MRC Cognition and Brain Sciences Unit
UNIVERSITY OF CAMBRIDGE

Functional Magnetic Resonance Imaging

GitHub https://github.com/dcdace/fMRI_training

Dace [datza] Apšvalka

February 2025

Outline

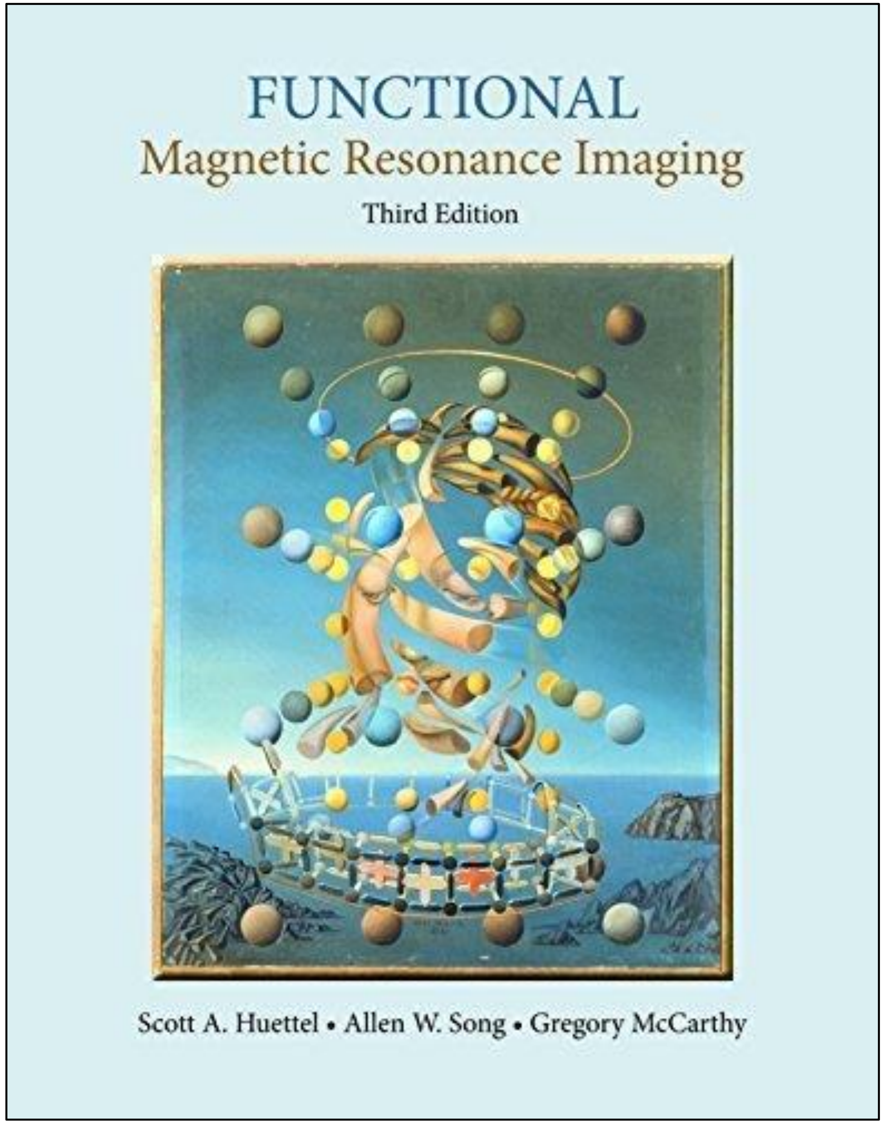
- Introduction
- Experimental design
- Data management
- Pre-processing
- Statistical analysis
- Practical demo

Materials

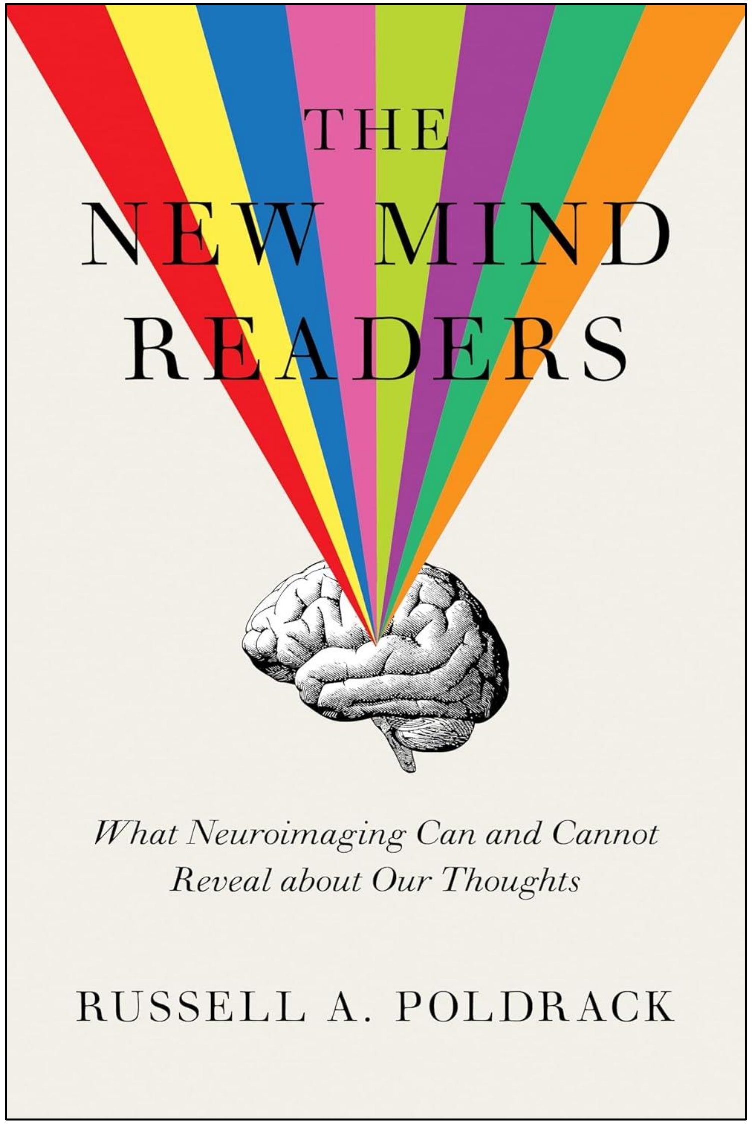
GitHub https://github.com/dcdace/fMRI_training

Example data (~6GB):
https://cloud.mrc-cbu.cam.ac.uk/index.php/s/gUJZ6Ehli92Sm6X
(email me for password)

Recommended books



University of Cambridge Library link

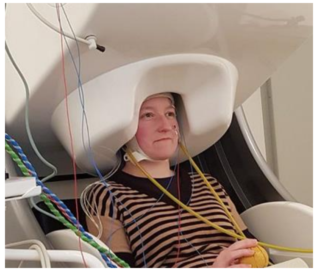


University of Cambridge Library link

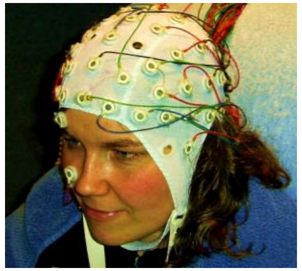
Introduction

Non-invasive functional brain imaging techniques

fMRI
Functional magnetic resonance imaging
1992



MEG
Magnetoencephalography
1968



EEG
Electroencephalography
1929

maturity level

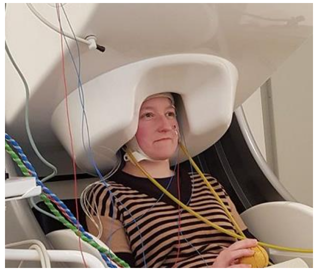
Non-invasive functional brain imaging techniques

