# IMAGING HUMAN BRAIN ANATOMY, FUNCTION AND CONNECTIVITY:

# ADVANCES ACHIEVED THROUGH NOVEL INSTRUMENTATION

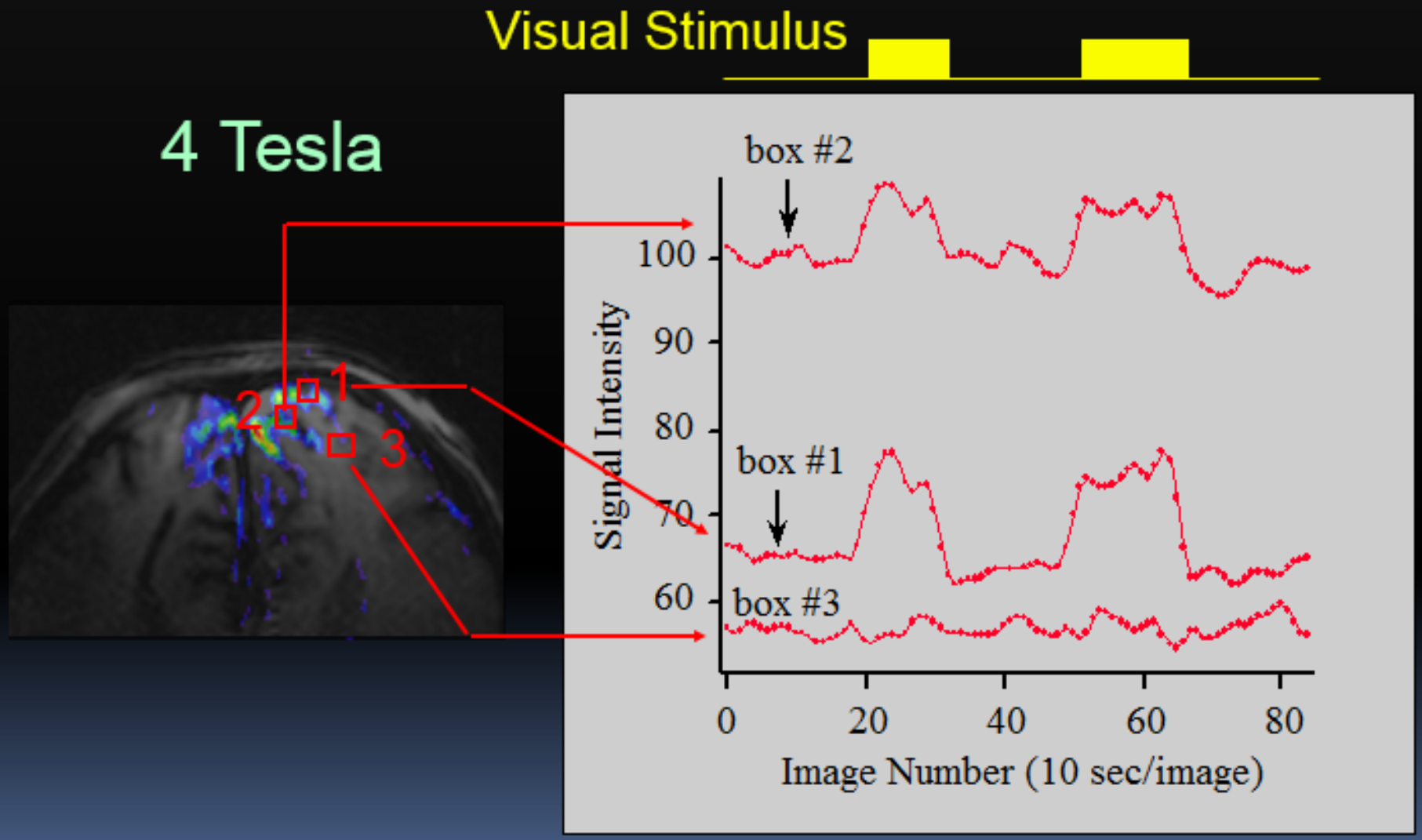
1992 First papers introducing FUNCTIONAL IMAGING in the HUMAN BRAIN (fMRI) appeared in Press

2012 We celebrated two-decades of fMRI

**TWO MAJOR INVESTMENTS in INSTRUMENTATION**

- UMinn: 4 Tesla HUMAN capable MR INSTRUMENT
- MGH: 1.5Tesla but Ultrafast Imaging Capable Instrument

