Curious Contrasts other than BOLD

Peter A. Bandettini, Ph.D.

Section on Functional Imaging Methods

Laboratory of Brain and Cognition

http://fim.nimh.nih.gov

&

Functional MRI Facility

http://fmrif.nimh.nih.gov

Contrasts other than BOLD

- Perfusion (IVIM)
- Volume (gadolinium)
- Volume (fuyrmoxotol)
- Perfusion (ASL)
- $\Delta CMRO_2$
- ΔVolume (VASO)
- Neuronal Currents
- Proton density? (SEEP)
- Diffusion coefficient
- Temperature
- Elastography
- Metabolic Contrasts

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Intravoxel Incoherent Motion (IVIM)

Denis Le Bihan, MD • Eric Breton, MS • Denis Lallemand, MD
• Philippe Grenier, MD • Emmanuel Cabanis, MD
• Maurice Laval-Jeantet, MD

Radiology, 1986

MR Imaging of Intravoxel Incoherent Motions: Application to Diffusion and Perfusion in Neurologic Disorders[1]

NeuroImage 187 (2019) 56–67

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage

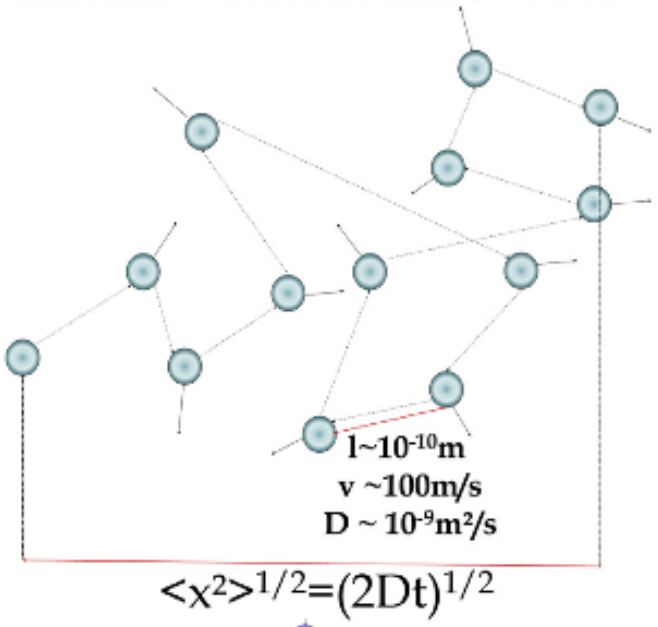
What can we see with IVIM MRI?

Denis Le Bihan

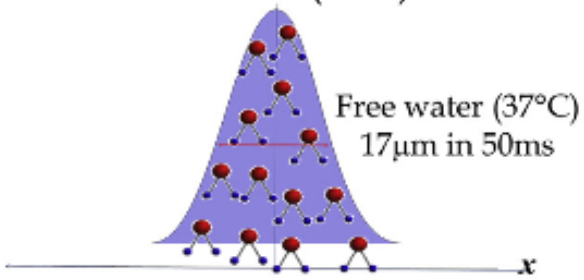
NeuroSpin, Frédéric Joliot Institute, Bât 145, CEA-Saclay Center, Gif-sur-Yvette, 91191 France

Intravoxel Incoherent Motion (IVIM)

***Individual* water molecular diffusion**

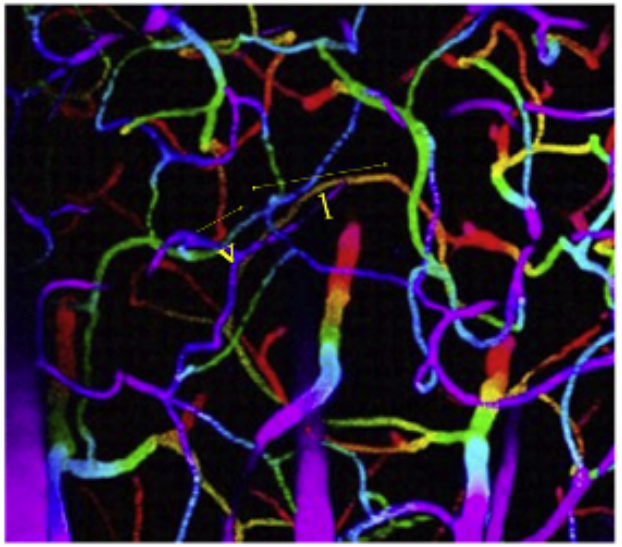


$\langle x^2 \rangle^{1/2} = (2Dt)^{1/2}$



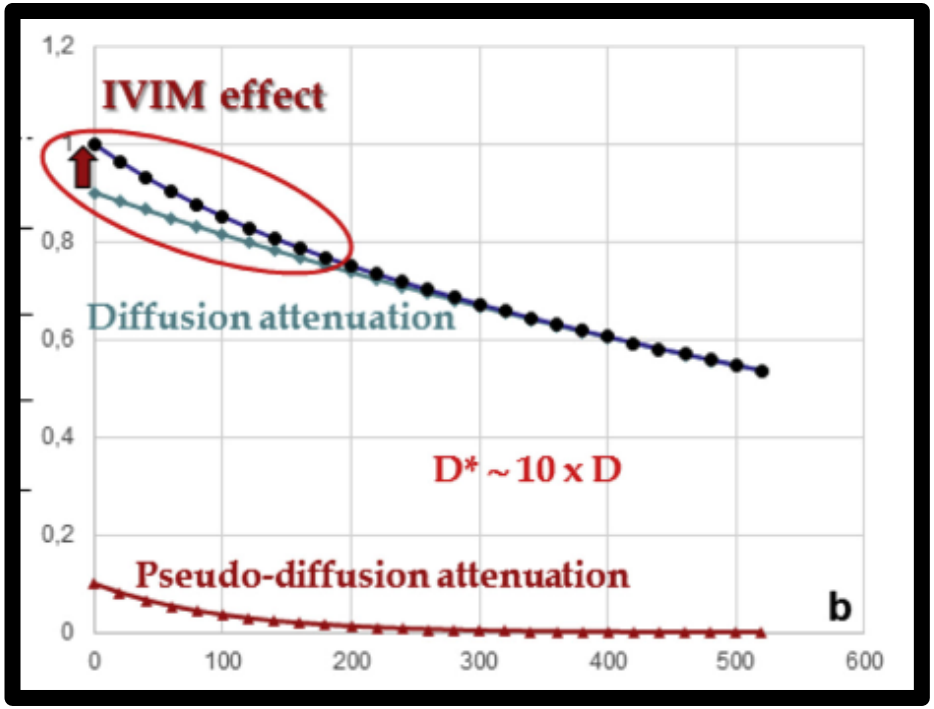
Molecular diffusion

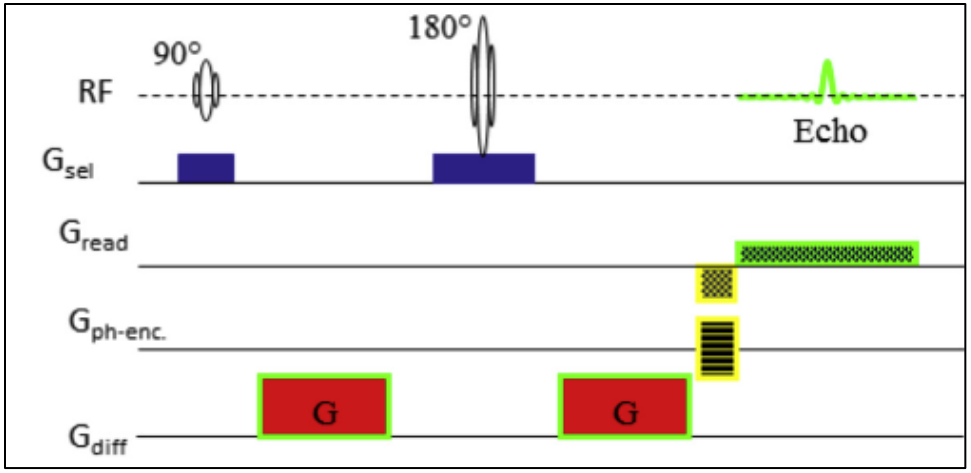
Blood pool
***collective* water flow**



$l \sim 10^{-4}$m
v ~1mm/s
$D^* \sim 10^{-8}$m²/s

Blood microcirculation (pseudo-diffusion)


1,2
IVIM effect
0,8
Diffusion attenuation
0,6
0,4
D* ~ 10 x D
0,2
Pseudo-diffusion attenuation
b
0
0
100
200
300
400
500
600


90°
180°
RF
Echo
G_{sel}
G_{read}
$G_{ph\text{-}enc.}$
G
G
G_{diff}

- **IVIM didn't work well in late 80's and early 90's because of CSF pulsation dominating signal as well as intrinsically low sensitivity.**

- **It was a nice idea that was partially implemented for removing intravascular signal to increase BOLD specificity.**

- **Still has potential clinical applications today…just not brain activation.**

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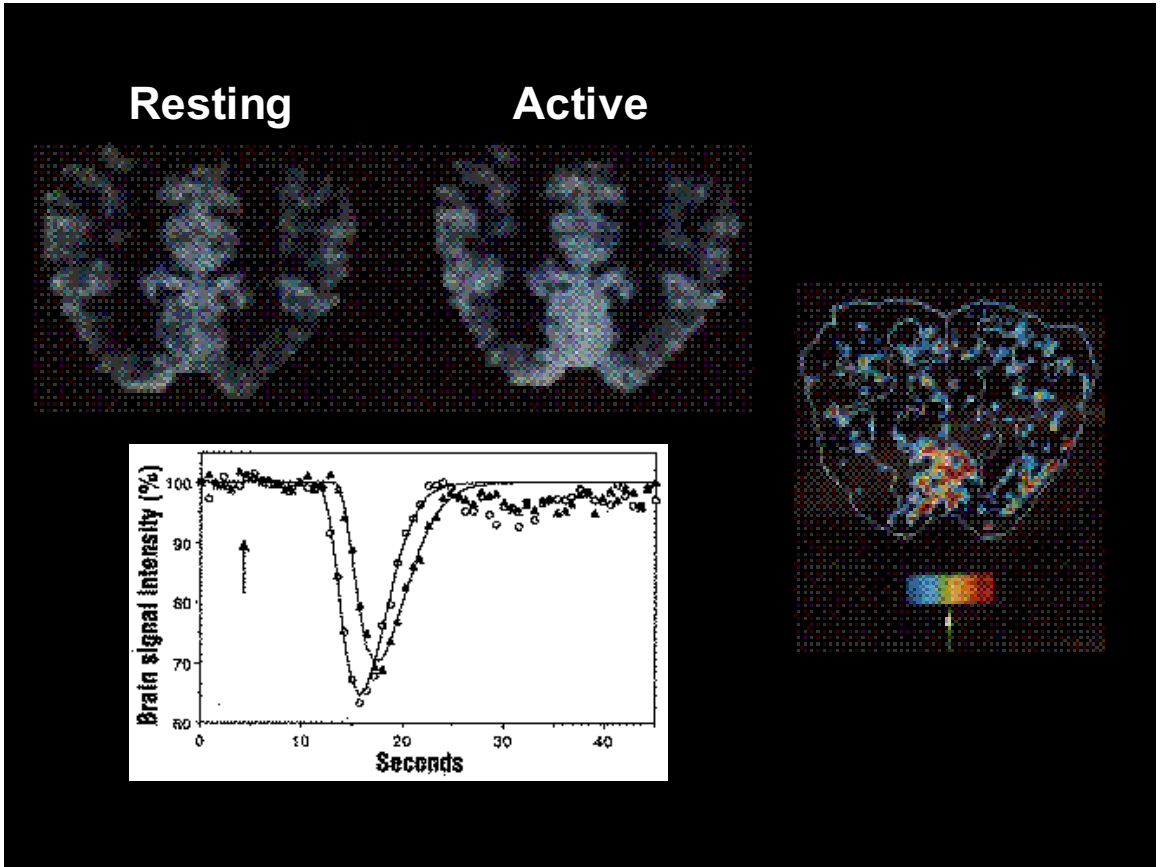
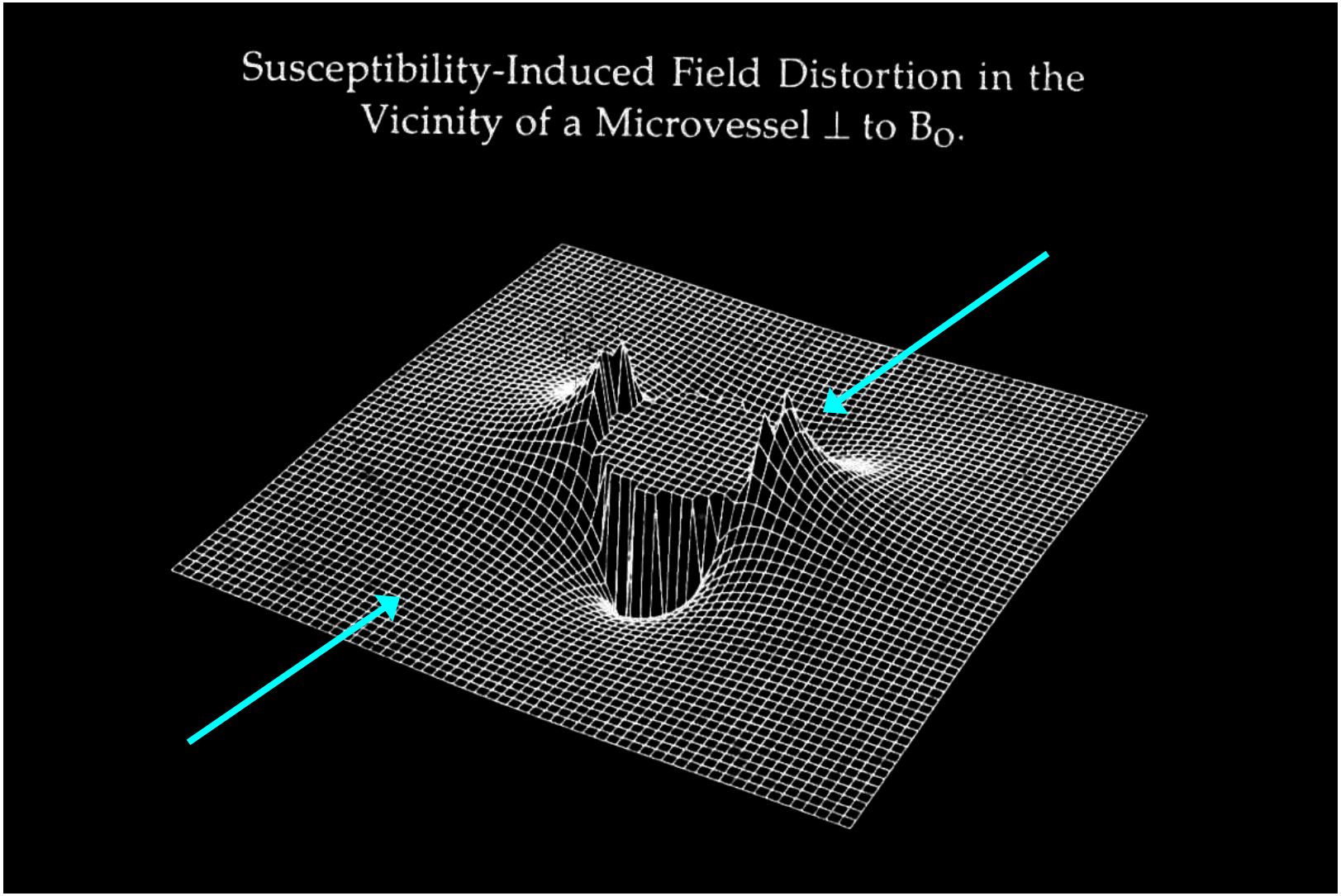
- Metabolic contrasts

Blood Volume Imaging

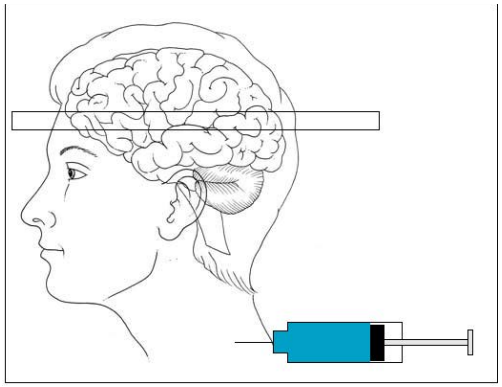
Susceptibility Contrast agent bolus injection and time series collection of T2* or T2 - weighted images

