



# FUNCTIONAL MAGNETIC RESONANCE IMAGING

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*EPFL and CIBM*

*CIBM translational MR neuroimaging & spectroscopy, 25.04.2023*



C I B M . C H

# FUNCTIONAL MAGNETIC RESONANCE IMAGING

## What it is about

### Keywords:

- Functional imaging, fMRI, BOLD, task and resting-state, block design, connectome

### Readings:

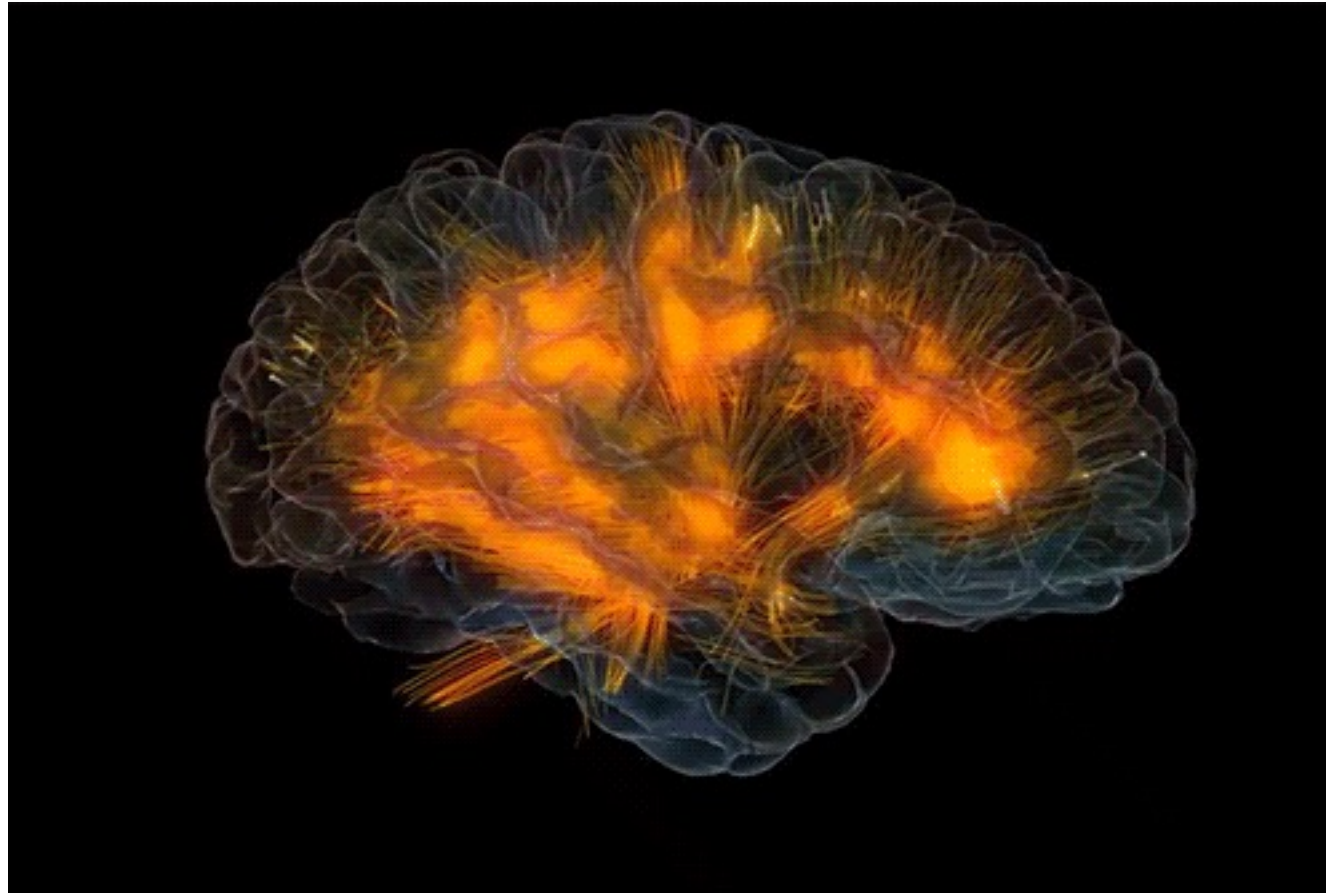
- Functional Magnetic Resonance Imaging (Huettel, Song, McCarthy)
- Fundamentals of Brain Network Analysis (Fornito, Zalesky, Bullmore)

### Complementary PHD courses :

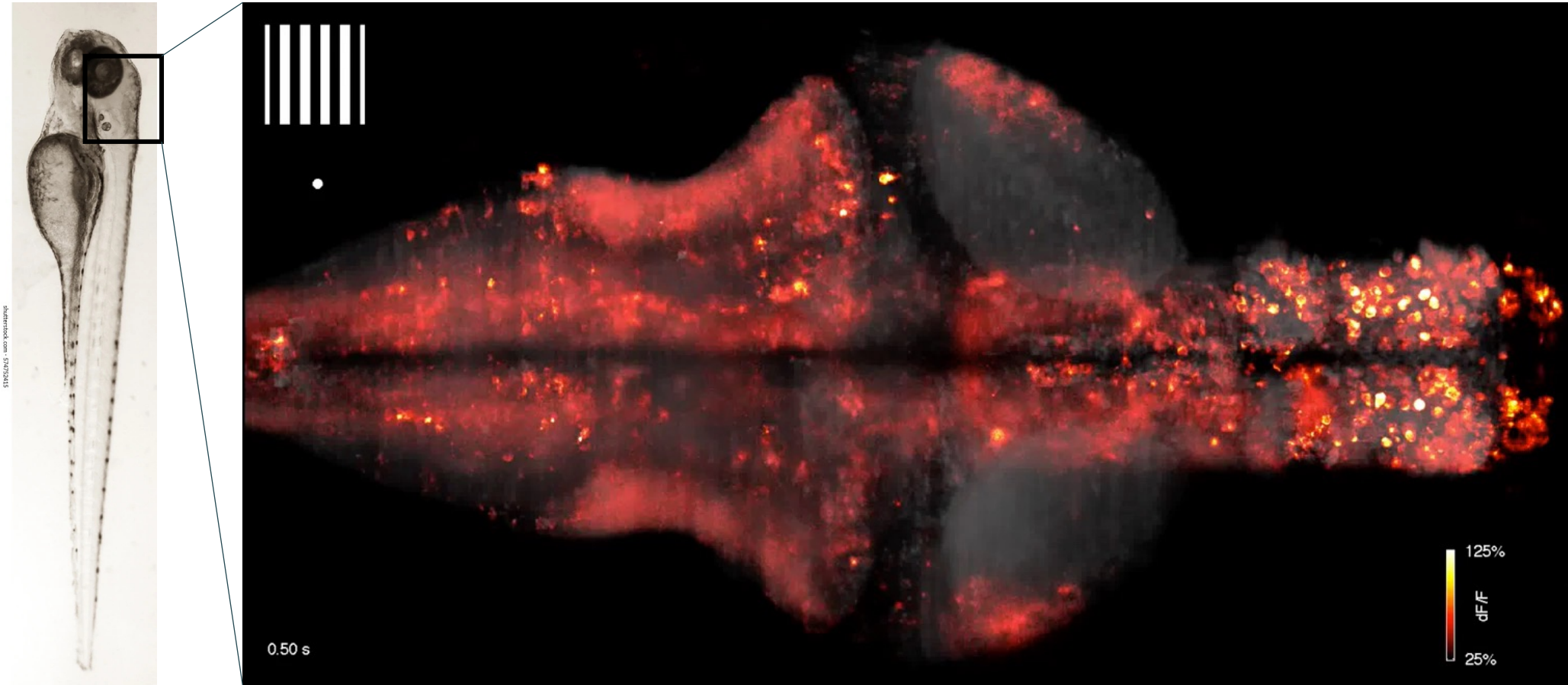
- Advanced topics in network neuroscience (Dr. Enrico Amico)



# FUNCTIONAL IMAGING OF BRAIN ACTIVITY



# FUNCTIONAL IMAGING OF BRAIN ACTIVITY



Credit: Misha Ahrens & Philipp Keller/Howard Hughes Medical Institute

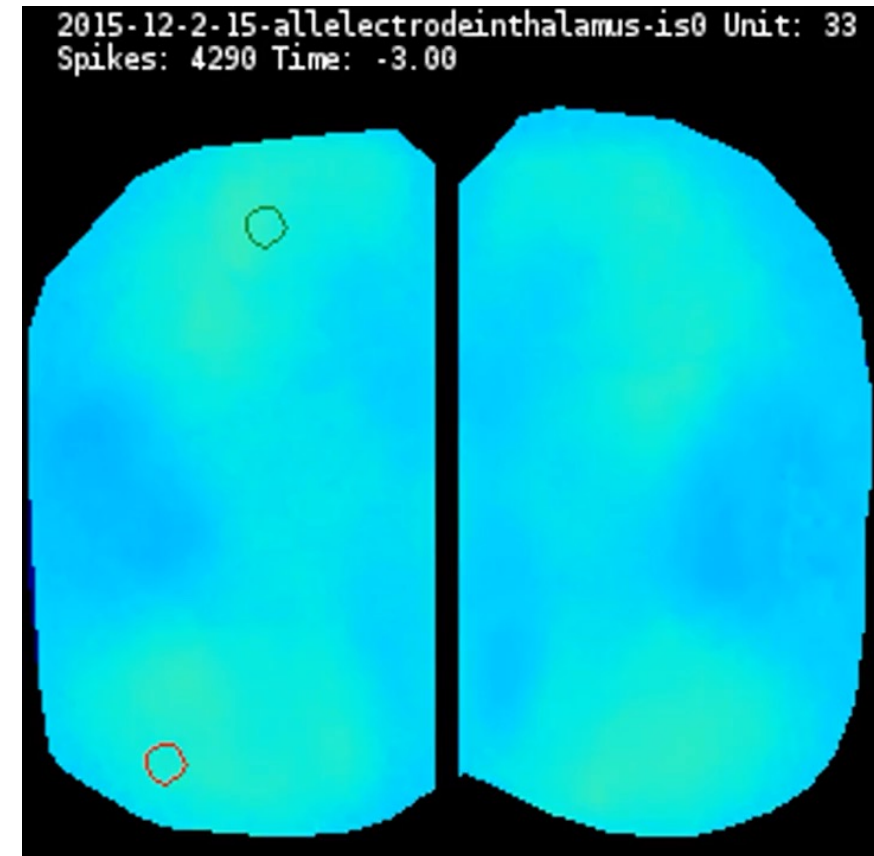
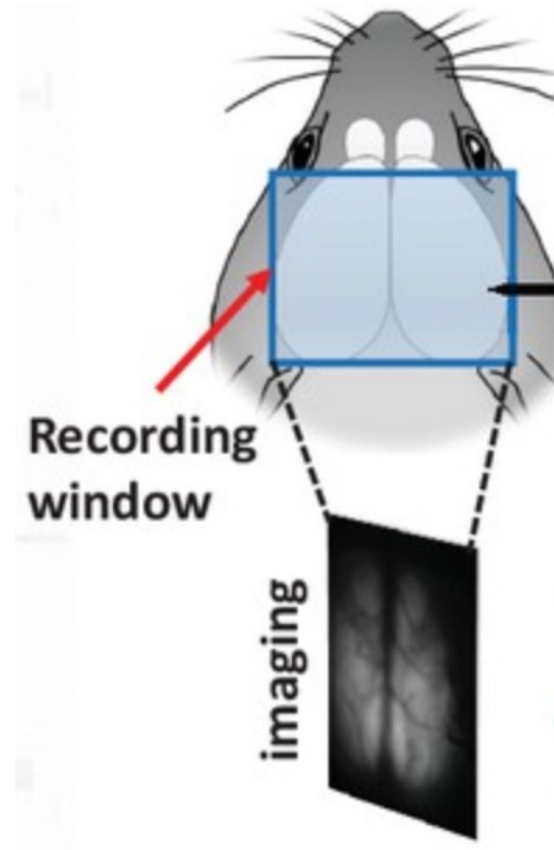
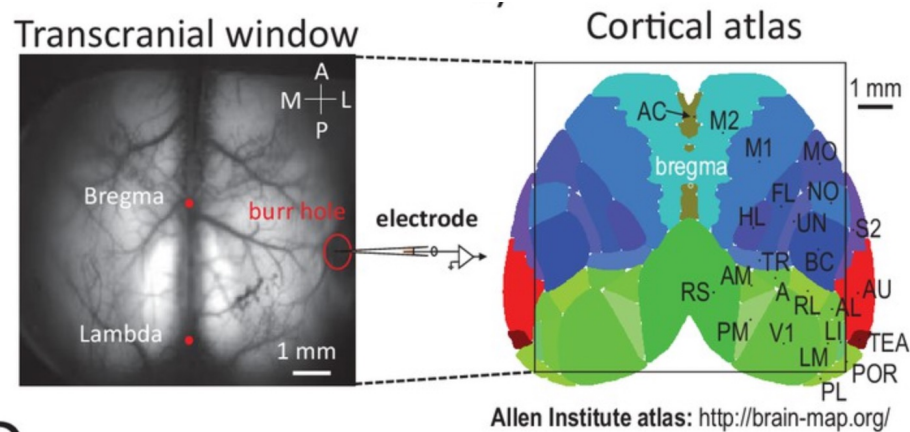


# FUNCTIONAL IMAGING OF BRAIN ACTIVITY

## Mapping cortical mesoscopic networks of single spiking cortical or sub-cortical neurons

Dongsheng Xiao, Matthieu P Vanni, Catalin C Mitelut, Allen W Chan, Jeffrey M LeDue, Yicheng Xie, Andrew CN Chen, Nicholas V Swindale, Timothy H Murphy

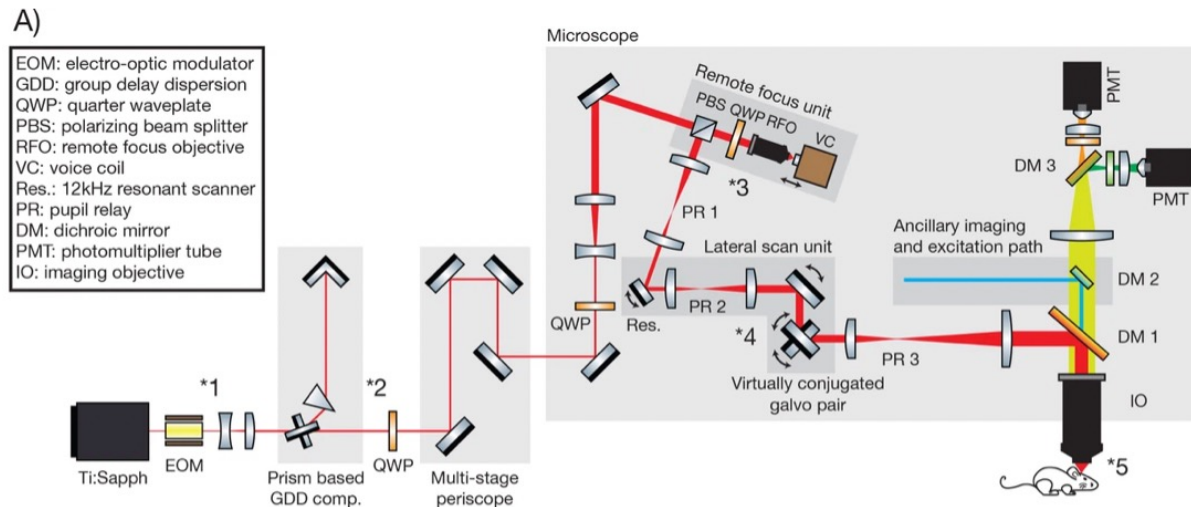
Kinsmen Laboratory of Neurological Research, Canada; Beijing Institute for Brain Disorders, Capital Medical University, China; Djavad Mowafaghian Centre for Brain Health, University of British Columbia, Canada; University of British Columbia, Canada



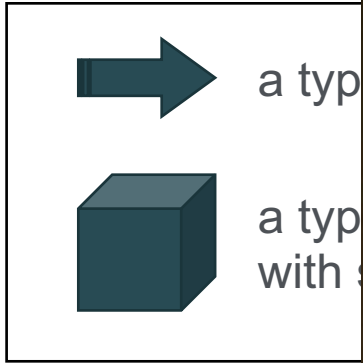
# FUNCTIONAL IMAGING OF BRAIN ACTIVITY

## A large field of view two-photon mesoscope with subcellular resolution for in vivo imaging

Nicholas James Sofroniew, Daniel Flickinger, Jonathan King, Karel Svoboda



# CAN WE IMAGE BRAIN ACTIVITY WITH MRI?



measure fast events?

events may be possible

single cells events?