# Functional Imaging with Magnetic Resonance



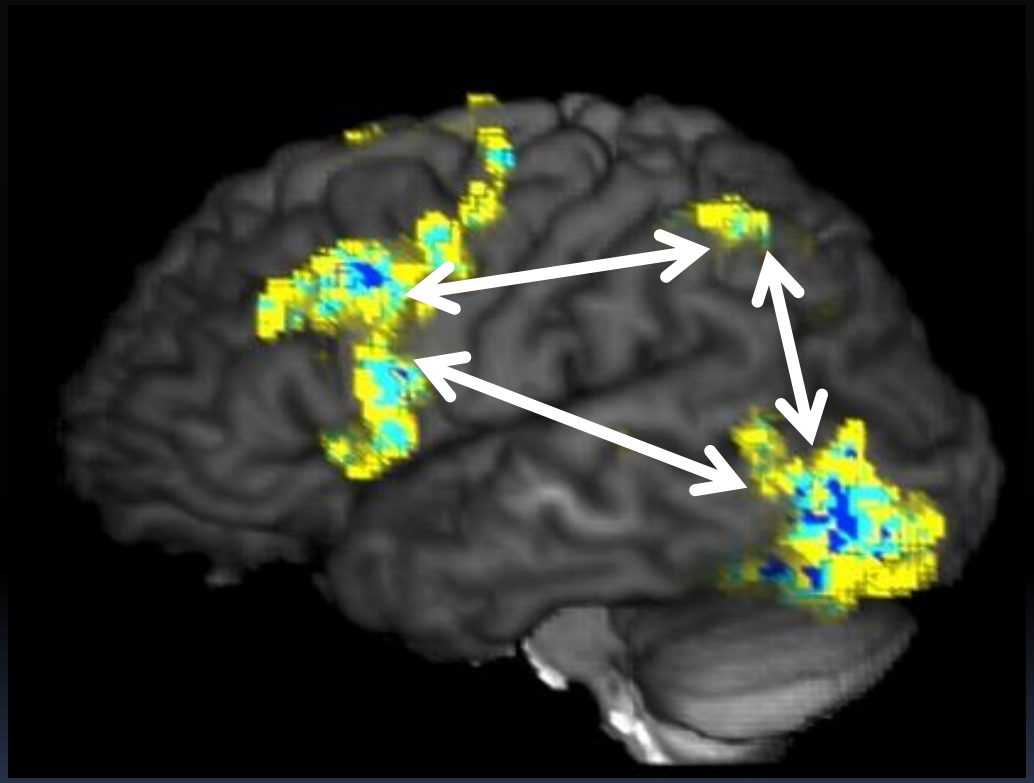

Ogawa et al. Proc Natl Acad Sci USA (1992) 89, 5951-5955

BEHAVIOR
or
PERCEPTION

NEURONAL
ACTIVITY

# The different SCALES of the BRAIN's FUNCTIONAL ORGANIZATION

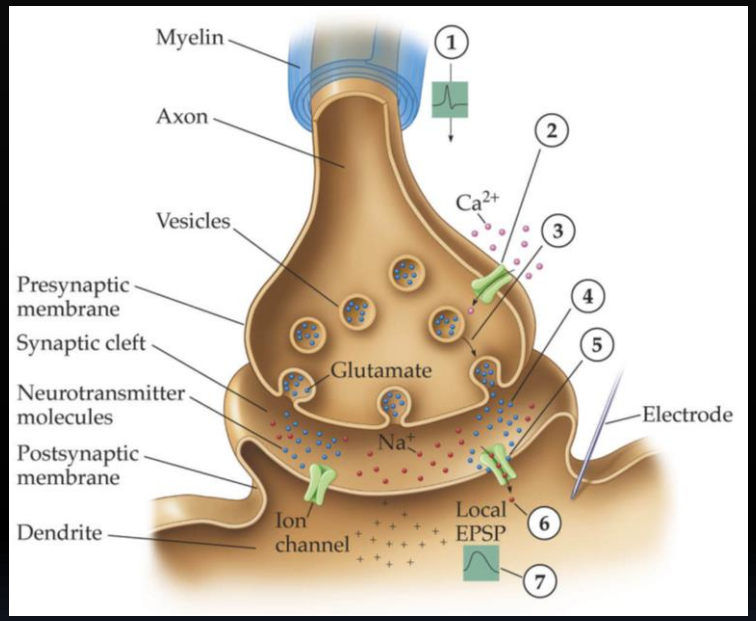
# Scales of the Brain

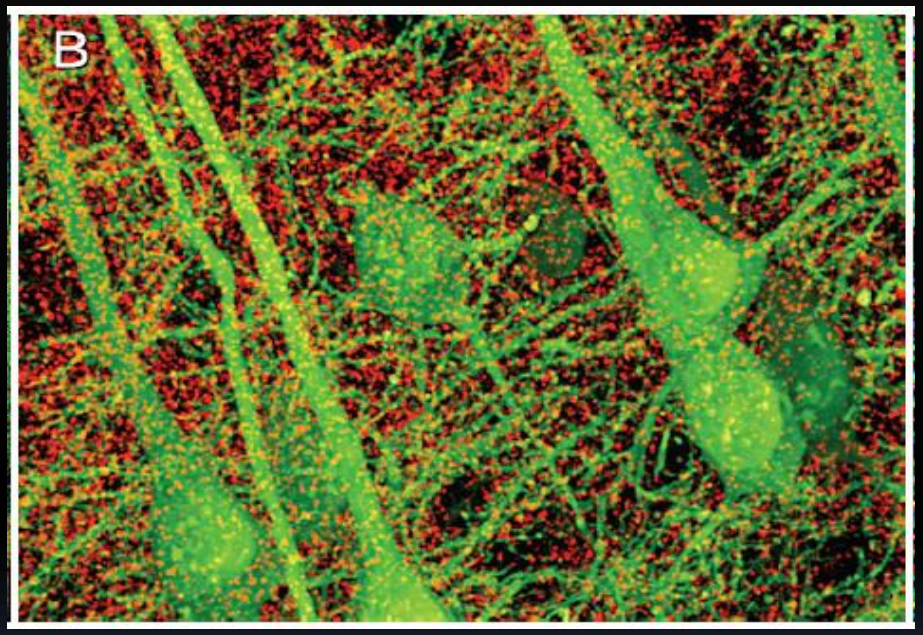


Silent Word Generation

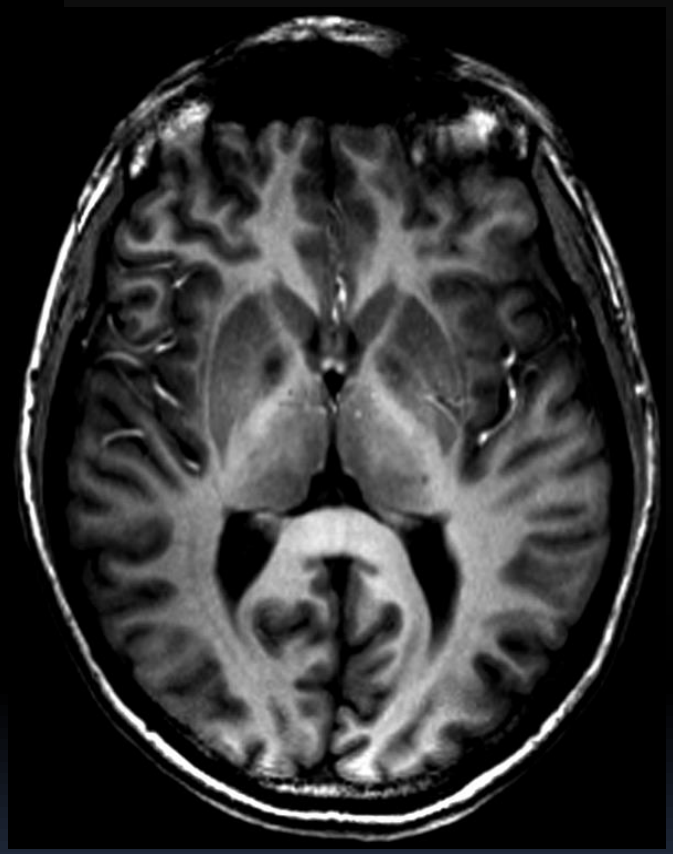
Global networks

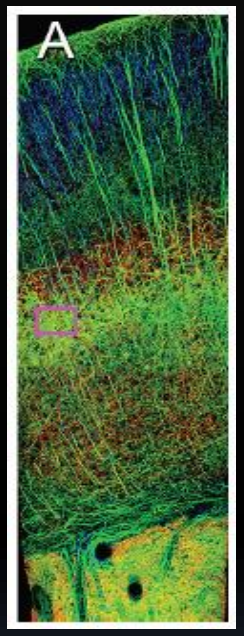
# Scales of the Brain

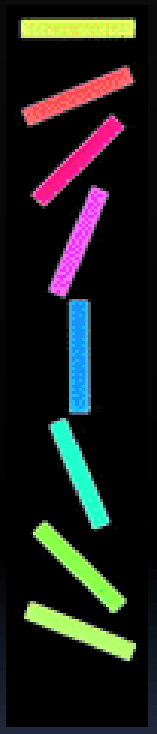


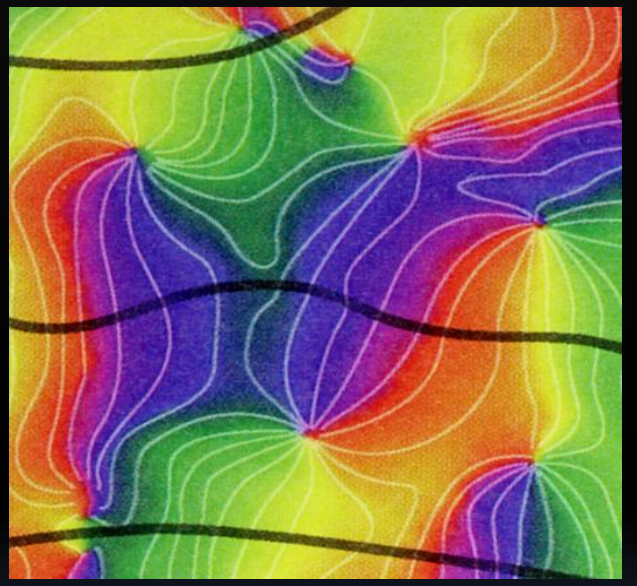
# Scales of the Brain





Orientation Domains in the Primary Visual Cortex

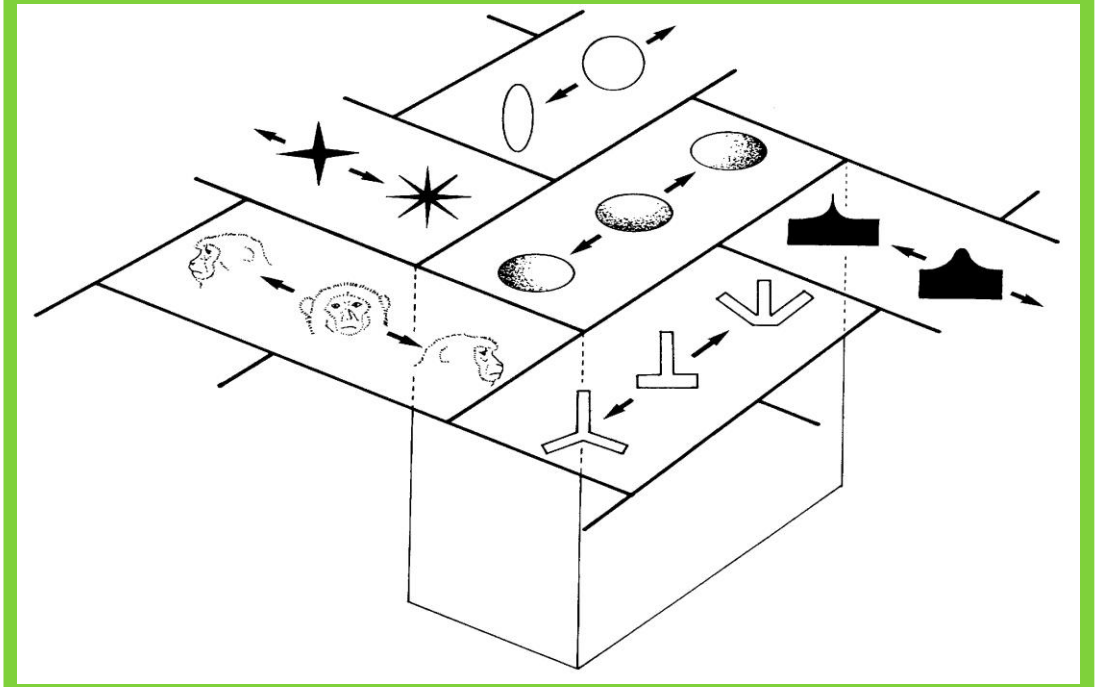


~4 mm

Monkey Cortex

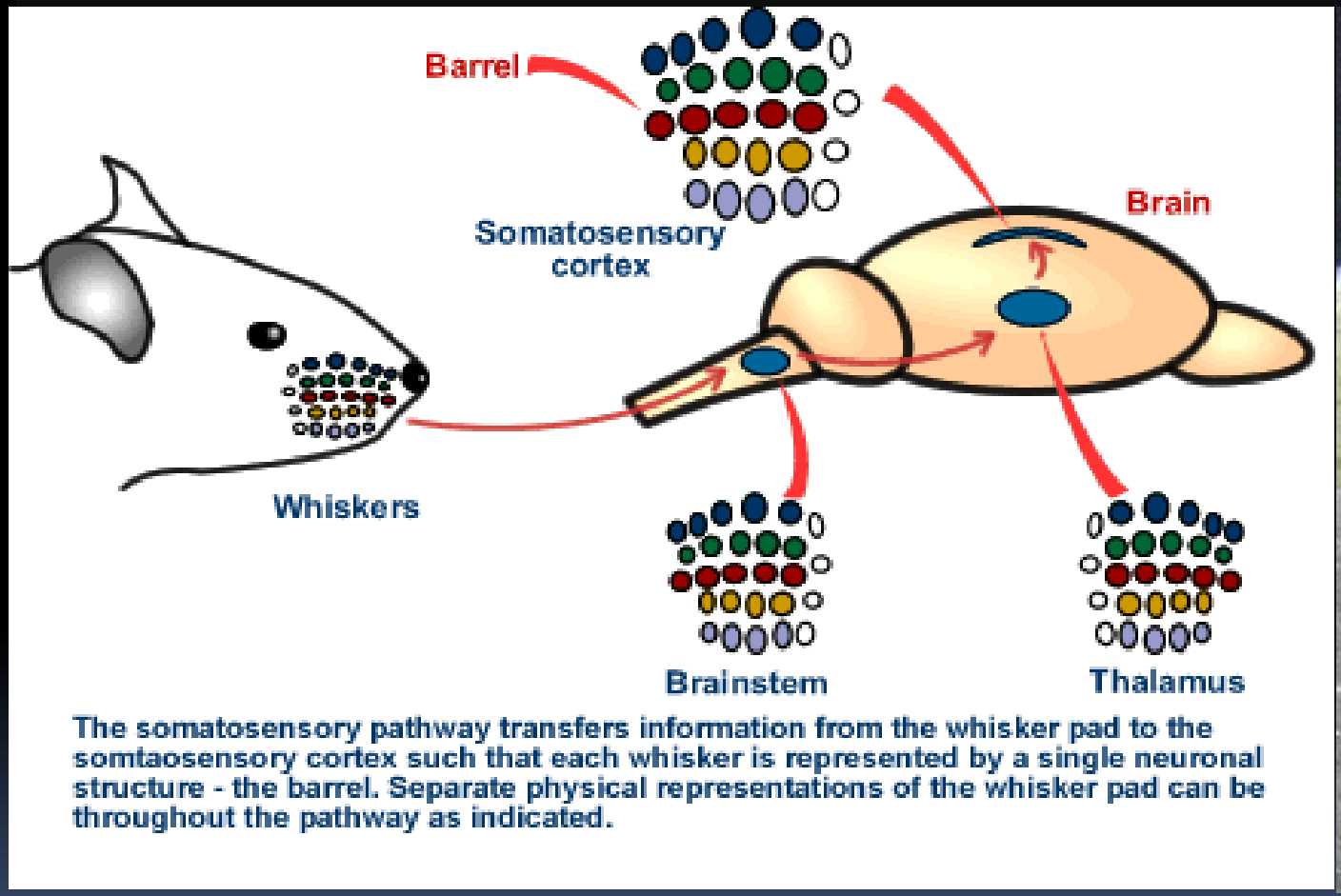
Optical Imaging

## Object selective columns in IT

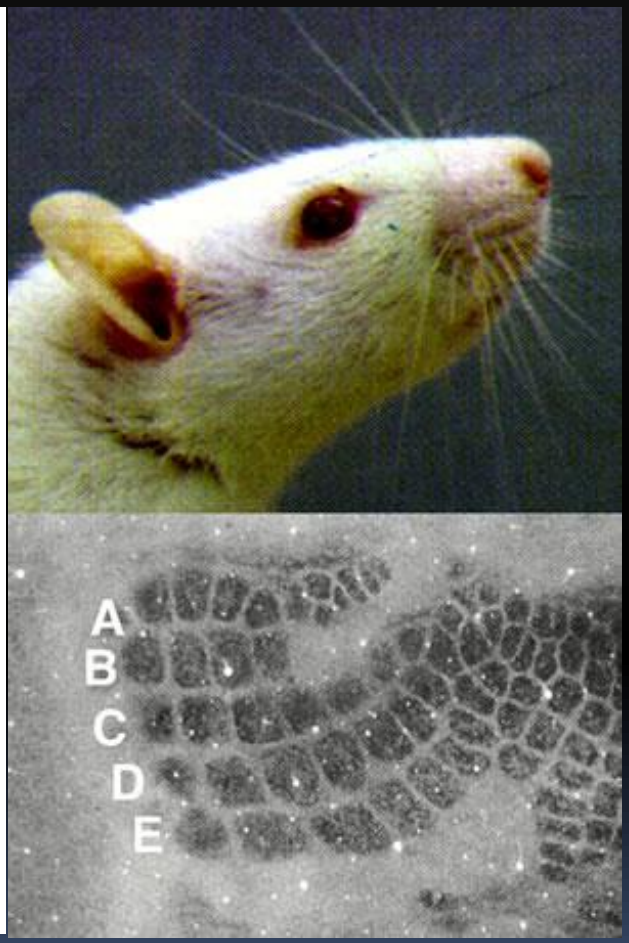


Tanaka, *Annu Rev Neurosci*, 1996

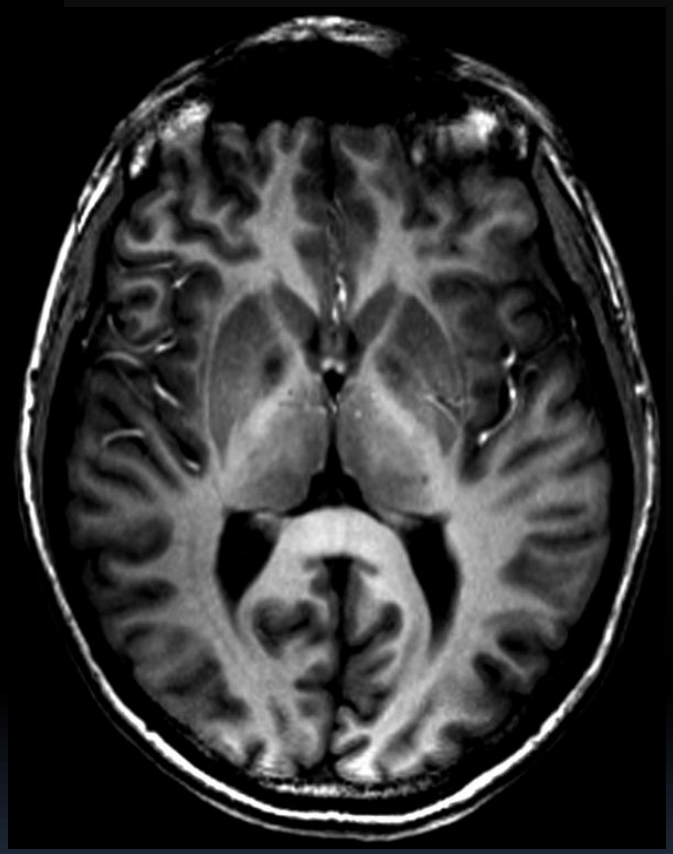
# Whisker Barrels

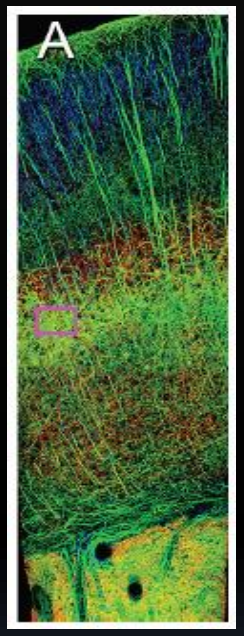


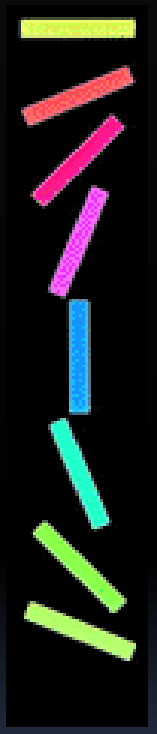

The somatosensory pathway transfers information from the whisker pad to the somtaosensory cortex such that each whisker is represented by a single neuronal structure - the barrel. Separate physical representations of the whisker pad can be throughout the pathway as indicated.



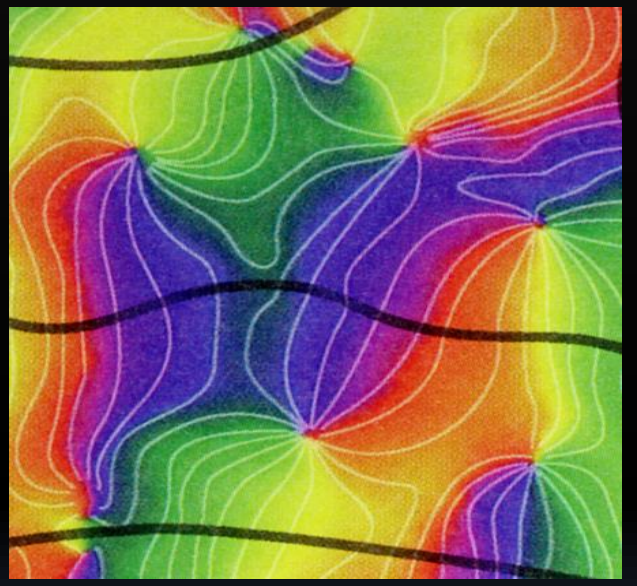
# Scales of the Brain





Orientation Domains in the Primary Visual Cortex



~4 mm

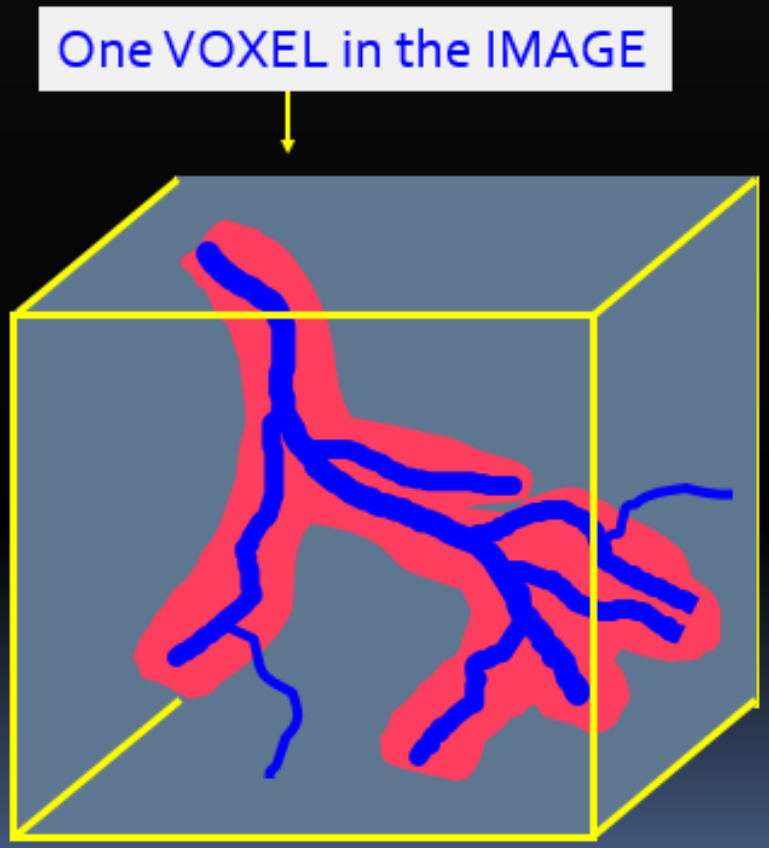
Monkey Cortex

Optical Imaging

FIRST QUESTION:

Is cerebral physiology compatible with MR imaging of functional activity at columnar level??

# BLOOD OXYGEN LEVEL DEPENDENT CONTRAST (BOLD)



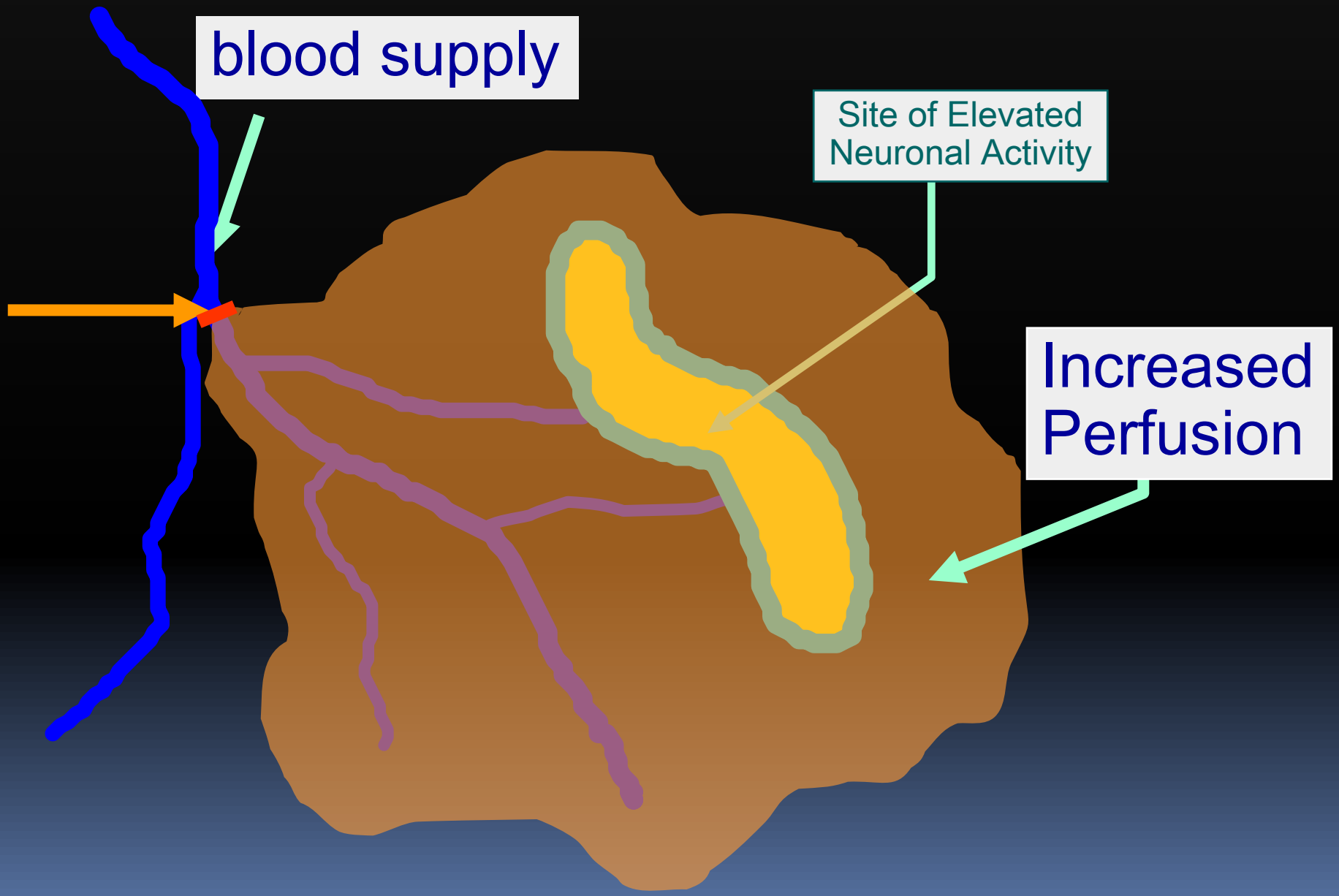

DEOXY-Hemoglobin
(Paramagnetic)

INCREASED NEURONAL ACTIVITY

INCREASE in REGIONAL BLOOD FLOW (& Volume)

*LOWER DEOXYHEMOGLOBIN CONTENT* per unit volume in the BRAIN if Cerebral Oxygen Consumption ($CMRO_2$) does not increase commensurately

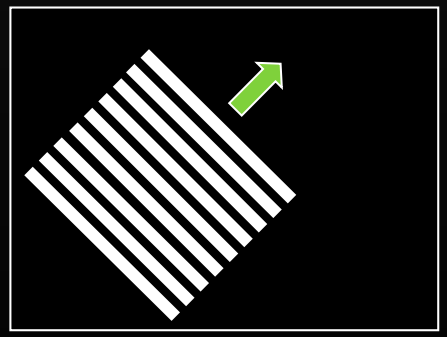
# SPECIFICTY of the METABOLIC and HEMODYNAMIC RESPONSES



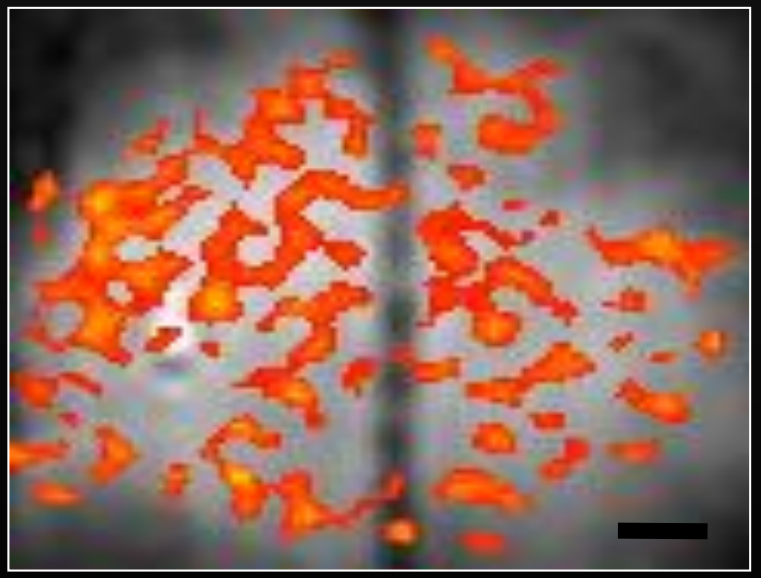
# 9.4 Tesla/ 31 cm Bore for animal model studies (~1994)

