MRC Cognition and Brain Sciences Unit

UNIVERSITY OF CAMBRIDGE

ChatGPT art

Functional Magnetic Resonance Imaging

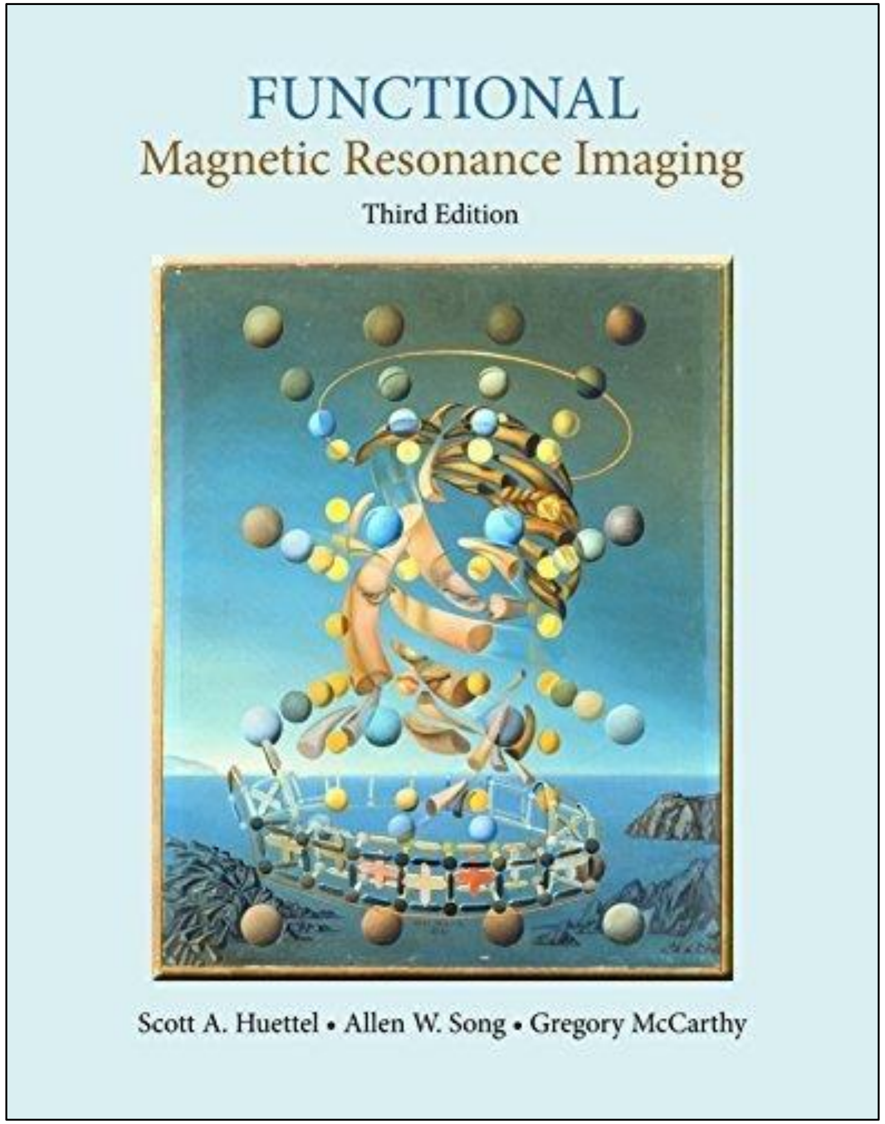
Dace Apšvalka

Winter, 2024

Outline

- Introduction
- Experimental design
- Data management
- Pre-processing
- Statistical analysis
- Practical demo

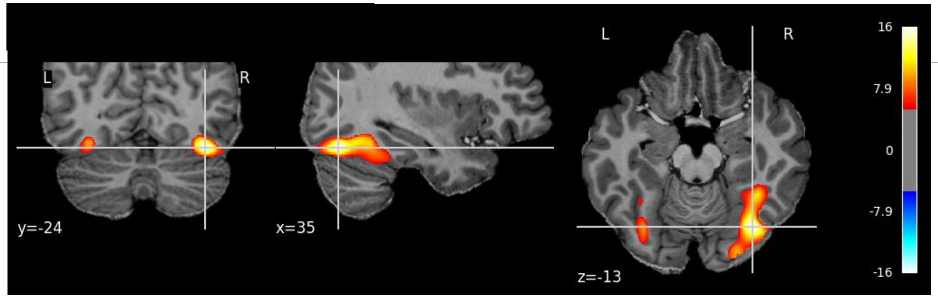
Recommended book



University of Cambridge Library link

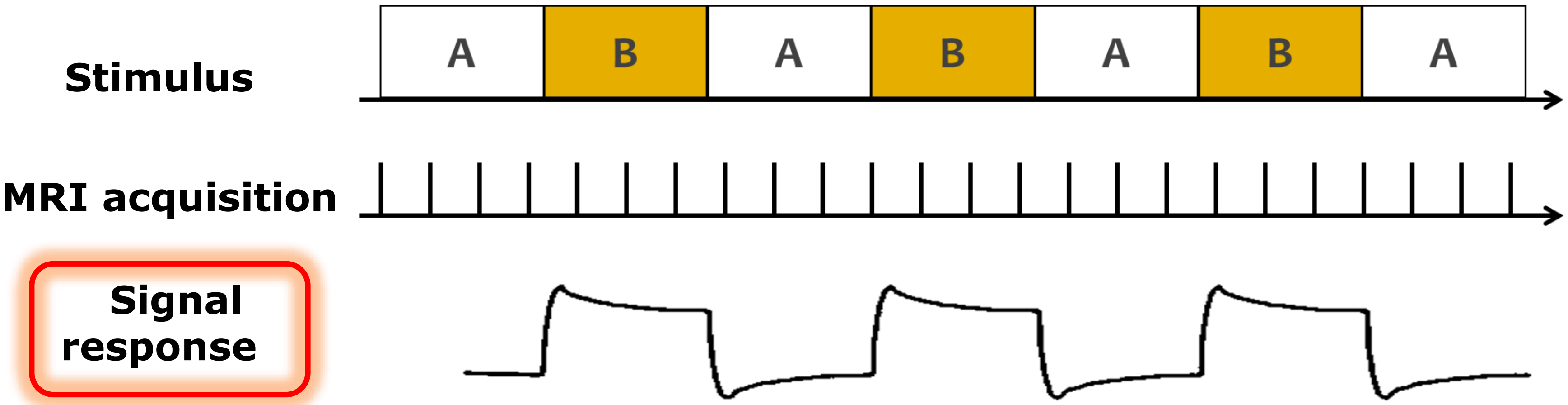
Introduction

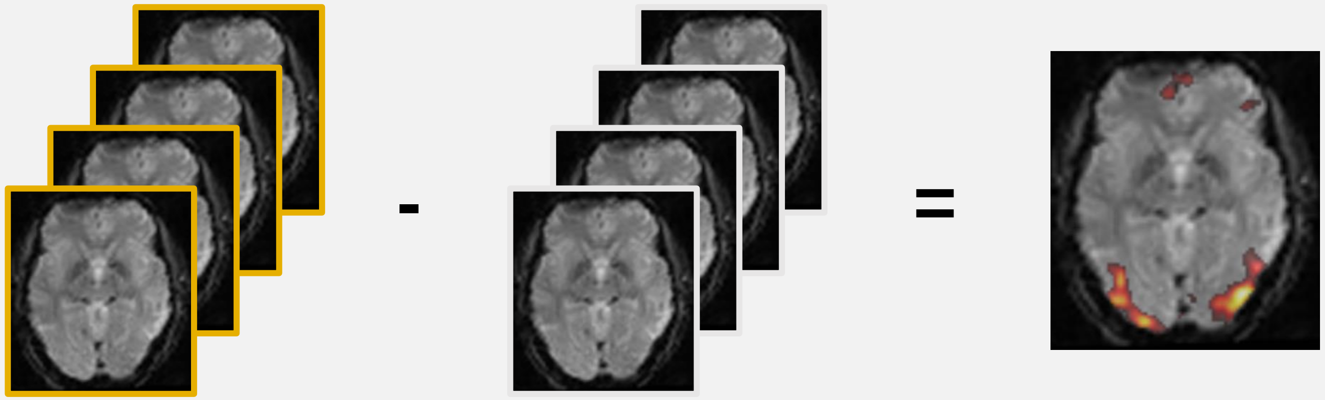
Functional MRI (fMRI)



- A brain imaging technique that uses an **MRI** scanner to measure and map **brain activity**
- It is **non-invasive**
- Can give **whole-brain** coverage
- It has the **highest spatial resolution** of any non-invasive imaging technique (typically 1-3 mm)
- It has a **reasonable temporal resolution** (typically 1-3 seconds)

