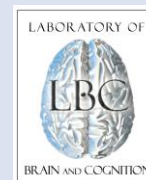# High-resolution CBV-fMRI allows mapping of laminar activity and connectivity of cortical input and output

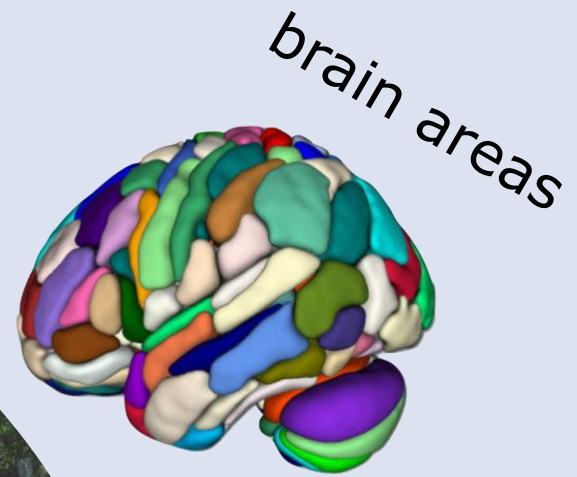Renzo (Laurentius) Huber

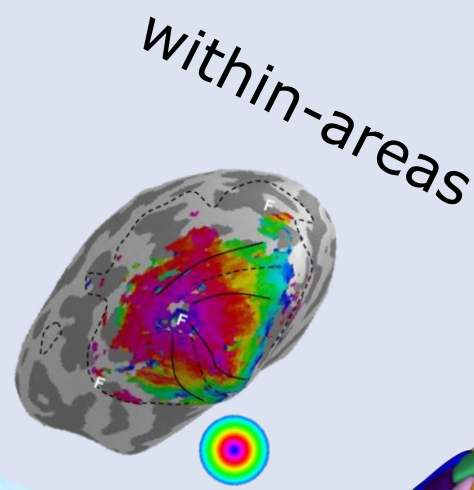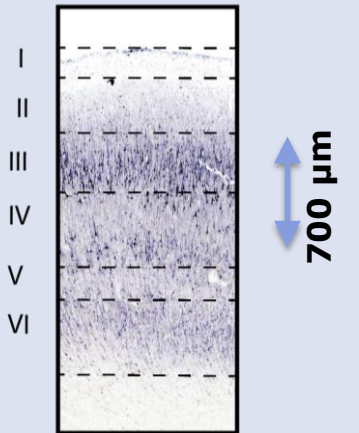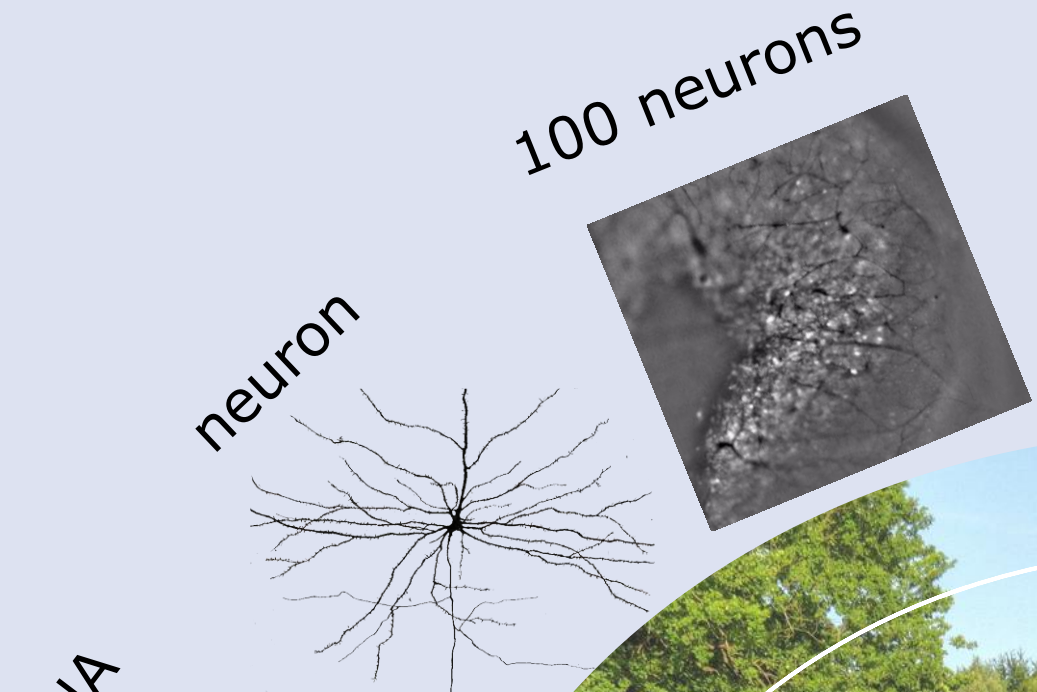SFIM, LBC, NIMH, NIH under Peter Bandettini

May 31st 2018

Esther Kühn's BrainInDepth conference

spatial scales in neuroscience

layers & columns

100 neurons

within-areas

brain areas

neuron

behavior

DNA

bridge metaphor idea from
Eric Wong and Bruce Rosen

2/35

higher hierarchy   lower hierarchy

cortical input

output

4 mm

700 µm

top-down

bottom up
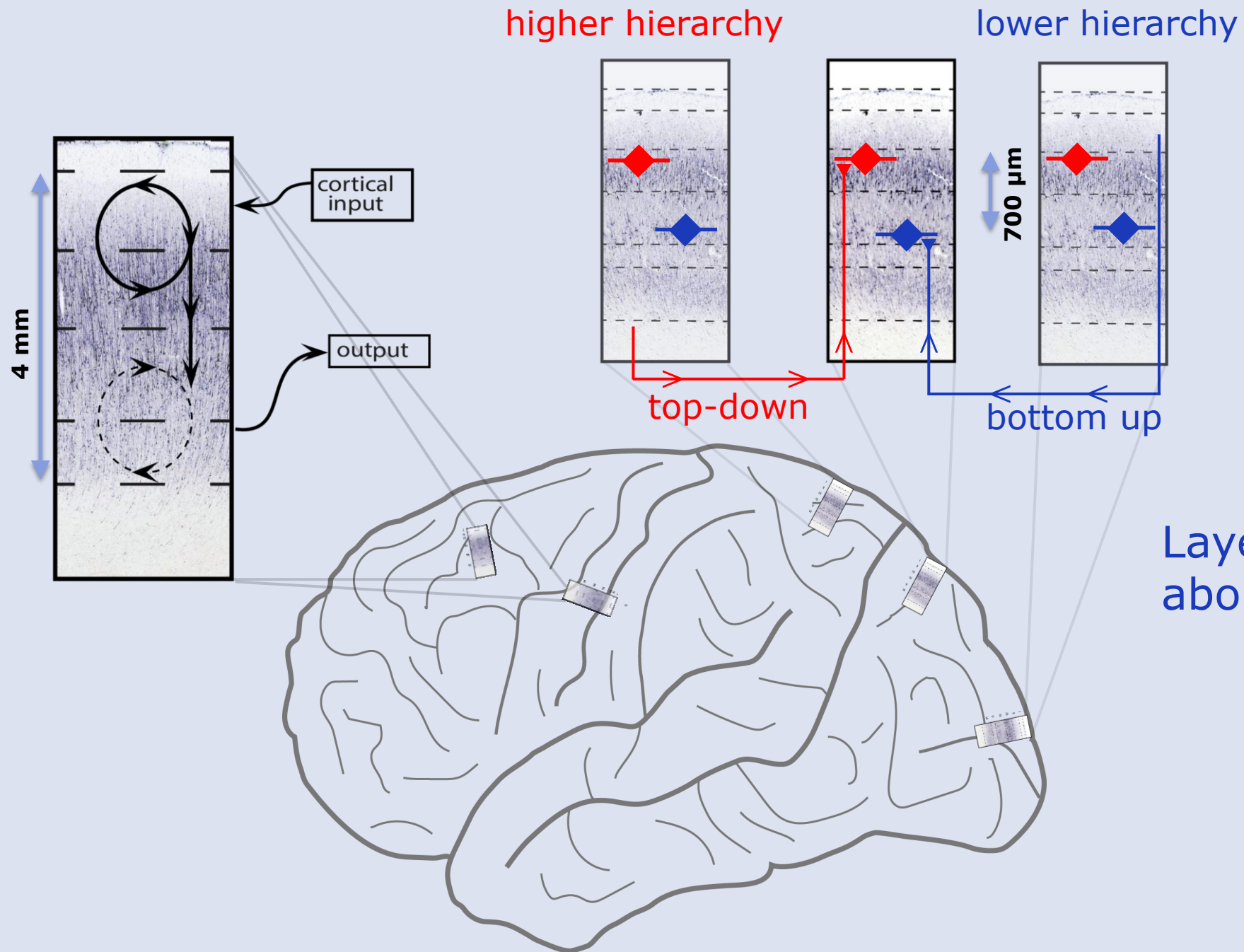
Layers provide information about directionality