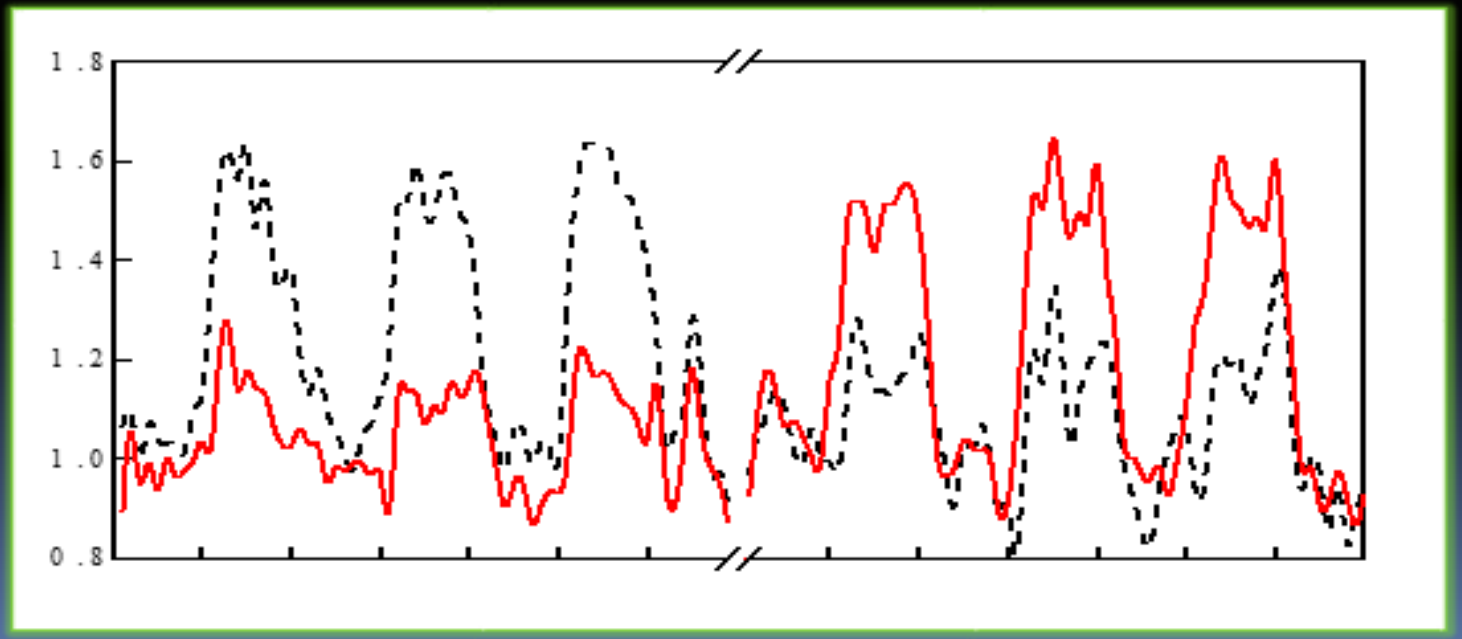
# ISO-ORIENTATION DOMAINS in the CAT VISUAL Area 18: SINGLE Orientation, SINGLE CONDITION

T. Duong, S-G. Kim et al., PNAS (2001): 98; 10904-10909



CBF





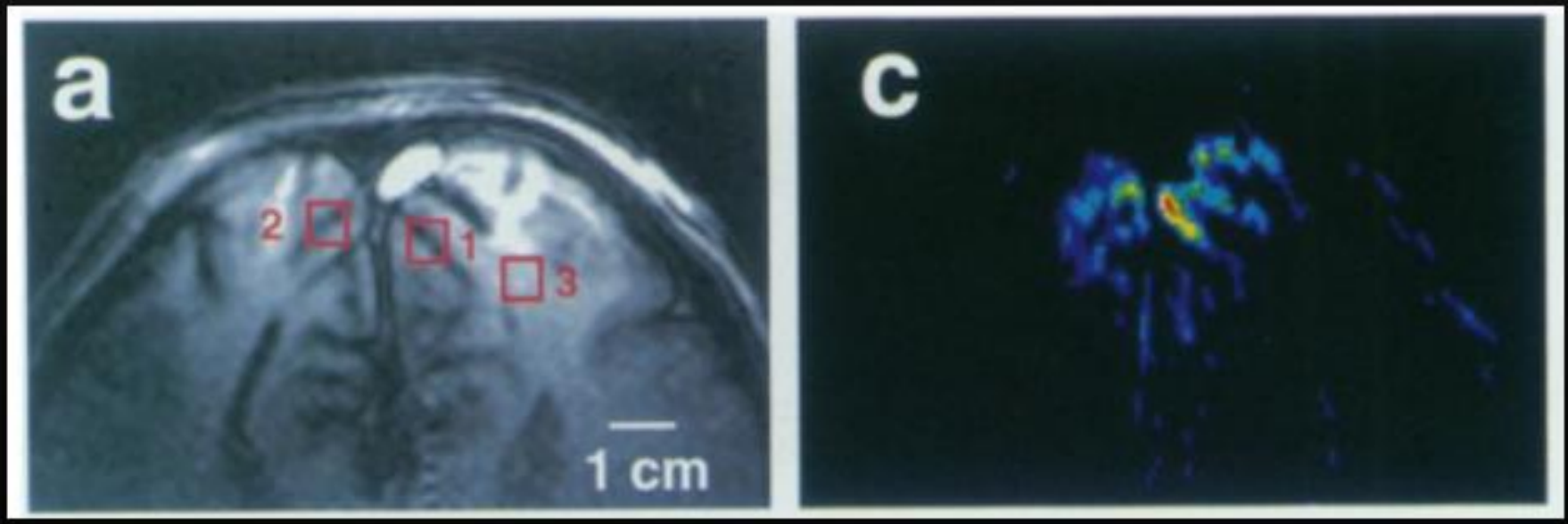
Duong, T.Q., D.S. Kim, K. Ugurbil, and S.G. Kim:
*Localized cerebral blood flow response at submillimeter columnar resolution*.
Proc Natl Acad Sci U S A, 2001. 98(19): p. 10904-10909.

→ CBF *is* regulated at he level of Cortical Columns

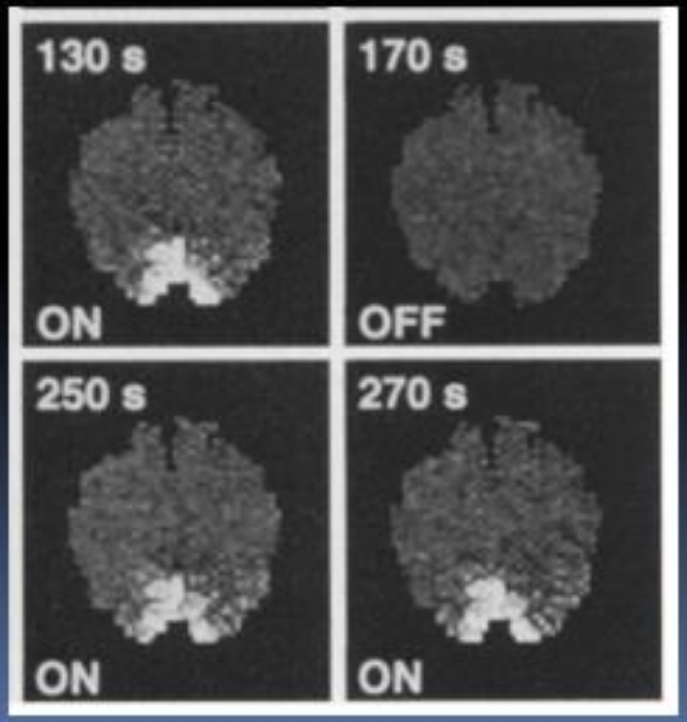
~~"brain waters the entire garden for the sake of a thirsty flower"~~

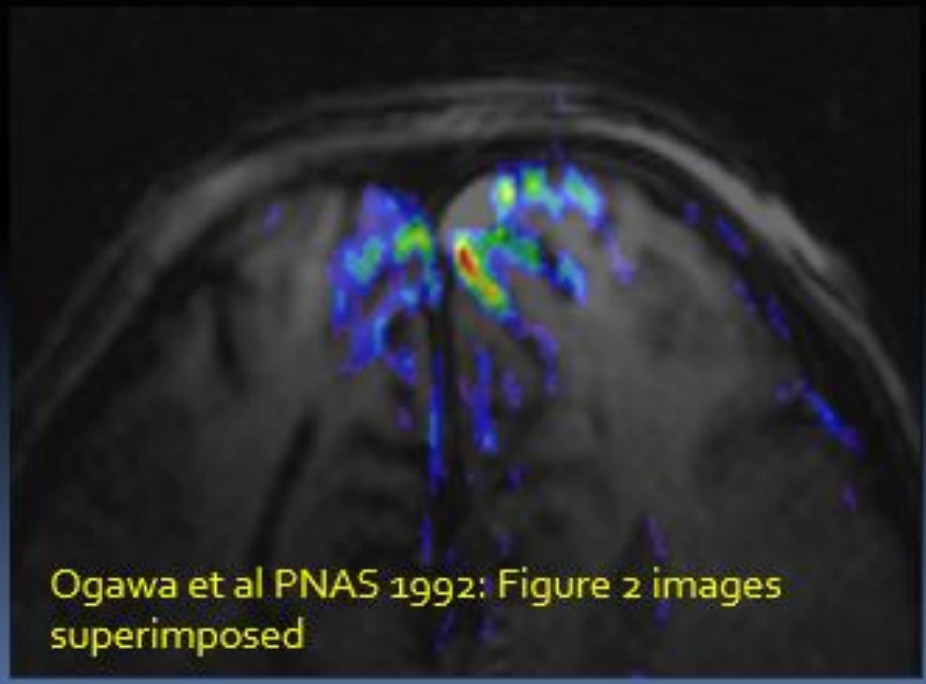
*"the brain really waters the thirsty flower while it sprinkles generously around it"*

From Ogawa et al 1992 PNAS Paper.

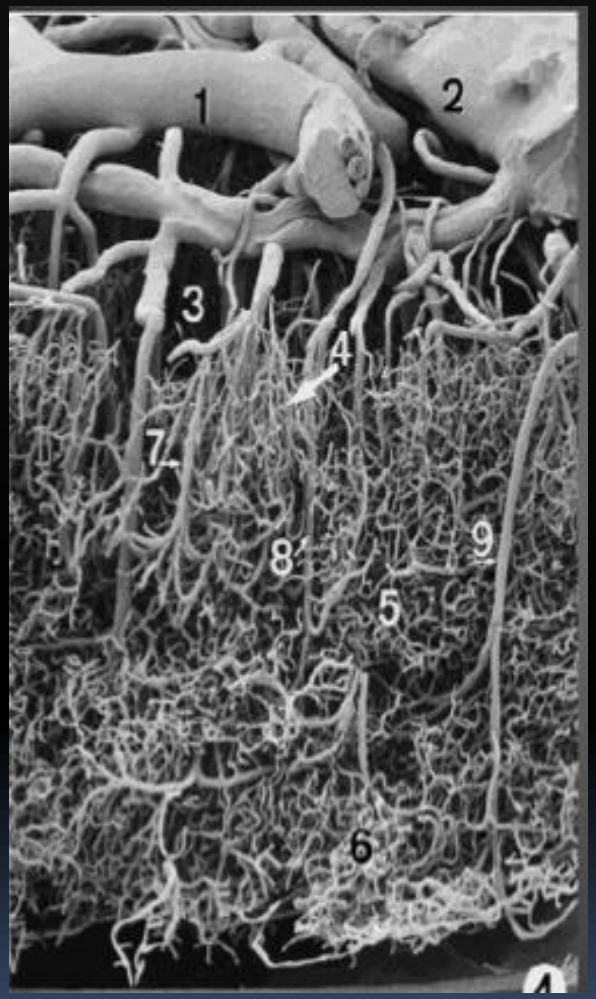



From Kwong et al 1992 PNAS paper



Cortical surface

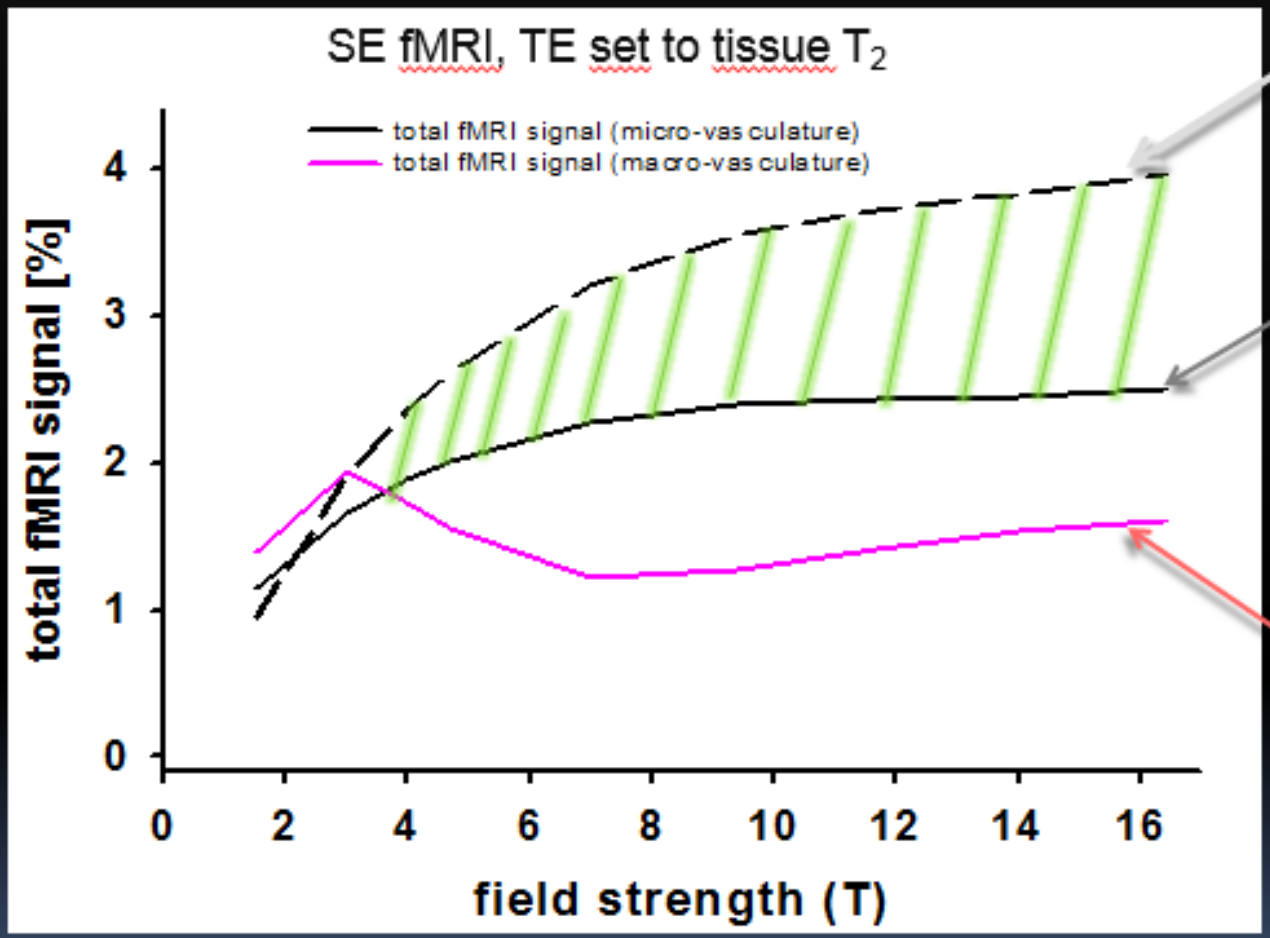



White Matter

ULTRAHIGH FIELDS
(7 Tesla or higher)

Image From: Reine-De La Torre et al. The Anatomical Record 251:87-96 (1998)