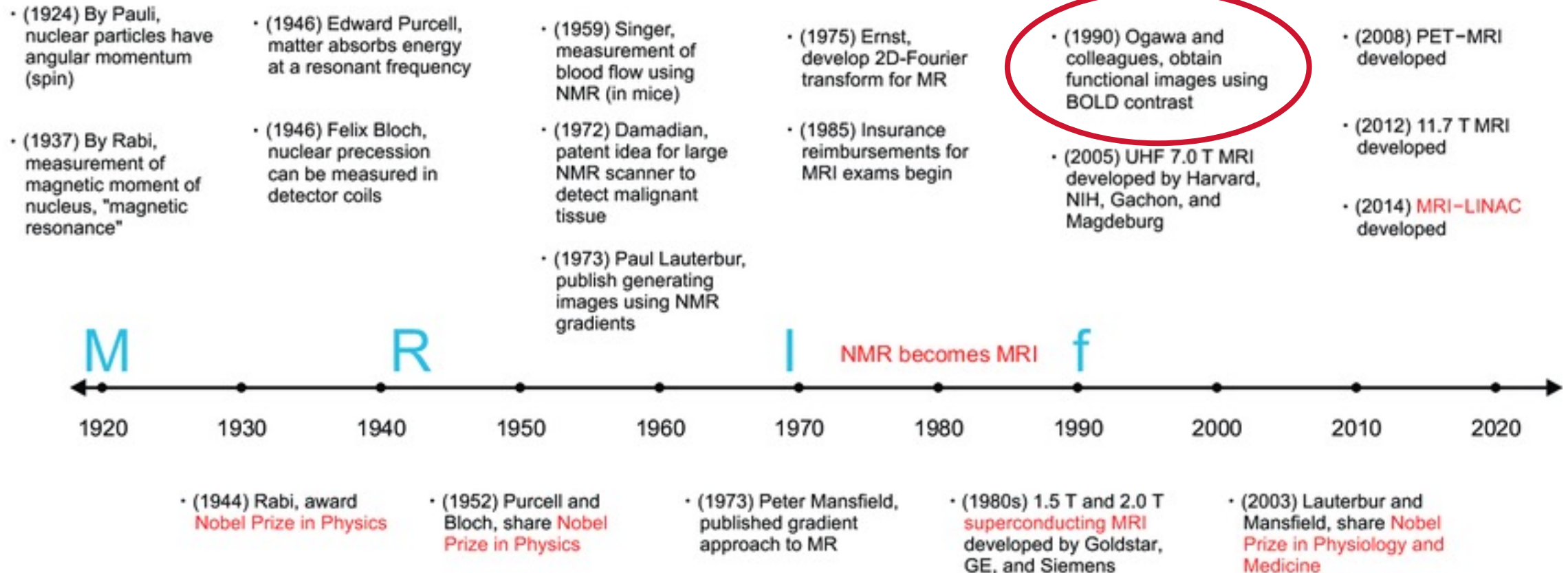
events may be possible

ne neuronal activity?

activity nonetheless

# 1990: THE ADVENT OF FUNCTIONAL MRI

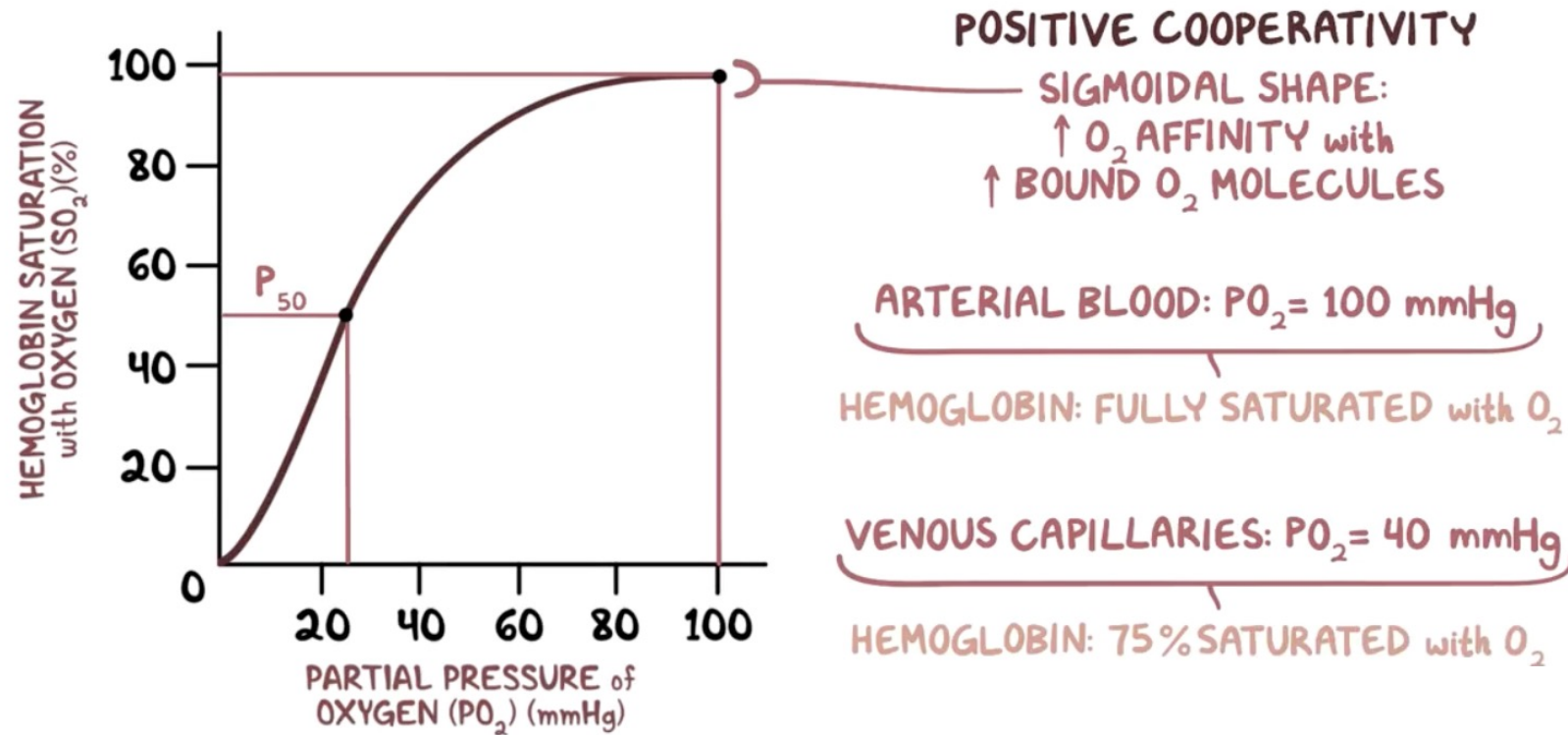
## Timeline of MRI



# CONTRAST SOURCE OF FMRI

## THE BOLD SIGNAL

Red Blood Cells

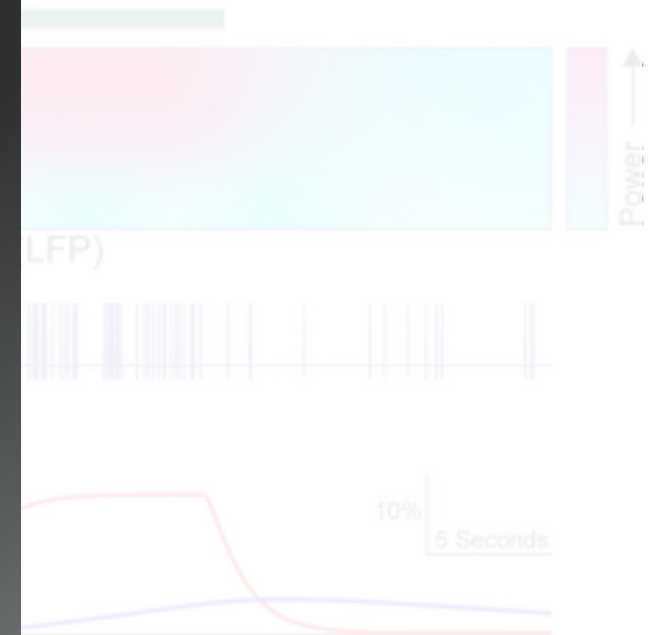
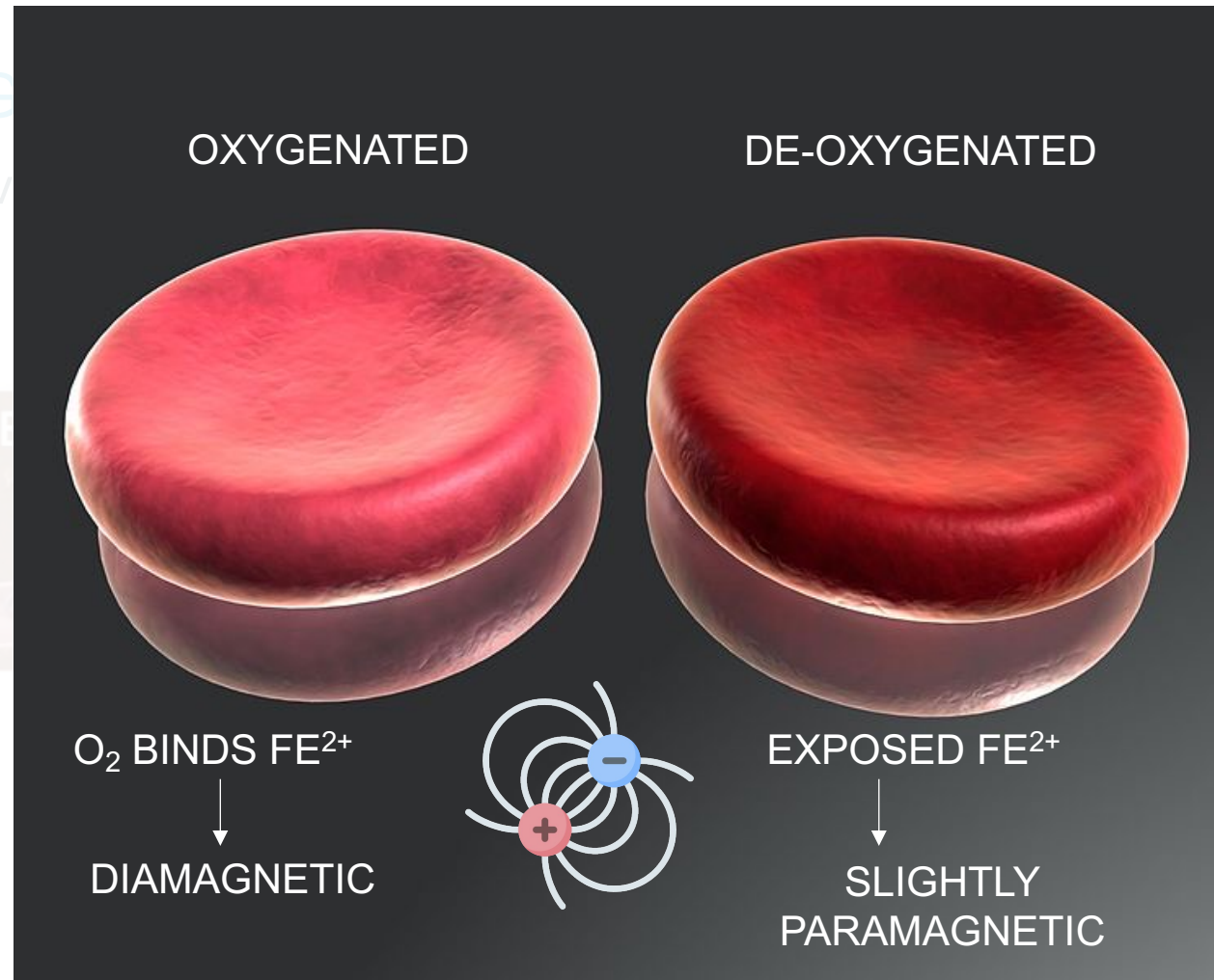
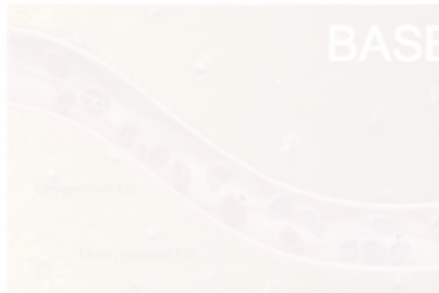




# CONTRAST SOURCE OF FMRI

## THE BOLD SIGNAL

The brain has developed lots of strategies to maintain oxygen availability high!