Functional MRI (fMRI)





B state images

A state images

Contrast/**B activation** map

Diagram adapted from Glover, 2011

fMRI signal

- Blood oxygen level-dependent (BOLD) signal

dampens the MRI signal

Oxygenated blood cells
HbO2

De-oxygenated blood cells
Hb

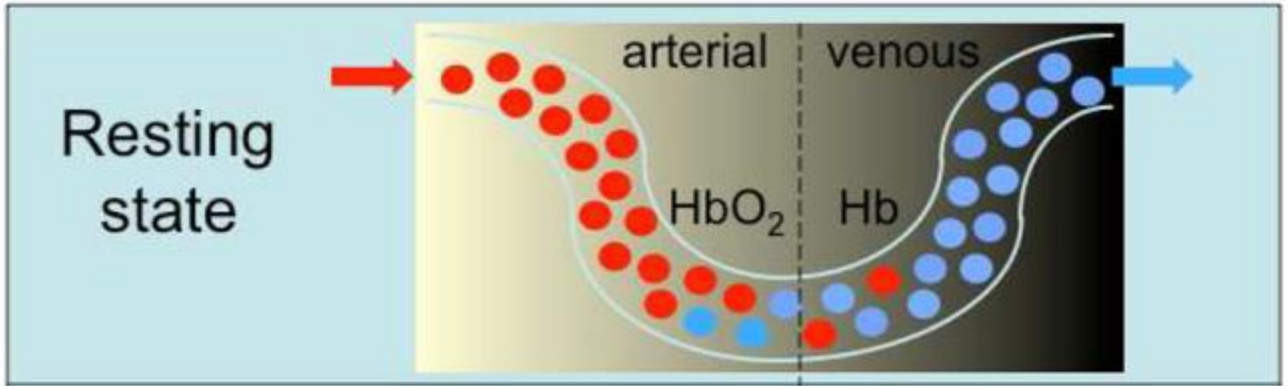


Diagram adapted from Glover, 2011

fMRI signal

- Blood oxygen level-dependent (BOLD) signal

→ **dampens the MRI signal**

Oxygenated blood cells
$HbO2$

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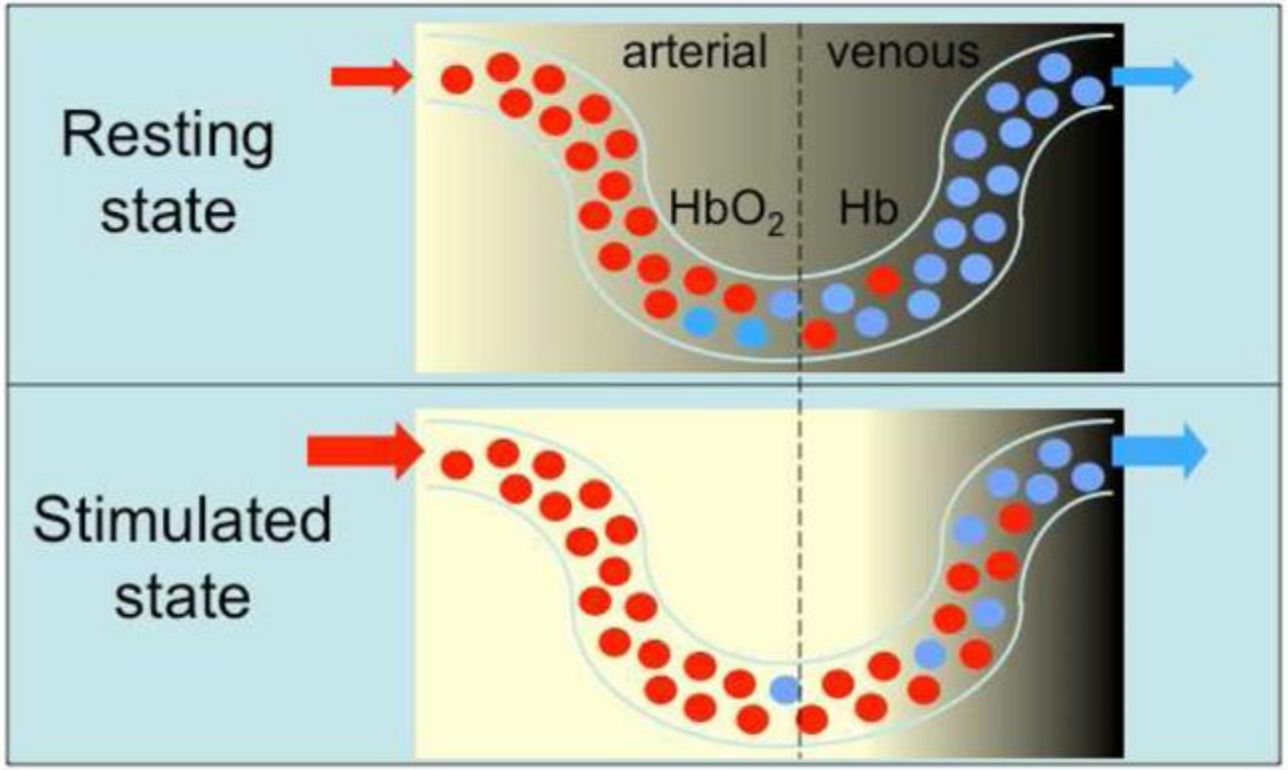
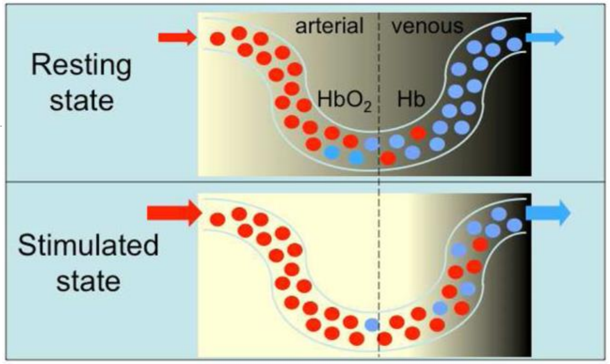


Neural activity-induced increase in blood flow **sweeps the "de-ox" away**, causing an MRI **signal increase**

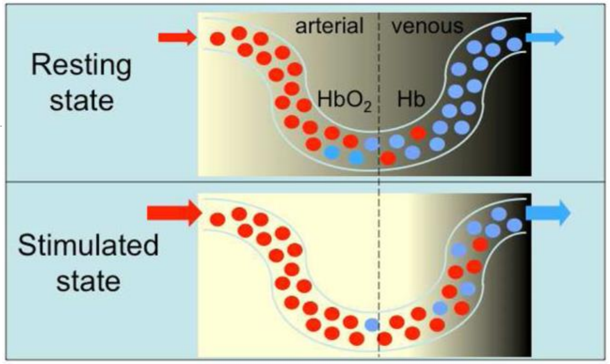
Diagram adapted from Glover, 2011

fMRI signal



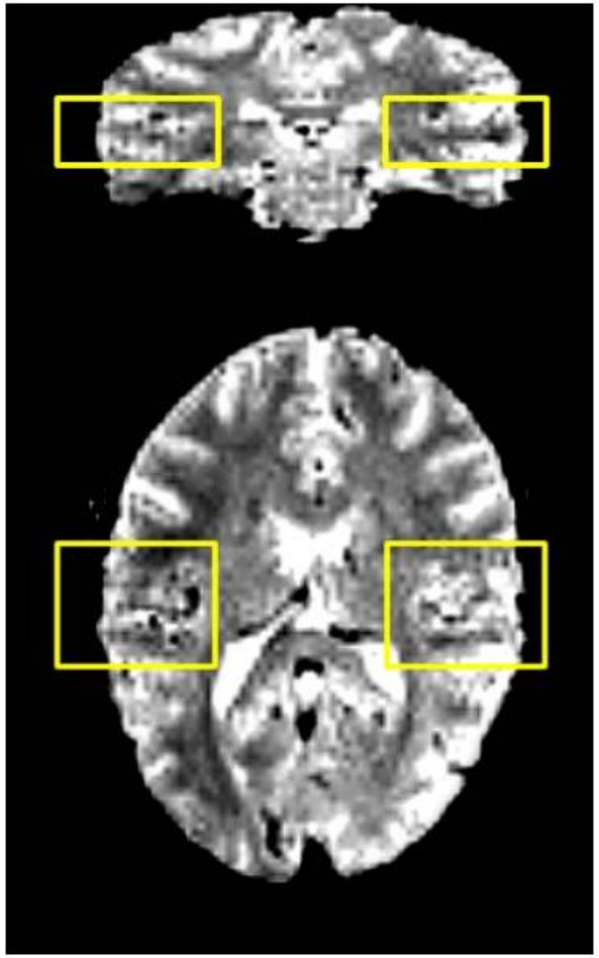
- **At rest,** the cerebral **metabolic rate of oxygen** (CMRO2) and cerebral **blood flow** (CBF) are tightly **coupled**
- During **increased neuronal activity** they become **uncoupled**, with CBF increasing relatively more than CMRO2 (Fox and Raichle, 1986)
  - ‘an overcompensation’
- The uncoupling leads to an **increase in oxygenated Hb** due to an influx of fresh blood which **‘flushes away’ the de-oxygenated Hb** and therefore increases the BOLD signal

