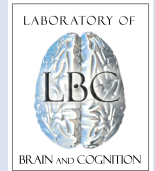


Layer specific fMRI: Limits, I am struggling with

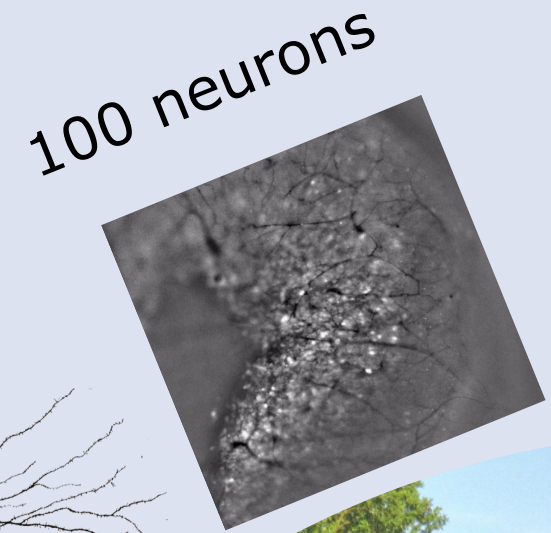
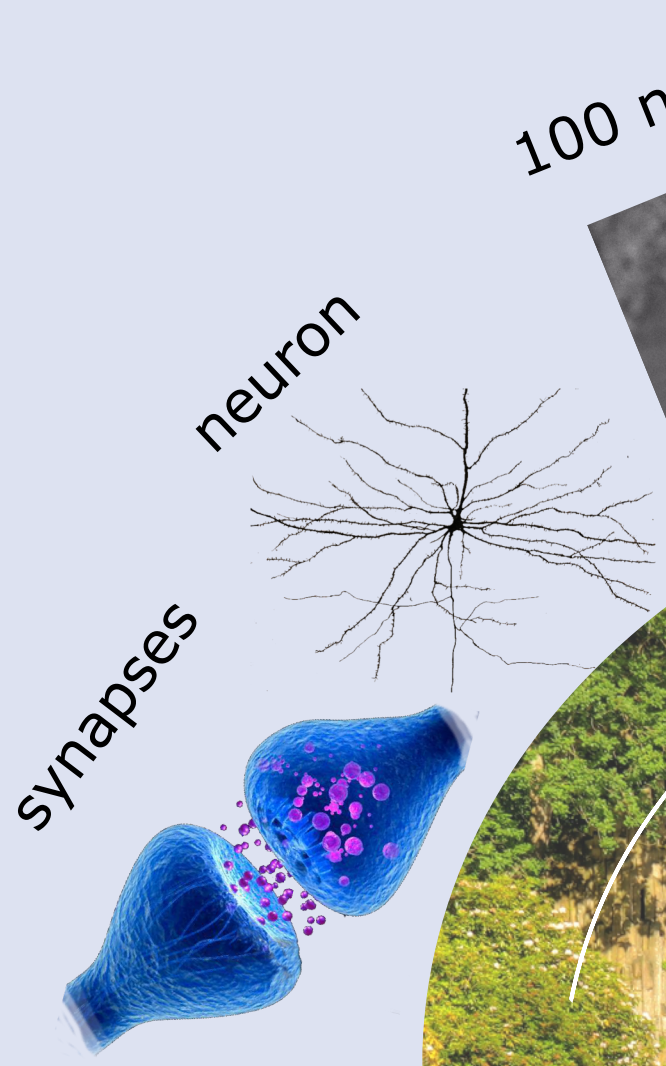
Renzo (Laurentius) Huber



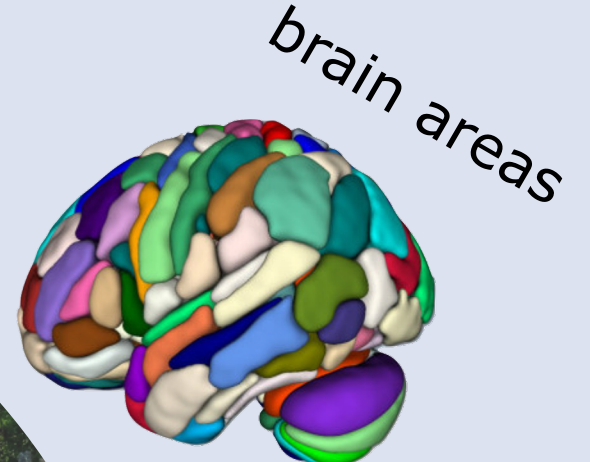
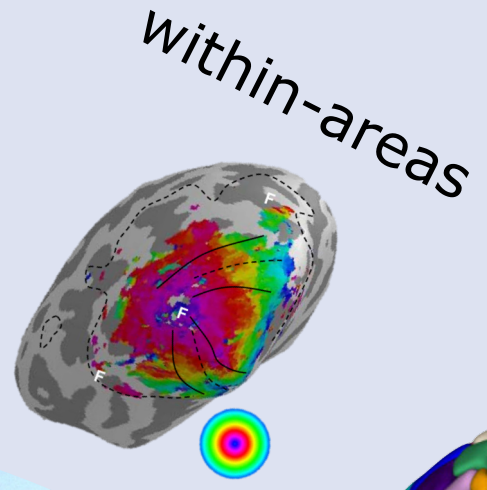
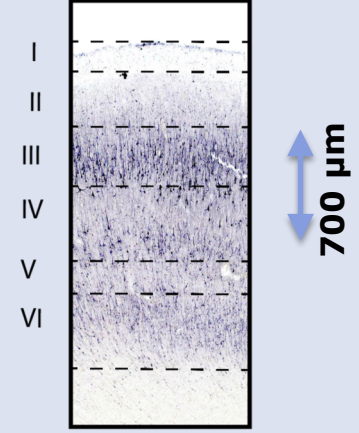
SFIM, NIMH, Bethesda, MD, United States
under Peter Bandettini

July 27th 2018

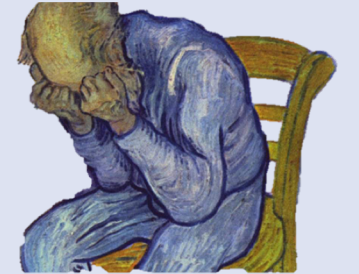
Spatial scales in neuroscience



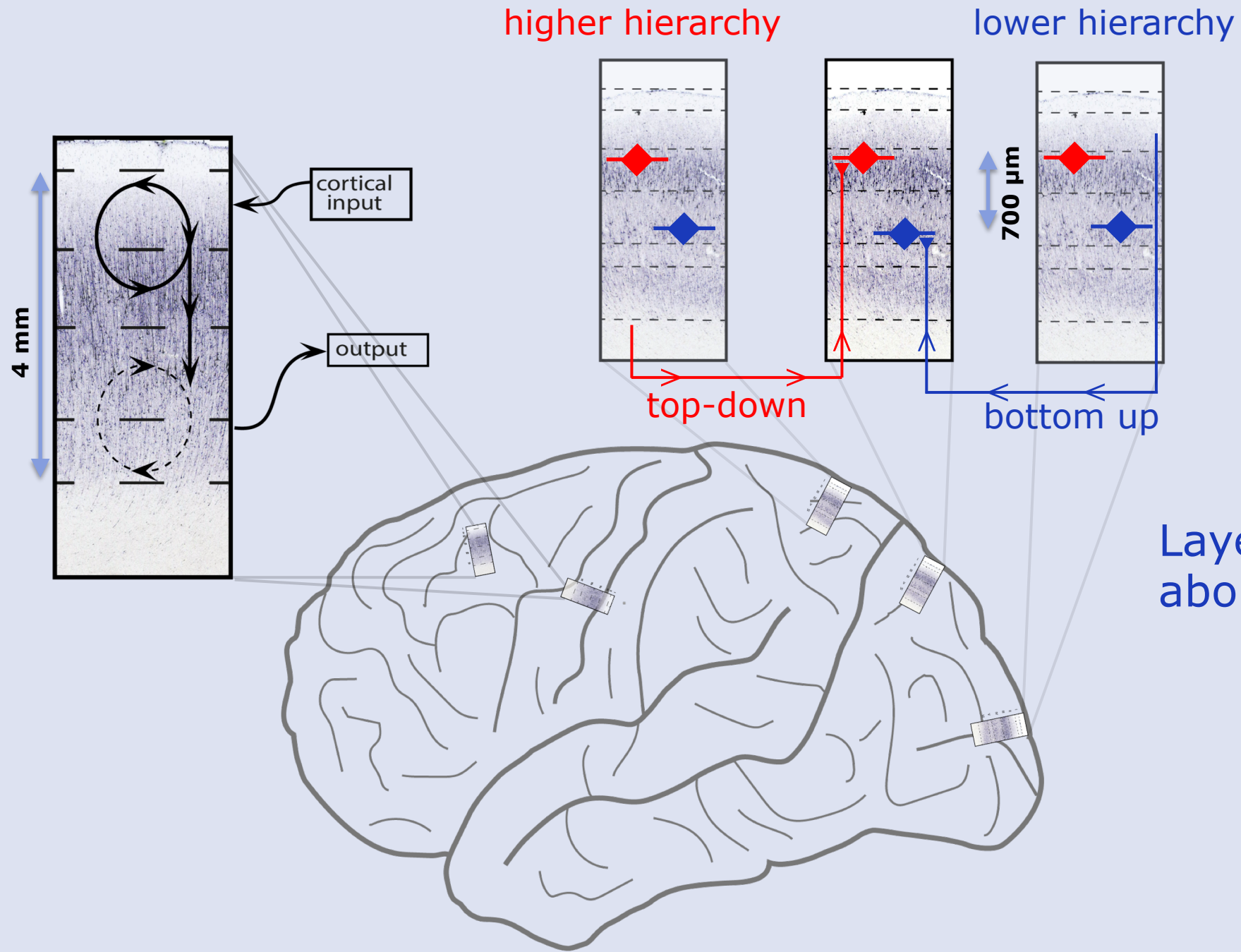
layers & columns



behavior



bridge metaphor idea from Eric Wong and Bruce Rosen

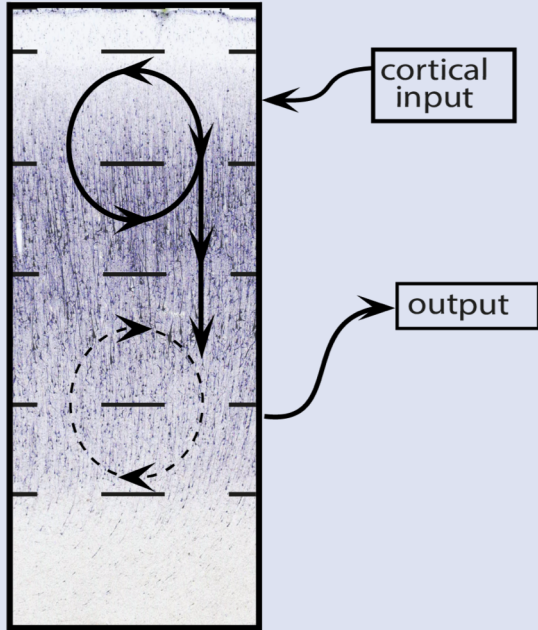


Layers provide information about directionality

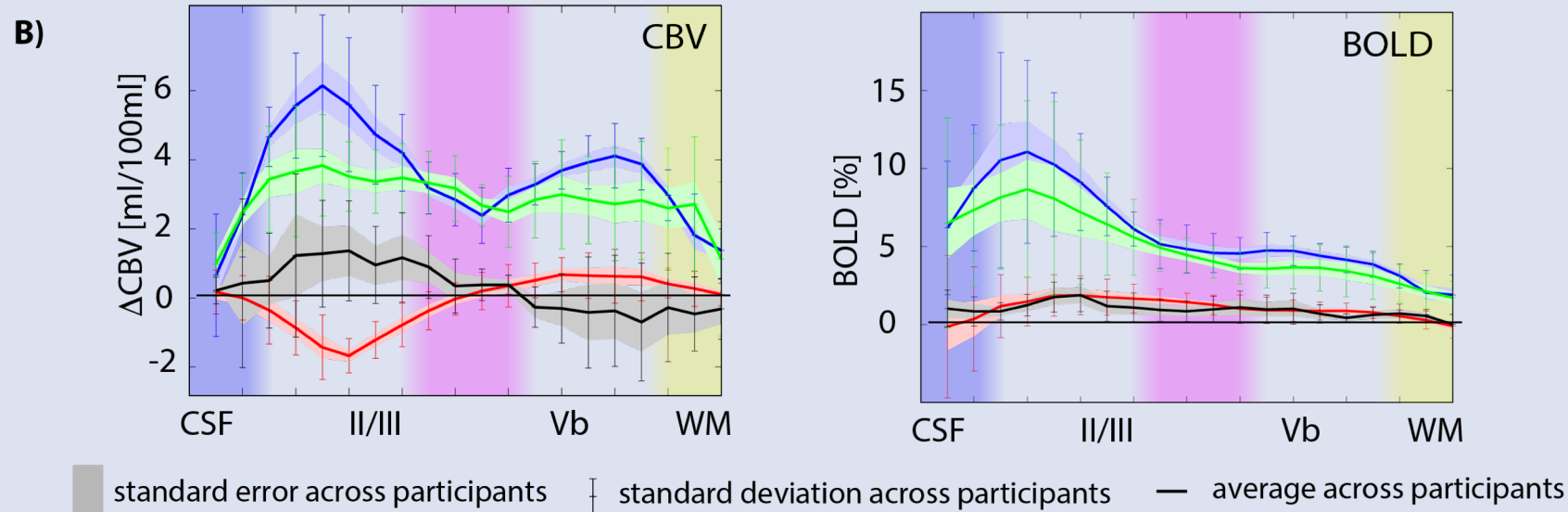
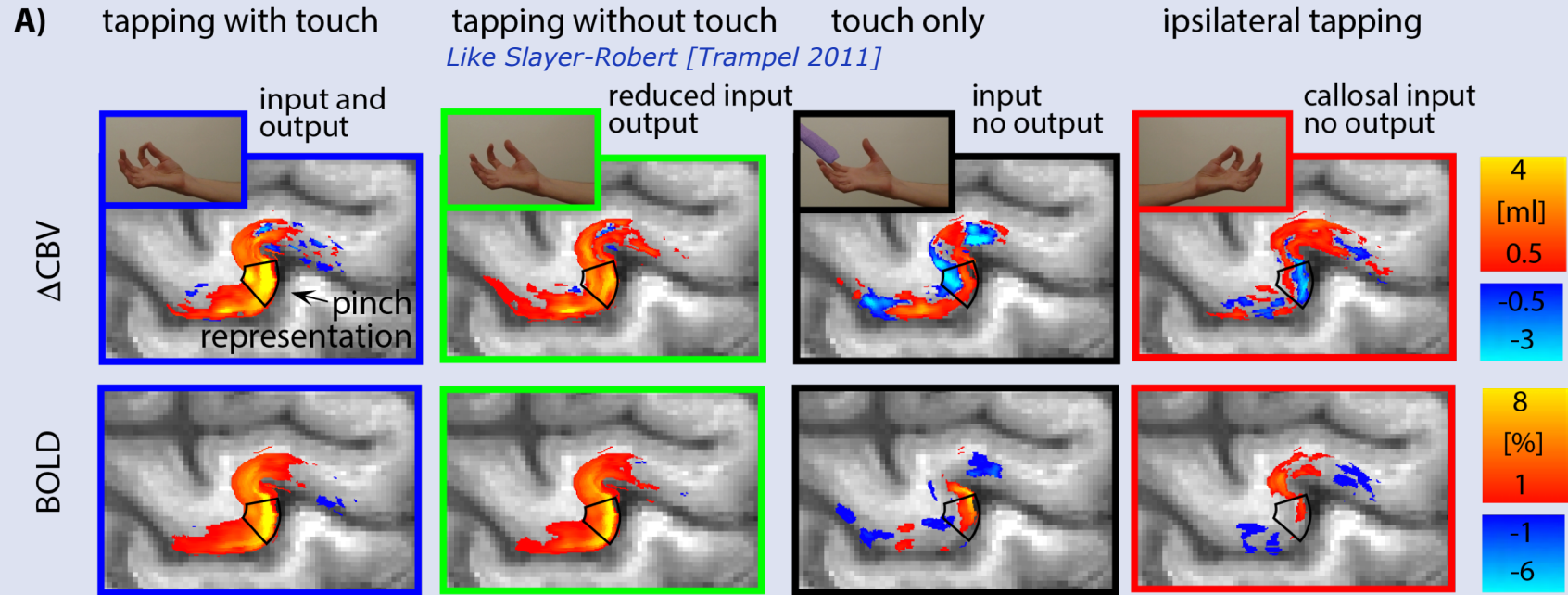
Hierarchical connectivity:
Felleman and Van Essen 1991

Input-output connectivity:
Goldman-Rakic et al. 1996
Pappale and Hooks 2017

Input vs. output in M1



N=9 participants

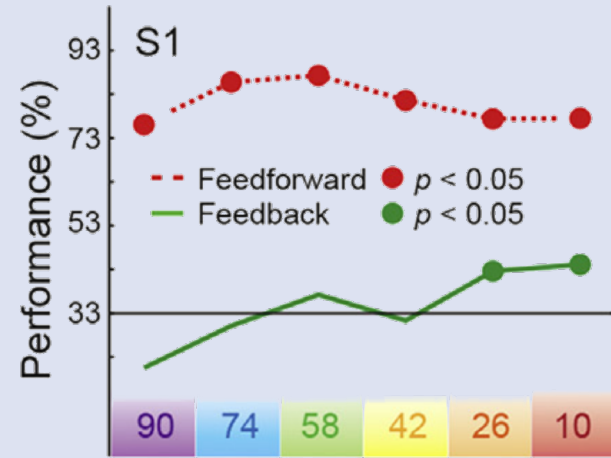


[Weiler, et al., 2008; Papale and Hooks, 2017, Mao, 2011]

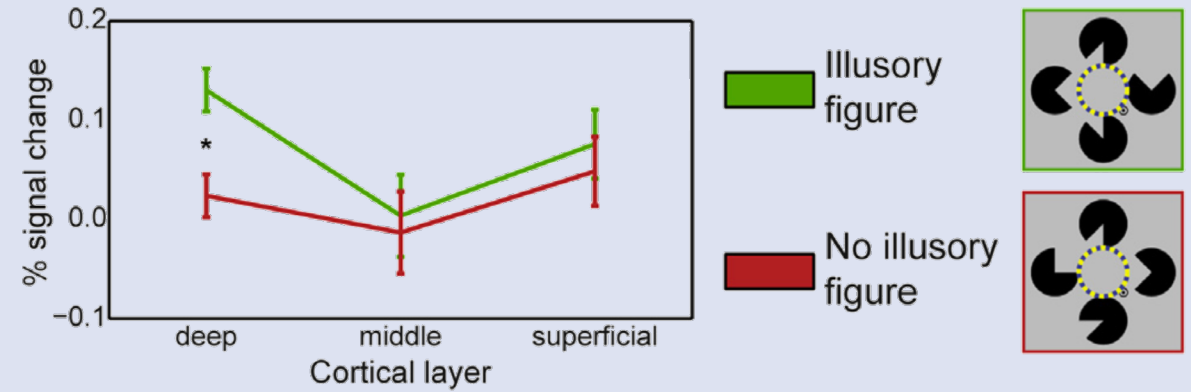
[Huber et al., Neuron, 2017]