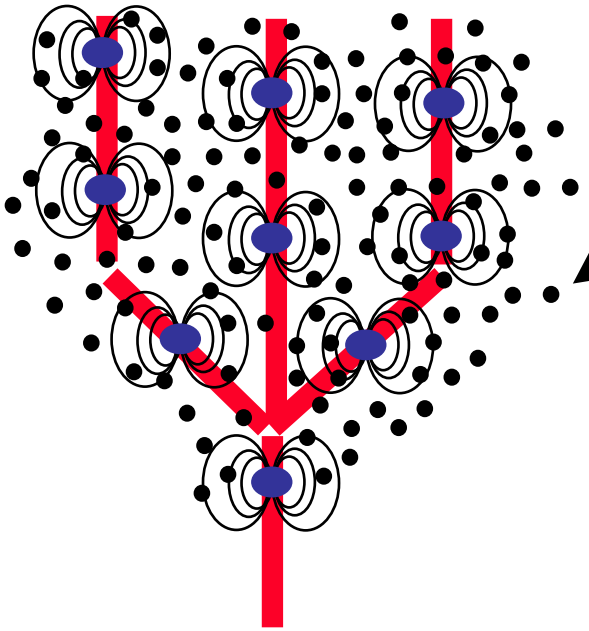


Susceptibility Contrast



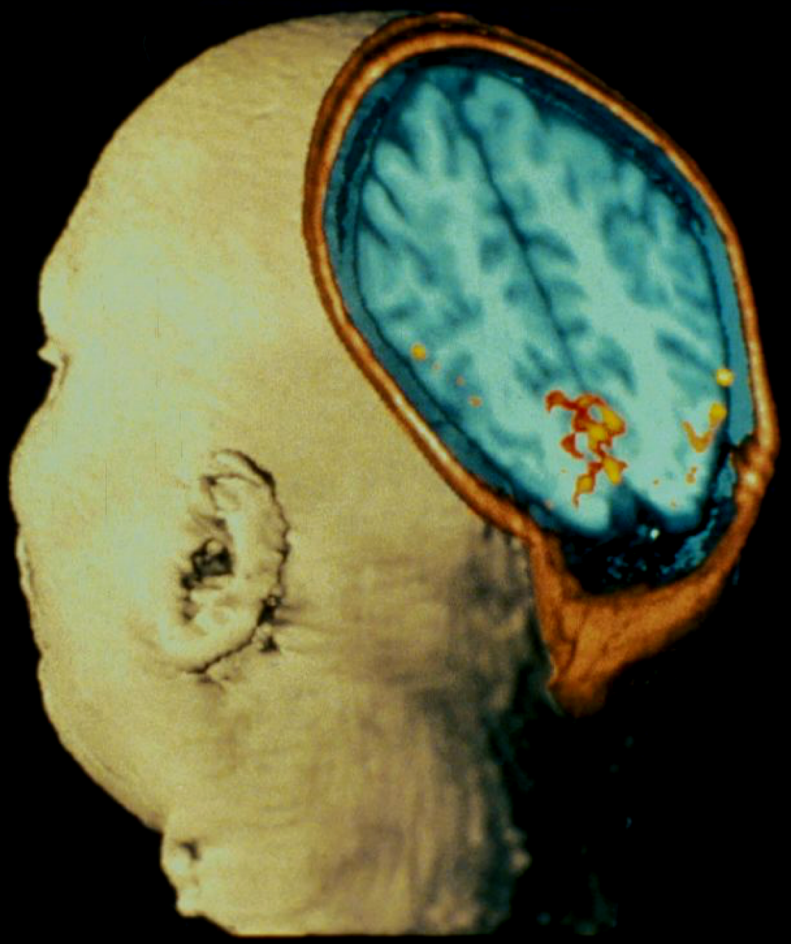
Addition of paramagnetic compound to blood





Courtesy Larry Wald

Photic Stimulation



MRI Image showing activation of the Visual Cortex

From Belliveau, et al. Science Nov 1991

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Fuyrmoxotol

- used by patients with iron deficiencies
- either taken orally or IV injection
- half life in blood of 10-15 hours.
- susceptibility contrast agent like gadolinium but doesn't "wash out"
- can be used to study blood volume dynamics and resting state blood volume fluctuations – in humans.

NeuroImage 181 (2018) 292–300

Contents lists available at ScienceDirect

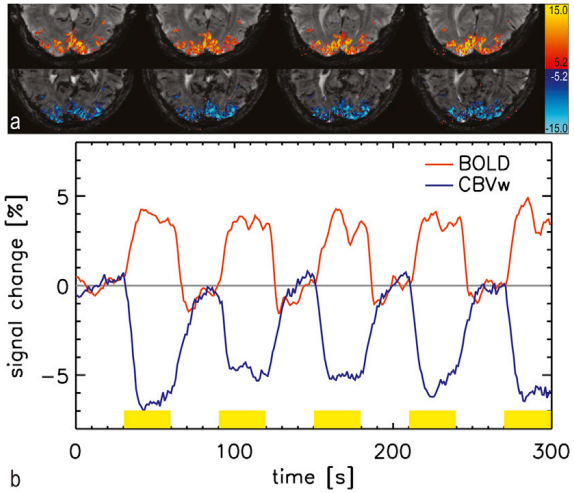
NeuroImage

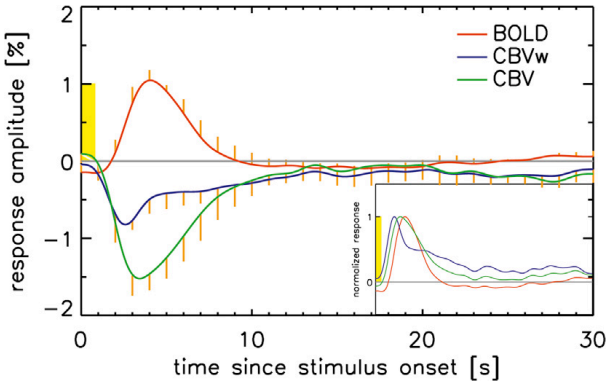
journal homepage: www.elsevier.com/locate/neuroimage

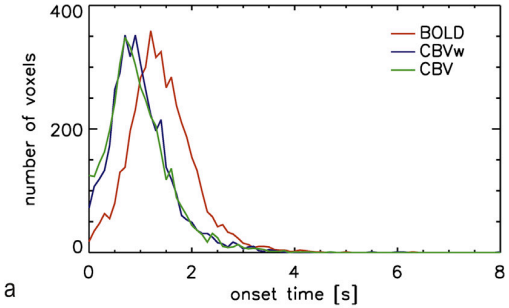
Impulse response timing differences in BOLD and CBV weighted fMRI

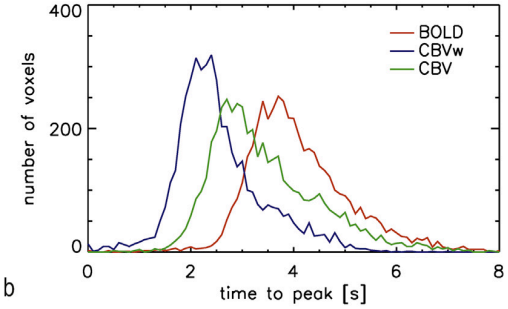
Jacco A. de Zwart [a,*], Peter van Gelderen [a], Matthew K. Schindler [b], Pascal Sati [b], Jiaen Liu [a], Daniel S. Reich [b], Jeff H. Duyn [a]

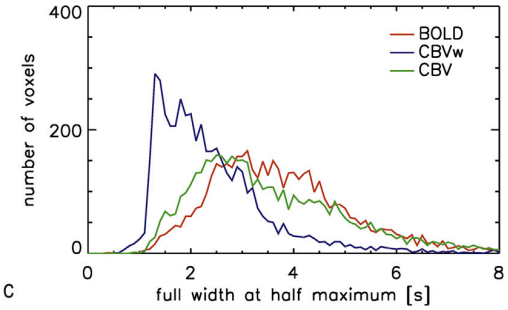
[a] Advanced MRI Section, Laboratory of Functional and Molecular Imaging, NINDS, National Institutes of Health, Bethesda, MD, United States
[b] Translational Neuroradiology Section, NINDS, National Institutes of Health, Bethesda, MD, United States











NeuroImage 83 (2013) 200–209

Contents lists available at ScienceDirect

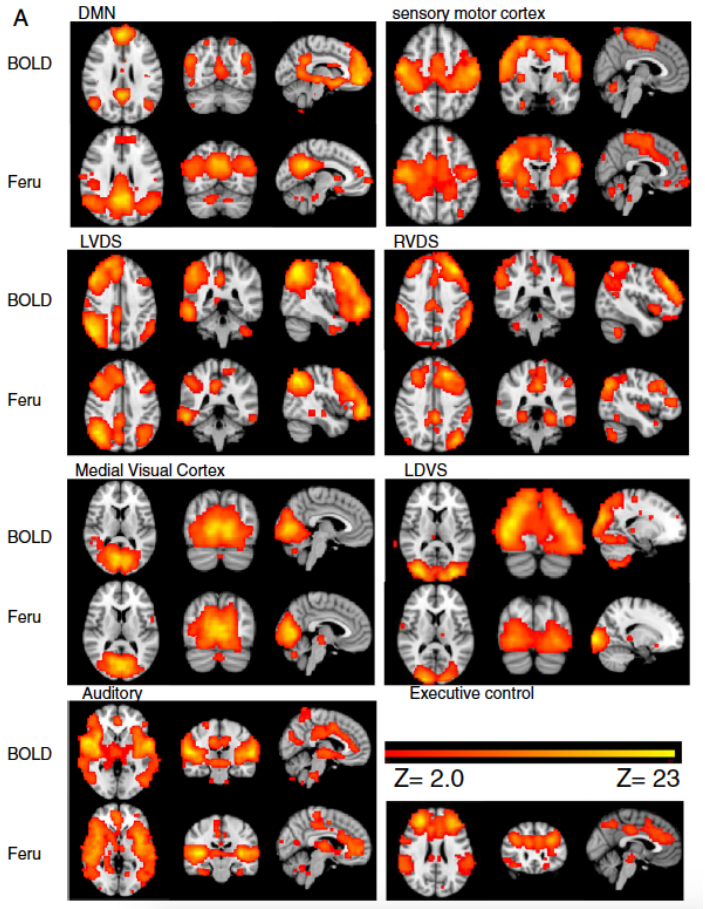
NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Ferumoxytol enhanced resting state fMRI and relative cerebral blood volume mapping in normal human brain

Helen D'Arceuil [a,*], Alexandre Coimbra [b], Pamela Triano [c], Margaret Dougherty [c], Julie Mello [c], Michael Moseley [a], Gary Glover [a], Maarten Lansberg [d], Francis Blankenberg [e]

[a] Dept. of Radiology, Stanford University, CA, USA
[b] Early Clinical Development, Genentech Inc., CA, USA
[c] Department of Rehabilitation Services, Stanford University, CA, USA
[d] Dept. of Neurology, Stanford University, CA, USA
[e] Pediatric Radiology, Stanford University, CA, USA



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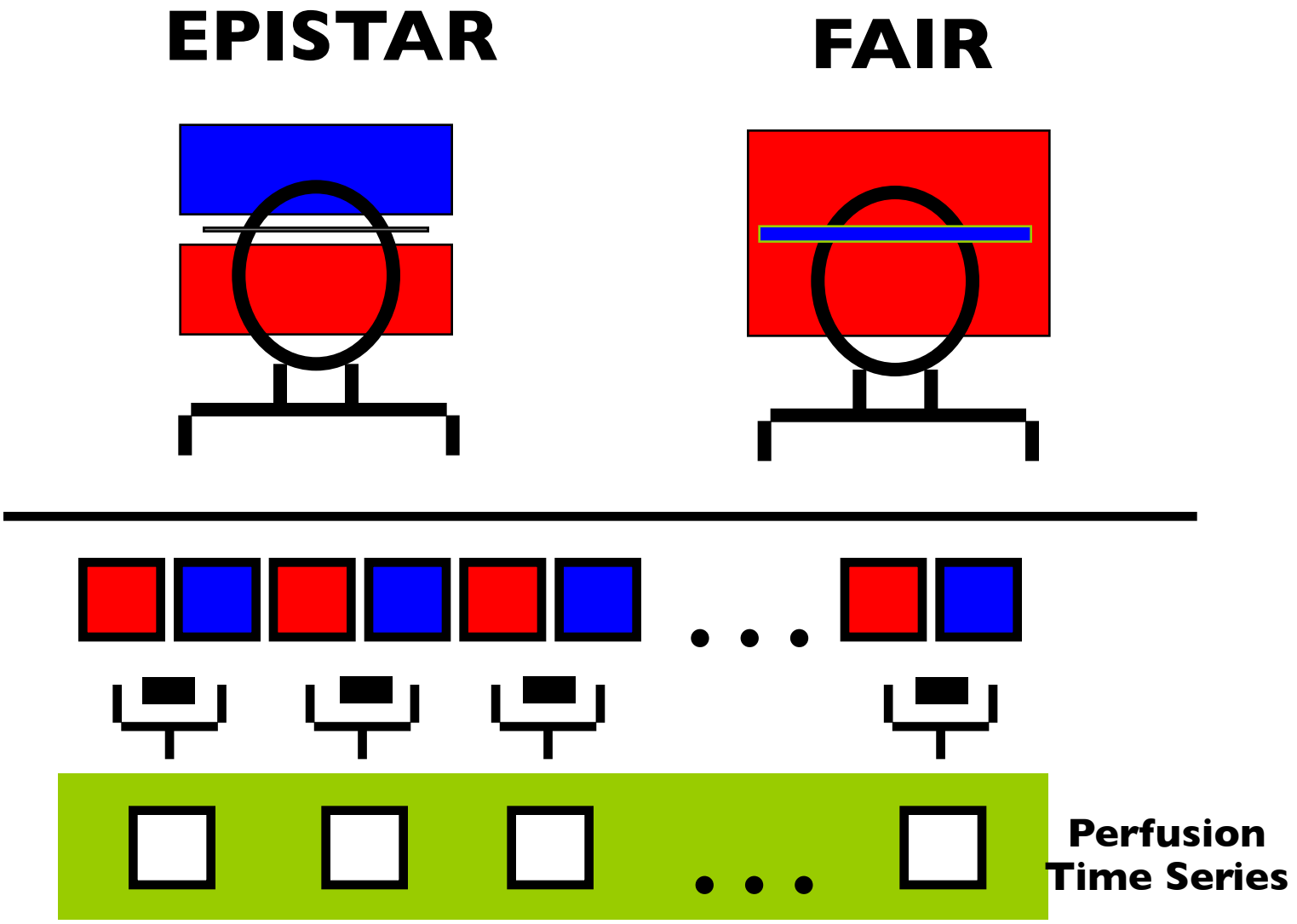
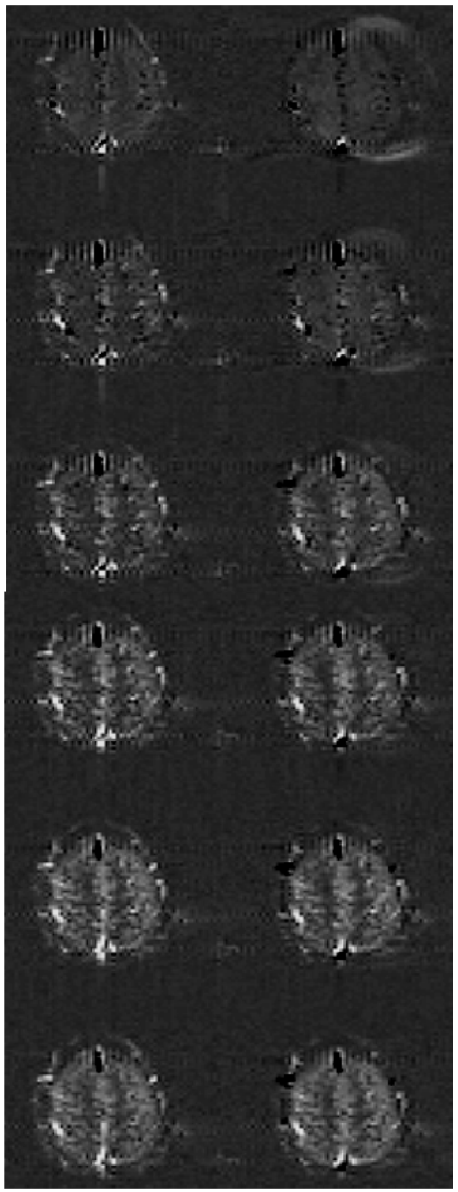
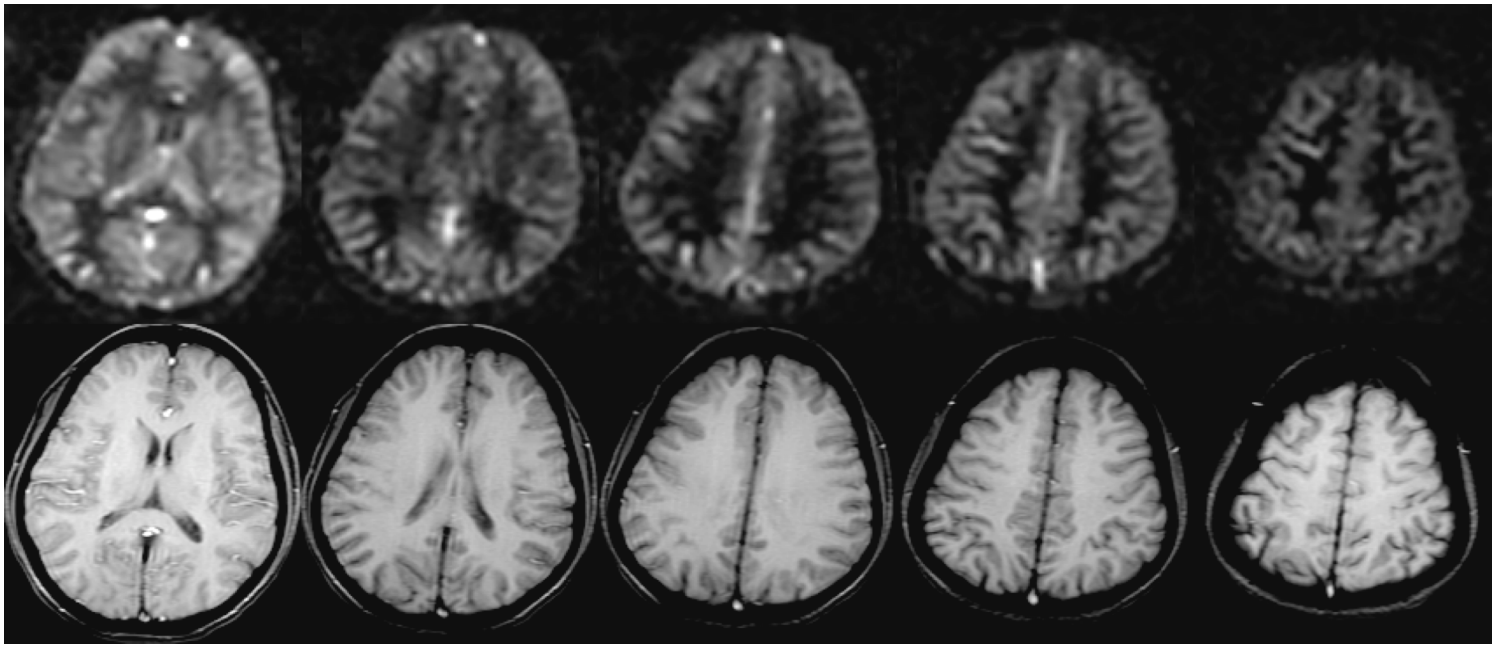
Perfusion Contrast