fMRI signal

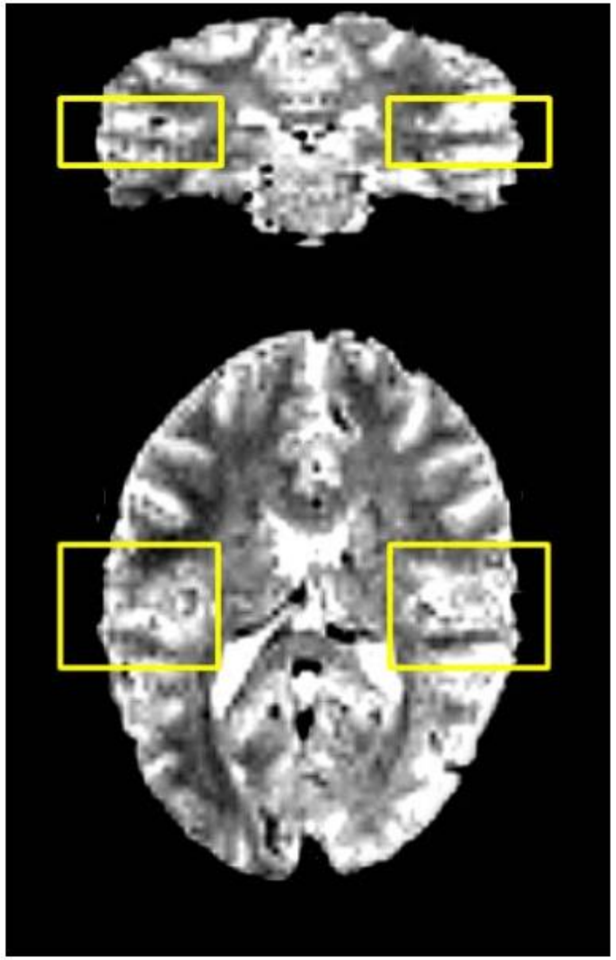


- An example of auditory cortex activation (from Marta's MRI physics slides)

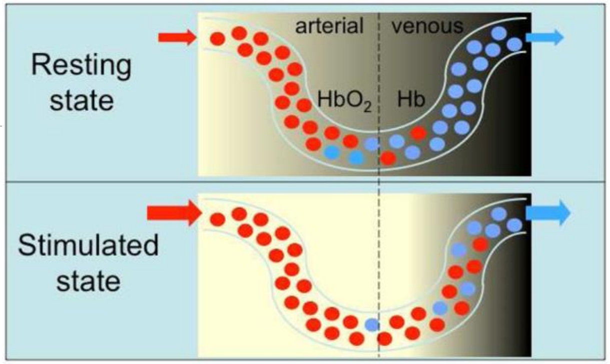
Baseline



Neural Activity



fMRI signal



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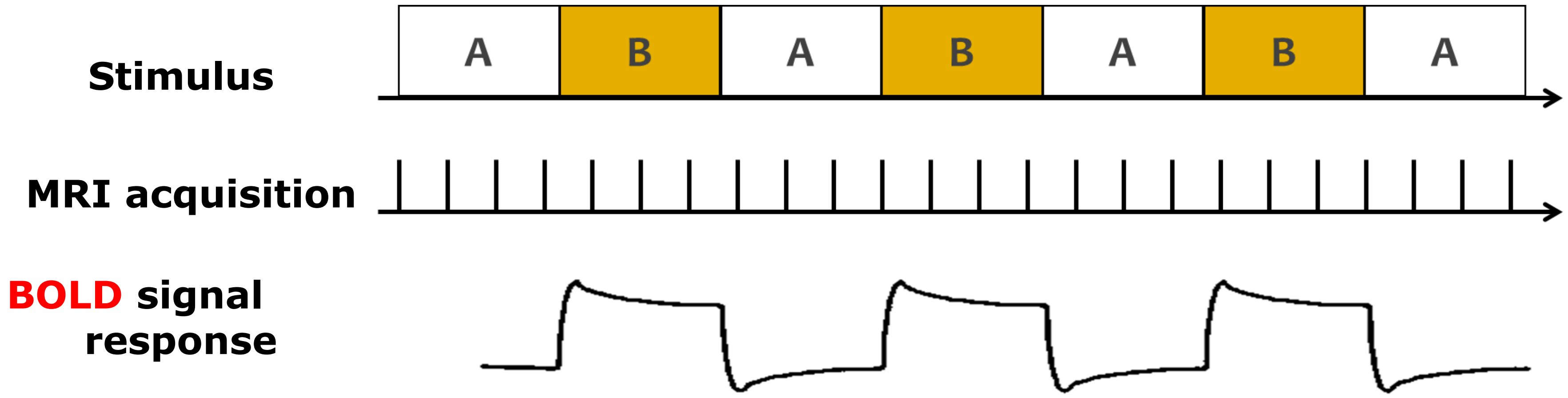
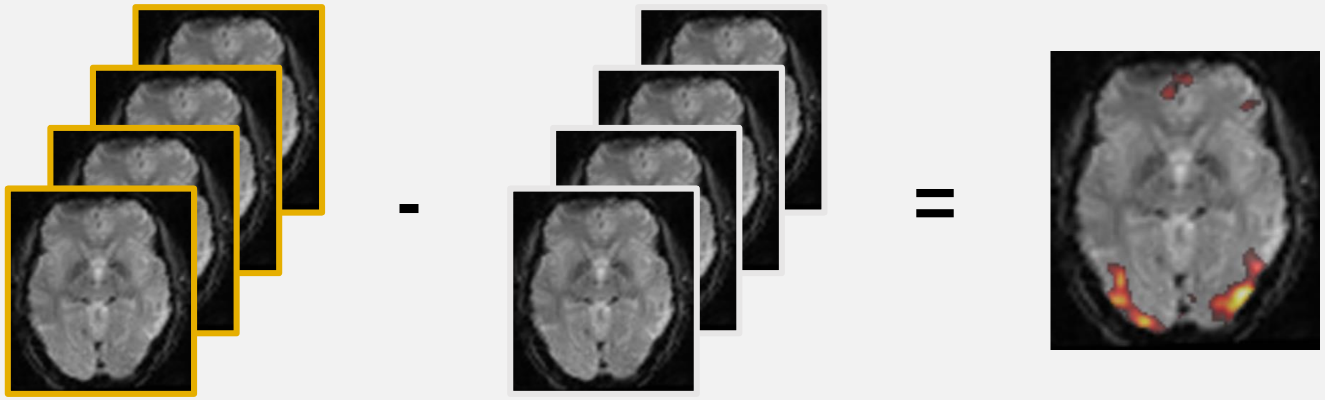
- This difference in the magnetic properties of de-oxygenated and oxygenated Hb is used in BOLD fMRI to create contrast in images – reflecting activity in different brain regions.
  - By controlling for all other factors, any observed differences in the BOLD signal are inferred to be due to differences in neuronal activity

Functional MRI (fMRI)





