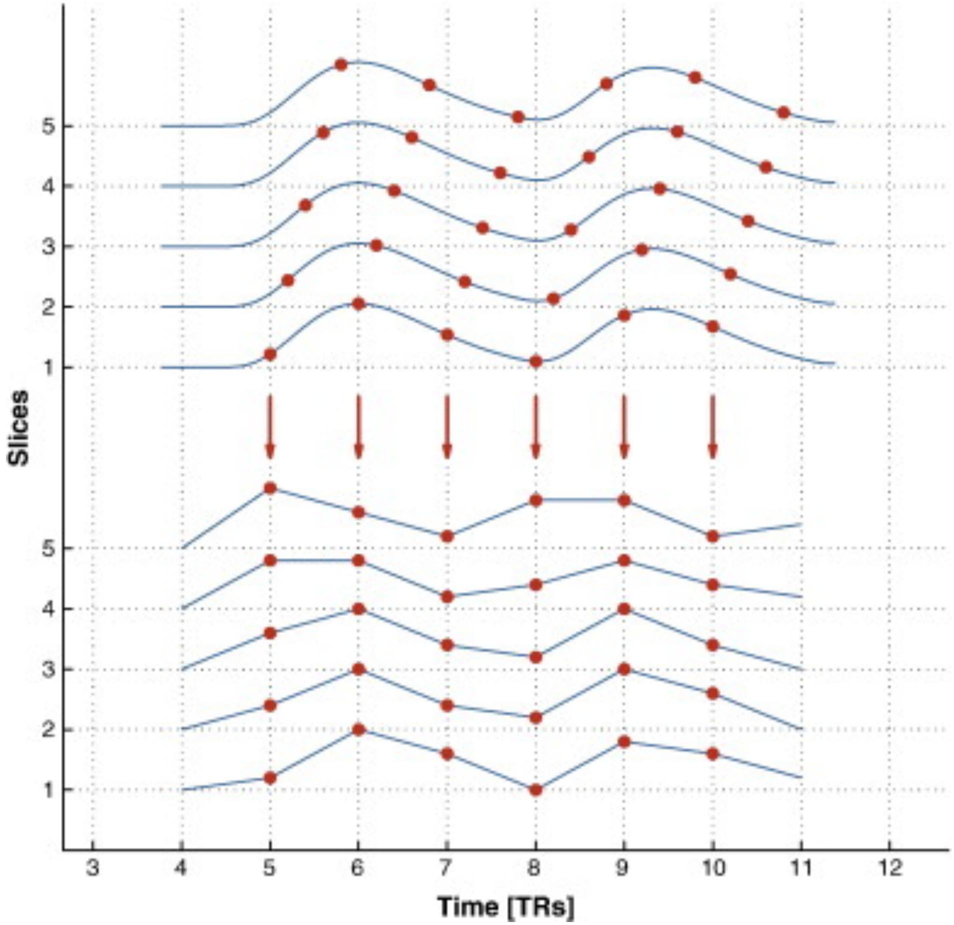
fMRI preprocessing

fMRI preprocessing in the year 2000s

1. **Slice timing correction**
2. **Head motion stabilization**
3. **Co-registration with individual's anatomical**
4. **Normalization with population average** (e.g. MNI template)
5. **Spatial filtering** (kernel smoothing)
6. **Temporal filtering** (high and/or low pass)

fMRI preprocessing in the year 2000s
Slice timing correction

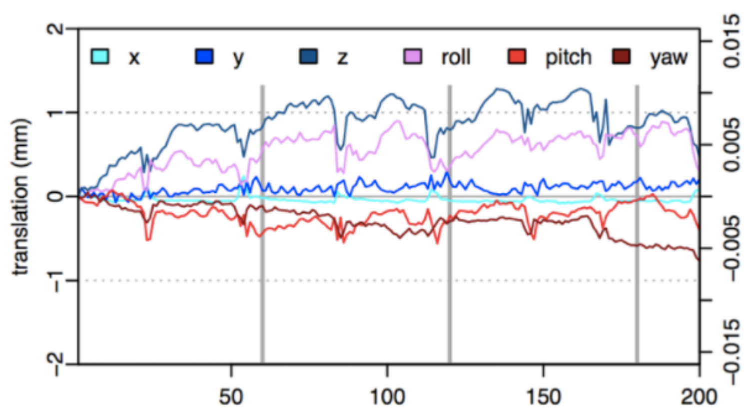
Compensate for the time delay of each acquired slice so that they are at the same time