TI (ms)	FAIR	EPISTAR
200		
400		
600		
800		
1000		
1200		



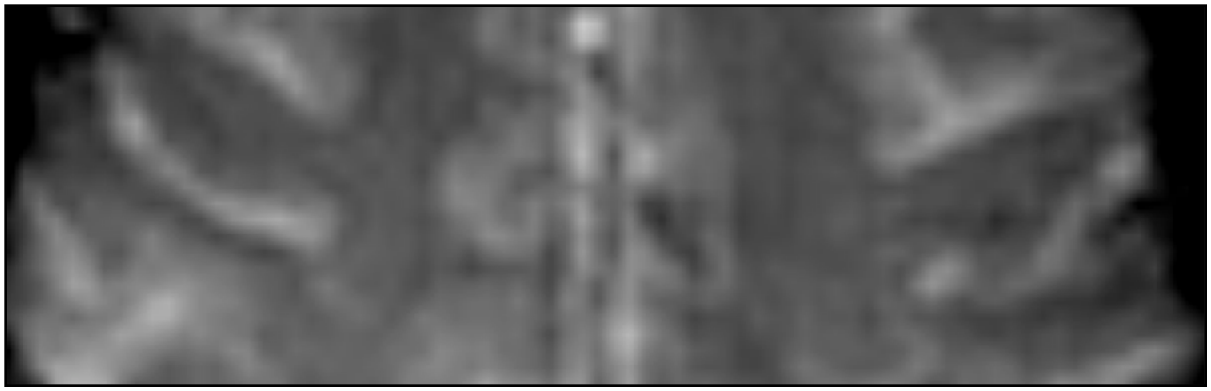
Williams, D. S., Detre, J. A., Leigh, J. S. & Koretsky, A. S. (1992) "Magnetic resonance imaging of perfusion using spin-inversion of arterial water." **Proc. Natl. Acad. Sci. USA 89, 212-216.**

Edelman, R., Siewert, B. & Darby, D. (1994) "Qualitative mapping of cerebral blood flow and functional localization with echo planar MR imaging ans signal targeting with alternating radiofrequency (EPISTAR)." **Radiology 192, 1-8.**

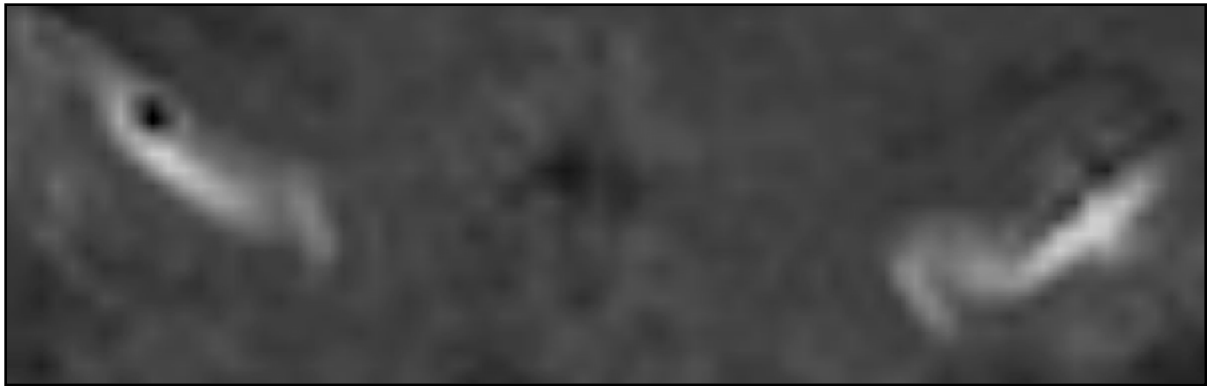
Kim, S.-G. (1995) "Quantification of relative cerebral blood flow change by flow-sensitive alternating inversion recovery (FAIR) technique: application to functional mapping." **Magn. Reson. Med. 34, 293-301**.

Kwong, K. K. et al. (1995) "MR perfusion studies with T1-weighted echo planar imaging."**Magn. Reson. Med. 34,878-887.**

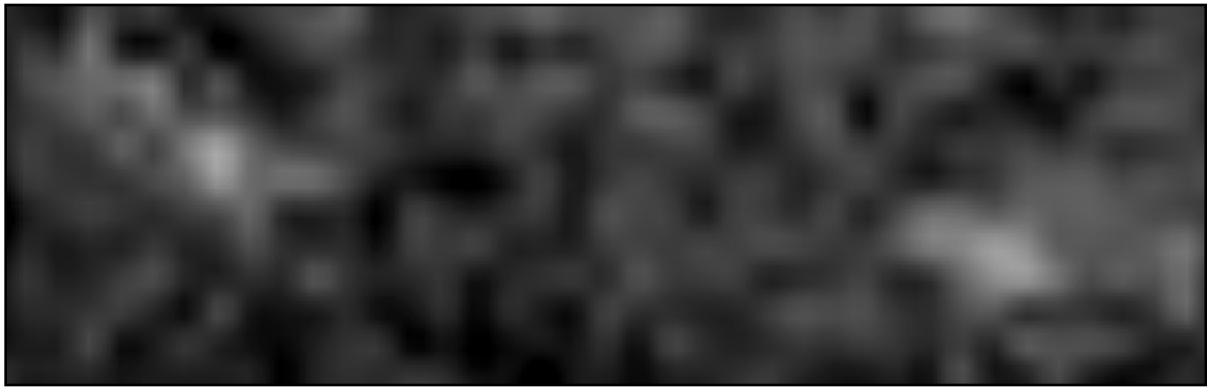
Anatomy



BOLD

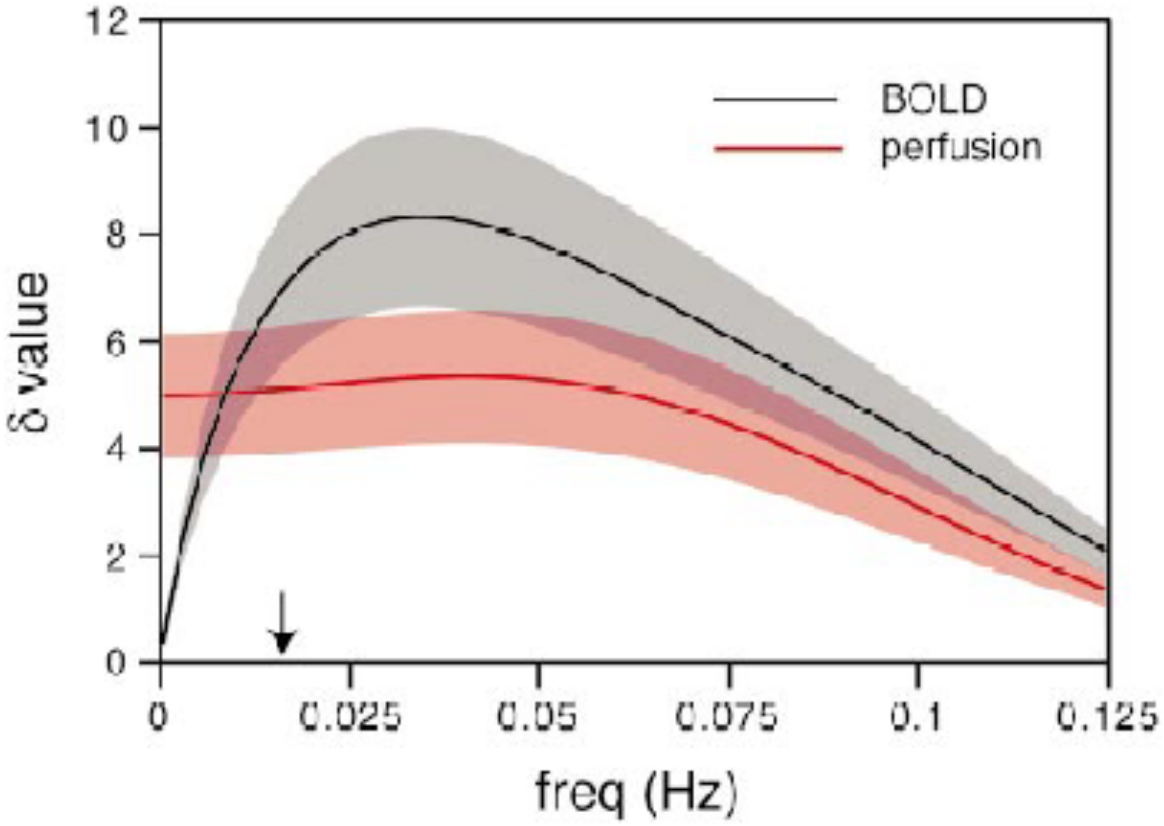


Perfusion



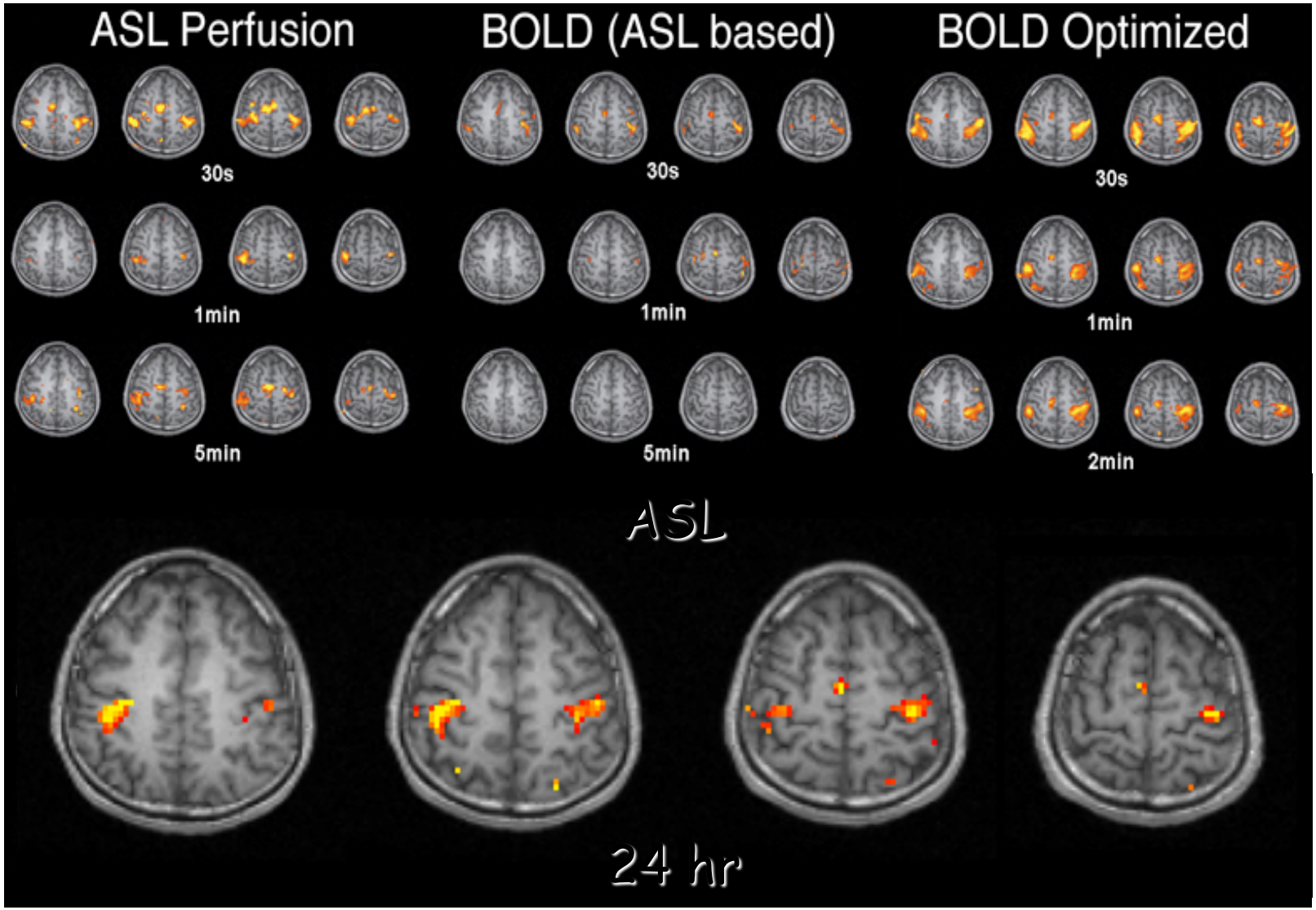
P. A. Bandettini, E. C. Wong, Magnetic resonance imaging of human brain function: principles, practicalities, and possibilities, *in* "Neurosurgery Clinics of North America: Functional Imaging" (M. Haglund, Ed.), p.345-371, W. B. Saunders Co., 1997.

Better than BOLD for long duration activation…



GK Aguirre et al, (2002) NeuroImage 15 (3): 488-500

Perfusion vs. BOLD: Low Task Frequency



New ASL techniques:

CASL (tagging based on location and velocity)
PCASL (pseudo-continuous CASL)
PASL (tagging based on location)
VS-ASL (tagging based on location and velocity)

TASL (territorial ASL)
VE-ASL (vessel encoded ASL)

ASL at multiple TI's

Arterial Spin Labeling in neuroimaging
Petcharunpaisan, Ramalho, Castillo
World Journal of Radiology, 2010

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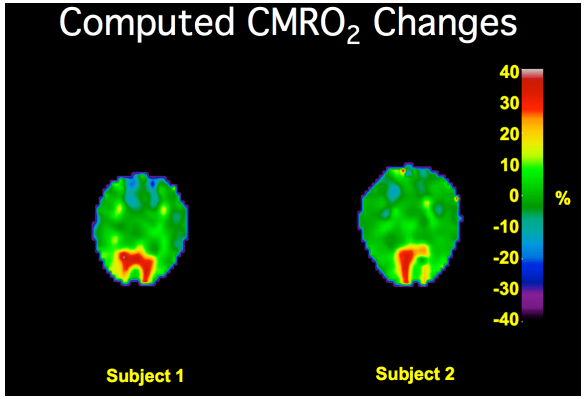
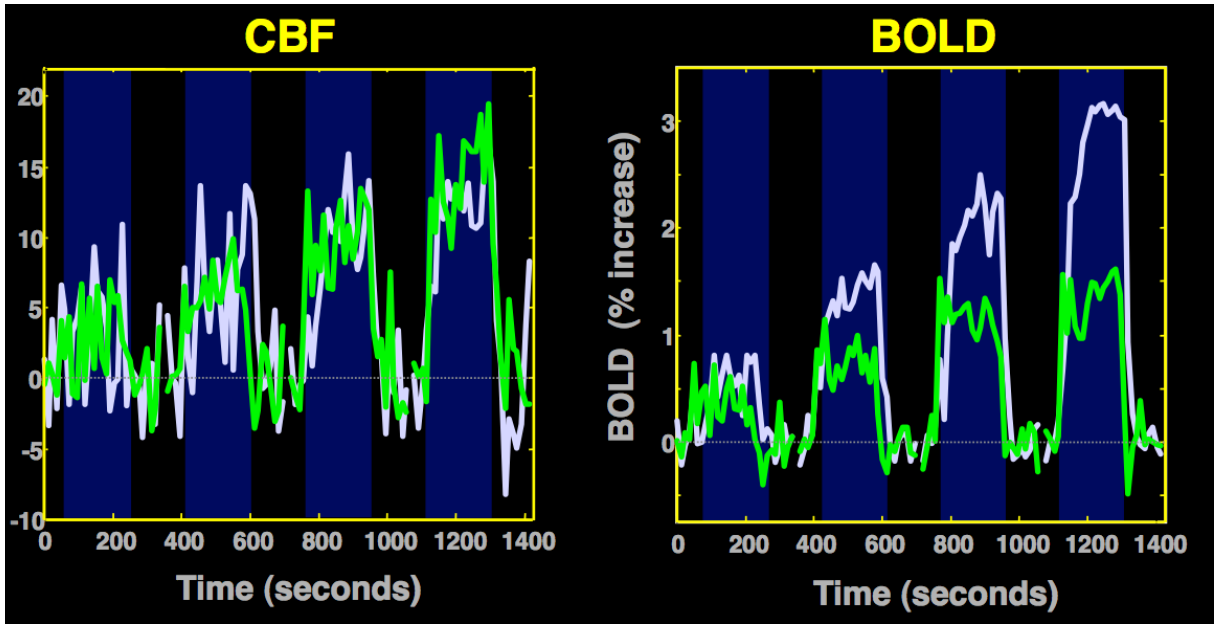
Activation-induced $CMRO_2$ changes