# AND of MR detected Mapping Signals and Physiologic Changes induced by Neuronal activity

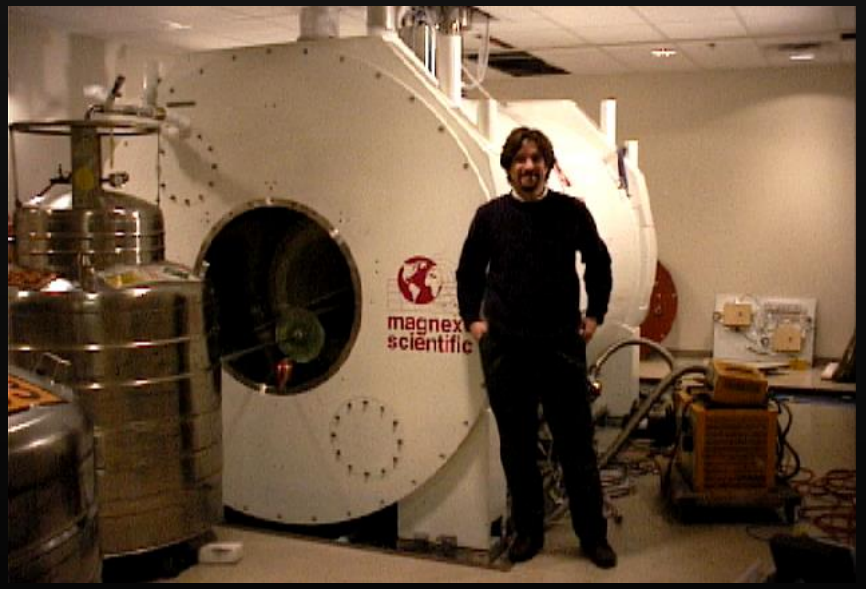


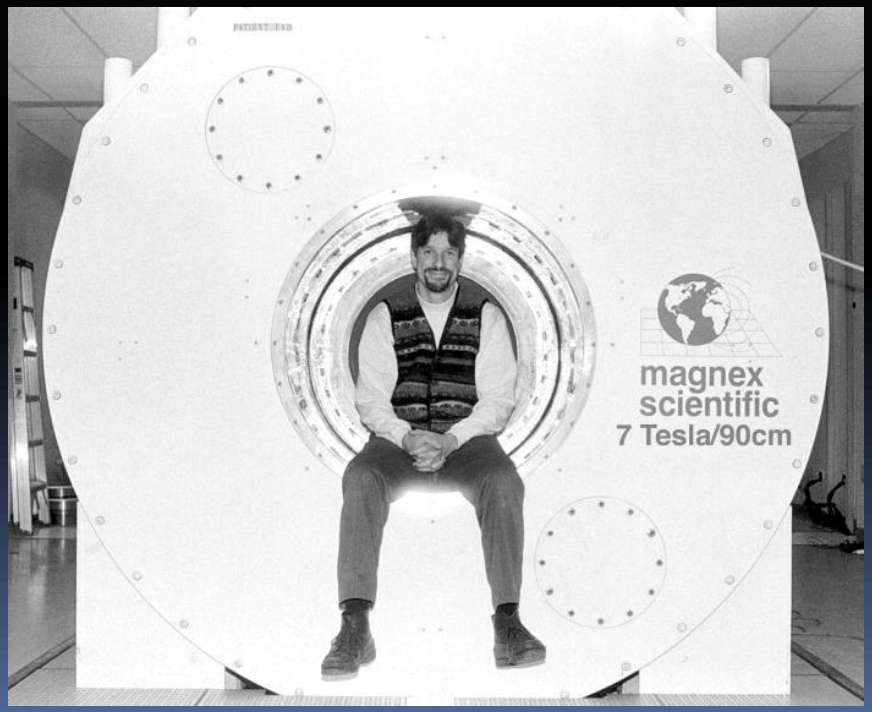

MICRO-Vasculature with ΔCBV=0

MICRO-Vasculature ΔCBV 16%

$CBV_{MACRO\ -vasc.}$=5%
Diameter, d = 200 μ
90° to $B_o$ !!!!
ΔCBV=0

K. Uludağ, B. Müller-Bierl, K. Uğurbil Neuroimage (2009) 48(1): p. 150-65.



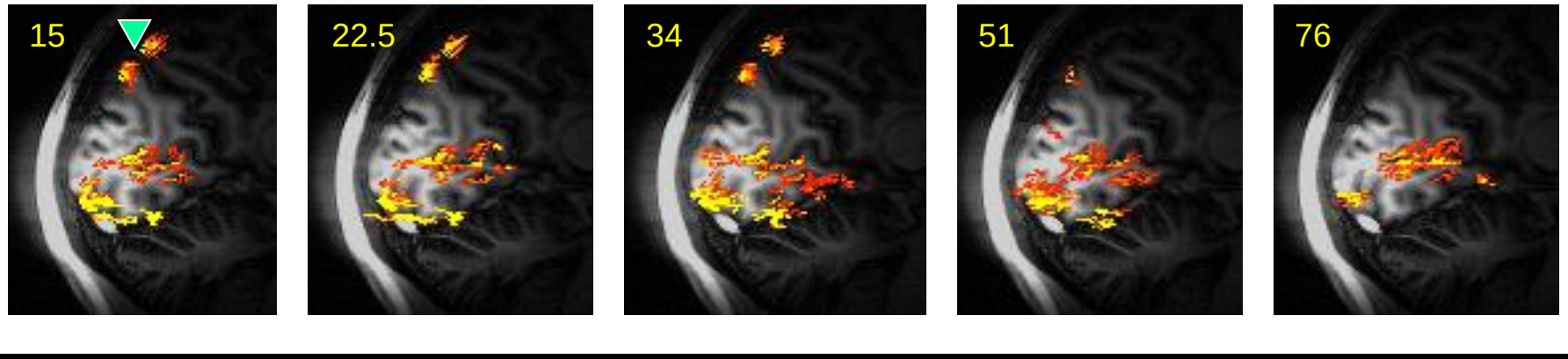




7 Tesla/90 cm bore

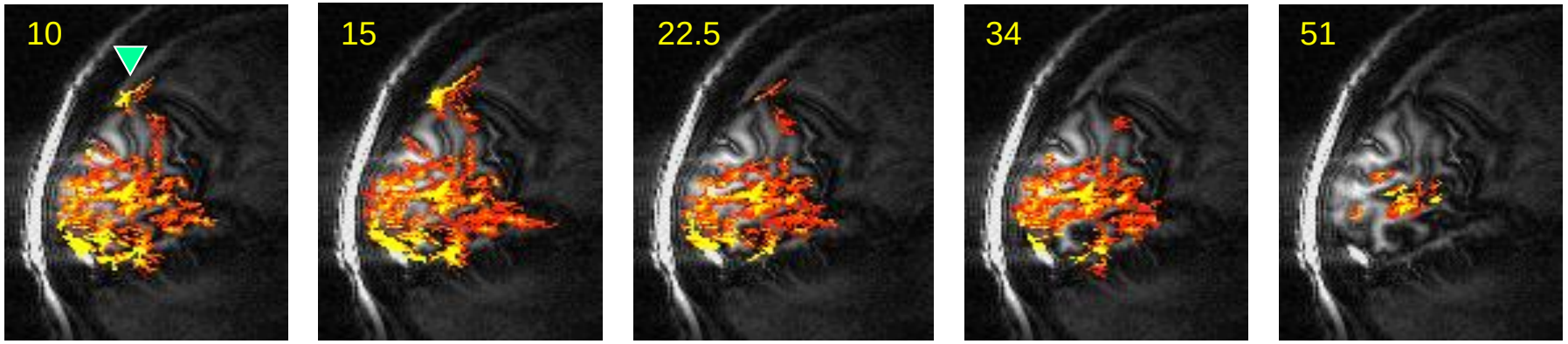
~1999

# GE BOLD fMRI 4 vs 7 Tesla, as a function of TE (ms)

## 4 TESLA




## 7 TESLA

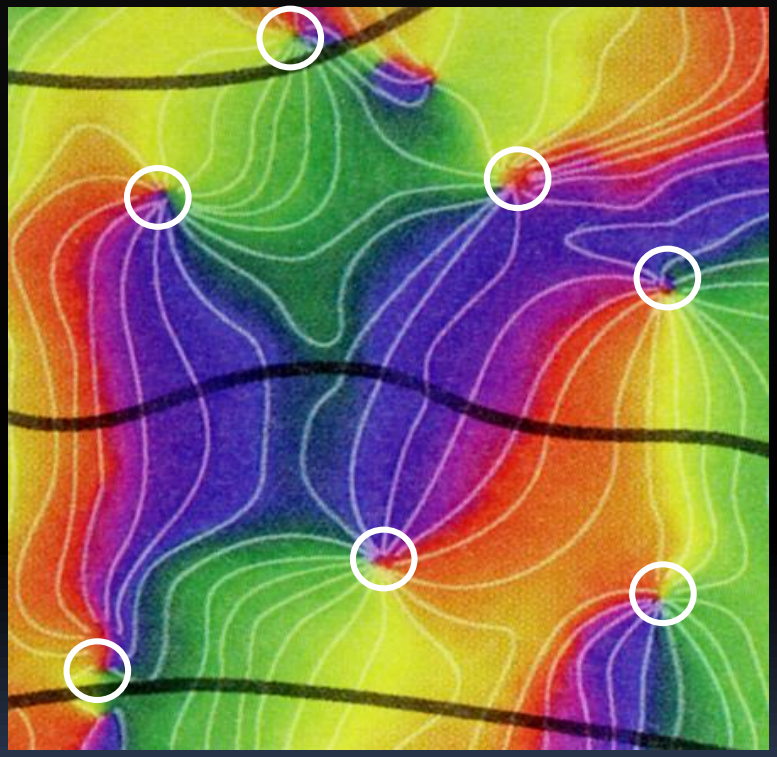


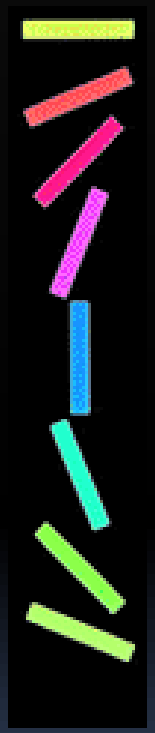

Yacoub E, et al. Magn Reson Med 2001;45(4):588-594

# Orientation Domains in the Primary Visual Cortex

Monkey

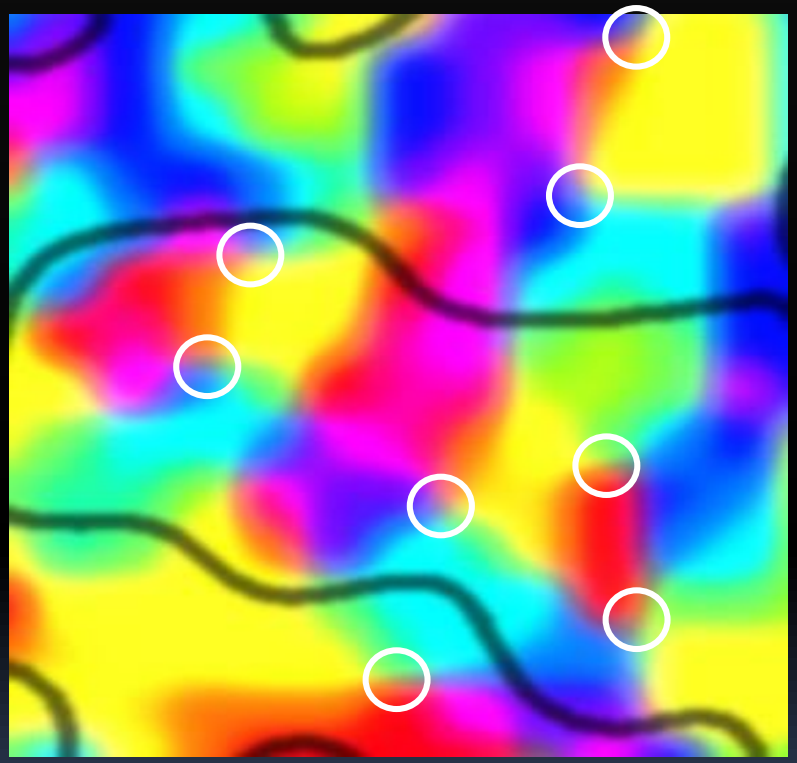
Optical Imaging





Human

fMRI (SE, 7 Tesla)

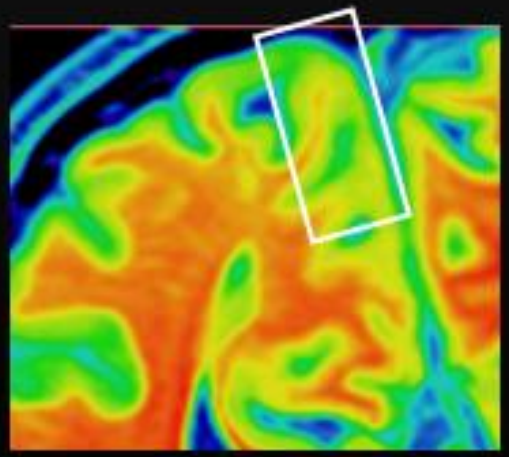


~4 mm

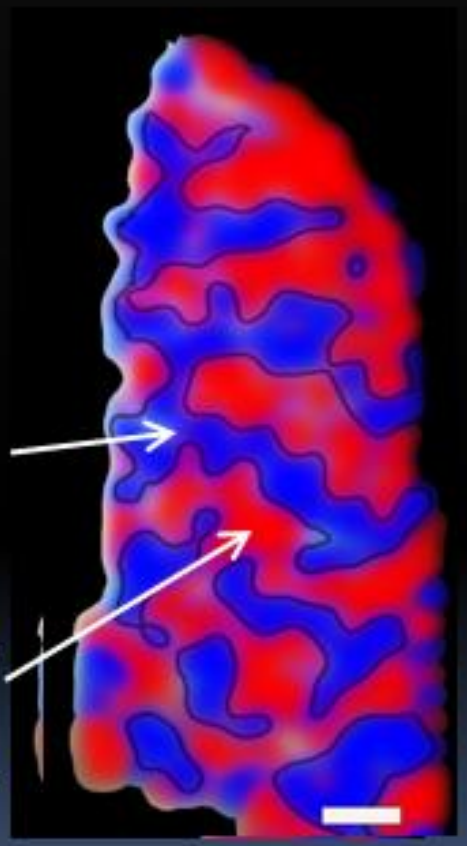
~4 mm

Yacoub, Harel, Uğurbil PNAS 2008

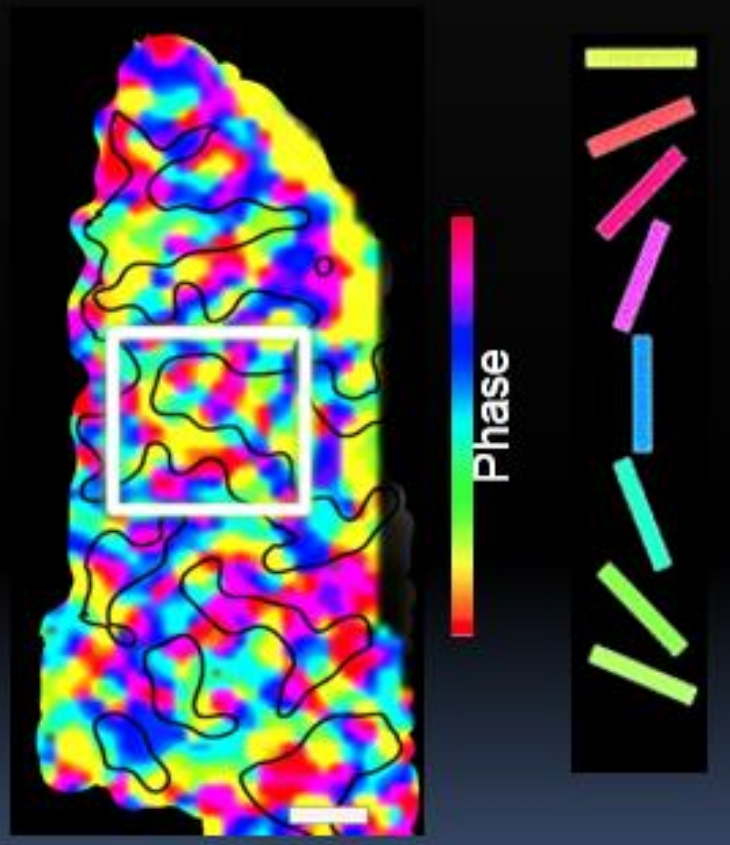
# Ocular Dominance (ODC) and Orientation maps in Human V1 (7 Tesla)