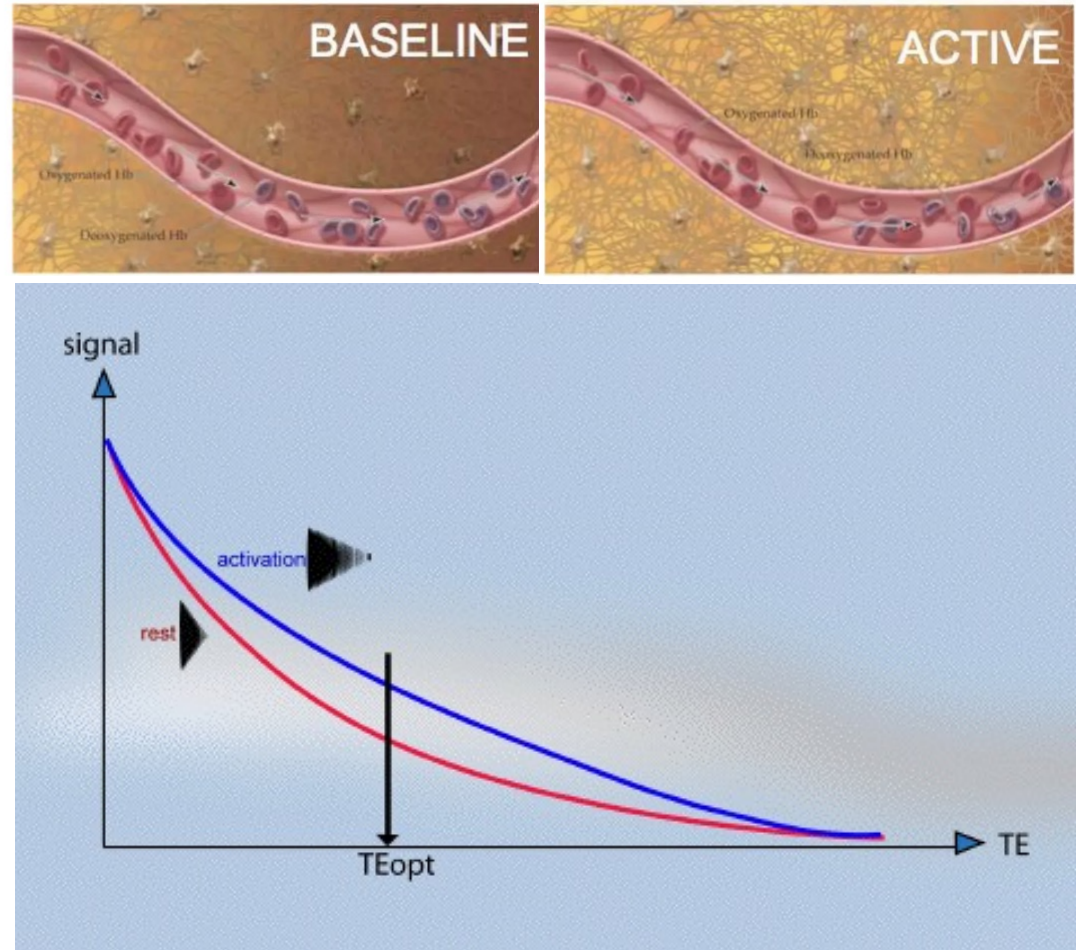




# CONTRAST SOURCE OF FMRI

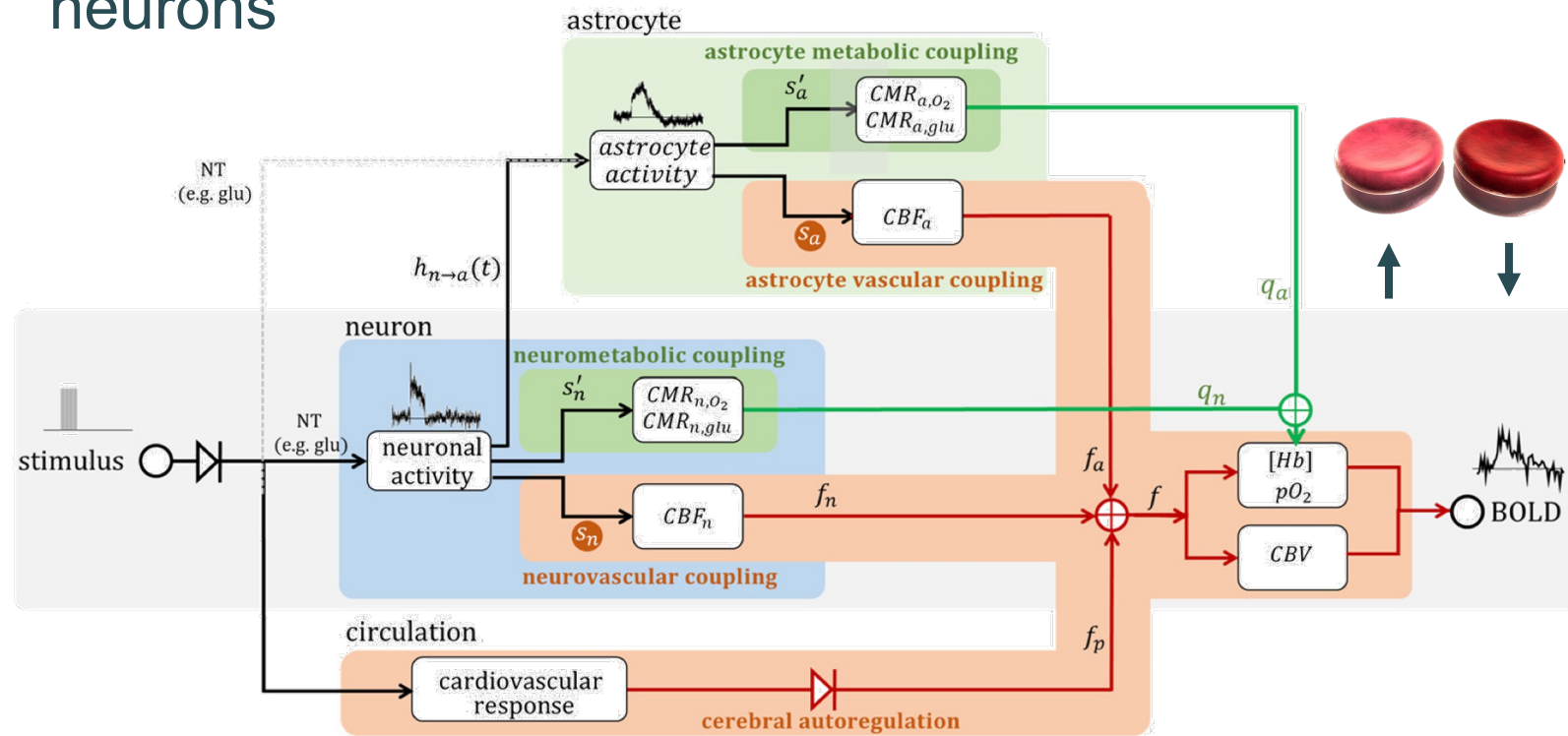
## THE BOLD SIGNAL

- neurons consume oxygen and nutrients
- increased neural activity requires increased supply of oxygen
- oxygen is bound to hemoglobin (oxyhemoglobin vs. de-oxyhemoglobin)
- to supply neurons with oxygen and glucose, blood flow is increased locally
- the local increase in blood flow leads to a displacement of de-oxyhemoglobin
- MR signal is higher for oxygenated compared to de-oxygenated blood



# THE HEMODYNAMIC RESPONSE

not only  
Made by neurons



Ioanas et al., *Neurophotonics* 2022

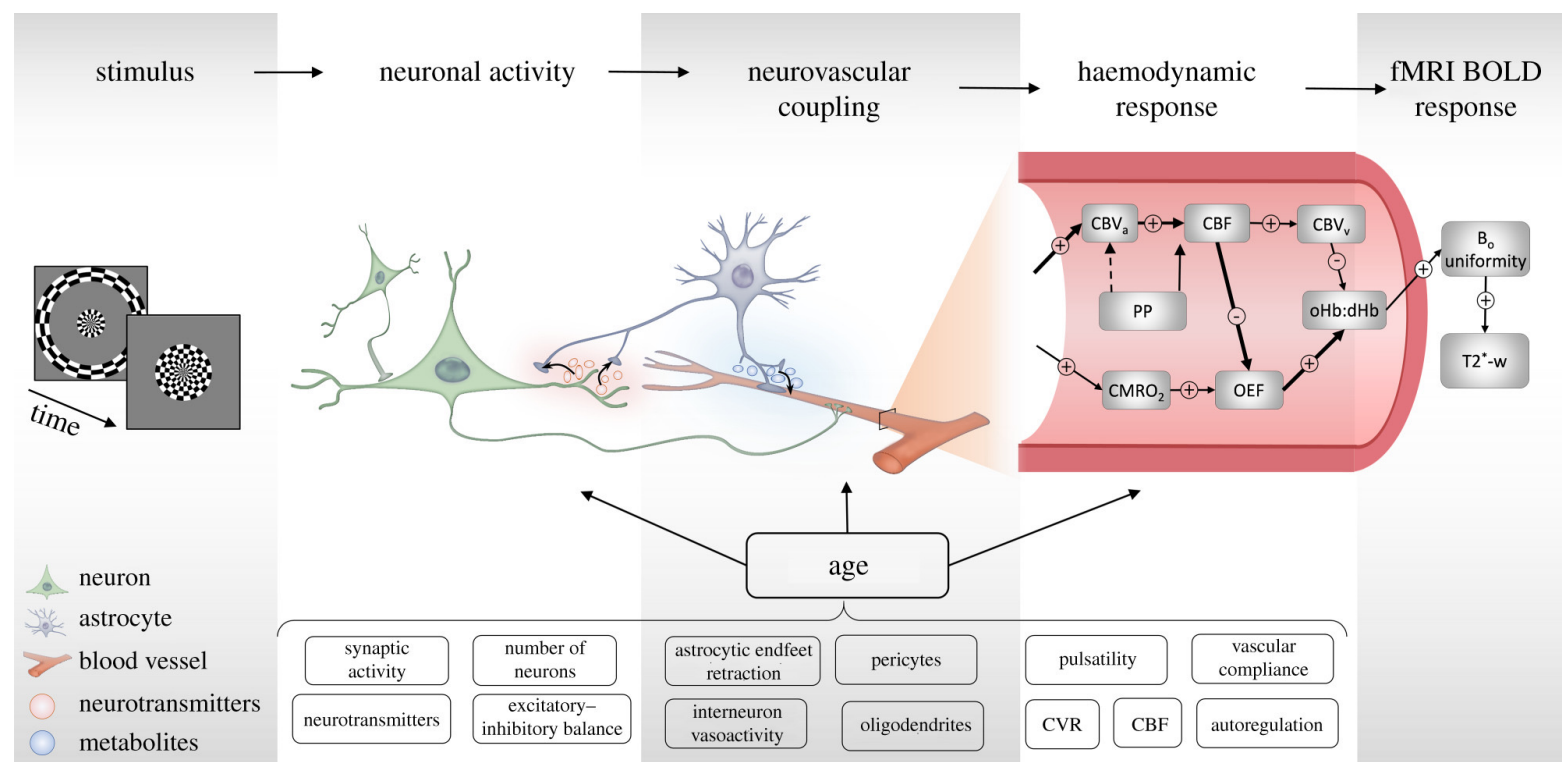
# CAREFUL ON THE INTERPRETATION OF FMRI

Review articles

## Separating vascular and neuronal effects of age on fMRI BOLD signals

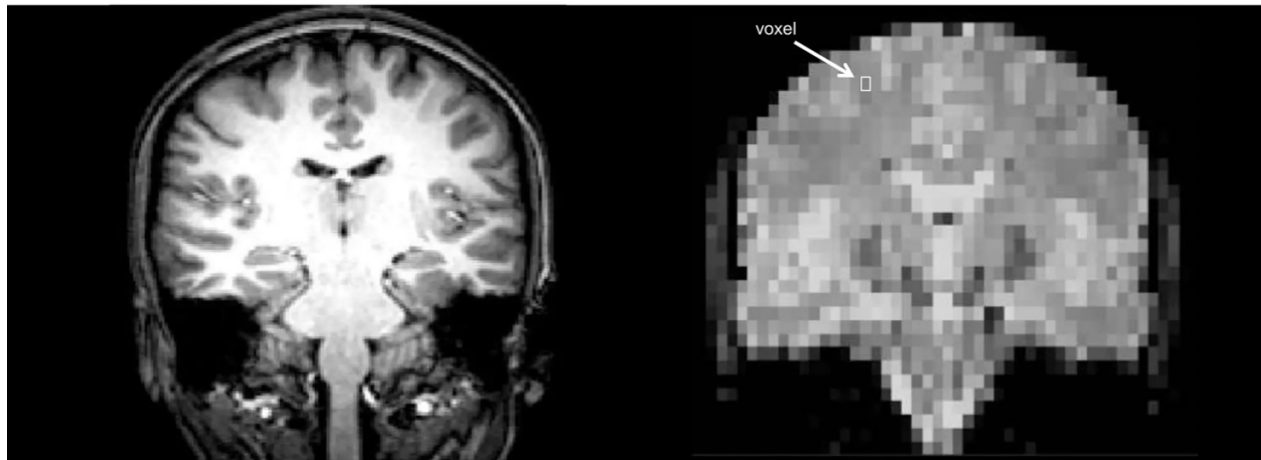
Kamen A. Tsvetanov ✉, Richard N. A. Henson and James B. Rowe

Published: 16 November 2020 | <https://doi.org/10.1098/rstb.2019.0631>



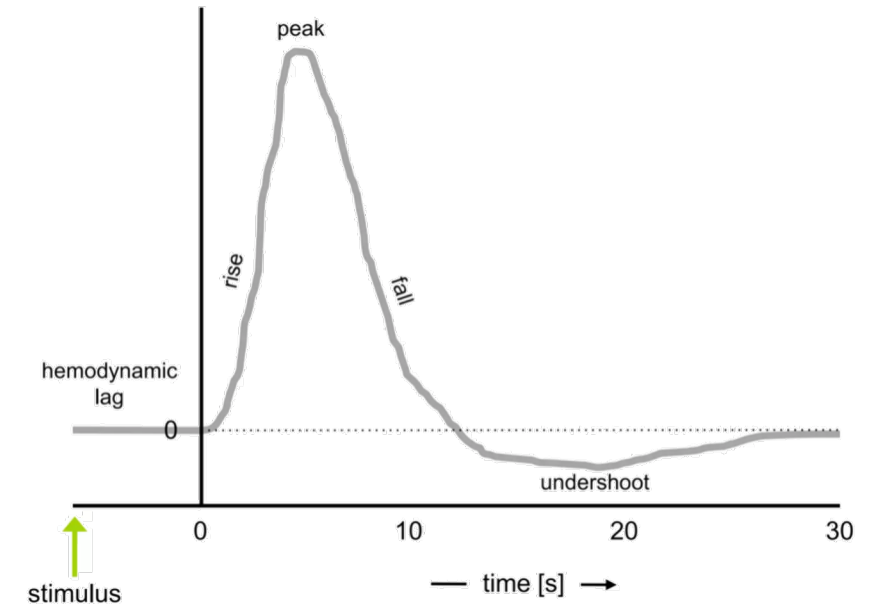
# THE HEMODYNAMIC RESPONSE

The neurovascular unit works as a low-pass filter!