-requires a global hemodynamic stress
-assumption is that $CMRO_2$ unchanged with global stress
-requires simultaneous flow and BOLD collection

R. D. Hoge, et al, PNAS 96: 9403-9408, 1999



Visual = green
Hypercapnia = white

NeuroImage 187 (2019) 128–144

Contents lists available at ScienceDirect

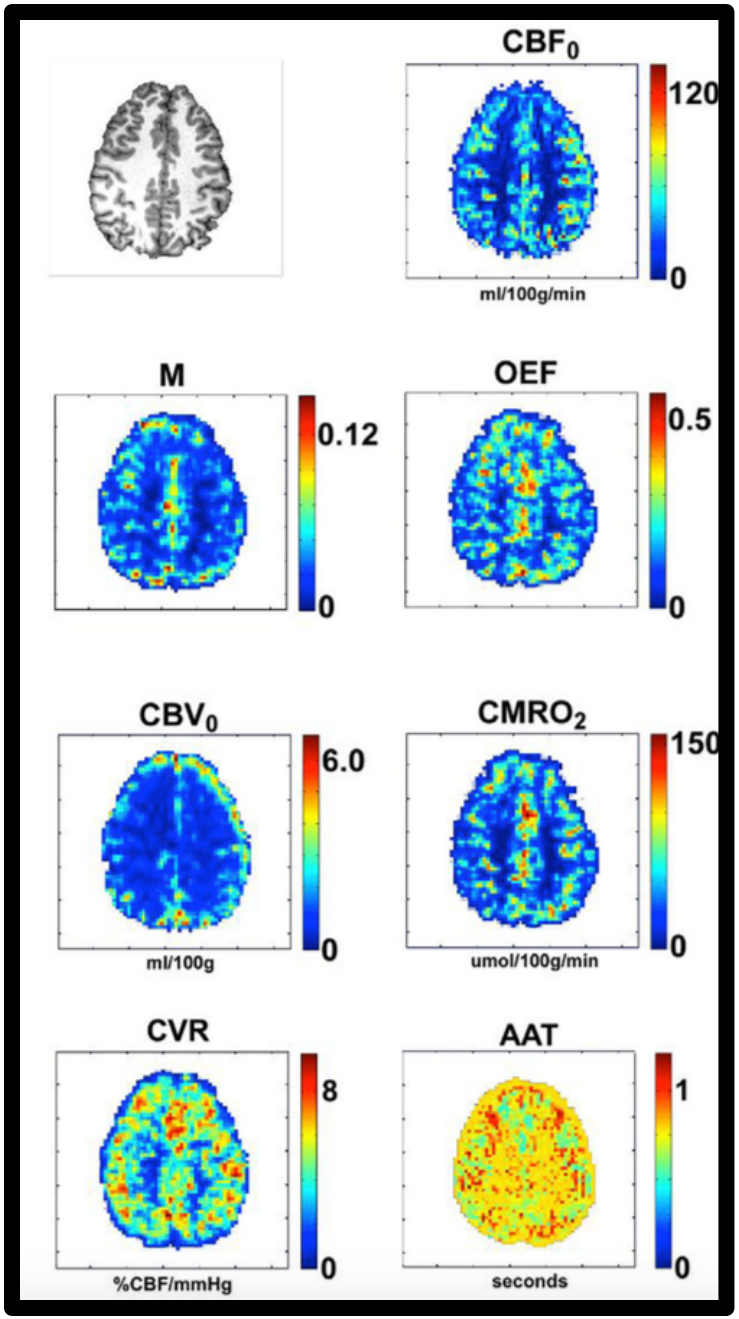
NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage

Multiparametric measurement of cerebral physiology using calibrated fMRI

Molly G. Bright [a,b], Paula L. Croal [c], Nicholas P. Blockley [d], Daniel P. Bulte [c,d,*]

[a] Sir Peter Mansfield Imaging Centre, School of Medicine, University of Nottingham, Nottingham, UK
[b] Department of Physical Therapy and Human Movement Sciences, Feinberg School of Medicine, Northwestern University, Chicago, IL, United States
[c] IBME, Department of Engineering Science, University of Oxford, Oxford, UK
[d] FMRIB, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK



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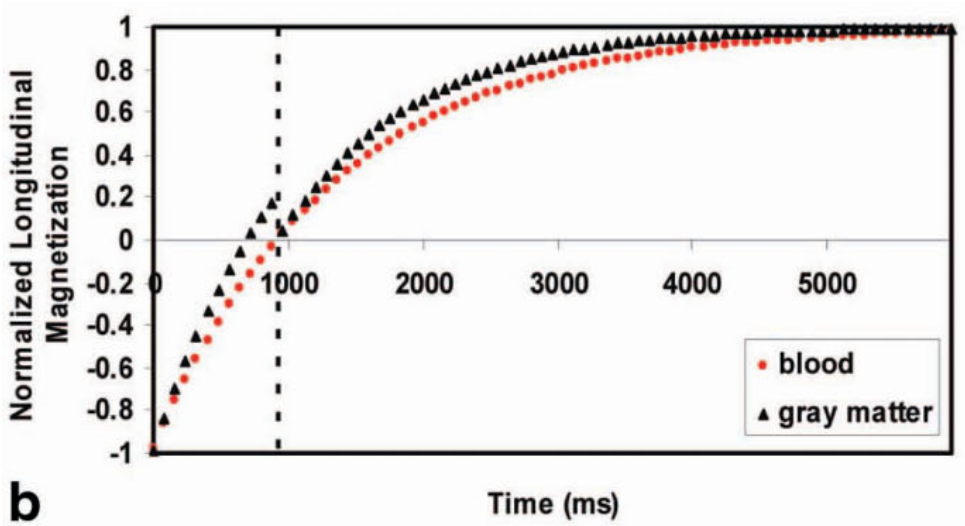
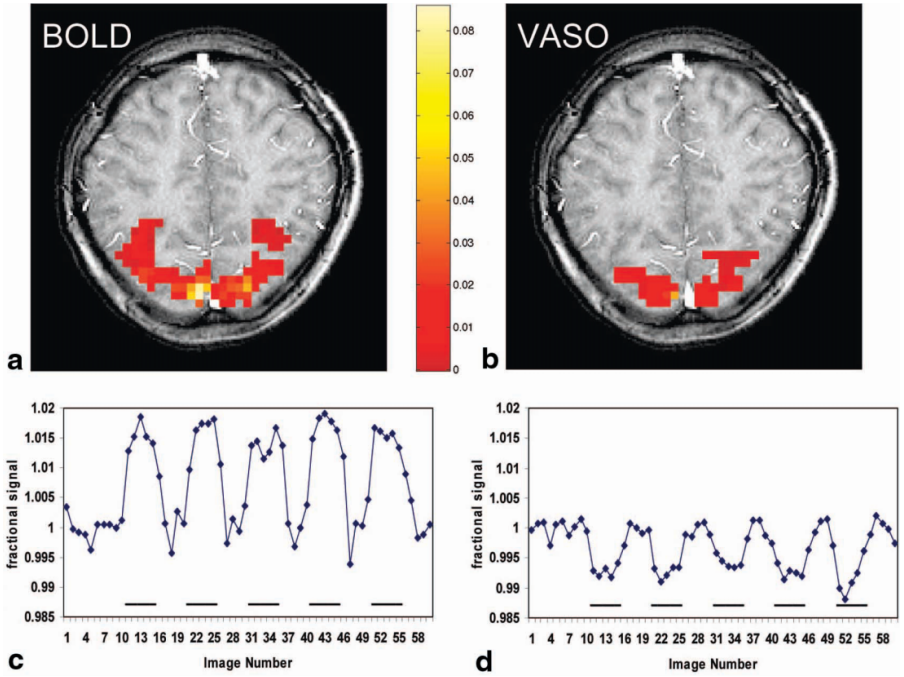
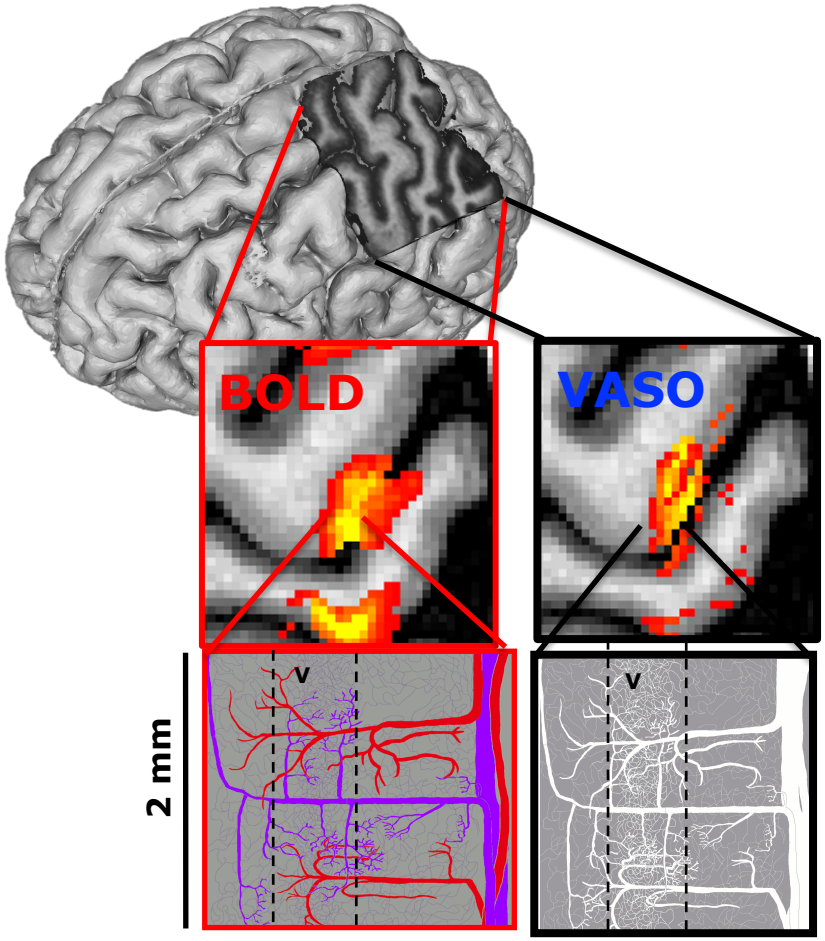
Activation-induced Blood Volume Changes: "VASO"

H. Lu, et al, MRM 50: 263-274, 2003



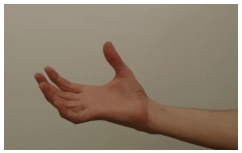


Null blood based on T1 difference between blood and tissue
..more blood -> less signal.



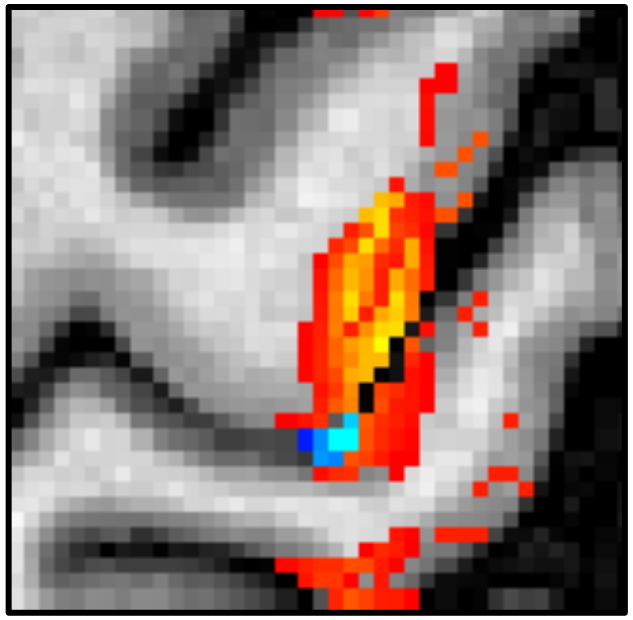
[Huber et al., NeuroImage, 2015] *[Lu et al., MRM, 2003]*

Functional Structure Changes < 0.8 mm

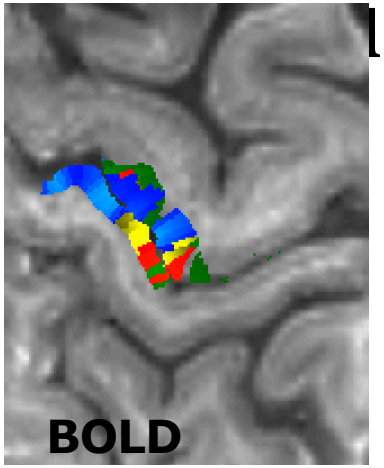


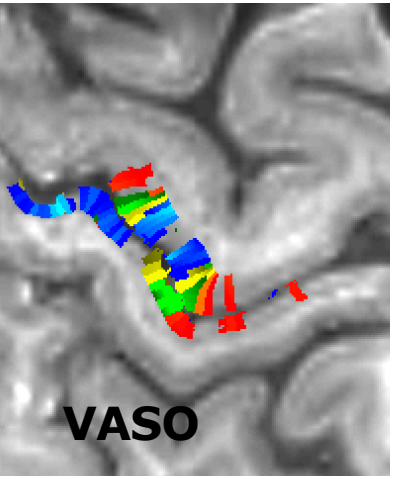
right tapping

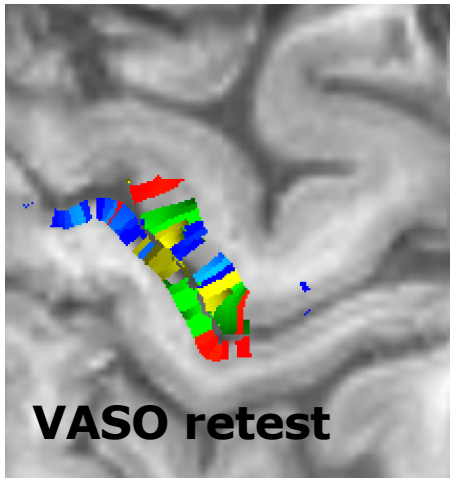
resol. 0.75mm

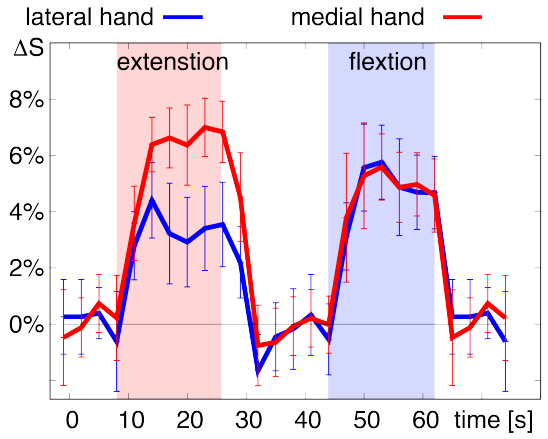


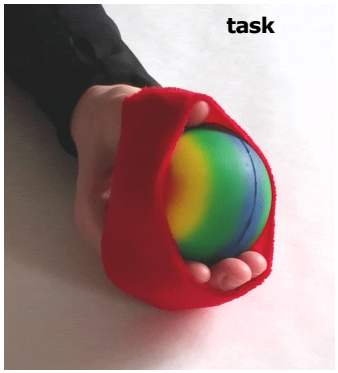
Digit Representation in M1

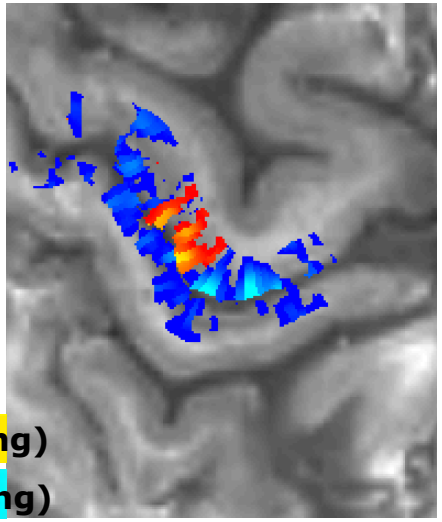










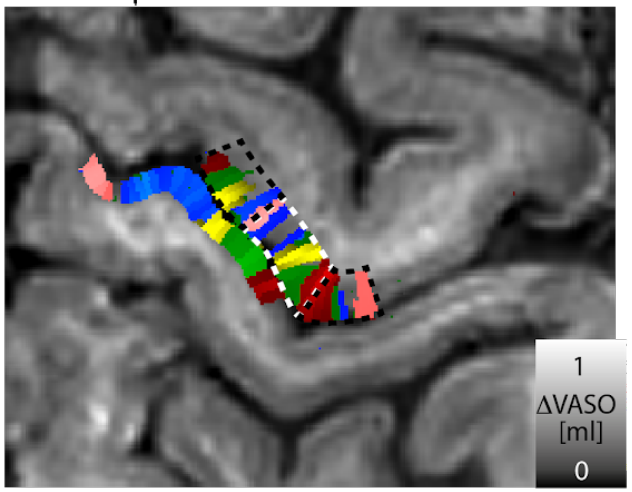


Extension (spreading)