Yacoub, Shmuel, et al.
Neuroimage (2007) 37(4): 1161-77

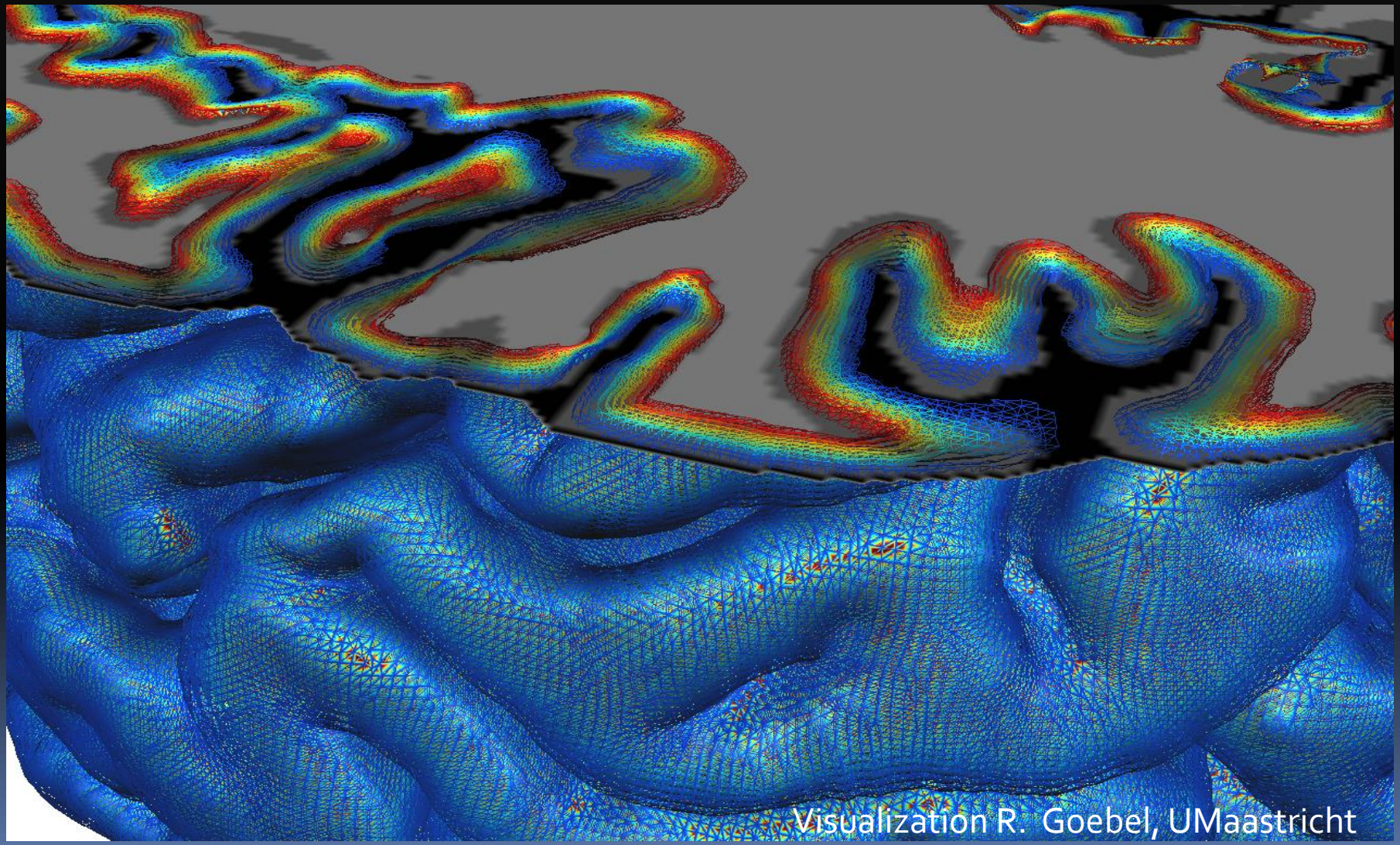


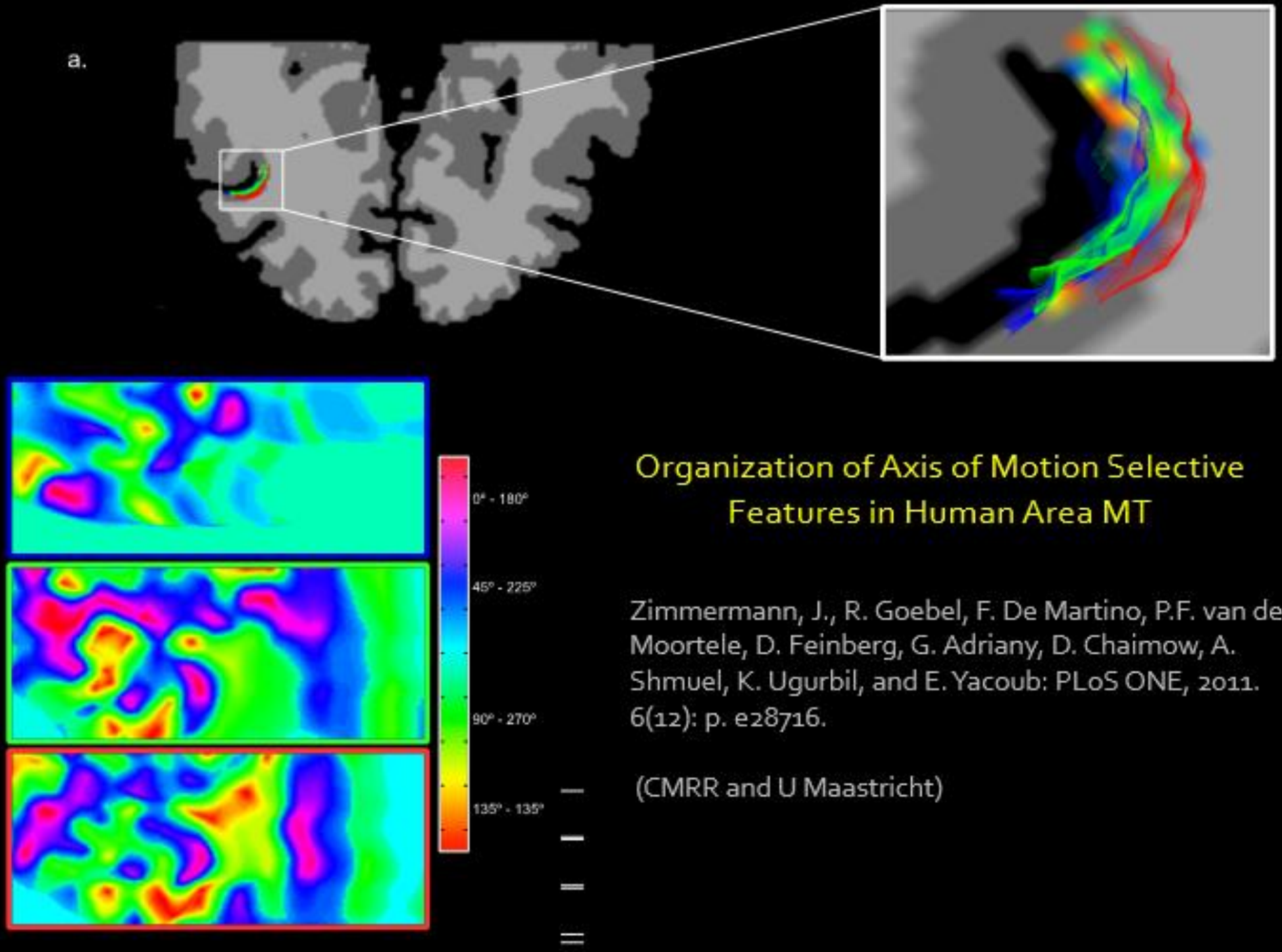

Yacoub, Harel, Uğurbil
PNAS (2008) 105(30): 10607-12

# Axis of Motion Selective Features in Human Area MT

3 D Volumetric Imaging (Restricted Volume);  0.8 mm isotropic resolution

Di Martino et al 2013 PlosOne, 8 (3) e60514






# Organization of Axis of Motion Selective Features in Human Area MT

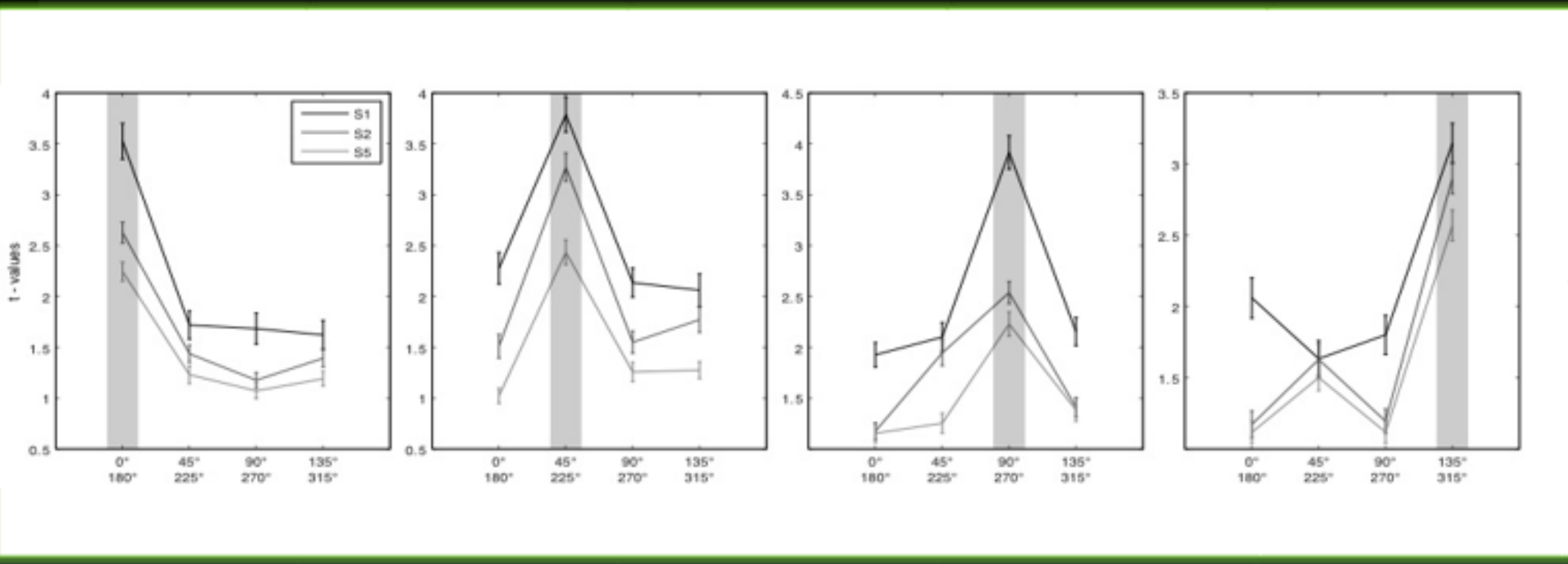
Zimmermann, J., R. Goebel, F. De Martino, P.F. van de Moortele, D. Feinberg, G. Adriany, D. Chaimow, A. Shmuel, K. Ugurbil, and E. Yacoub: PLoS ONE, 2011. 6(12): p. e28716.

(CMRR and U Maastricht)

# Axis of Motion Selective Features in Human Area MT

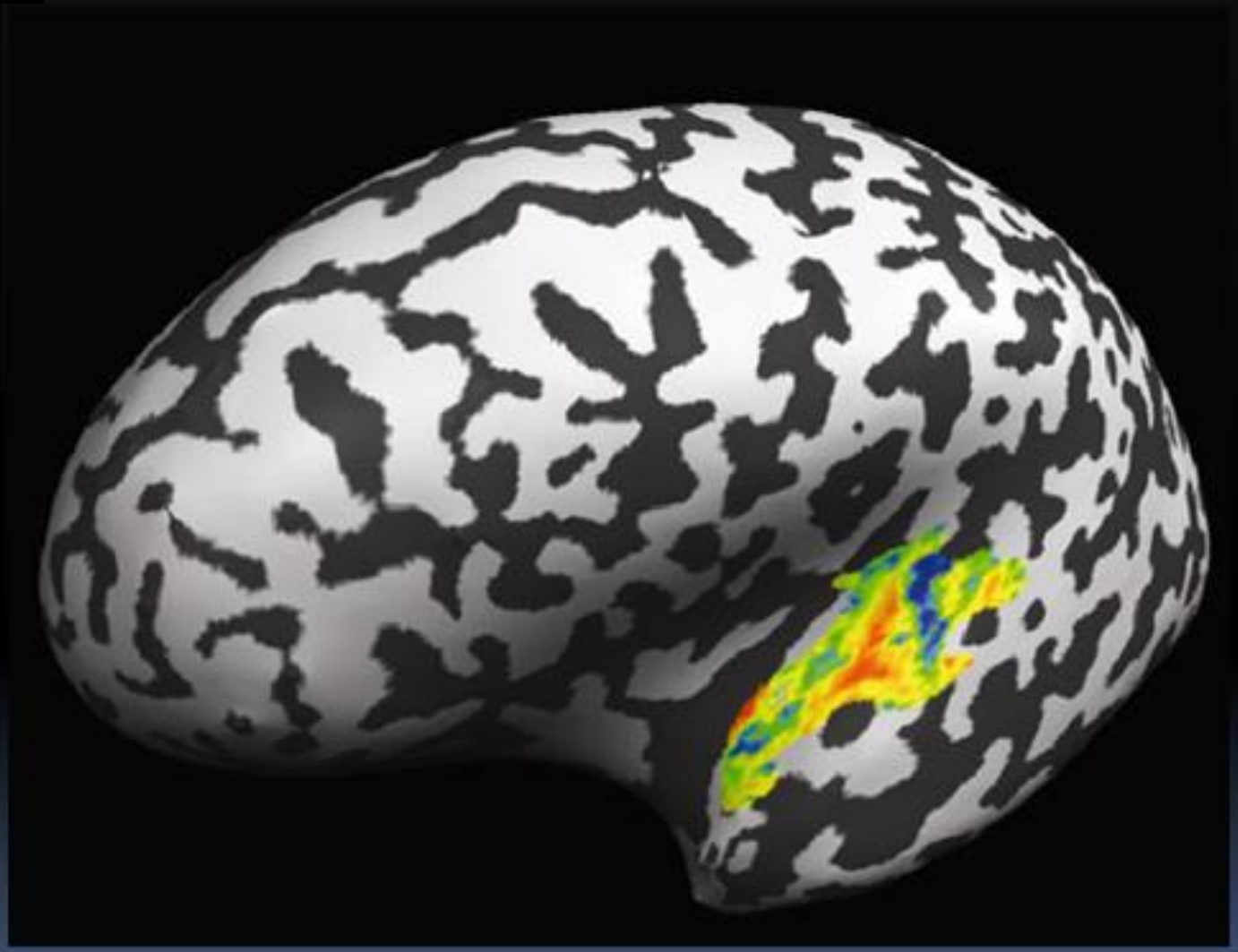
Zimmermann, et al PLoS ONE **6**(12): e28716. (2011)

# Tuning Curves in Human Area MT for Axis of Motion




Di Martino et al 2013 PlosOne, 8 (3) e60514 (CMRR & UMaastricht)

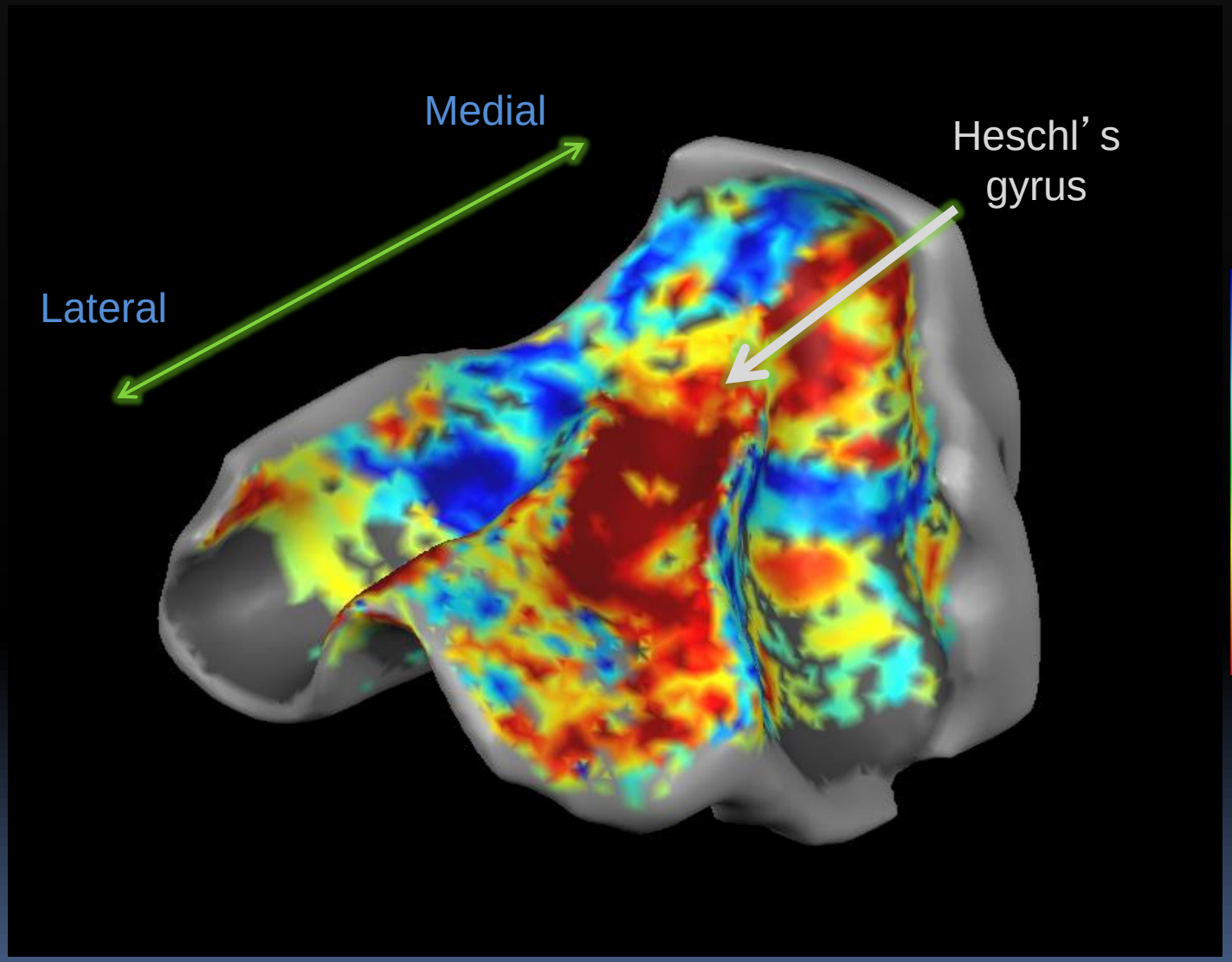
# Tonotopic Mapping in Human Primary Auditory Cortex



7 T GE fMRI
1.2x1.5x2.4 $mm^3$

Formisano, et al
NEURON 40, 859 (2003)

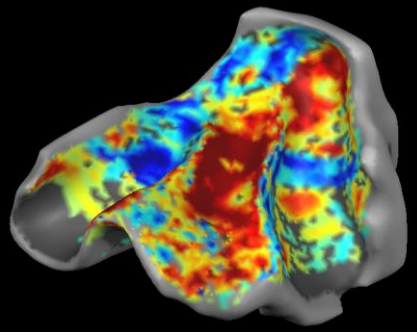
# Sub millimeter predominantly T2 weighted functional responses in human area A1.