Hierarchical connectivity:
Felleman and Van Essen 1991

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

Challenge 1: Sensitivity

Challenge 2: Specificity
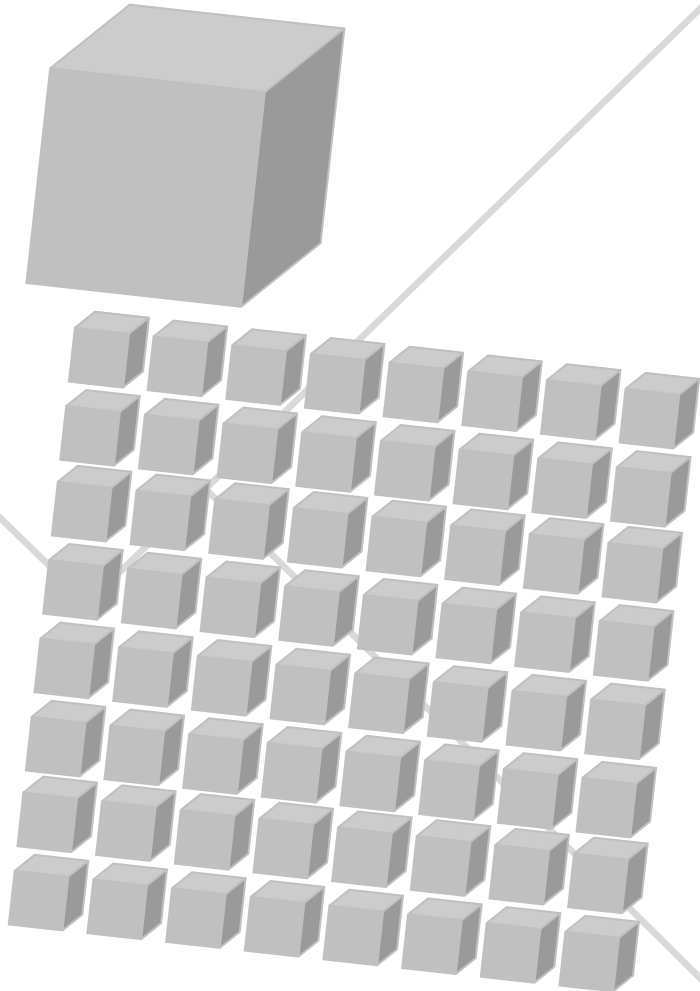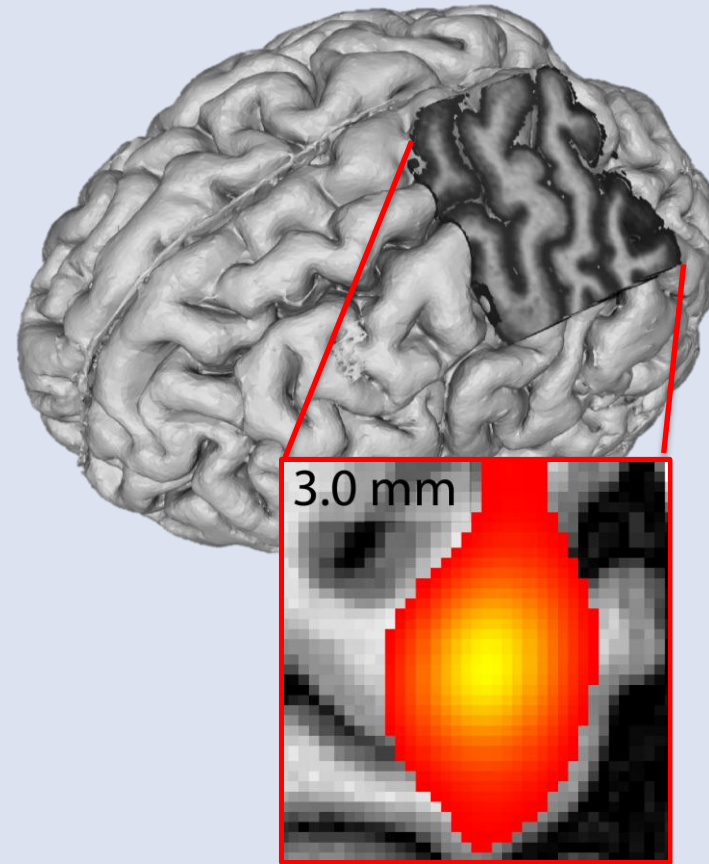
$SNR \sim \Delta x^3$

going from 3 mm

to 0.75 mm voxels
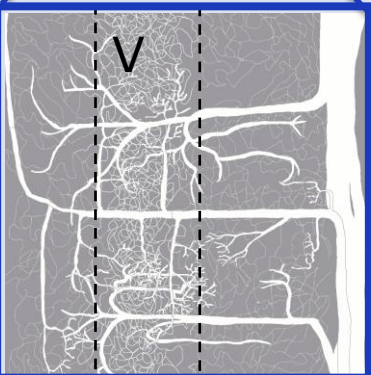
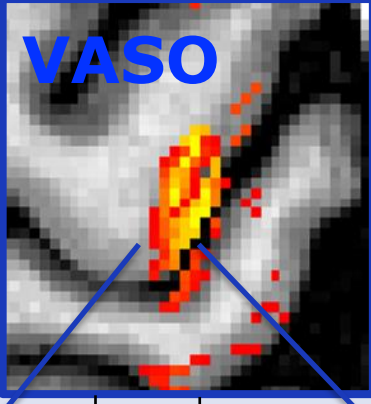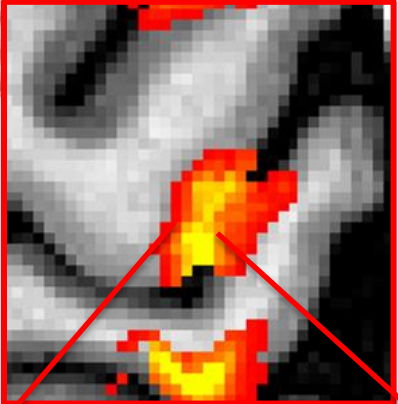64 fold reduction

➤ 4096 times
   longer averaging!
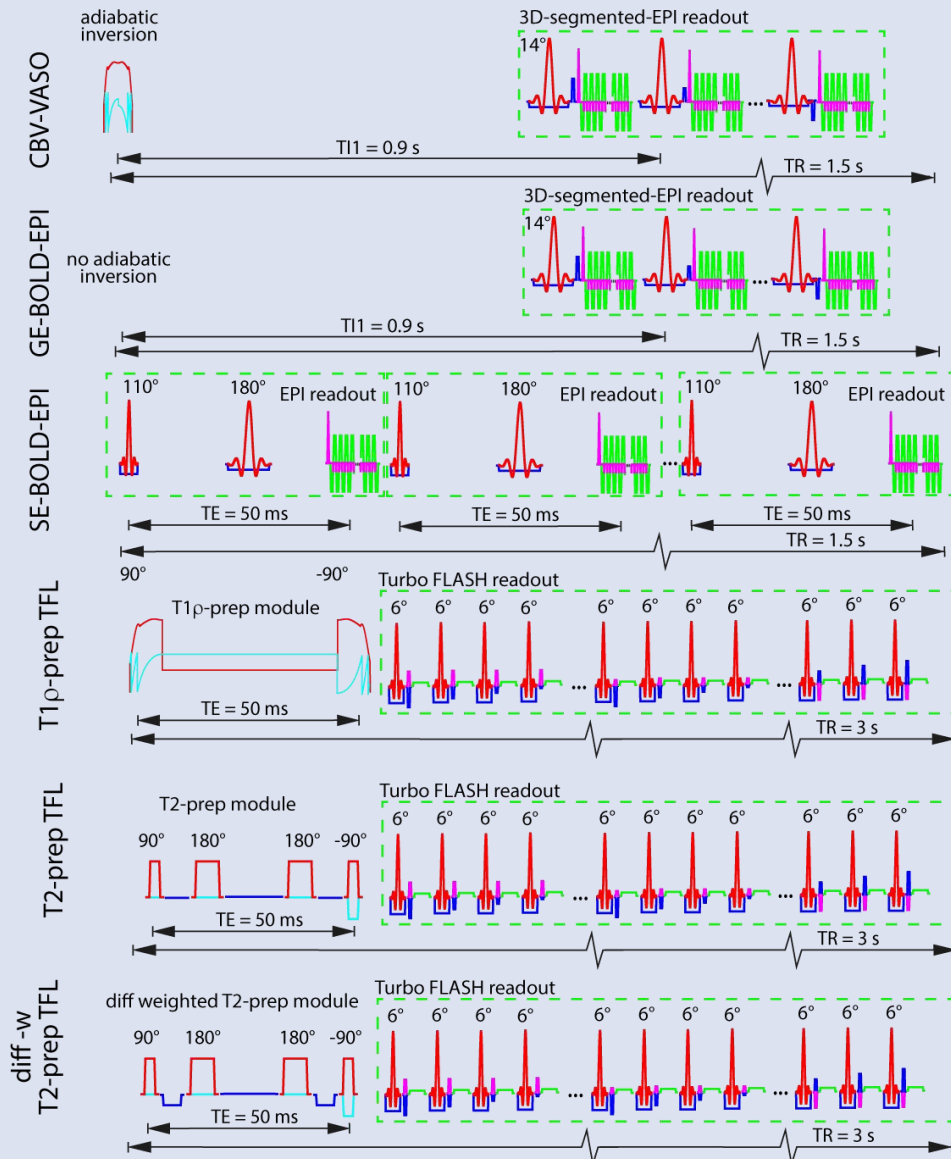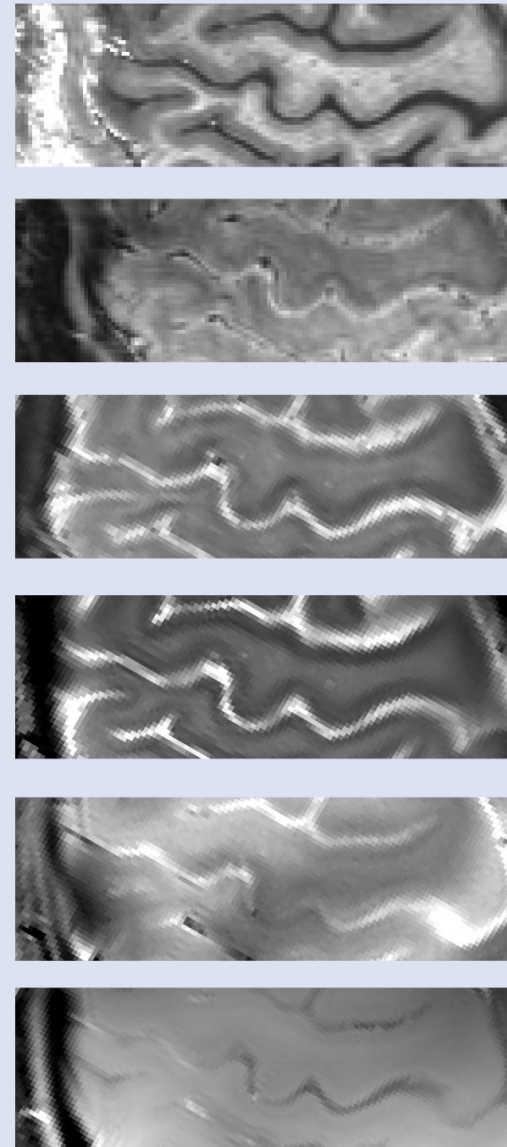
➤ 48 Tesla