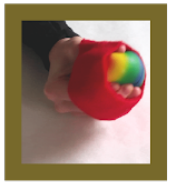
Flexion (compressing)

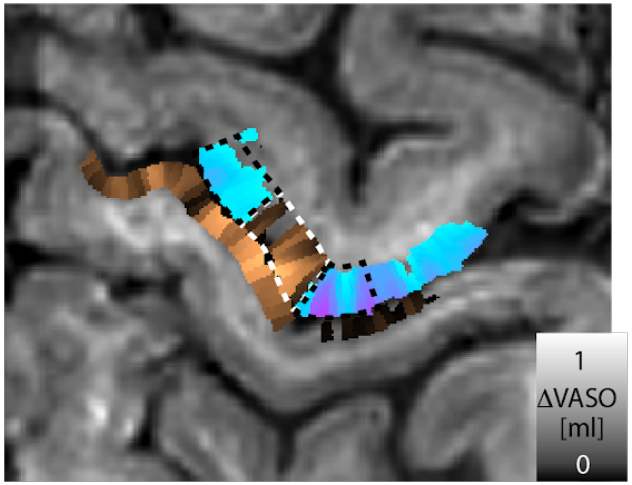
Digit representations appear to be organized by opposing movements

five-finger tapping

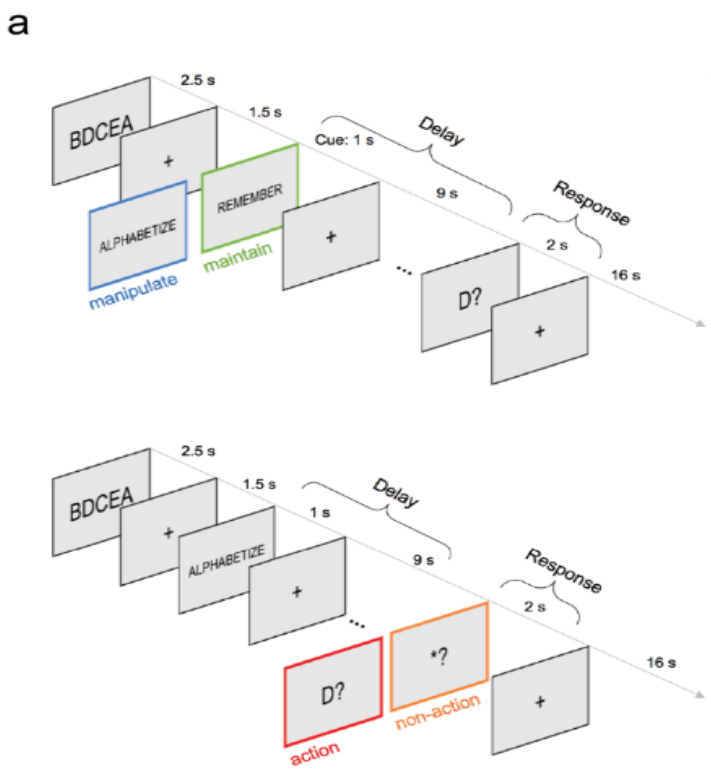


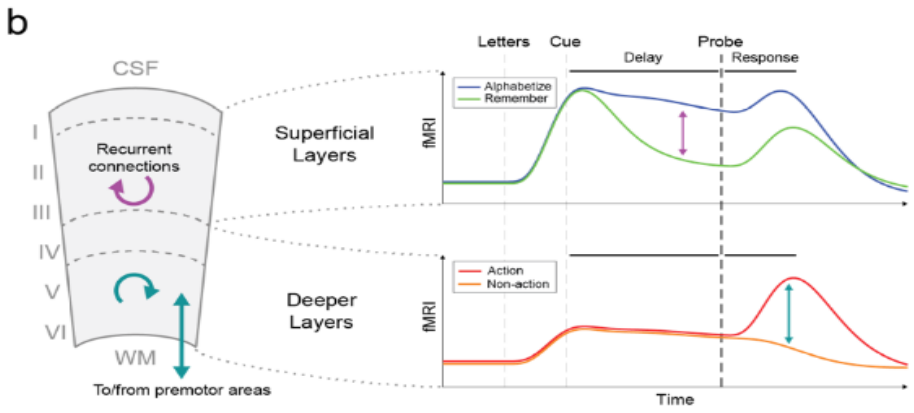
finger flexion vs. finger extension

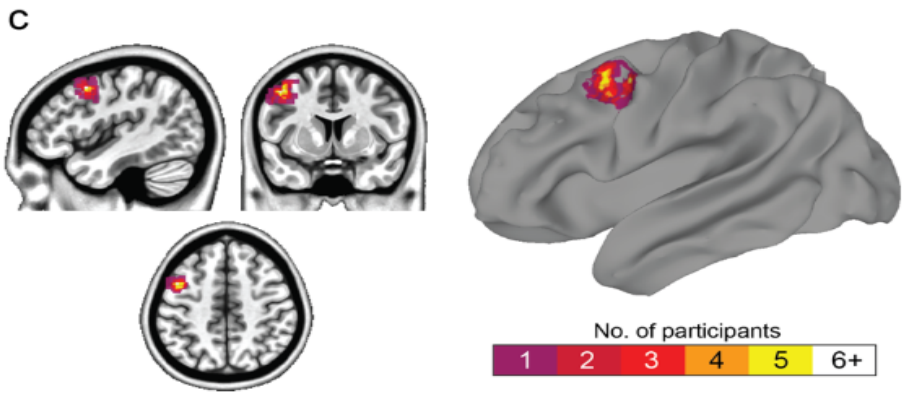




Layer Activation in a Working Memory task



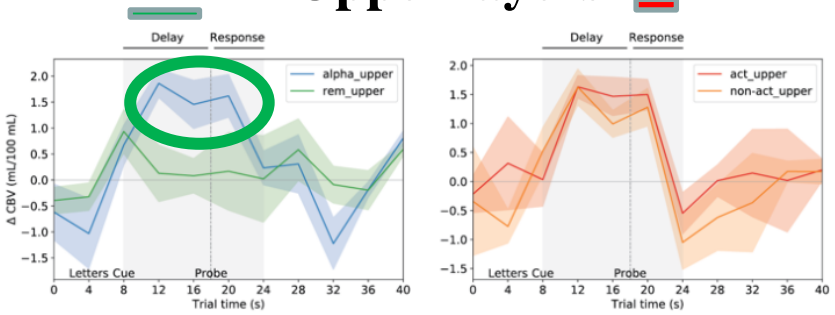


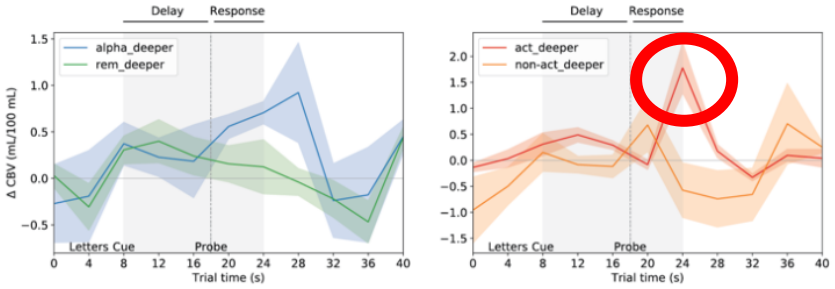


Maintain & Manipulate

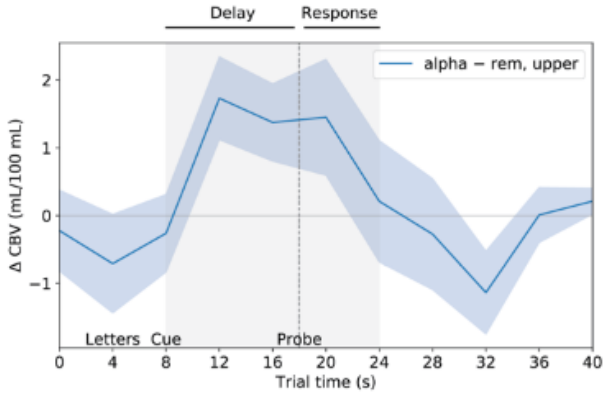
Go & No-Go

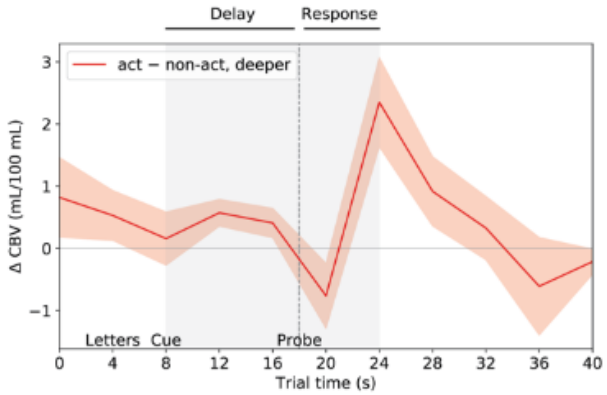
Upper layers





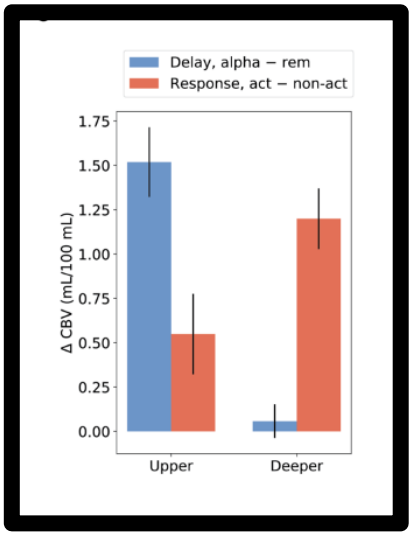
Deeper layers

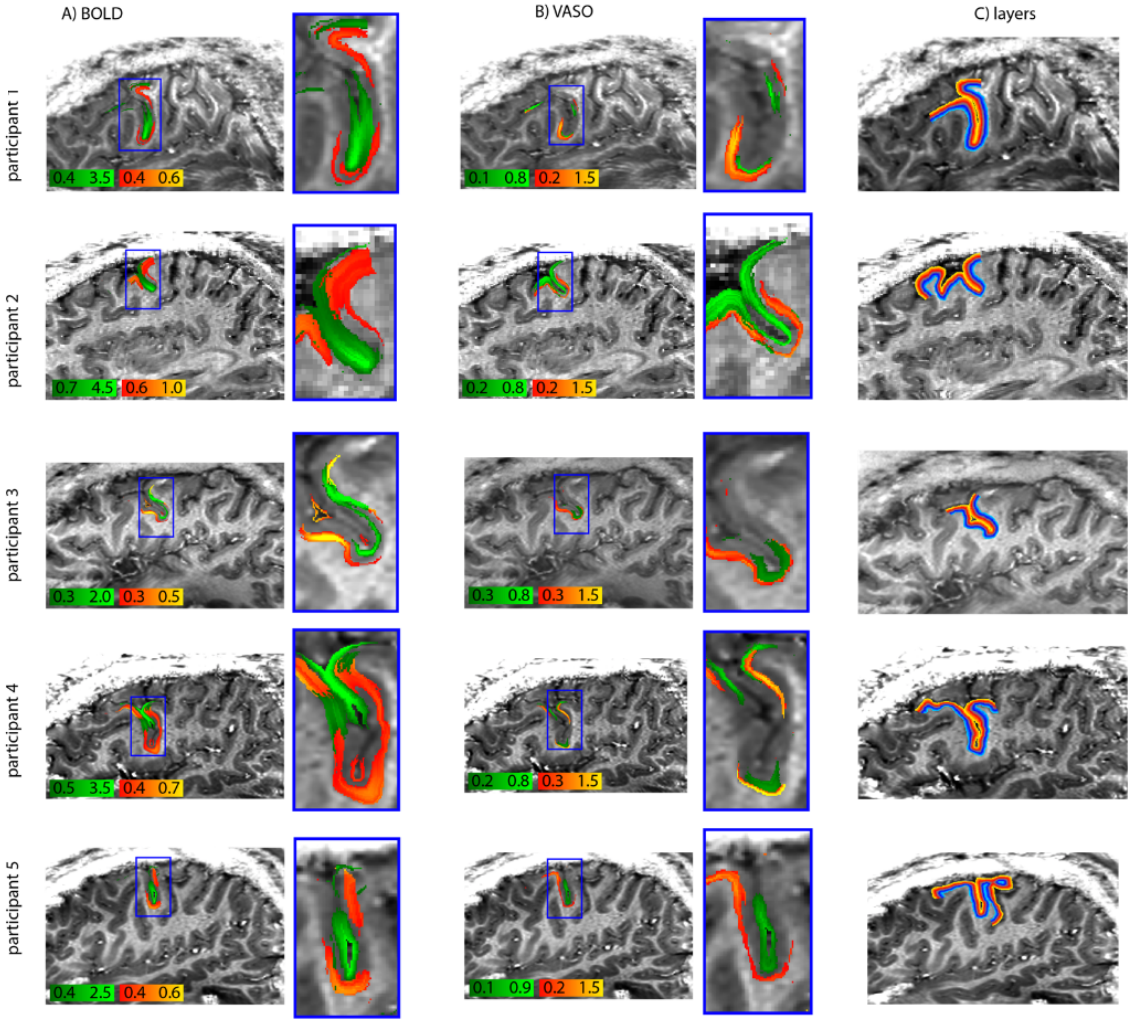




signal of alphabetizing minus signal of remembering [%] (overlay)

signal during responding minus signal during rest [%] (underlay)

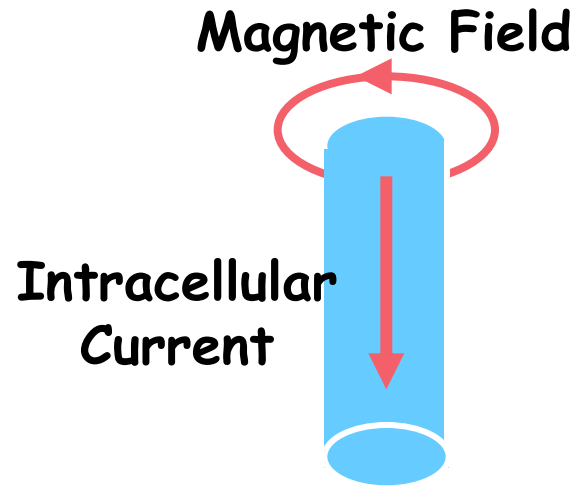


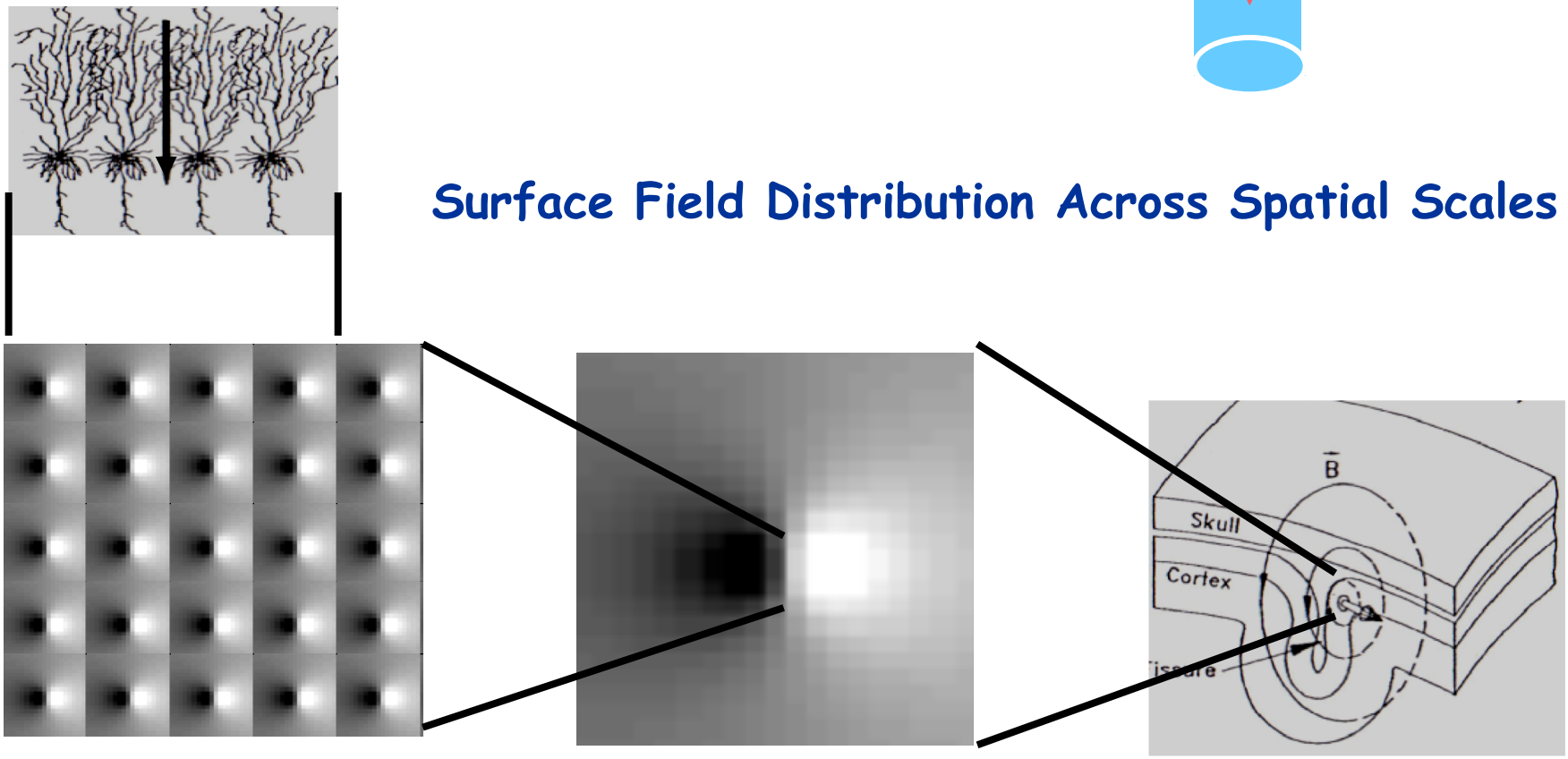


Contrasts other than BOLD

- Perfusion (IVIM)
- Volume (gadolinium)
- Volume (fuyrmoxotol)
- Perfusion (ASL)
- $\Delta CMRO_2$
- ΔVolume (VASO)
- **Neuronal Currents**
- Proton density? (SEEP)
- Diffusion coefficient
- Temperature
- Elastography
- Metabolic Contrasts

