BOLD, etc

What are we measuring, really?

Tomas Knapen, Brain Imaging 2022

Discovery of fMRI

How does a new field of science start?

- Scientific measurements are often serendipitously discovered, and quite contrived.
- For instance, we can *measure precipitation using cell phone towers*
- If we know the physics behind phenomena, we can use them as measurements of other phenomena of interest.

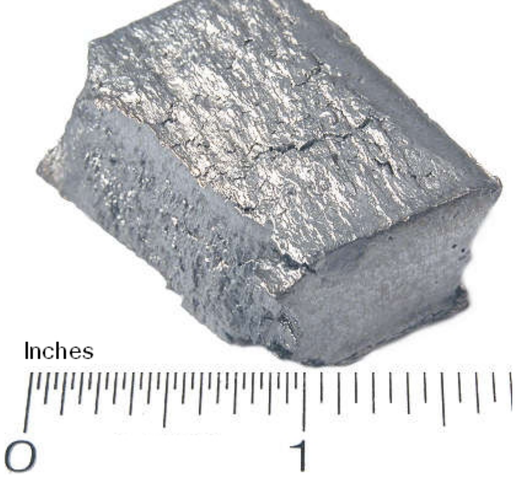
Functional Mapping of the Human Visual Cortex by Magnetic Resonance Imaging

J. W. Belliveau,* D. N. Kennedy, R. C. McKinstry, B. R. Buchbinder, R. M. Weisskoff, M. S. Cohen, J. M. Vevea, T. J. Brady, B. R. Rosen

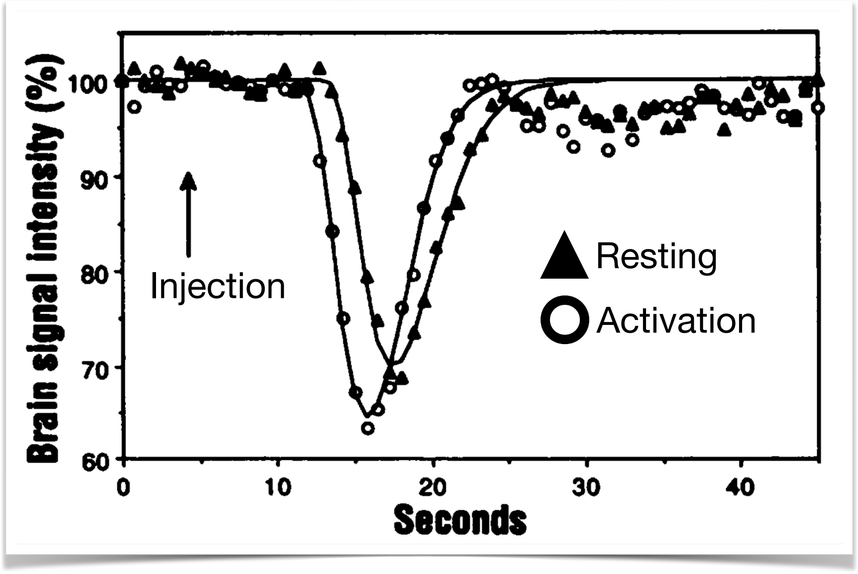
Science, 1991

Contrast Agent fMRI

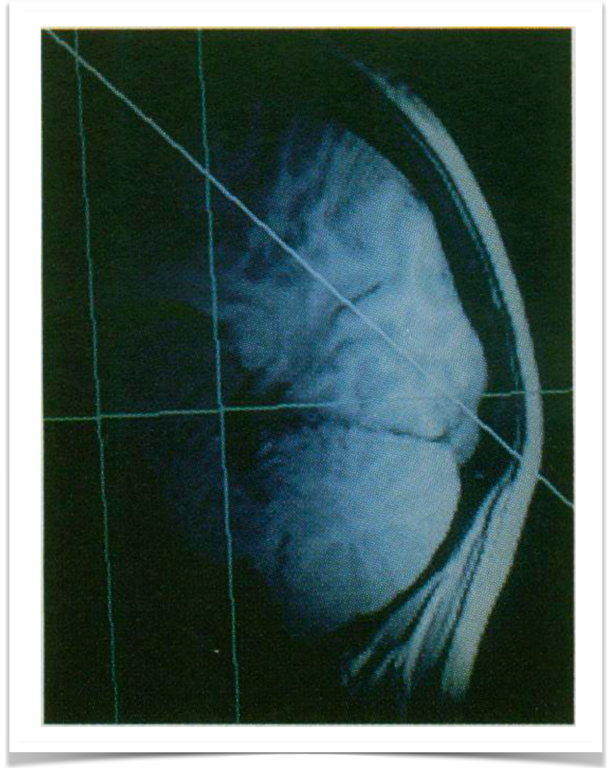
Just like PET: invasive. Just not radioactive :-)



- Gadolinium is the most paramagnetic element at body temperature
- Inject it, and it will permeate the bloodstream and give you a way to MR-image how much blood volume is present in a voxel:
  *Cerebral **Blood Volume** **(CBV)** measurements*
- Then, the difference between ‘resting’ and ‘activation’ is a sign of activation-induced changes in perfusion

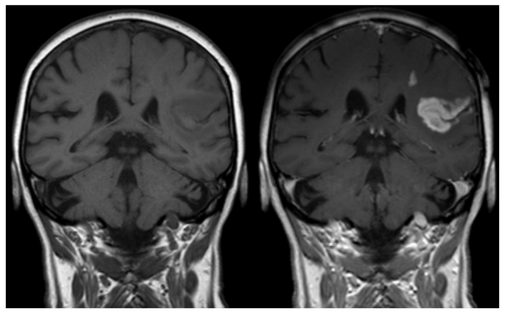


Local coil on Occipital Lobe



Downsides

Invasive Measurements are Limited



- Great for angiography and oncological diagnostics: ***very sensitive.***
- MION (manganese-iron contrast agent) is used in ***monkey fMRI***.
- Can’t keep injecting people over and over for cognitive neuroscience experiments!