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

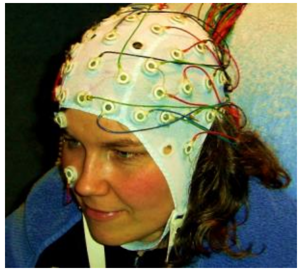


MEG
Magnetoencephalography
1968

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



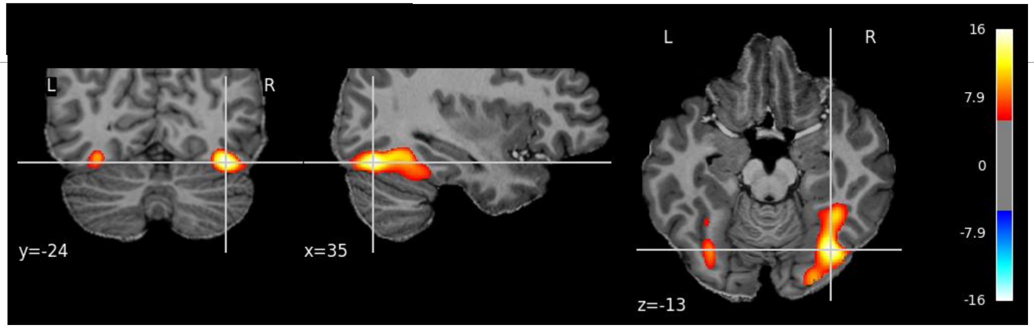
EEG
Electroencephalography
1929

Direct
the electrical activity of the brain

Spatial resolution
Poor
~10 mm
cortical surface

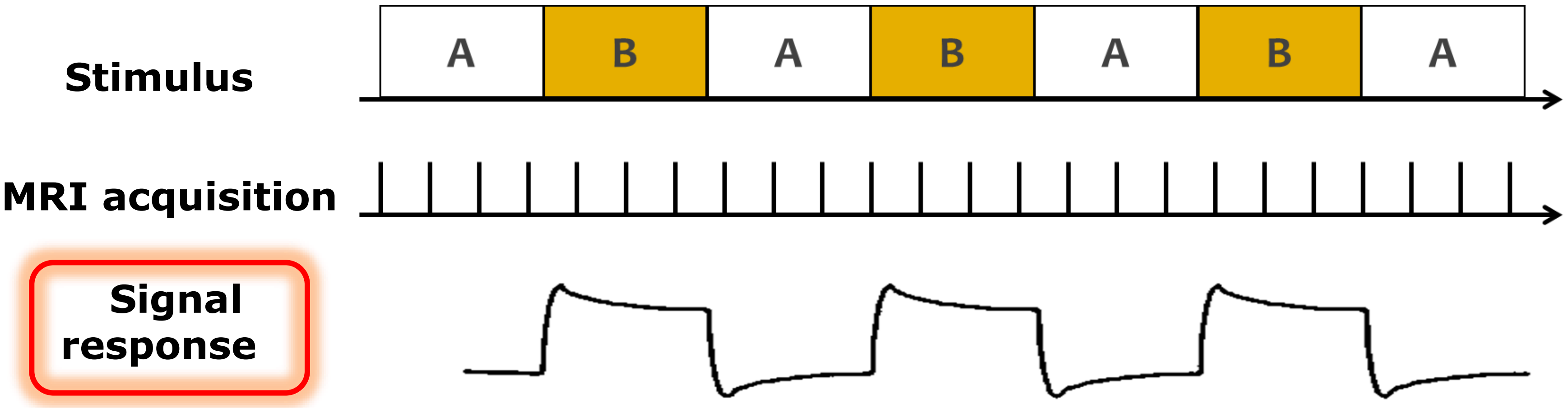
Temporal resolution
Excellent
~1-10 milliseconds

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)