Neuronal Currents



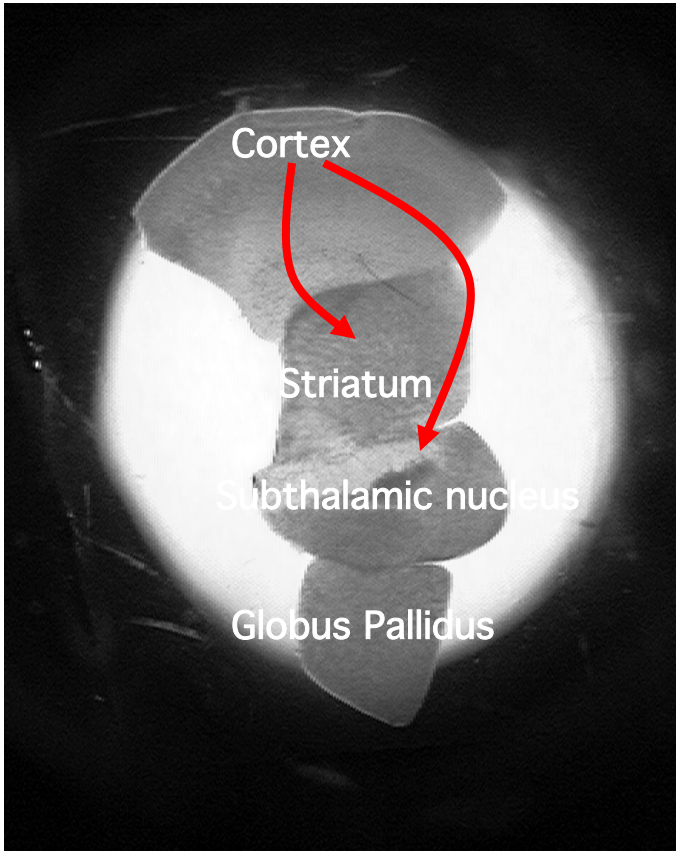


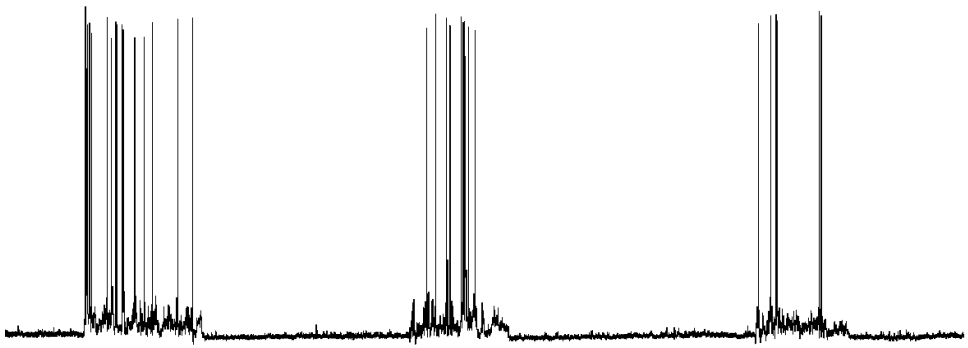
Surface Field Distribution Across Spatial Scales

Adapted from: J.P. Wikswo Jr et al. *J Clin Neurophy* 8(2): 170-188, 1991

In Vitro Results

Newborn rat brains have been found to exhibit spontaneous and synchronous firing at specific frequencies

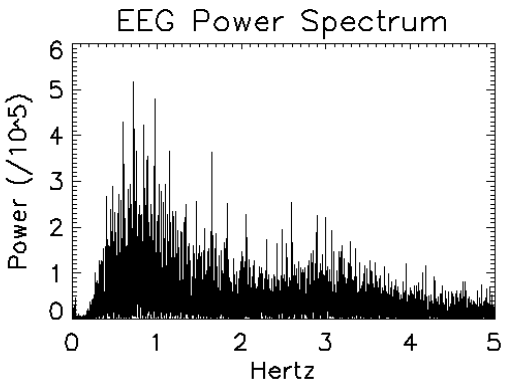


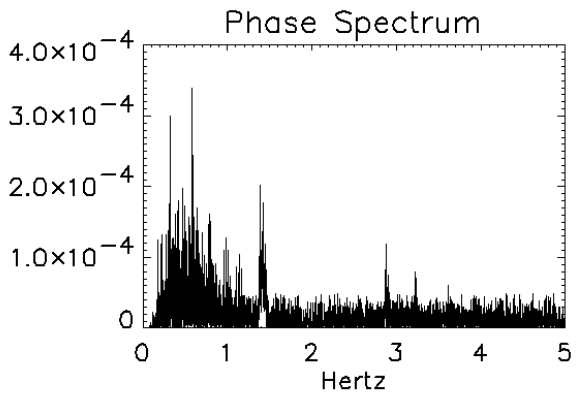


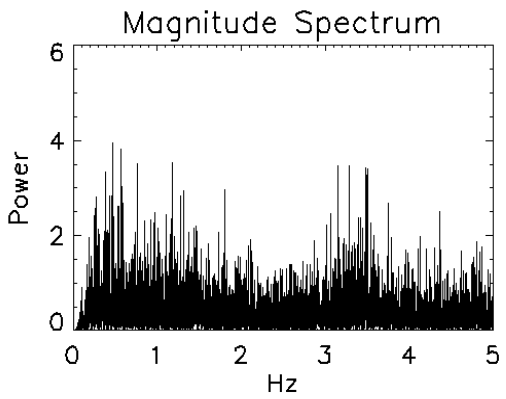
Plenz, D. and S.T. Kital. Nature, 1999. 400: p. 677-682.

EEG

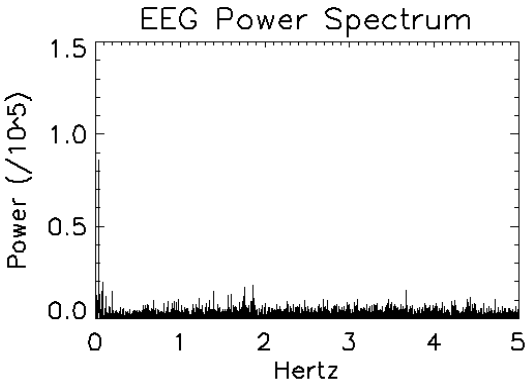
MR (7T)

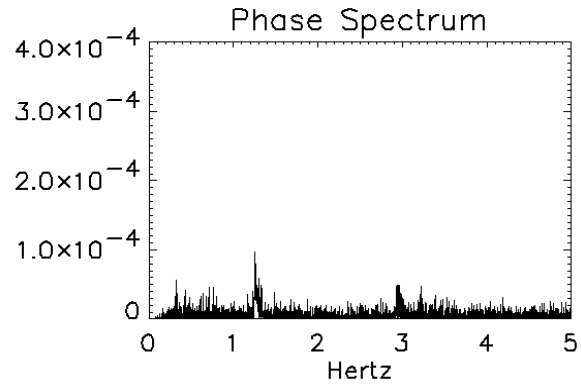


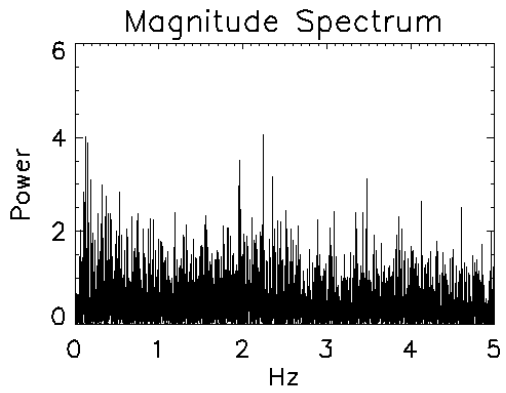




TTX







Power decrease between PRE & TTX EEG : ~ 81%

Decrease between PRE & TTX MR phase: ~ 70%

Decrease between PRE & TTX MR magnitude: ~ 8%

N. Petridou, D. Plenz, A. C. Silva, J. Bodurka, M. Loew, P. A. Bandettini, *Proc. Nat'l. Acad. Sci. USA*. 103, 16015-16020 (2006).

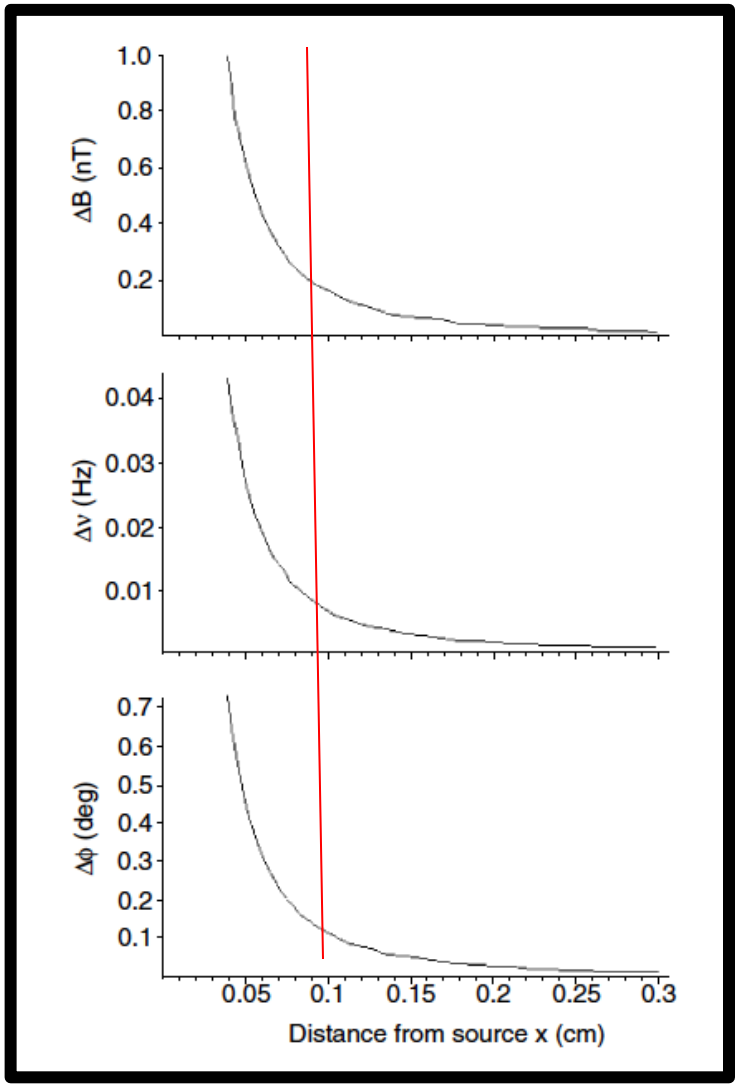
Direct Detection of Neuronal Activity with MRI: Fantasy, Possibility, or Reality?

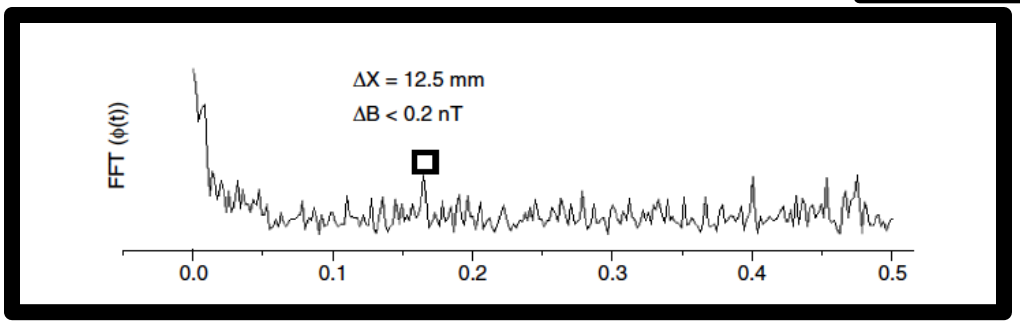
P. A. Bandettini[1,2], **N. Petridou**[1], and **J. Bodurka**[2]

[1] Unit on Functional Imaging Methods, Laboratory of Brain and Cognition and
[2] Functional MRI Facility, National Institute of Mental Health, National Institutes of Health, Bethesola, Maryland, USA

Received November 29, 2004; revised January 7, 2005

- A single dendrite produces a field of about 0.002 fT at the surface of the skull
- MEG field measurement at surface of skull = 100 fT, produced by about 50K dendritic bundles
- If these bundles are clustered in a voxel (containing the dipole), then within the voxel, they would produce a field shift of 0.2 nT.

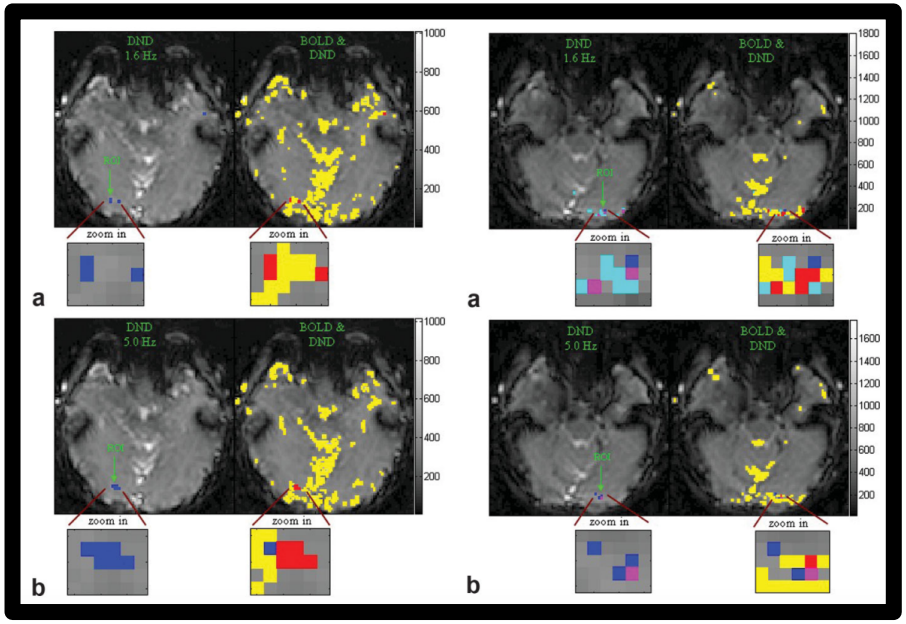


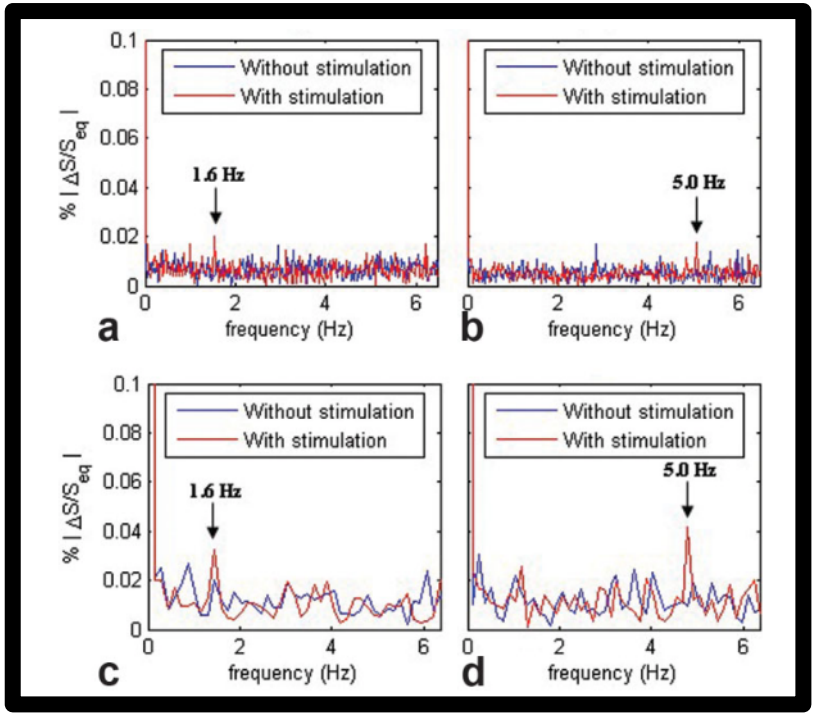


Magnetic Resonance in Medicine 60:1147–1154 (2008)