B state images | **A state** images | Contrast/**B activation** map

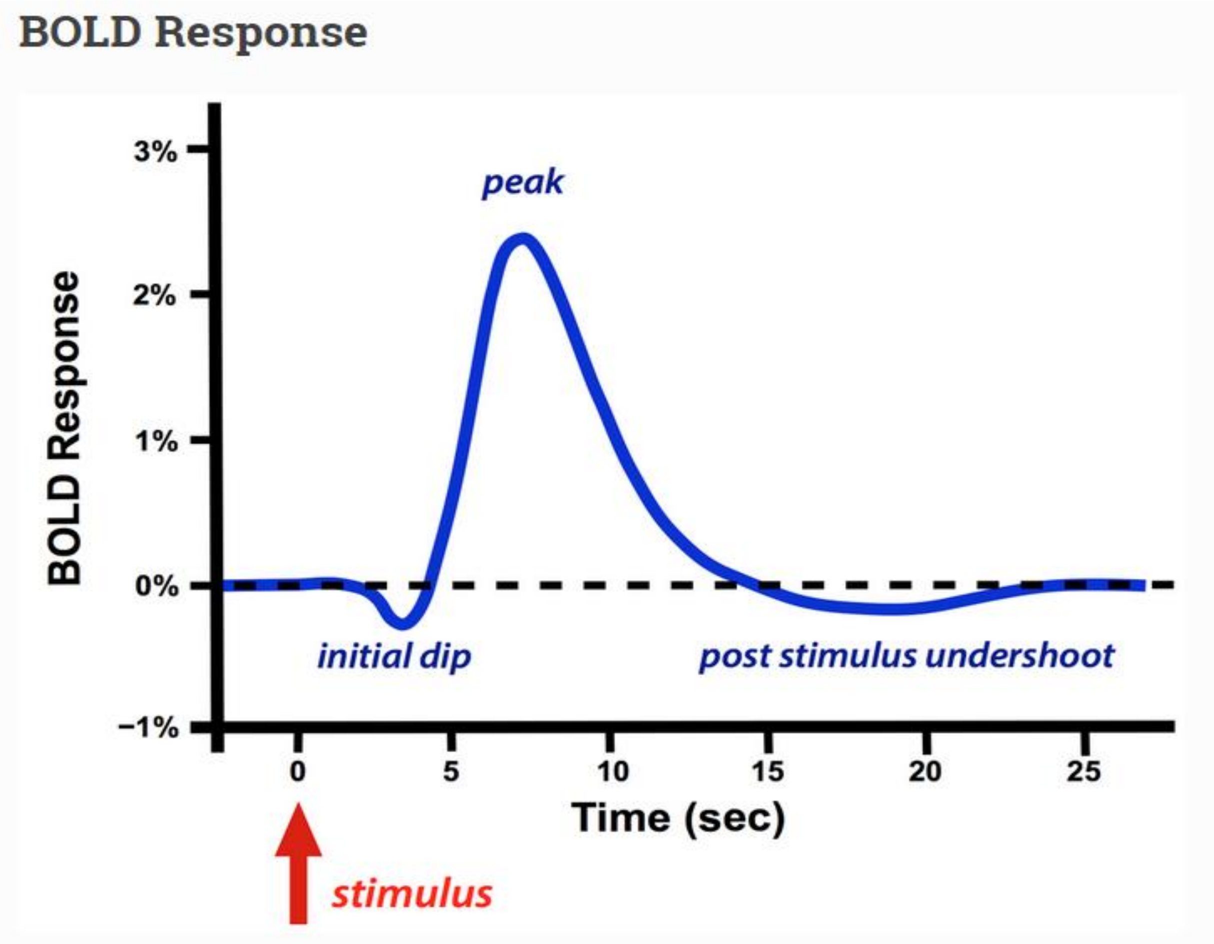
Diagram adapted from Glover, 2011

fMRI signal

- Blood oxygen level-dependent (BOLD) signal
- BOLD fMRI detects the changes in blood oxygenation that occur in response to neural activity
- The BOLD signal is well detectable with MRI
- However, BOLD is an indirect measure of neural activity
- More direct methods have failed due to poor signal

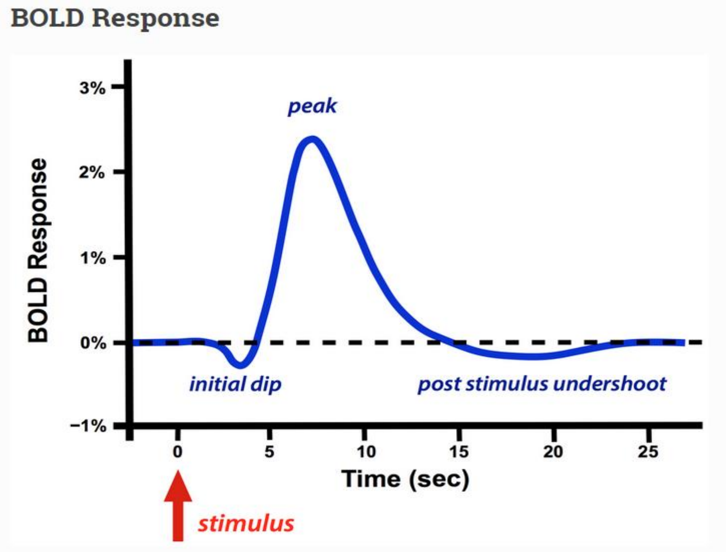
BOLD response

Hemodynamic response function (HRF)



©Andy Jahn

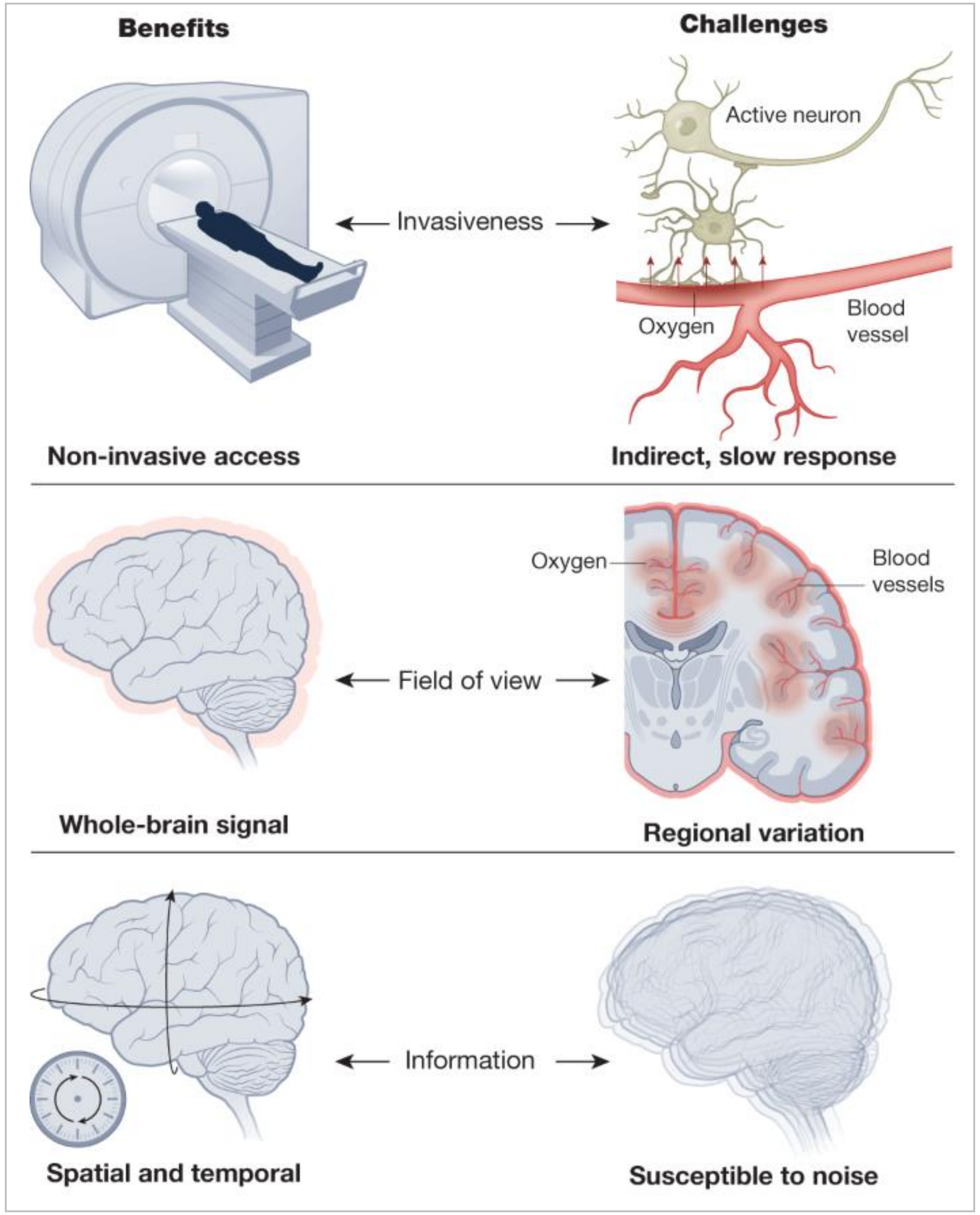
Hemodynamic response function (HRF)



- Depends on stimulus intensity and duration
- Varies across individuals
- Varies with healthy ageing and development
- Varies with common stimulants such as caffeine
- Varies across the brain, both at a distant and local scale

- The most common solution to HRF variability is to pretend it doesn’t exist and use a generic model for all participants