Layer fMRI in visual cortex

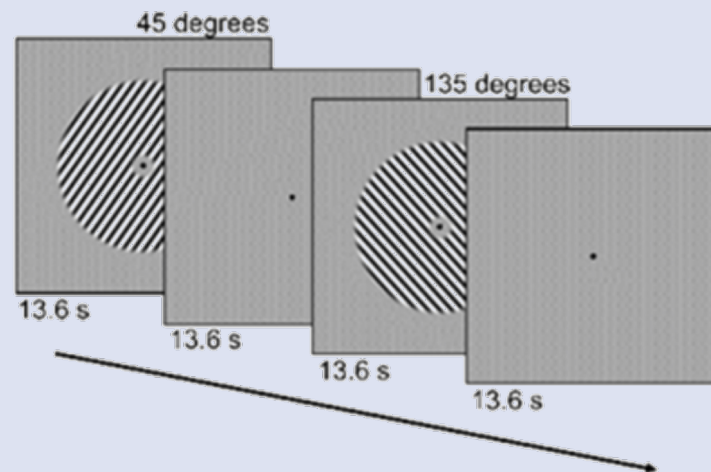
Muckli, Curr Biol, 2015



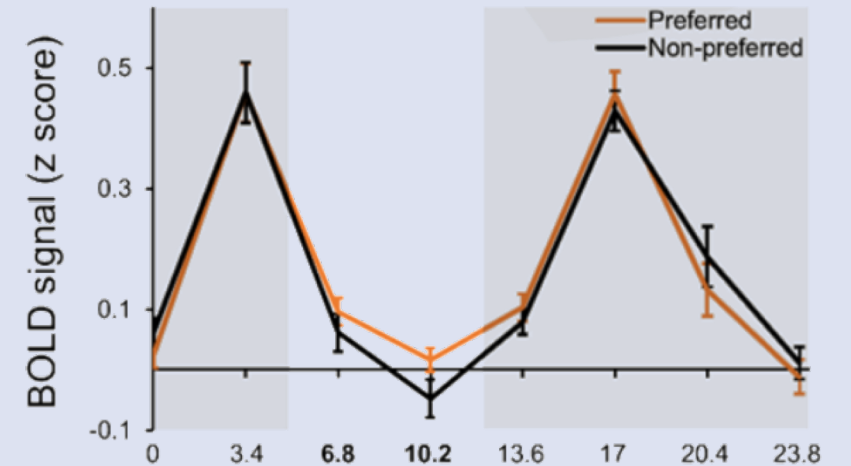
Kok, Curr Biol, 2015



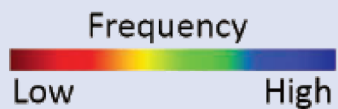
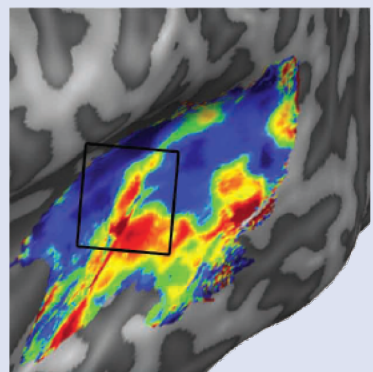
Lawrence et al., 2018



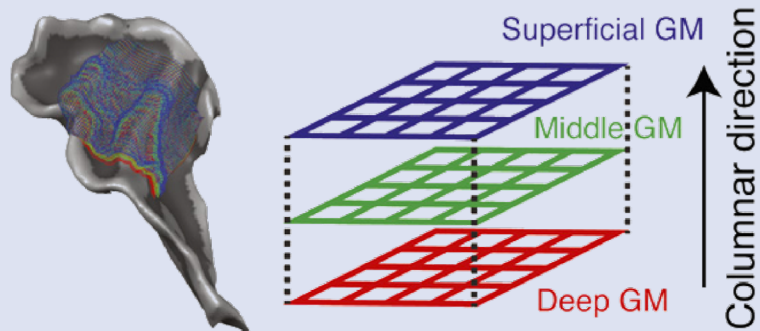
V1



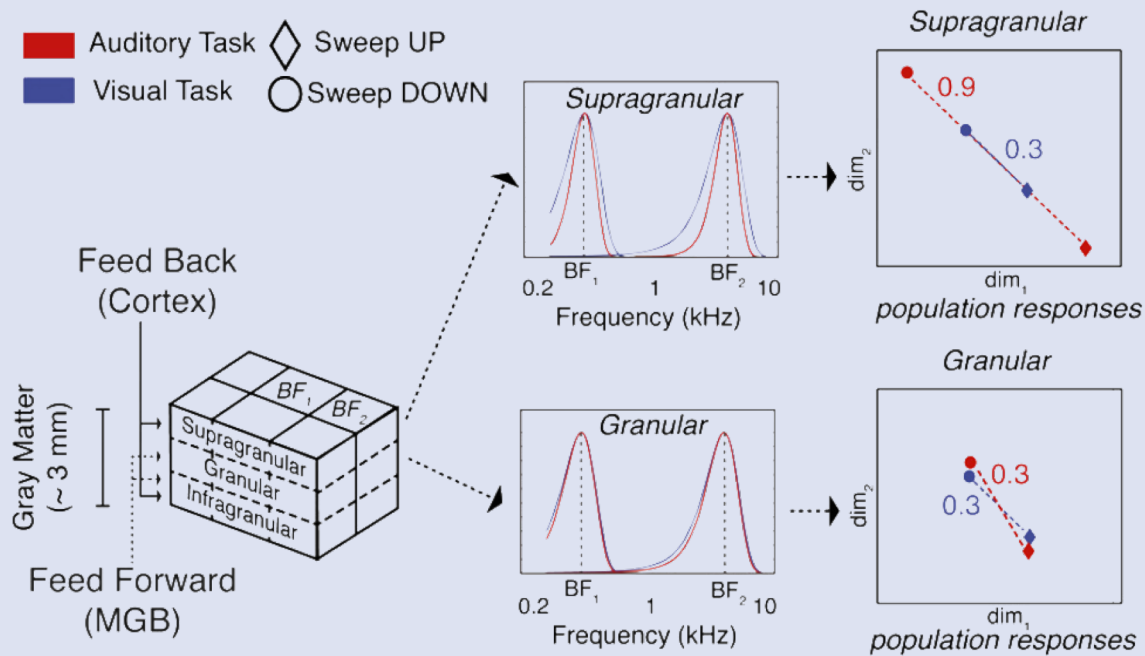
Layer fMRI in auditory cortex



Moerel et al., 2014

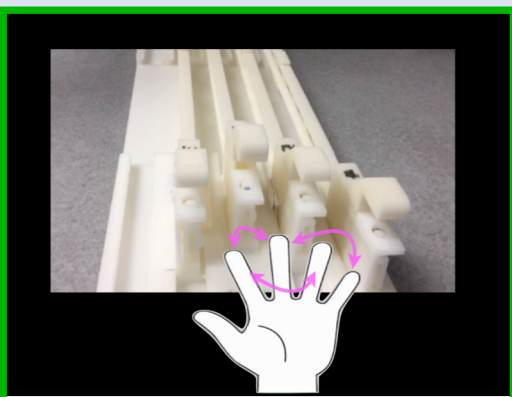
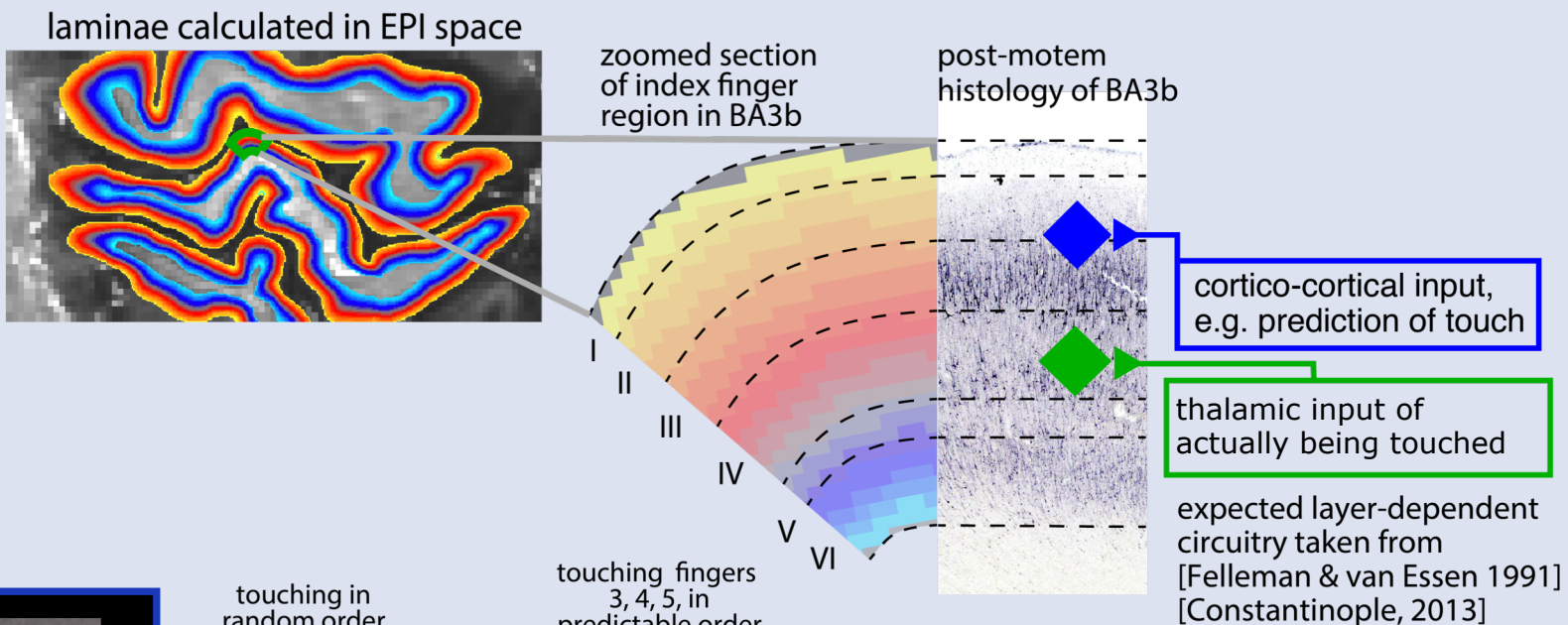


De Martino et al., 2015



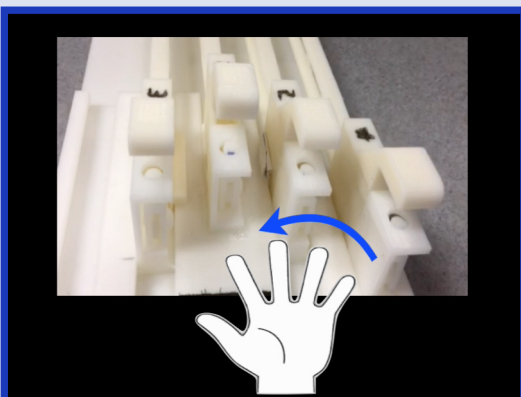
Layer-fMRI in somatosensory cortex

In collaboration with **Yinghua Yu**



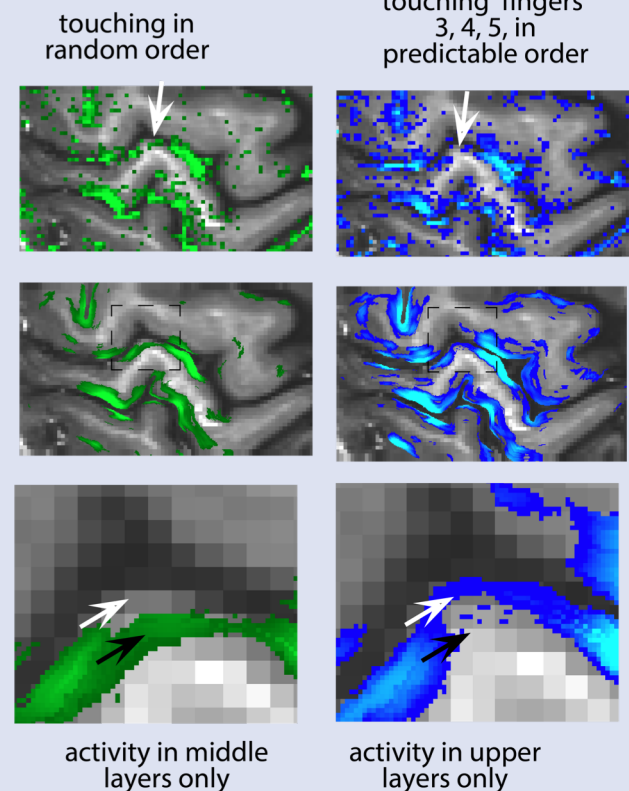
random touching of all fingers

index finger is touched (unexpectedly)

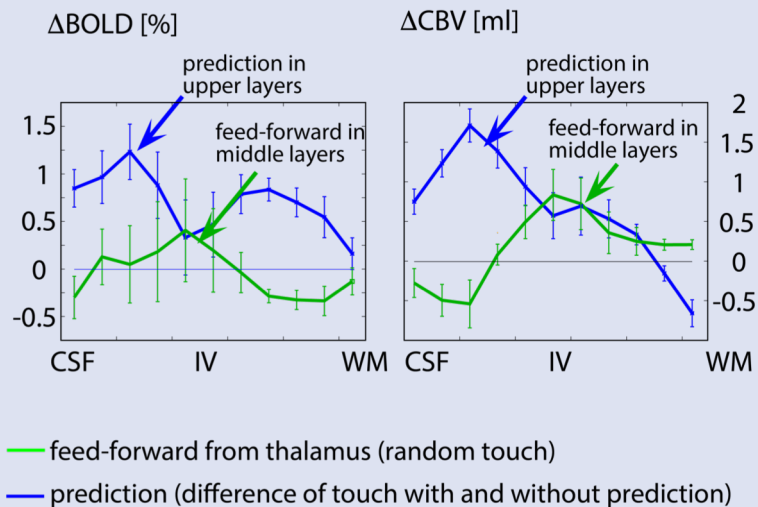


touching sequence of fingers 3,4,5

index finger is expected to be touched only



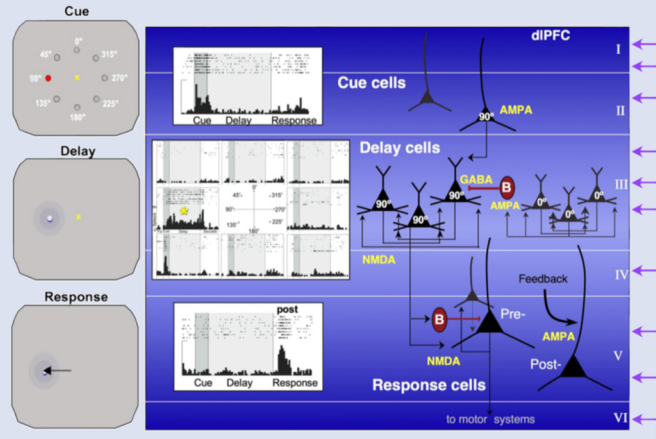
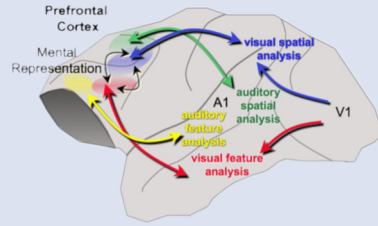
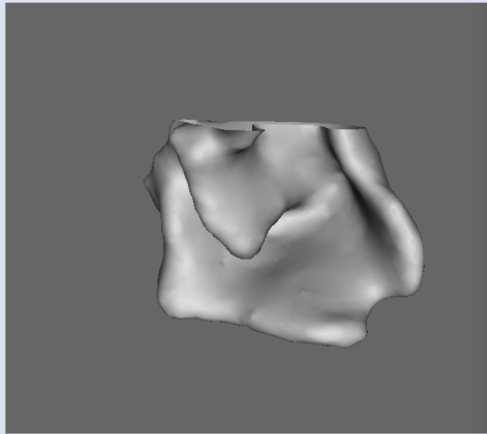
N=6 participants



Layer fMRI in cognitive area DLPFC

In collaboration with **Emily Finn**

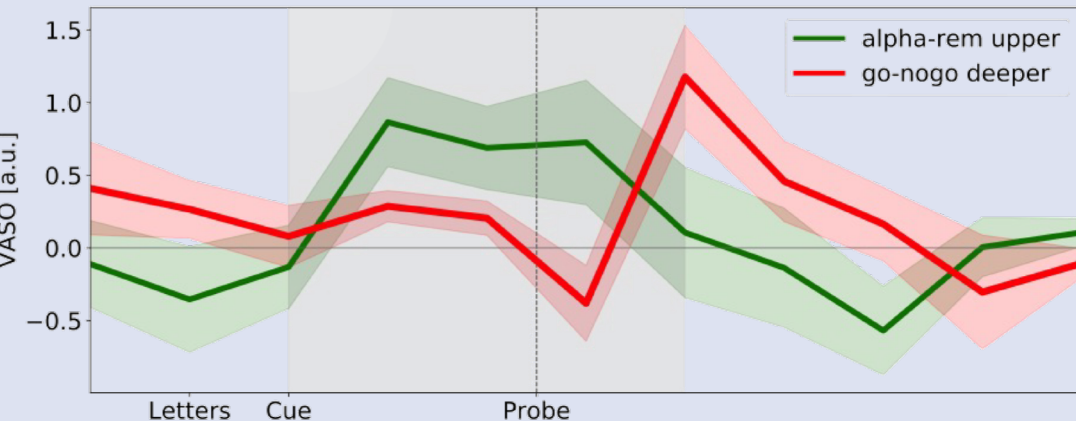
geometry



[Goldman-Rakic et al., 1996] [Arnseten 2012, Neuron]

N = 6 participants

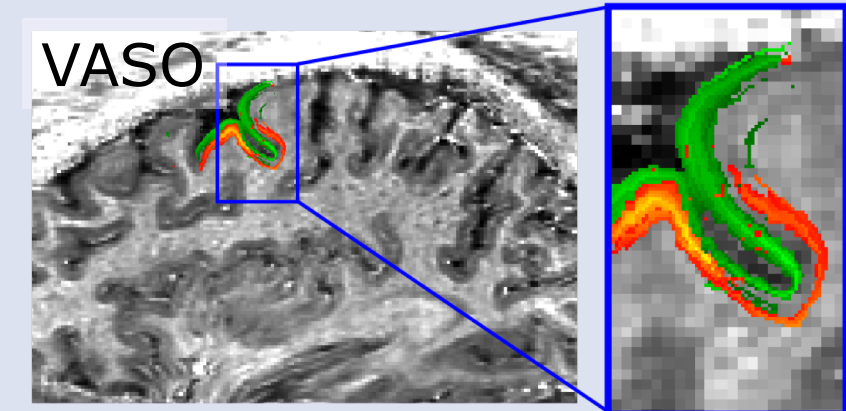
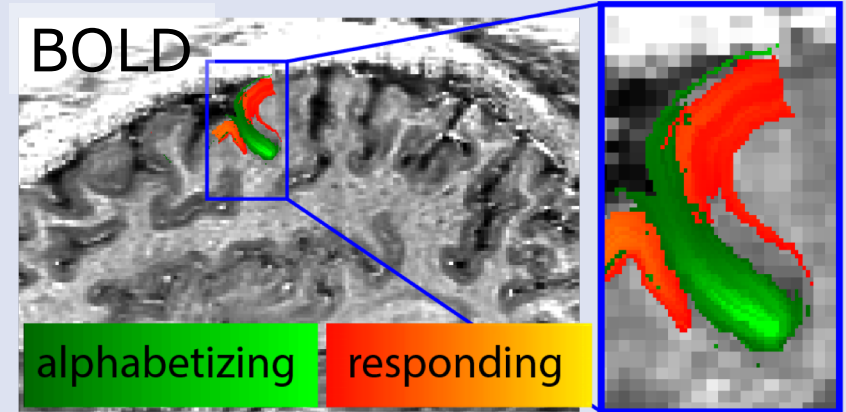
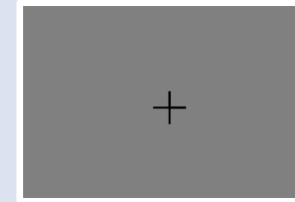
Delay Response



Task:

~~alphabetize~~

[D'Esposito et al., 1999]