Comparison of BOLD and Direct-MR Neuronal Detection (DND) in the Human Visual Cortex at 3T

Li Sze Chow,[1*] Andrew Dagens,[1] Ying Fu,[2] Greg G. Cook,[2] and Martyn N.J. Paley[1]





Magnetic resonance imaging of oscillating electrical currents

PNAS

Nicholas W. Halpern-Manners[a], Vikram S. Bajaj[a,1], Thomas Z. Teisseyre[a,b], and Alexander Pines[a]

[a]Materials Sciences Division, Lawrence Berkeley National Laboratory and Department of Chemistry, University of California, Berkeley, CA 94720; and [b]Joint Graduate Group in Bioengineering, University of California, Berkeley, CA 94720, and University of California, San Francisco, CA 94158

Contributed by Alexander Pines, March 25, 2010 (sent for review January 11, 2010)

Received: 14 June 2018 | Revised: 12 November 2018 | Accepted: 13 December 2018

DOI: 10.1002/mrm.27654

FULL PAPER

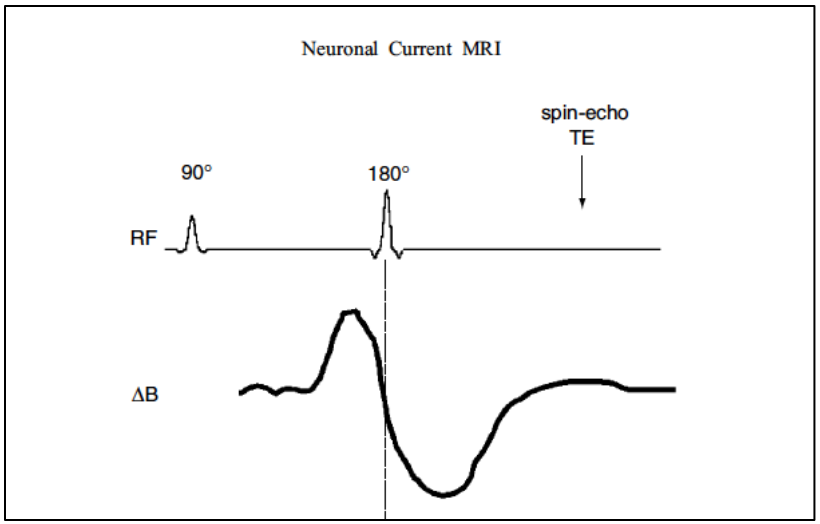
Magnetic Resonance in Medicine

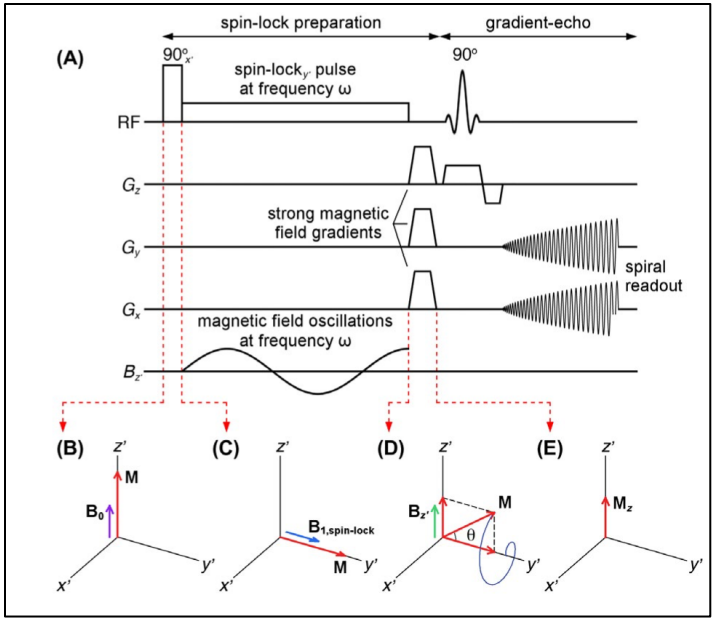
Toward direct MRI of neuro-electro-magnetic oscillations in the human brain

Trong-Kha Truong[1] | Kenneth C. Roberts[2] | Marty G. Woldorff[2] | Allen W. Song[1]

[1]Brain Imaging and Analysis Center, Duke University, Durham, North Carolina

[2]Center for Cognitive Neuroscience, Duke University, Durham, North Carolina





ELSEVIER

NeuroImage

www.elsevier.com/locate/ynimg
NeuroImage 39 (2008) 310–317

Toward direct neural current imaging by resonant mechanisms at ultra-low field

R.H. Kraus Jr.,* P. Volegov, A. Matlachov, and M. Espy

Los Alamos National Laboratory, Los Alamos, NM, USA

Received 22 June 2006; revised 19 June 2007; accepted 31 July 2007
Available online 16 August 2007

Contrasts other than BOLD

- Perfusion (IVIM)
- Volume (gadolinium)
- Volume (fuyrmoxotol)
- Perfusion (ASL)
- $\Delta CMRO_2$
- ΔVolume (VASO)
- Neuronal Currents
- Proton density? (SEEP)
- Diffusion coefficient
- Temperature
- Elastography
- Metabolic Contrasts

Signal Enhancement by Extravascular Water Protons (SEEP)

ELSEVIER

Available online at www.sciencedirect.com

ScienceDirect

Magnetic Resonance Imaging 28 (2010) 1234–1243

MAGNETIC RESONANCE IMAGING

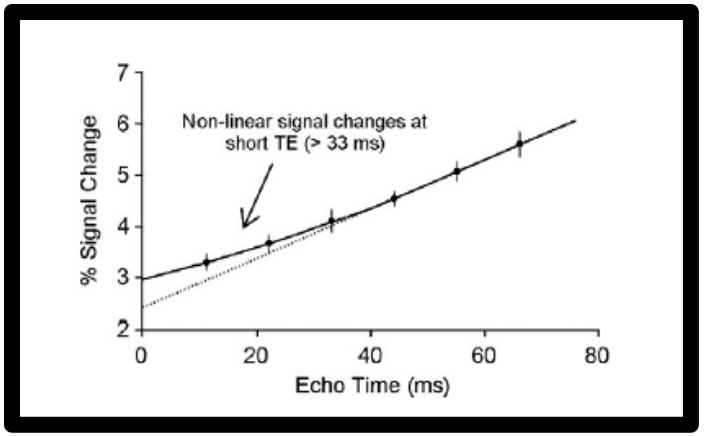
In contrast to BOLD: signal enhancement by extravascular water protons as an alternative mechanism of endogenous fMRI signal change

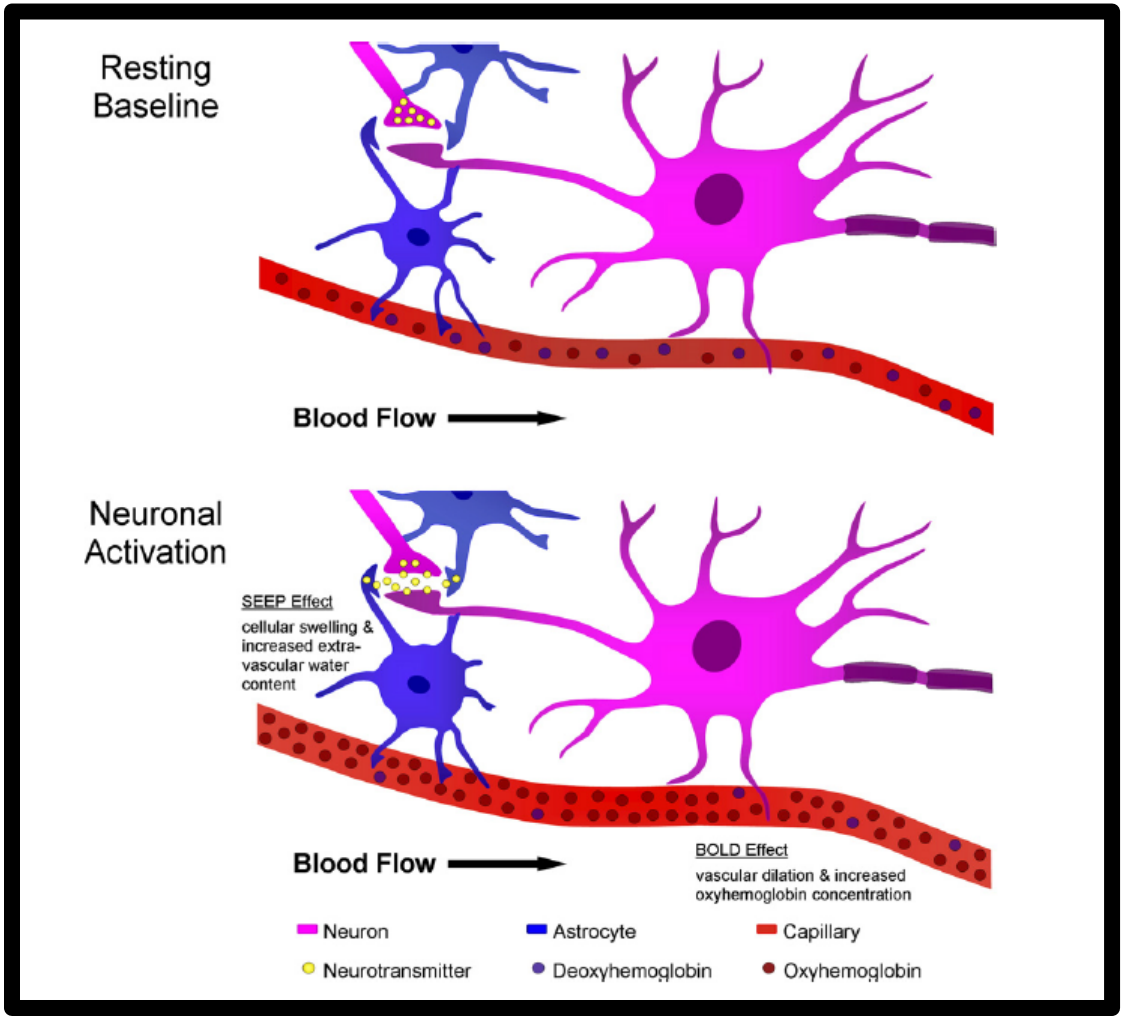
Chase R. Figley[a], Jordan K. Leitch[a], Patrick W. Stroman[a,b,c,*]

[a]*Centre for Neuroscience Studies, Queen's University, Kingston, Ontario, Canada K7L 3N6*
[b]*Department of Diagnostic Radiology, Queen's University, Kingston, Ontario, Canada K7L 3N6*
[c]*Department of Physics, Queen's University, Kingston, Ontario, Canada K7L 3N6*

Received 7 October 2009; revised 23 December 2009; accepted 8 January 2010

Signal Enhancement by Extravascular Water Protons (SEEP)





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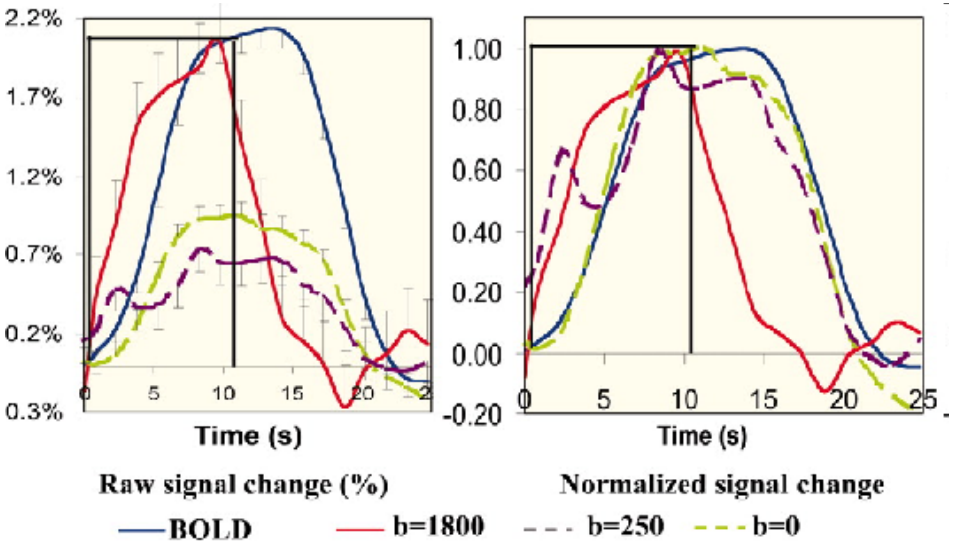
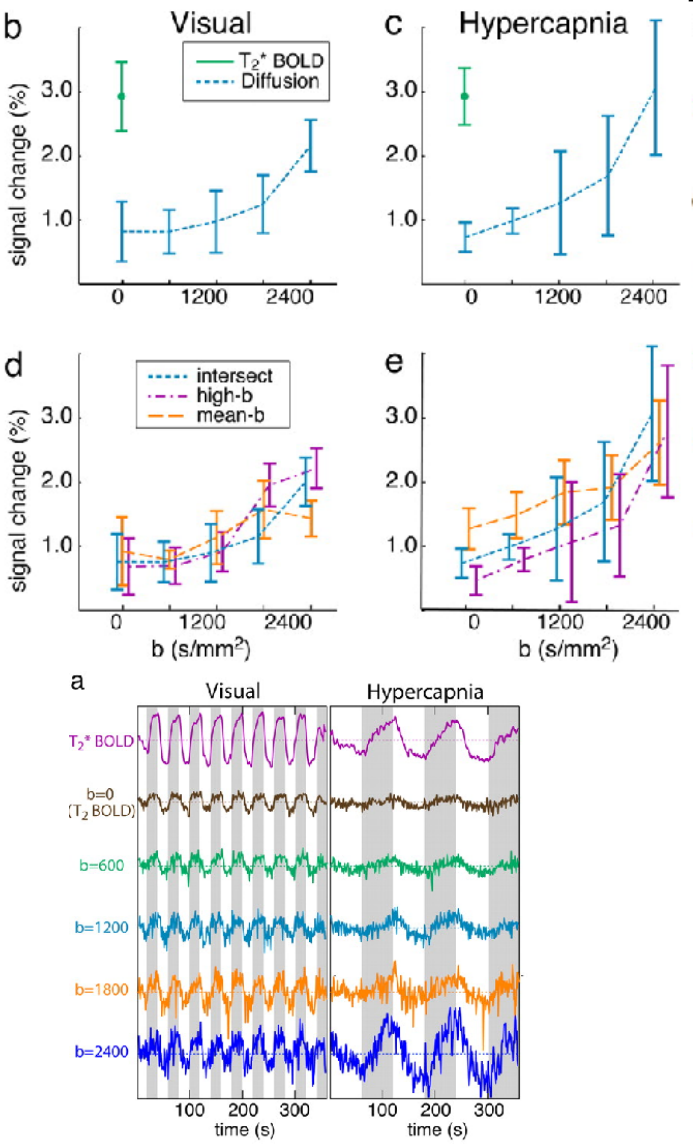
- Perfusion (ASL)
- $\Delta CMRO_2$
- ΔVolume (VASO)
- Neuronal Currents
- Proton density? (SEEP)
- Diffusion coefficient
- Temperature
- Elastography
- Metabolic Contrasts

Decrease in diffusion coefficient with cell swelling?