Proc. Natl. Acad. Sci. USA
Vol. 87, pp. 9868–9872, December 1990
Biophysics

Brain magnetic resonance imaging with contrast dependent on blood oxygenation

(cerebral blood flow/brain metabolism/oxygenation)

S. OGAWA, T. M. LEE, A. R. KAY, AND D. W. TANK

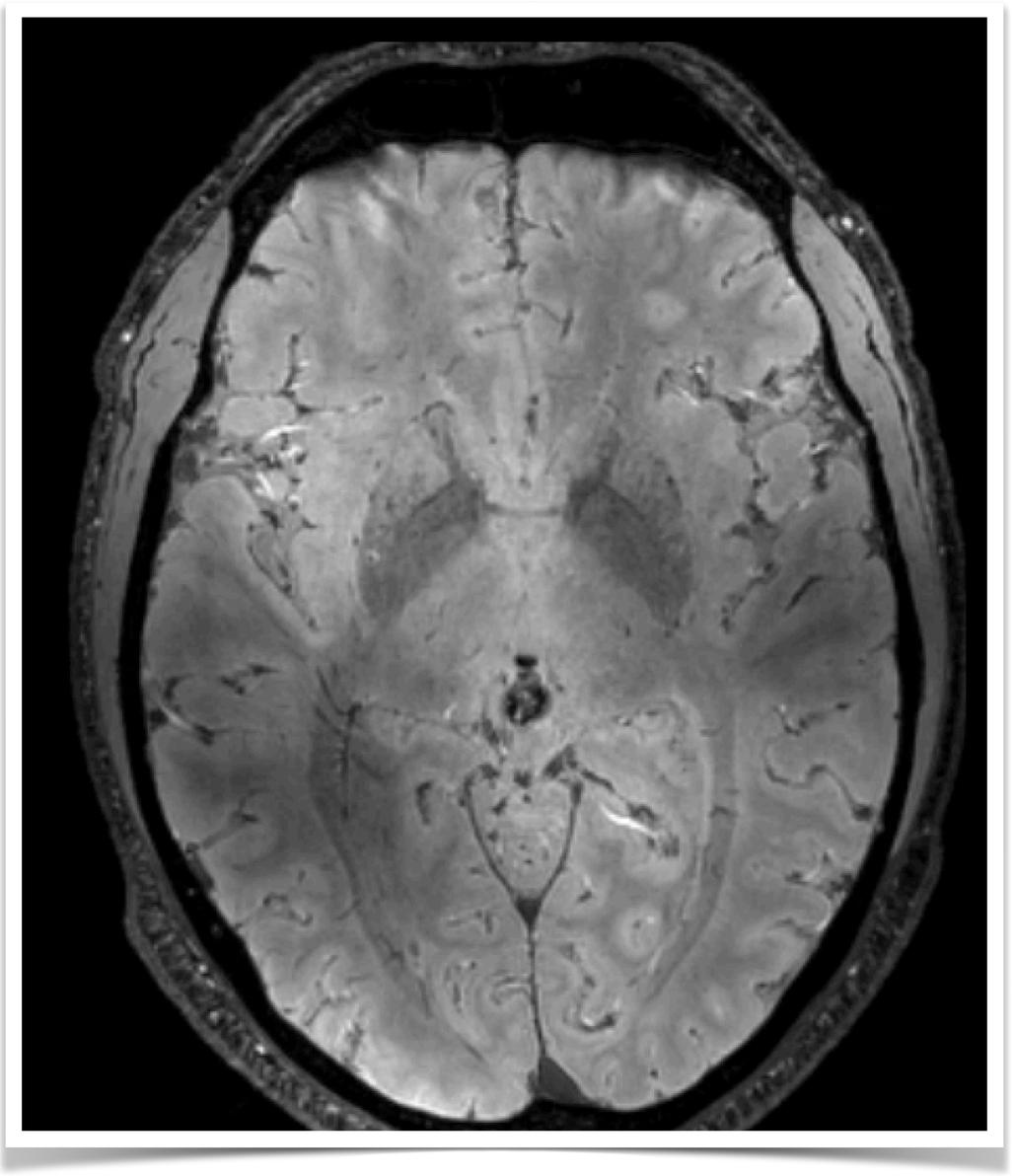
Biophysics Research Department, AT&T Bell Laboratories, Murray Hill, NJ 07974

Communicated by Frank H. Stillinger, September 24, 1990 (received for review August 1, 1990)

The solution:

Endogenous contrast agent

- Blood oxygenation turns out to influence its magnetic properties!
- Oxygenated haemoglobin is diamagnetic, deoxygenated it's paramagnetic.
- The T_2^* MR contrast is sensitive to this!
- T_2^* values *decrease as result of deoxygenation*



BOLD

Blood Oxygenation Level Dependent

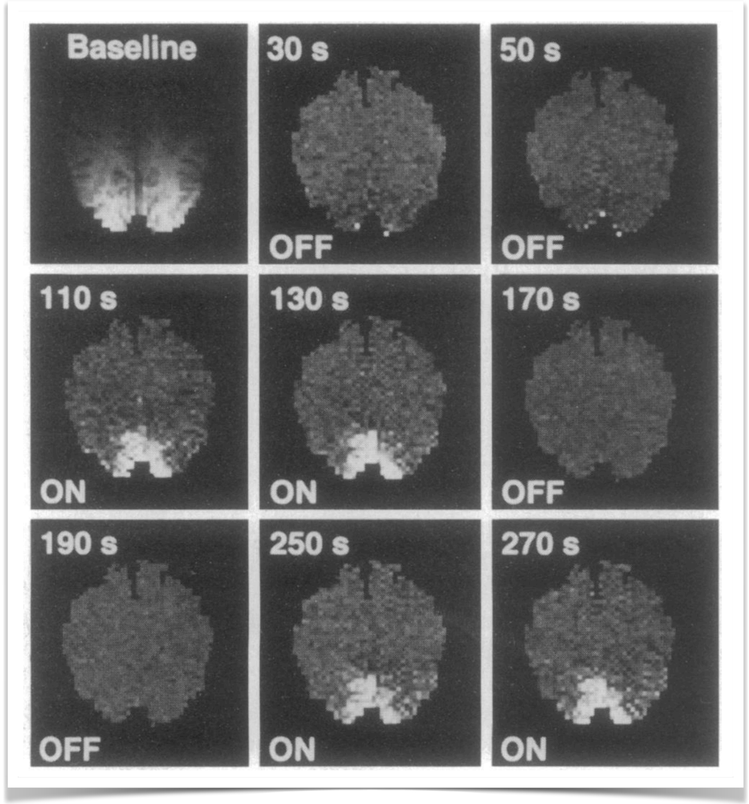
Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation

KENNETH K. KWONG†, JOHN W. BELLIVEAU†, DAVID A. CHESLER†, INNA E. GOLDBERG†, ROBERT M. WEISSKOFF†, BRIGITTE P. PONCELET†, DAVID N. KENNEDY†, BERNICE E. HOPPEL†, MARK S. COHEN†, ROBERT TURNER‡, HONG-MING CHENG§, THOMAS J. BRADY†, AND BRUCE R. ROSEN†

†MGH–NMR Center, Department of Radiology, Massachusetts General Hospital and Harvard Medical School, Charlestown, MA 02129; ‡National Institutes of Health, Laboratory of Cardiac Energetics, National Heart, Lung, and Blood Institute, Bethesda, MD 20892; and §Howe Laboratory of Ophthalmology, Massachusetts Eye and Ear Infirmary and Harvard Medical School, Boston, MA 02114

