Using MRI to link Microstructure and Macrostructure

Bruce Fischl

MGH ATHINOULA A. MARTINOS CENTER
Harvard Medical School

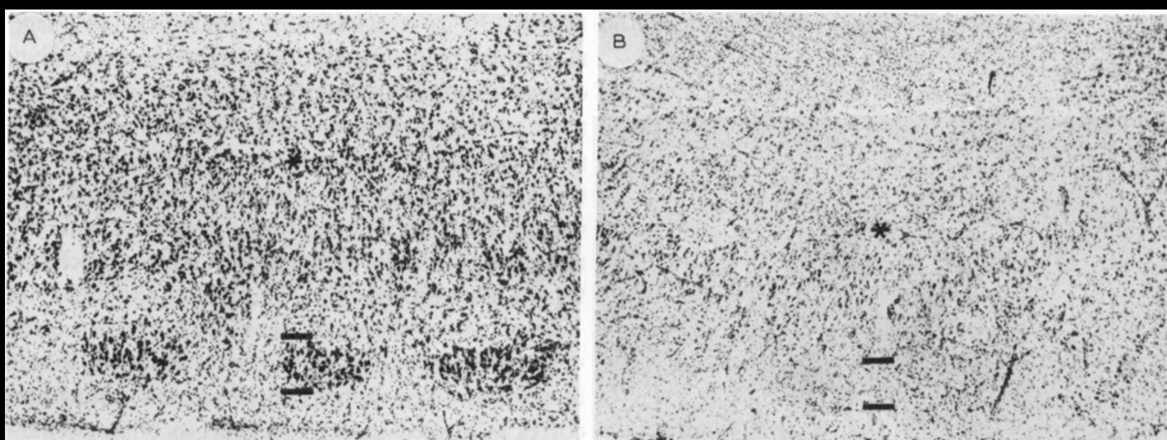
MIT CSAIL/HST

MASSACHUSETTS GENERAL HOSPITAL

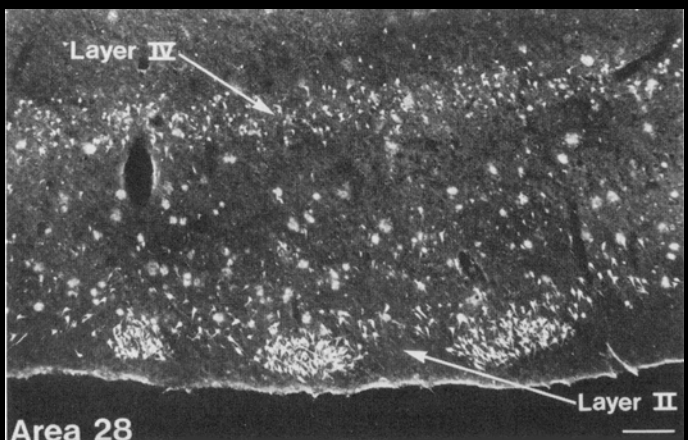
Histology in Alzheimer's Disease

(entorhinal cortex=BA28)