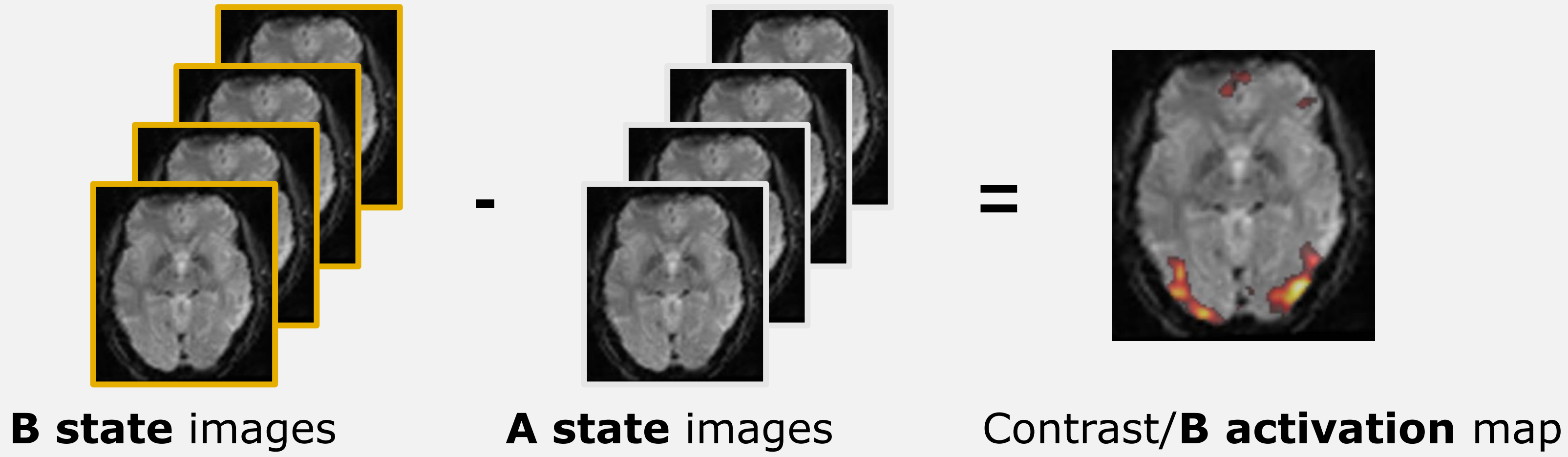


Diagram adapted from Glover, 2011

fMRI signal

- Blood oxygen level-dependent (BOLD) signal

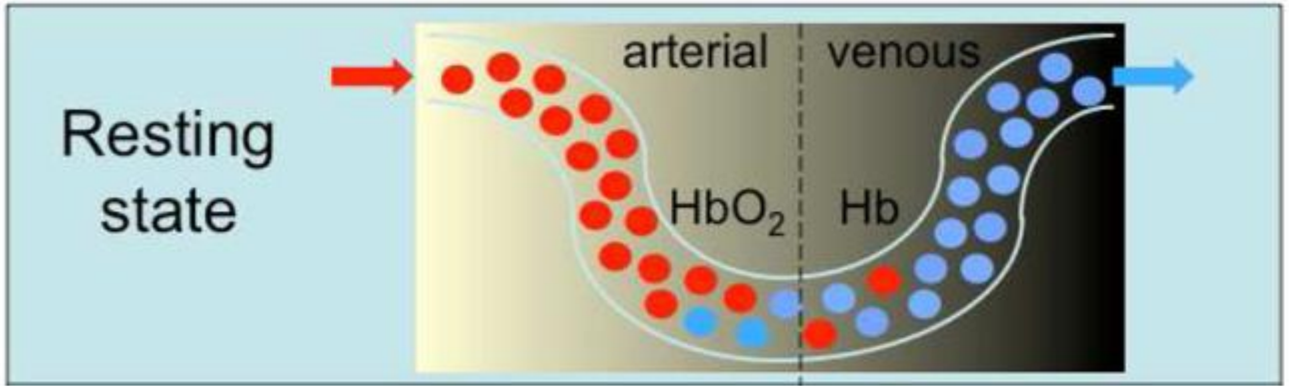


Diagram adapted from Glover, 2011

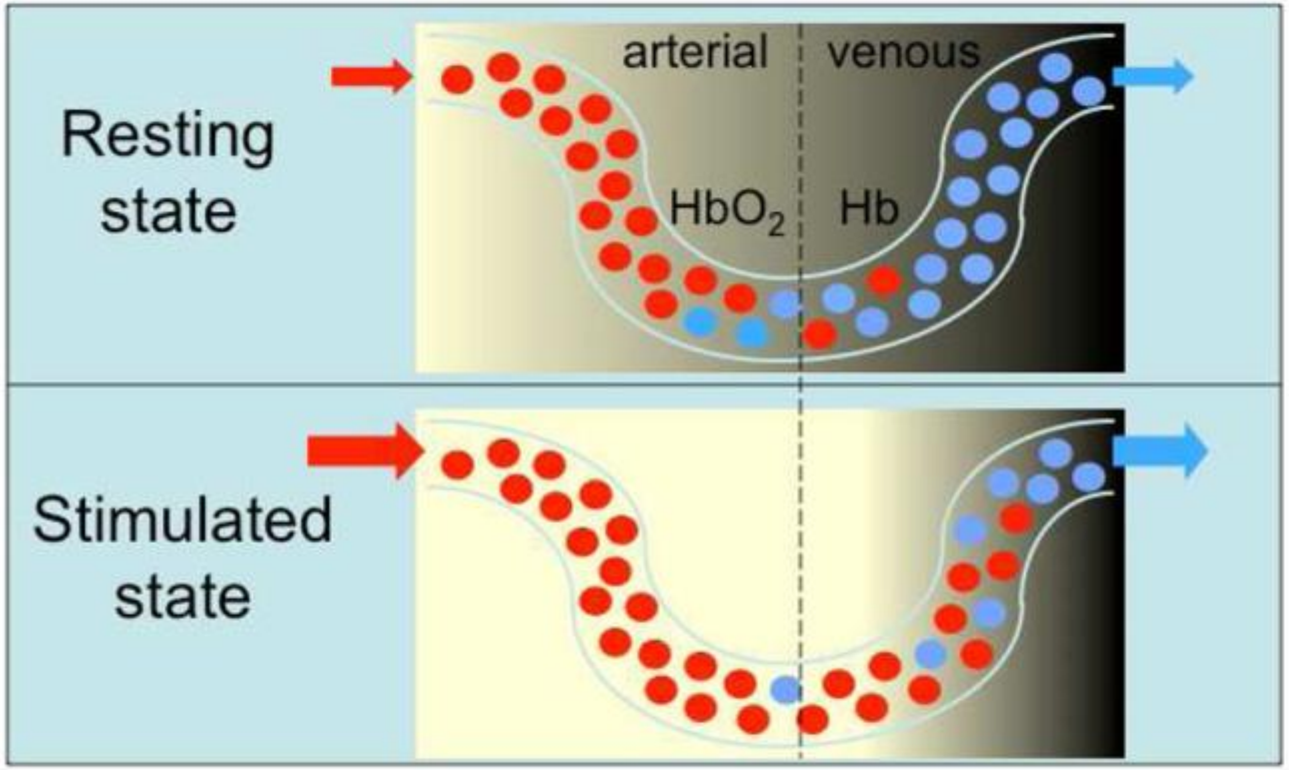
fMRI signal

- Blood oxygen level-dependent (BOLD) signal

dampens the MRI signal

Oxygenated blood cells
HbO2

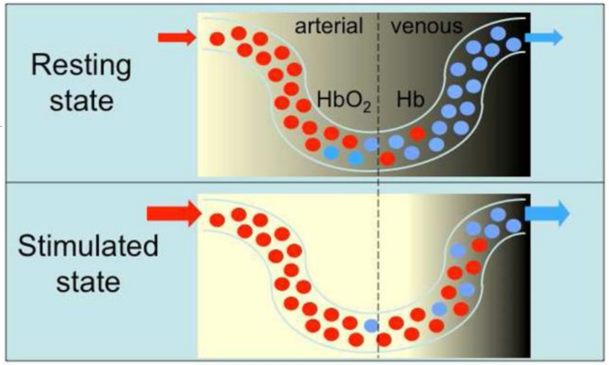
De-oxygenated blood cells
Hb



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

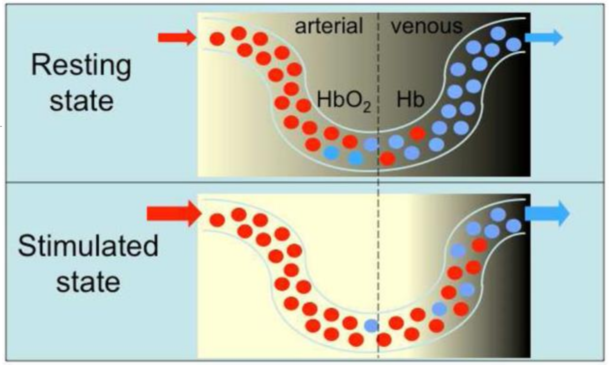
Diagram adapted from Glover, 2011

fMRI signal



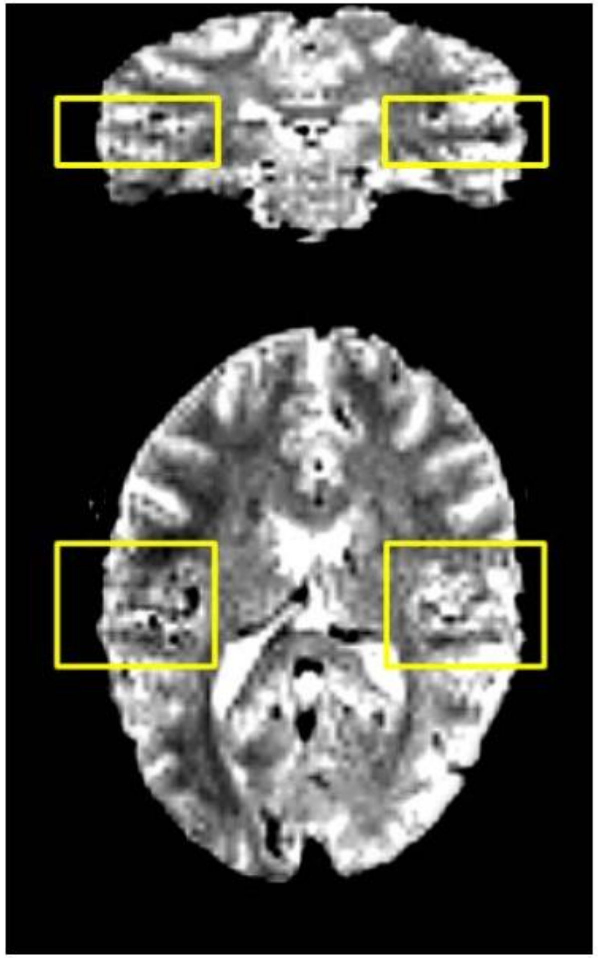
- **At rest,** the cerebral **metabolic rate of oxygen** (CMRO2) and cerebral **blood flow** (CBF) are tightly **coupled**
- During **increased neuronal activity** they become **uncoupled**, with CBF increasing relatively more than CMRO2 (Fox and Raichle, 1986)
    - ‘an overcompensation’
- The uncoupling 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

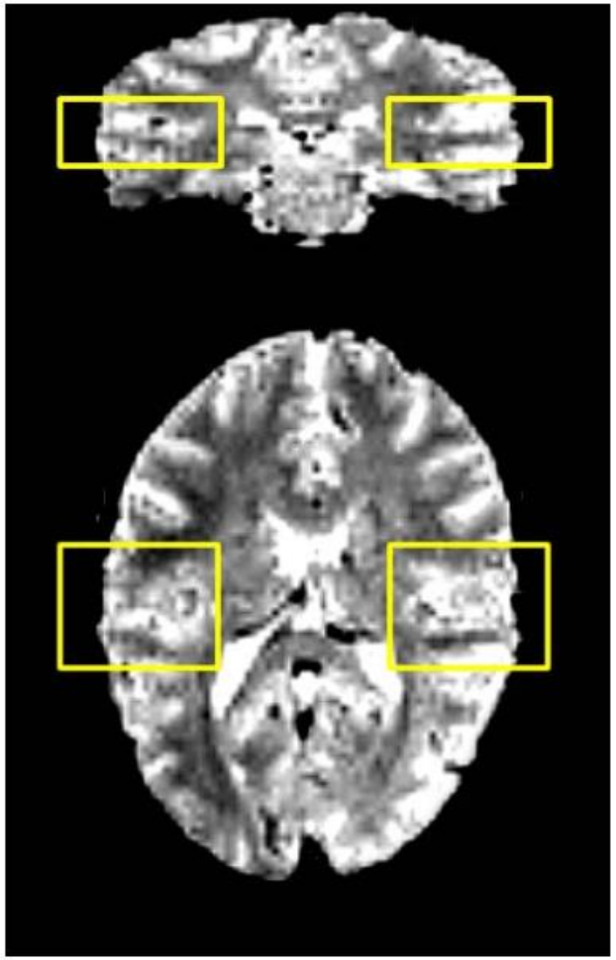


- An example of auditory cortex activation (from Marta's MRI physics slides)