3.0 mm

specificity

VASO
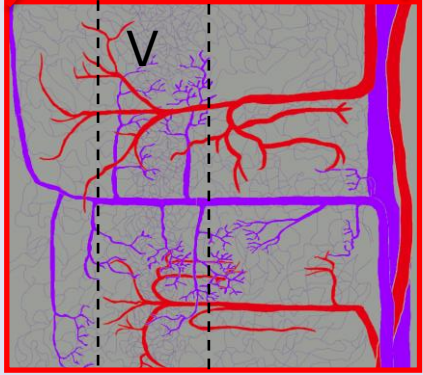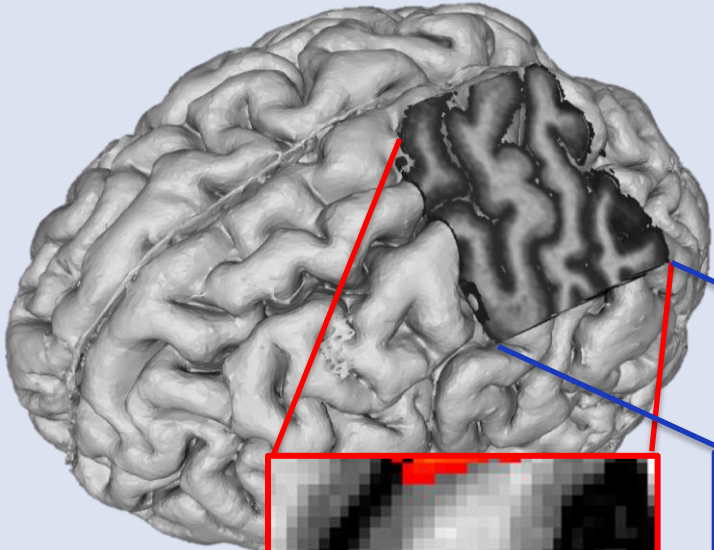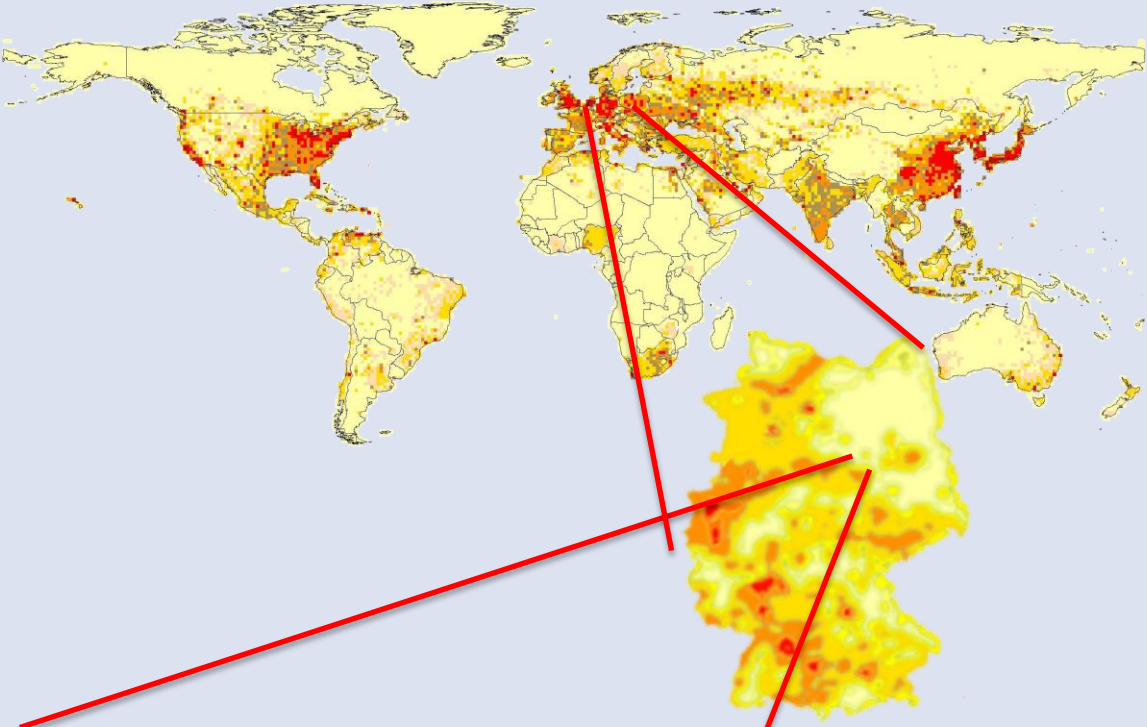
comparing contrast mechanisms

sequence   MRI contrast   fMRI signal change

[Huber et al., ISMRM, 2017a]

comparing contrast mechanisms

GRASE BOLD

GRASE VASO

CBF — BOLD
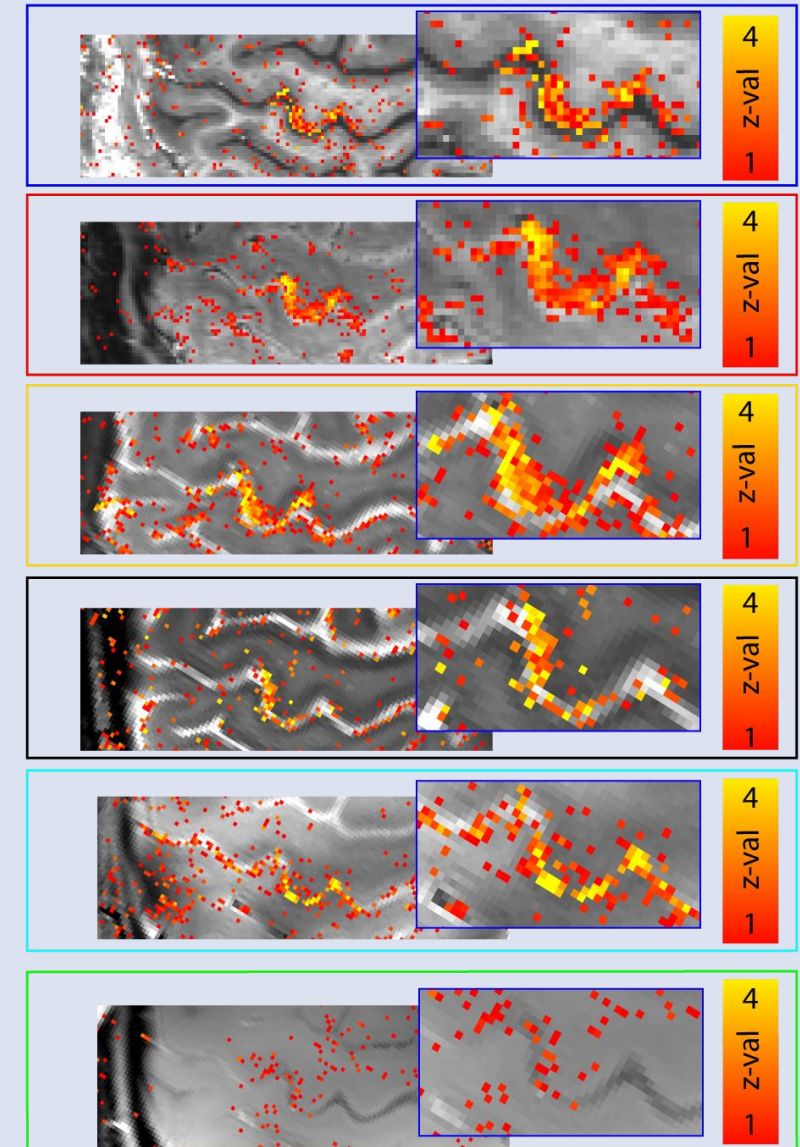
Acquired in collaboration with Tania Dadakova and David Feinberg

GE-BOLD

GRASE-BOLD

SE-BOLD

VASO-3D EPI

VASO-GRASE

$T_1\rho$-prep
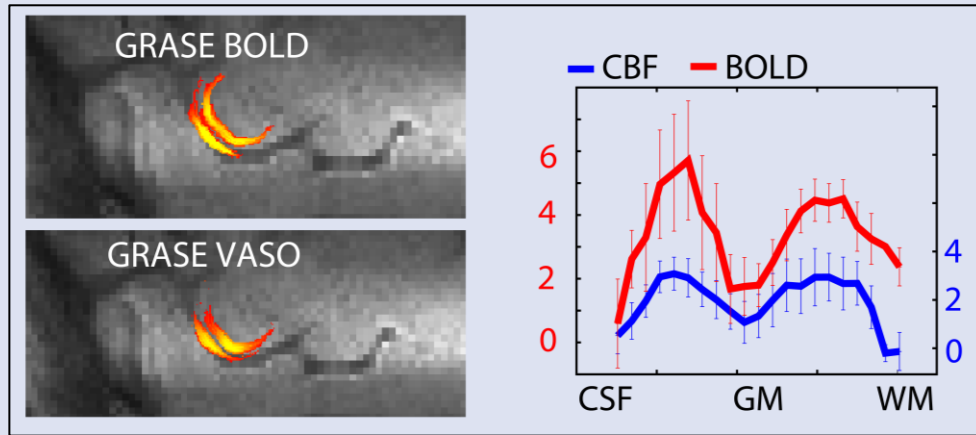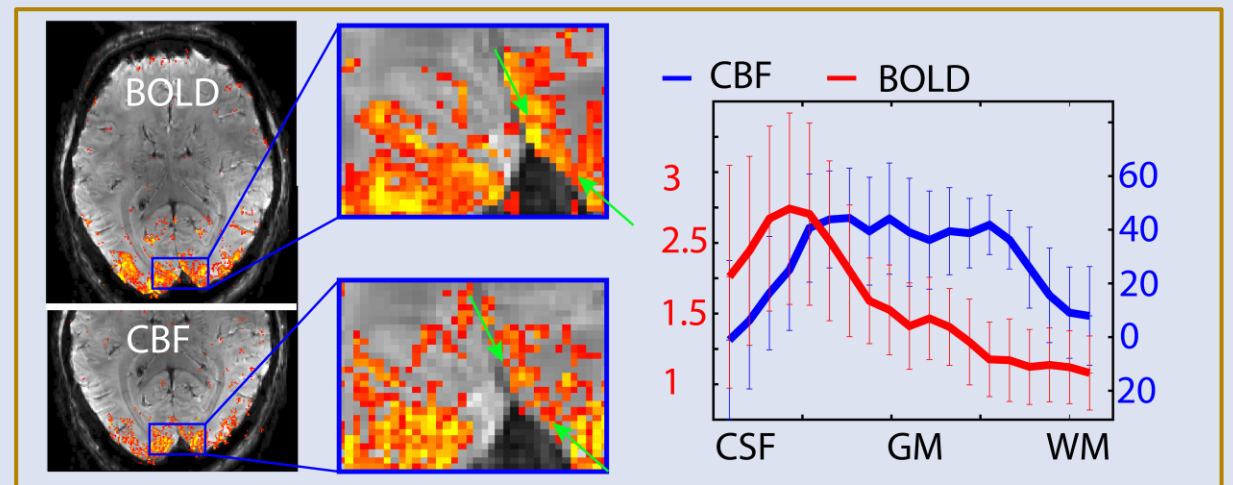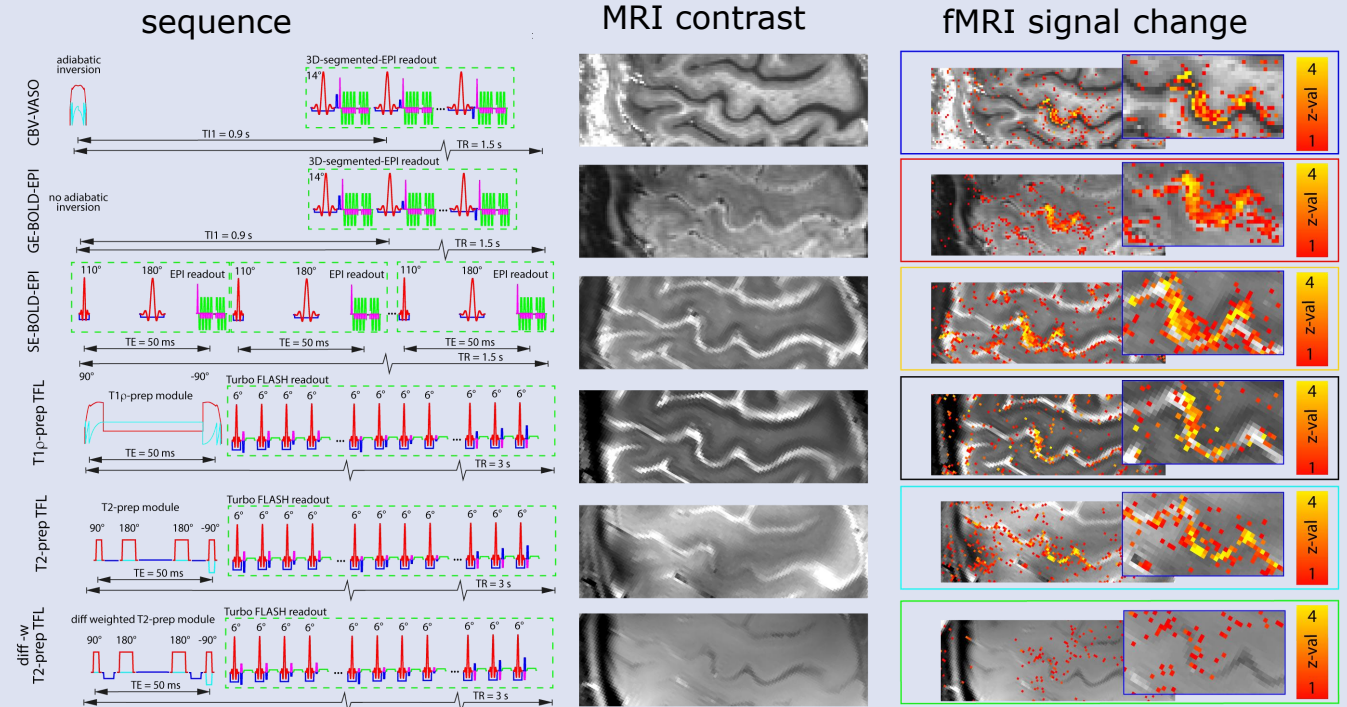
ASL