CONTROL AD



Nissl Stain



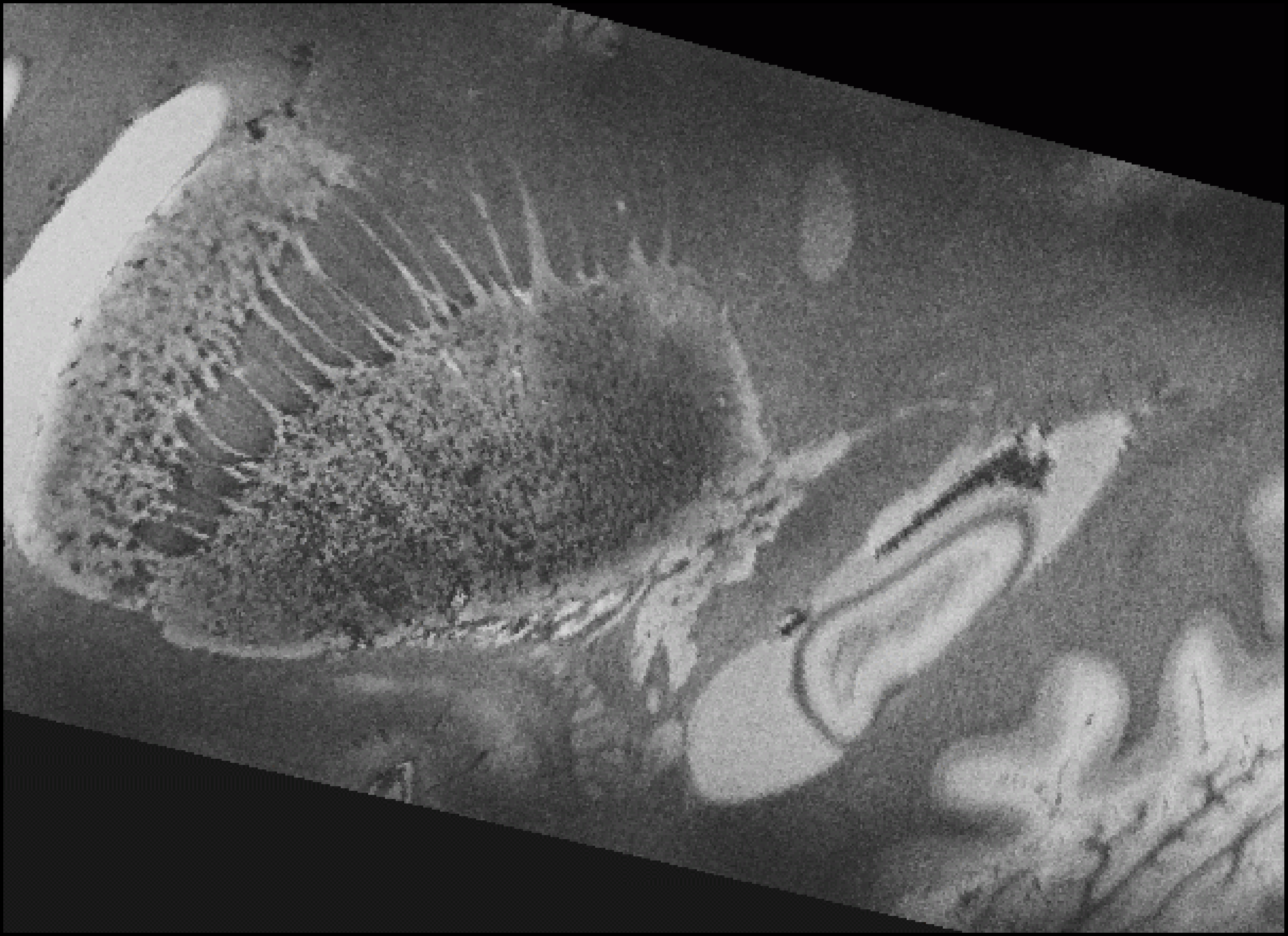
thioflavin S
(neurofibrillary tangles and neuritic plaques)

Thanks to Brad Hyman and Jean Augustinack for this slide.

Why Image *ex vivo* brains?