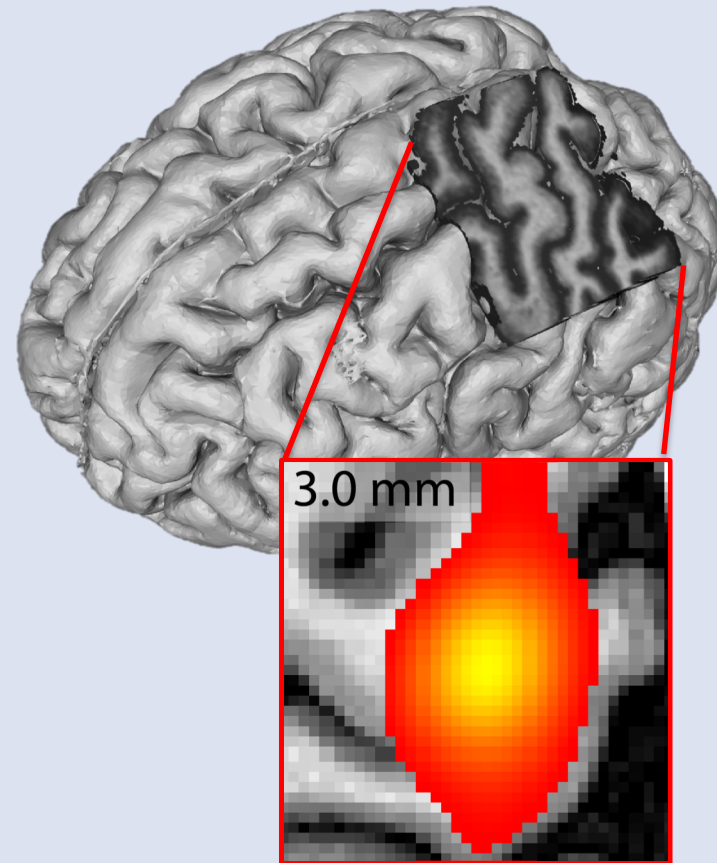


7T, 32ch.
Nova,
Inpl. resol.
0.79mm,
pF = 6/8,
24 slices

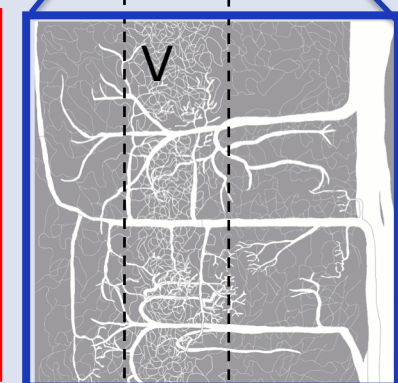
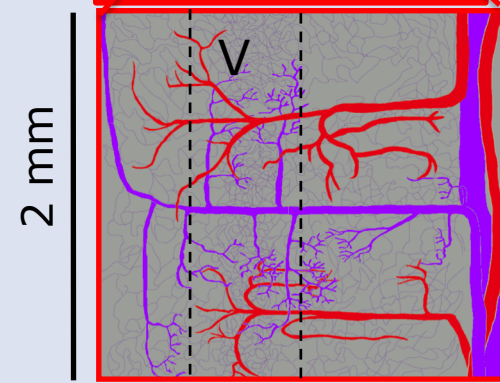
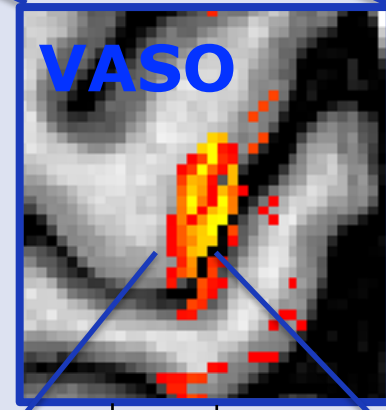
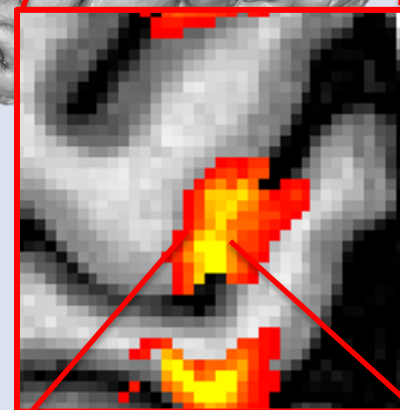
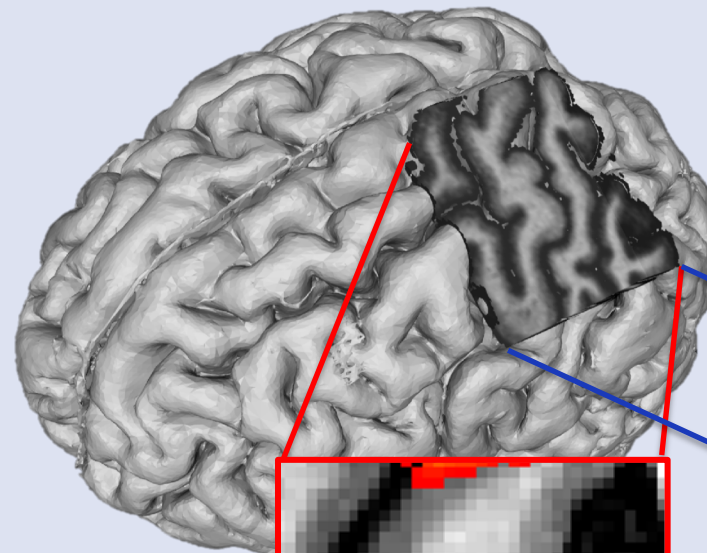
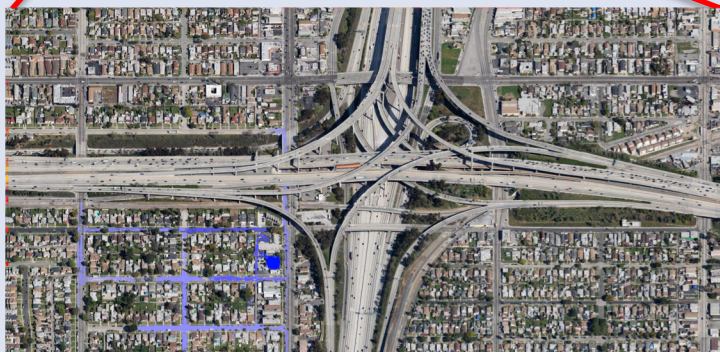
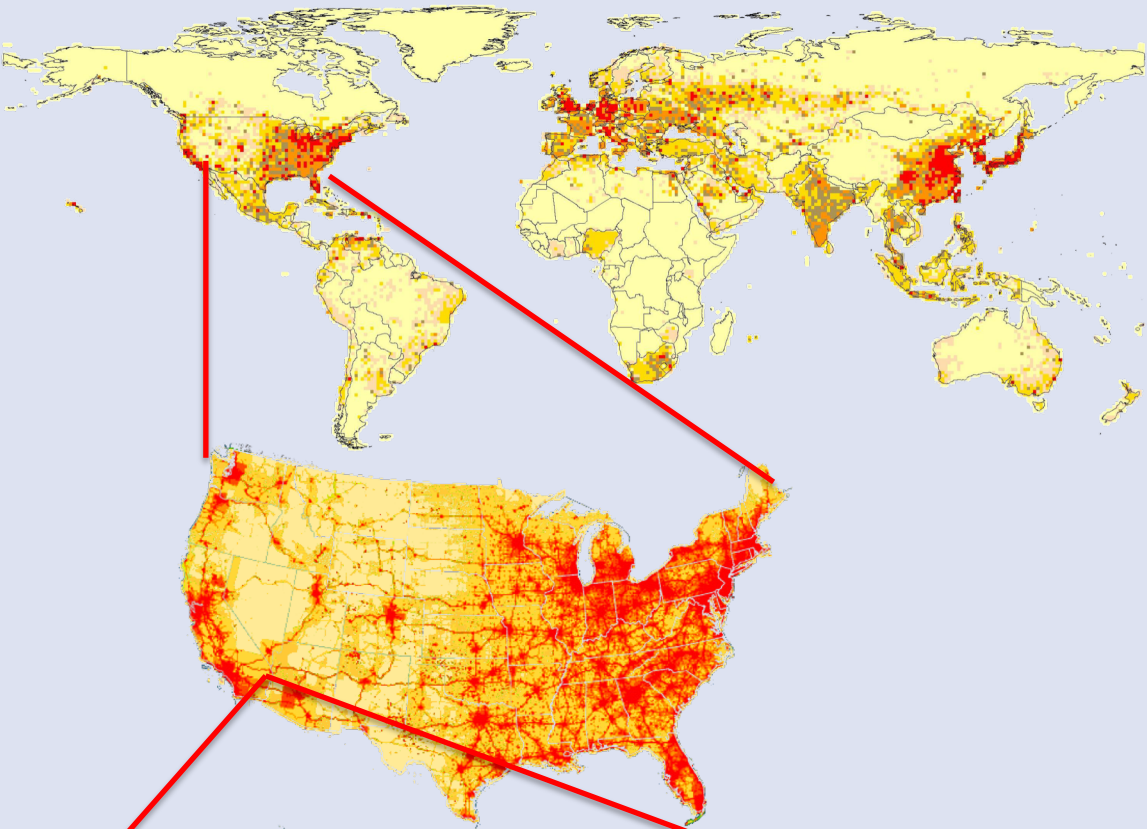
Limits of layer fMRI

- Localization specificity limits
- Calibrating “cortical depths” to “cortical layers”
- Anatomically meaning full estimation of cortical depth
- Statistical interpretation
- HRF modeling
- Signal leakage across layers
- Cortical thickness
- Columnar variability
- Coverage
- Inter-subject variability
- Interconnection between layers
- Future challenges