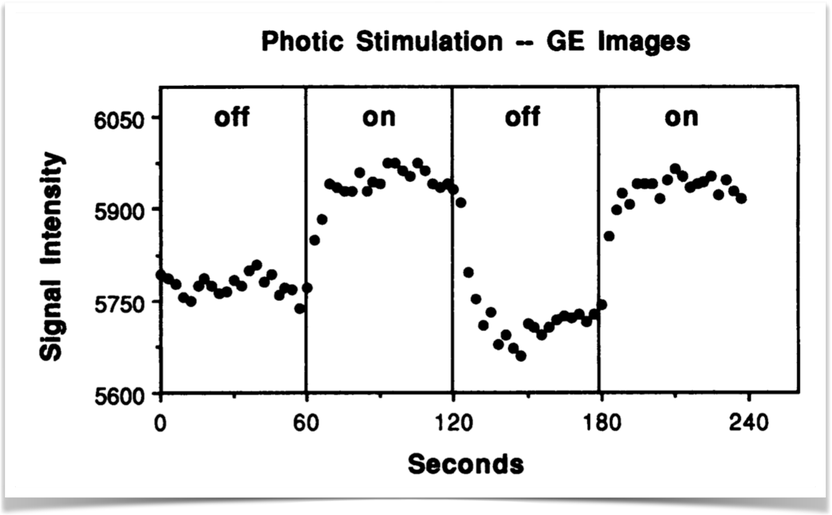
Communicated by David H. Hubel, March 26, 1992

PNAS, 1992



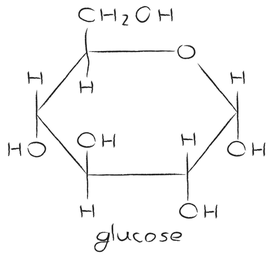
- We can non-invasively measure human brain activations in vivo!
- *Signal intensity should go down, right?*

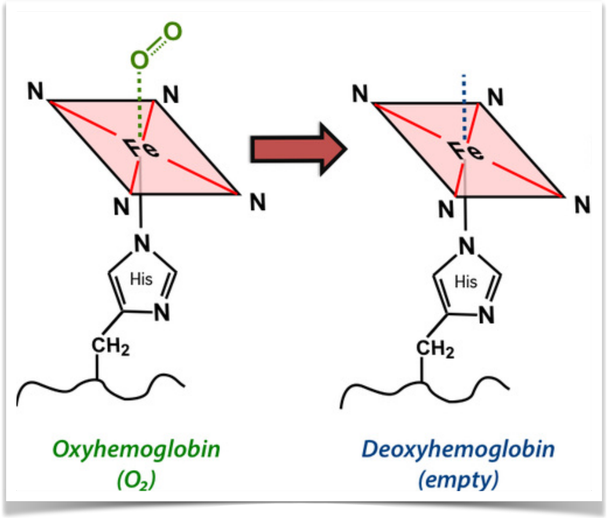
Wrong



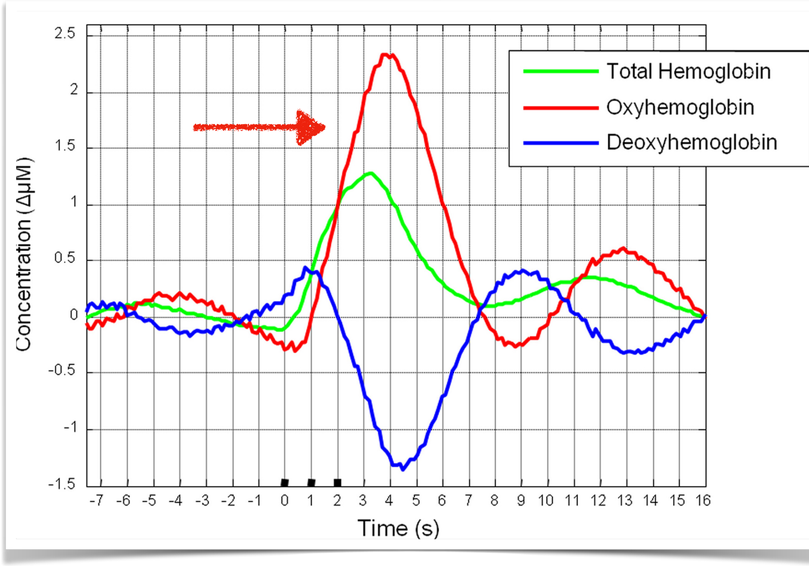
Haemodynamics

Why this positive BOLD response?





- Neural activations cause changes in
  - Cerebral Metabolic Rate of Glucose (CMRGlu) ***(PET)***
  - Cerebral Metabolic Rate of Oxygen ($CMRO_2$) ***(PET)***
  - Cerebral Blood Flow (CBF) ***(MRI - ASL)***
  - Cerebral Blood Volume (CBV) ***(MRI - contrast agent)***
  - And: Haemoglobin Oxygenation
- So, our measurement is a complex, compound response.



- ***But why a positive response?***
  - The vasculature 'overreacts' and oversupplies new, oxygenated blood to tissue

What else?

How does the BOLD response relate to other measures?

Like, electrophysiology?

What are we measuring?