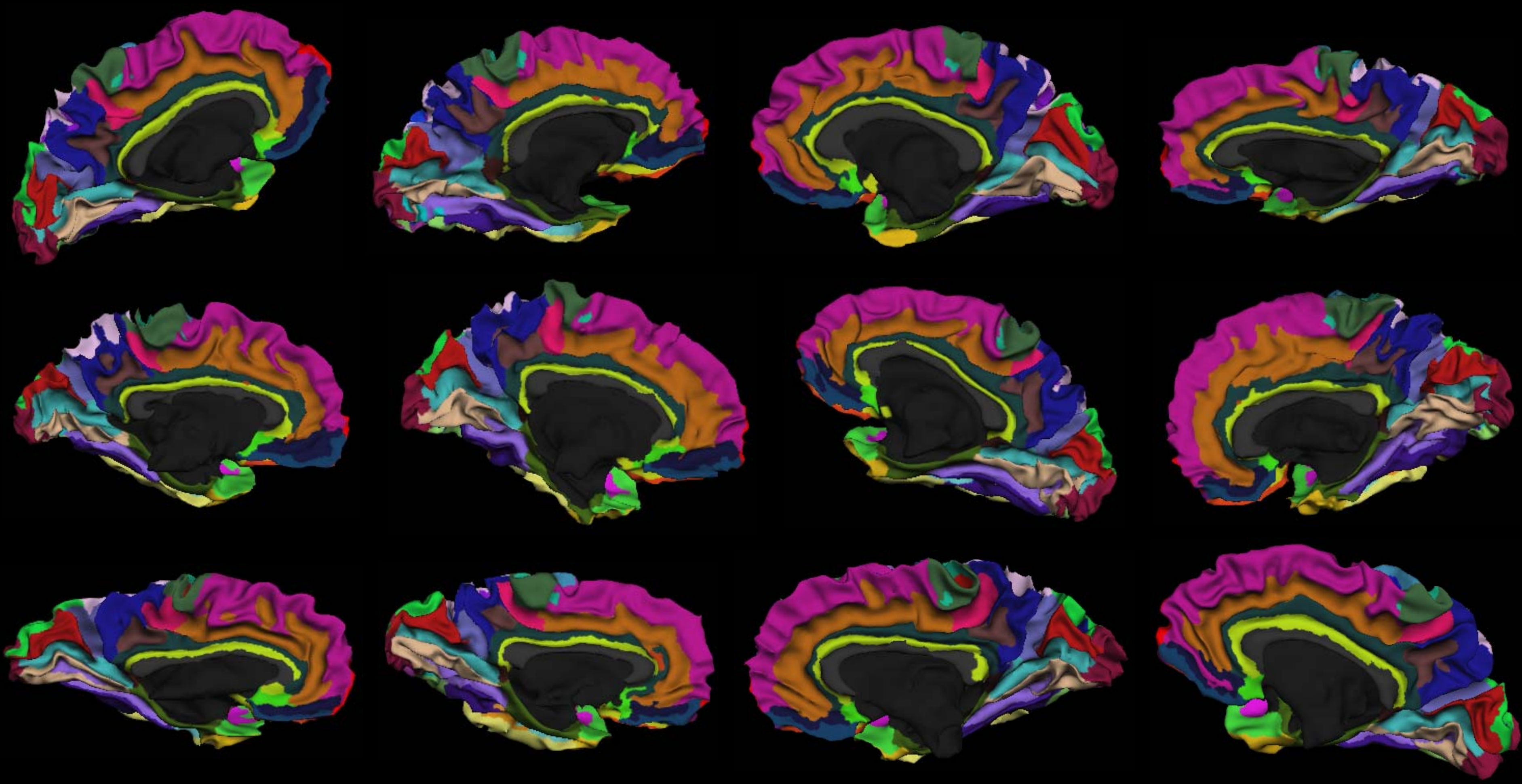
Can obtain orders of magnitude more SNR than *in vivo*, allowing the direct visualization of otherwise (almost) undetectable histological properties.

Imaging Cytoarchitecture (150μm)