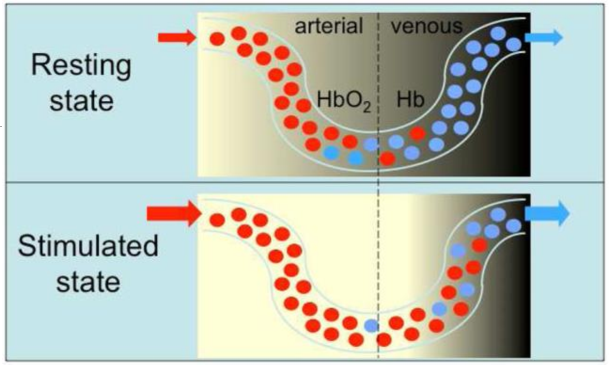
Baseline



Neural Activity



fMRI signal



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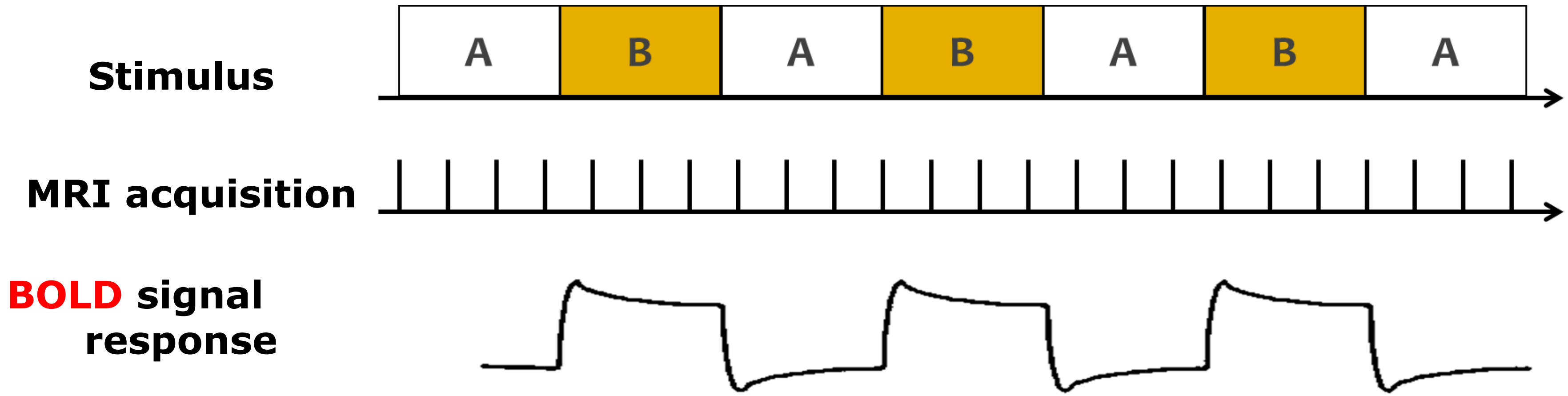
- This difference in the magnetic properties of de-oxygenated and oxygenated Hb is used in BOLD fMRI to create contrast in images – reflecting activity in different brain regions.
  - By controlling for all other factors, any observed differences in the BOLD signal are inferred to be due to differences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

Functional MRI (fMRI)