T_2-prep

diffw T_2-prep

senstivity [a.u]

specificity [%]

sequence

MRI contrast

fMRI signal change

CBF — BOLD

BOLD

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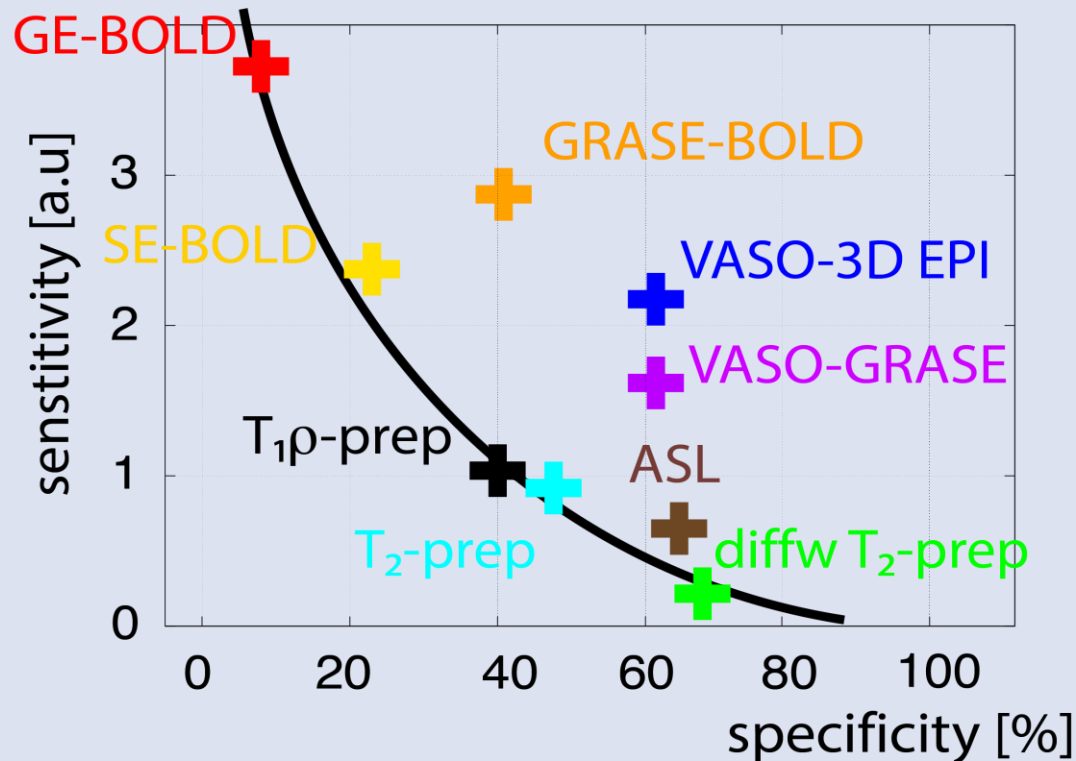
[Huber et al., NeuroImage 2018], acquired from Dimo Ivanov

field strength

3T

7T

9.4T

ΔCBV [ml]

2

1
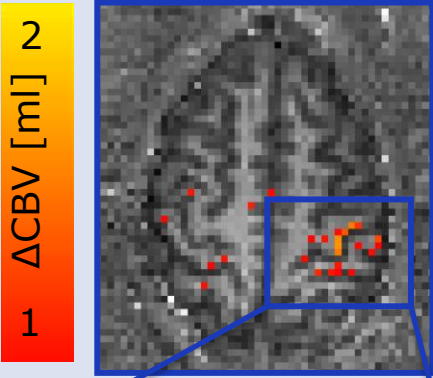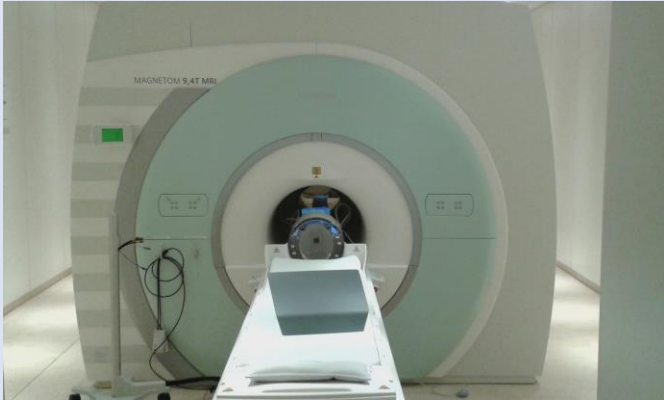
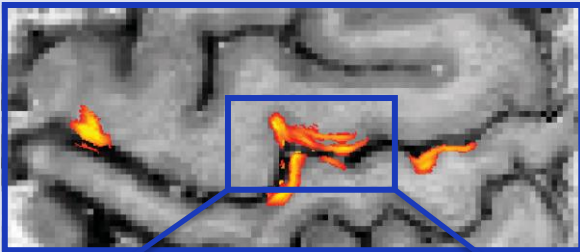3 mm resol.
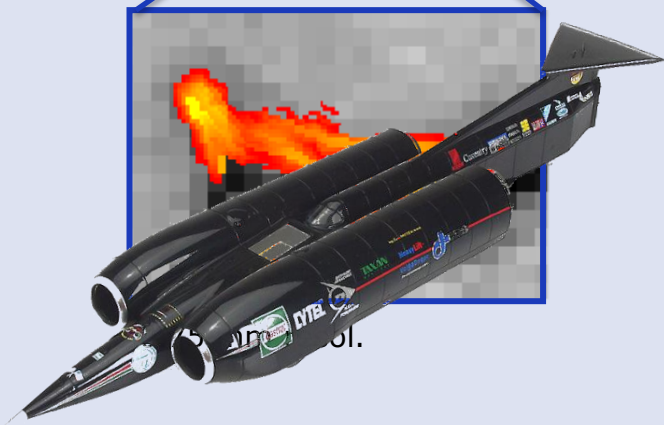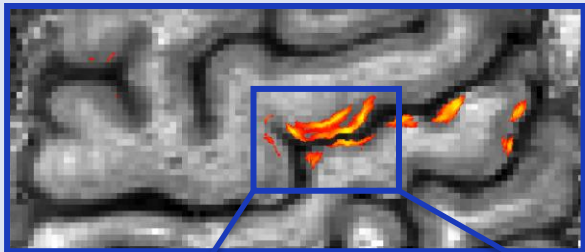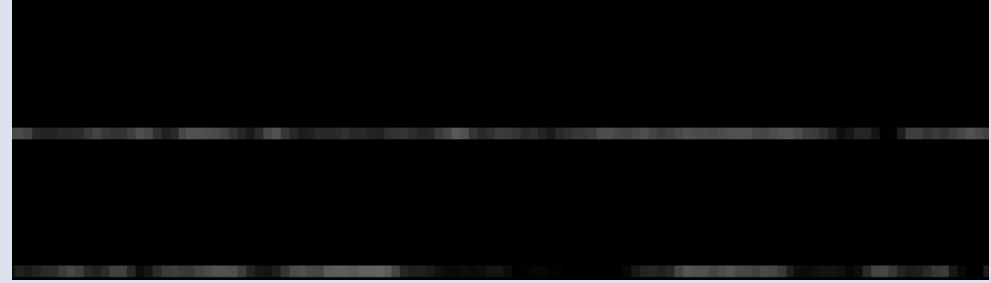
readout

2D-SMS-EPI

[Setsompop, 2012]

readout

3D-EPI

2D-SMS-EPI
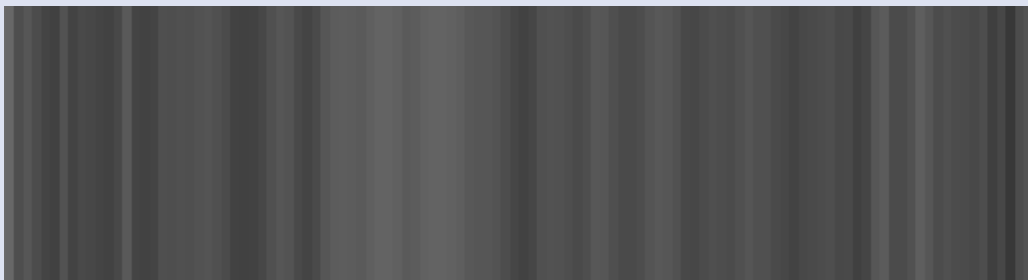
[Poser, 2010, 2013]

[Setsompop, 2012]

3 mm

3D-EPI

2D-SMS

0.75 mm

3D-EPI

2D-SMS

temporal signal to noise ratio in N=4 participants

relative SNR

voxel volume [µl]