(Sladky et al 2011 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3167249/)

fMRI preprocessing in the year 2000s
Head motion stabilization

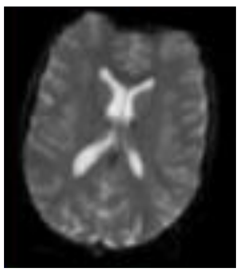
- **Head motion stabilization** just estimates rigid rotations and translations.
- For 3D images this means 6 degrees of freedom (translation x y z, rotations yaw, pitch, roll)
- 6 motion parameters are estimated



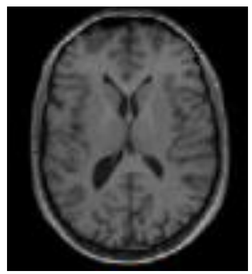
Source: https://practicalfmri.blogspot.fi/2016/10/motion-traces-for-respiratory.html

fMRI preprocessing in the year 2000s
Co-registration and normalization

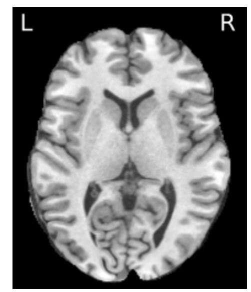
- **Transformations in space so that functional data can be compared across subjects**



1) Affine Tf (7dof)



2) Affine (12dof) or non linear



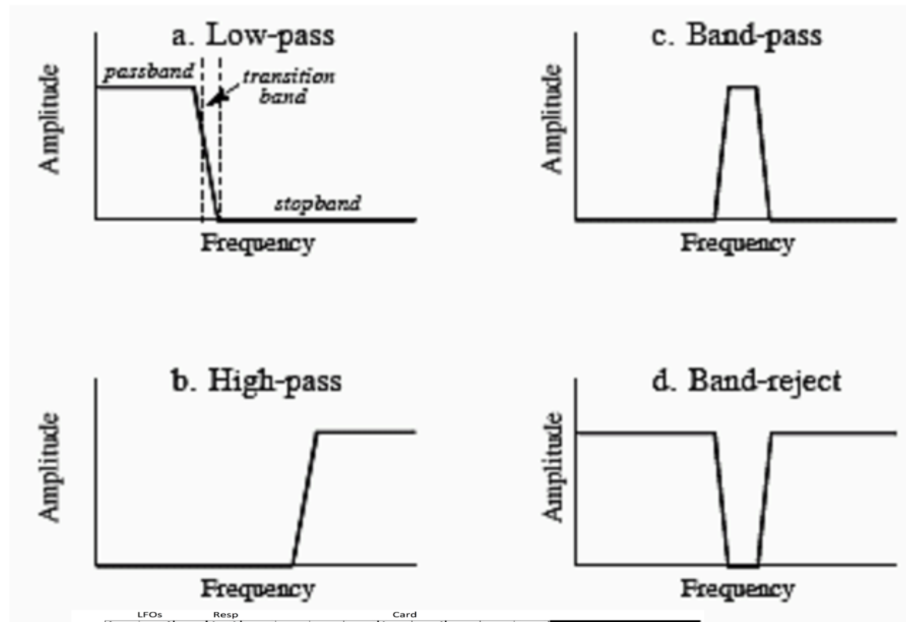
1. As the subject's head does not change, rigid body (6dof) and a scaling factor (1dof) is enough
2. If linear, rigid (6dof), scale (3dof), skew (3dof)

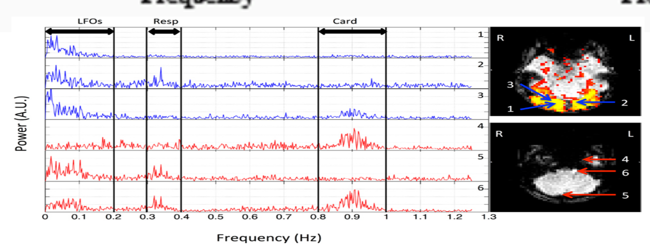
fMRI preprocessing in the year 2000s
Spatial filtering

- **Smoothing just means that the image is blurred**
- It gets rid of spatial noise
- Improves normalization and inter-individual similarities
- Increases statistical power

fMRI preprocessing in the year 2000s
Temporal filtering

- **Same as smoothing, but this time it happens in time**
- Can get rid of unwanted signal components that are frequency specific like scanner drift (due to heating) or cardiac and respiratory noise.