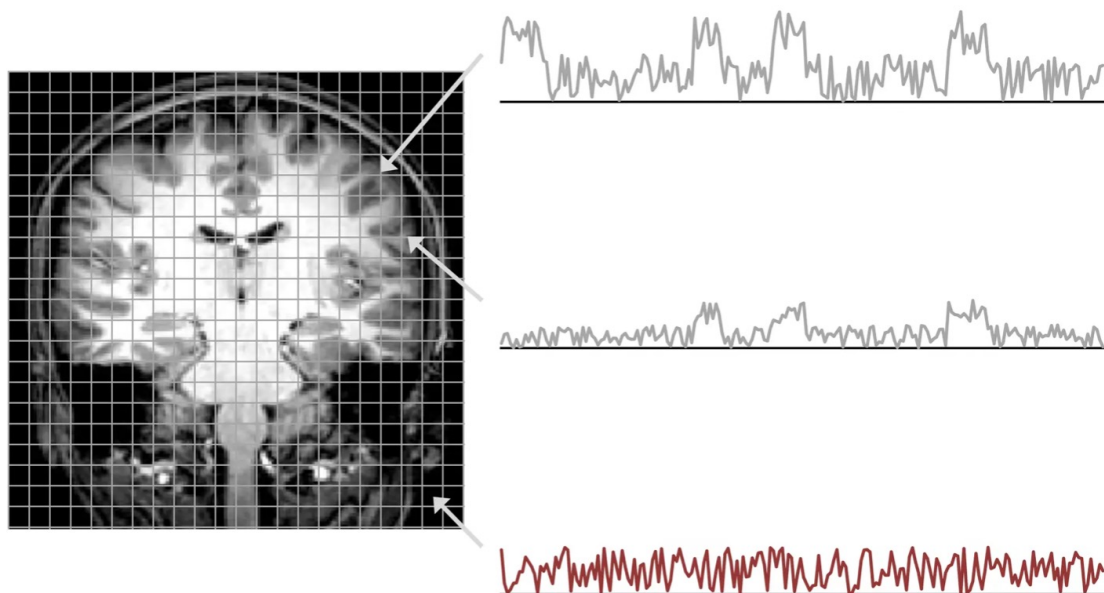
MRI

functional MRI

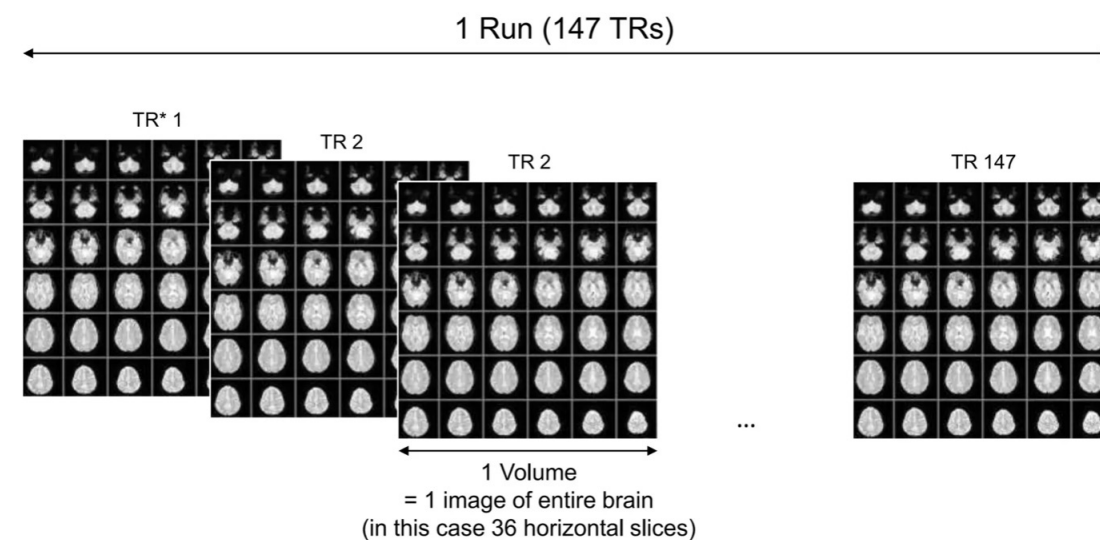


# VOXEL RESOLUTION

A [BOLD] response is measured for every voxel



## 4-D datasets



\*TR = Time of Repetition = time it takes to acquire one volume



# FMRI DATA ANALYSIS

## Regression in fMRI

**Core idea:** observed data can be explained by a combination of weighted regressors

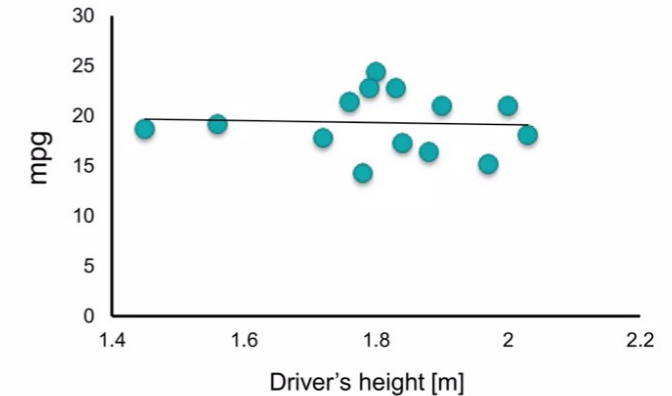
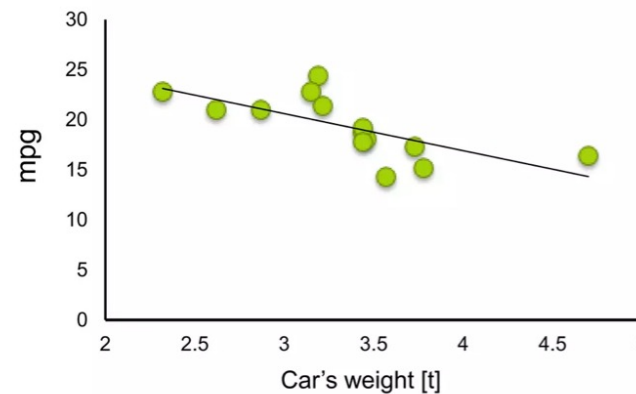
**Example:** explain fuel consumption of a car (miles per gallon), based on the car's weight and the driver's height

Observed data: mpg

Regressor: car's weight, driver's height

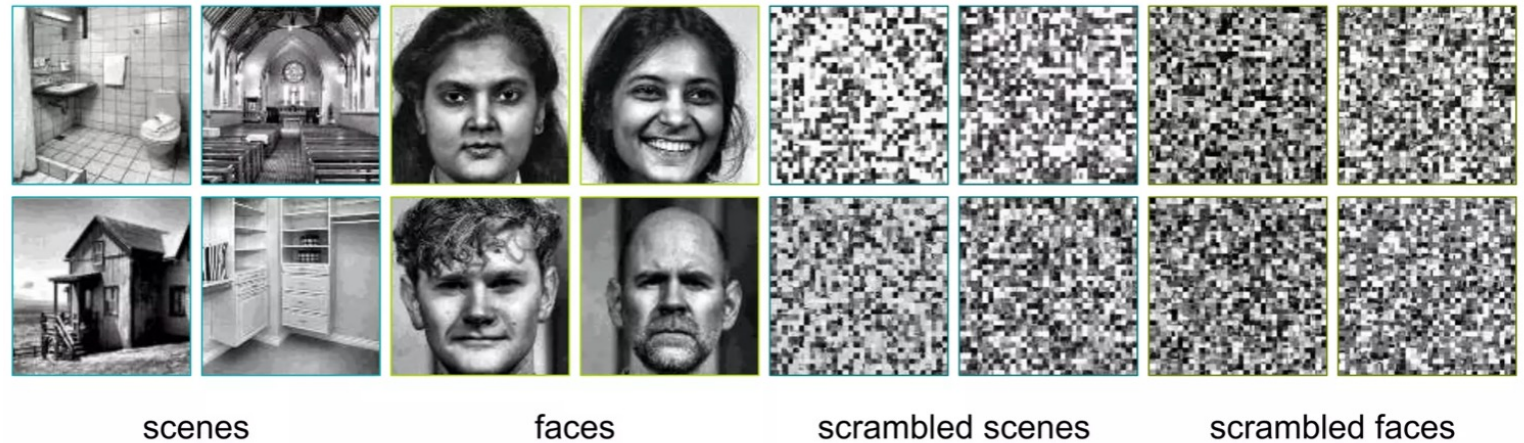
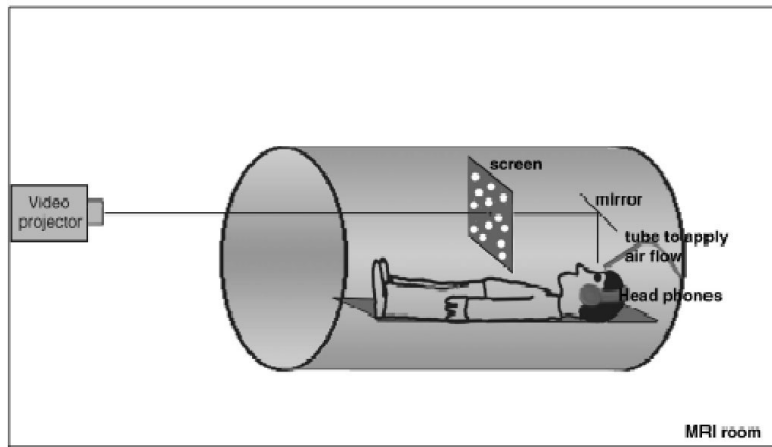
Weights:  $\beta_{\text{car's weight}} = \text{high}$

$\beta_{\text{driver's height}} = \text{low}$

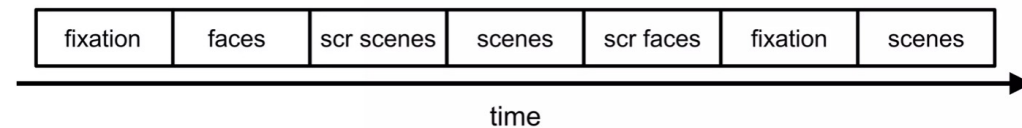


# FMRI DATA ANALYSIS

Research question: which brain areas decode for scene/faces from scrambled images?

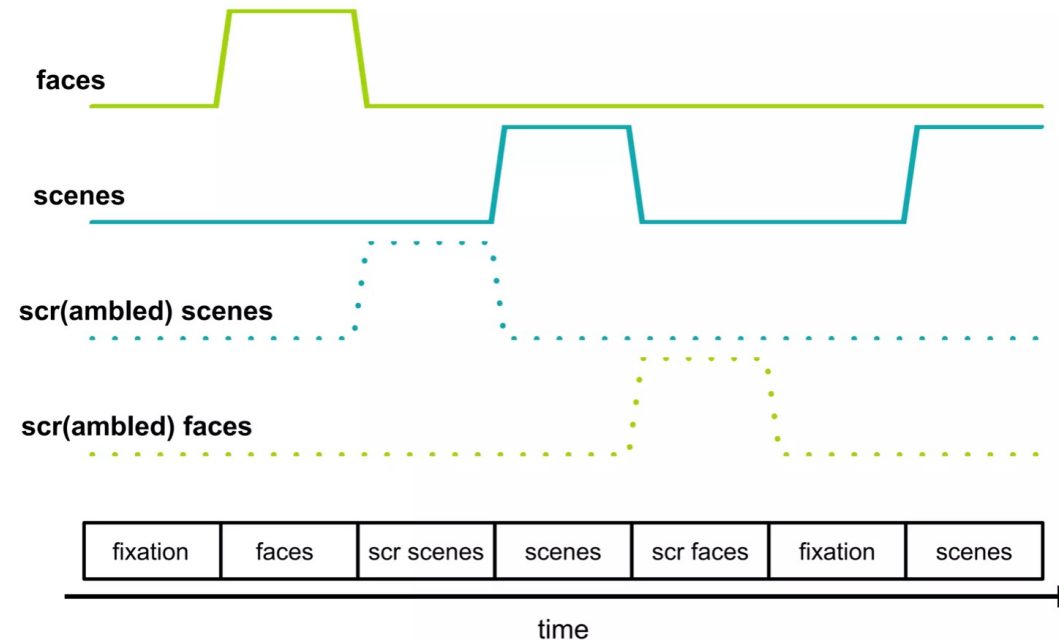


Stimuli are presented in a blocked design:



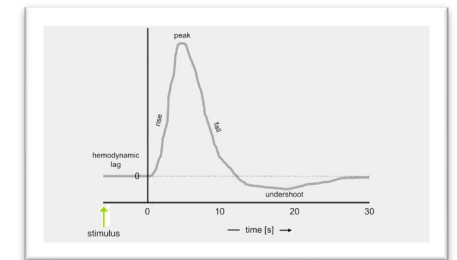
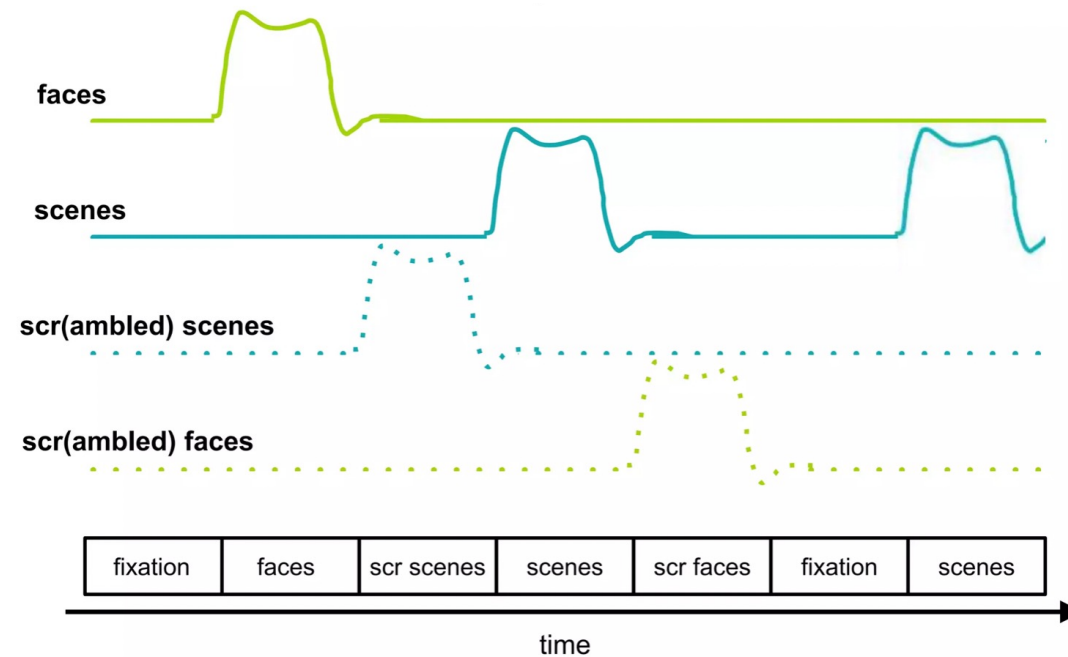
# FMRI DATA ANALYSIS

Regressors: timing of conditions combined with assumptions about the shape of the BOLD response



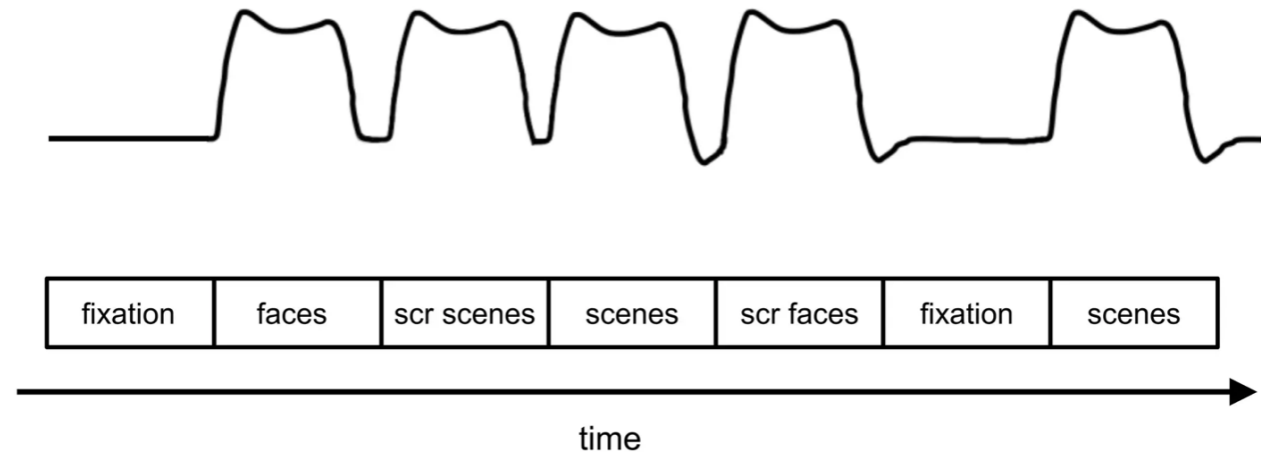
# FMRI DATA ANALYSIS

Regressors: timing of conditions combined with assumptions about the shape of the BOLD response