Challenge #1: Specificity

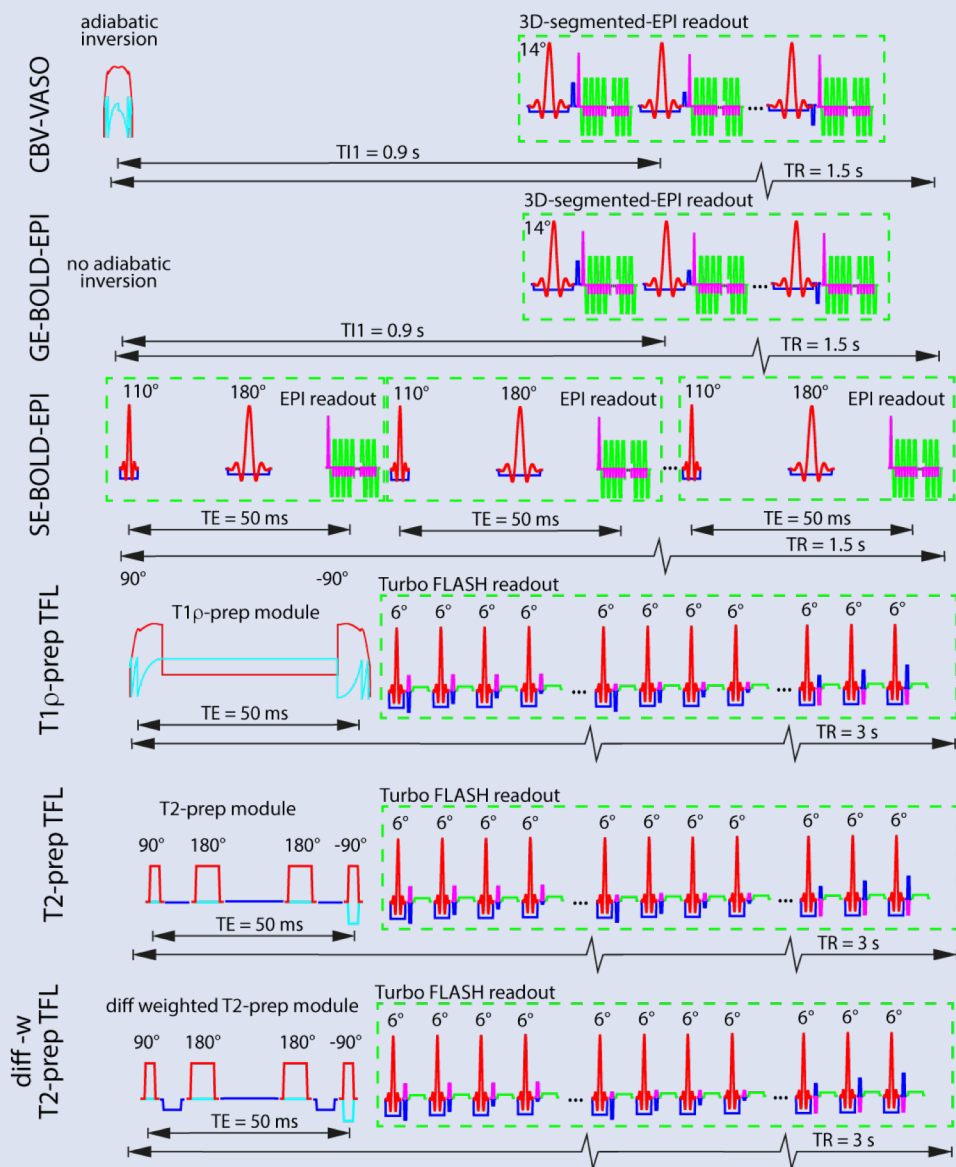


Specificity

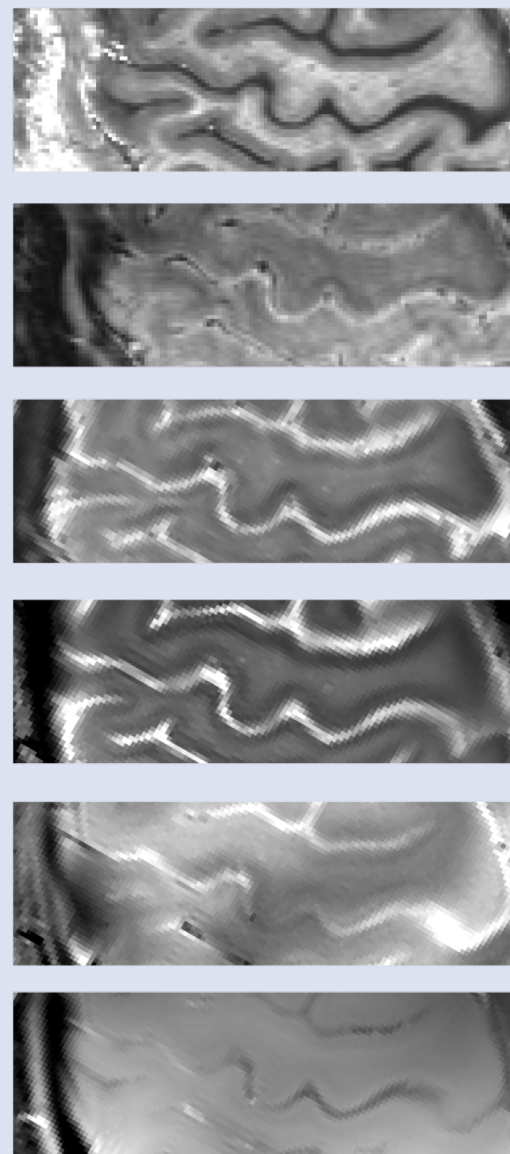


Comparing contrast mechanisms

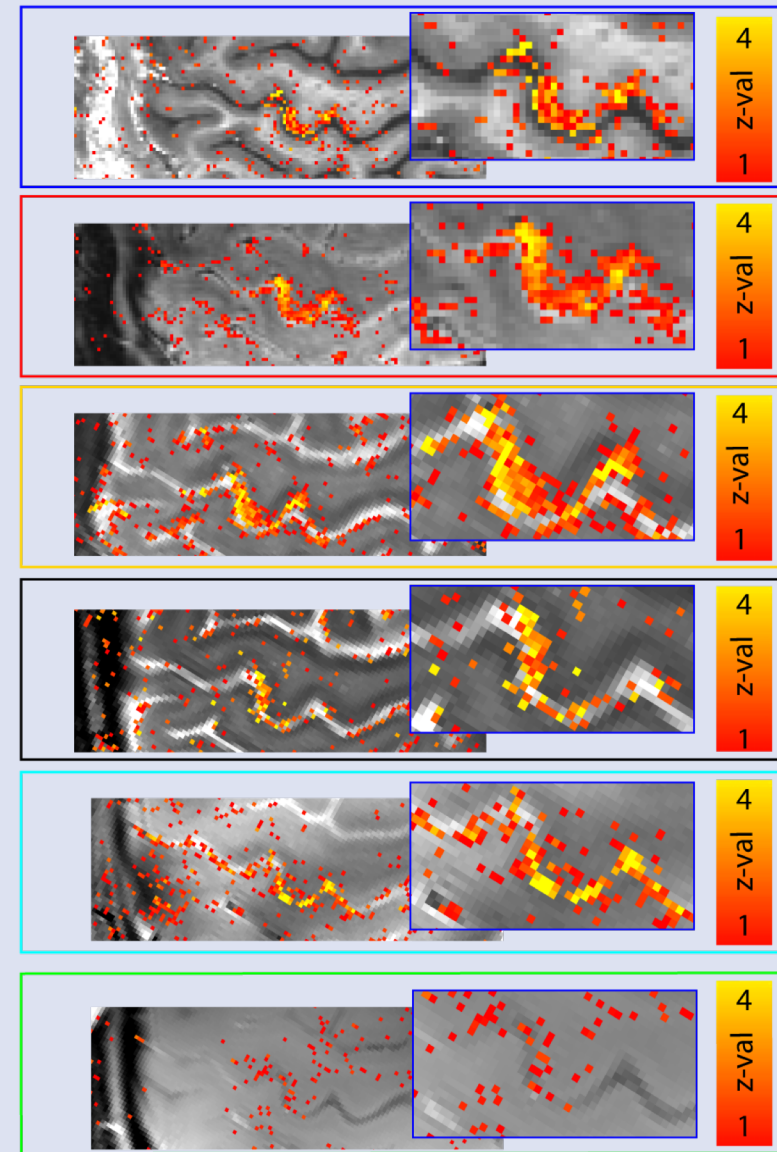
sequence



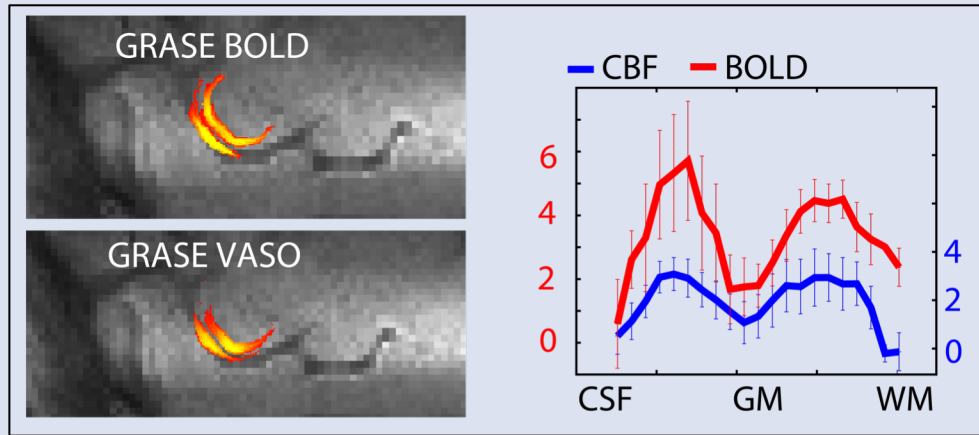
MRI contrast



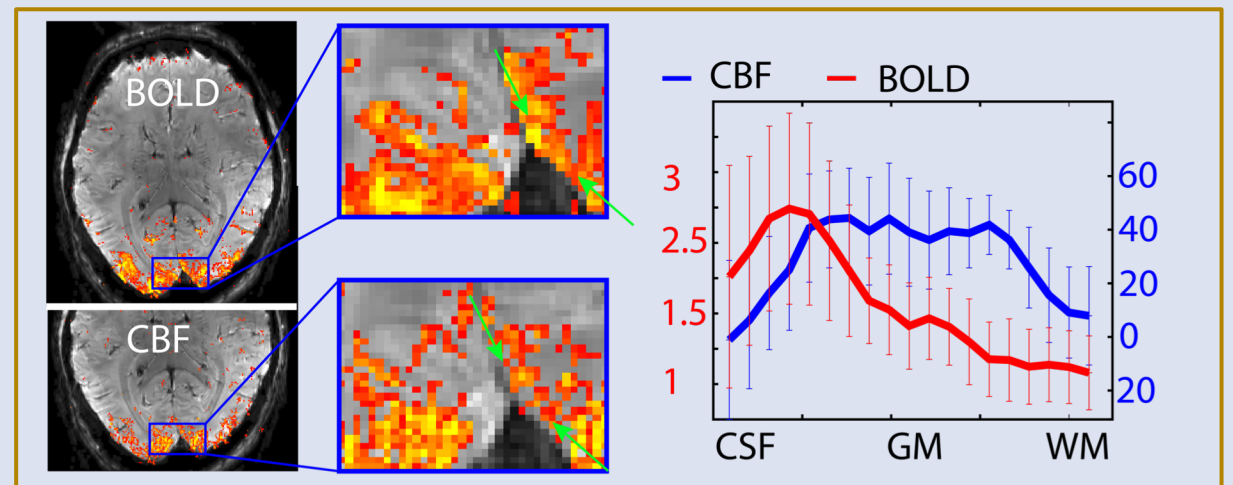
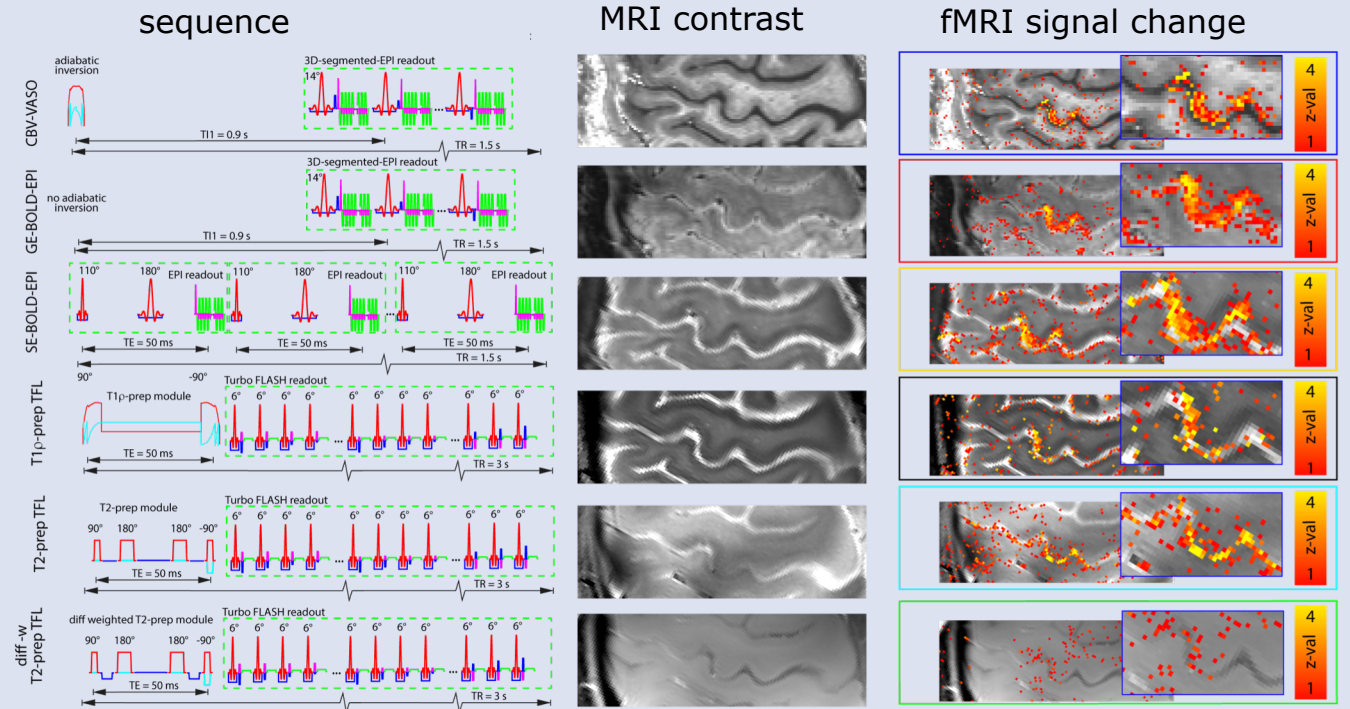
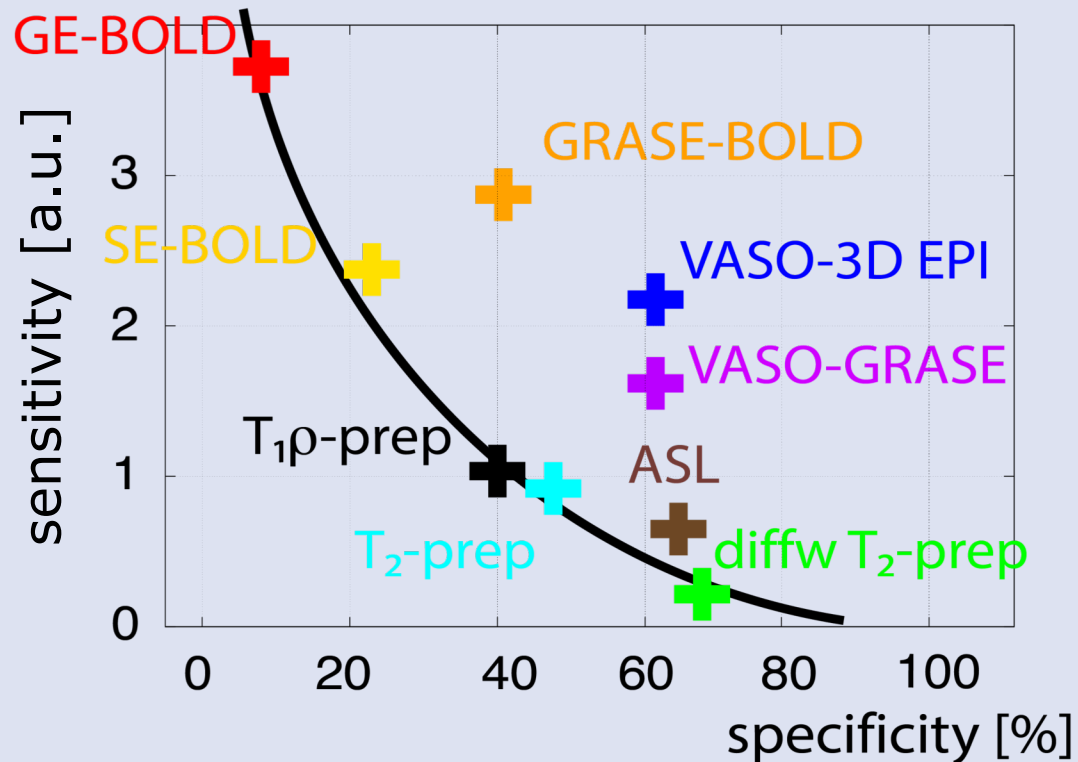
fMRI signal change



Comparing contrast mechanisms



Acquired in collaboration with Tania Dadakova and David Feinberg

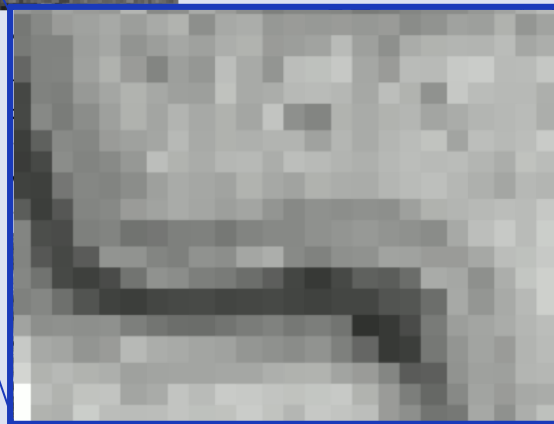
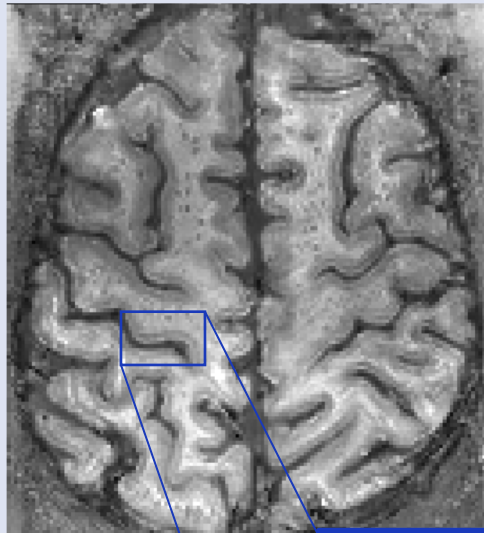


[Huber et al., NeuroImage 2018], acquired from Dimo Ivanov

Limits of layer fMRI

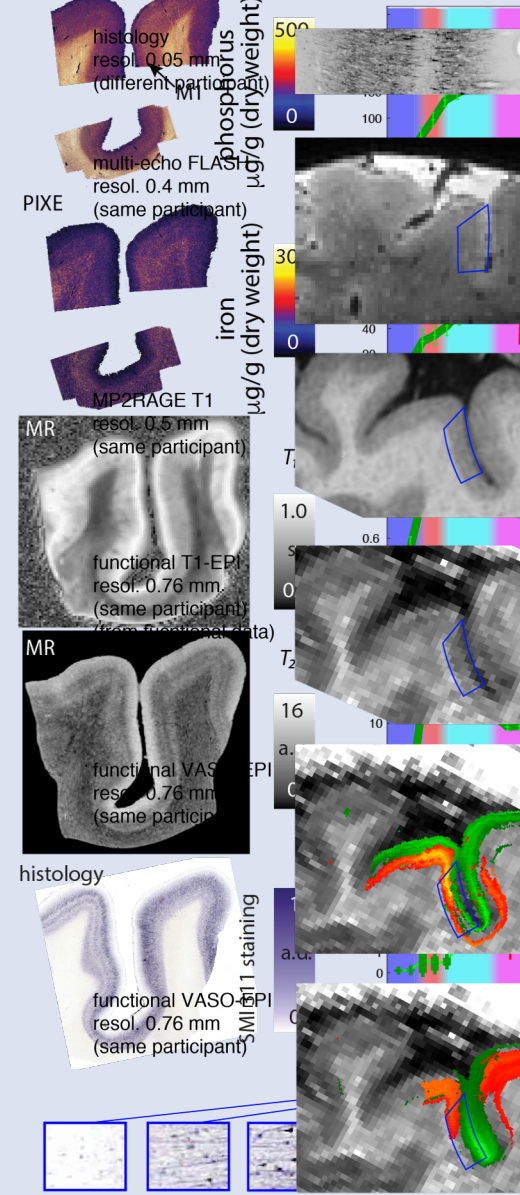
- Localization specificity limits
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Normalizing "depths" to layers



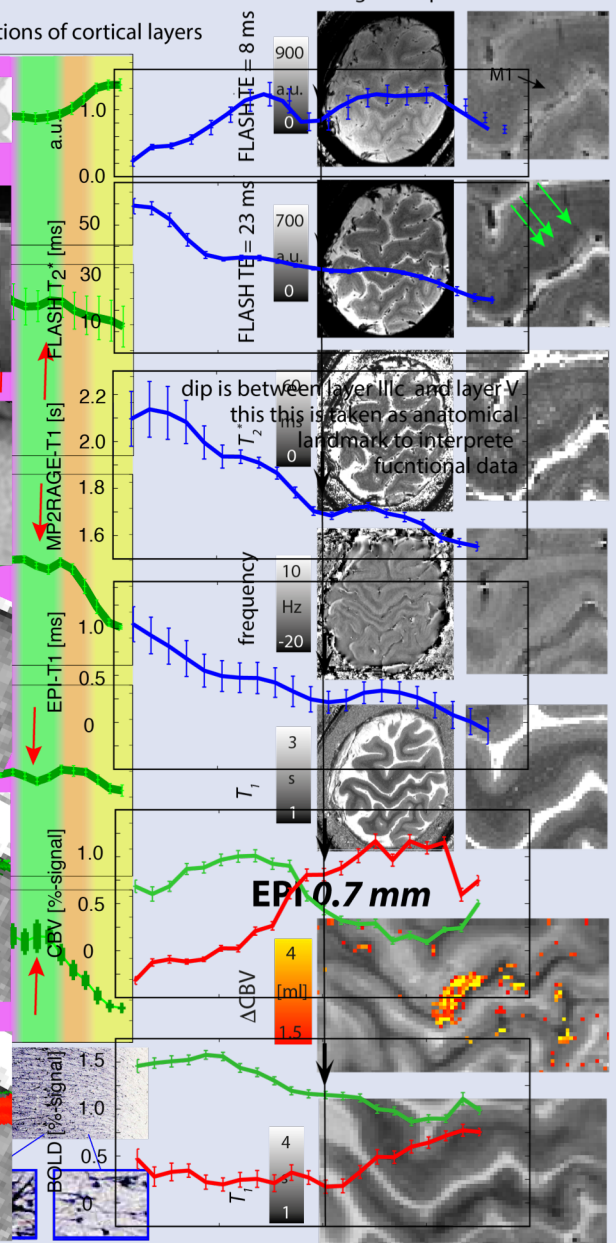
in DLPEC Post Mortem 0.2 mm

PIXE Calibrating position of cortical depth to positions of cortical layers

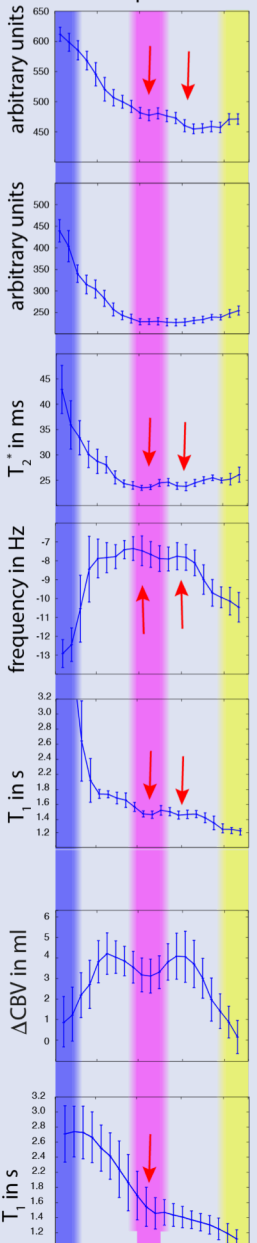


in vivo 0.35 mm

signal map zoomed on M1



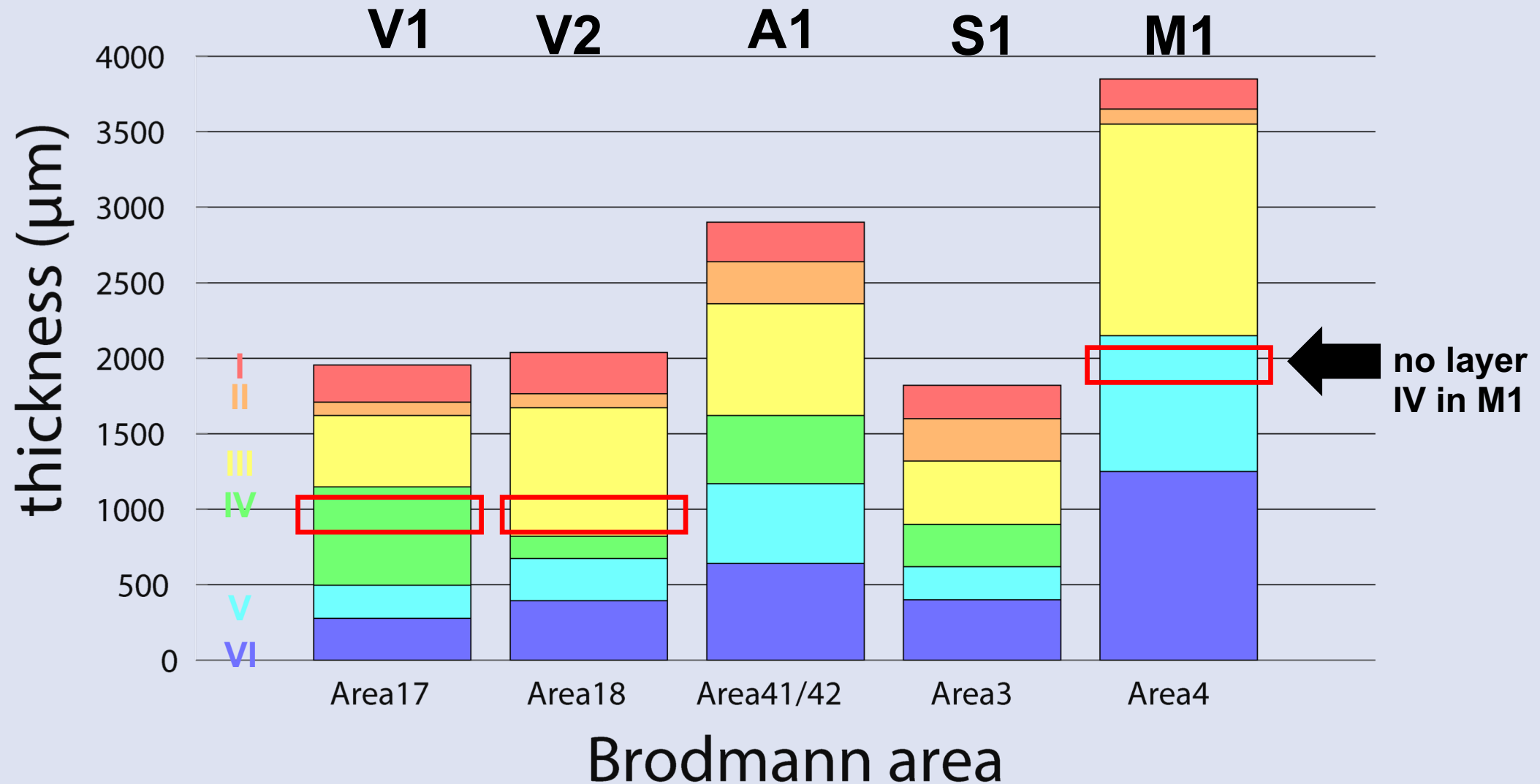
cortical profiles



CSF I II III Va Vb VI WM
area of interest that is co-registered across the different contrasts in the same participant
arrow points to the border between "superficial" and "deeper" layers
[Hubel et al., *Neuron*, 2017, a collaboration with Carsten Stueber, Cornell]