Reference: Smith "The Scientist and Engineer's Guide to Digital Signal Processing" http://www.dspguide.com/ch14/4.htm

Is this the state of the art?

fMRI preprocessing state of the art

- Within last 5 years neuroscience (and psychology) have undergone a **methodological audit** to increase reproducibility and validity of the results
- Reflection: **is it methodological terrorism?** No
- With increased power (better SNR in tools, more subjects, more data) **it becomes more easier to detect trivial effects** that can be explained by confounds

fMRI preprocessing in the year 2017

1. **Compensation for heart and breathing rates**
2. **Slice timing correction**
3. **Head motion stabilization**
4. **Co-registration with individual's anatomical**
5. **Normalization with population average** (e.g. MNI template) **using bias field info or EPI template**
6. **Denoising (remove low frequency drift, remove motion related time-courses)**
7. **Spatial filtering** **…maybe don't do it**
8. **Temporal filtering** **…maybe don't do it**

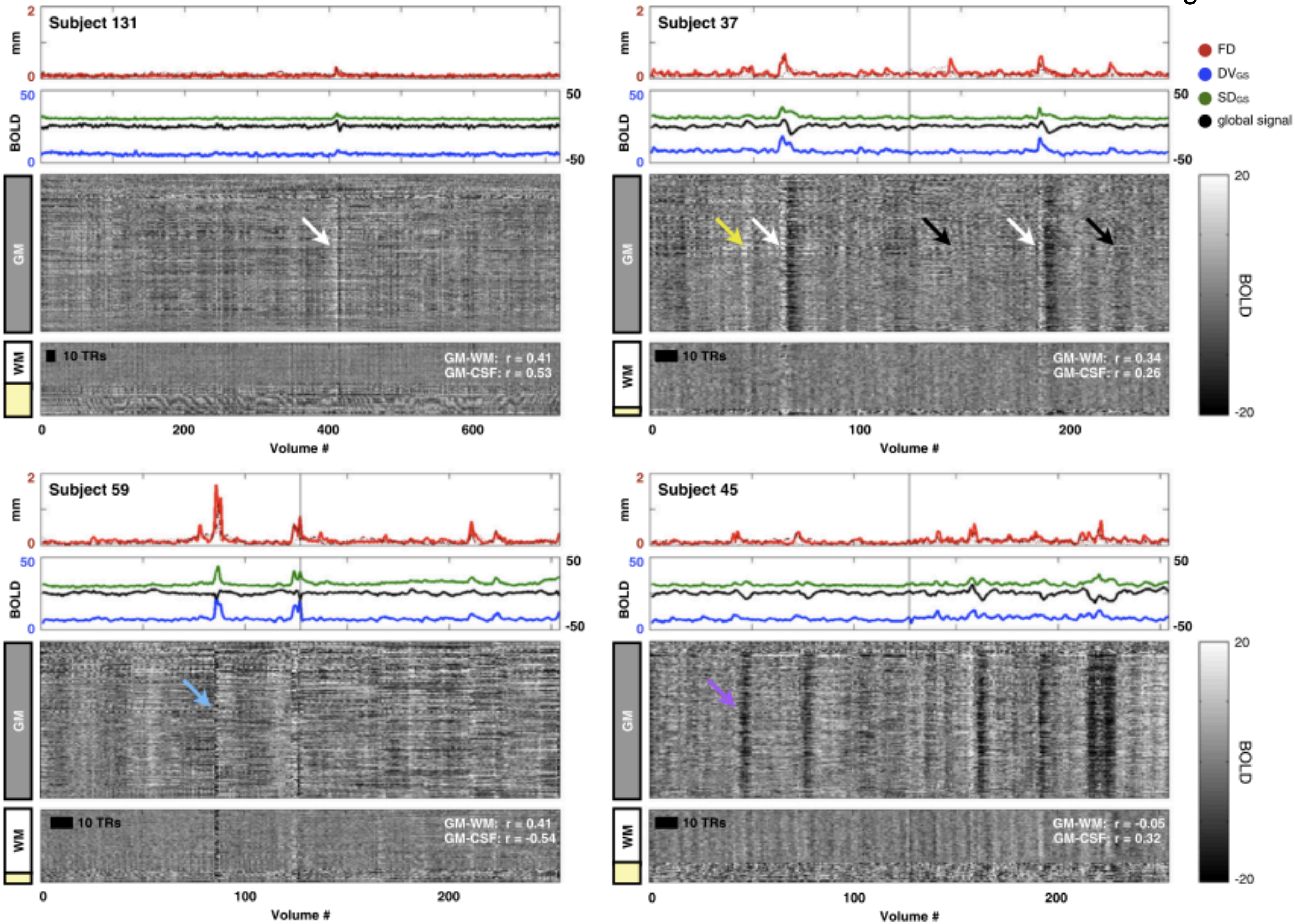
fMRI preprocessing state of the art
heart and breathing