# FMRI DATA ANALYSIS

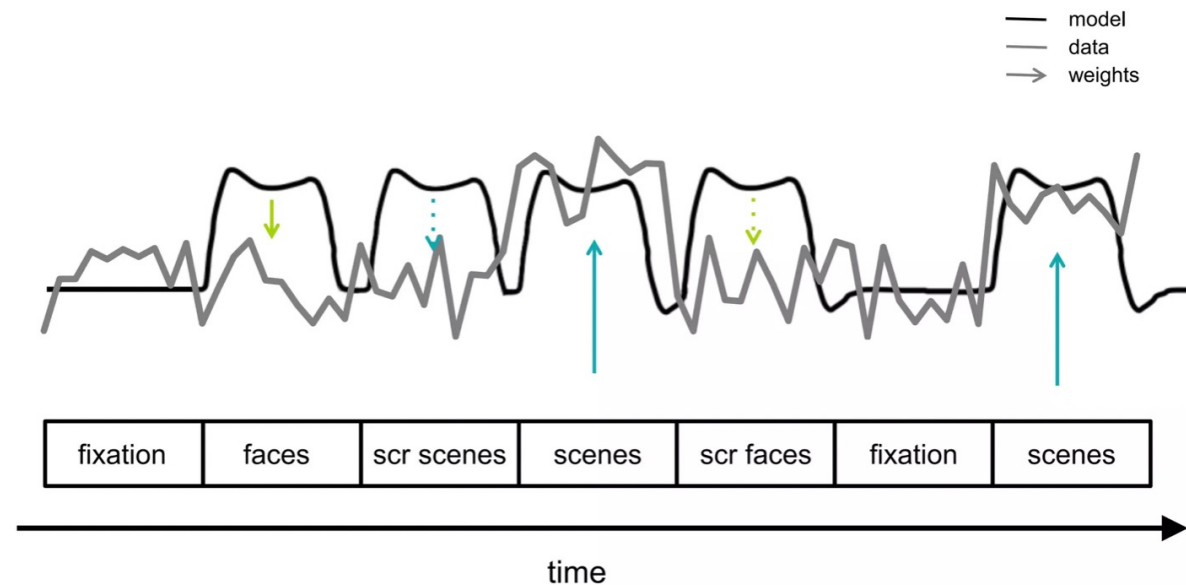
Regressors: timing of conditions combined with assumptions about the shape of the BOLD response





# FMRI DATA ANALYSIS

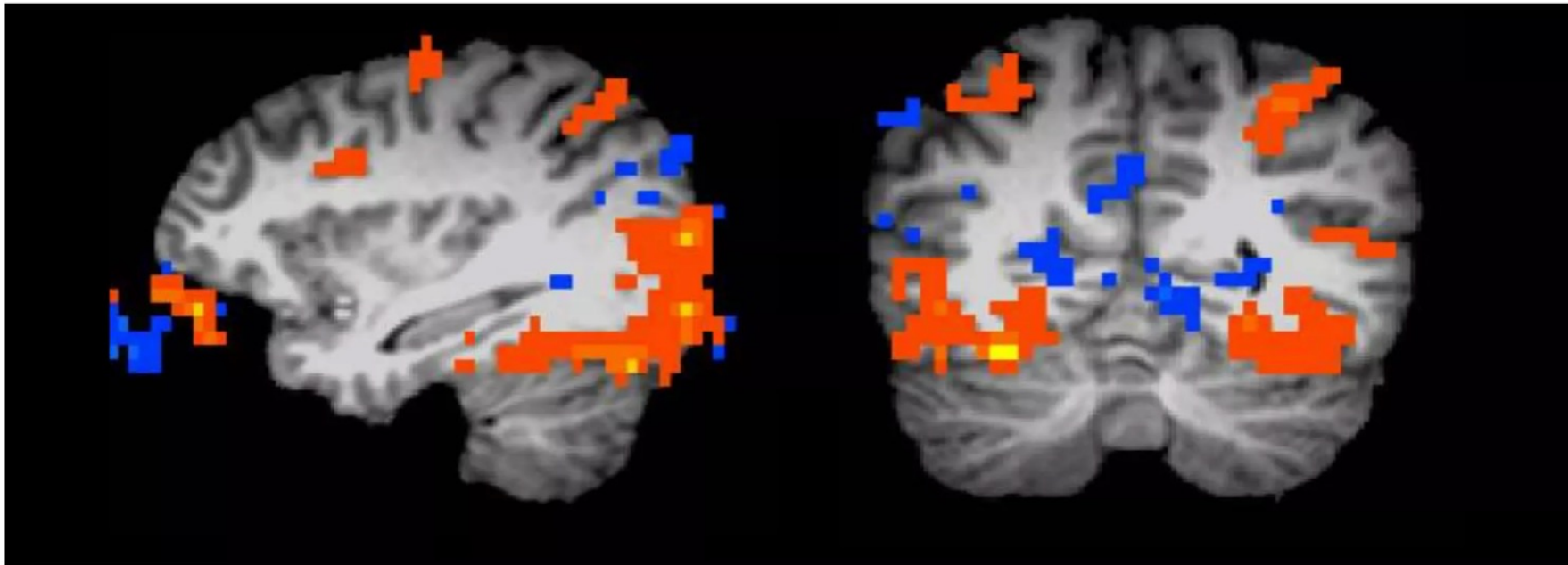
Regressors: timing of conditions combined with assumptions about the shape of the BOLD response



**Regressors that account for a lot of variance in the signal receive high beta values (weights)!**

# FIRST LEVEL ANALYSIS

**Weights are plotted as statistical parametric maps**

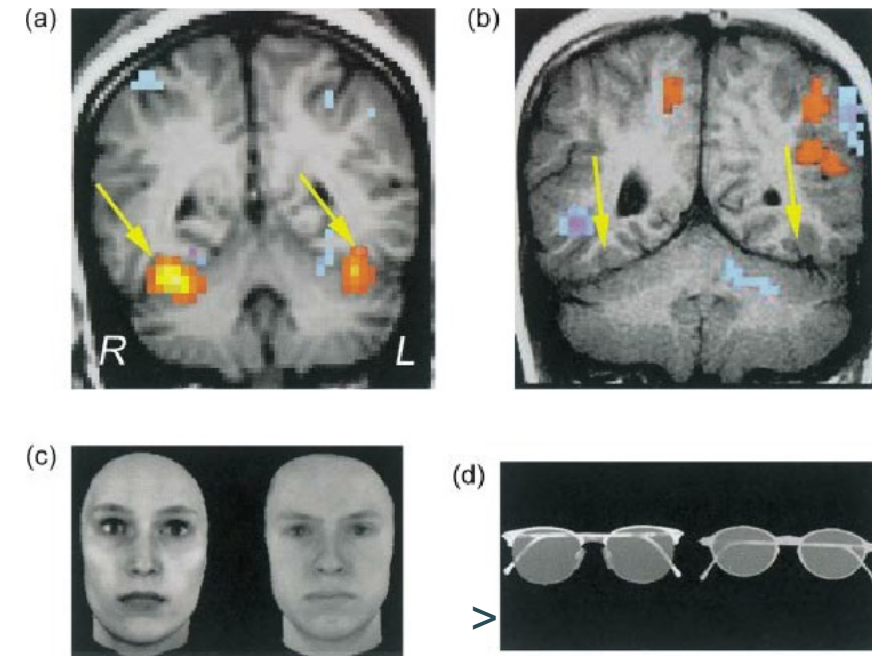
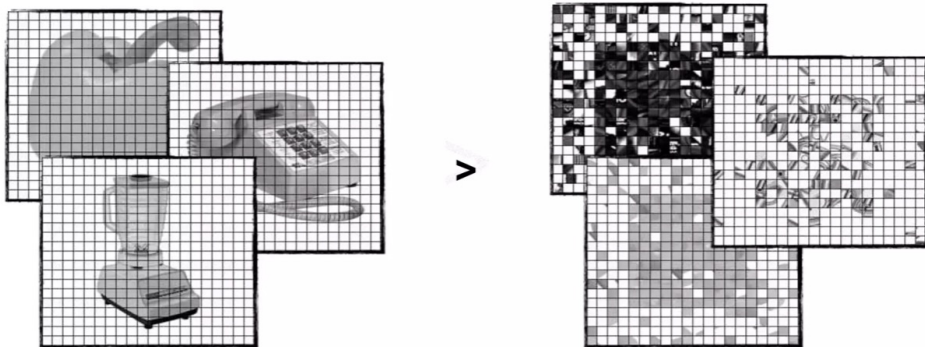
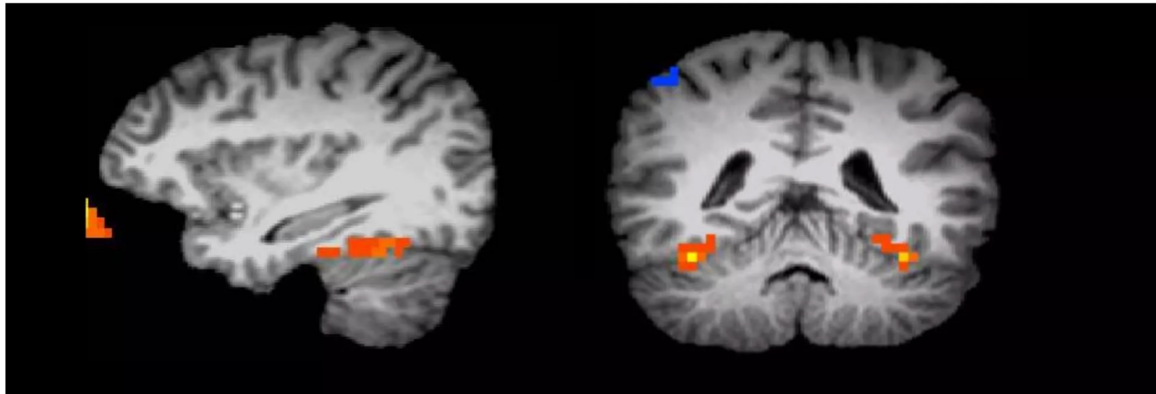


Eg. Voxels that get significantly activated during scenes

# SECOND LEVEL ANALYSIS

**Contrasts** are used to test for differences among the levels of a factor:

**Contrasts: intact vs. scrambled objects**



[Review](#) > [Dev Psychobiol.](#) 2002 Apr;40(3):213-25. doi: 10.1002/dev.10028.

**Social interest and the development of cortical face specialization: what autism teaches us about face processing**

David J Grelotti<sup>1</sup>, Isabel Gauthier, Robert T Schultz

Affiliations + expand

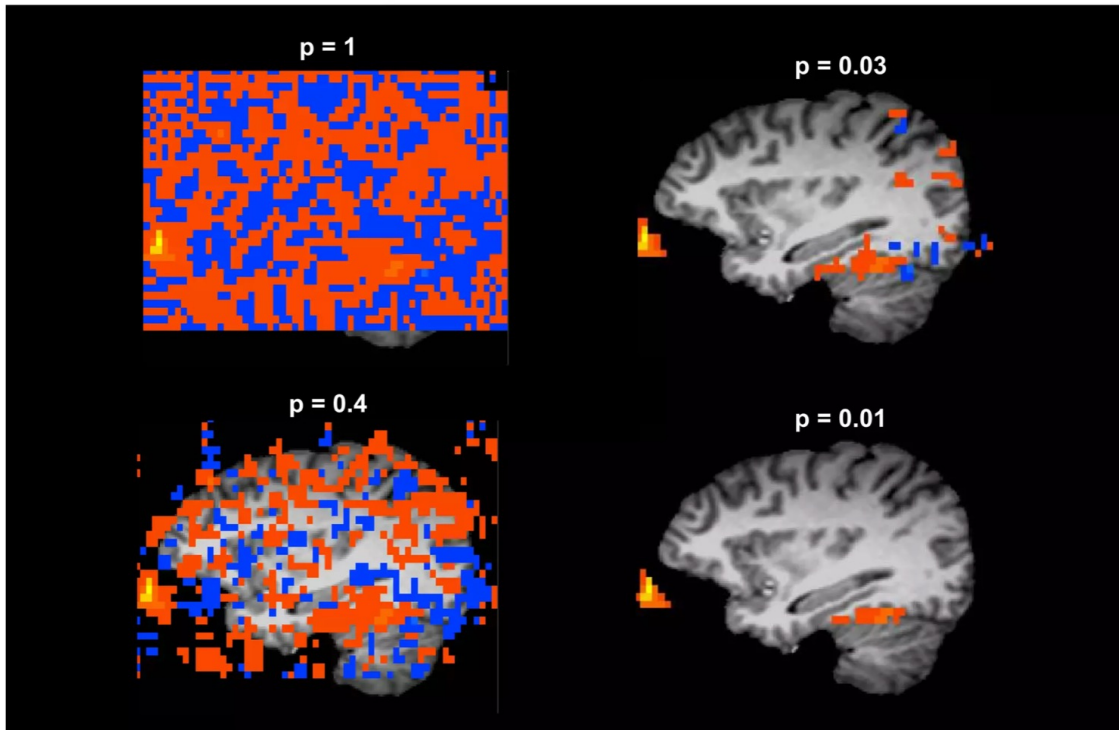
PMID: 11891634 DOI: 10.1002/dev.10028

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# THE DEAD SALMON



Significance thresholds



## IgNobel Prize in Neuroscience: The dead salmon study

Bennett et al. "Neural Correlates of Interspecies Perspective Taking in the Post-Mortem Atlantic Salmon: An Argument For Proper Multiple Comparisons Correction" *Journal of Serendipitous and Unexpected Results*, 2010.