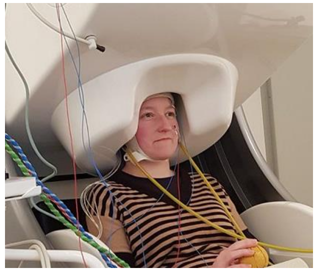
Benefits and challenges of fMRI



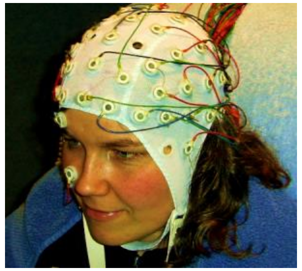
Finn, E.S., Poldrack, R.A. & Shine, J.M. *Nature*, 2023. https://doi.org/10.1038/s41586-023-06670-9

Non-invasive functional brain imaging techniques

fMRI
Functional magnetic resonance imaging
1992



MEG
Magnetoencephalography
1968



EEG
Electroencephalography
1929

maturity level

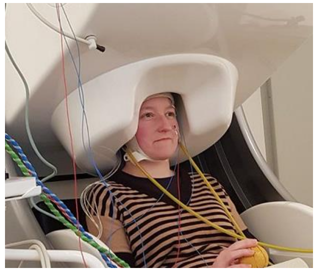
Non-invasive functional brain imaging techniques

fMRI
Functional magnetic resonance imaging
1992

Indirect
increased metabolic
demands of active neurons

Spatial resolution
Excellent
~1-3 mm
whole-brain

Temporal resolution
Not-so-good
~1-4 seconds

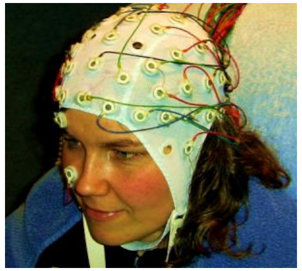


MEG
Magnetoencephalography
1968

Direct
the magnetic field generated by
the electrical activity of neurons

Spatial resolution
Not-so-good
~5 mm
limited for deep structures

Temporal resolution
Excellent
~1 millisecond



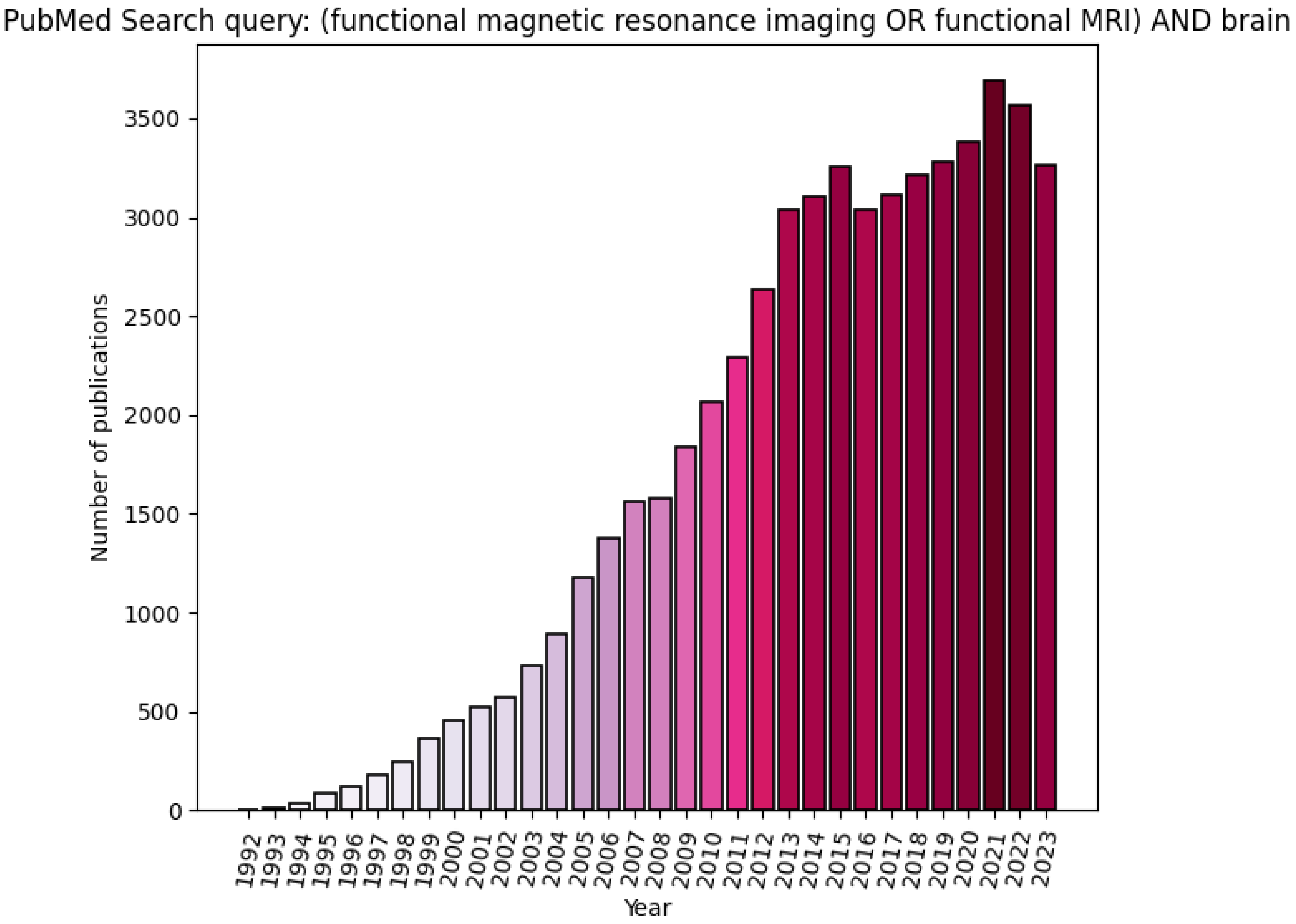
EEG
Electroencephalography
1929

Direct
the electrical activity
of the brain

Spatial resolution
Poor
~10 mm
cortical surface

Temporal resolution
Excellent
~1-10 milliseconds

fMRI popularity



Experimental design

Experimental constraints

- **Physical constraints**
  - Strong magnetic field
  - Small space
  - Loud
  - Horizontal position

Some equipment won't work
Limited range of motion
Limited peripheral vision
Difficulty hearing
Uncomfortable

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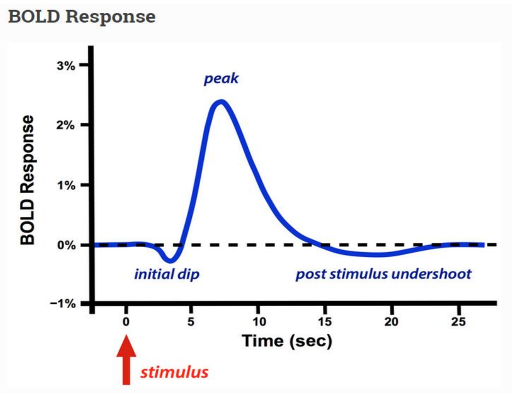
- **Physiological constraints**
  - BODL is slow
  - BOLD is a relative measure – the absolute values are meaningless
  - The data are continuous time-series, not discrete events



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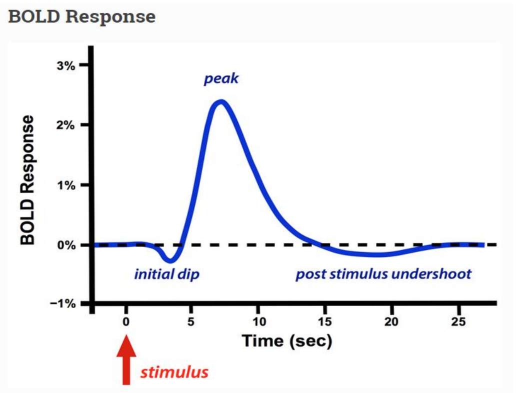