- **Heart rate and breathing rate** are present in the BOLD. With fast TR ***most*** of the signal is outside the BOLD neural spectrum… but arousal and other mental process co-vary with them
- BOLD TR ~ 2s i.e. **0.5 Hz sampling frequenc**y
- Shannon theorem tells us that we cannot actually see those faster frequencies
- Brain tissues close to large vessels are affected (default mode areas, insula and amygdala)
- **S.o.t.A : record breathing and pulse and/or use MultiBand EPI** (cheap solution is to regress out white matter and cerebral spinal fluid voxels activity)

fMRI preprocessing state of the art
head motion

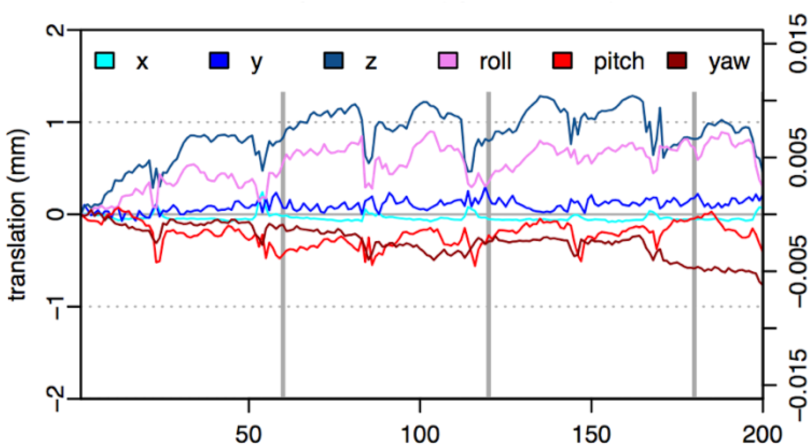
- **Head motion** (even less than 1 mm) destroys the BOLD signal.

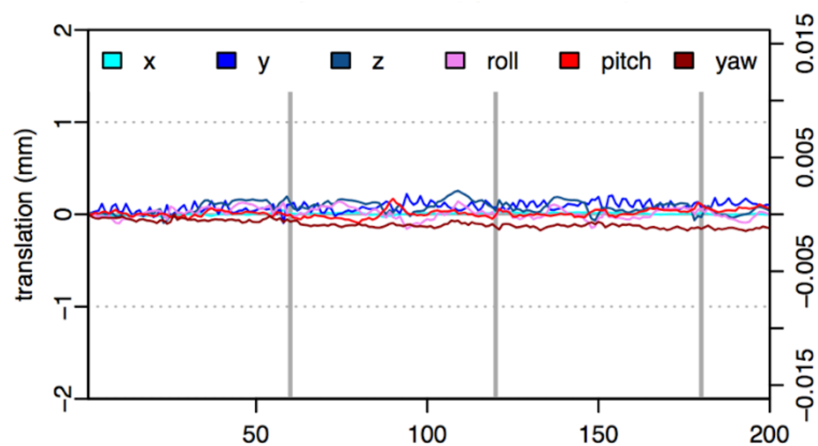
Power et al 2014, Neuroimage



fMRI preprocessing state of the art
head motion

- **Head motion** (even less than 1 mm) destroys the BOLD signal.
- The best way to fix it is to use **better head restraints**