# FMRI: STRENGTH IN NUMBERS

## Number of articles with “fMRI” in their abstract

RESULTS BY YEAR

599,066 results

Page 1 of 59,907



Source: pubmed.com



# FMRI: STRENGTH IN NUMBERS

## fMRI is still controversial today

### nature

Explore content ▾ About the journal ▾ Publish with us ▾

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Article | [Open Access](#) | [Published: 16 March 2022](#)

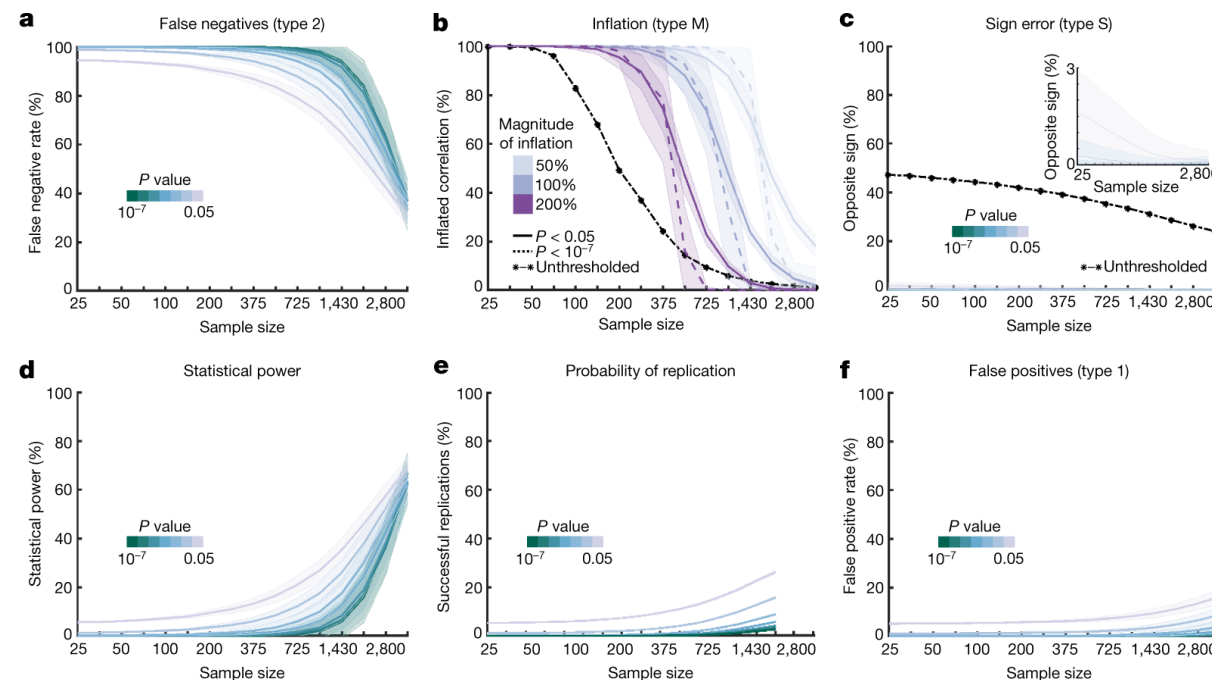
### Reproducible brain-wide association studies require thousands of individuals

[Scott Marek](#) , [Brenden Tervo-Clemmens](#) , [Finnegan J. Calabro](#), [David F. Montez](#), [Benjamin P. Kay](#), [Alexander S. Hatoum](#), [Meghan Rose Donohue](#), [William Foran](#), [Ryland L. Miller](#), [Timothy J. Hendrickson](#), [Stephen M. Malone](#), [Sridhar Kandala](#), [Eric Feczko](#), [Oscar Miranda-Dominguez](#), [Alice M. Graham](#), [Eric A. Earl](#), [Anders J. Perrone](#), [Michaela Cordova](#), [Olivia Doyle](#), [Lucille A. Moore](#), [Gregory M. Conan](#), [Johnny Uriarte](#), [Kathy Snider](#), [Benjamin J. Lynch](#), [James C. Wilgenbusch](#), [Thomas Pengo](#), [Angela Tam](#), [Jianzhong Chen](#), [Dillan J. Newbold](#), [Annie Zheng](#), [Nicole A. Seider](#), [Andrew N. Van](#), [Athanasia Metoki](#), [Roselyne J. Chauvin](#), [Timothy O. Laumann](#), [Deanna J. Greene](#), [Steven E. Petersen](#), [Hugh Garavan](#), [Wesley K. Thompson](#), [Thomas E. Nichols](#), [B. T. Thomas Yeo](#), [Deanna M. Barch](#), [Beatriz Luna](#), [Damien A. Fair](#)  & [Nico U. F. Dosenbach](#)  — [Show fewer authors](#)

[Nature](#) **603**, 654–660 (2022) | [Cite this article](#)

**64k** Accesses | **277** Citations | **1511** Altmetric | [Metrics](#)

“A primary challenge has been replicating associations between inter-individual differences in brain structure or function and complex cognitive or mental health phenotypes (brain-wide association studies (BWAS))”



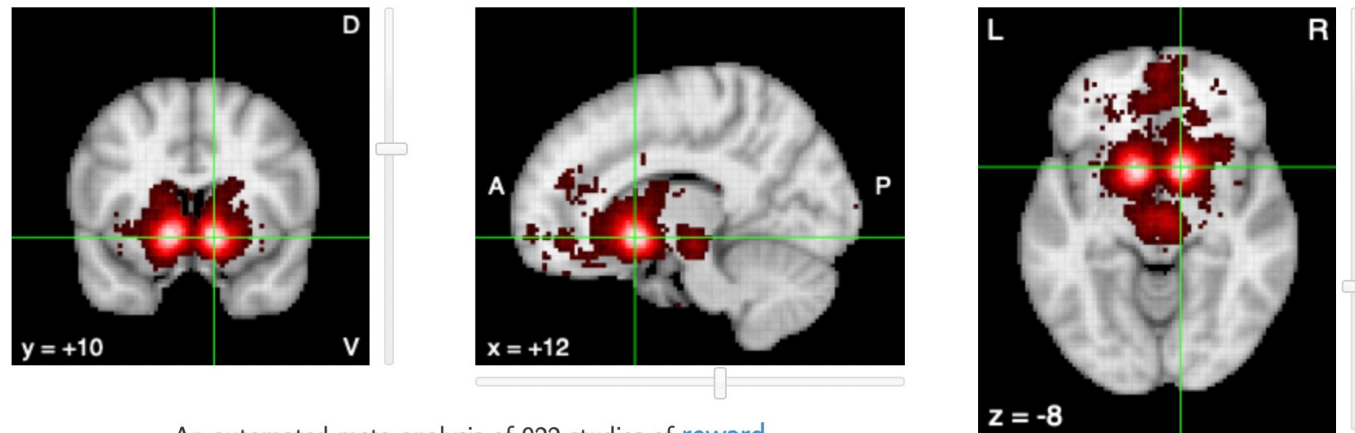


# FMRI: STRENGTH IN NUMBERS

## neurosynth.org

Neurosynth is a platform for large-scale, automated synthesis of functional magnetic resonance imaging (fMRI) data.

It takes thousands of published articles reporting the results of fMRI studies, chews on them for a bit, and then spits out images that look like this:



An automated meta-analysis of 922 studies of [reward](#)

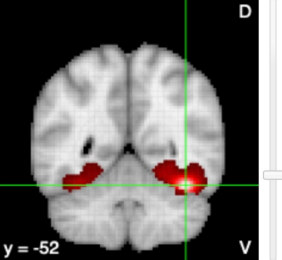
# FMRI: STRENGTH IN NUMBERS

Data for coordinates:

Maps Studies Associations FAQs

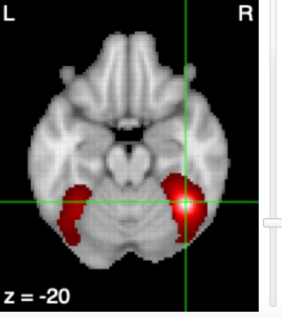
### Functional connectivity and coactivation maps

D



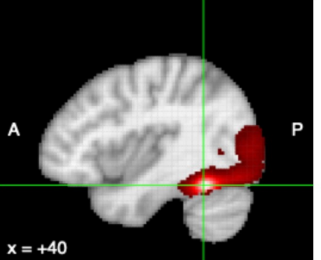
y = -52

L



z = -20

A



x = +40

Layers

- Functional connectivity
- Meta-analytic coactivation
- anatomical

Color palette:

- red

Positive/Negative:

- positive

Thresholds:

- 0.2 0.2

Opacity:

- 1

☒ Crosshairs

- ☐ Pan/zoom
- ☒ Labels

corr. (r): 1

What's here?

X:  Y:  Z:

Description

This image displays resting-state functional connectivity for the seed region in a sample of 1,000 subjects. To reduce blurring of signals across cerebro-cerebellar and cerebro-striatal boundaries, fMRI signals from adjacent cerebral cortex were regressed from the cerebellum and striatum. For details, see [Yeo et al \(2011\)](#).

Data for coordinates:

Maps Studies Associations FAQs

### Associations with meta-analysis maps

Show  entries Search:

|                  | Individual voxel |                 | Seed-based network |                          |
|------------------|------------------|-----------------|--------------------|--------------------------|
| Name             | z-score          | Posterior prob. | Func. conn. (r)    | Meta-analytic coact. (r) |
| face             | 24.19            | 0.88            | 0.48               | 0.75                     |
| fusiform face    | 22.26            | 0.92            | 0.43               | 0.68                     |
| fusiform         | 21.72            | 0.86            | 0.53               | 0.75                     |
| face ffa         | 19.68            | 0.93            | 0.41               | 0.65                     |
| faces            | 19.6             | 0.85            | 0.41               | 0.67                     |
| ffa              | 19.22            | 0.92            | 0.41               | 0.66                     |
| face recognition | 13.85            | 0.91            | 0.31               | 0.48                     |
| fusiform gyrus   | 13.77            | 0.82            | 0.47               | 0.69                     |
| viewing          | 8.37             | 0.76            | 0.37               | 0.52                     |
| recognition      | 7.72             | 0.71            | 0.29               | 0.49                     |

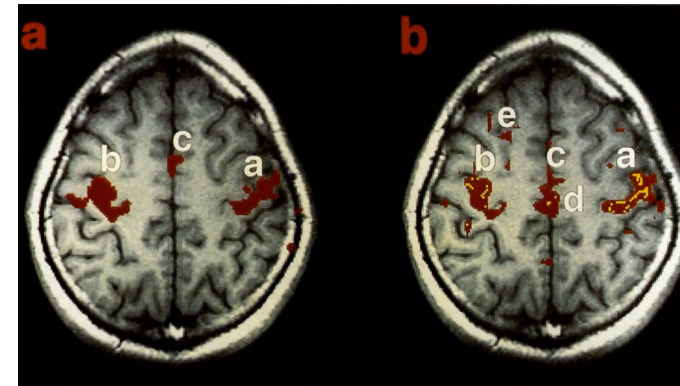
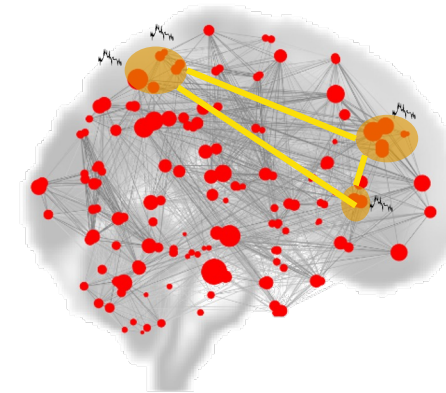
Showing 1 to 10 of 1,334 entries

First Previous **1** 2 3 4 5 ... 134 Next Last

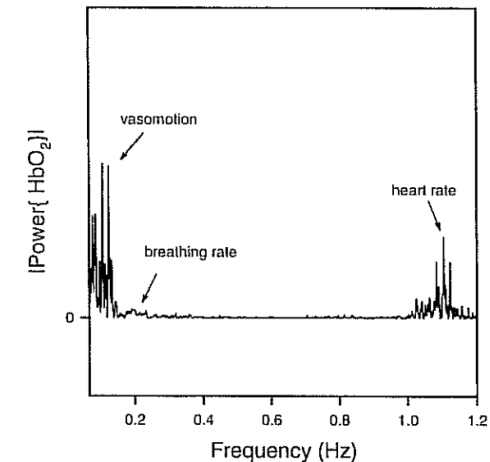
# CAN WE MEASURE MEANINGFUL BRAIN ACTIVITY IN THE ABSENCE OF A TASK?

## → RESTING-STATE fMRI

- the brain is always active, even in the absence of explicit input or output
  - task-related changes in neuronal metabolism are only about 5% of brain's total energy consumption
- what is the “noise” in standard activation studies?
  - peaks in frequency oscillations from 0.01 – 0.10 Hz
  - distinct from faster frequencies of respiratory and cardiac responses

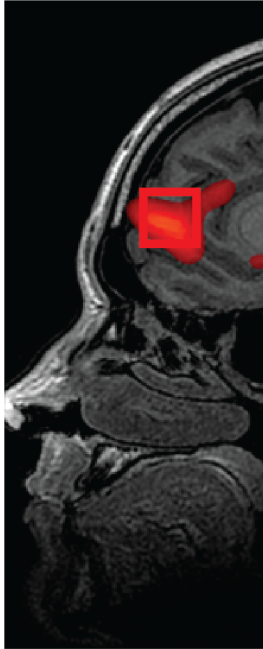


Biswal et al., 1995

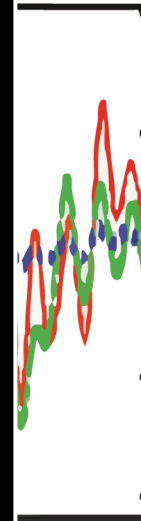
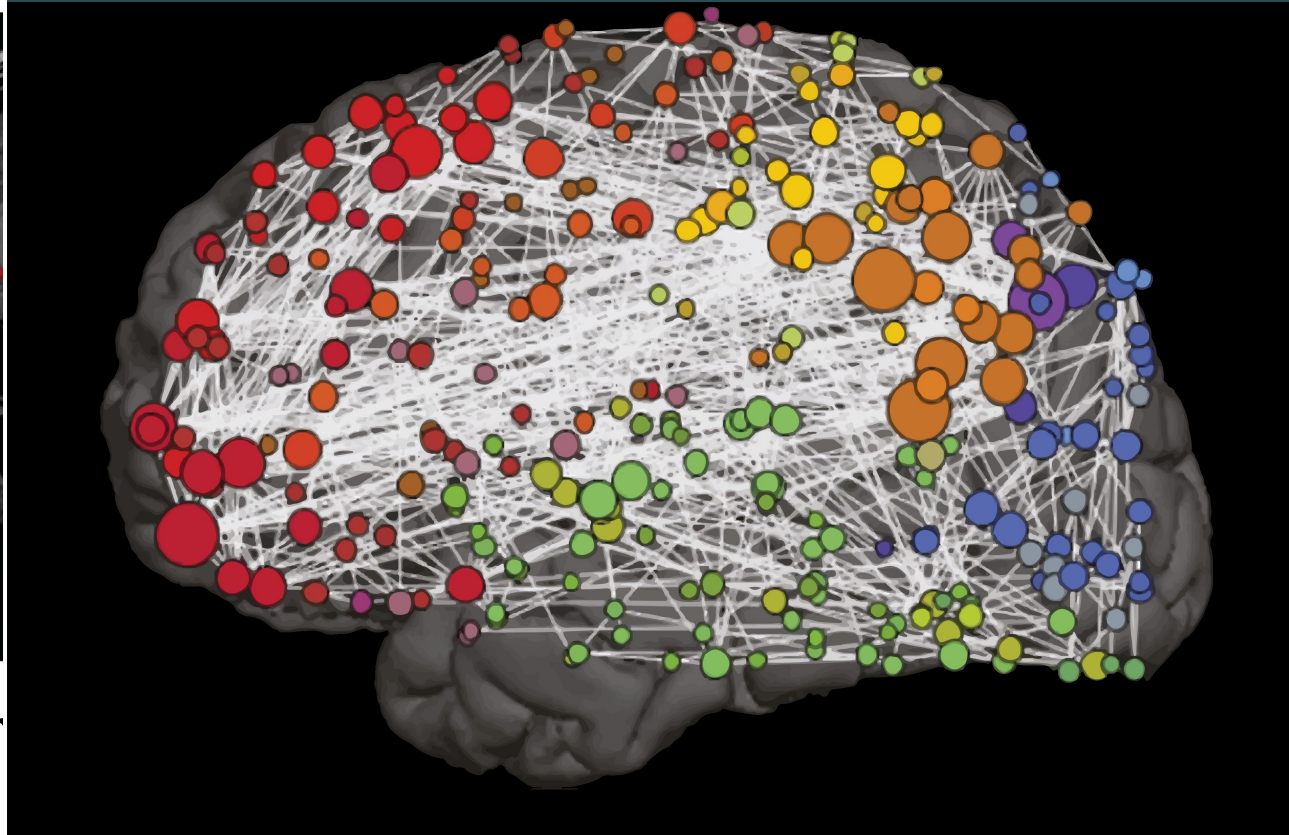


# CAN WE MEASURE MEANINGFUL BRAIN ACTIVITY IN THE ABSENCE OF A TASK?

## Resting-state functional CONNECTOME



Similar

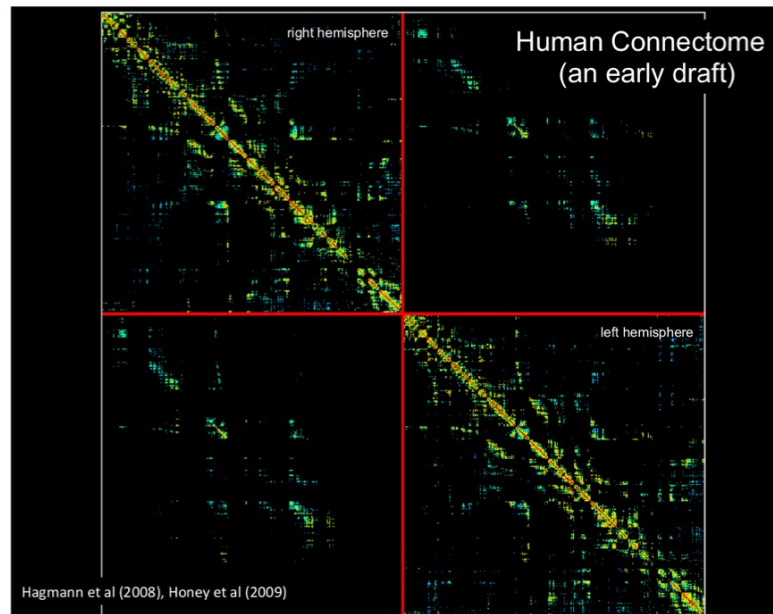


ected!