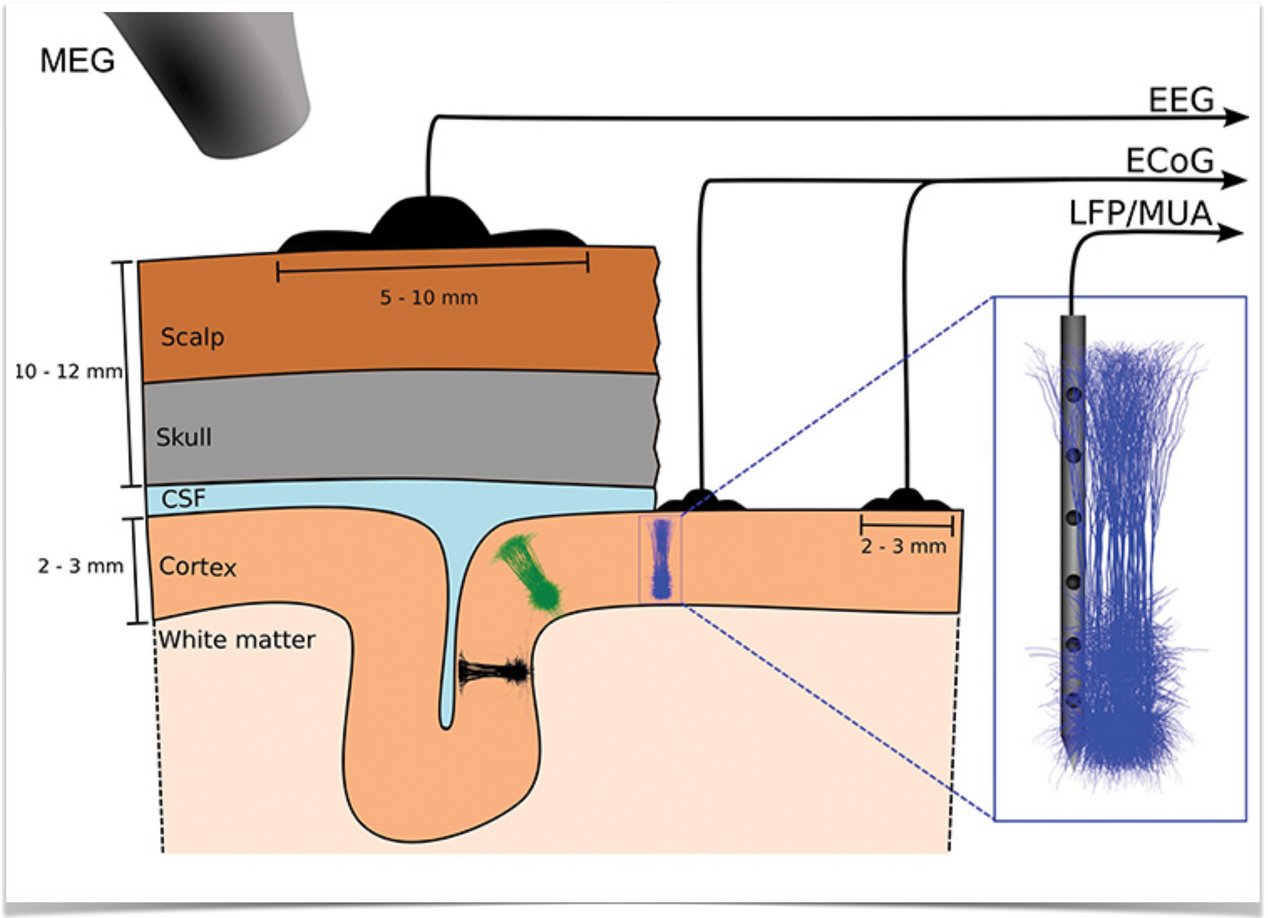
BOLD vs electrophysiology

- Neural spiking is the *output* of a given area. It is often measured as multi-unit activity (***MUA,*** *or electrical signals > 250 Hz*).

- Local field potential (***LFP***) is thought to reflect the input onto an area more than its own activity

- Low, Theta/Alpha (4-12 Hz) more long-range, Beta/Gamma (20-100 Hz) more local

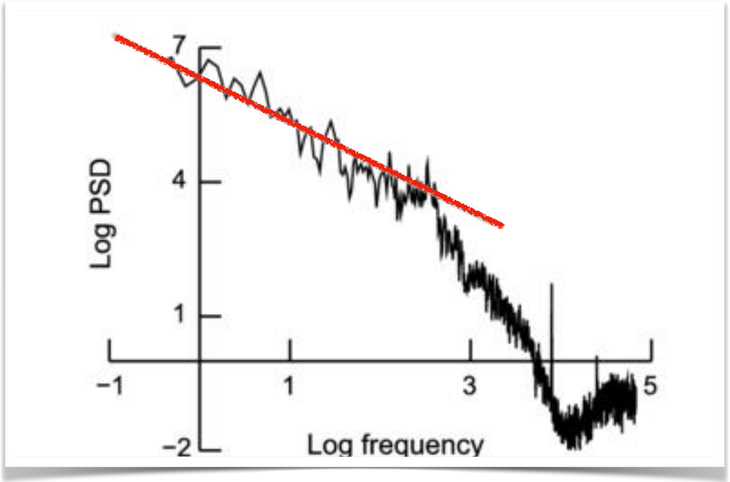
- Does ***BOLD*** correlate with ***MUA*** or with ***LFP?***
  and ***if LFP, which bands?***

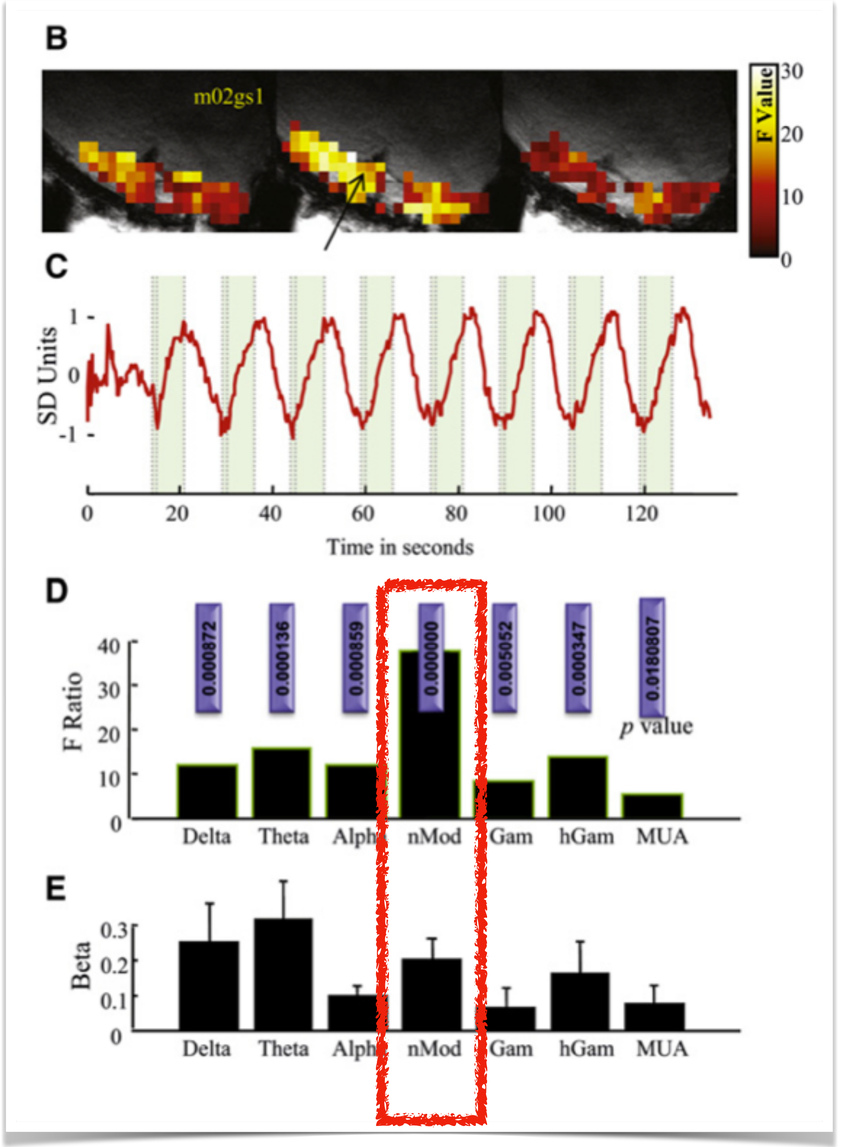


What are we measuring?