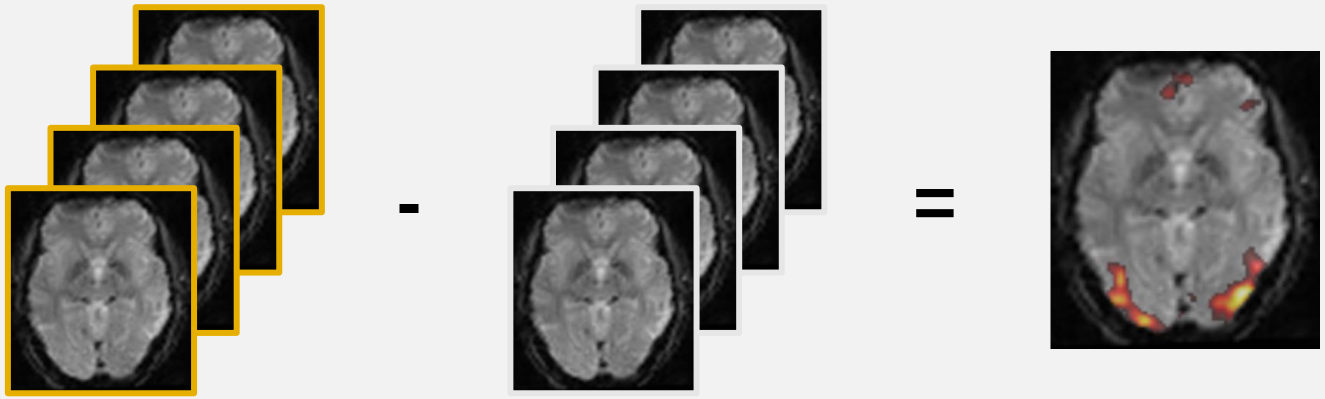


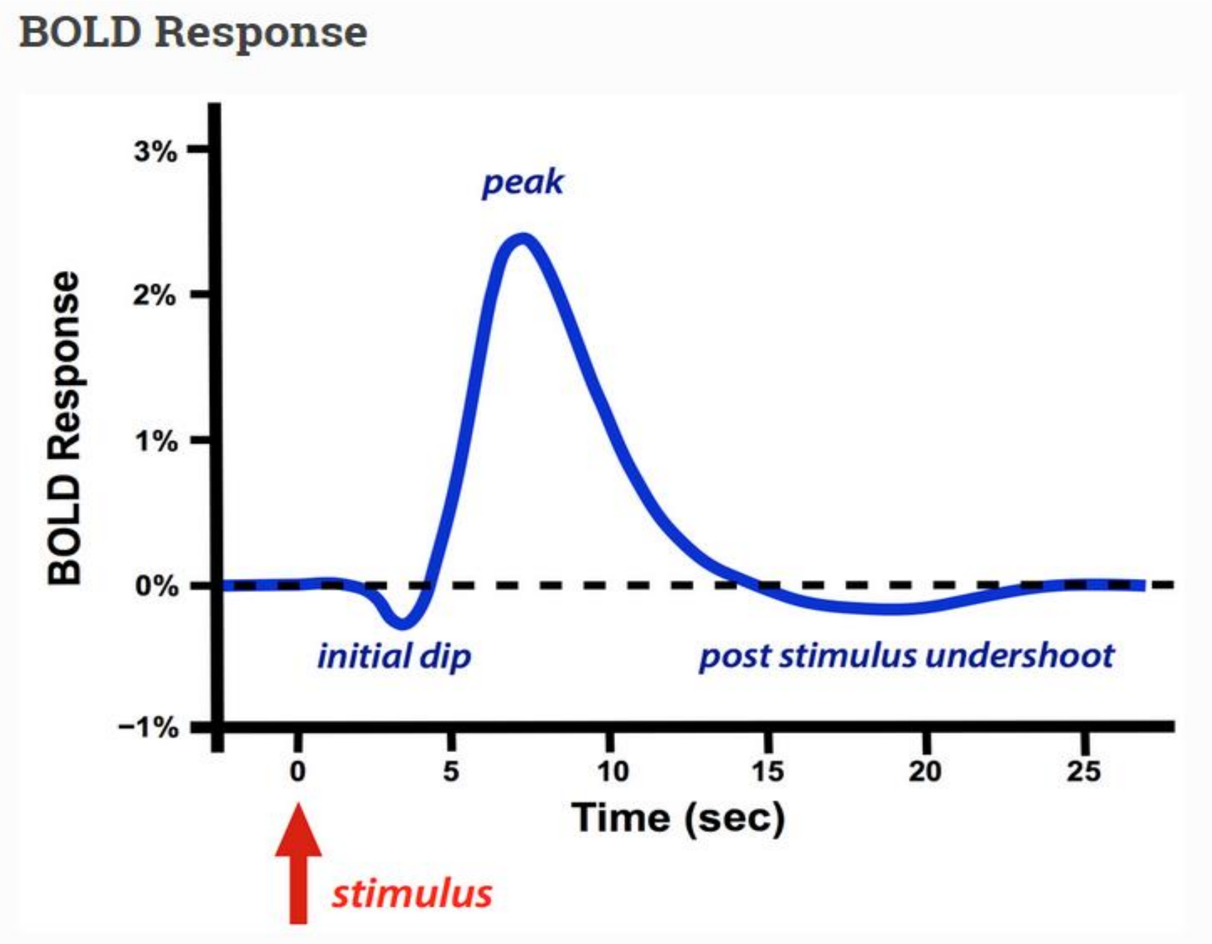
Diagram adapted from Glover, 2011

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

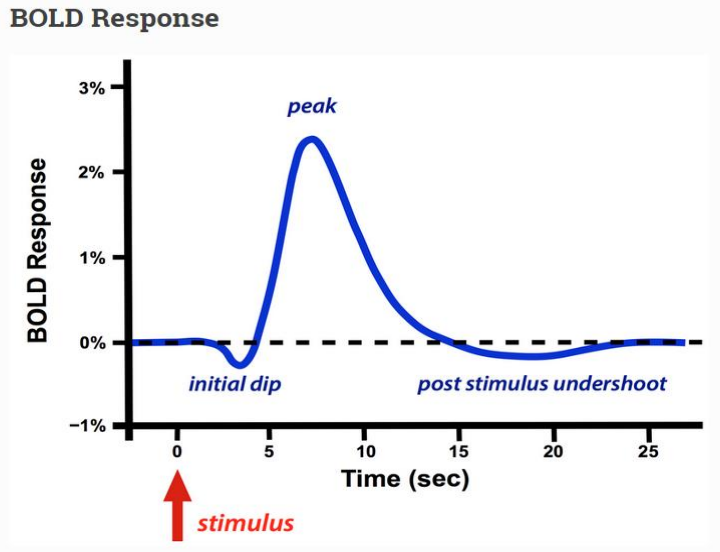
BOLD response

Hemodynamic response function (HRF)



©Andy Jahn

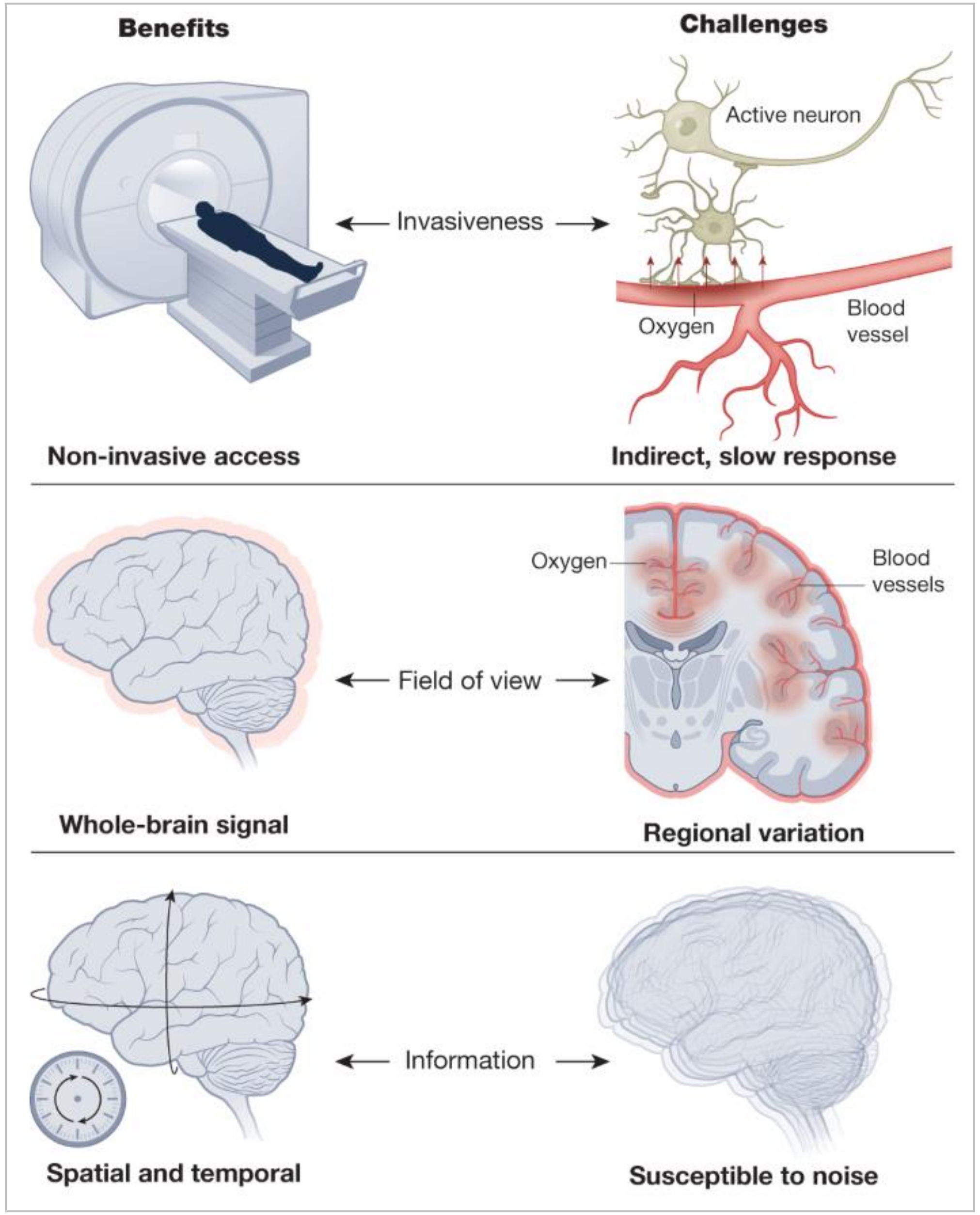
Hemodynamic response function (HRF)



- 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

Origins of Functional MRI

- 1970s – 1980s: MRI Foundations
  - **Paul Lauterbur** and **Peter Mansfield** developed MRI technology
- 1990: Key Breakthrough
  - Seiji Ogawa demonstrated **Blood Oxygenation Level-Dependent (BOLD) contrast**
  - The “father” of modern functional brain imaging

MAGNETIC RESONANCE IN MEDICINE **14**, 68–78 (1990)

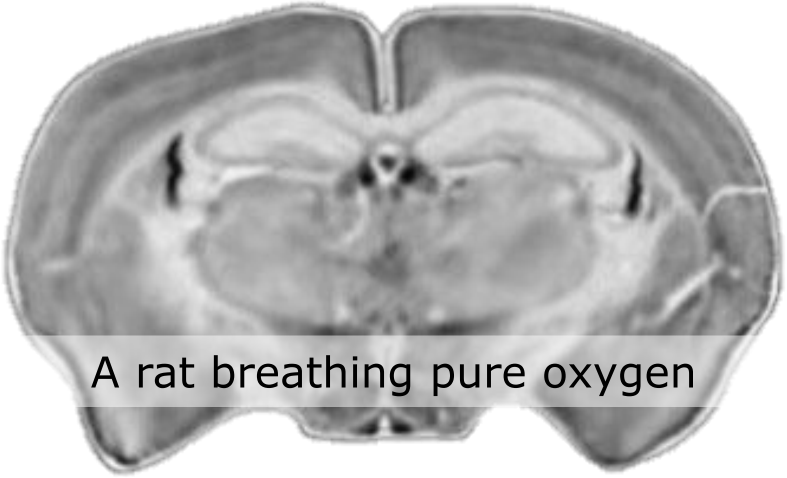
Oxygenation-Sensitive Contrast in Magnetic Resonance Image of Rodent Brain at High Magnetic Fields