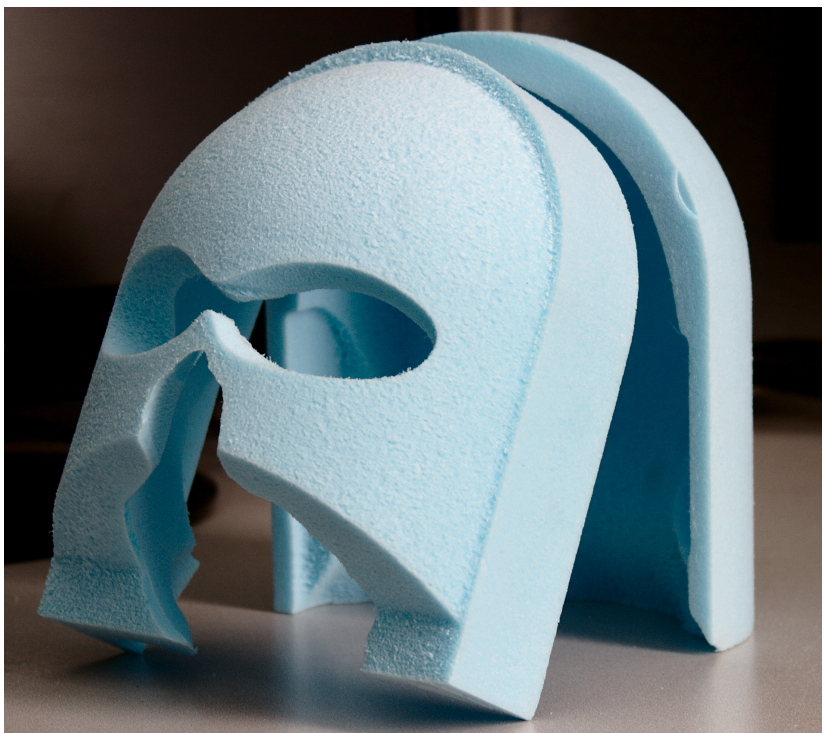




Source: https://practicalfmri.blogspot.fi/2016/10/motion-traces-for-respiratory.html

fMRI preprocessing state of the art
head motion

https://caseforge.co/



Jack Gallant
@gallantlab
Following

High-quality non-invasive brain-reading devices will likely be common long before invasive ones. Hopefully they won't look as silly as this.

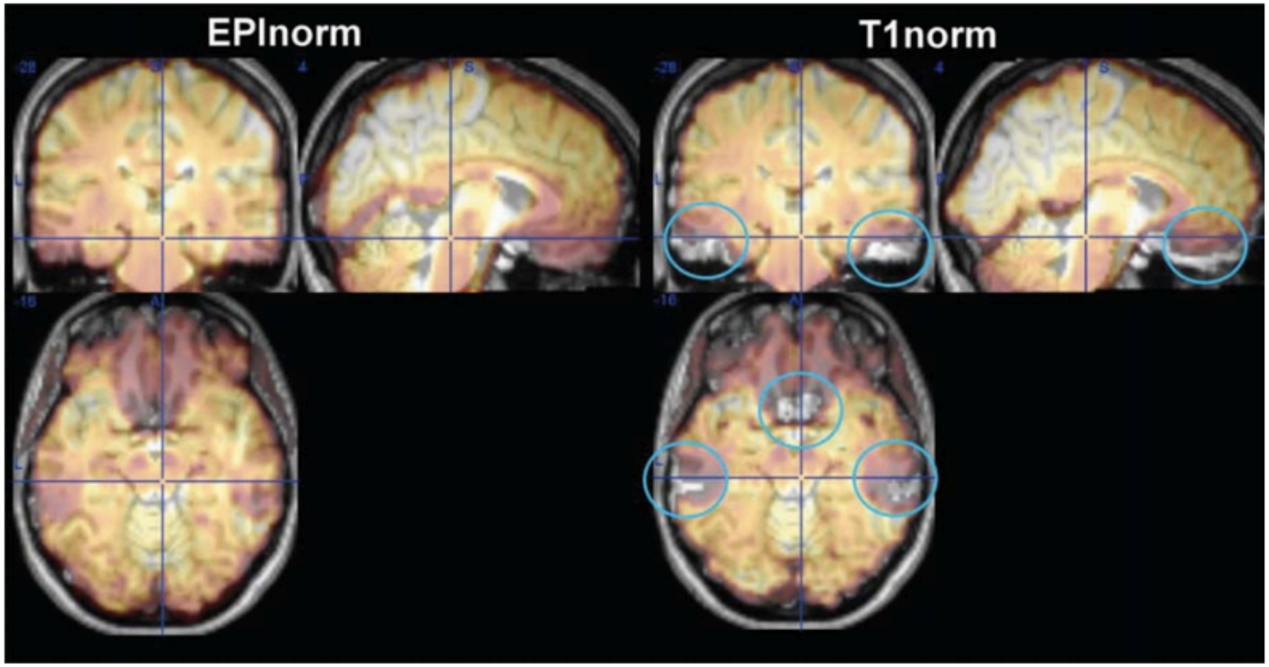
8:03 PM - 23 Apr 2017

fMRI preprocessing state of the art
head motion

- **Head motion** (even less than 1 mm) destroys the BOLD signal.
- The best way to fix it is to use **better head restraints**
- We can remove what is explained by head motion building **regressors based on estimated motion parameters** or – the state of the art – **ICA denoising tools** such as **ICA-AROMA**
- **S.o.t.A.: caseforge and ICA-AROMA**