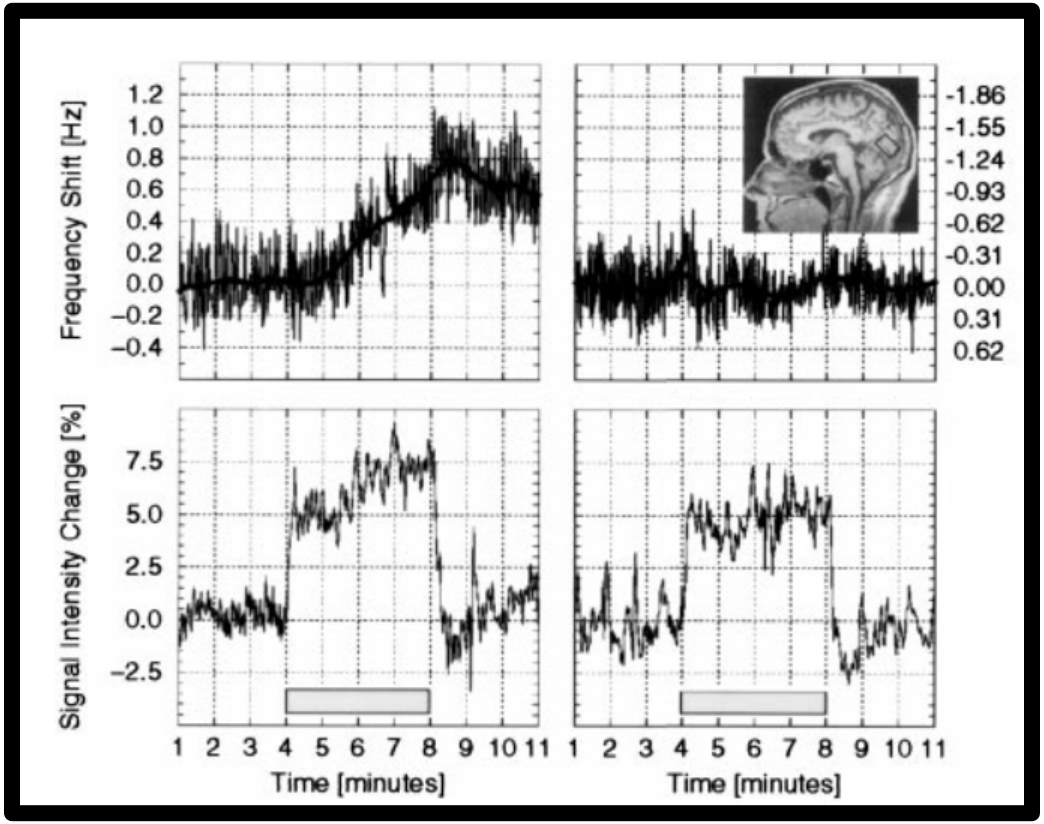
D. Le Bihan, et al Proceedings of the National Academy of Sciences of the United States of America 103 (21), pp. 8263-8268

K. Miller, et al Proceedings of the National Academy of Sciences of the United States of America 104 (52), pp. 20967-20972

Contrasts other than BOLD

- Perfusion (IVIM)
- Volume (gadolinium)
- Volume (fuyrmoxotol)
- Perfusion (ASL)
- $\Delta CMRO_2$
- ΔVolume (VASO)
- Neuronal Currents
- Proton density? (SEEP)
- Diffusion coefficient
- Temperature
- Elastography
- Metabolic Contrasts

The frequency of the MR signal of water depends on temperature and changes with a coefficient of about 0.01 ppm / degree C



Yablonskiy, D. A., J. J. H. Ackerman, et al. (2000). "Coupling between changes in human brain temperature and oxidative metabolism during prolonged visual stimulation." Proceedings of the National Academy of Sciences of the United States of America 97(13): 7603-7608

Contrasts other than BOLD

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- Volume (gadolinium)
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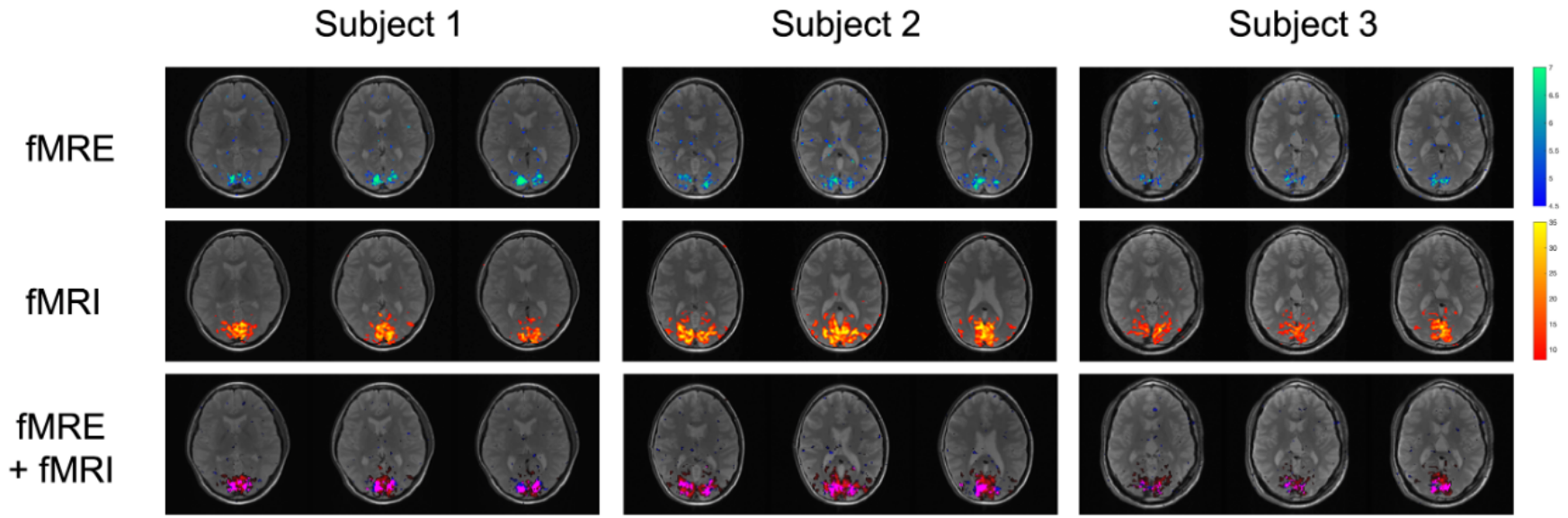
- Perfusion (ASL)
- $\Delta CMRO_2$
- ΔVolume (VASO)
- Neuronal Currents
- Proton density? SEEP
- Diffusion coefficient
- Temperature
- Elastography
- Metabolic Contrasts

Increases in Stiffness…

ISMRM 2019

Simultaneous fMRE and fMRI measures the viscoelastic and BOLD responses of the human brain to functional activation in the visual cortex

Patricia S. Lan[1], Kevin J. Glaser[2], Richard L. Ehman[2], and Gary H. Glover[3]



Increases in Stiffness for slow on/off

Decreases in Stiffness for fast on/off

ISMRM 2019

Spatial-temporal dynamics of the visual cortex stiffness driven by a flashing checkerboard stimulus

Jose de Arcos[1], Daniel Fovargue[1], Radhouene Neji[2], Sam Patz[3], and Ralph Sinkus[4]

36 second on / 36 sec off: Increase in shear modulus of 0.37kPA

hemodynamic effect

840ms on / 840ms off: Decrease in shear modulus of 0.4kPA

"One potential mechanism is water influx after ionic changes that translates cellular osmotic pressure into hydrostatic pressure."

Contrasts other than BOLD

- Perfusion (IVIM)
- Volume (gadolinium)
- Volume (fuyrmoxotol)
- Perfusion (ASL)
- $\Delta CMRO_2$
- ΔVolume (VASO)
- Neuronal Currents
- Proton density? SEEP
- Diffusion coefficient
- Temperature
- Elastography
- Metabolic Contrasts

frontiers in Psychiatry

Front Psychiatry. 2018; 9: 76.
Published online 2018 Mar 12. doi: 10.3389/fpsyt.2018.00076

PMCID: PMC5857528
PMID: 29593585

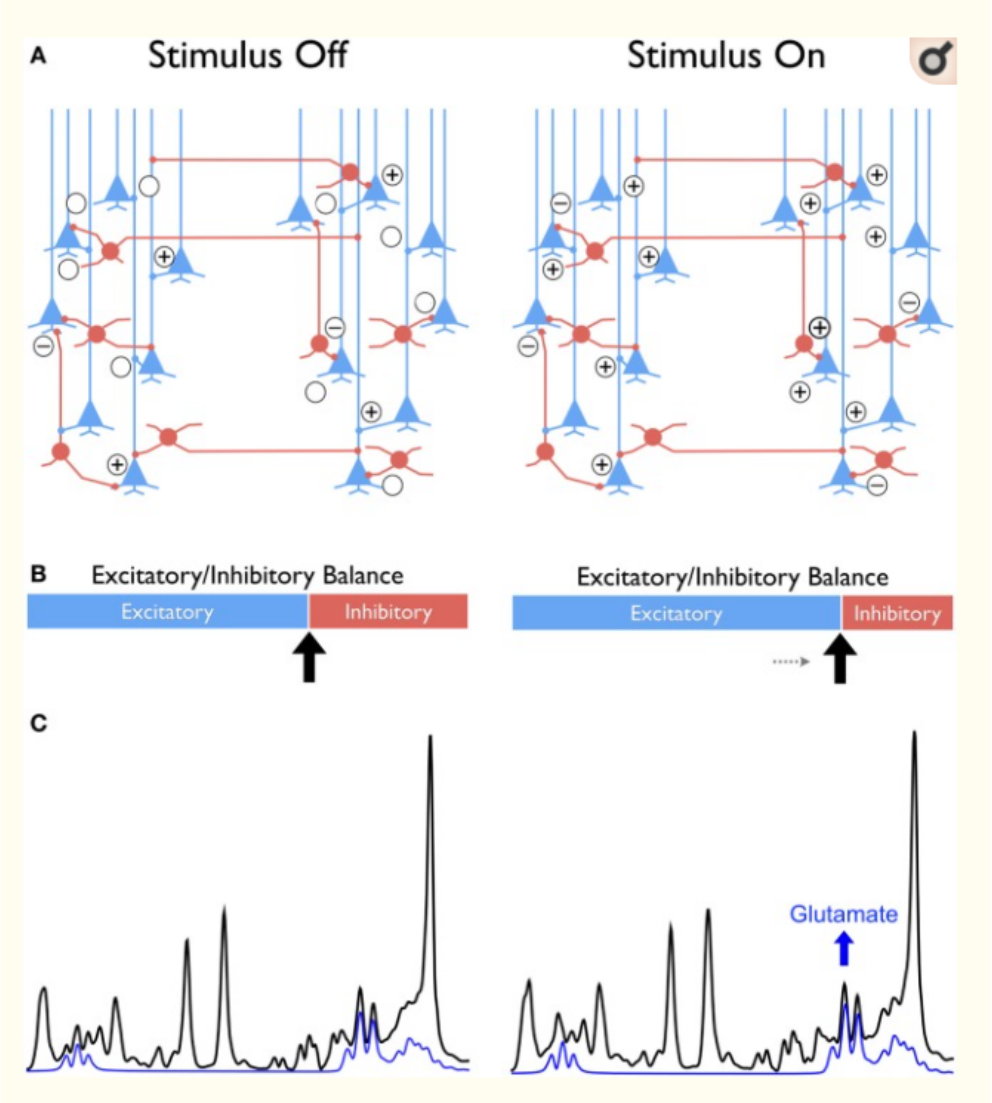
Functional Magnetic Resonance Spectroscopy: The "New" MRS for Cognitive Neuroscience and Psychiatry Research

Jeffrey A. Stanley[1,*] and Naftali Raz[2,3,4]

▸ Author information ▸ Article notes ▸ Copyright and License information Disclaimer

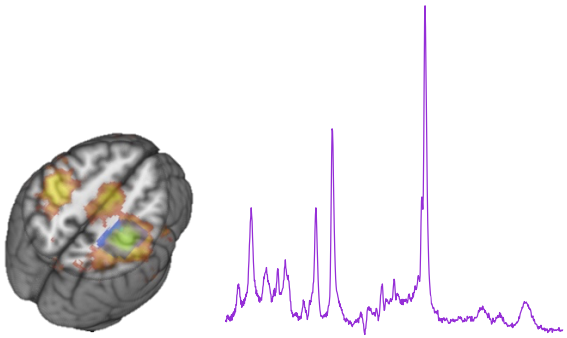
Imaging of glutamate and γ-aminobutyric acid (GABA)

80% neurons excitatory (Glutamate is neurotransmitter)
20% neurons inhibitory (GABA is neurotransmitter)



7T Combined fMRI-fMRS Multiscale Investigation of the Motor Cortex during Active and Resting States

Jacob M. Levenstein, University of Oxford / NIH
PhD Supervisors:
Prof. Charlotte J. Stagg, University of Oxford
Dr. Peter Bandettini, National Institutes of Health

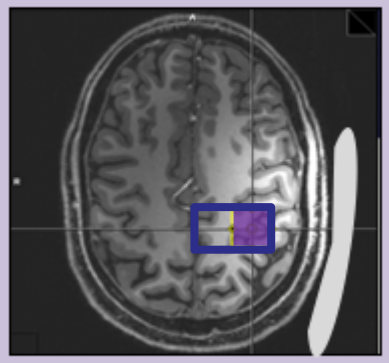


Poster and Contact information:
Poster: M407
Abstract ID: 1845
Email: Jacob.Levenstein@ndm.oc.ac.uk

NIH Oxford-Cambridge Scholars Program

Functional Magnetic Resonance Spectroscopy + fMRI

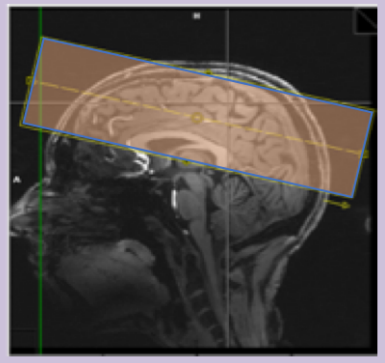
MRS Positioning,
Left hand knob, 2cm^3



Sequence: Semi-LASER
(TE = 36ms)

+

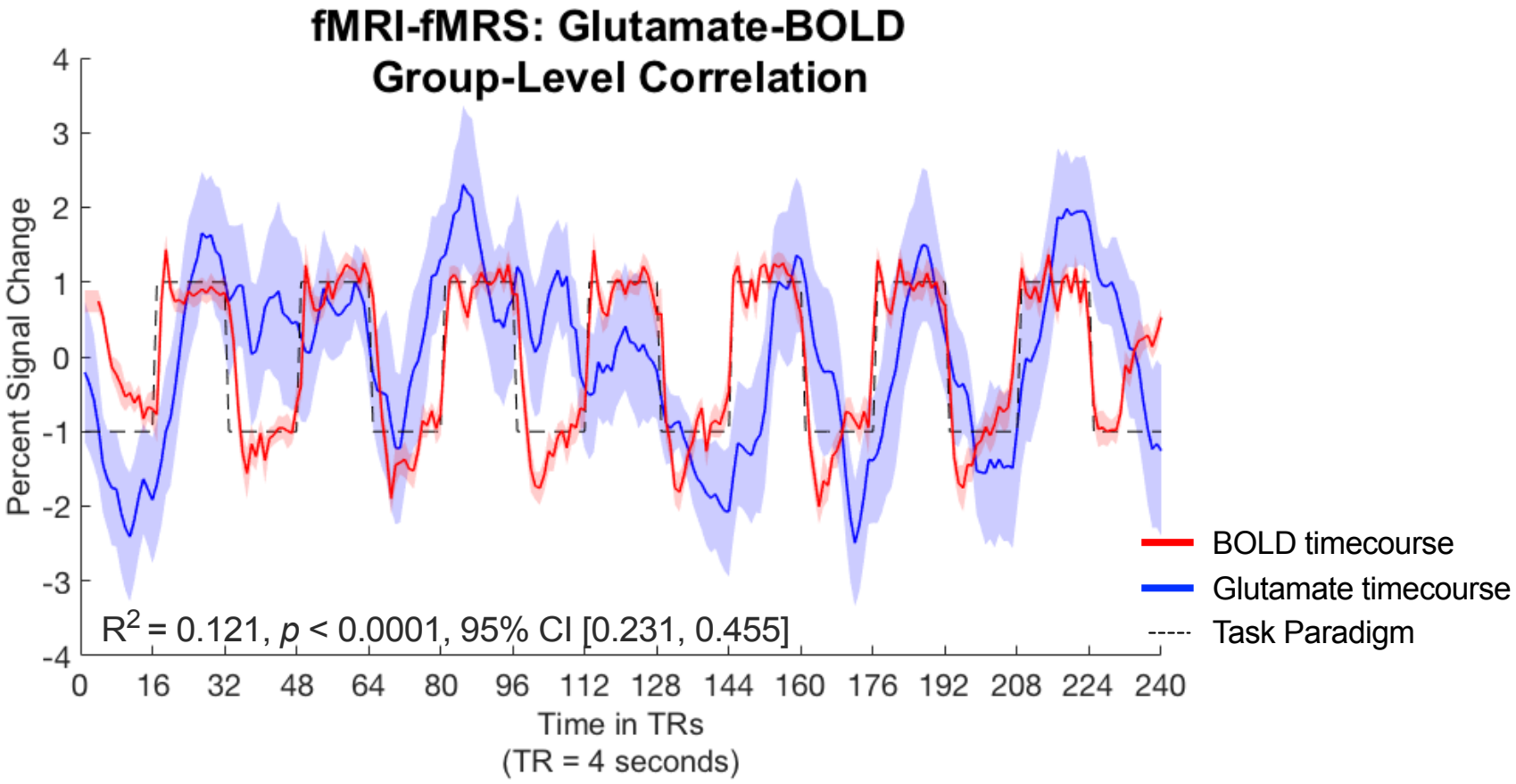
Limited FOV
Voxel size 4.3mm^3



Sequence: 3D EPI
(TR = 40ms, TE = 25ms)

Collective TR = 4 seconds

Adjust Volume = Green
40mm x 20mm x 20mm



Possible delay in depletion of glutamate pool

Contrasts other than BOLD

- Perfusion (IVIM)
- Volume (gadolinium)
- Volume (fuyrmoxotol)
- Perfusion (ASL)
- $\Delta CMRO_2$
- ΔVolume (VASO)
- Neuronal Currents
- Proton density? (SEEP)
- Diffusion coefficient
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- Elastography
- Metabolic Contrasts