# THE CONNECTOME

In 2005, Dr. Olaf Sporns at Indiana University and Dr. Patric Hagmann at Lausanne University Hospital independently and simultaneously suggested the term "**connectome**" to refer to a map of the neural connections within the brain. This term was directly inspired by the ongoing effort to sequence the human genetic code—to build a genome. "**Connectomics**" (Hagmann, 2005) has been defined as the science concerned with assembling and analyzing connectome data sets.



“a comprehensive  
description of all the  
network of elements and  
connections forming the  
brain”.



# THE CONNECTOME

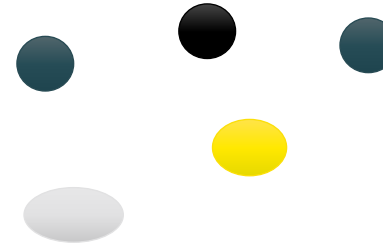
Connectome (Google search, 2005) = “Connect home?”

Connectome (Google search, 2020) = 1.500.000 results

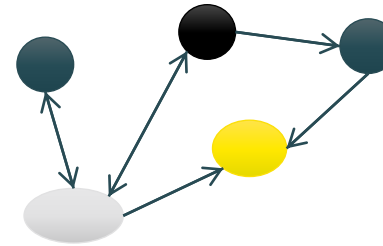


# THE CONNECTOME

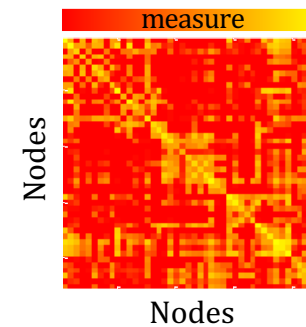
Step 1: define “nodes” (brain regions)



Step 2: define “edges” (brain connections)



Step 3: analysis of the connectivity matrix



# THE CONNECTOME

- From an anatomical perspective, the connectome is the ensemble of all brain neurons of axonal origin, termination, and trajectory relative to other structures



Structural/Anatomical connectome



Functional connectome

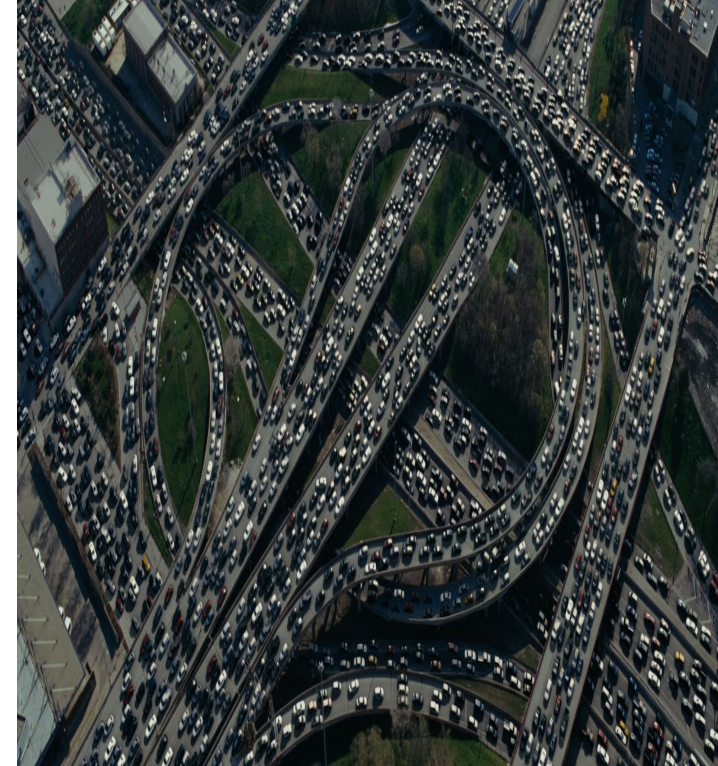


# THE CONNECTOME

- From a functional perspective, the connectome is the description of how neurons/areas interact with each other

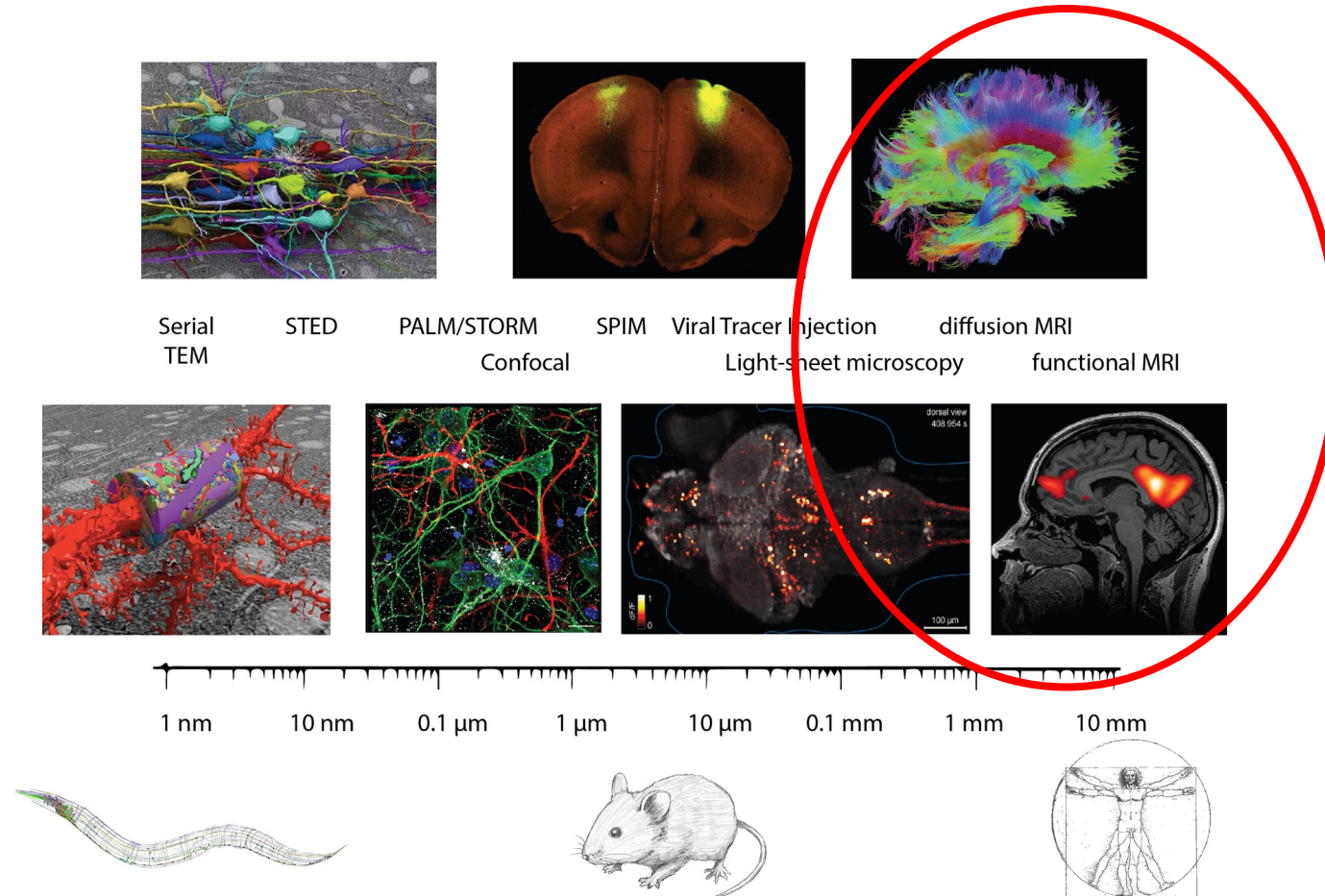


Structural/Anatomical connectome

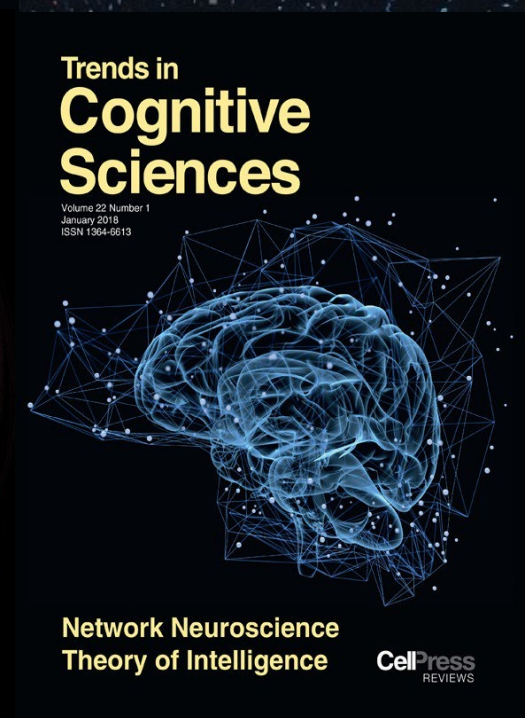
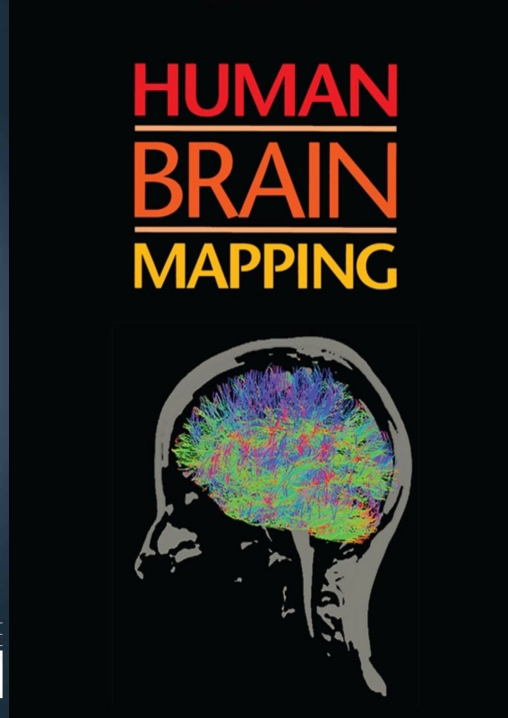
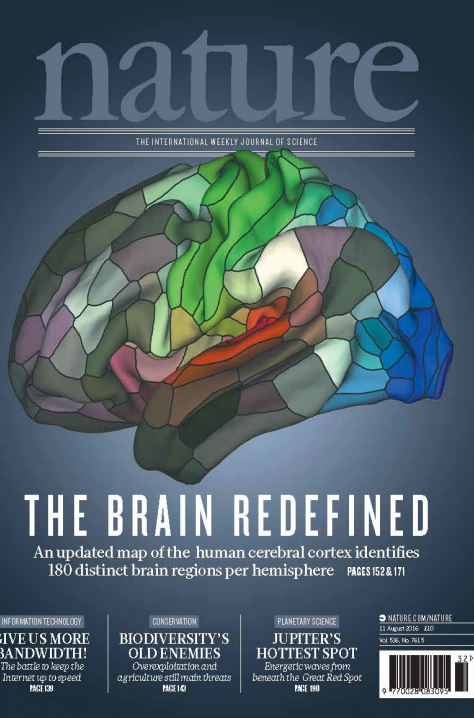
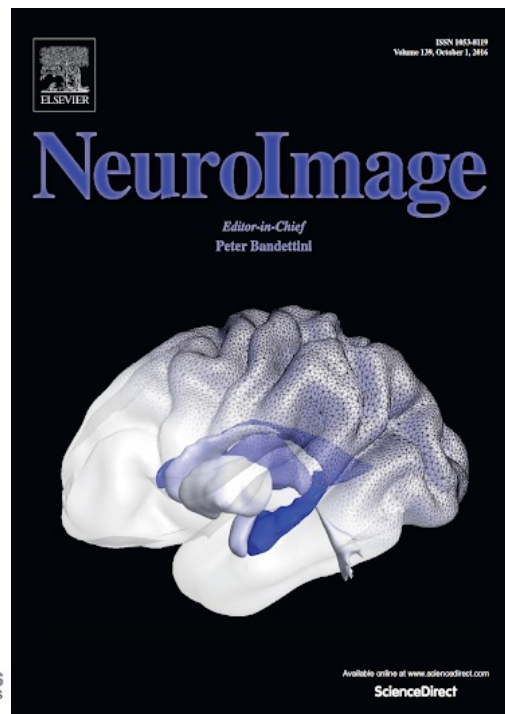
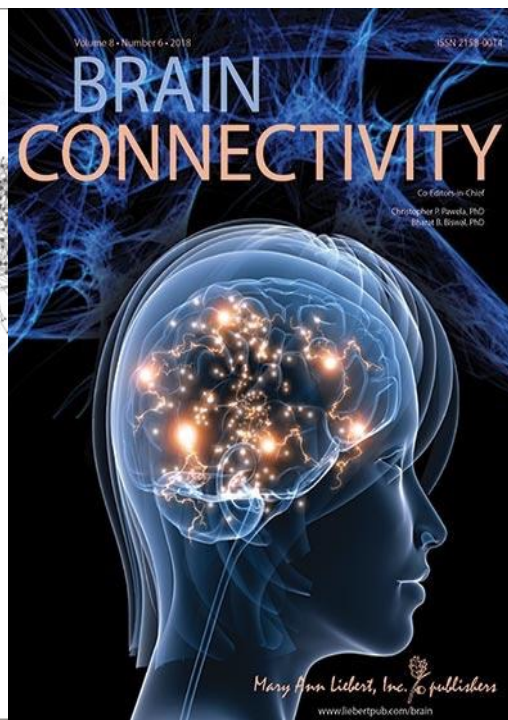
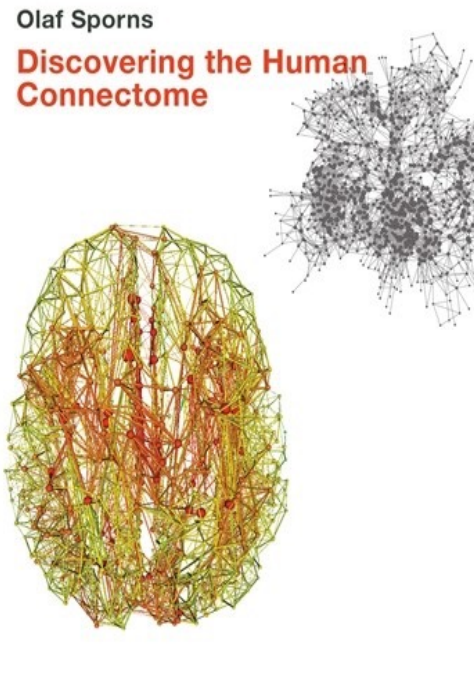