Varying thickness and position of cortical layers across areas

slide curtesy from Jonathan Polimeni

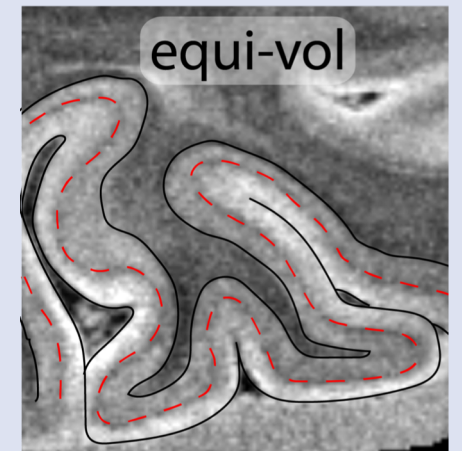
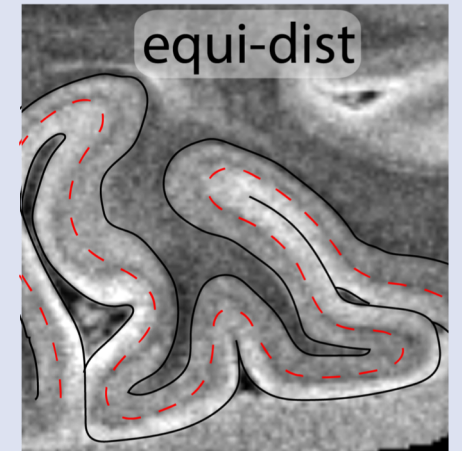
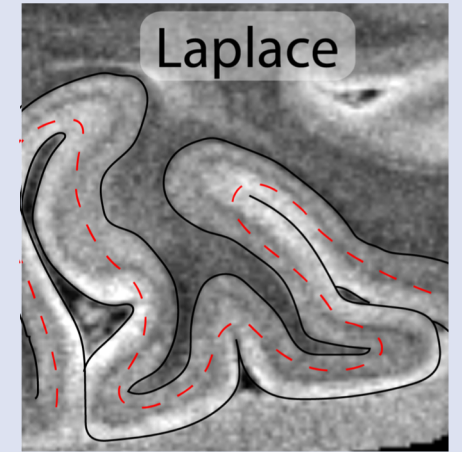
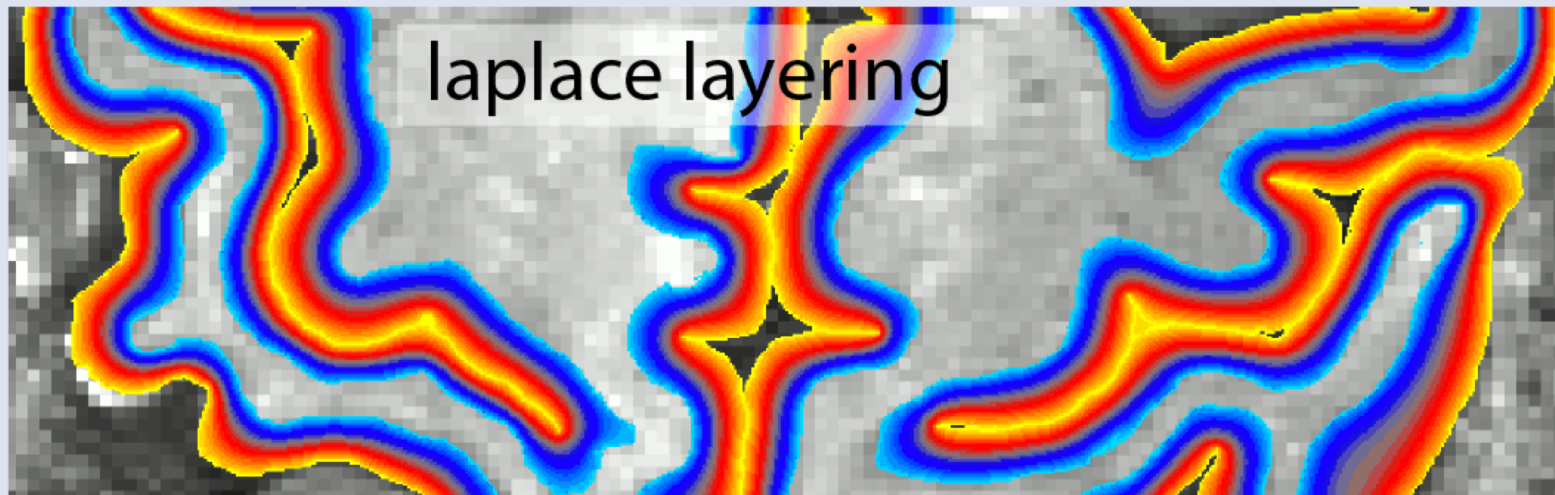
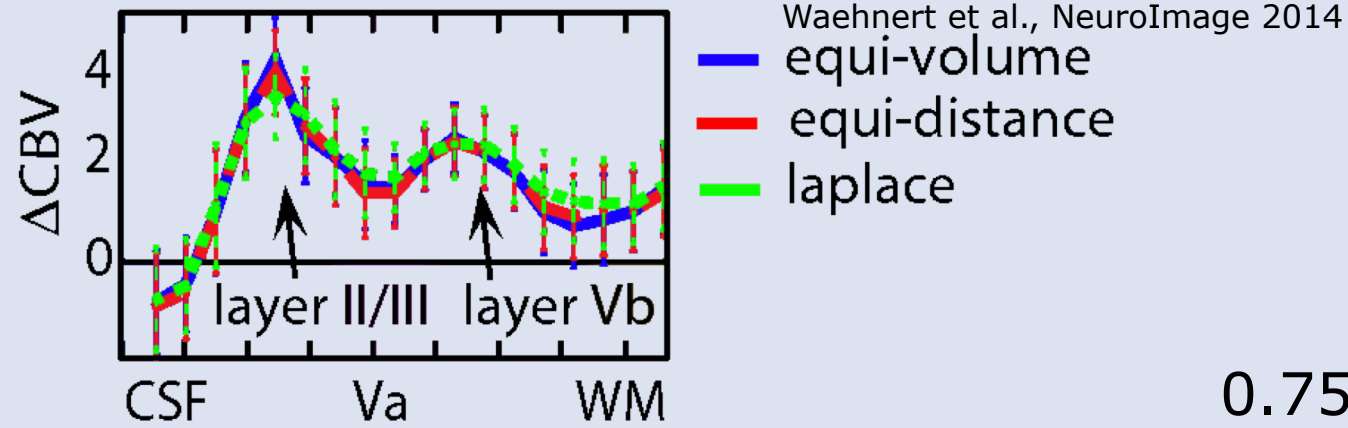


Limits of layer fMRI

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Layering algorithm

functional layer profiles



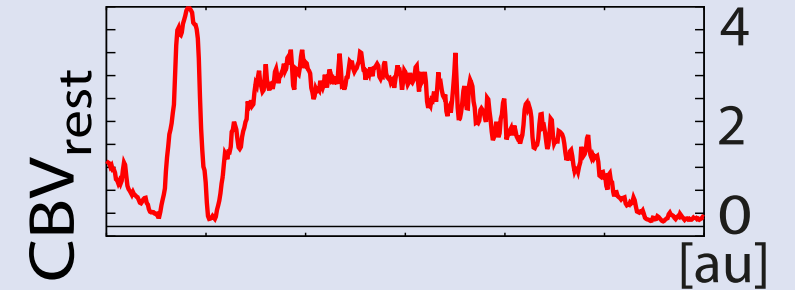
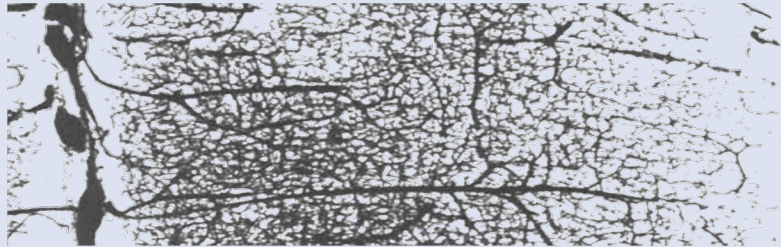
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Quantitative analysis vs. statistical analysis

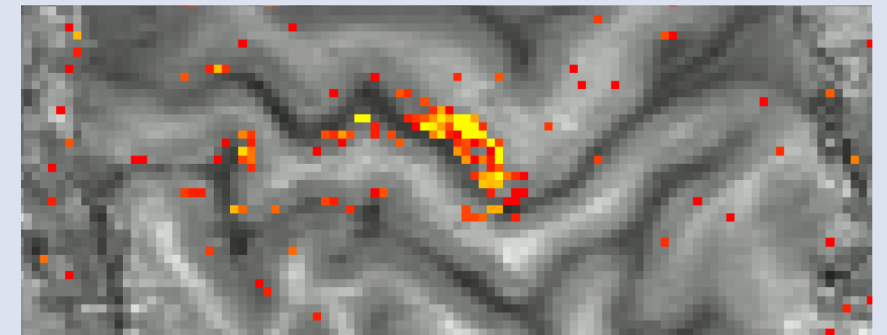
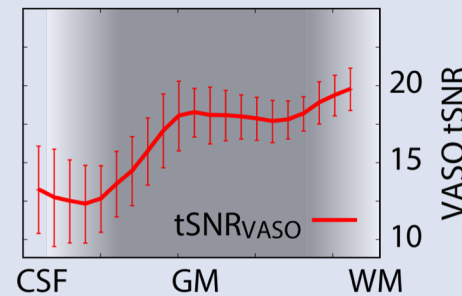
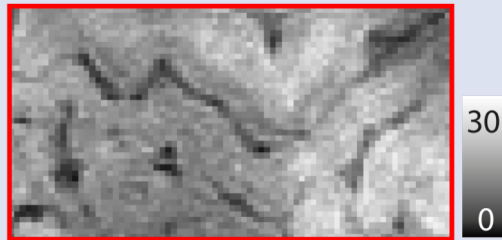
The baseline is heterogeneous

CBV_{baseline}:



tSNR:

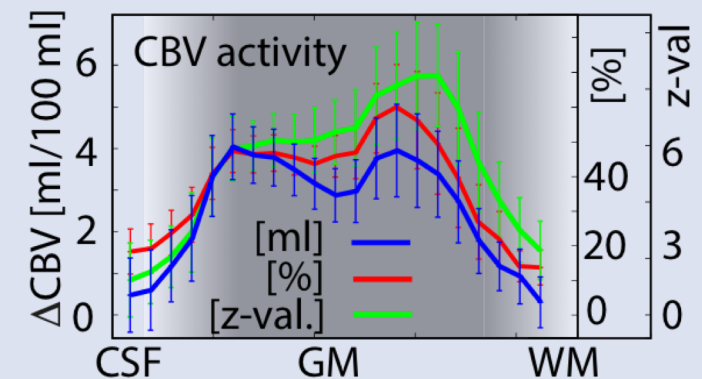
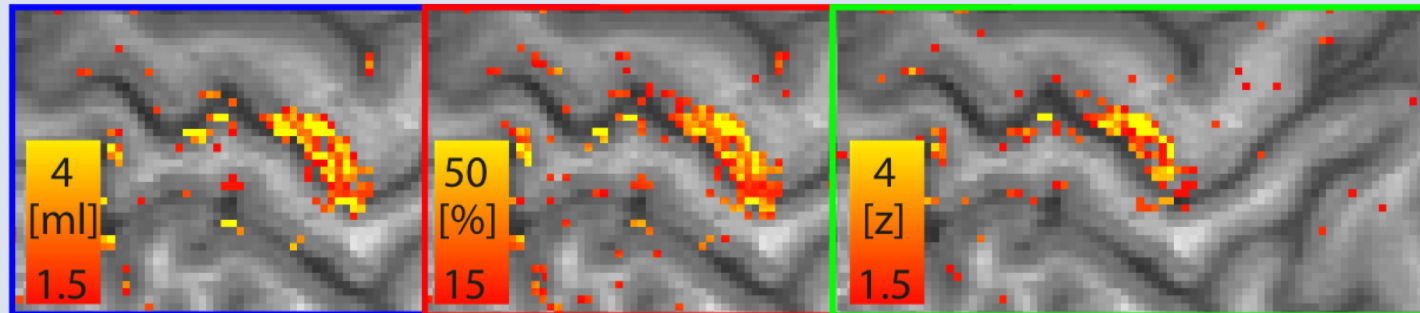
tSNR of VASO



Δ CBV in ml/100 ml

Δ CBV in %

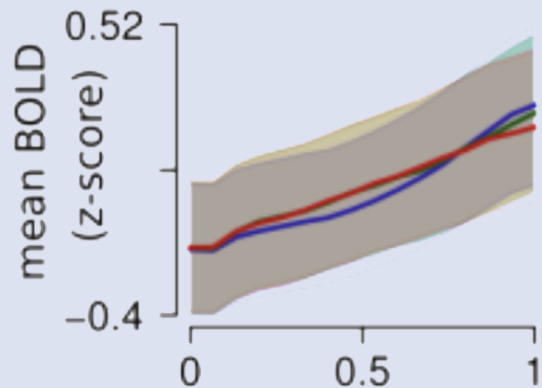
stat. CBV activity in z-values



biases in statistical models

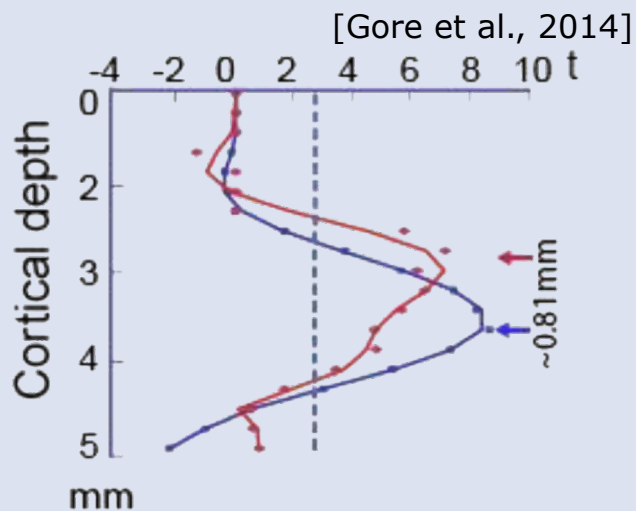


z-score



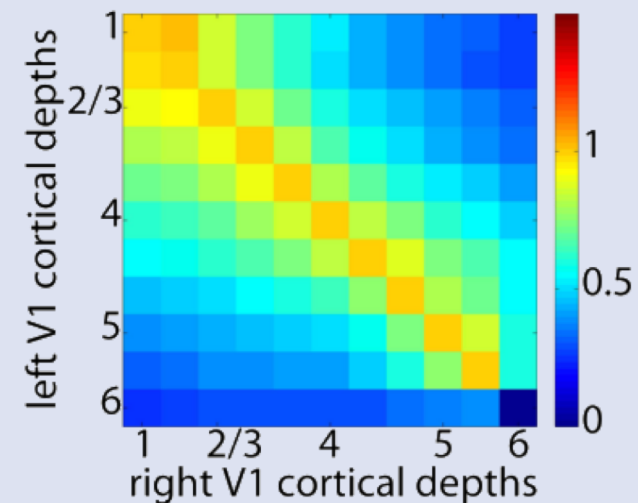
cortical depth [Francasso, NI, 2016]

t-score

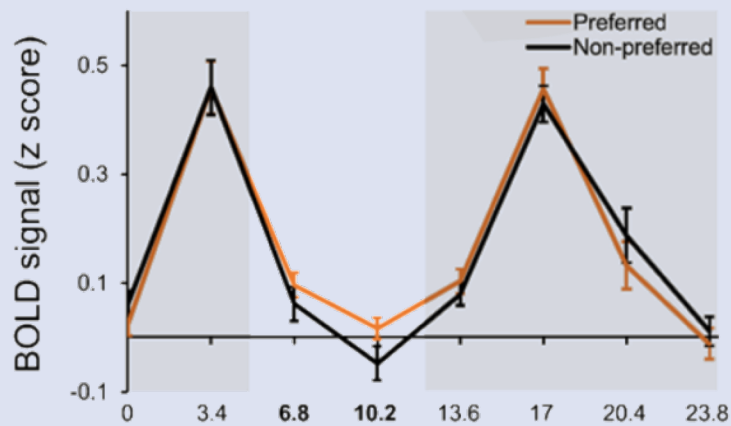


[Gore et al., 2014]

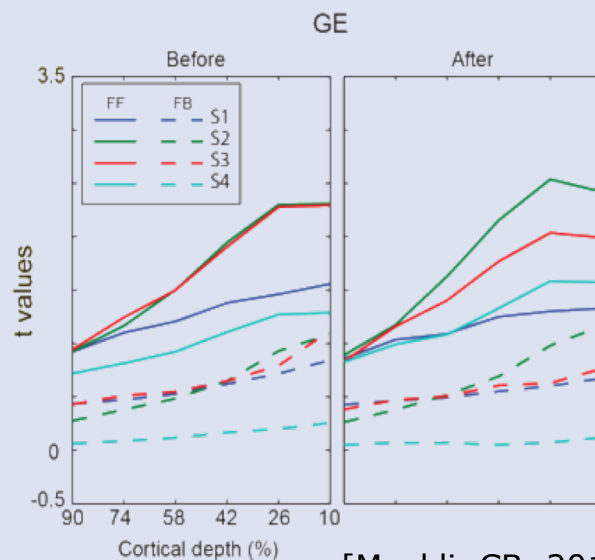
r-correl.



[Polimeni, 2010]



Lawrence, 2018]



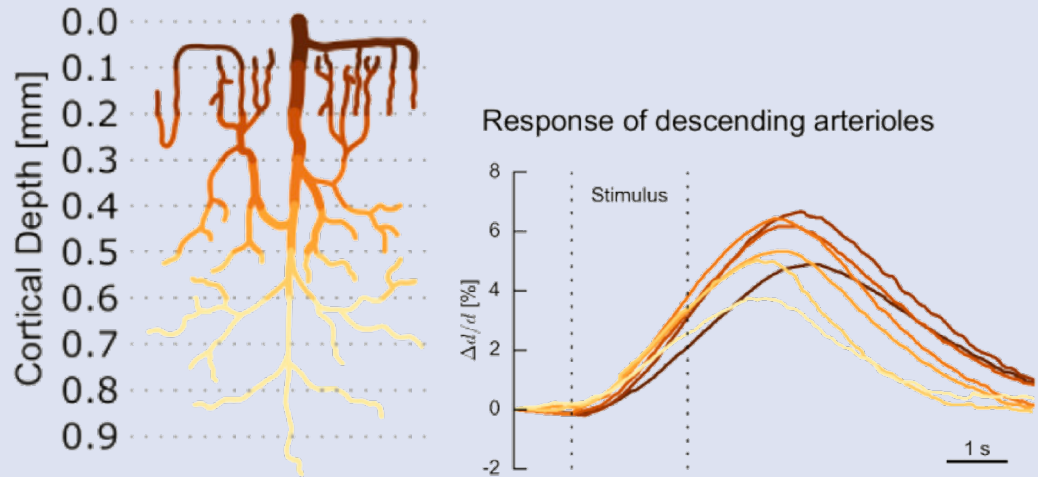
[Muckli, CB, 2015]

V1

limits of layer fMRI

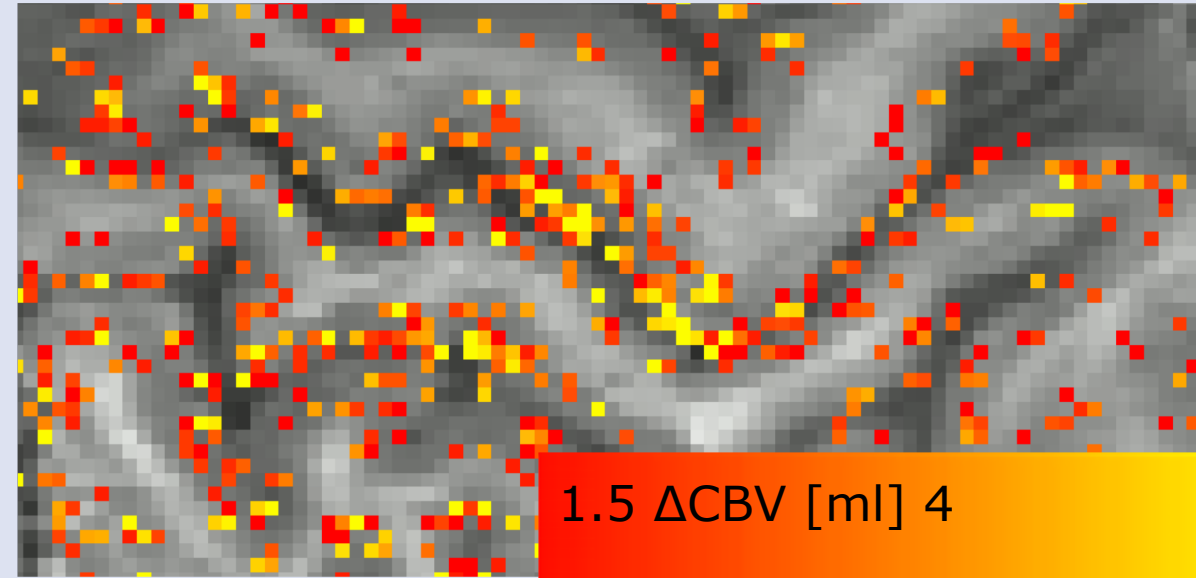
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Layer-dependent timing of vessel control

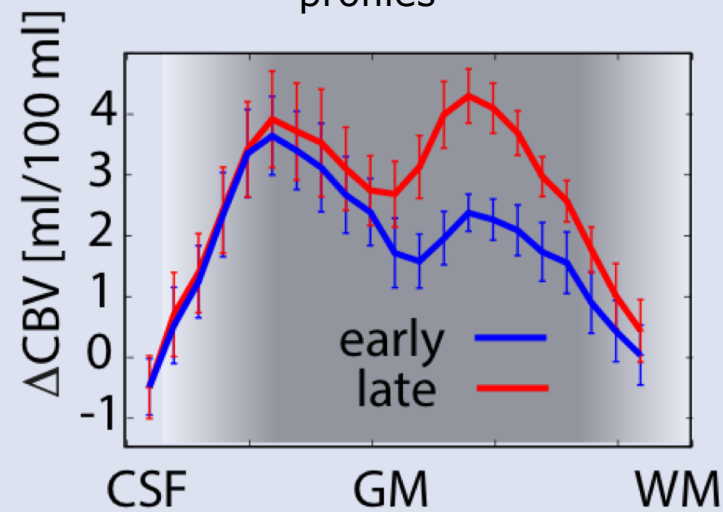


[Uhlirva *et al.* 2016, *eLife*] [Schmid *et al.* 2018, *NeuroImage*]