— 3D EPI
— 2D EPI
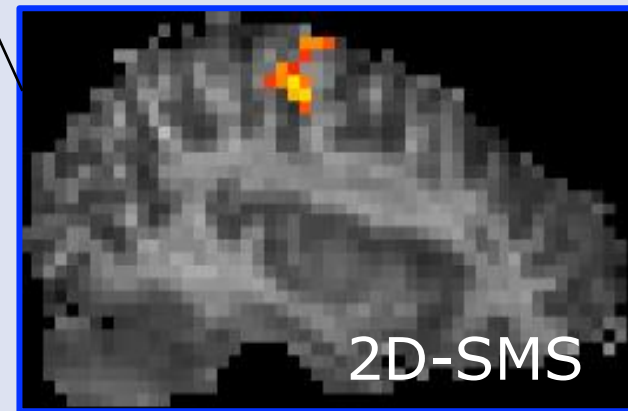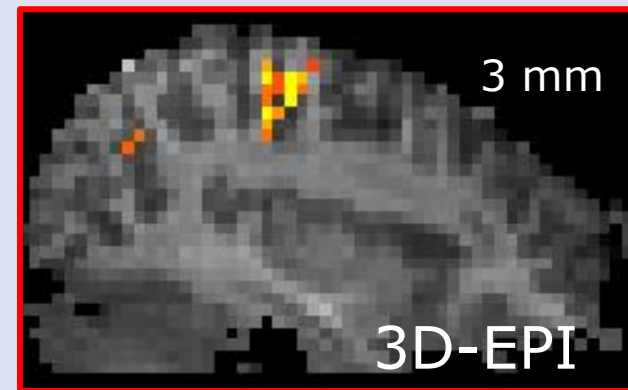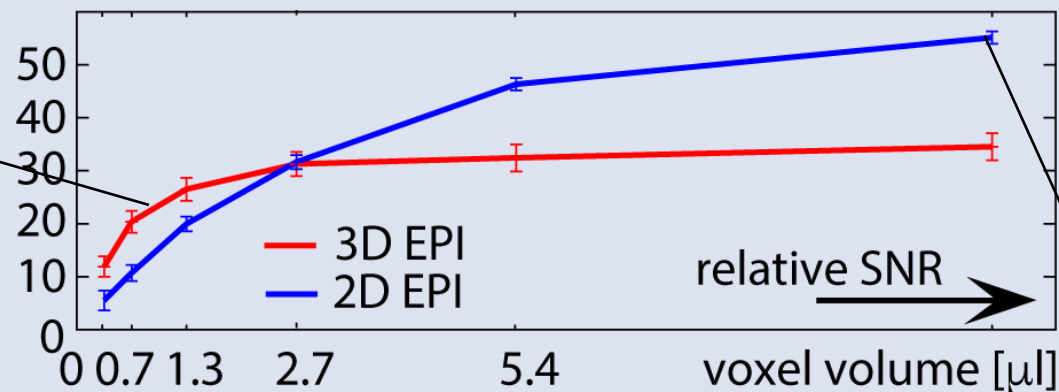
[Huber et al., NeuroImage, 2018]

motion

- participant training
- padding

field motion is biggest motion
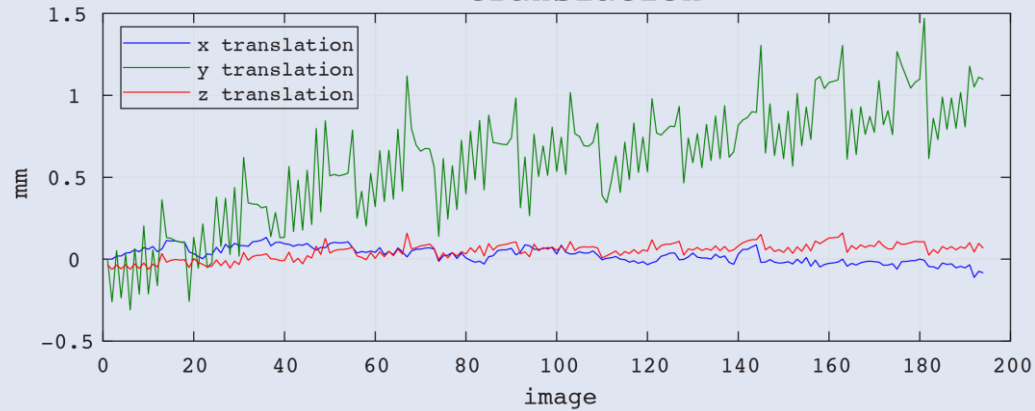
Valsalva breath holding respiration task
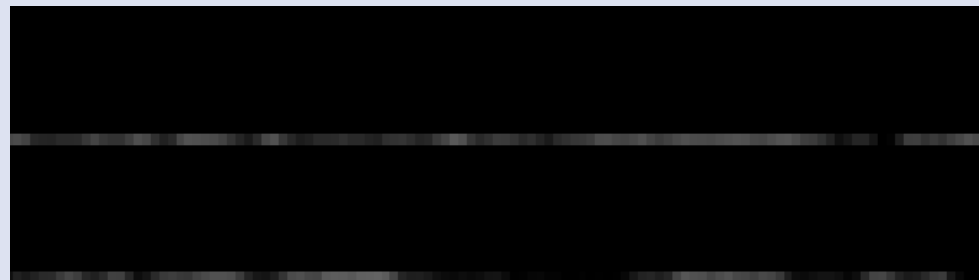

local motion correction

surface analysis
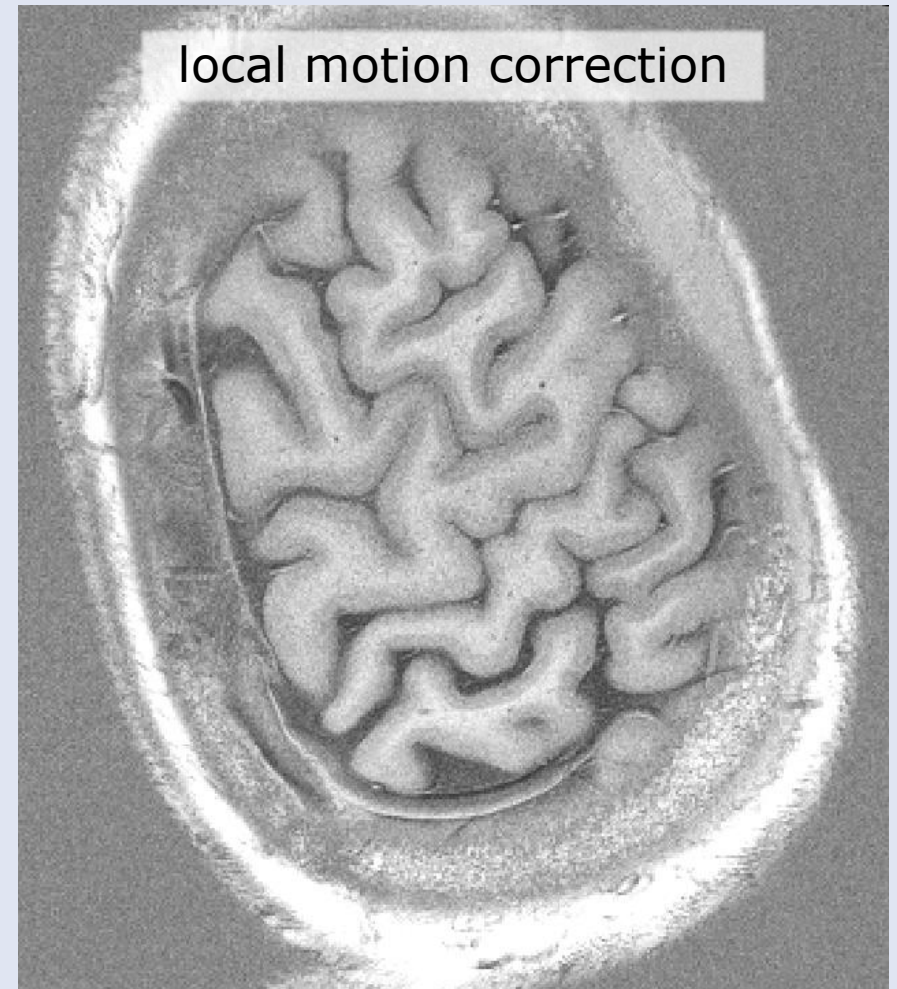
equi-distant and equi-volume surfaces
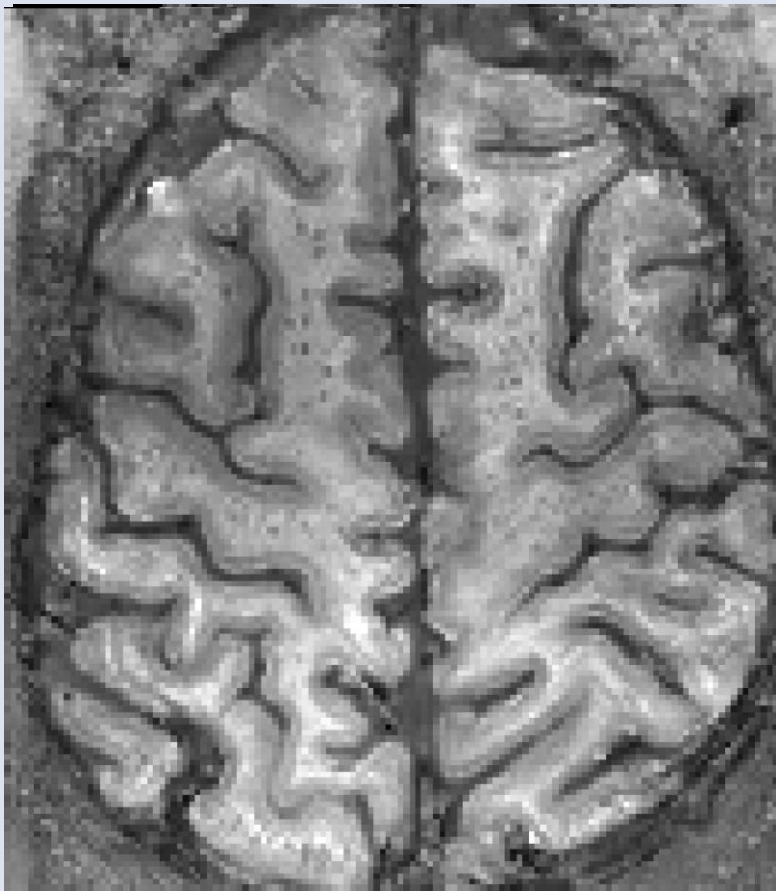
0.79 mm isotropic
24 slices, 7T, SC72
Nova head coil