Functional connectome

# CONNECTOMICS AT DIFFERENT SCALES









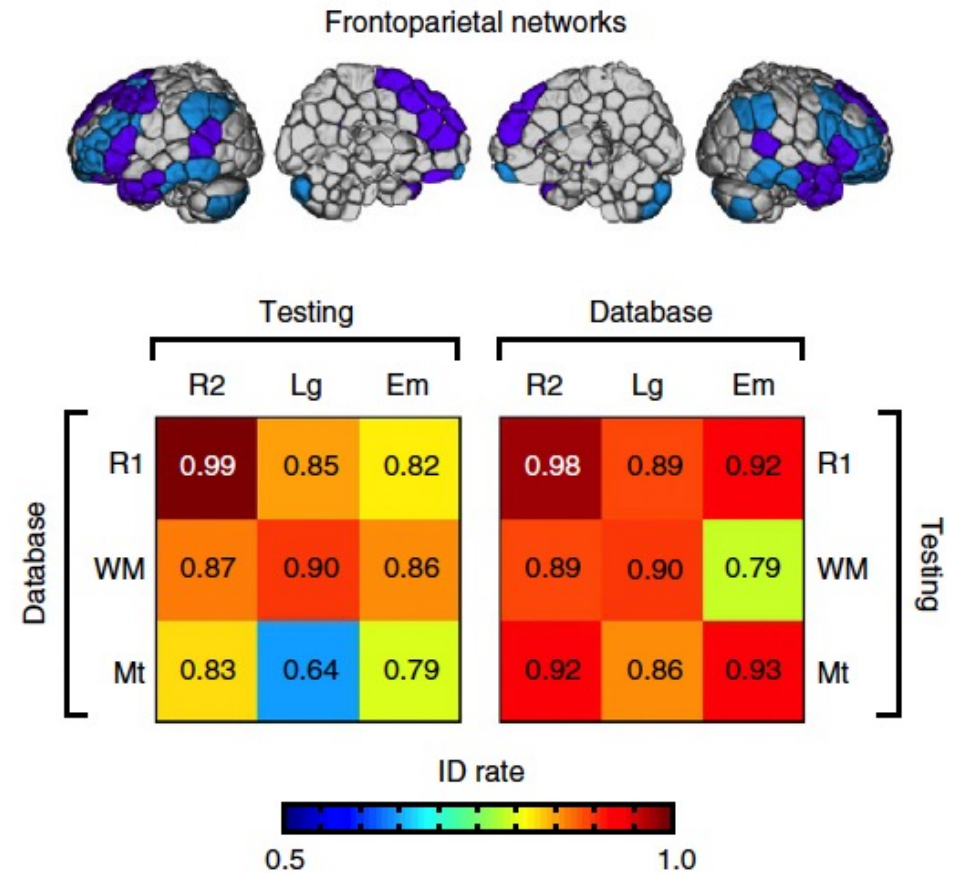
# CONNECTOME: ONE APPLICATION

## Resting-state fMRI

### Functional connectome fingerprinting: identifying individuals using patterns of brain connectivity

Emily S Finn<sup>1,7</sup>, Xilin Shen<sup>2,7</sup>, Dustin Scheinost<sup>2</sup>, Monica D Rosenberg<sup>3</sup>, Jessica Huang<sup>2</sup>, Marvin M Chun<sup>1,3,4</sup>, Xenophon Papademetris<sup>2,5</sup> & R Todd Constable<sup>1,2,6</sup>

nature  
neuroscience



# Human Connectome Project

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## The Human Connectome Project

Navigate the brain in a way that was never before possible; fly through major brain pathways, compare essential circuits, zoom into a region to explore the cells that comprise it, and the functions that depend on it.

The Human Connectome Project aims to provide an unparalleled compilation of neural data, an interface to graphically navigate this data and the opportunity to achieve never before realized conclusions about the living human brain.

[Download Data](#)

Laboratory of Neuro-Imaging

### News

[RSS News](#)

**National Geographic features the Human Connectome Project**

New research from members of our HCP team suggests that brain circuitry is organized more like Manhattan's street grid than London's chaotic tangle of random

[ABIDE I](#)[ABIDE II](#)[Manuscripts](#)[ABIDE I Preprocessed](#)

# Welcome to the Autism Brain Imaging Data Exchange!



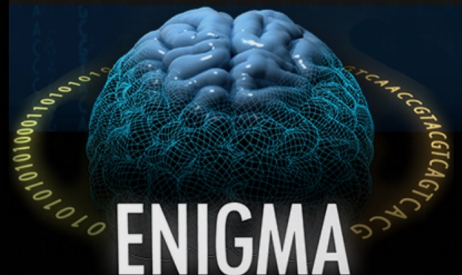
Autism Brain Imaging  
Data Exchange

## Introduction

Autism spectrum disorder (ASD) is characterized by qualitative impairment in social reciprocity, and by repetitive, restricted, and stereotyped behaviors/interests. Previously considered rare, ASD is now recognized to occur in more than 1% of children. Despite continuing research advances, their pace and clinical impact have not kept up with the urgency to identify ways of determining the diagnosis at earlier ages, selecting optimal treatments, and predicting outcomes. For the most part this is due to the complexity and heterogeneity of ASD. To face these challenges, large-scale samples are essential, but single laboratories cannot obtain sufficiently large datasets to reveal the brain mechanisms underlying ASD. In response, the Autism Brain Imaging Data Exchange (ABIDE) initiative has aggregated functional and structural brain imaging data collected from laboratories around the world to accelerate our understanding of the neural bases of autism. With the ultimate goal of facilitating discovery science and comparisons across samples, the ABIDE initiative now includes two large-scale collections: ABIDE I and ABIDE II. Each collection was created through the aggregation of datasets independently collected across more than 24 international brain imaging laboratories and are being made available to investigators throughout the world, consistent with open science principles, such as those at the core of the International Neuroimaging Data-sharing Initiative. For details about these initiatives visit the collection specific pages: [ABIDE I](#) and [ABIDE II](#).

Last Updated March 27, 2017.






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# ENIGMA

## ENHANCING NEURO IMAGING GENETICS THROUGH META ANALYSIS

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### What is ENIGMA?

**The ENIGMA Consortium brings together researchers in imaging genomics to understand brain structure, function, and disease, based on brain imaging and genetic data. We welcome brain researchers, imagers, geneticists, methods developers, and others interested in cracking the neuro-genetic code!**

**The ENIGMA Consortium has several goals:**

- ① To create a network of like-minded individuals, interested in pushing forward the field of imaging genetics.
- ② To ensure promising findings are replicated via member collaborations.
- ③ To share ideas, algorithms, data, and information on research studies and methods.
- ④ To facilitate training, including workshops and conferences on key methods and emerging directions in imaging genetics.

There are 50 active ENIGMA working groups!! Full details of each ENIGMA project can be accessed by clicking on the links provided. If you are interested in joining and contributing to a current group, or would like to propose a group you do not see listed, please contact us at [enigma.usc.edu](mailto:enigma.usc.edu)

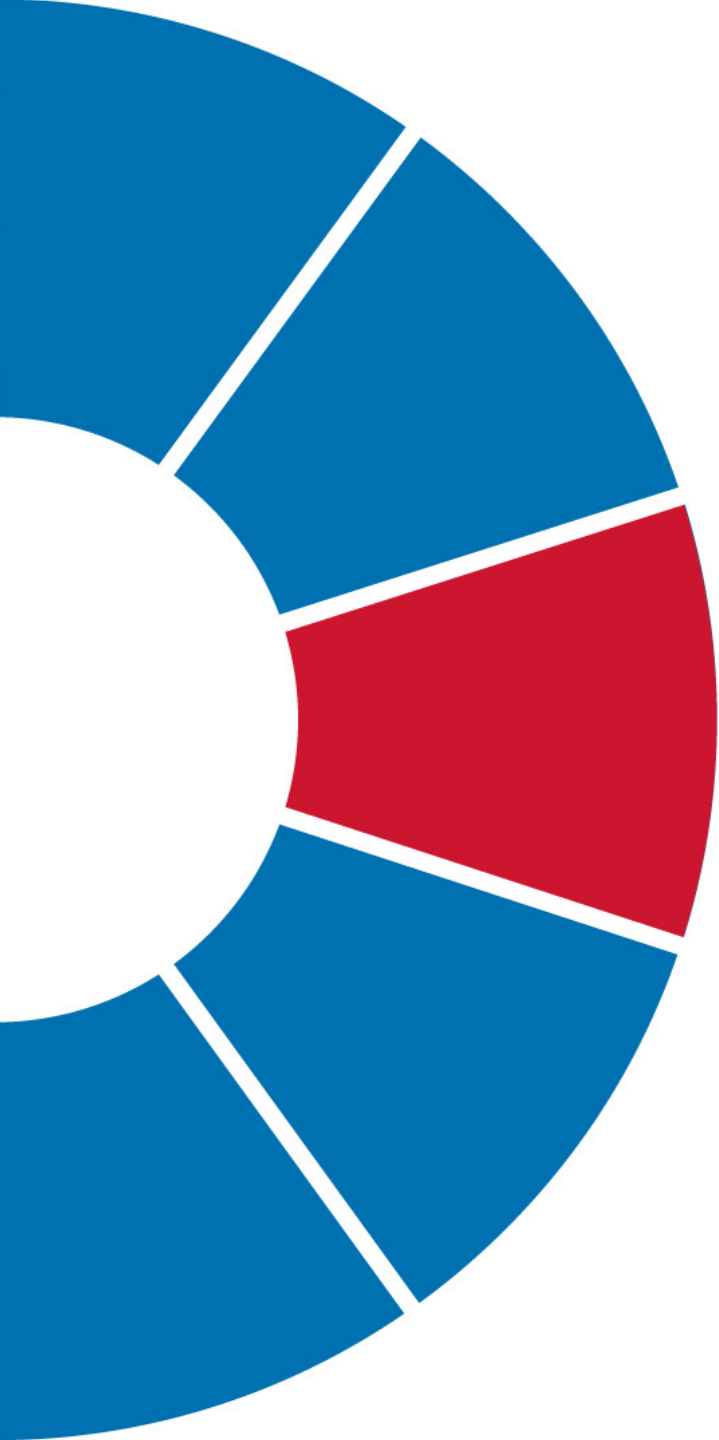




THANK YOU FOR YOUR ATTENTION

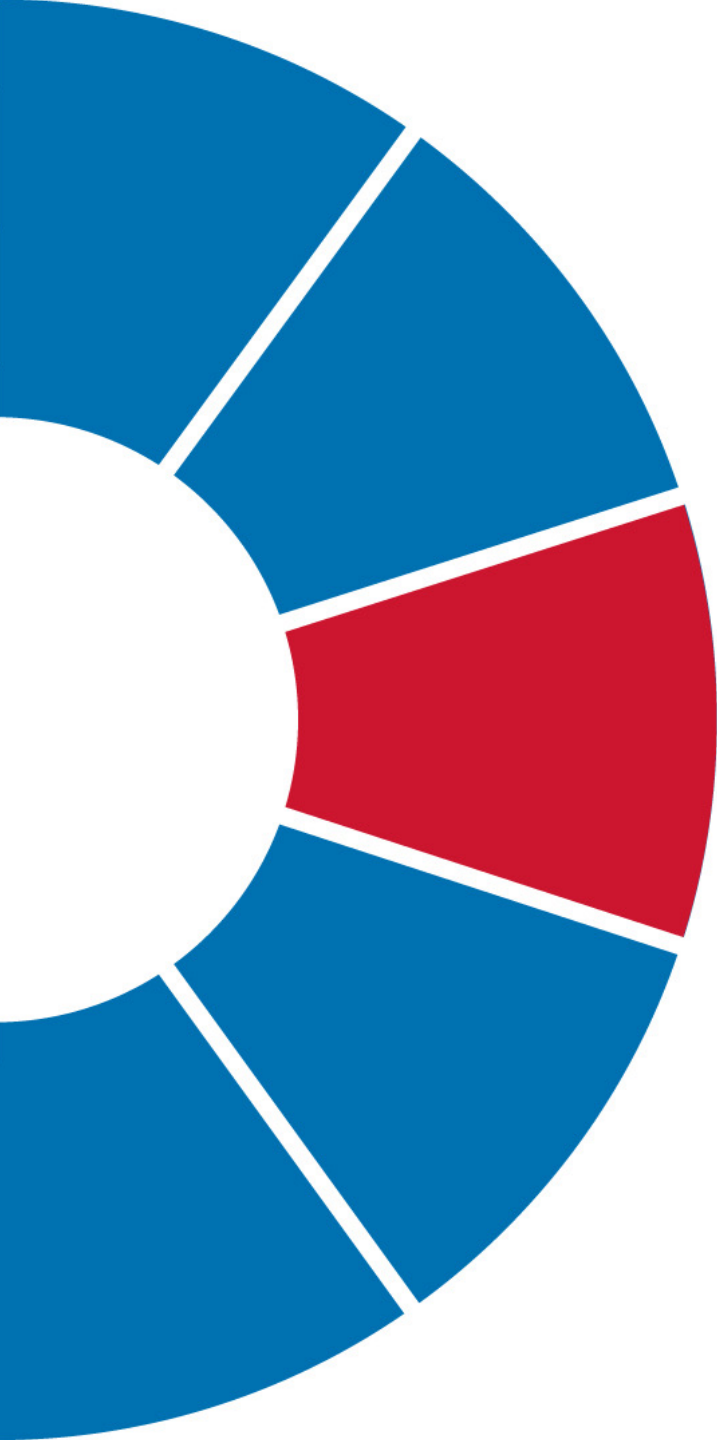


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FOR ANY QUESTIONS YOU MAY HAVE,  
PLEASE WRITE AT:

[VALERIO.ZERBI@EPFL.CH](mailto:VALERIO.ZERBI@EPFL.CH)



## MR COIL WORKSHOP – TOMORROW, WEDNESDAY 26<sup>TH</sup>

### **Group1 (Morning) 8.15am-12am:**

Francesca Barcellini  
Gercek Berk  
Jenifer Miehlbradt  
Guibert Fabrice Jean  
Brayan Alves  
Huang Zhiwei

### **Group2 (Afternoon) 13.15-17:**

Liu Chang  
Jan Luxemburg  
Nikolaos Molochidis  
Mustafa Arslan  
Mark Stephan Widmaier