Reference: Parkes et al 2017 “An evaluation of the efficacy, reliability, and sensitivity of motion correction strategies for resting-state functional MRI”
https://www.biorxiv.org/content/early/2017/06/27/156380

fMRI preprocessing state of the art



If you cannot estimate the bias field distortion, use EPI template (single step normalization)

Reference: Calhun et al 2017 “The Impact of T1 Versus EPI Spatial Normalization Templates for fMRI Data Analyses” https://www.ncbi.nlm.nih.gov/pubmed/28745021

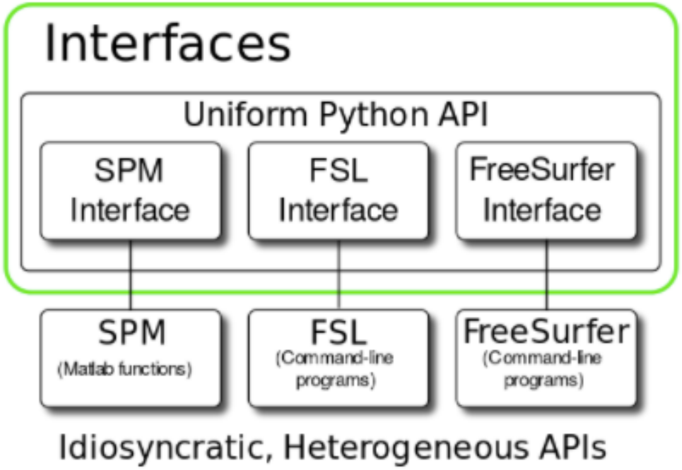
fMRI preprocessing state of the art
smoothing and filtering

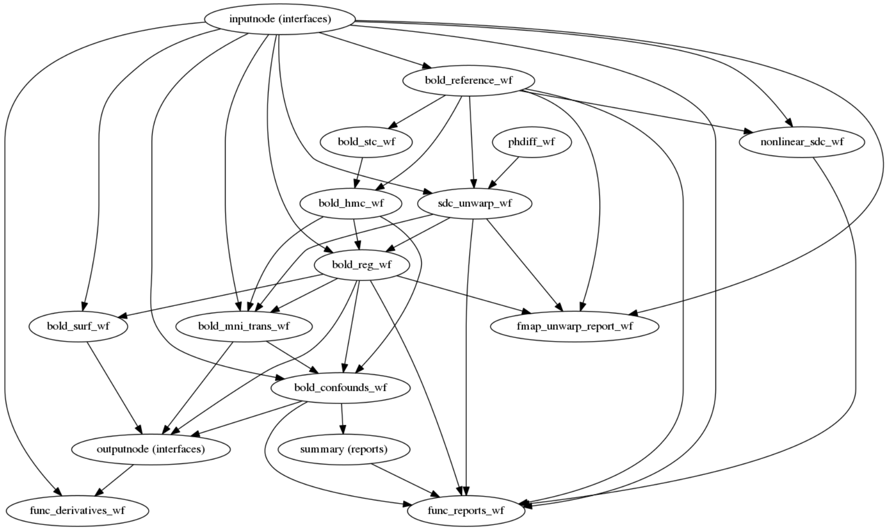
- **The state of the art depends on what you need to do: KWYAD** (know-what-you-are-doing)
- Smoothing increases **spatial autocorrelation** (information at one voxel is able to predict information on the neighbouring voxel) -> it can affect statistical estimate.
- Smoothing is not recommended with techniques such as **MVPA** and **connectivity**
- **It's not as simple as it relates with the point spread function** (about 3mm)

What is the best way to do it in practice?

fMRI preprocessing state of the art
tools

- **Multiple tools**: the best solution is to use the best of each.
- **fMRIprep** is a tool based on nipype
  https://fmriprep.readthedocs.io
- It is based on containers, faster to install and run.
- It can be run from the web if you can share the data one day





Take home messages

fMRI preprocessing
take home messages

- **fMRI preprocessing** is a necessary step if you work with fMRI, but remember to **KWYAD** (know-what-you-are-doing)

- **Follow the literature** as the field is still evolving (twitter and blogs can help you with that like practicalfMRI)

- **Don’t reinvent wheels**: pick up tools that are easy and that allows you to get the job done while trusting who is behind