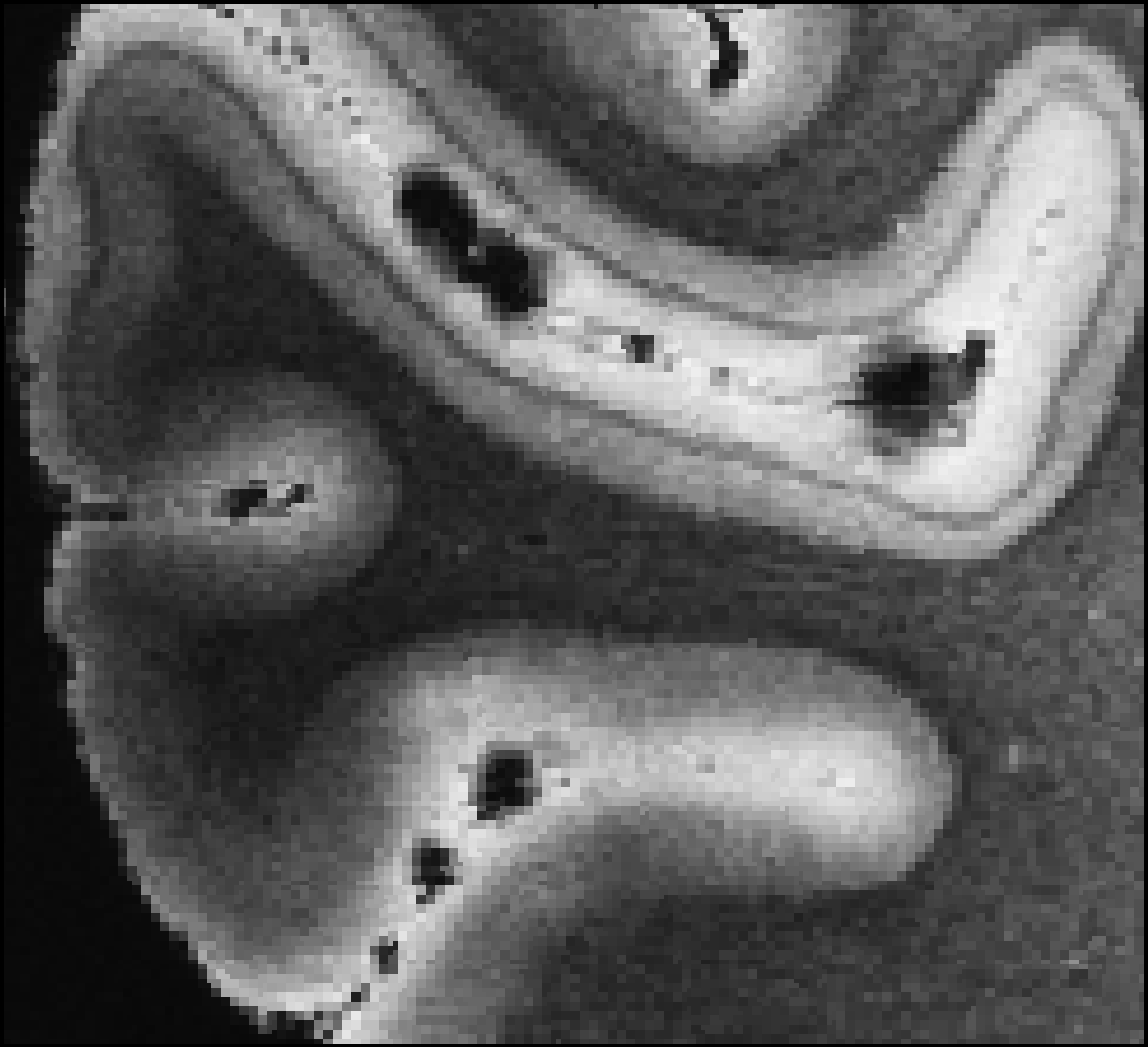
(that’s why they call it the striatum)