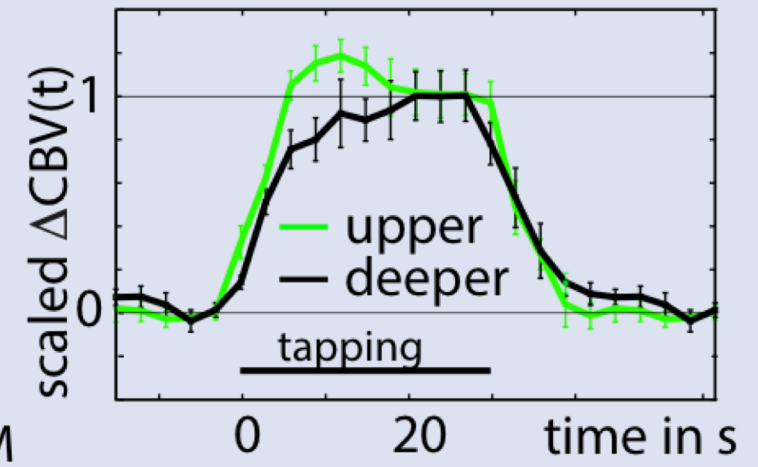
Early (9-18 sec) vs. late (21-30sec)



profiles



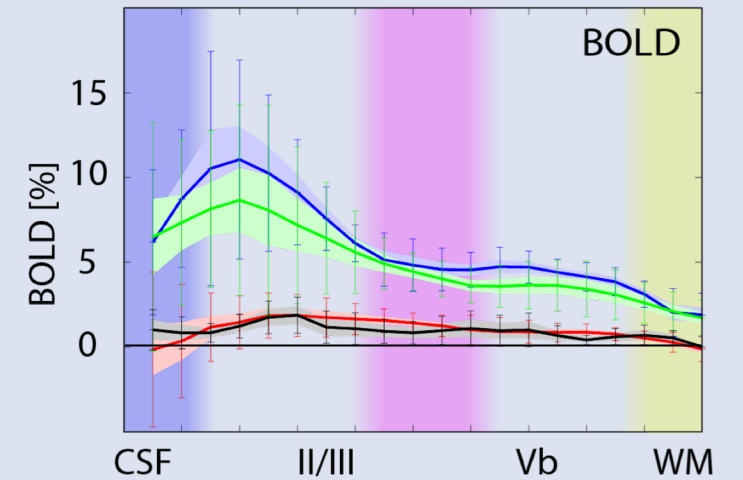
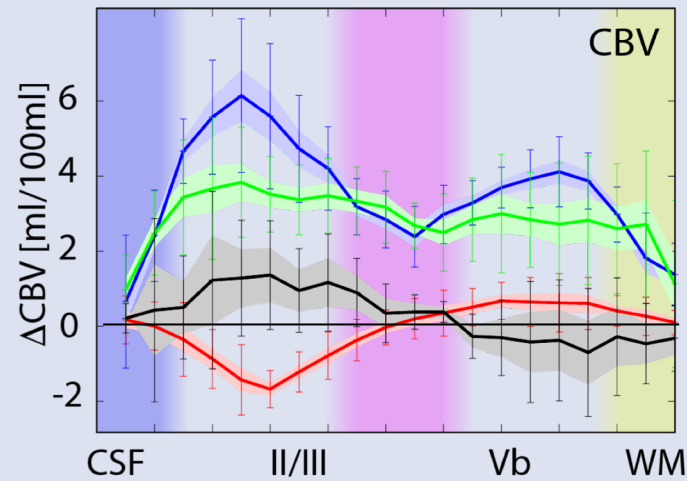
time courses



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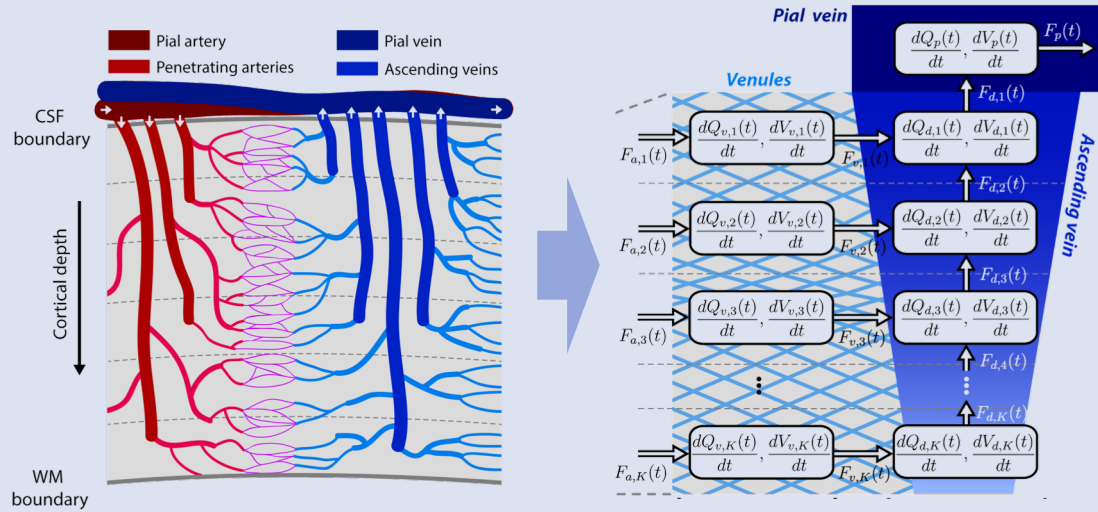
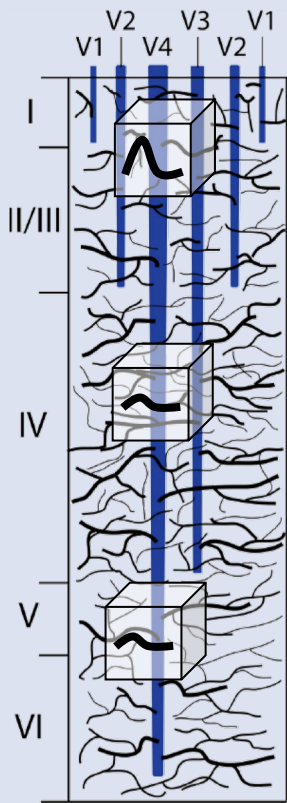
Vascular bias correction



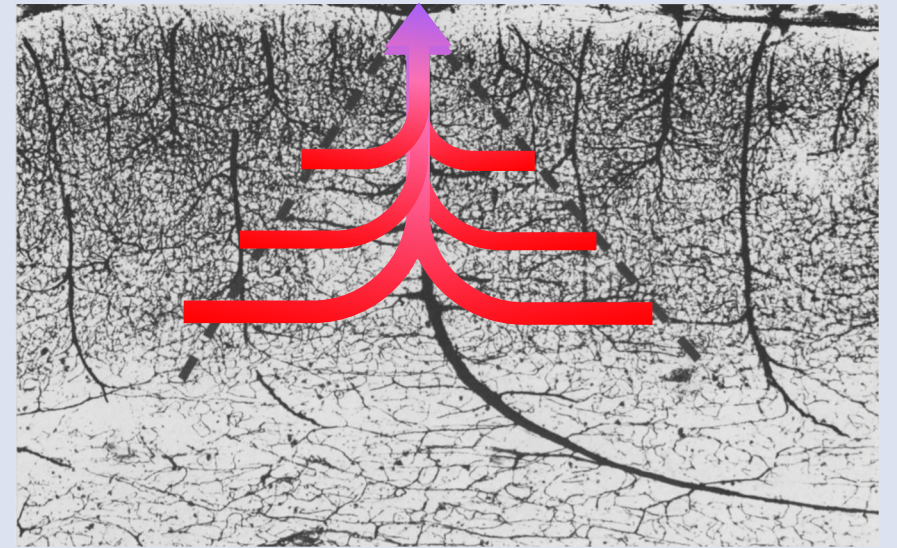
■ standard error across participants | standard deviation across participants — average across participants

[Huber et al., Neuron, 2017]

Vascular bias correction

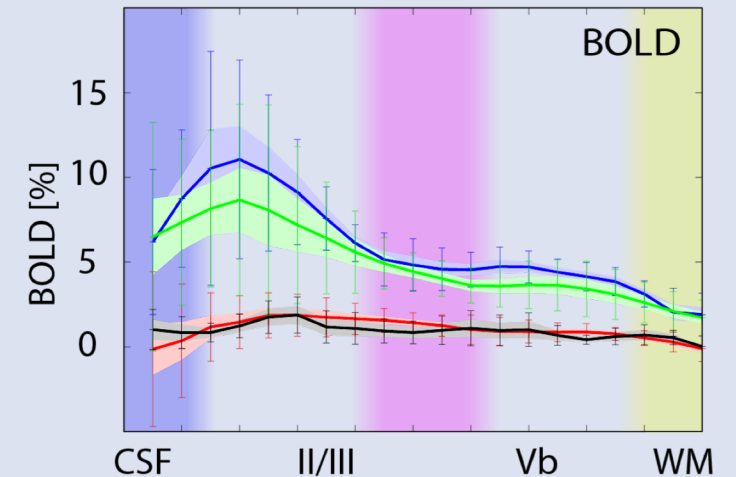
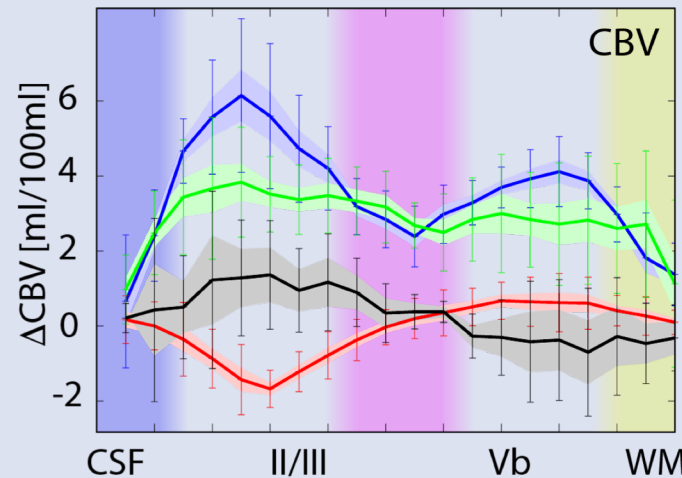


Uludag & Havlicek ISMRM2018



$$\tau_u \frac{dv_u}{dt} = f_u - v_u \frac{1}{\alpha} + \lambda_d v_i^*$$

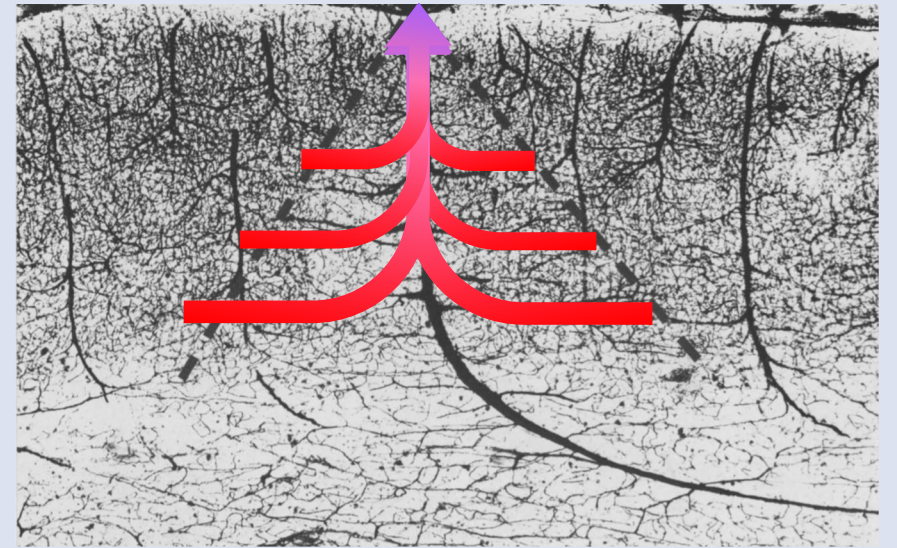
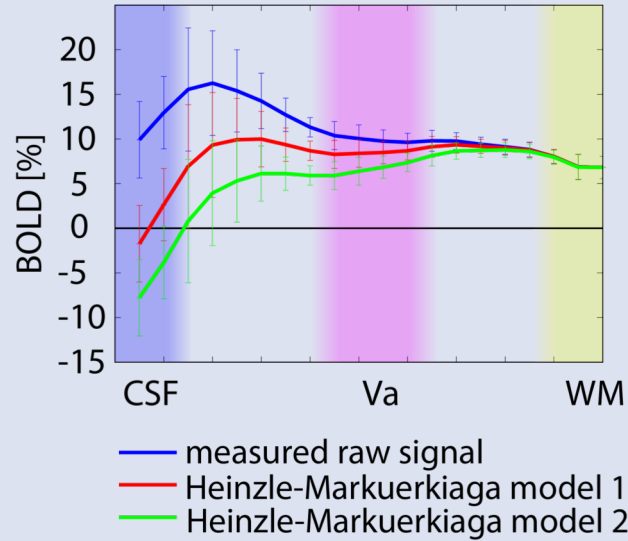
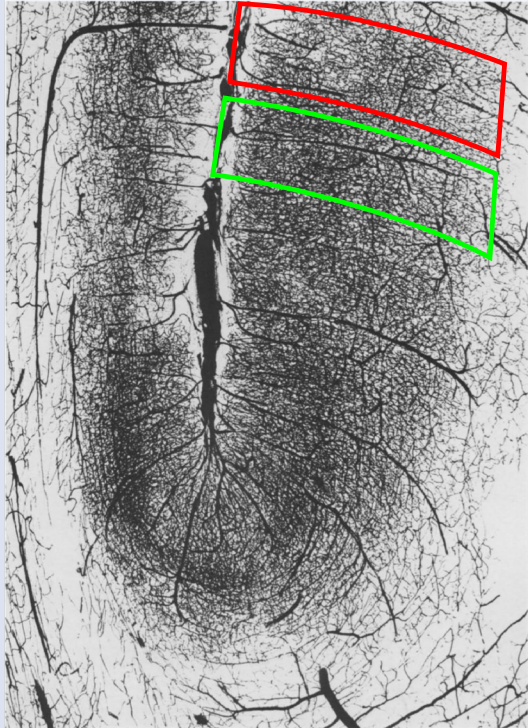
[Heinzle et al., NeuroImage, 2016]



■ standard error across participants
 | standard deviation across participants
 — average across participants

[Markuerkiaga et al. 2016, NeuroImage]

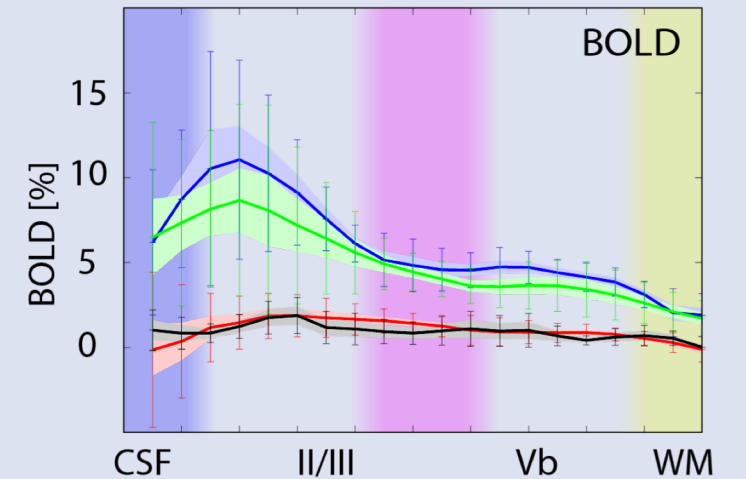
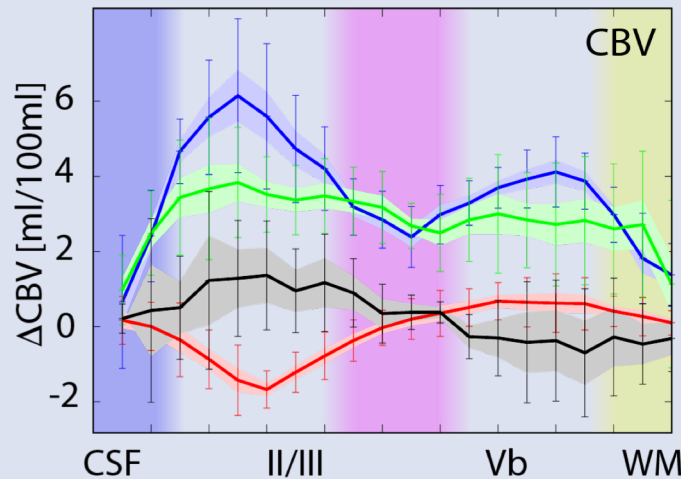
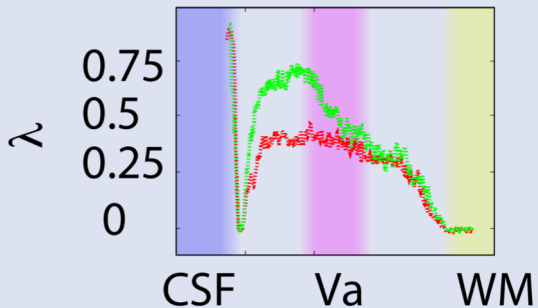
Vascular bias correction



$$\tau_u \frac{dv_u}{dt} = f_u - v_u \frac{1}{\alpha} + \lambda_d v_l^*$$

[Heinzle et al., NeuroImage, 2016]

model assumption:
 λ taken from baseline
 CBV of two 'columns'



Limits of layer fMRI

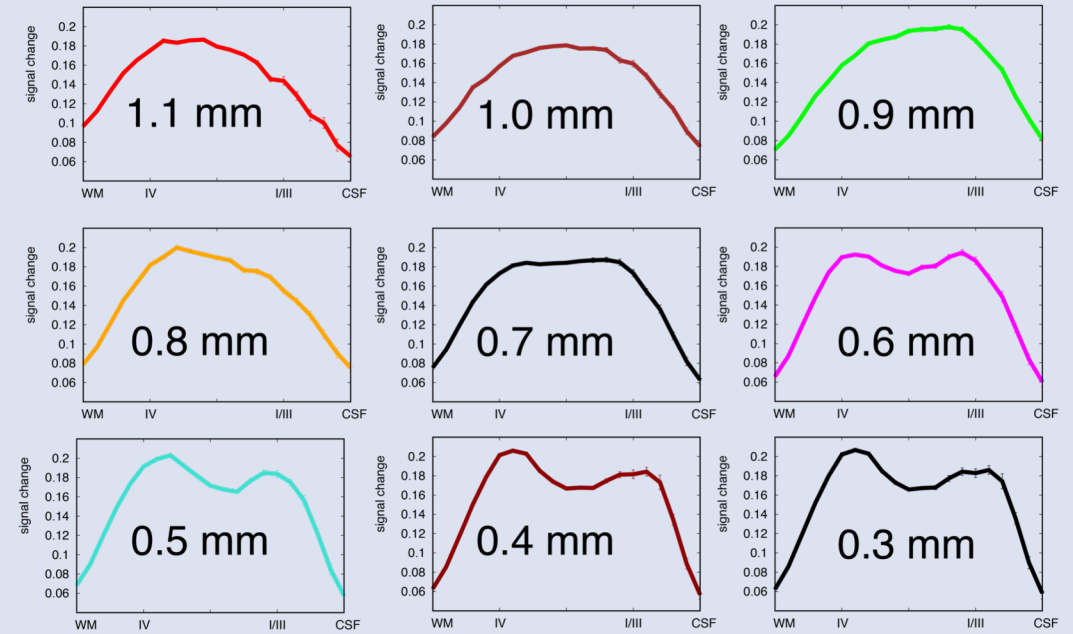
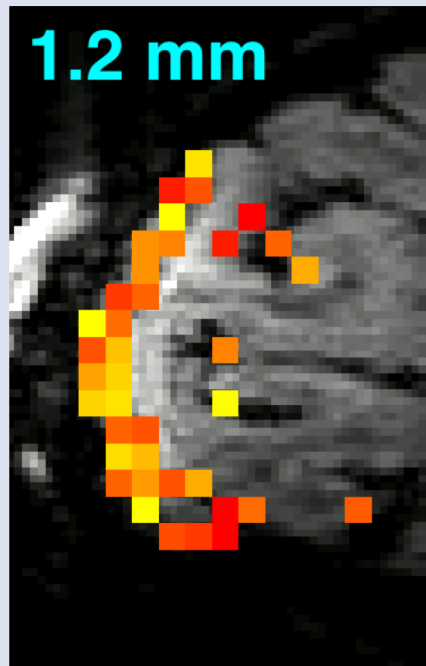
- Localization specificity limits
- Calibrating “cortical depths” to “cortical layers”
- Anatomically meaning full estimation of cortical depth
- Statistical interpretation
- HRF modeling
- Signal leakage across layers
- Cortical thickness
- Columnar variability
- Coverage
- Inter-subject variability
- Interconnection between layers
- Future challenges