BOLD vs electrophysiology

- Simultaneous electrophysiology and BOLD show that all bands correlate with BOLD
- But the strongest correlation with BOLD is in the γ range (nMod, right)
- Statistics correct for 1/f power distribution
- *BOLD reflects more local processing*



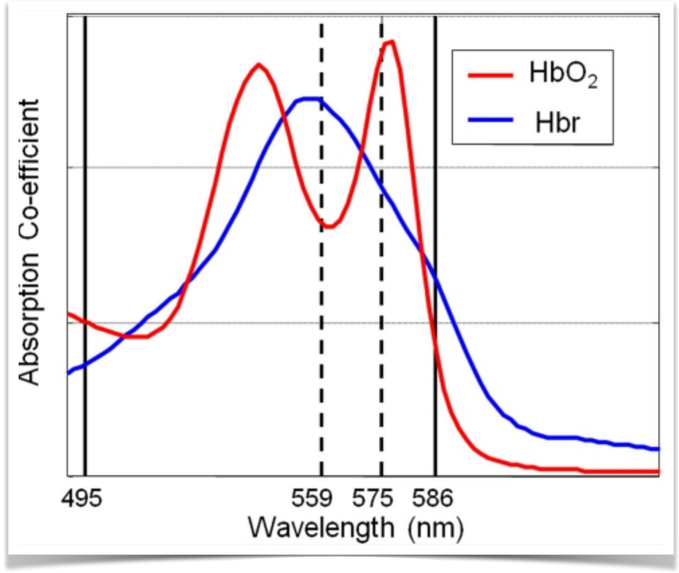


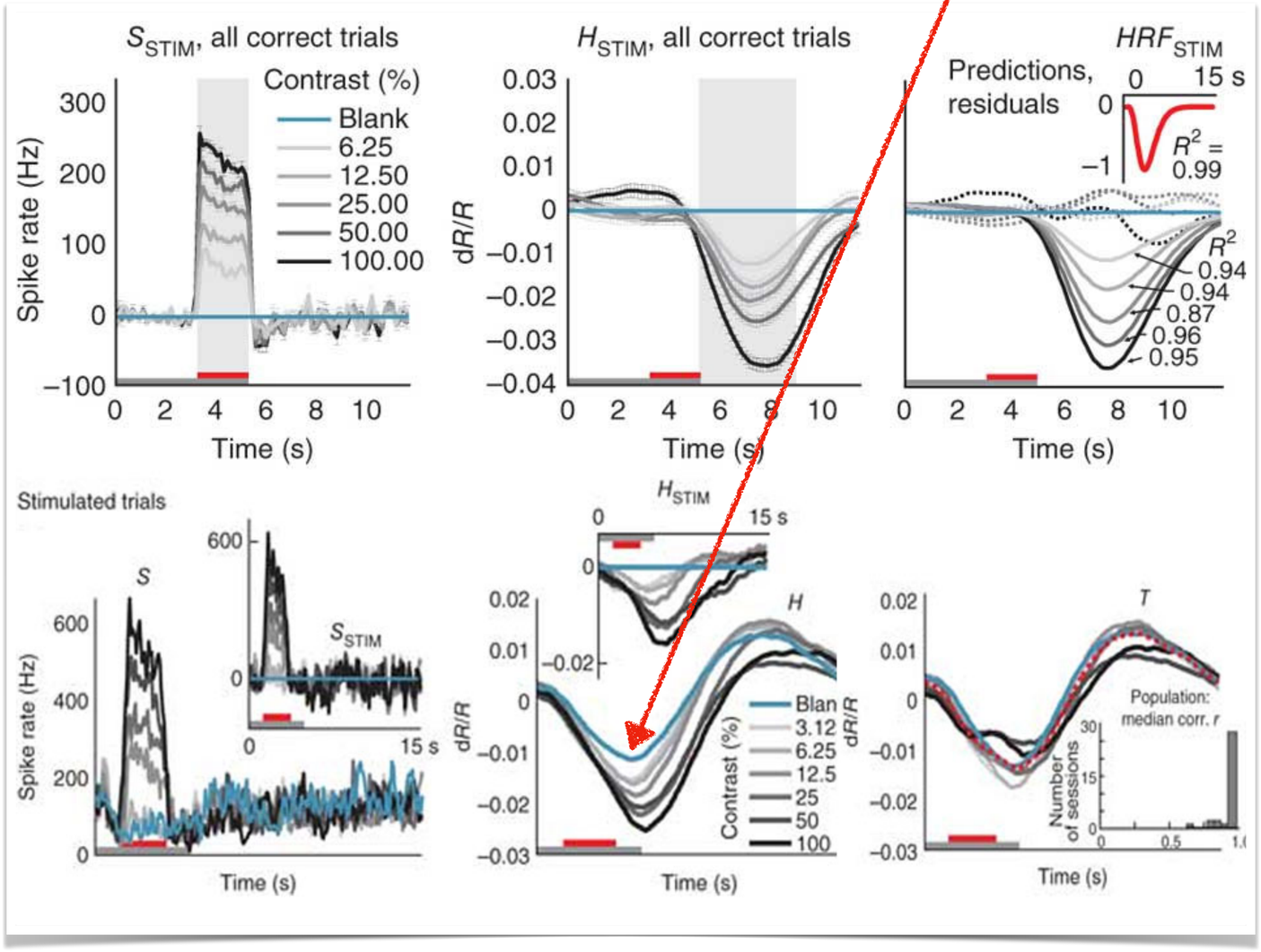
What are we measuring?

BOLD vs electrophysiology - *again!*

What's this doing here!

- This isn't the final story.
- Recent findings show that transient BOLD responses can occur without neural firing!





OK, so what has happened since 2015?