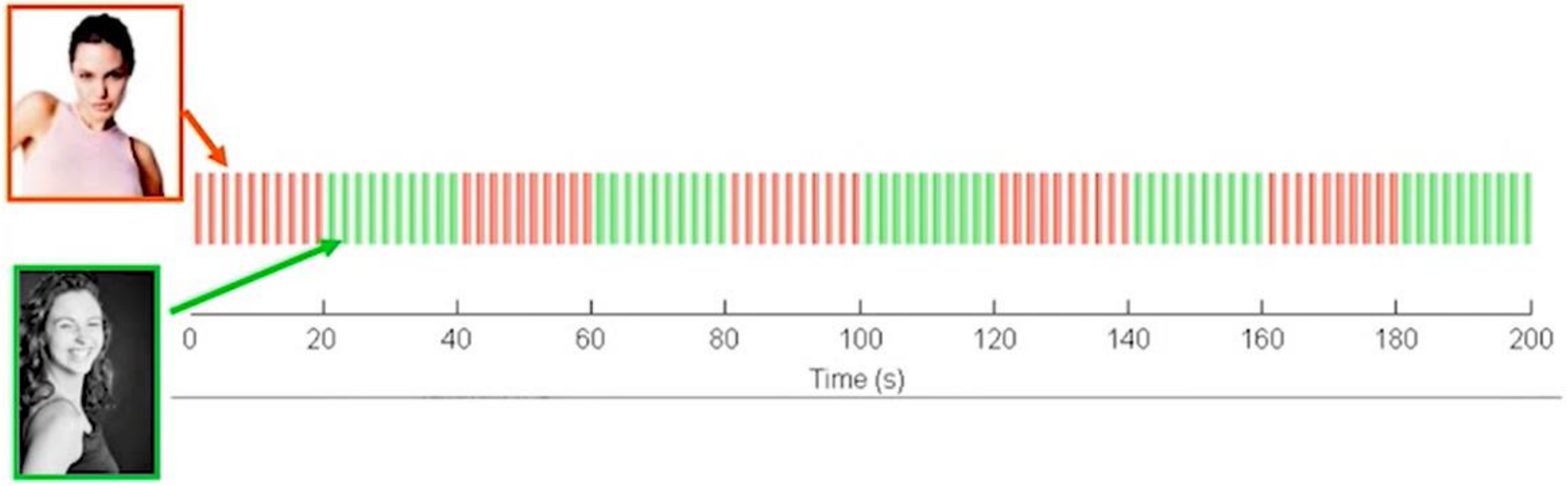
- **Psychological constraints**
  - Stimulus predictability
  - Time on task
  - Participant strategies
  - Temporal precision of the cognitive process
  - Unintended cognitive activity

Good practices in fMRI experimental design (Huettel, Song & McCarthy, 2009)

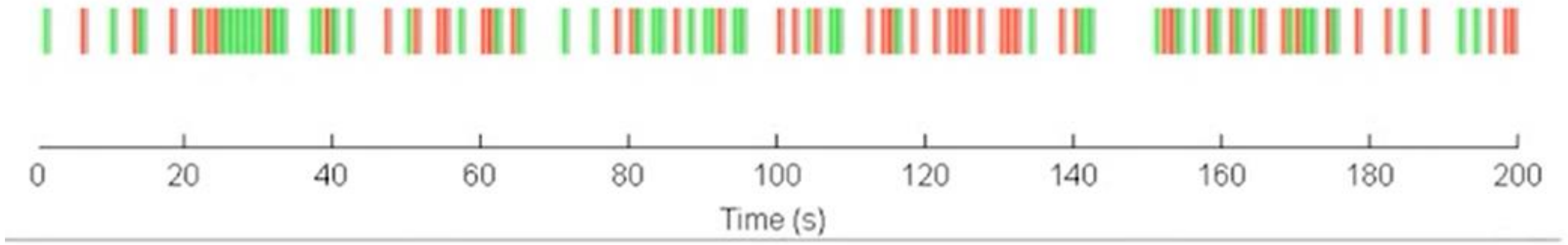
1. Evoke cognitive processes of interest
   - What will subjects do
2. Collect as much data as possible from each subject
   - How many trials do I need
3. Collect data from as many subjects as possible
   - What statistical power can I achieve
4. Choose your stimulus conditions and the timings of their presentations to evoke maximal changes in the cognitive processes of interest
   - How to increase the efficiency of the experiment
5. Organise the timings of experimental stimuli so that successively elicited processes of interest are minimally correlated with each other, over time
   - Variable intervals between successive events
6. Where possible, obtain measures of your subject's behaviour that can be related to the fMRI activation
   - task performance, memory effects, personality traits

Types of designs

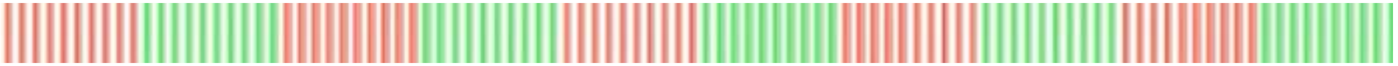
- **Block design**: similar events are grouped



- **Event-related design**: events are mixed



Block designs



- Advantages
  - Maximal efficiency
    - A 2-condition 16-20 second block design (~ duration of HRF) is optimal for power
  - Reduced task-switching costs
  - Forgiving with respect to the exact form of the HRF
- Problems
  - Stimulus predictability (e.g., in Go/No-go task: N B M V X X X X)
  - Chance to apply strategy (e.g., in the Stroop task: blue, red, green; blue, red, green)
  - Cannot detect rapid/transient events
- Note
  - Too short blocks don’t let HRF return to the baseline – the signal will be reduced
  - Too long blocks are confounded by low-frequency noise (MRI scanner drift)
  - Not recommended to have more than 4 conditions

Event-related designs

- Advantages
  - Avoid predictability and strategy
  - Can detect transient effects
  - More flexible - can accommodate more complex experimental designs and a wider variety of stimuli or tasks
- Problems
  - Lower detection power - requires more trials to achieve the same level of statistical power as block designs
  - Enhanced task-switching costs
  - Strong effect on presentation rate – requires design optimization (e.g. Optseq2 tool)
  - Sensitive to the exact form of the HRF
- Note
  - Each event is separated in time from the previous event with an inter-stimulus-interval (ISI)
  - Short 2-6 second jittered ISIs improve efficiency

Kinds of designs

- Subtractions designs
  - Basic contrast between task and control or between two task
- Individual differences
  - Correlations with behaviour or traits
- Process overlap/dissociation designs
  - Multiple subtractions
- Factorial designs
  - ANOVA designs
- Parametric modulation
  - Performance-related effects within subjects

https://youtu.be/ofl4p1Pyqes?si=UNQ1o8vd-BVcbfKV

Design trade-offs

- Fewer conditions and contrasts
  - + more power
  - - less generalizable

Good for the first studies in a new area of research

- Many comparisons
  - + high potential for specificity of inference
  - - low power

Good for the later studies with more complete information

https://youtu.be/ofl4p1Pyqes?si=UNQ1o8vd-BVcbfKV

More information! https://imaging.mrc-cbu.cam.ac.uk/imaging/DesignEfficiency

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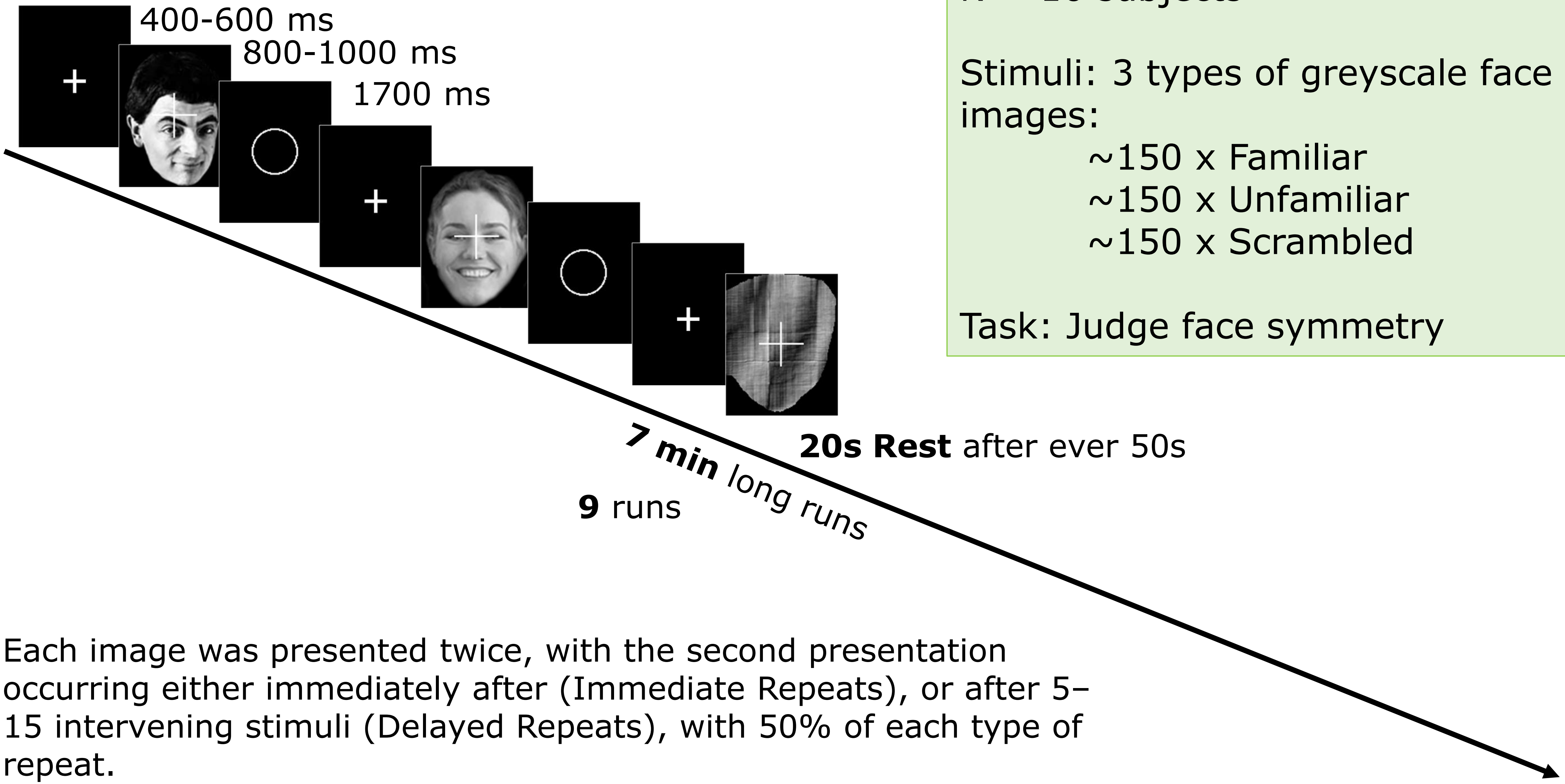
Design efficiency in FMRI