Layer-fMRI in V1



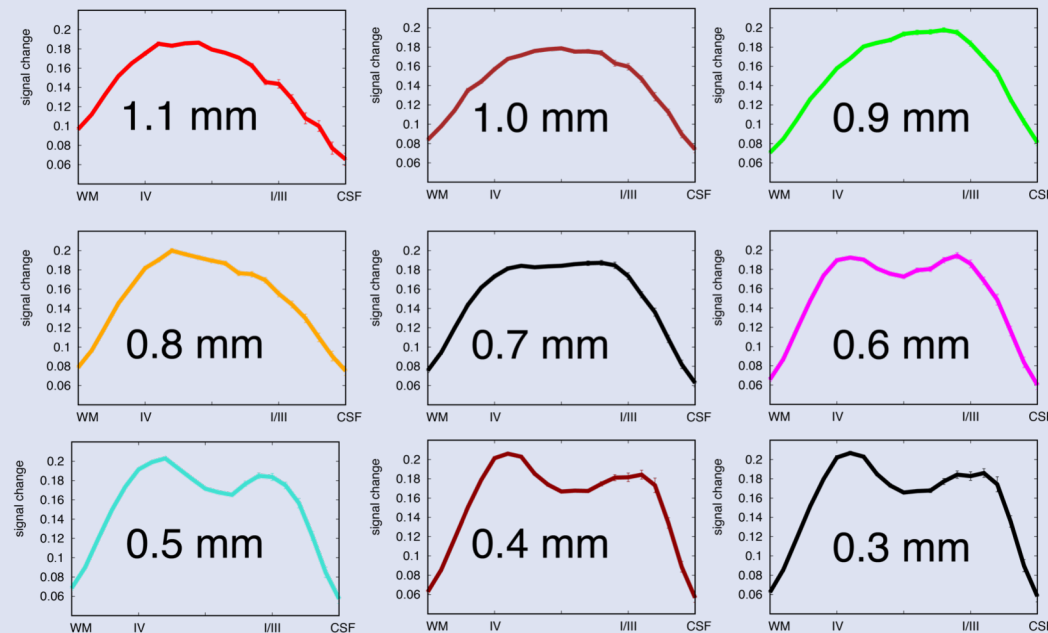
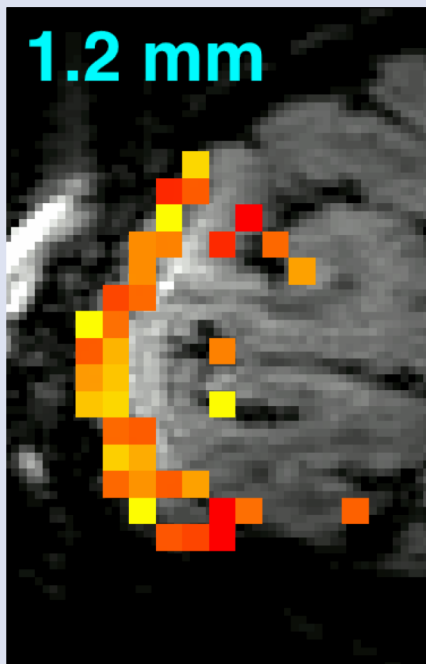
Huber et al. NeuroImage 2014, in collaboration with Jozien Goense

Layer-fMRI in V1



Huber et al. NeuroImage 2014, in collaboration with Joziën Goense

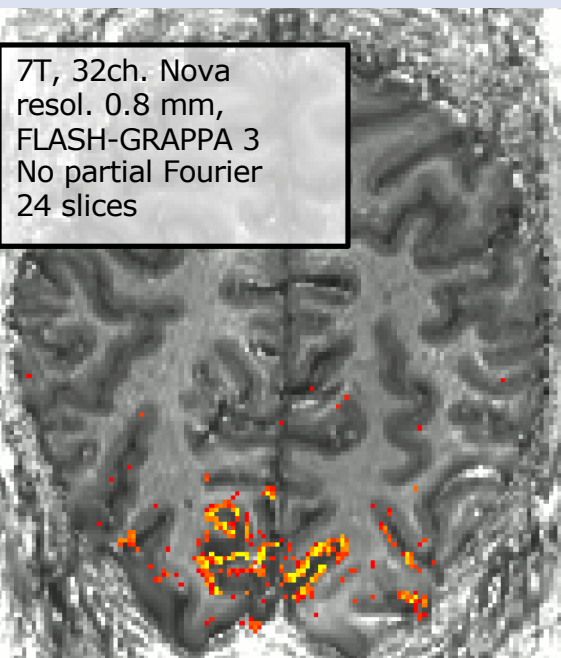
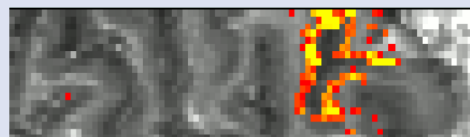
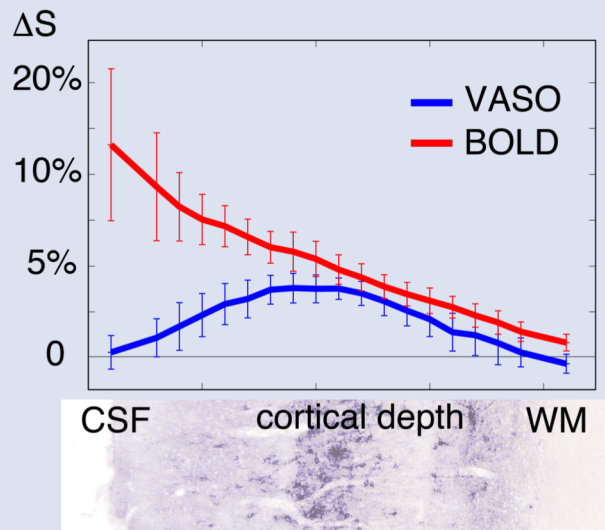
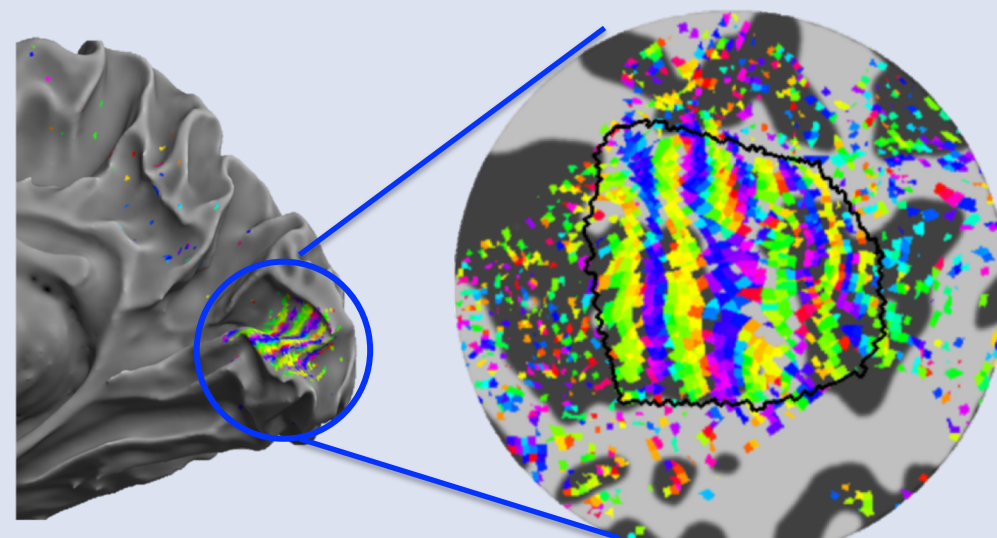
Layer-fMRI in V1



In collaboration with **Eli Merriam** and **Zvi Roth**

Huber et al. NeuroImage 2014, in collaboration with **Joziën Goense**

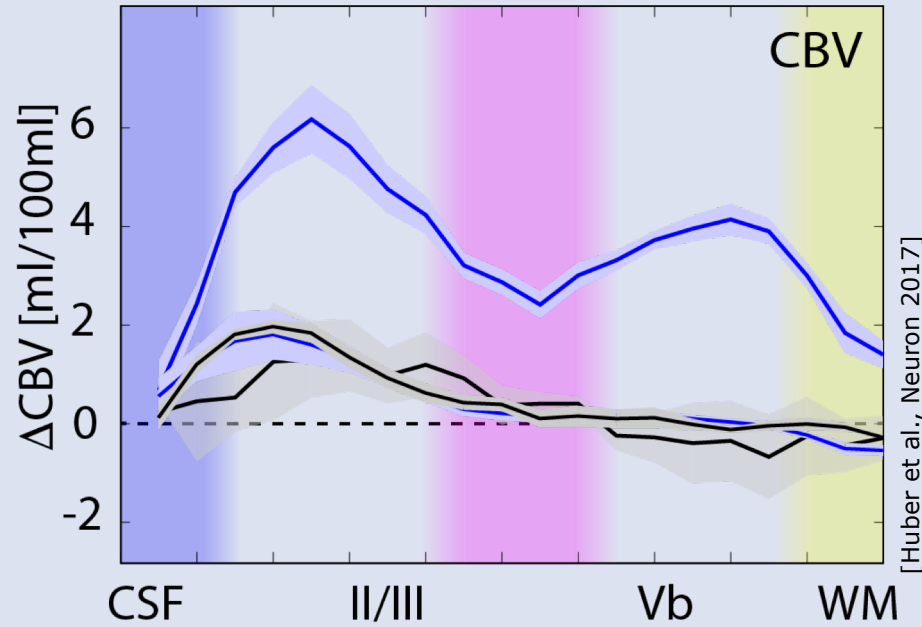
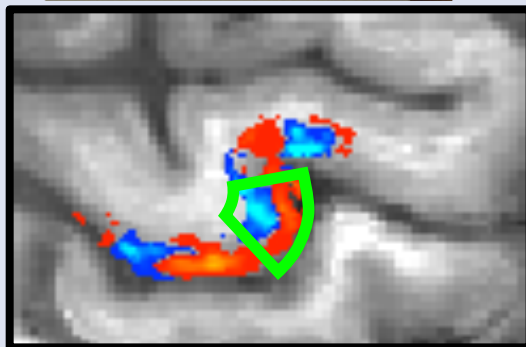
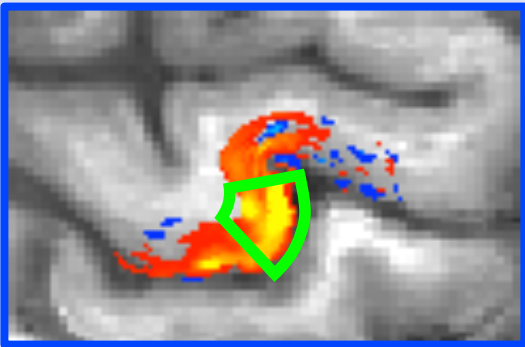
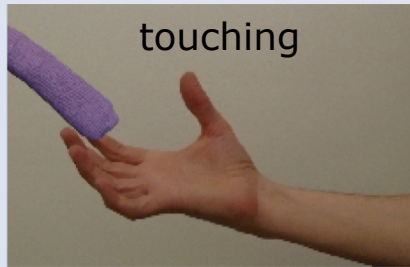
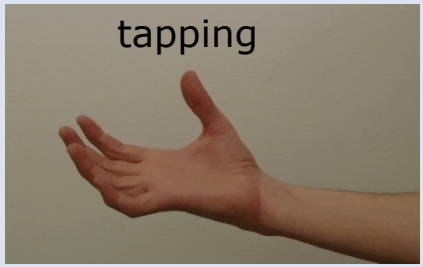
Data from Eli Merriam and Zvi Roth



Limits of layer fMRI

- Localization specificity limits
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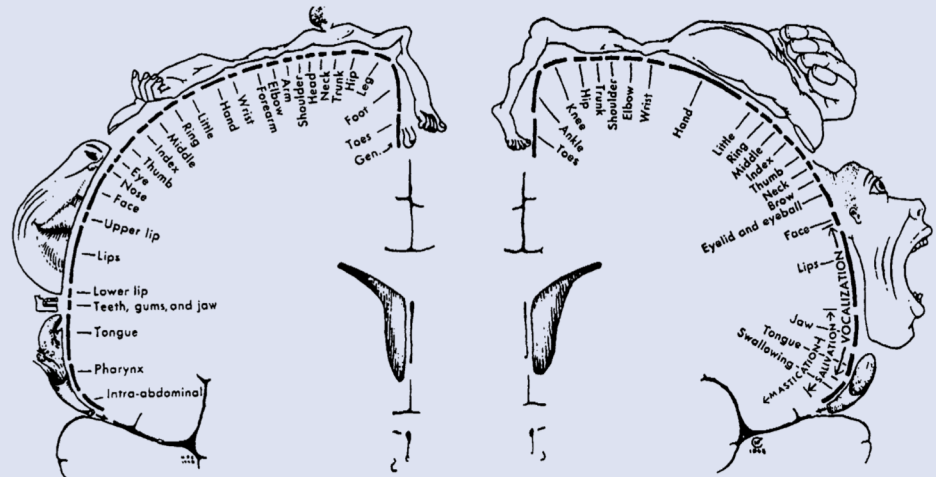
Every column is different



Tasks for columnar representations

Test bed for topology tools

M1: body part map



somatosensory area (left) and primary motor area (right).

finger tapping (64 min)

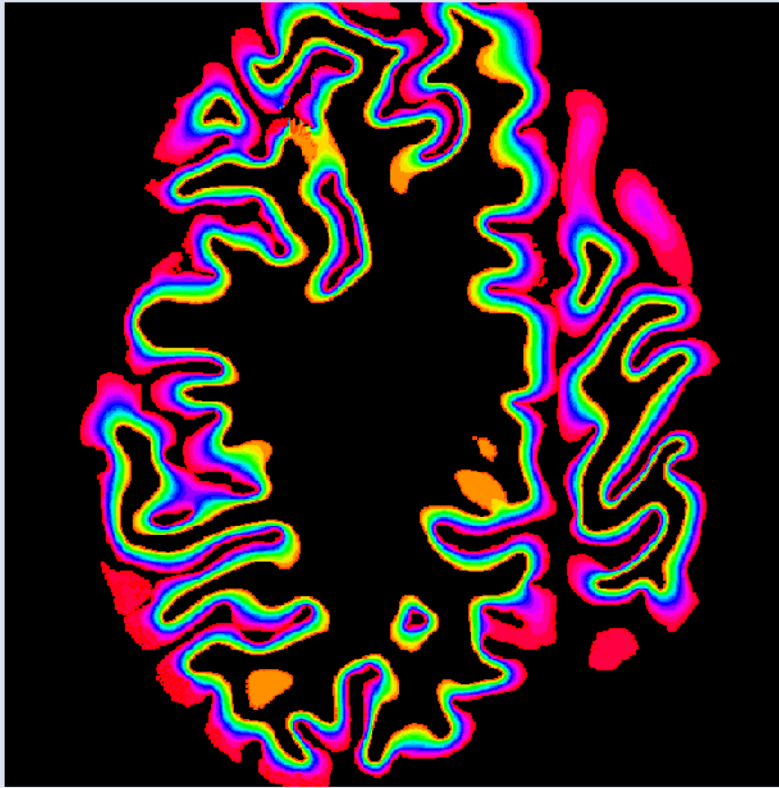


- index finger tapping (0.75 Hz)
- middle finger tapping (0.75 Hz)
- ring finger tapping (0.75 Hz)
- little finger tapping (0.75 Hz)
- thumb tapping (0.75 Hz)



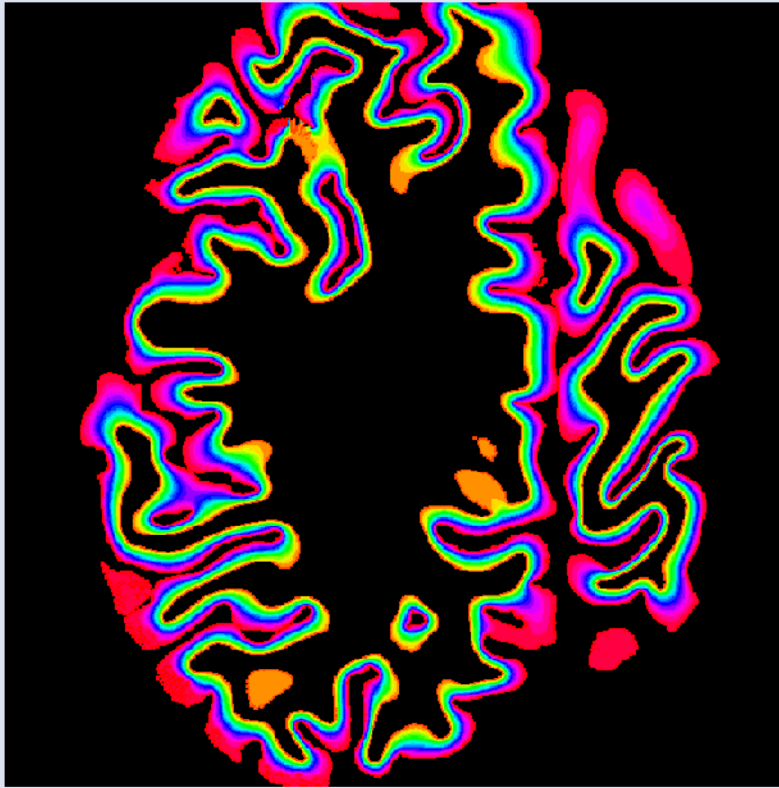
From layers to columns

Layers in 3D



From layers to columns

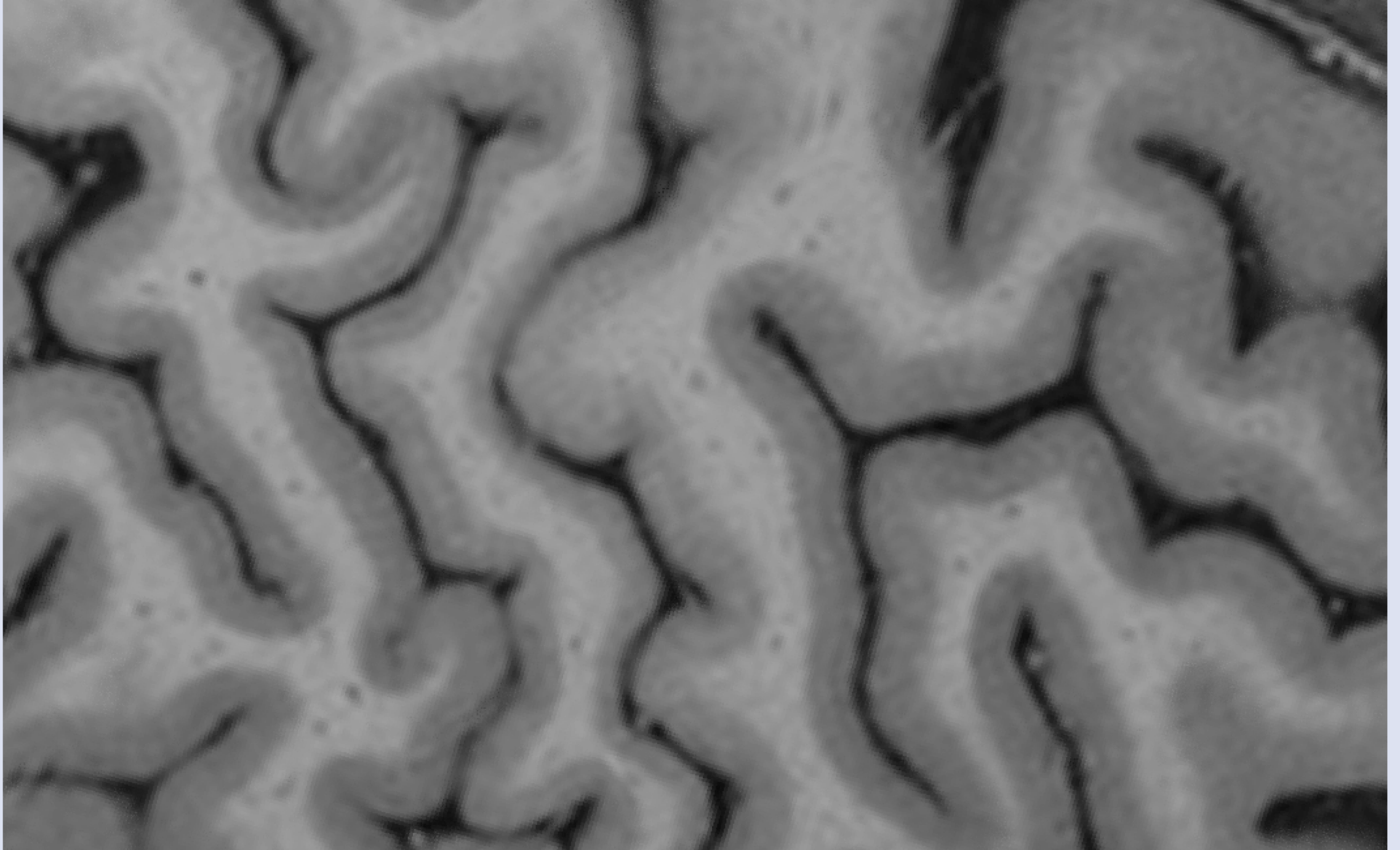
Layers in 3D



Crawlers to span sheet



Different than Freesurfer because it works with slabs
In voxel space

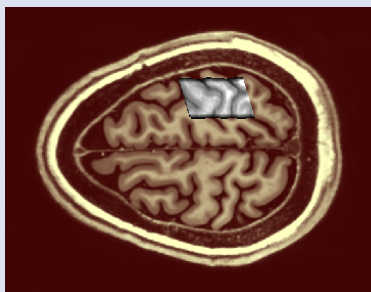


Limits of layer fMRI

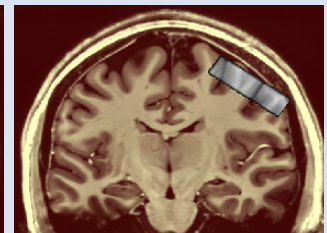
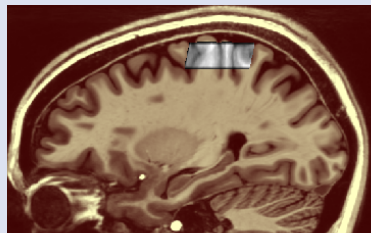
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Coverage