Automatic Parcellation of *ex vivo* Hemispheres



Thanks to Brian T Quinn for helping generate these results

Delineating Area 17

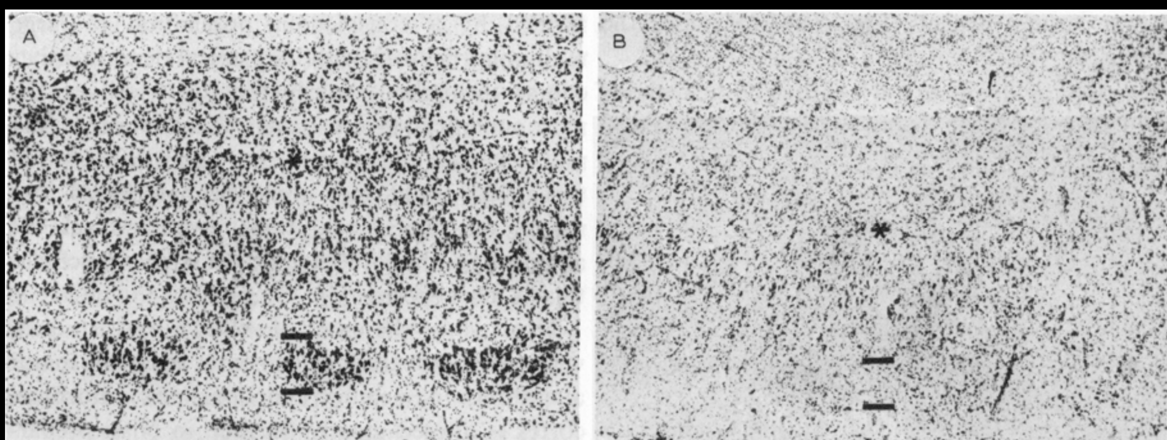


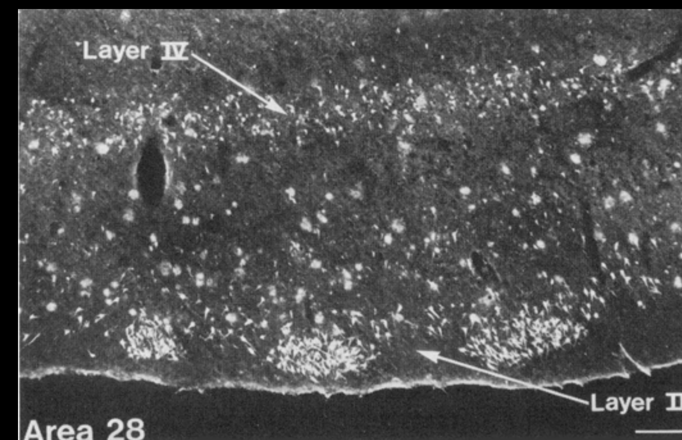
7T, 160μm isotropic, NEX=2, 4 echos, TR=55 ms, esp 13ms, α=10°

Histology in Alzheimer's Disease

(entorhinal cortex=BA28)

CONTROL AD



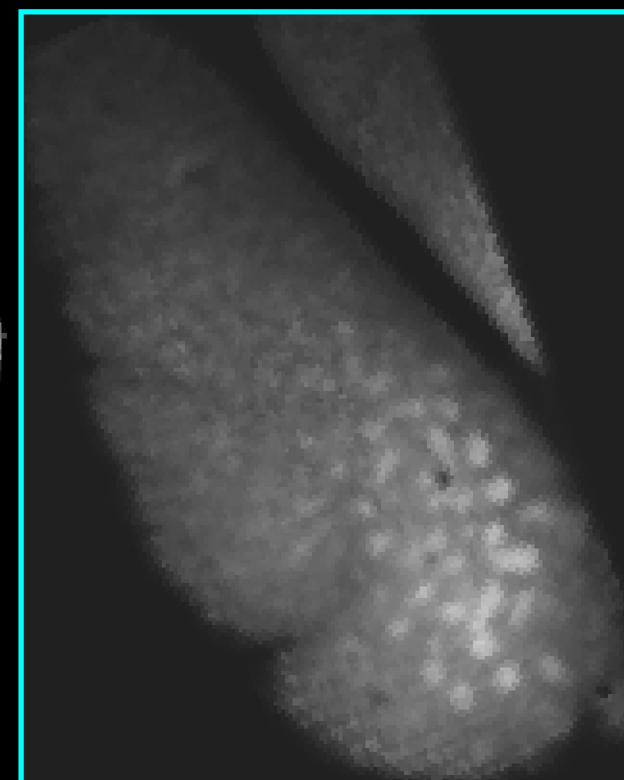


Nissl Stain

thioflavin S (neurofibrillary tangles and neuritic plaques)

Thanks to Brad Hyman and Jean Augustinack for this slide.