Contents

1. Design efficiency in FMRI
    1. General Advice
        1. Scan for as long as possible.
        2. Keep the subject as busy as possible.
        3. Do not contrast trials that are far apart in time.
        4. Randomise the order, or SOA, of trials close together in time.
    2. Theoretical Background
        1. The BOLD impulse response (IR)
    3. Signal-processing
    4. Mathematics (statistics)
        1. Impact of nonlinearities on efficiency
    5. Correlation between regressors
    6. Common Questions
        1. I. What is the minimum number of events I need?
        2. II. Doesn't shorter SOAs mean more power simply because of more trials?
        3. III. What is the maximum number of conditions I can have?
        4. IV. Should I use null events?
        5. V. What is the difference between 'detection power' and 'estimation efficiency' ?
        6. VI. Should I generate multiple random designs and choose the most efficient one ?
        7. VII. Should I treat my trials as events or epochs ?
    7. Acknowledgements

Example Experiment: Face Recognition



N = 16 subjects

Stimuli: 3 types of greyscale face images:

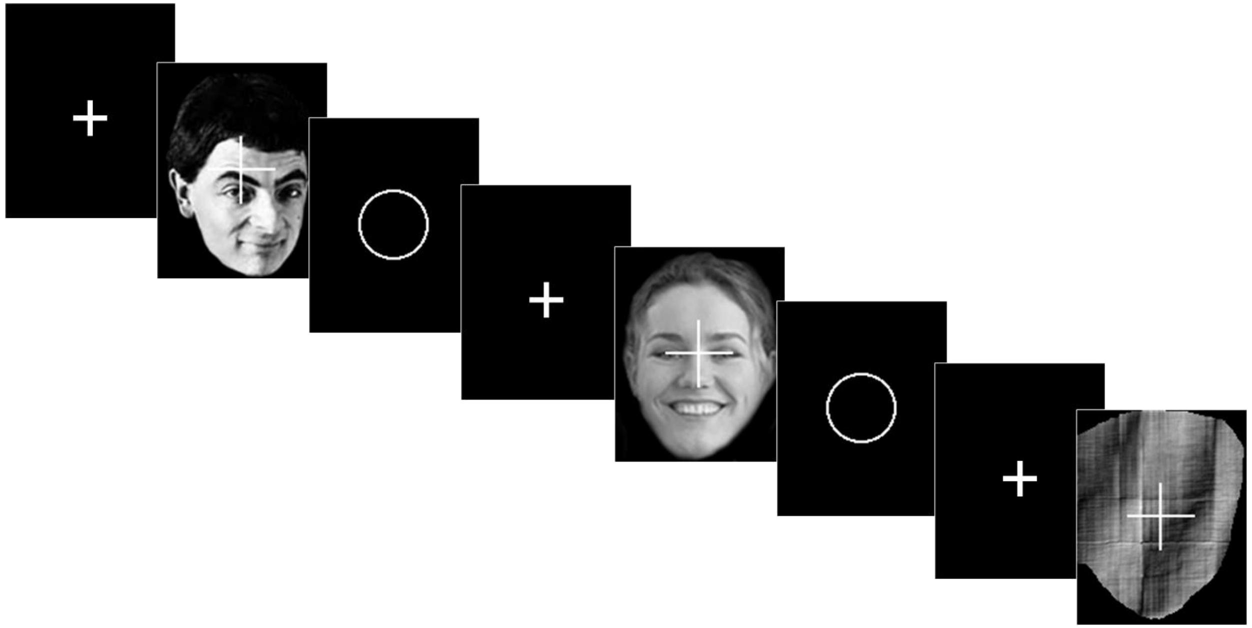
- ~150 x Familiar
- ~150 x Unfamiliar
- ~150 x Scrambled

Task: Judge face symmetry

Each image was presented twice, with the second presentation occurring either immediately after (Immediate Repeats), or after 5–15 intervening stimuli (Delayed Repeats), with 50% of each type of repeat.

Example Experiment: Face Recognition

- Conditions
  - Familiar faces
  - Unfamiliar faces
  - Scrambled faces
  - Initial presentation
  - Immediate repeat
  - Delayed repeat
- Possible questions to investigate
  - Brain areas for Faces
  - Brain areas for Face Familiarity
  - Response to Initial vs Repeated presentations
  - Response to the Repetition of Familiar vs Repetition of Unfamiliar
  - ...



Example Dataset

https://openneuro.org/datasets/ds000117/versions/1.0.5

www.nature.com/scientificdata

SCIENTIFIC DATA

OPEN

SUBJECT CATEGORIES

» Electroencephalography -EEG

» Brain imaging

» Functional magnetic resonance imaging

» Cognitive neuroscience

A multi-subject, multi-modal human neuroimaging dataset

Daniel G. Wakeman[1,2] & Richard N. Henson[2]

We describe data acquired with multiple functional and structural neuroimaging modalities on the same nineteen healthy volunteers. The functional data include Electroencephalography (EEG), Magnetoencephalography (MEG) and functional Magnetic Resonance Imaging (fMRI) data, recorded while the volunteers performed multiple runs of hundreds of trials of a simple perceptual task on pictures of familiar, unfamiliar and scrambled faces during two visits to the laboratory. The structural data include T1-weighted MPRAGE, Multi-Echo FLASH and Diffusion-weighted MR sequences. Though only from a small sample of volunteers, these data can be used to develop methods for integrating multiple modalities from multiple runs on multiple participants, with the aim of increasing the spatial and temporal resolution above that of any one modality alone. They can also be used to integrate measures of functional and structural connectivity, and as a benchmark dataset to compare results across the many neuroimaging analysis

Received: 07 April 2014

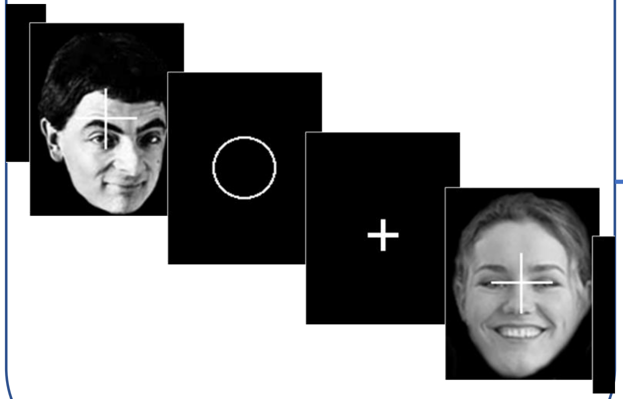
Accepted: 05 January 2015

Published: 2

Wakeman & Henson (2015), *Scientific Data,* http://www.nature.com/articles/sdata20151