All done in EPI Software package: LAYNII
https://github.com/layerfMRI

Software tutorials: https://layerfmri.com

Thanks to Daniel Glen and
Rick Reynolds for their nii I/O
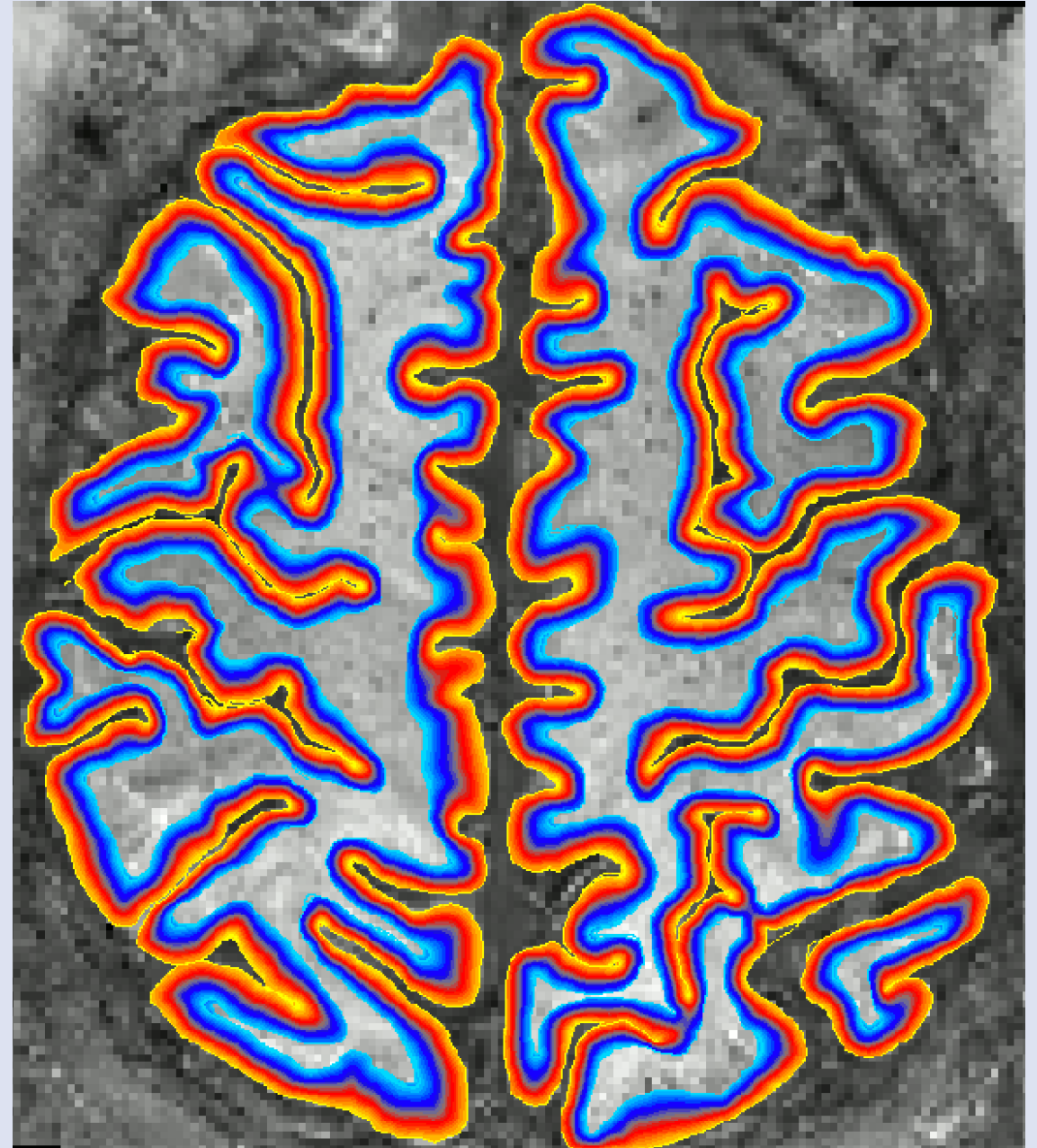
normalizing "depths" to layers
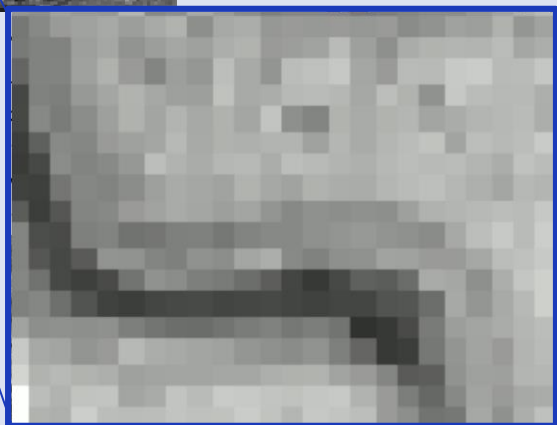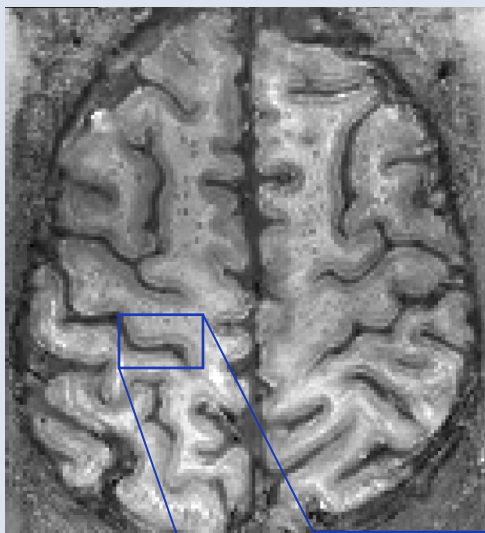
200 μm ex-vivo
[In collaboration with Carsten Stüber]

in vivo 0.35 mm

CSF | I | II | III | Va | Vb | VI | WM
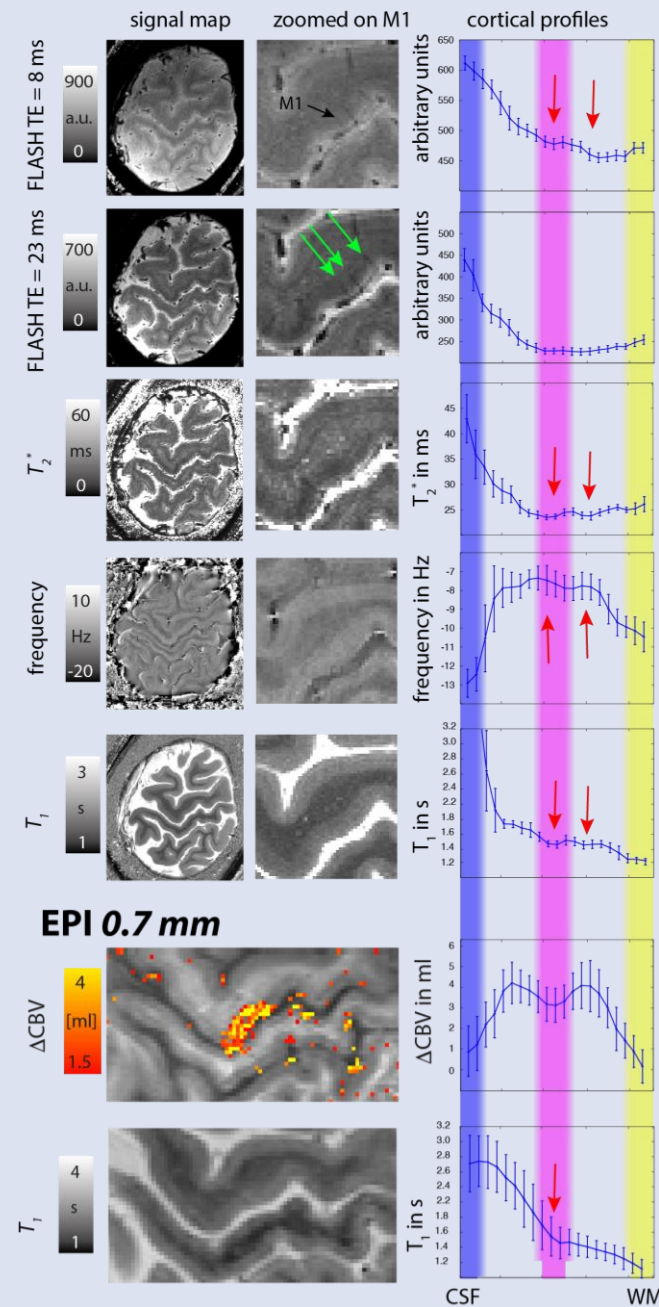
[Huber et al., Neuron, 2017 , a collaboration with Carsten Stüber, Cornell]

input vs. output in M1
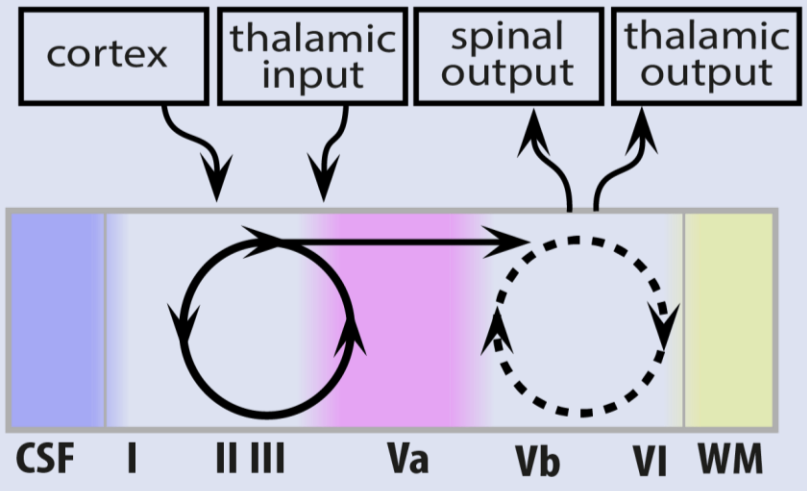
[Weiler, et al., 2008; Papale and Hooks, 2017, Mao, 2011]

A) tapping with touch, tapping without touch *Like Slayer-Robert [Trampel 2011]*, touch only, ipsilateral tapping

input and output, reduced input output, input no output, callosal input no output
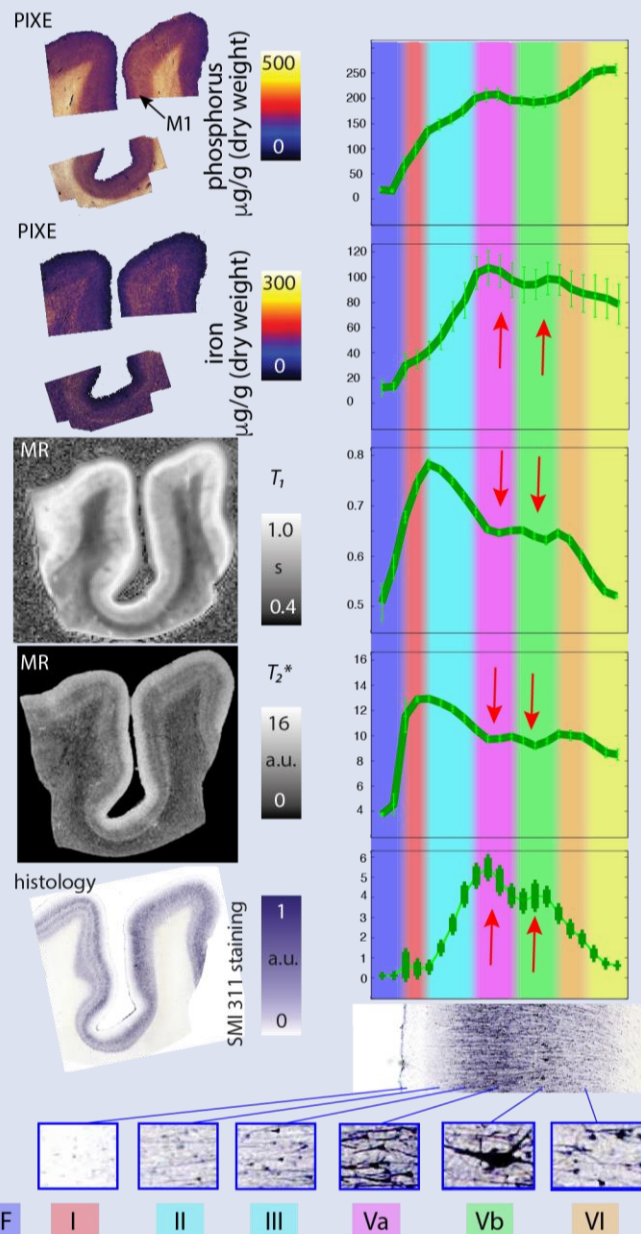
pinch representation