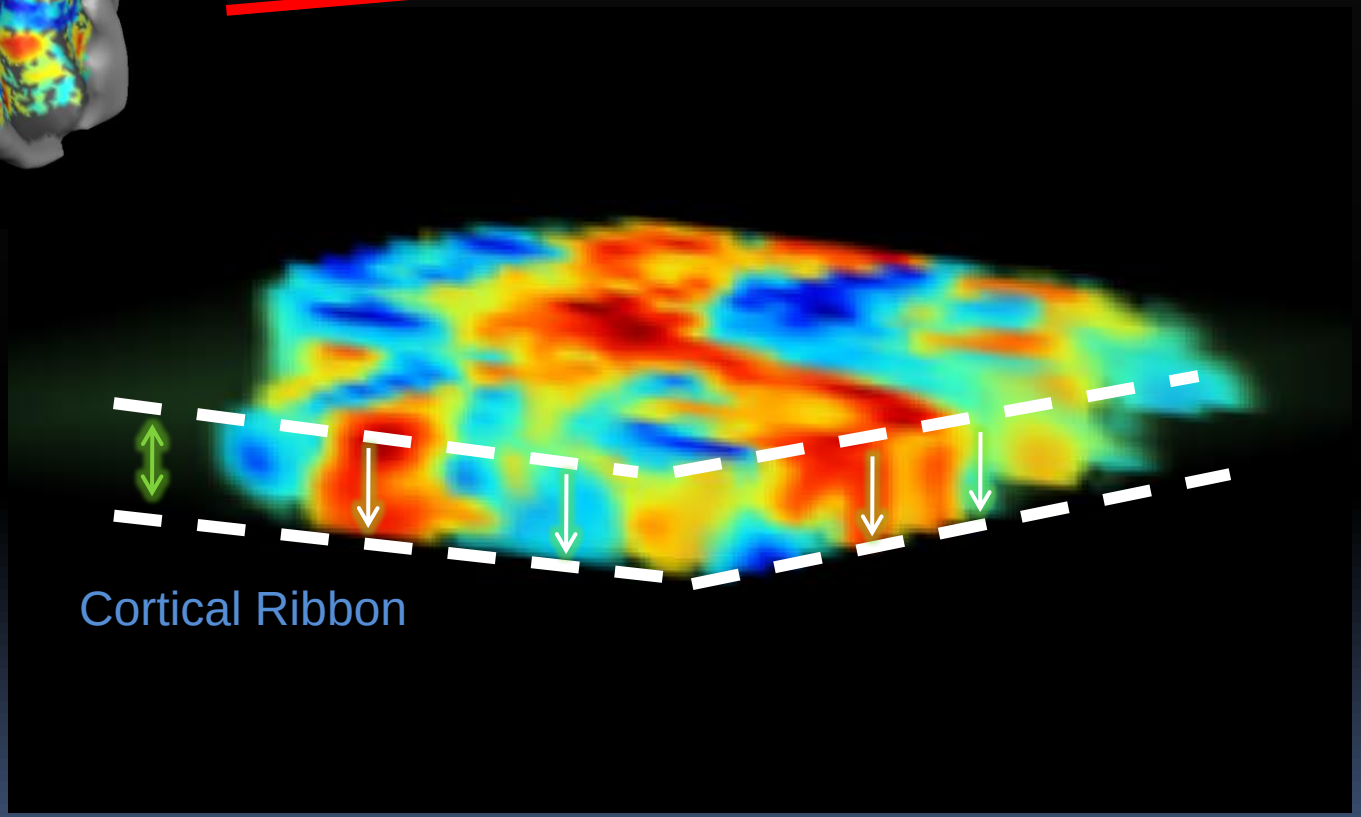



F. De Martino, E. Yacoub , E. Formisano et al.

UMMU

# Frequency preference orthogonal to the brain surface (tonotopic columns).






High (200)

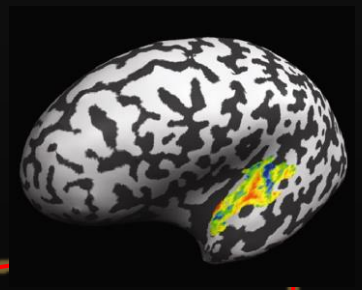
Frequency (Hz)

Low (6400)

F. De Martino, E. Yacoub , E. Formisano et al.

# Mapping low level acoustical properties with natural sounds
# 7 Tesla SINGLE SUBJECT

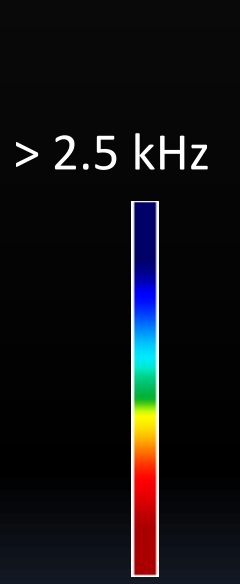
F. De Martino, E. Yacoub, E. Formisano et al. (CMRR & U Maastricht)

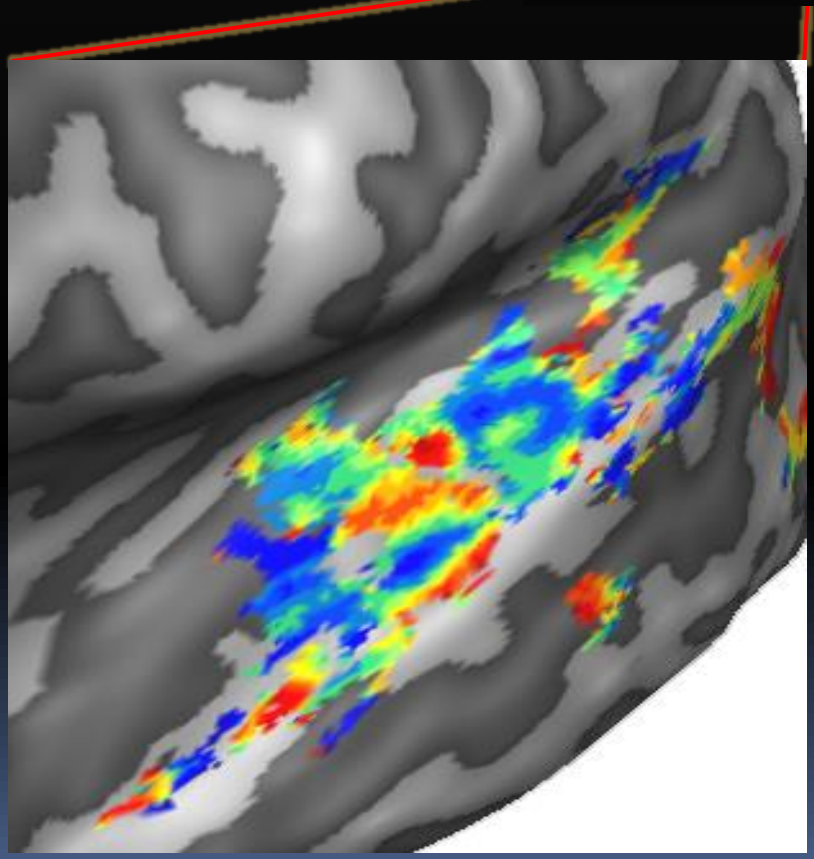


NATURAL SOUNDS

NEURONAL ACTIVATION

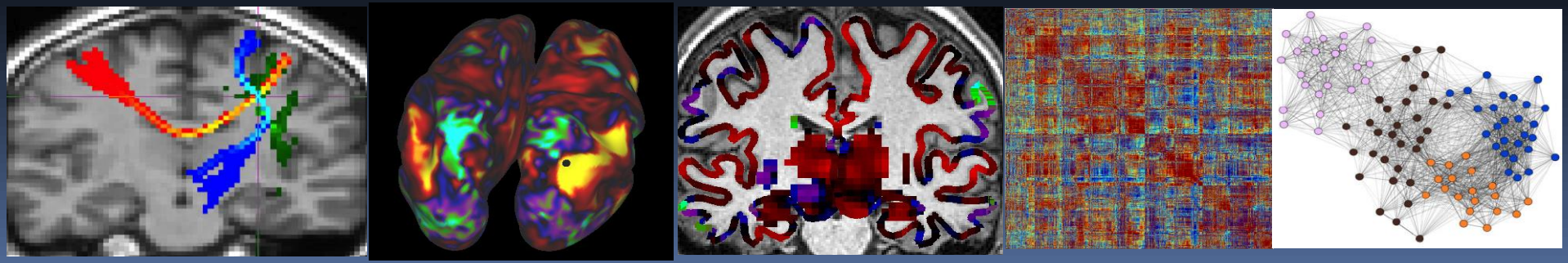
Model Based Decoding



# WASHINGTON UNIVERSITY-UNIV. OF MINNESOTA (WU-MINN) CONSORTIUM

Principal Investigators:
David C. Van Essen and Kamil Ugurbil



HUMAN
Connectome
PROJECT

Mapping structural and functional connections in the human brain

# HUMAN CONNECTOME

Description of the functional and structural connections among gray matter locations in the human brain

- spontaneous fluctuations in an fMRI time series (i.e. "Resting State" fMRI ) to deduce '*functional connectivity*'

and/or

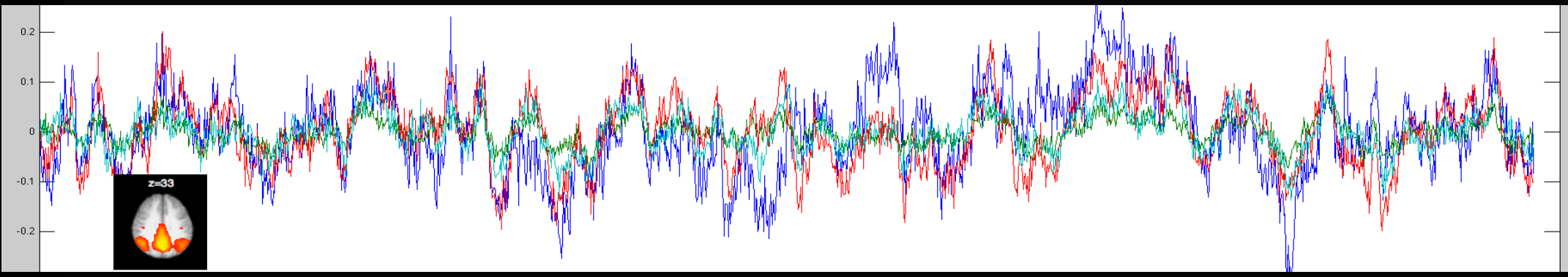
- Diffusion weighted MRI to infer '*structural connectivity*'

Complemented by

- Morphological imaging
- Task fMRI
- Phenotyping
- Genotyping

# Resting-State Networks (RSNs)

SLIDE COURTESY of STEVEN SMITH
OXFORD UNIVERSITY



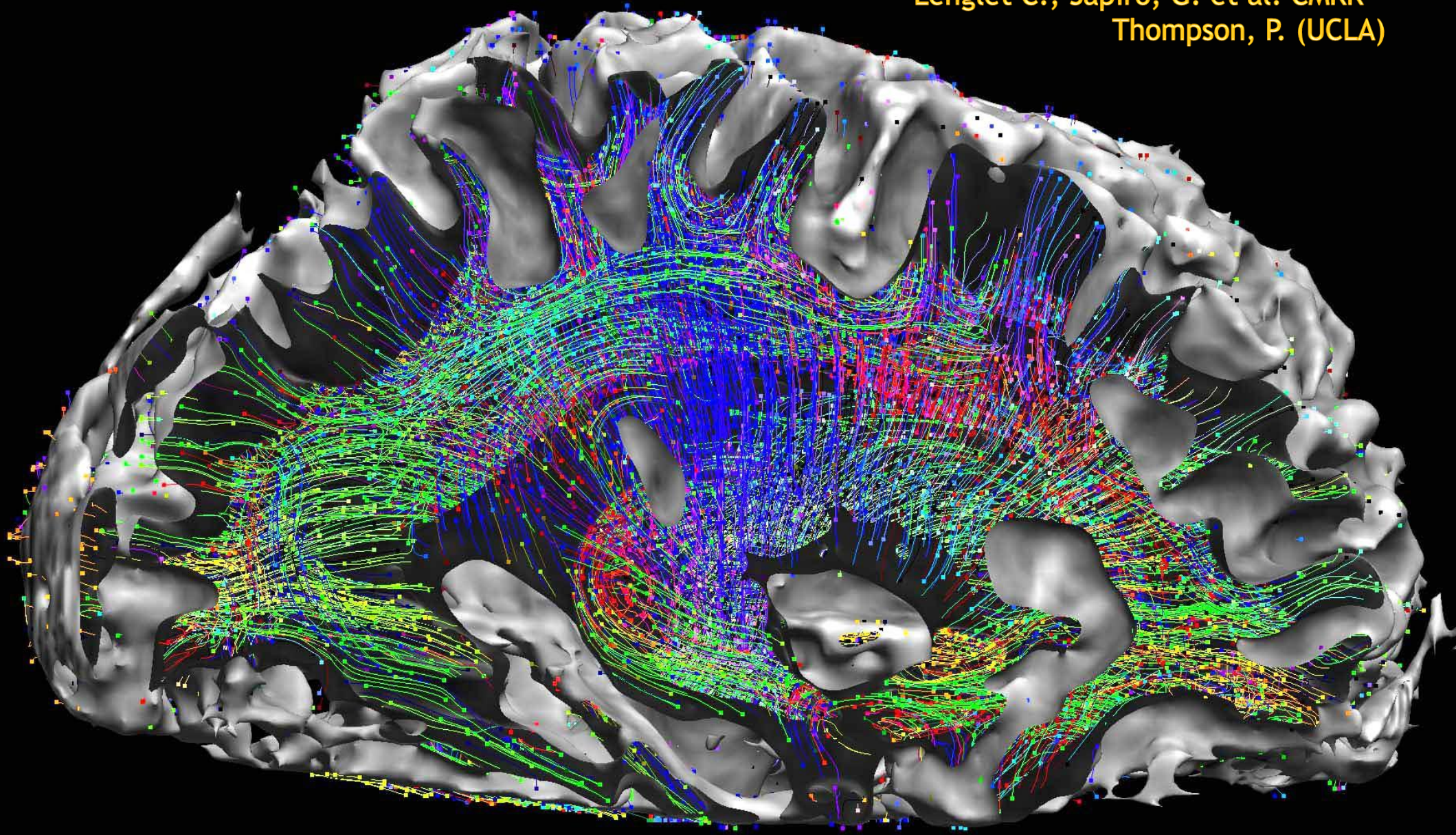

Time ⟶

*Spatial patterns* of correlated temporal dynamics, resembling activation maps

# DIFFUSION IMAGING

## 7T DWI Data (CMRR)

Lenglet C., Sapiro, G. et al. CMRR
Thompson, P. (UCLA)

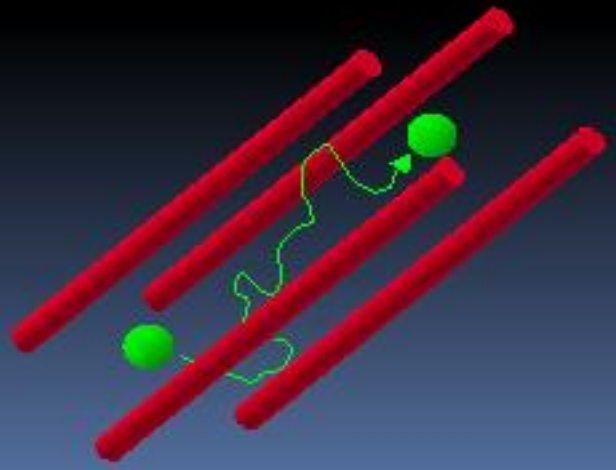


# *In vivo* labeling of axonal fibers using Diffusion Tensor Imaging (DTI)

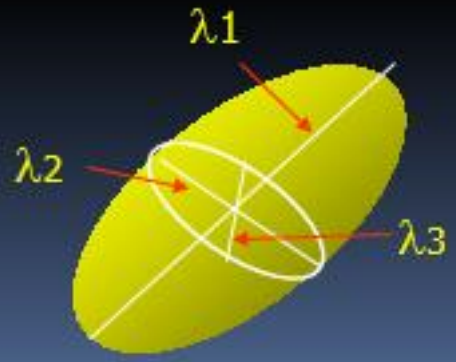
**Free diffusion**

**Isotropic diffusion**

**Restricted diffusion**



**Anisotropic diffusion**



# CHALLENGES IN THE HCP GOAL:

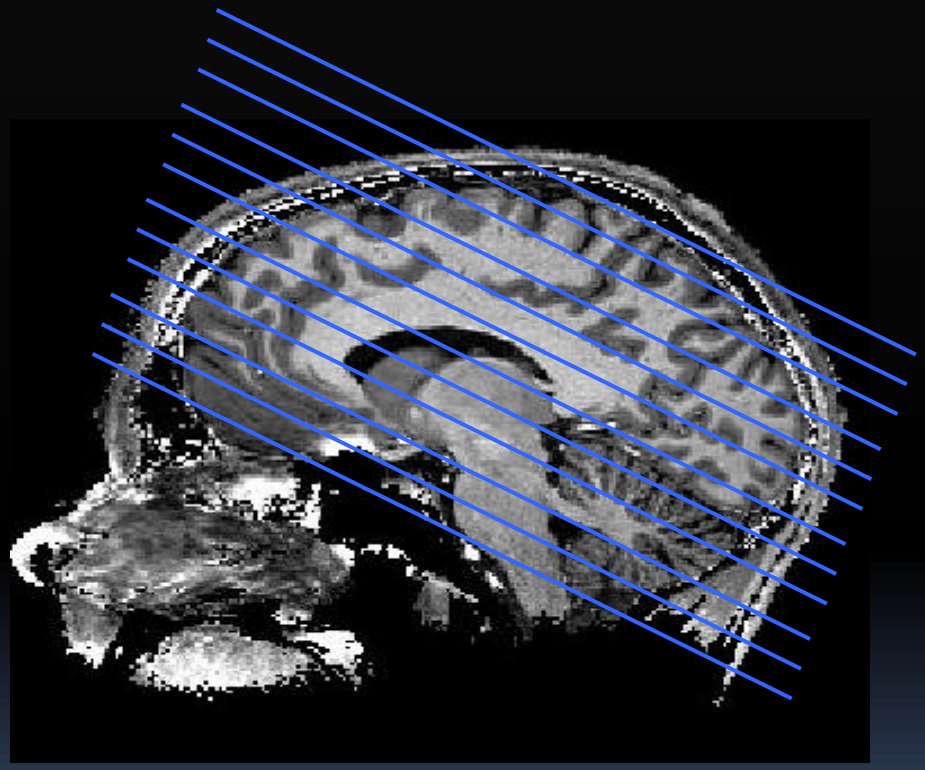
- **HIGH SPATIAL RESOLUTION over the WHOLE BRAIN !!!!!**

→ *MAXIMIZE SNR*

→ *FASTER DATA ACQUISITION SPEED without SIGNIFICANTLY SACRIFICING SNR*

# Conventional Multi-slice Imaging

Whole Volume TR
= $N_{slice}$ x Time per slice



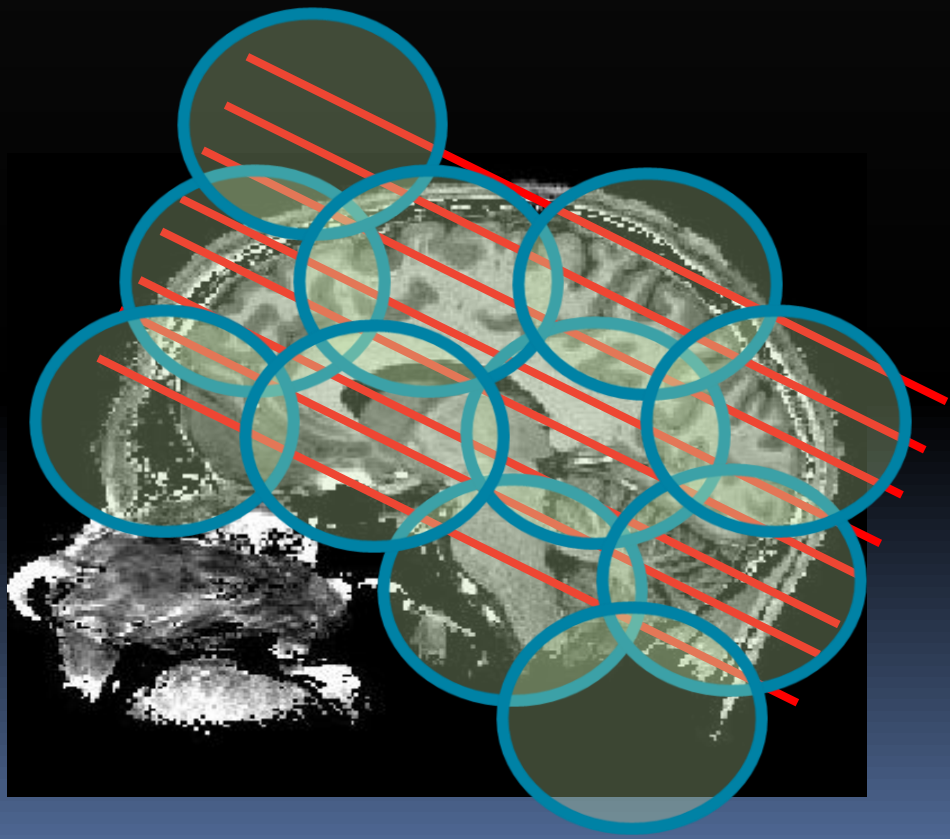
# IMPROVED IMAGING STRATEGIES

## Slice Accelerated, Simultaneous Multi Slice, Multiband Imaging

- Larkman et al JMRI 2001 (leg)
- Moeller, Yacoub, Auerbach, Ugurbil ISMRM 2008; # 236
- Moeller et al. Magn Reson Med, 2010; 63(5): p. 1144-53
- Setsompop et al. Magn Reson Med, 2012; 67, 1210-1224.