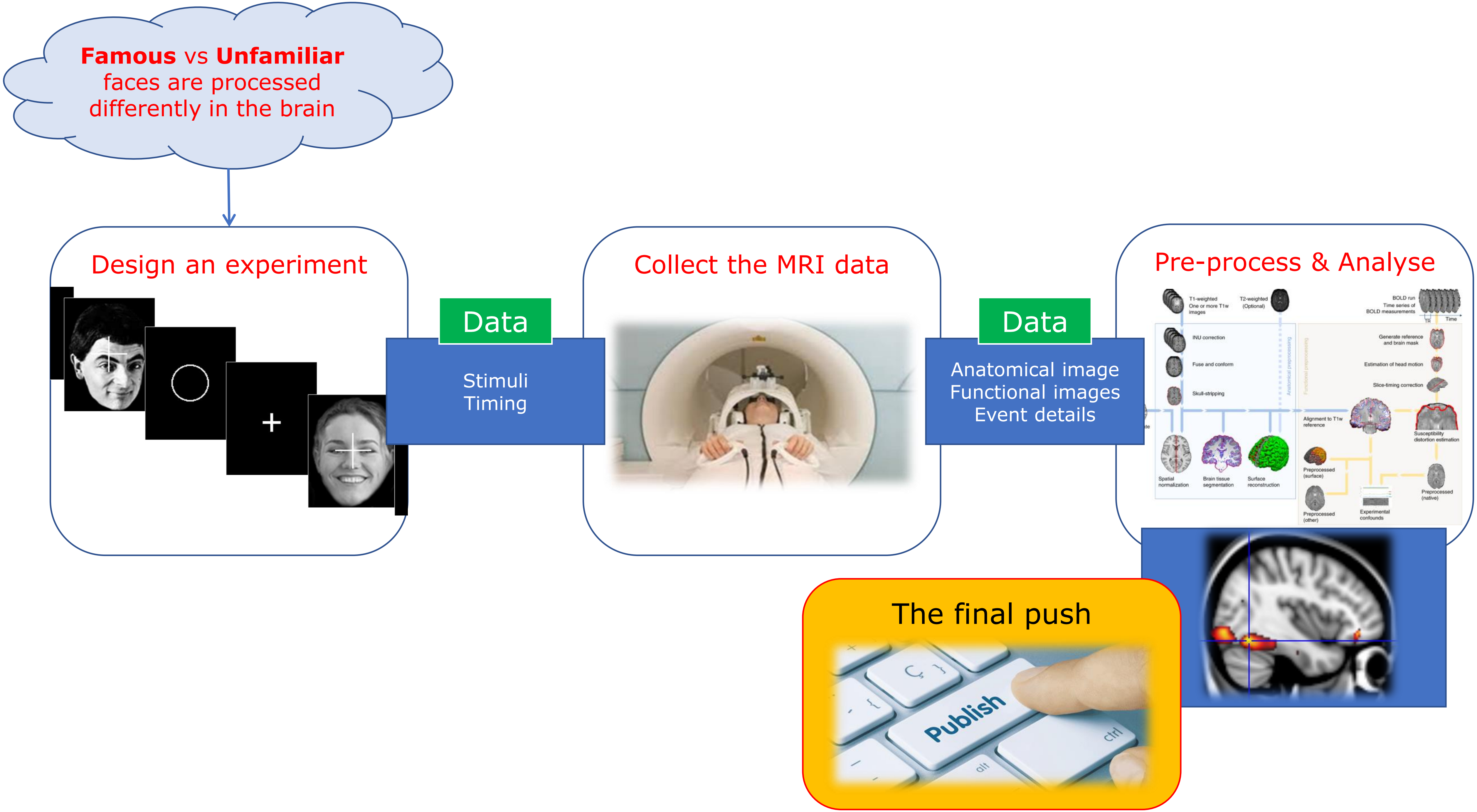
Famous vs **Unfamiliar** faces are processed differently in the brain

Design an experiment



Collect the MRI data

What do we do now?



Famous vs Unfamiliar
faces are processed
differently in the brain
Design an experiment
Data
Stimuli
Timing
Collect the MRI data
Data
Anatomical image
Functional images
Event details
Pre-process & Analyse
The final push
Publish

Famous vs **Unfamiliar** faces are processed differently in the brain

Design an experiment

Data

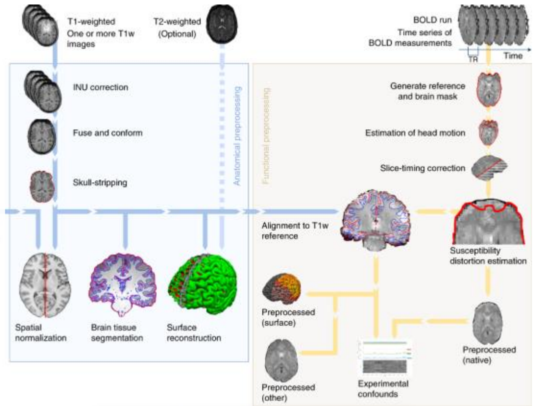
Stimuli Timing

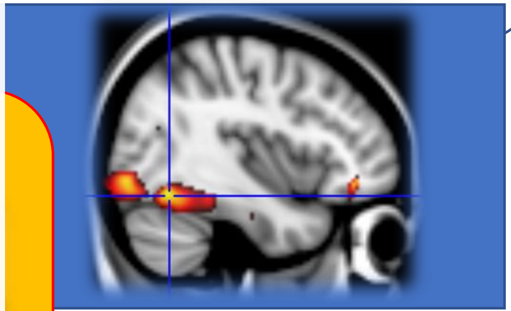
Collect the MRI data

Data

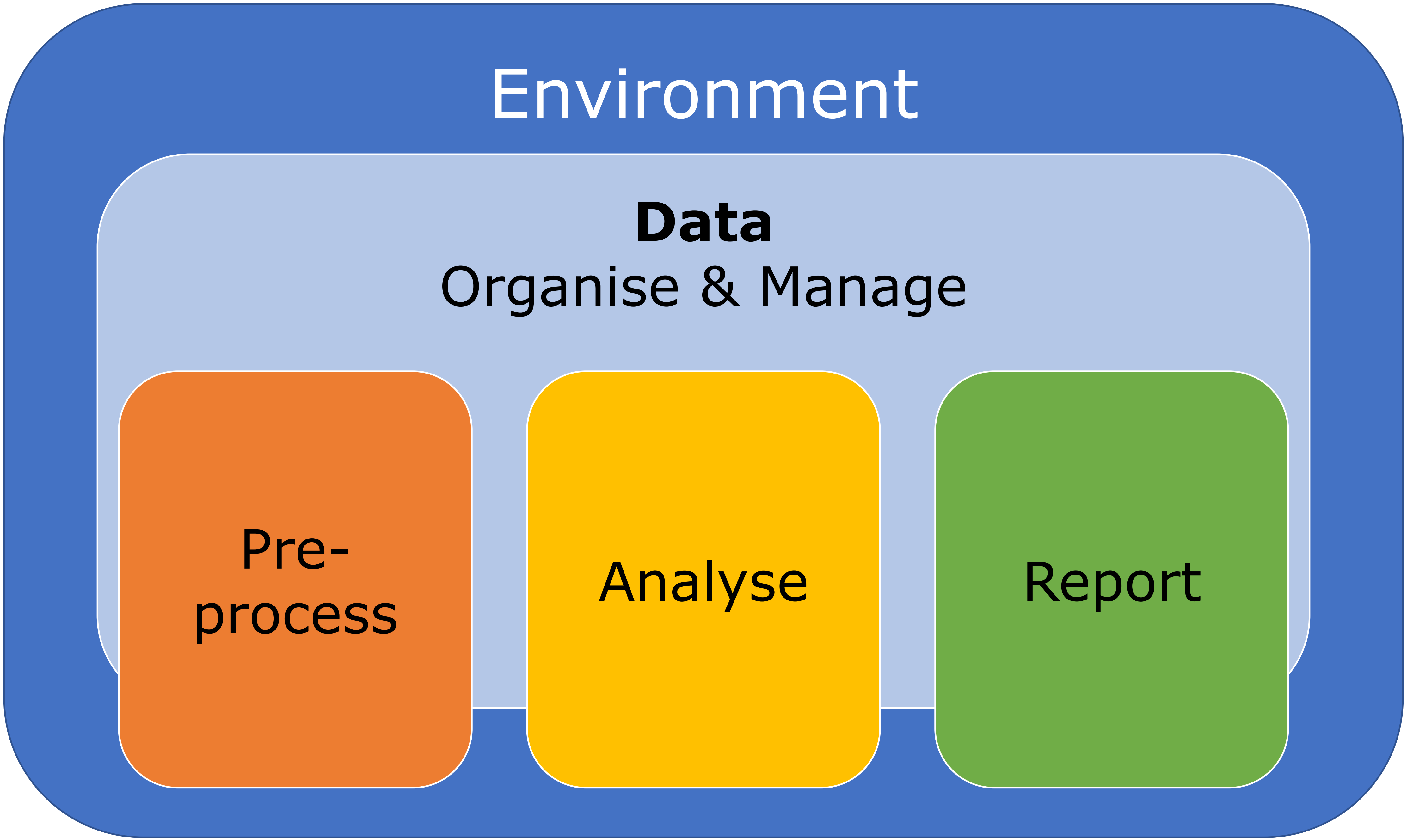
image Functional images

Pre-process & Analyse





The final push


Environment
Data
Organise & Manage
Pre-
process
Analyse
Report

Outline

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- Practical demo