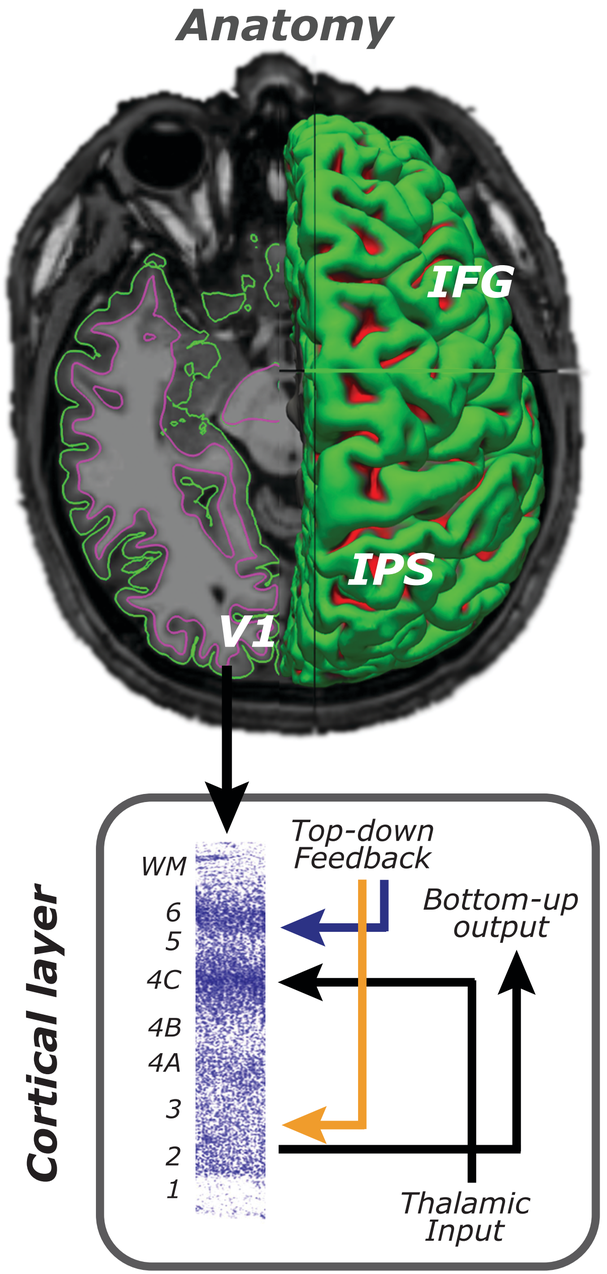
What are the developments since the YouTube channel aired?

Progress report

Measurement settings

Scanner can do many things

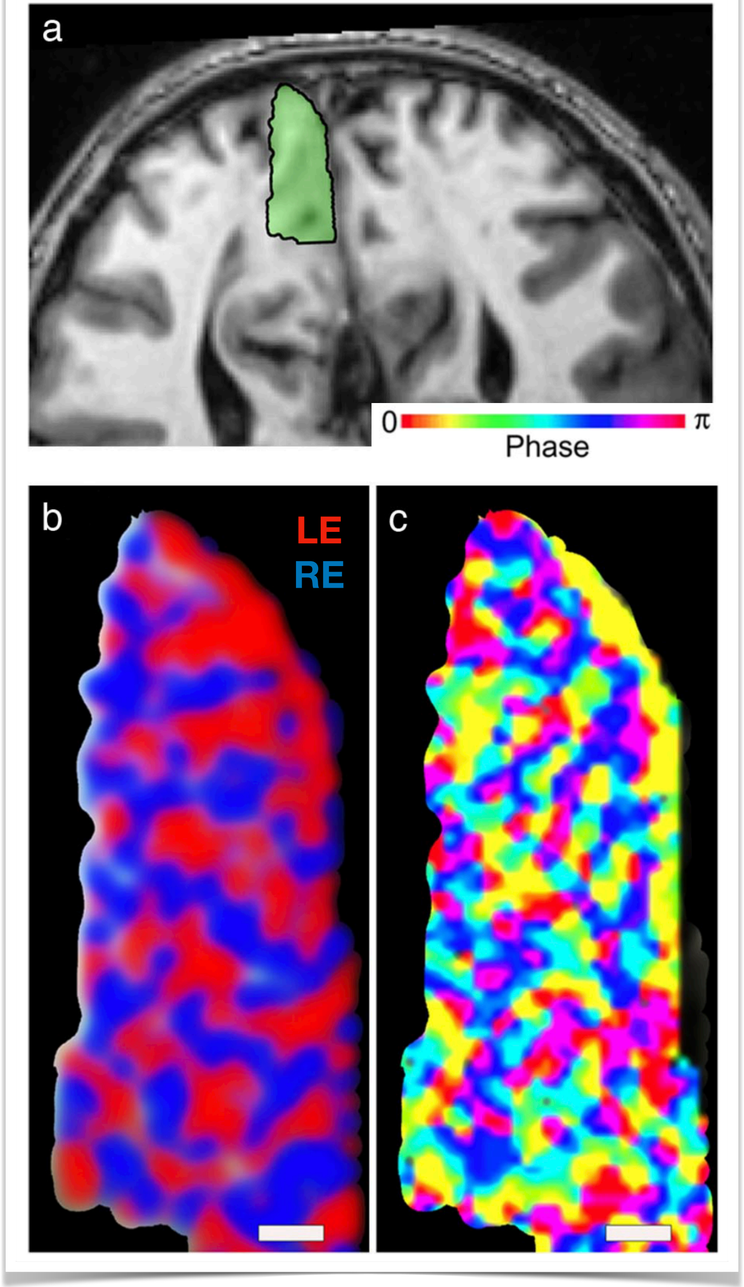
- With higher field strengths and improved sequences, we can approach the biological level in 2 ways:
  - ***Scan faster*** (faster connectivity, cardiac denoising)
  - ***Scan smaller*** (voxels <1mm have ‘laminar’ resolution)
- *Different depths have different computational roles*
- Laminar fMRI is a new field, but:
  Details matter!