ΔCBV, BOLD

4 [ml] 0.5, -0.5 -3, 8 [%] 1, -1 -6

B) CBV, BOLD
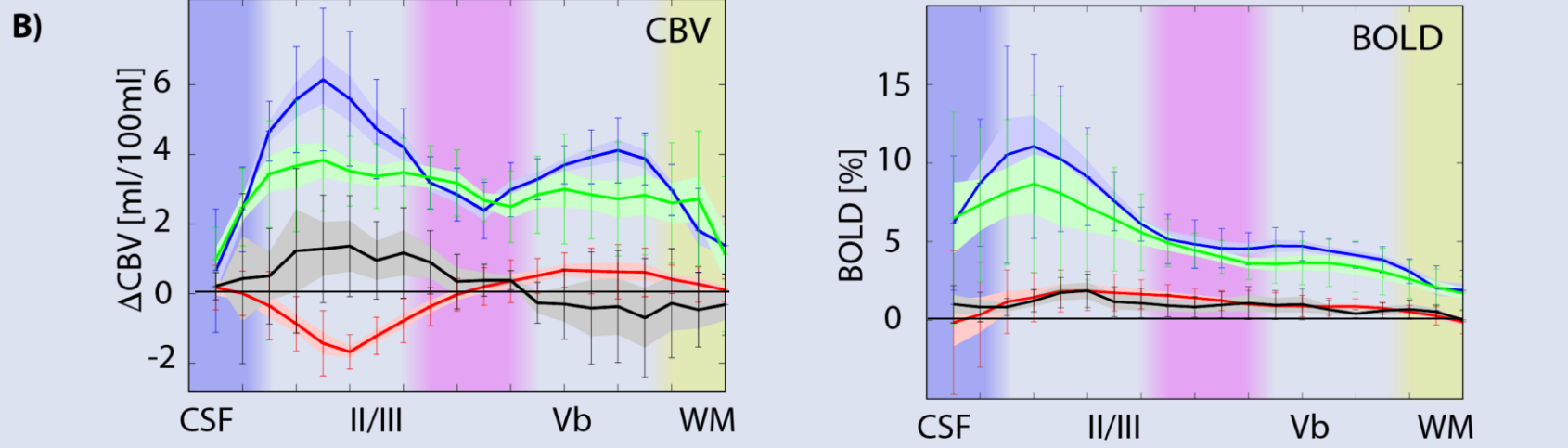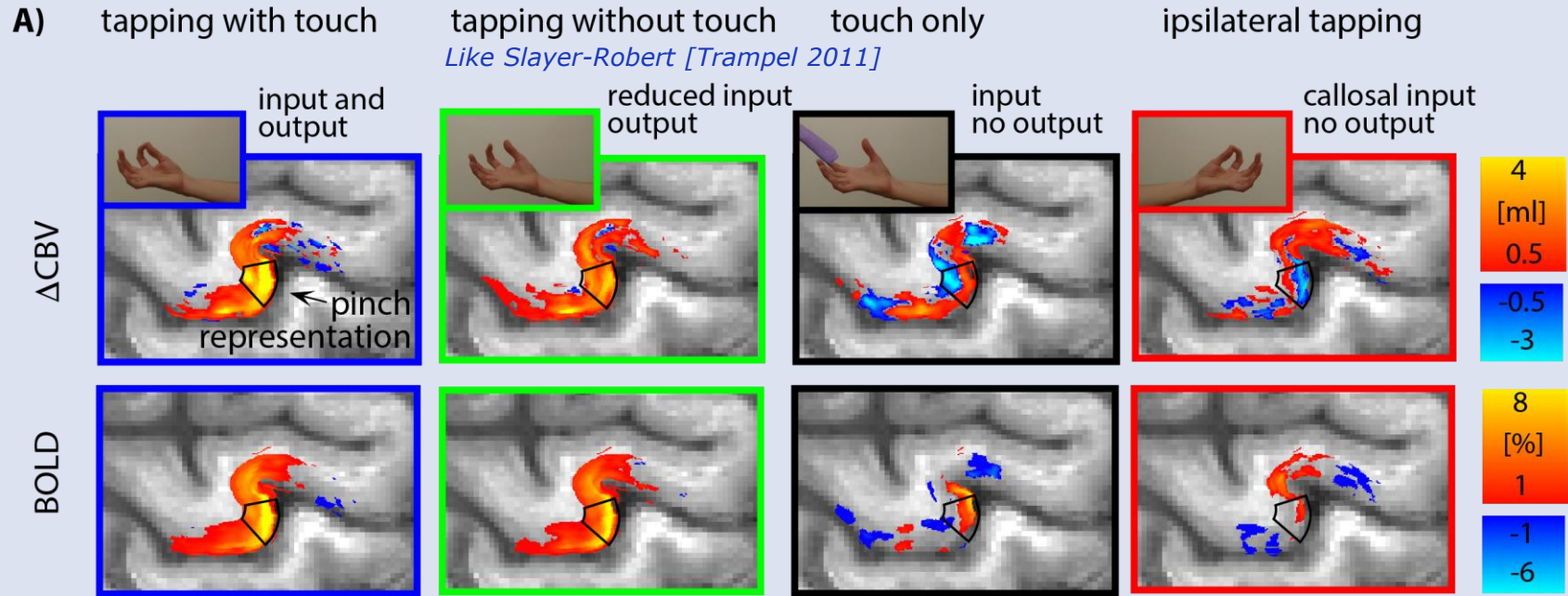
standard error across participants — standard deviation across participants — average across participants

[Huber et al., Neuron, 2017]

Vascular bias correction

ΔCBV [ml/100ml]

CSF Va WM
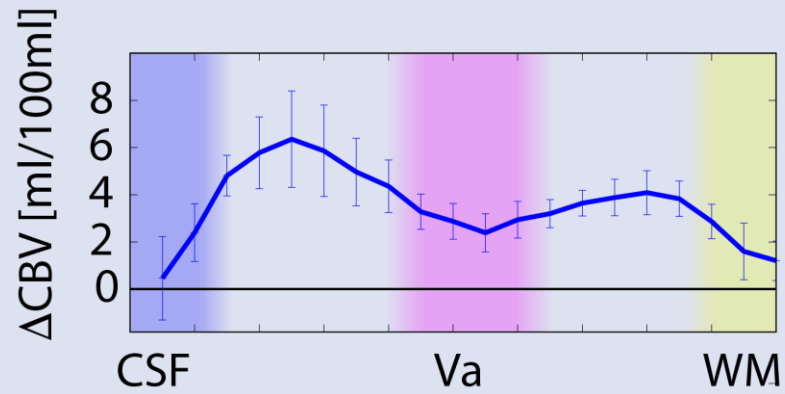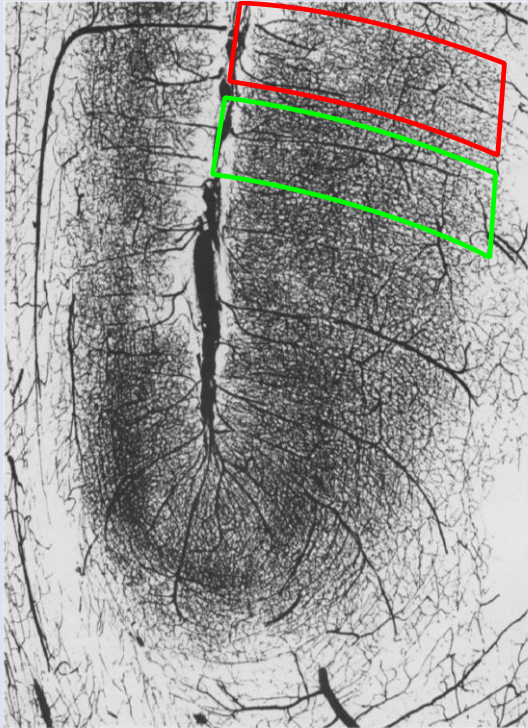
— measured raw signal
— Heinzle-Markuerkiaga model 1
— Heinzle-Markuerkiaga model 2

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

BOLD [%]

CSF Va WM
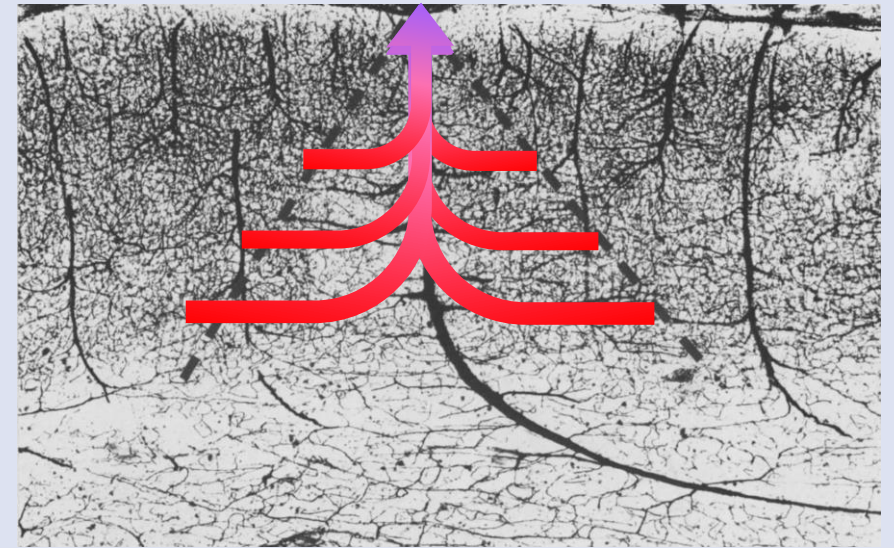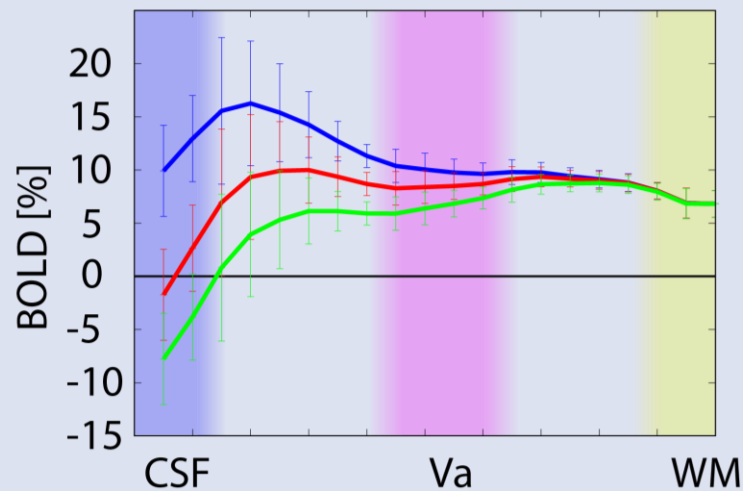
$$\tau_u \frac{d\nu_u}{dt} = f_u - \nu_u^{\frac{1}{\alpha}} + \boxed{\lambda_d \nu_l^*}$$

[Heinzle et al., NeuroImage, 2016]

BOLD

BOLD [%]