SEIJI OGAWA, TSO-MING LEE, ASHA S. NAYAK,* AND PAUL GLYNN

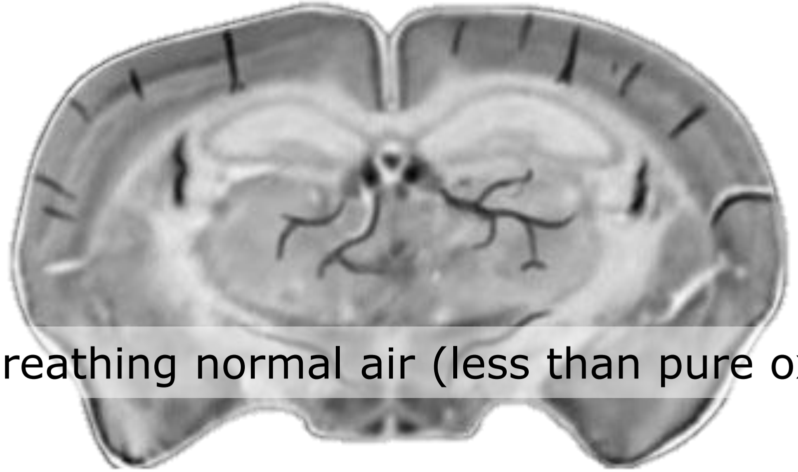
AT&T Bell Laboratories, Murray Hill, New Jersey 07974

- Oxygenated blood – no signal loss
- Deoxygenated blood – **signal loss**

- In 1990 Ogawa published several papers on BOLD contrast in rats and
  - suggested that BOLD contrast **functional MRI could potentially also be used in humans**



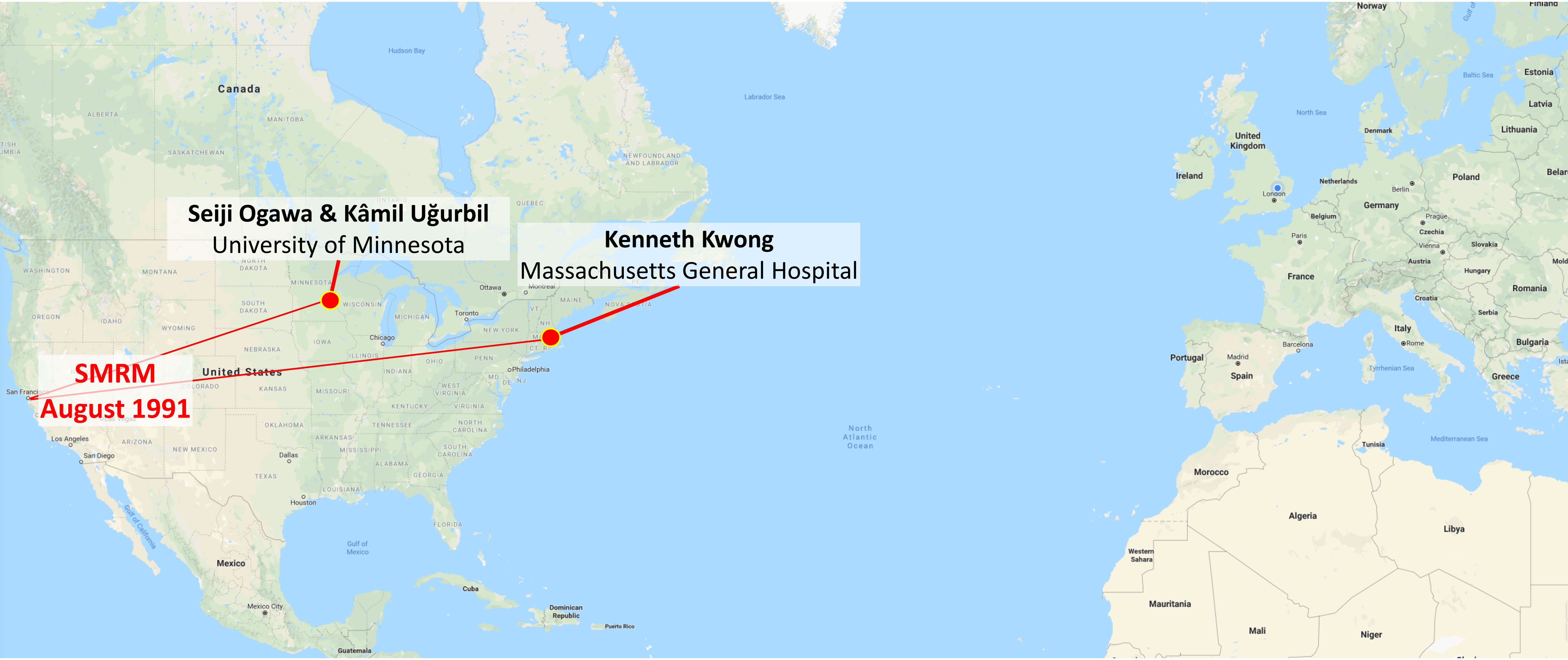
A rat breathing pure oxygen



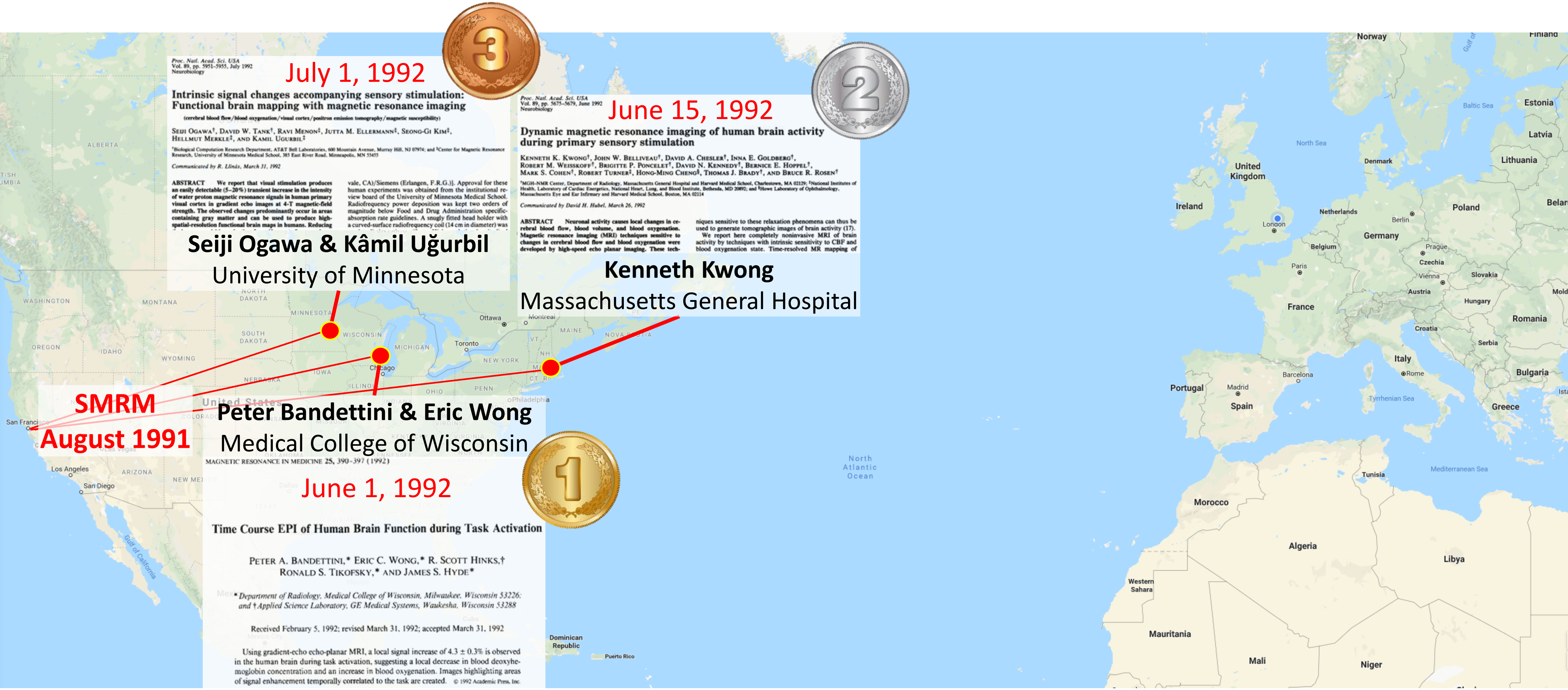
A rat breathing normal air (less than pure oxygen)