- Excite ***multiple*** slices simultaneously

- Use Parallel Imaging and Multichannel receive coil array to unalias simultaneously acquired images



# CHALLENGES IN THE HCP GOAL:

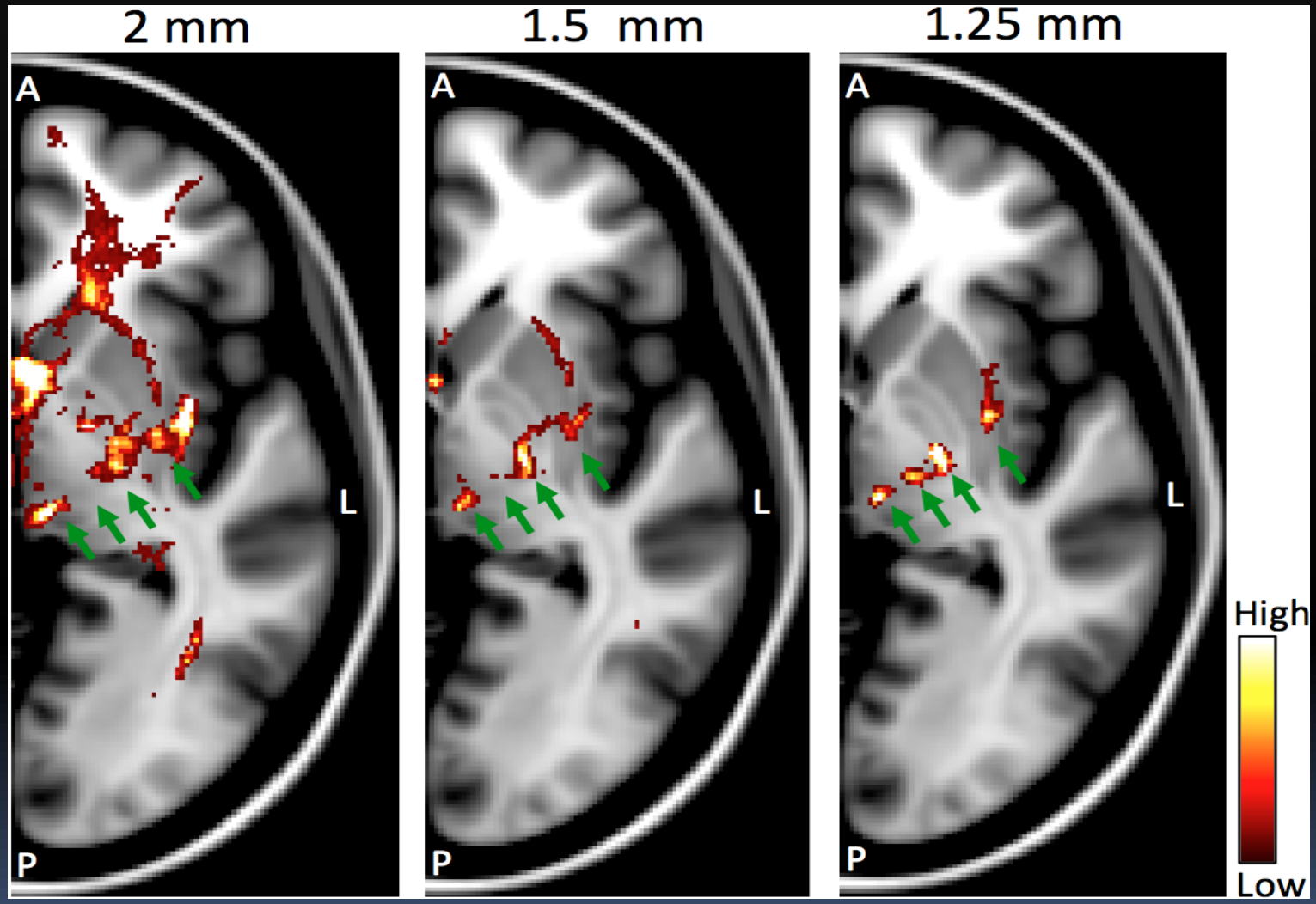
## INSTRUMENTATION

- ***3 TESLA equipped with 100 mT/m Gradients***

  CONVENTIONAL INSTRUMENTS operate with ~40 mT/m Gradients

- ***7 Tesla***

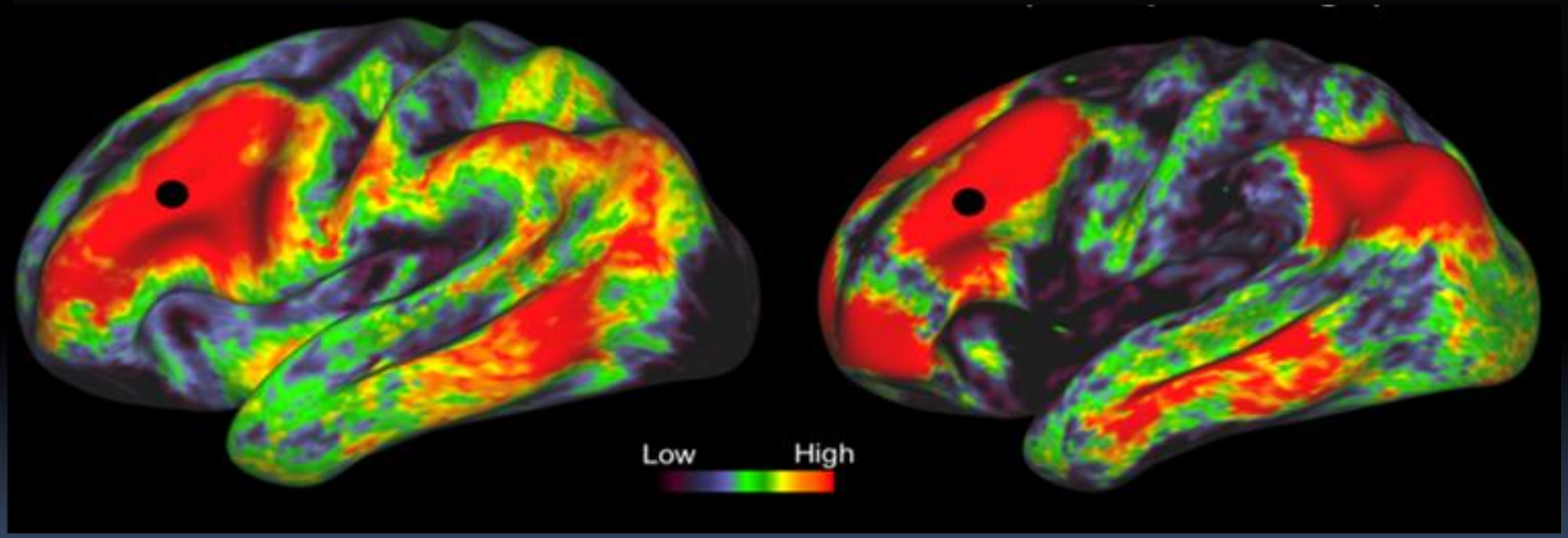
**PROBABILISTIC TRACTOGRAPHY**: medial to lateral : cortico-thalamic, cortico-bulbar, cortico-spinal and cortico-striatal projections. Images are shown in radiological view.



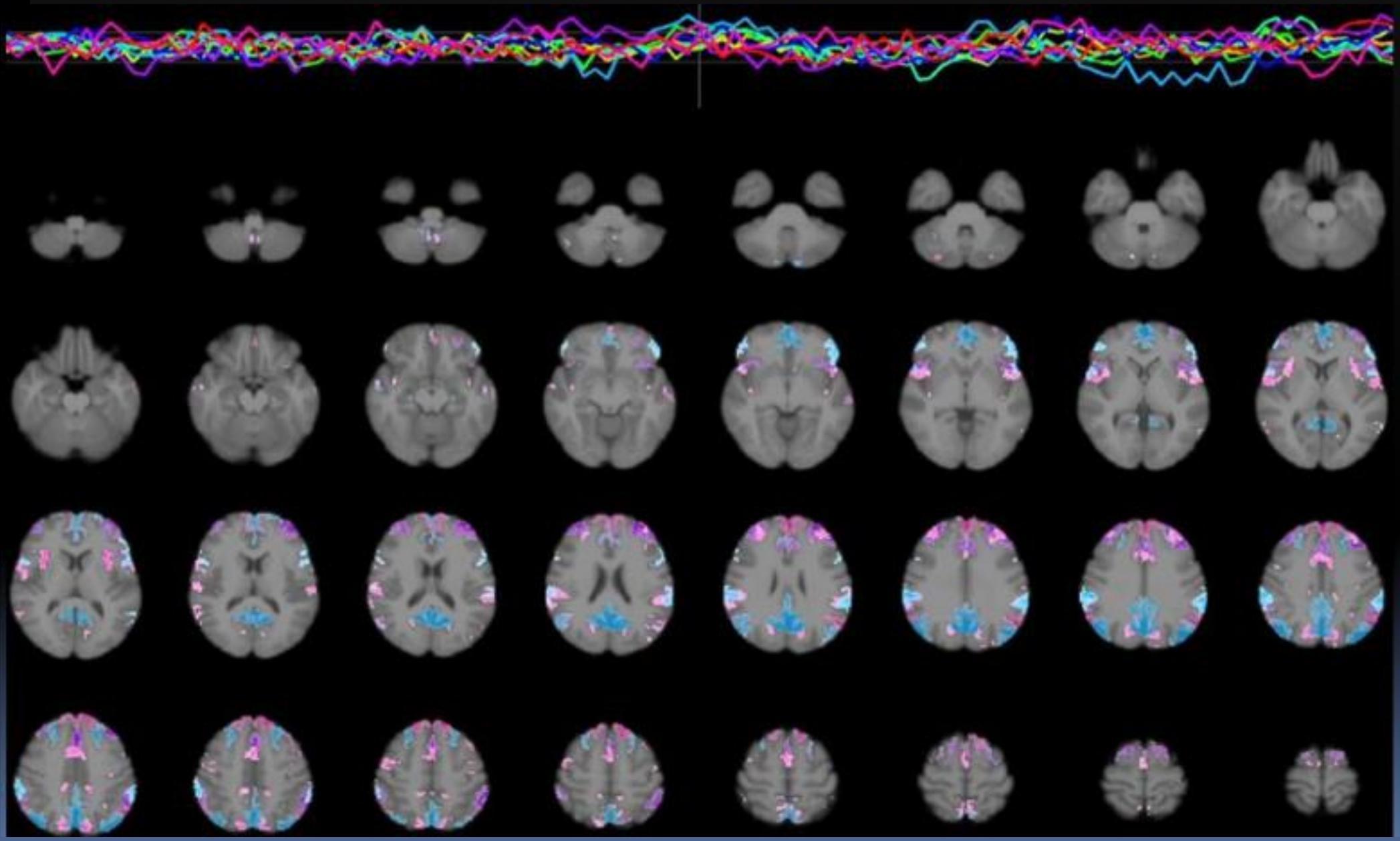

Sotiropoulos, S. N., Jbabdi, S., Xu, J., Andersson, J. L., Moeller, S., Auerbach, et al. & - for the WU-Minn HCP Consortium.

STRUCTURAL Connectivity
(Group average 9 subjects)

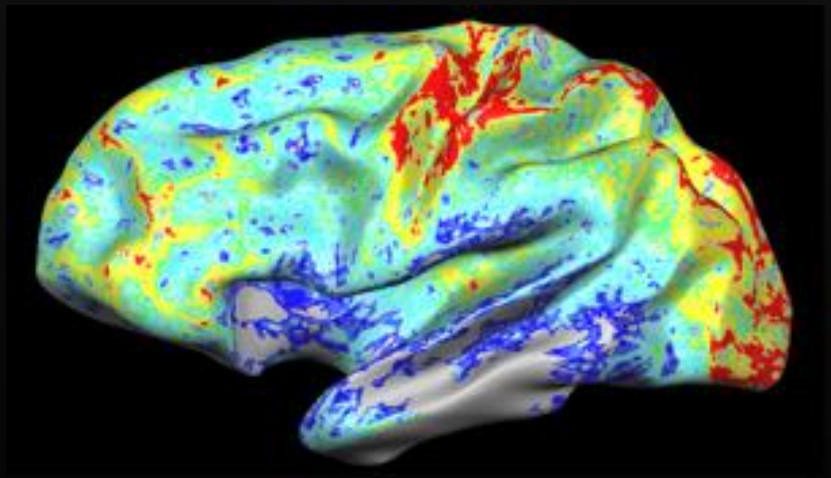
FUNCTIONAL Connectivity
(Group average 9 subjects)

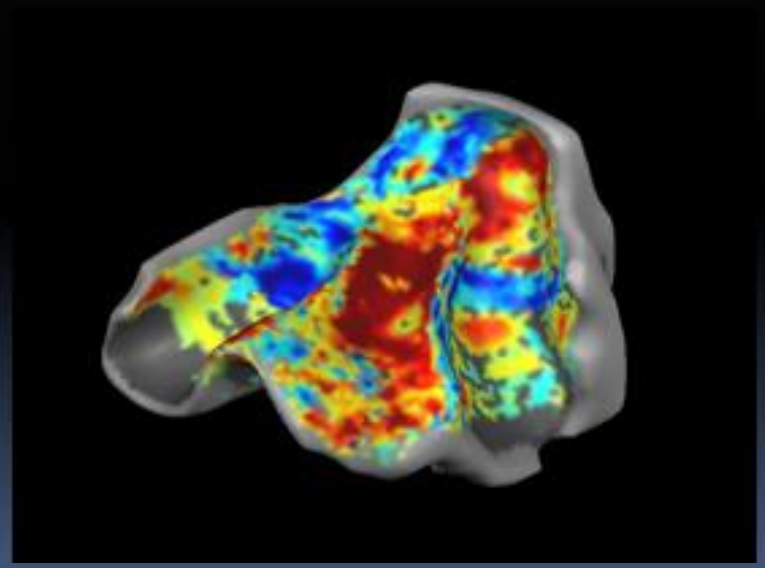


TFMs from HCP Phase II, released Data (Higher  spatial (2 vs 3 mm iso.) and temporal resolution (0.7 vs 0.8 s )



Intracortical myelin Content
(CMRR and UMaastricht)

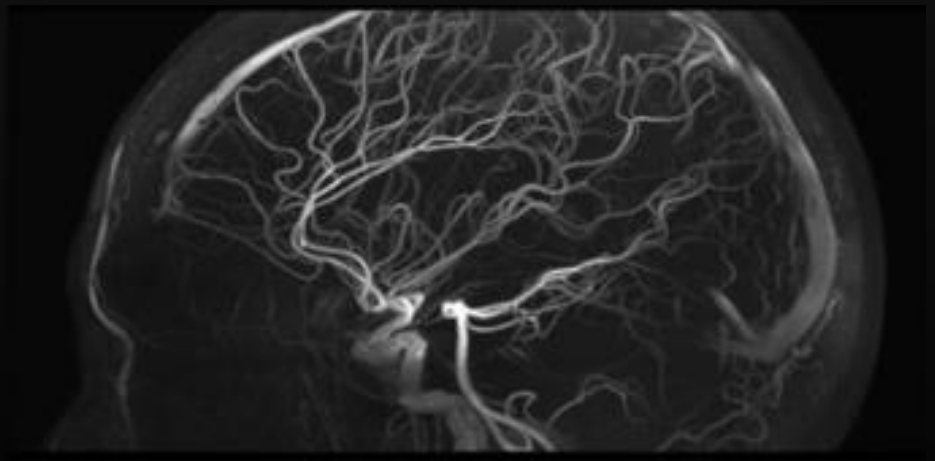




7 Tesla High Resolution fMRI

De Martino et al (CMRR and U Maastricht)

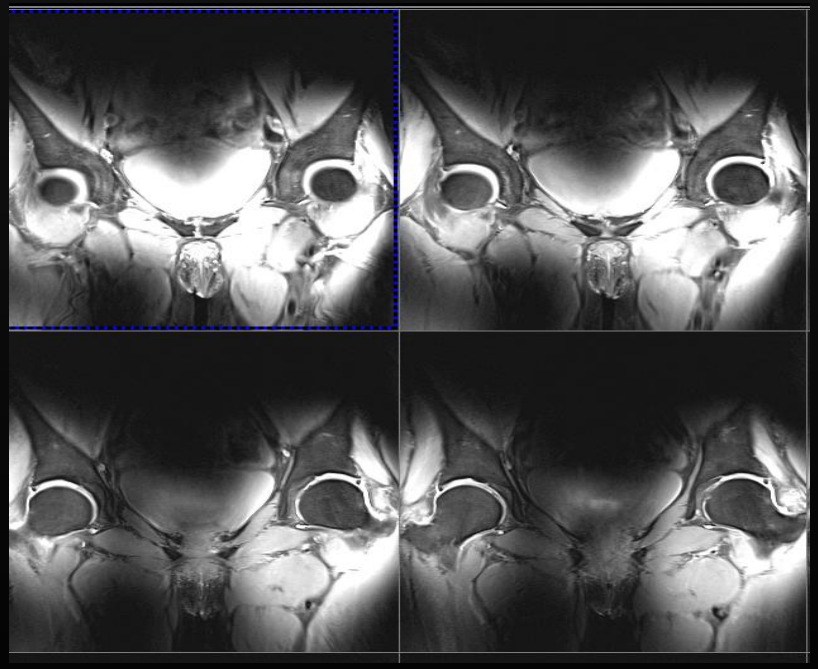
TOF angiography at 7 Tesla at 0.4 mm isotropic
S. Schmitter et al (CMRR)



**7 Tesla** CMRR

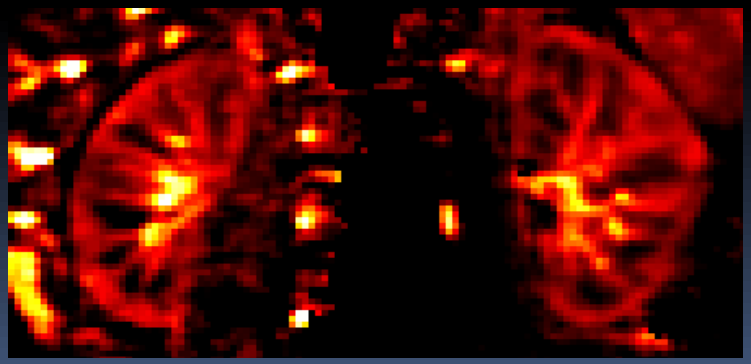
Henry, T.R., et al Radiology, 2011; 261(1): p. 199-209.