CSF II/III Vb WM
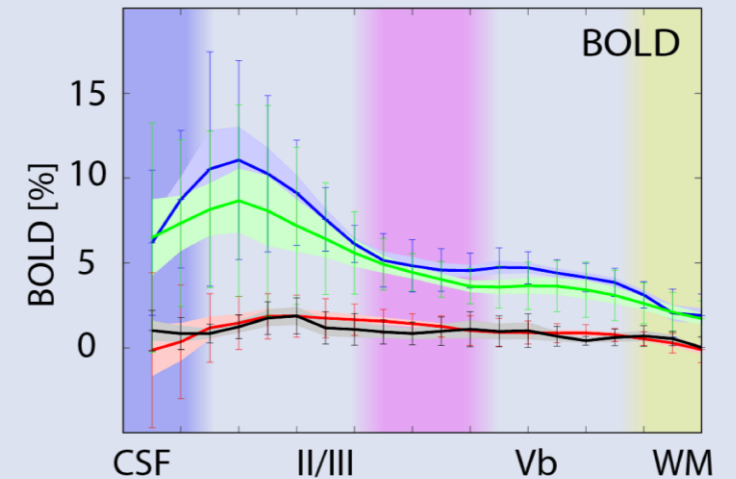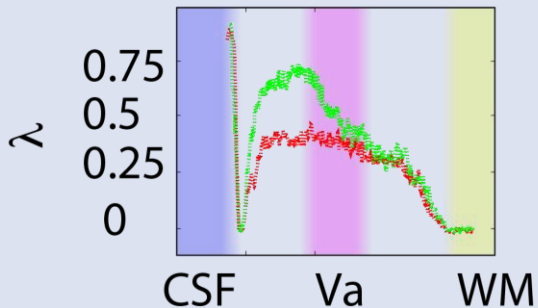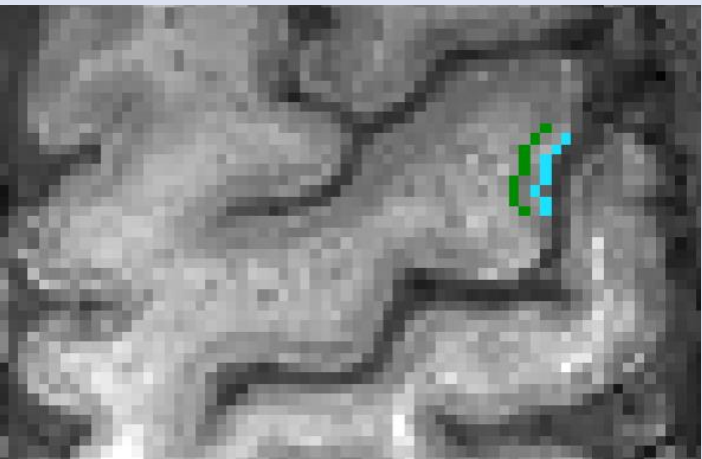
resting state   seed in superficial layers   seed in deep layers

seed across areas

comparing with random control seeds

S1 seed

pre motor seed

0.5 ΔCBV [ml/100ml] 3

seeds:

ROIs

connectivity with M1

ΔCBV in M1

upper peak

seed in S1

ΔCBV in M1

double peak

seed in pre motor

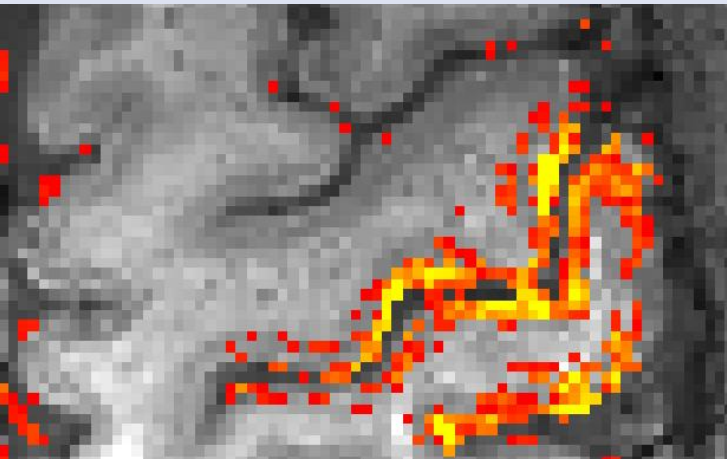* significant connectivity with S1 cortex ($p < 0.05$ uncorr.)

* significant connectivity with pre-motor cortex ($p < 0.05$ uncorr.)

* significantly more connectivity with S1 compared to premotor cortex ($p < 0.05$ uncorr.)

— pre motor
— S1
├──┤ stdev across participants
▨ uncertainty level from control seeds
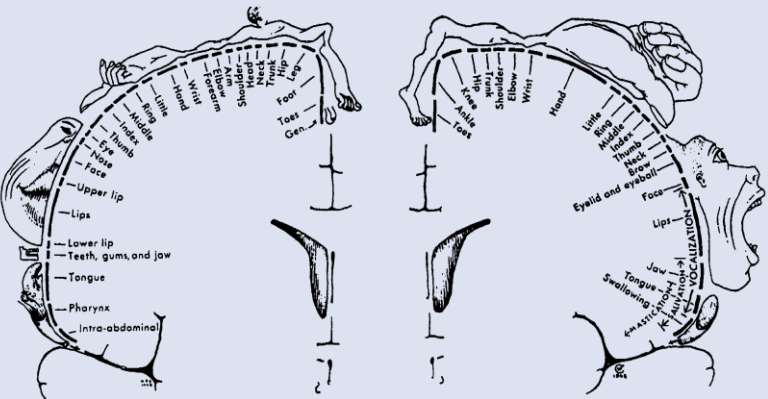
17/35

From layers to columns

Tasks used here:

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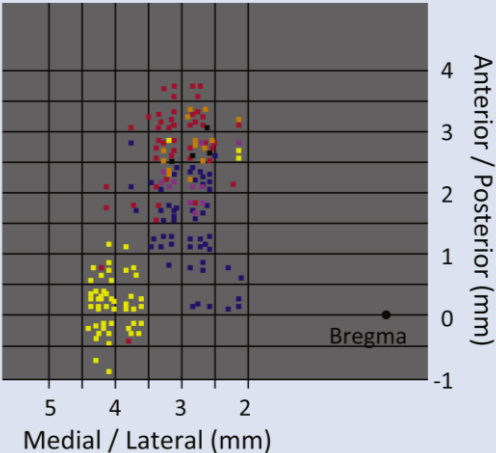- —— thumb tapping (0.75 Hz)

'columnar' topology in M1

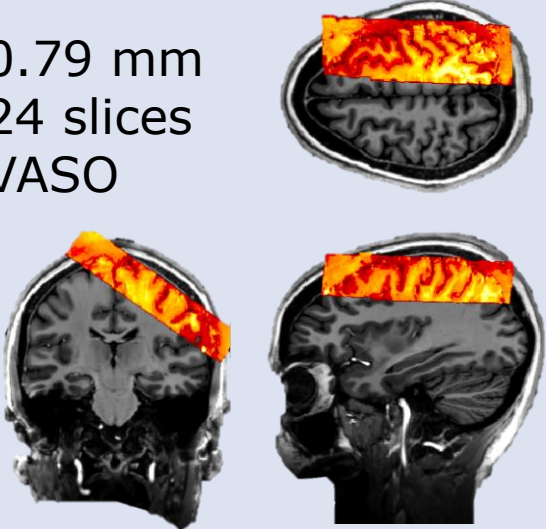somatosensory area (**left**) and primary motor area (**right**).

Action map

Reach ▇

Grasp ▇

Retract ▇

Graziano (2016) Cell

Anterior / Posterior (mm)
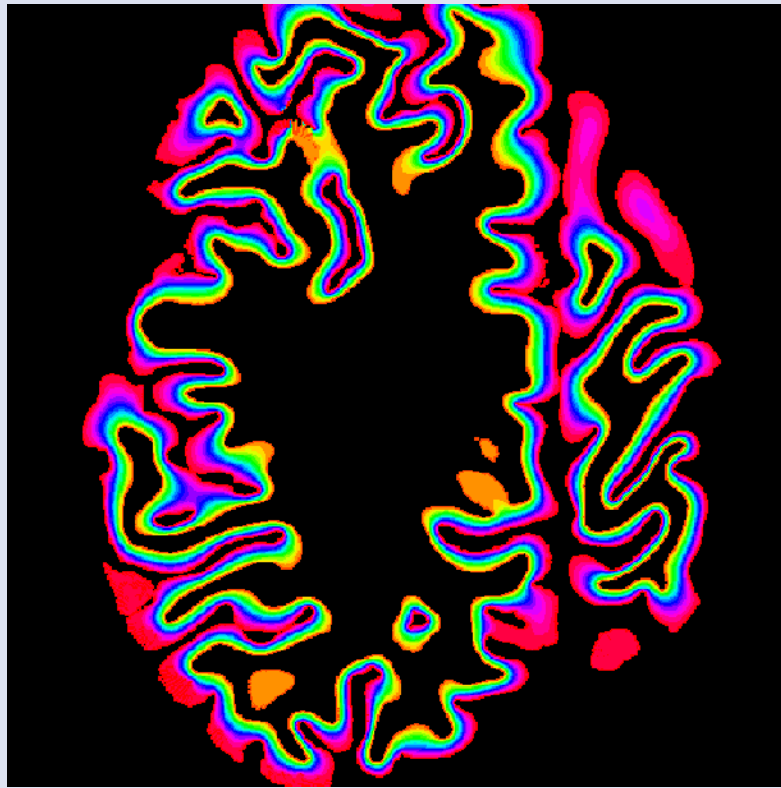
Bregma

Medial / Lateral (mm)

Data used here:

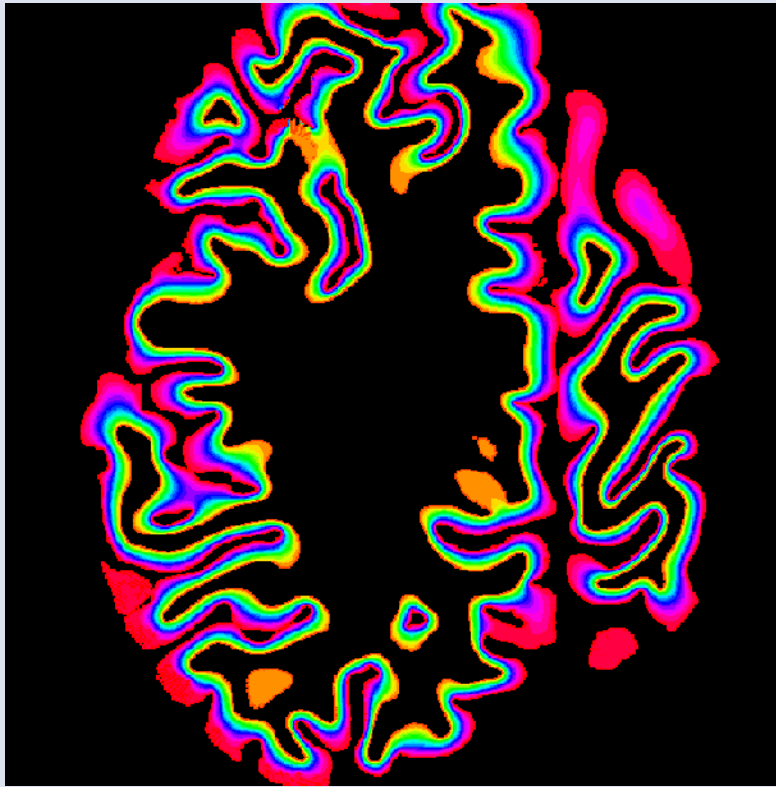- 0.79 mm
- 24 slices
- VASO

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