Images from Huettel, Song & McCarthy, 2004, Functional Magnetic Resonance Imaging

The start of the human BOLD fMRI, **1990-1992**



The start of the human BOLD fMRI, **1990-1992**



The start of the human BOLD fMRI, **1990-1992**

Bandettini et al., MRM, 1992

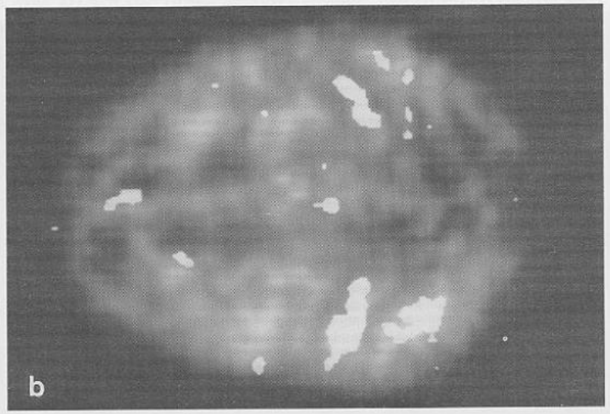
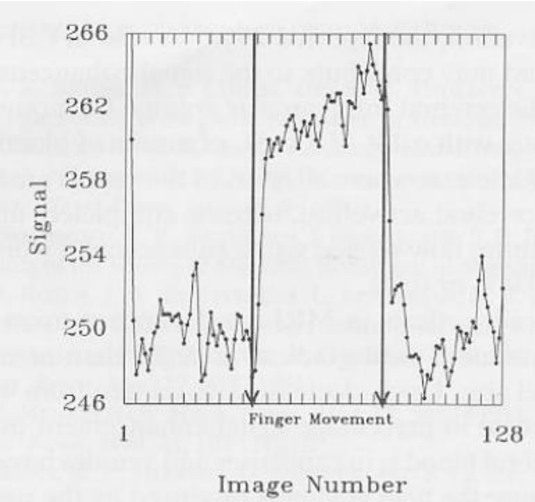


FIG. 2. Representative gradient-echo echo-planar images from each of the two series. TE = 50 ms. Slice thickness = 25 mm. Threshold images from the corresponding brain activity images are superimposed. (a) Coronal image from the 128-image series. A threshold image of Fig. 1a is superimposed. (b) Axial image from the 72-image series. A threshold image of Fig. 1b is superimposed.



Kwong et al., PNAS, 1992

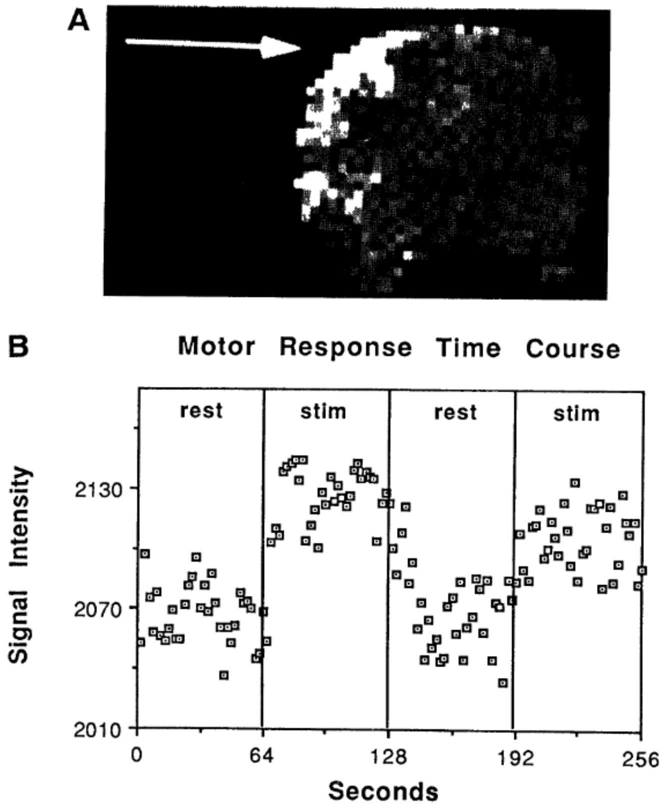
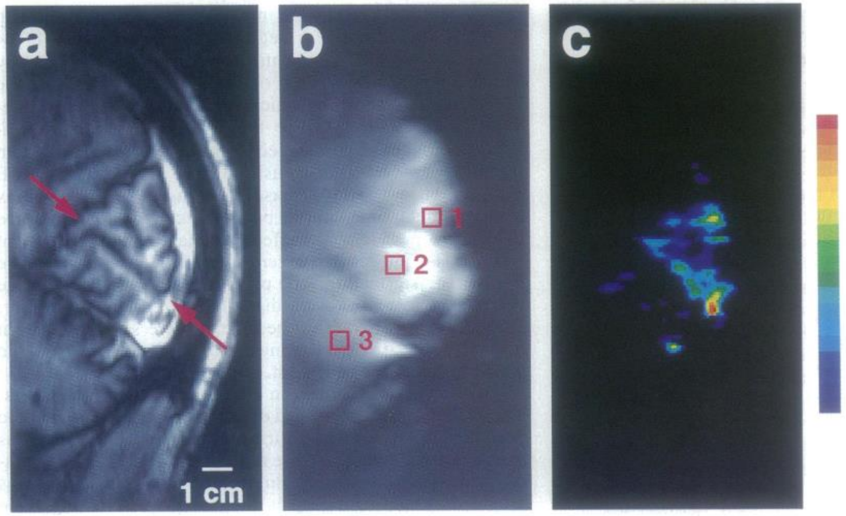


FIG. 5. (*A*) M1 activation (arrow) during repetitive contralateral hand squeezing. This coronal subtraction image (stimulated minus unstimulated) was acquired by a GE technique (TR = 2000 ms; TE = 60 ms) with the image plane obliquely aligned along the precentral gyrus. (*B*) Temporal response.