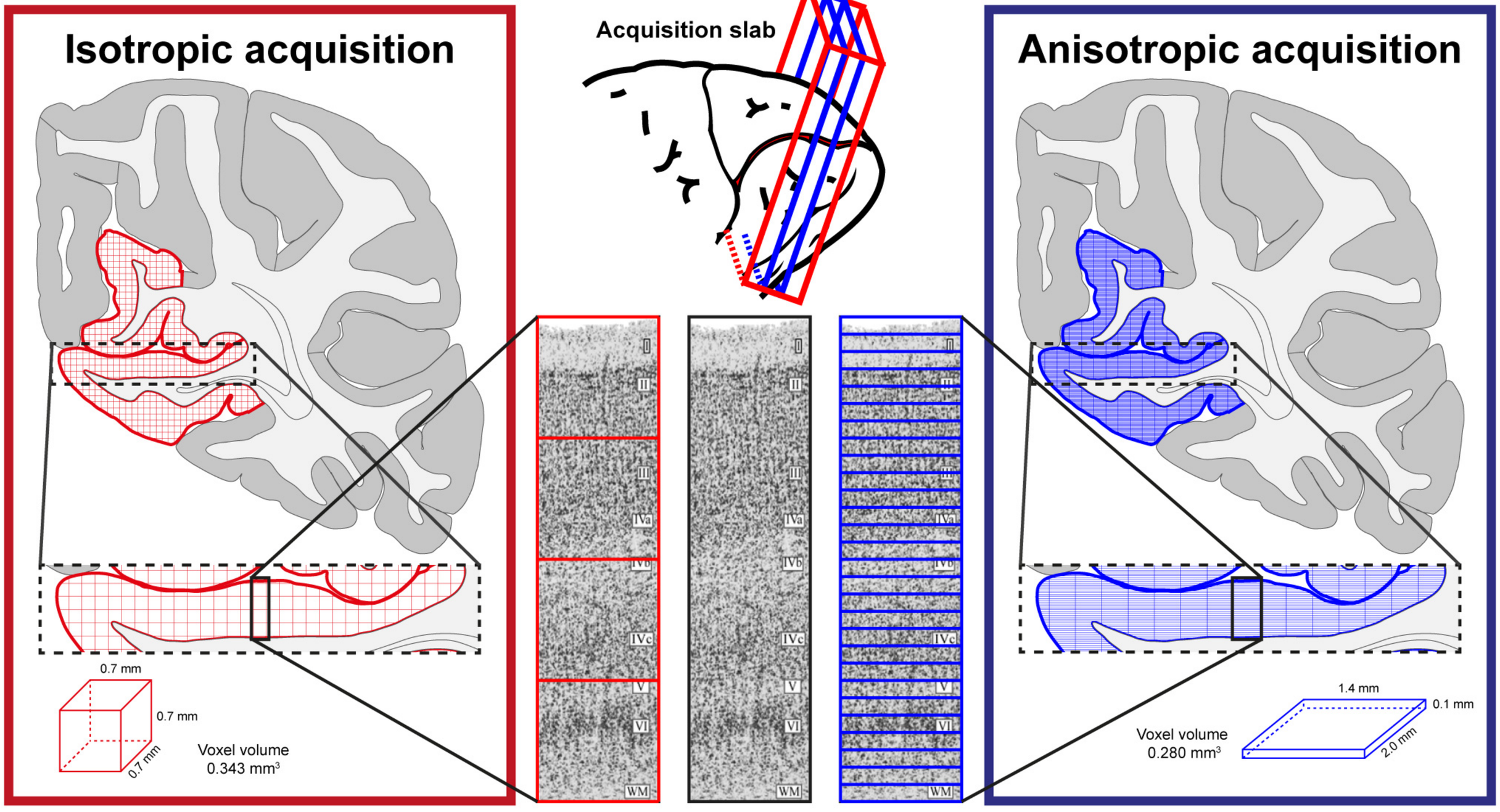
The promise of High-Resolution

“Mesoscale” imaging

- Image both the laminar and columnar organization of the living human brain
- V1 Columns:
  - Ocular Dominance Columns, and
  - Orientation Pinwheel Columns
- This is hard. We need to push the scanner, focus on a small part of the brain, and know our MR physics & analysis stuff.



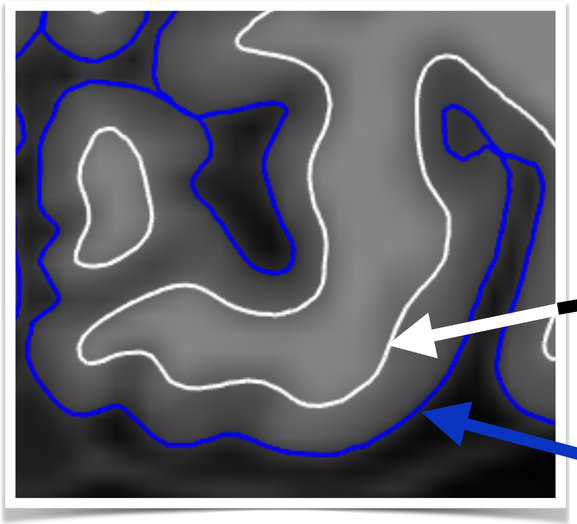
Yacoub et al, PNAS 2008

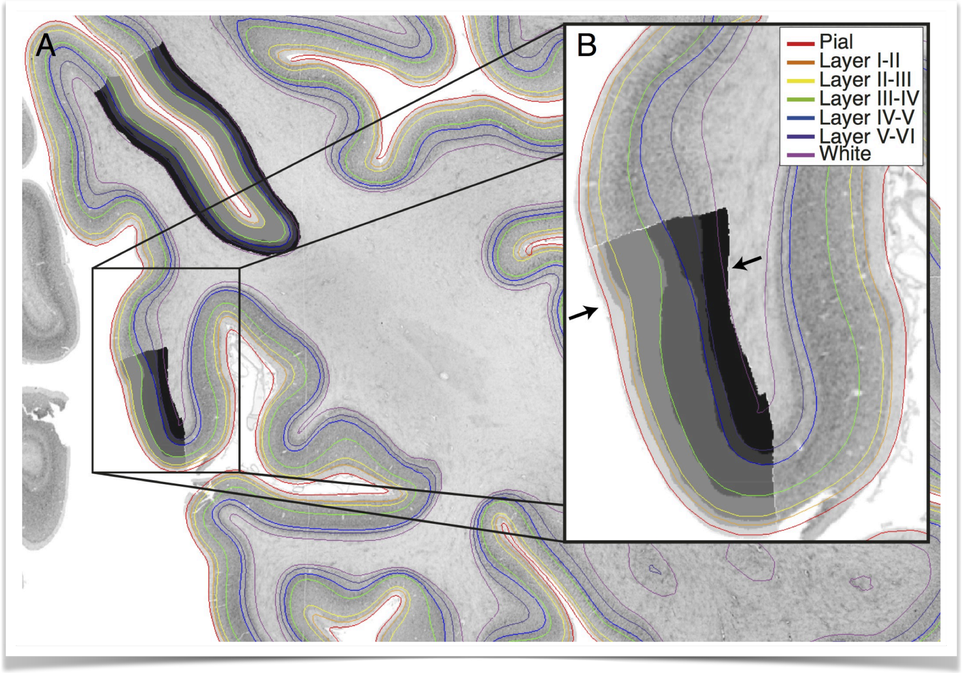

Isotropic acquisition
Acquisition slab
Anisotropic acquisition
I
II
III
IVa
IVb
IVc
V
VI
WM
0.7 mm
0.7 mm
0.7 mm
Voxel volume
0.343 mm3
1.4 mm
0.1 mm
2.0 mm
Voxel volume
0.280 mm3

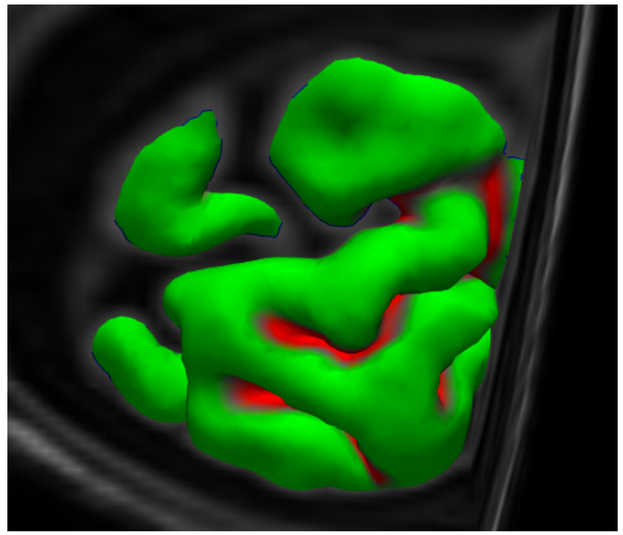
The pitfalls of High-Resolution

Analysis matters a lot!