Bilateral Hip Imaging 7 T

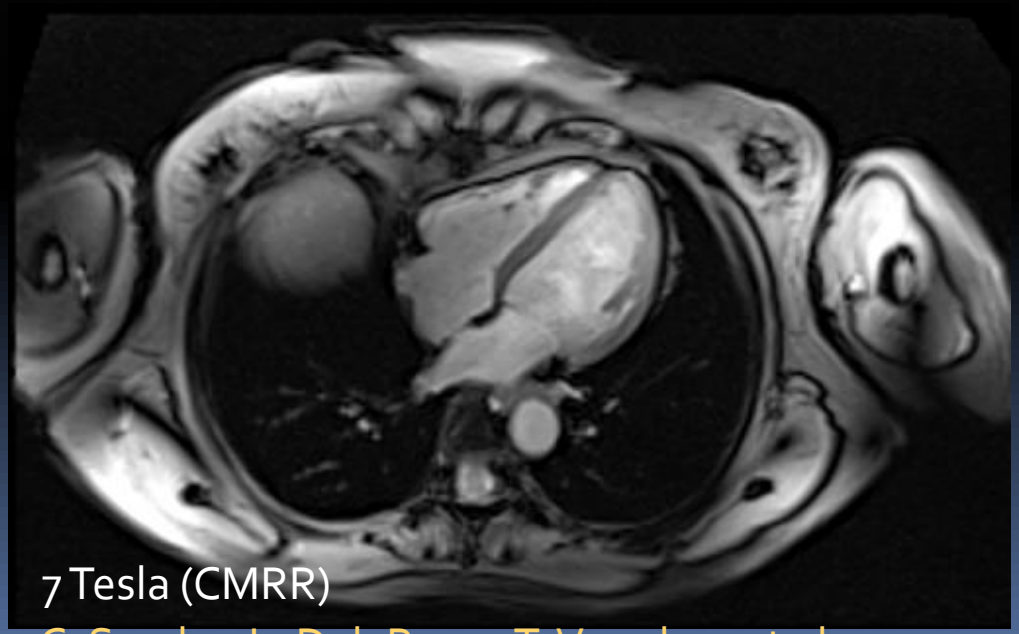


*Ellermann et al. NMR in Biomed 2012; 25, 1202-8*

7T Kidney Angiography (CMRR)
Metzger, G. J. (2013) Magn Reson Med **69,** 114

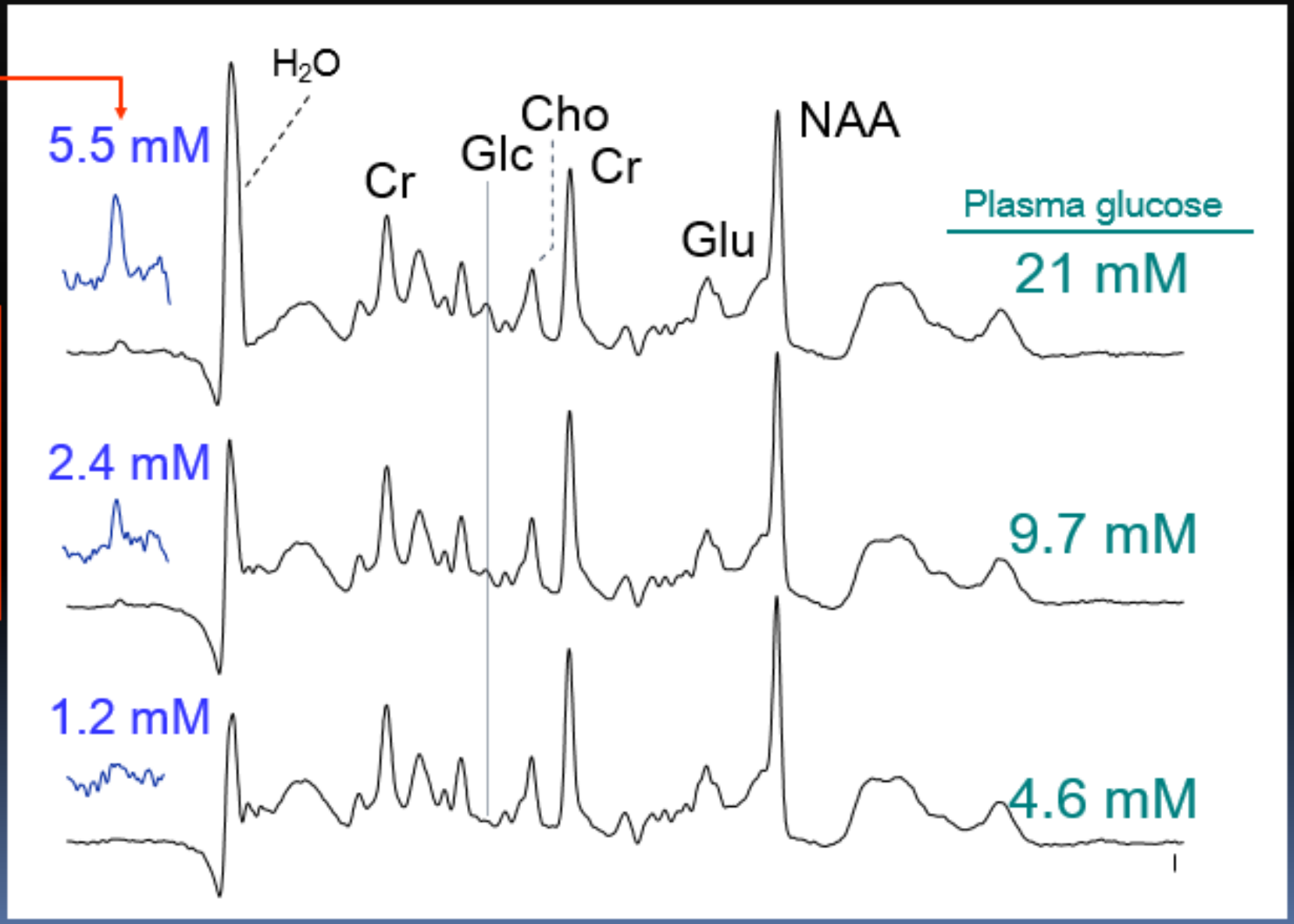


7T Kidney PERFUSION
Metzger et al. (CMRR)



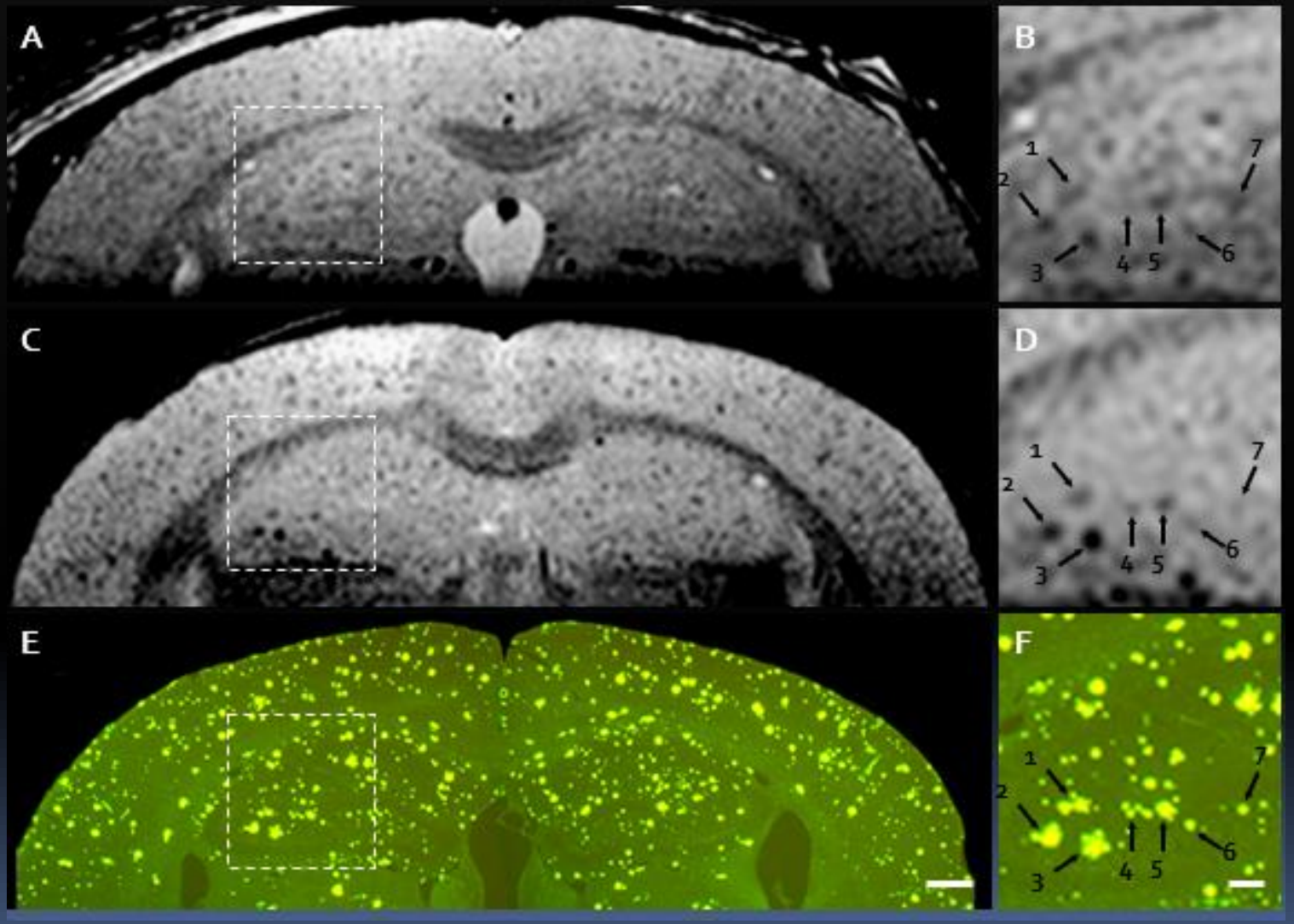
7 Tesla (CMRR)
C. Snyder, L. DelaBarre, T. Vaughan et al.

# Localized Human Brain $^{1}H$ Spectrum at 7 Tesla



# Three-way correlation in a 26 month AD mouse

**C. R. Jack, Jr., M. Garwood, et all MRM** 2004. **52**(6): p. 1263-71.




in vivo

ex vivo

**Histology**
(thioflavin S stained)

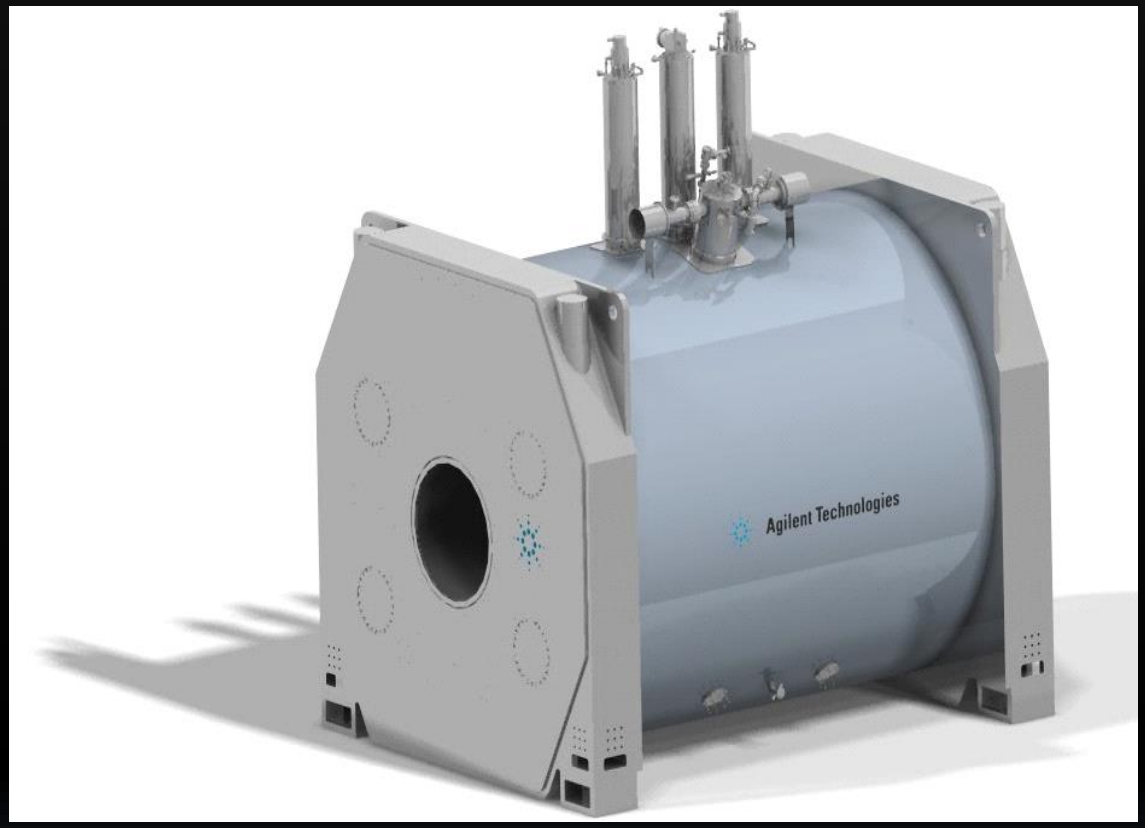
9.4 T MRI resolution: 60 µm x 60 µm x 120 µm

9.4 Tesla/31 cm bore ~1994

7 Tesla/90 cm bore ~1999

- **INCESSENT advances in Instrumentation intricately tied to Discoveries/Improvements in Methods of Image acquisition and reconstruction.**

# 10.5T System




Field / diameter 10.5T/88cm
Manufacturer Siemens / Agilent
Temporal Stability 0.03 ppm/hr
Spatial Homogeneity< 0.07 ppm/25cm dsv
Stored Energy 280 MJ

Conductor NbTi / 433 km
Temperature 3K
Size 4.1 x 3.2 m
Weight 110 tons
Delivery End of November


Completed Magnet former before assembly

# A New Factory Floor


80 Ton cold mass (magnet in helium can) being loaded into the cryostat using a specially commissioned 10 Ton "H" beam.

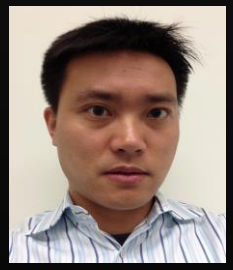
# CENTER for MAGNETIC RESONANCE RESEARCH (CMRR)

## PULSE SEQUENCE, IMAGE RECONSTRUCTION and EVALUATION

Steen Moeller

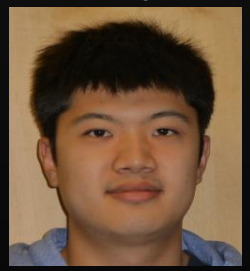
Eddie Auerbach

Gordon Xu

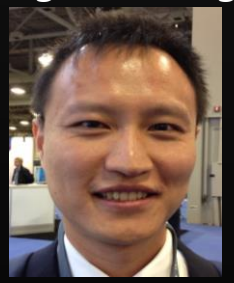


Essa Yacoub

An (Joseph) Vu



Dingxin Wang

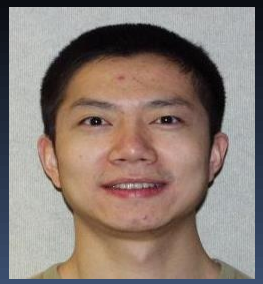


## DIFFUSION IMAGING

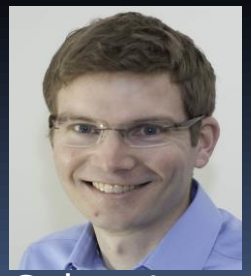
Christophe Lenglet

Center for Magnetic Resonance Research UMinn

## PARALLEL TRANSMIT PULSE DESIGN



Xiaoping Wu



Sebastian Schmitter

Pierre Francois Van de Moortele

## *DIFFUSION IMAGE ACQUISITION, PROCESSING and ANALYSIS*

Tim Behrens

Stam Sotiropoulos

Saad Jbabdi

Jesper Andersson

## *RESTING STATE ANALYSIS*

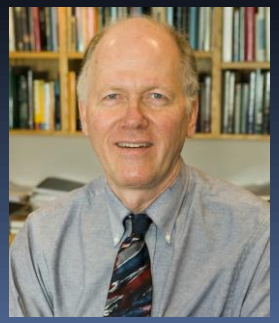
Steve Smith

Karla Miller

FMRIB

UNIVERSITY OF OXFORD

Matt Glaser



David Van Essen

Washington University in St. Louis