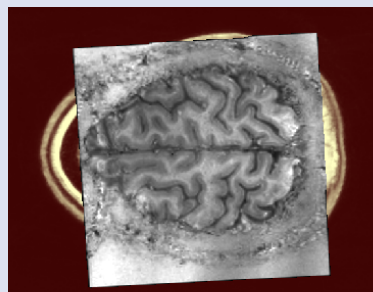
$$8 \times 32 \times 96 = 0.86\%$$



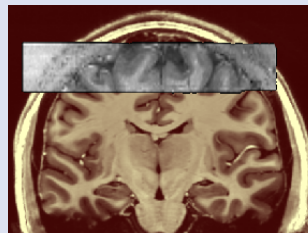
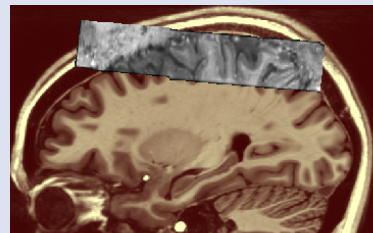
Original CBV-coverage for layer resolutions



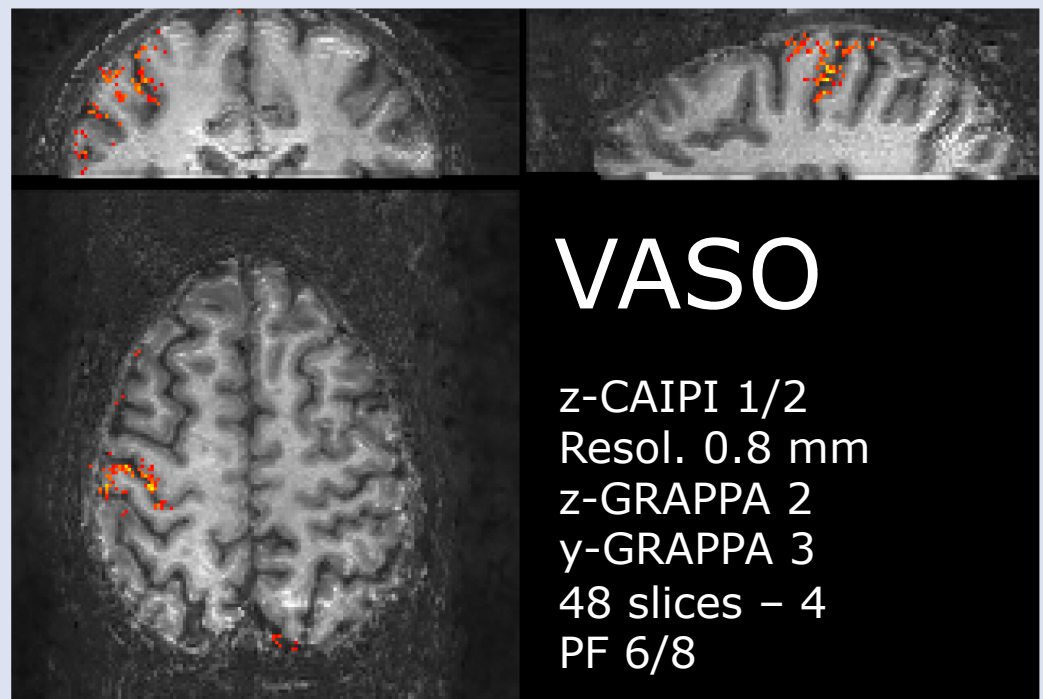
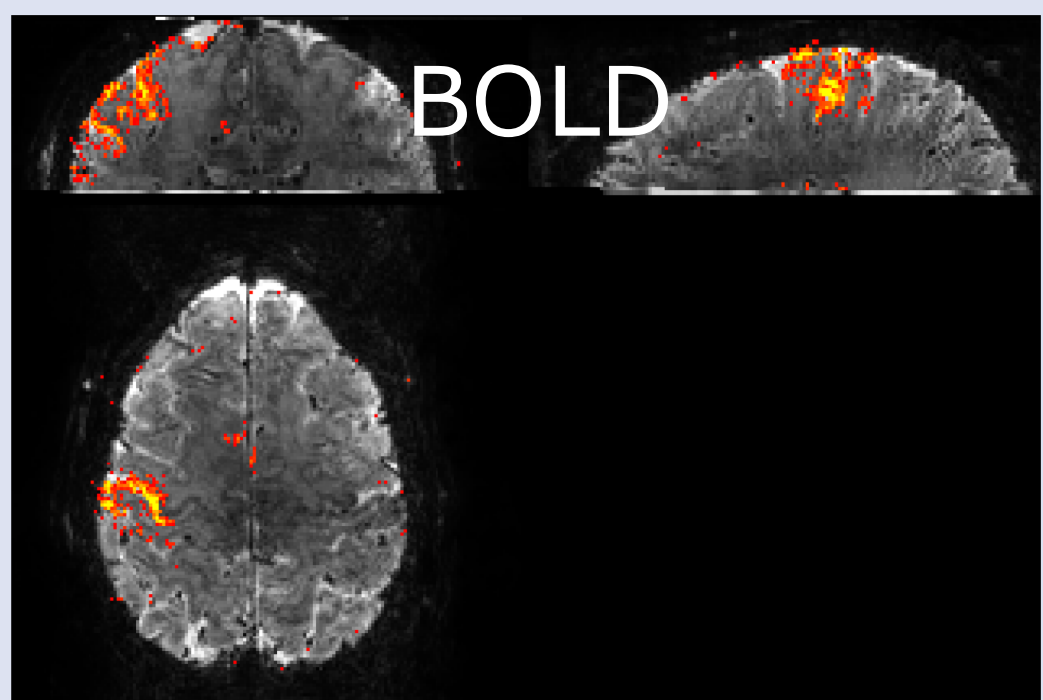
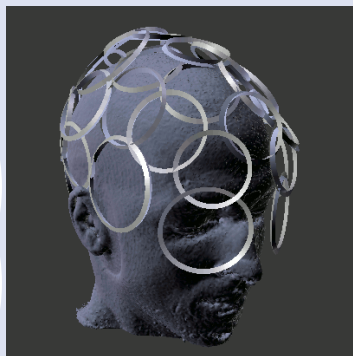
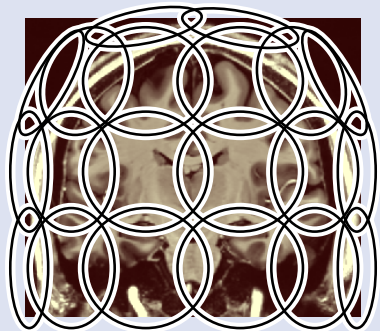
$$24 \times 162 \times 162 = 14\%$$



CBV-coverage for layer resolutions with 3D-EPI slab



RF-channel size is comparable to 3D-EPI slab coverage



Limits of layer fMRI

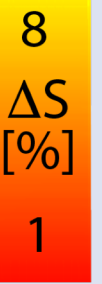
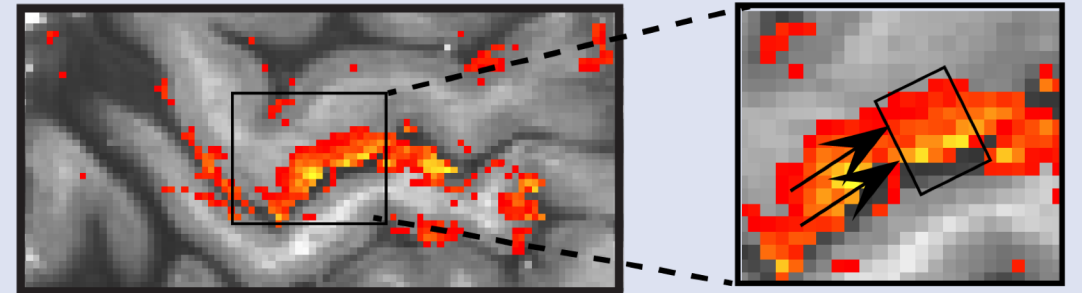
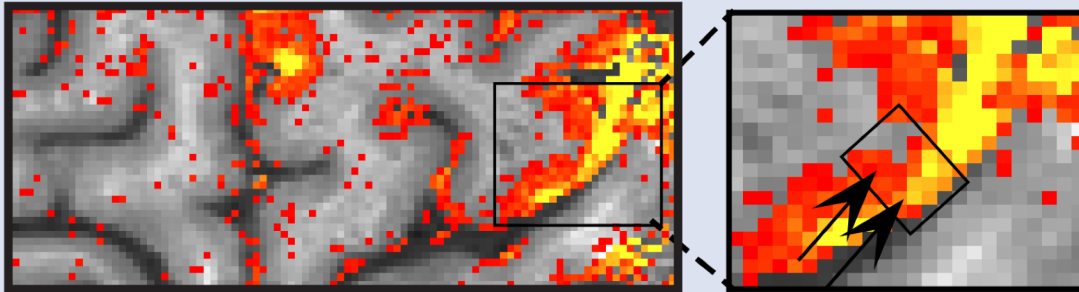
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Why does it work in some people better than in others?

volunteer A

volunteer B

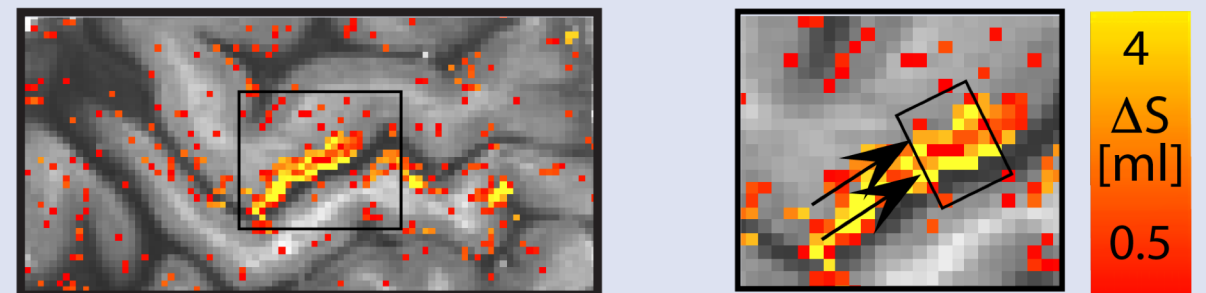
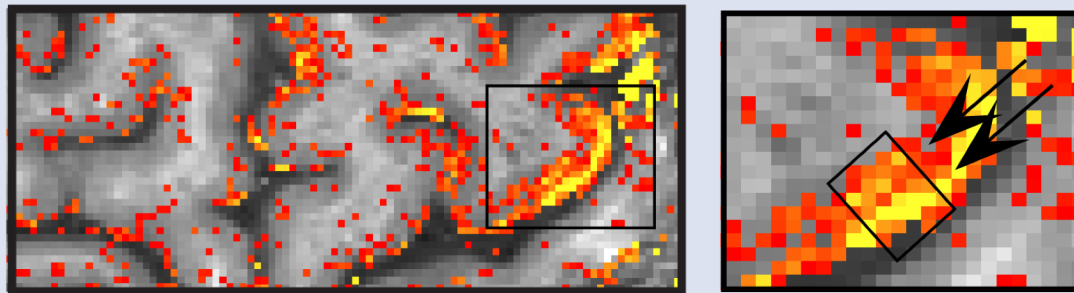
GE-BOLD



very strong response in upper layers
minimal response in deeper layers

weaker response in superficial layers
secondary response in deeper layers

CBV



CBV fMRI can resolve the inconsistencies in BOLD.

In CBV fMRI, both participants have a similar response amplitudes and the same double-layer feature

Limits of layer fMRI

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Open questions, unmet needs

- **Specialized streamlined analysis tools needed for high-res/laminar fMRI**
 - bundle tools into a common framework/package
- **More complete characterization of vascular bias**
 - ultimate specificity *still unknown*, may vary across regions/columns
- **How to move past current limits to *imaging* resolution?**
 - smarter sequences? faster gradients? denser coils? bigger magnets? *all four?*

More resources

NeuroImage special issue on laminar MRI

Prospects for cortical laminar MRI: functional and anatomical imaging of cerebral cortical layers

Editors: Jonathan R. Polimeni
David G. Norris

Call for Submissions

This special issue will focus on the developing field of cortical laminar MRI, which seeks to image structural and functional properties of the layers of the cerebral cortex. The goals of this issue will be: to survey laminar MRI methodologies and technical challenges; to review recent studies investigating the functional and anatomical properties of the cortical layers; to address which neuroscientific questions that can be addressed through neuroimaging of cortical layers; and to provide a wider intellectual framework for why cortical laminar MRI should be pursued.

All layer fMRI papers focusing on human can be found here:

<https://goo.gl/kh5DjG>

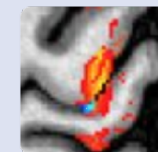
All layer fMRI researchers and corresponding email list-

serv: laminar.imaging.network@gmail.com <https://goo.gl/BJufev>

Repository of layerfMRI analysis code repositories: <https://goo.gl/Lb6Ps7>

Blog: www.layerfMRI.com

News of talks/abstracts/papers/artifacts: [@layerfMRI](#)



layerfMRI
@layerfMRI

Thank you

NIMH:

- Daniel Handwerker
- Emily Finn
- Yuhui Chai
- Dave Jangraw
- Arman Khojandi
- Sean Marrett
- Vinai Roopchansingh
- Andy Derbyshire
- Kenny Chung
- Javier Gonzales
- Adam Thomas
- Peter Bandettini

comments and questions are appreciated:

Laurentius.Huber@nih.gov

MPI CBS Leipzig:

- Harald Möller
- Bob Turner
- Robert Trampel
- Maria Guidi

University of Glasgow:

- Jozien Goense

University of Sheffield:

- Aneurin Kennerley

Cornell University Hospital

- Carsten Stüber

University of Maastricht:

- Benedikt Poser
- Dimo Ivanov

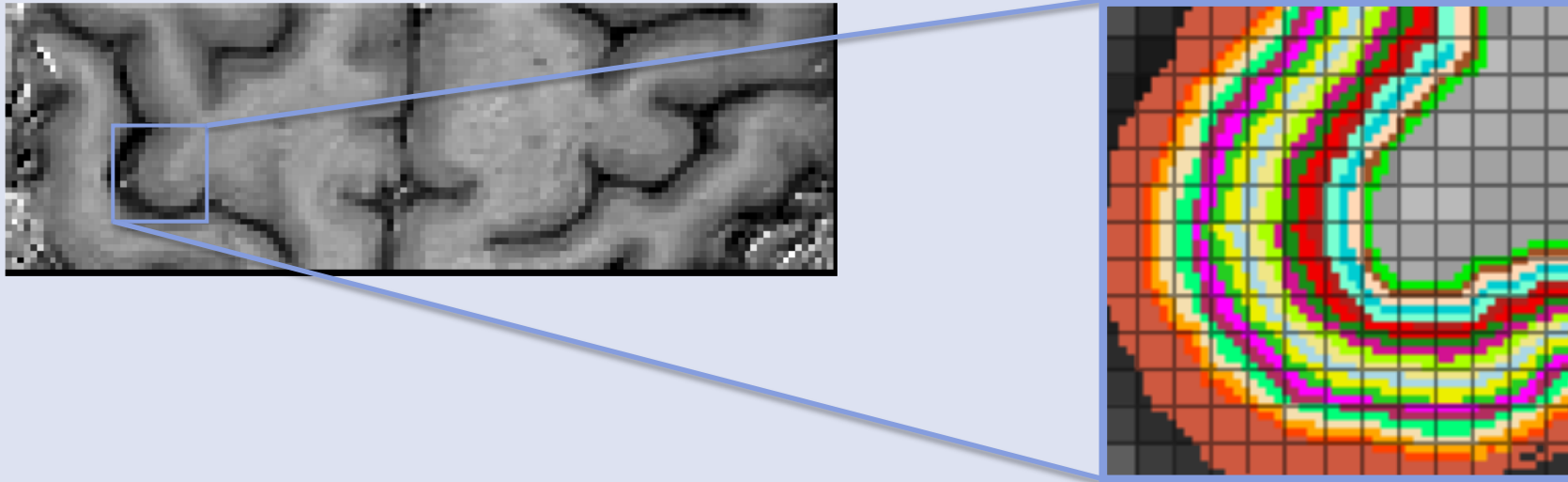


Supported by the NIMH Intramural Research Program

Decision 7: layers in sub-voxel space

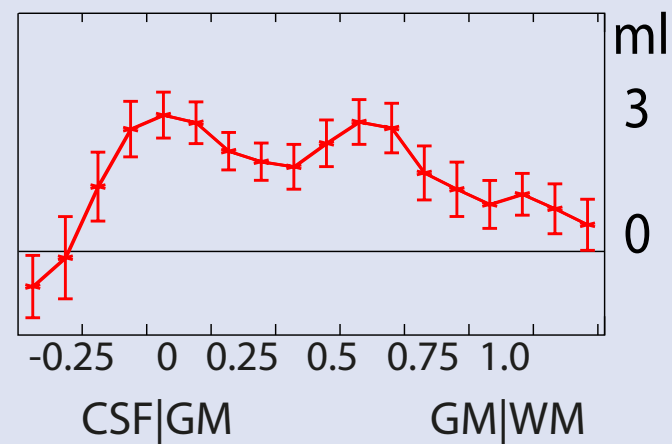
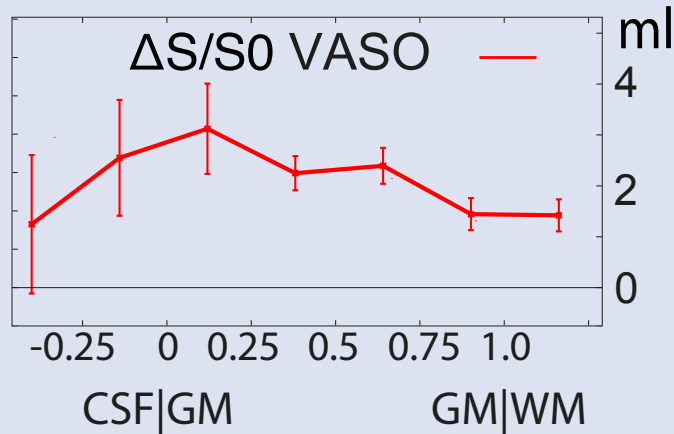
CSF-GM border from T1 weighting

20 layers (effective: 6-8.5)



[Huber Neuroimage 2015]

new



People react strong on the word 'interpolation'