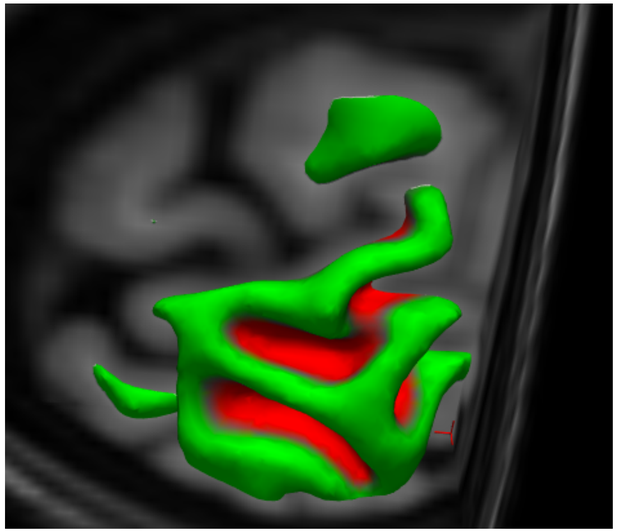
- Cannot use standard analysis routines, because half a mm error is disastrous!
- Hardly room for error, both in anatomical segmentation, and for functional alignment







Pial surface



White-Gray matter boundary

Different Sequences

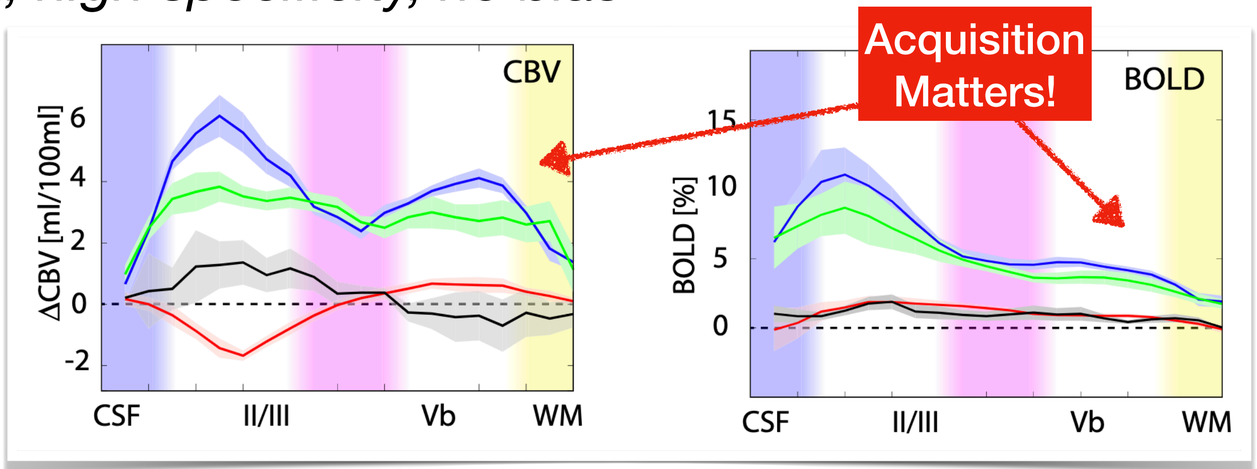
Scanner can do many things - again!

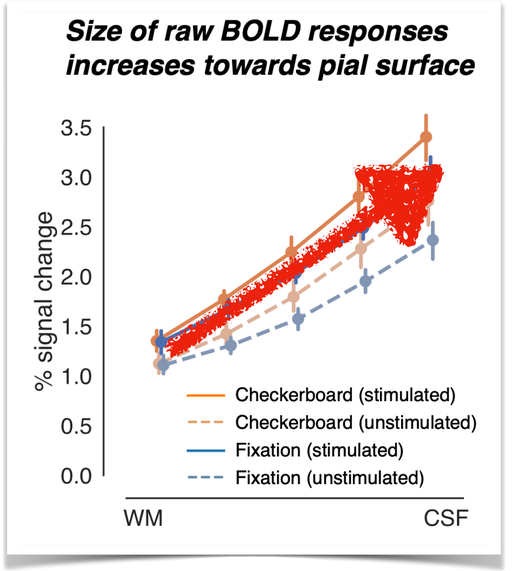
- Same scanner, different acquisitions:
  scan different aspects of blood response

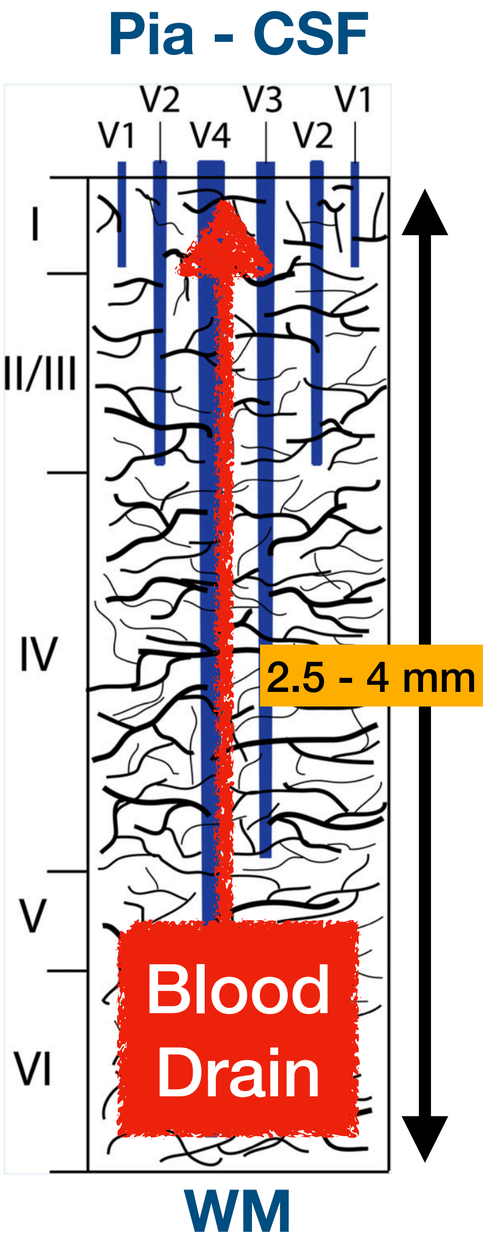
- Gradient Echo (GRE) **BOLD**:
  High SNR, low specificity, bias to larger draining veins

- Spin Echo (SE) **BOLD**:
  Lower SNR, higher specificity, bias to smaller draining veins

- Vascular-Space Occupancy (VASO) **BOLD & CBV**:
  Lower SNR, high specificity, no bias







BOLD is blood:
Vascular structure

Demo

Combined laminar-columnar work from the lab

http://aeneas.labs.vu.nl/odc/sub-07/ses-odc1/