Ogawa et al., PNAS, 1992



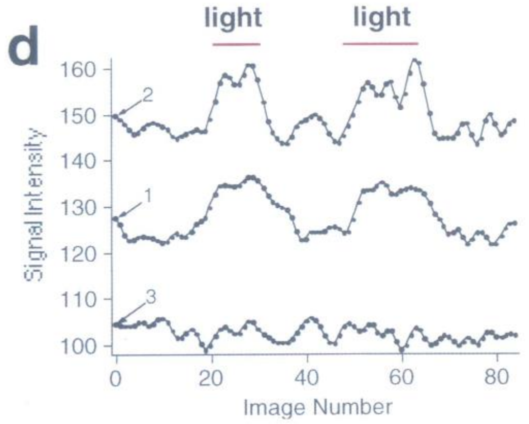
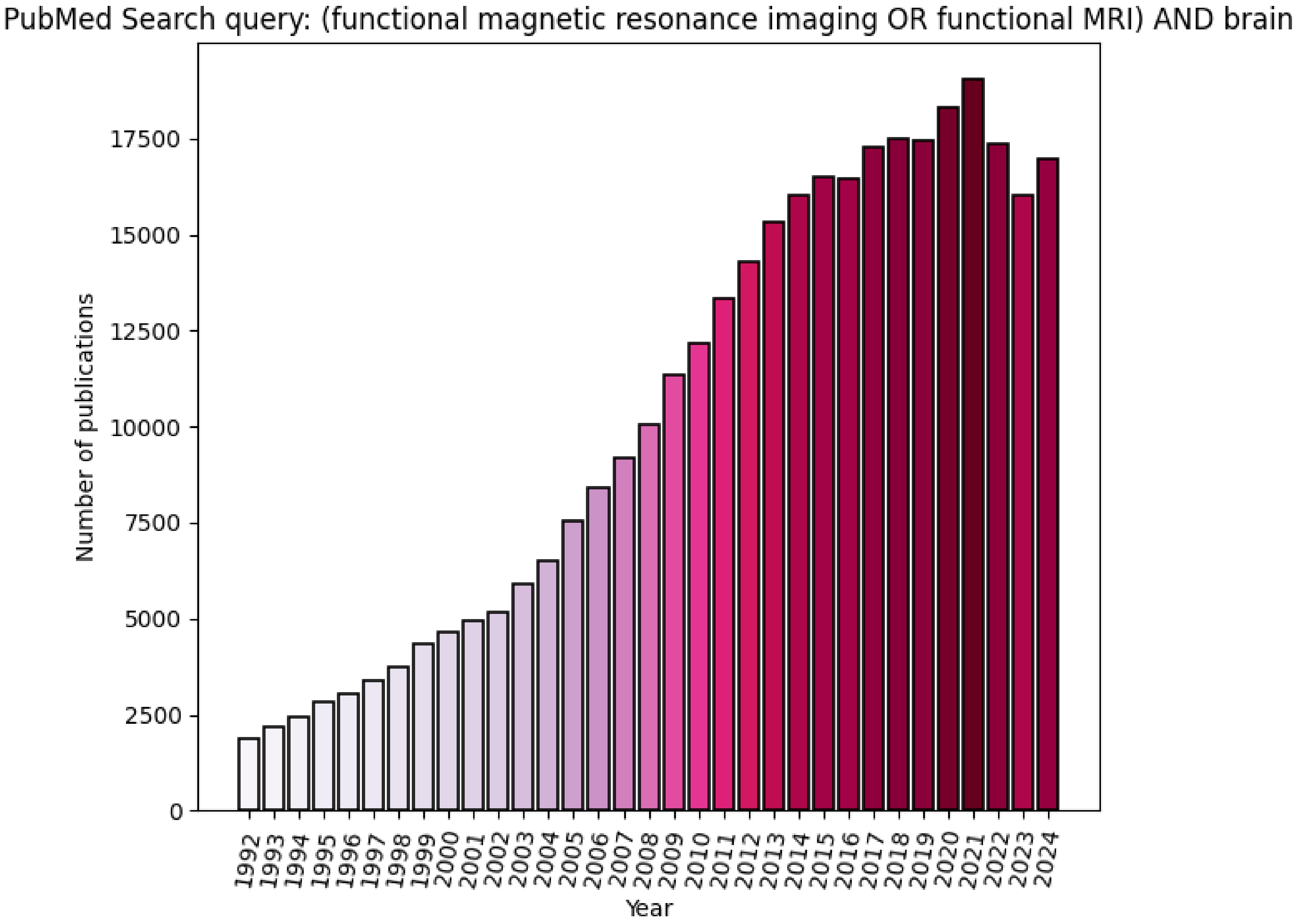


FIG. 1. Intrinsic signal changes in sagittal-brain images produced by photic stimulation. (*a*) Sagittal-slice image of the occipital pole taken with an inversion recovery pulse sequence. The oblique line is oriented along the bank of the calcarine fissure. (*b*) Gradient echo image (FISP sequence; TE = 40 ms) at the same anatomical location. (*c*) Pseudocolor map of the difference in signal intensity between the average of eight images acquired during photic stimulation and eight images taken in the dark. (*d*) Time course of signal-intensity changes (in arbitrary units) for regions indicated by the three boxes outlined in *b*.

fMRI popularity



Evolution and Key Milestones

- 1990s: Rapid adoption in cognitive neuroscience
  - Mapping visual, motor, and cognitive functions
  - Earliest fMRI experiments used “on-off” block designs: task (e.g., 30s of finger tapping) vs. rest
  - Provided robust signals but limited insight into transient cognitive states

- Late 1990s – 2000s: Advancements analysis methods
  - Rise of event-related fMRI (Bandettini et al.), enabling detection of transient brain responses
  - Rise of resting-state fMRI (Biswal et al.), revealing functional connectivity in the brain
  - Improved image resolution and advanced statistical methods enhanced analysis
  - Statistical Parametric Mapping, developed by Karl Friston, laid the foundation for modern fMRI analysis

- 2010s-Present: Continuing innovations and clinical applications
  - Multi-voxel pattern analysis and machine learning
  - Combining fMRI with EEG, MEG, and PET for multimodal imaging
  - Ultra-high field MRI (7T and above) achieves sub-millimetre spatial resolution enabling smaller functional units, such as cortical layers and columns
  - Improved acquisition techniques, allowing faster acquisitions
  - Big Data and deep learning approaches

MRI Fads, Overuses, and Overinterpretations

- The Neuro-Hype Era (Early 2000s)
  - “Neuro-everything": The explosion of fMRI studies linking brain activity to complex behaviours (e.g., love, morality, political beliefs)
  - Misleading Media Headlines: Over-simplified claims about single brain regions controlling emotions or decisions

- The Voodoo Correlations Controversy
  - Critique of inflated correlations in social neuroscience studies due to poor statistical practices (Vul et al., 2009)

- The Dead Salmon Study
  - Demonstrated significant brain activity in a dead salmon using flawed statistical thresholds, highlighting issues in multiple comparisons correction (Bennett et al., 2009)

- Functional Localisation Overreach
  - Over-reliance on mapping single regions to specific cognitive functions ("the brain’s love centre")

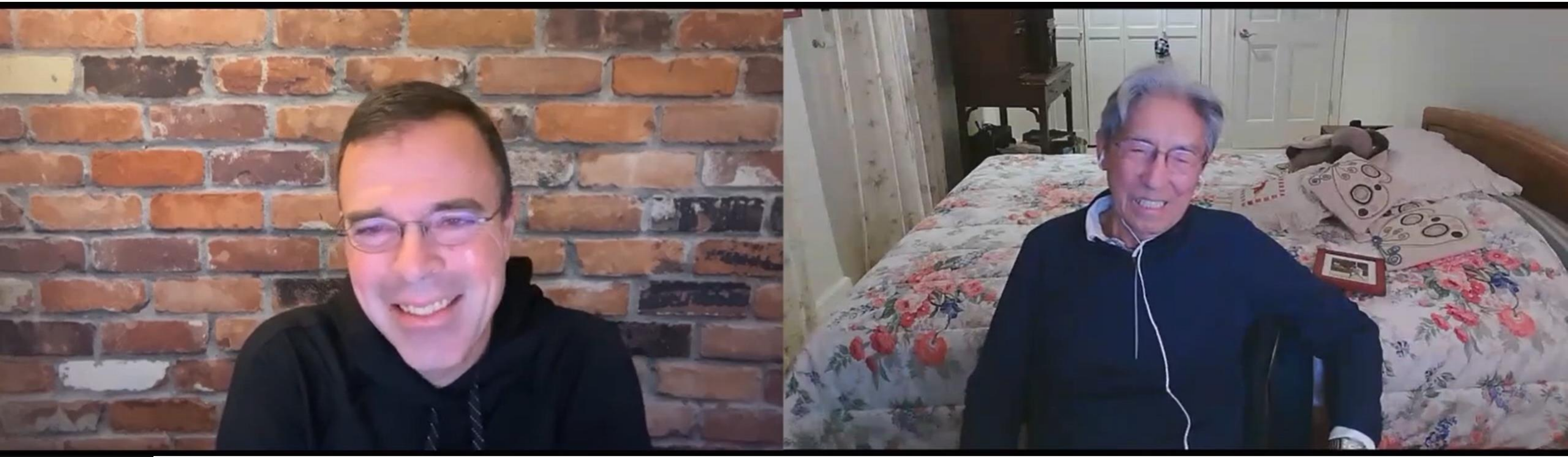
- Reverse Inference
  - Inferring cognitive states from observed brain activity without robust experimental validation
    - *"If the amygdala is activated, the person must be experiencing fear."*
    - *"If the insula is active, the person must be feeling disgust or pain."*
    - *"Increased mPFC activity means the person is engaging in moral reasoning."*

Moving Beyond Overinterpretation

- Shift toward larger samples
- Increased focus on reproducibility and robust statistics
- Transparent data (and code) sharing
- Shift toward network-level analysis vs isolated localisation

The discoverer of the BOLD contrast and fMRI

P.Bandettini's interview with S.Ogawa
January 2025



YouTube GB https://youtu.be/6gBKnxJD9v8?si=yvqXdA5xWHWHhILC

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