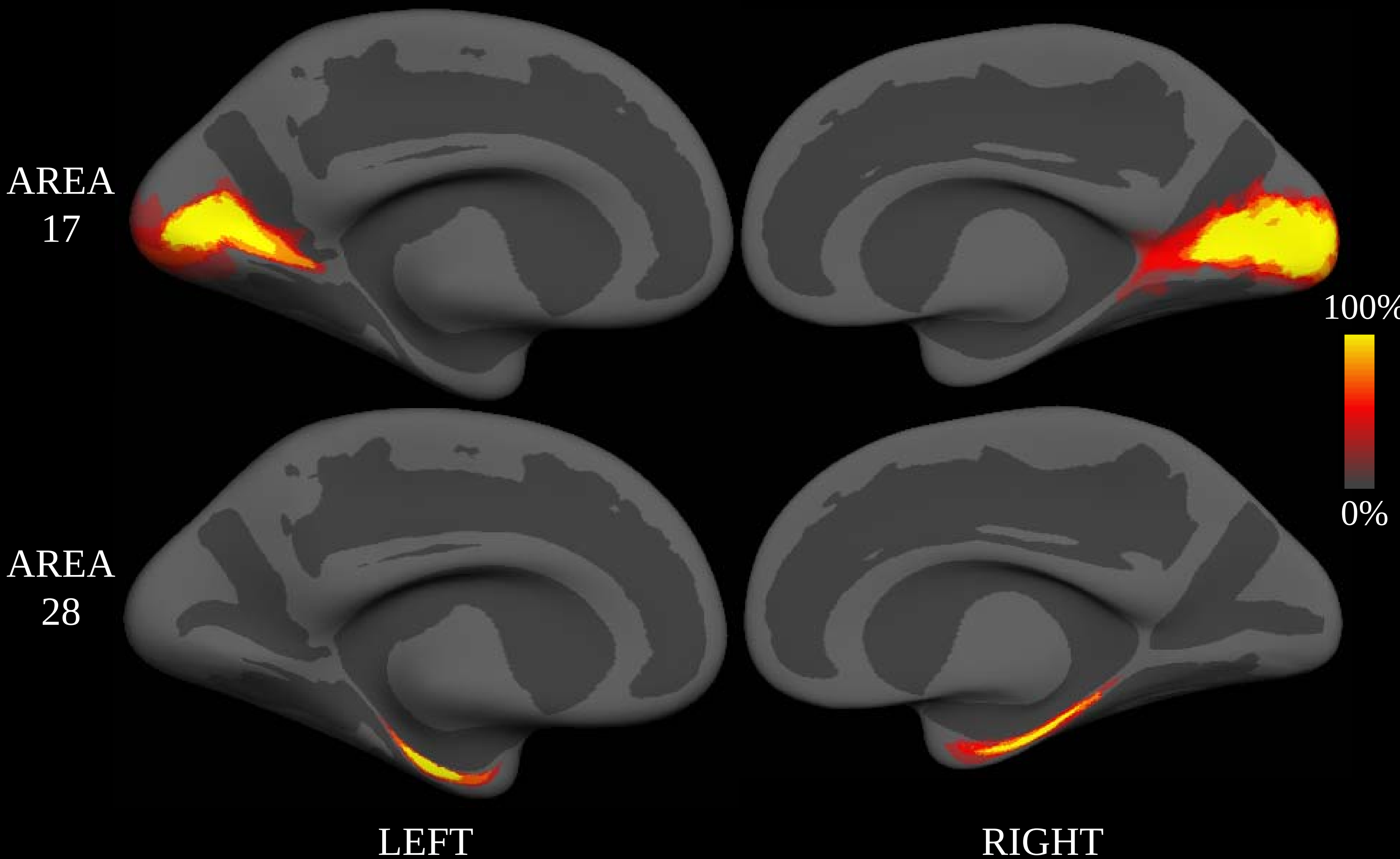
Delineating Area 28



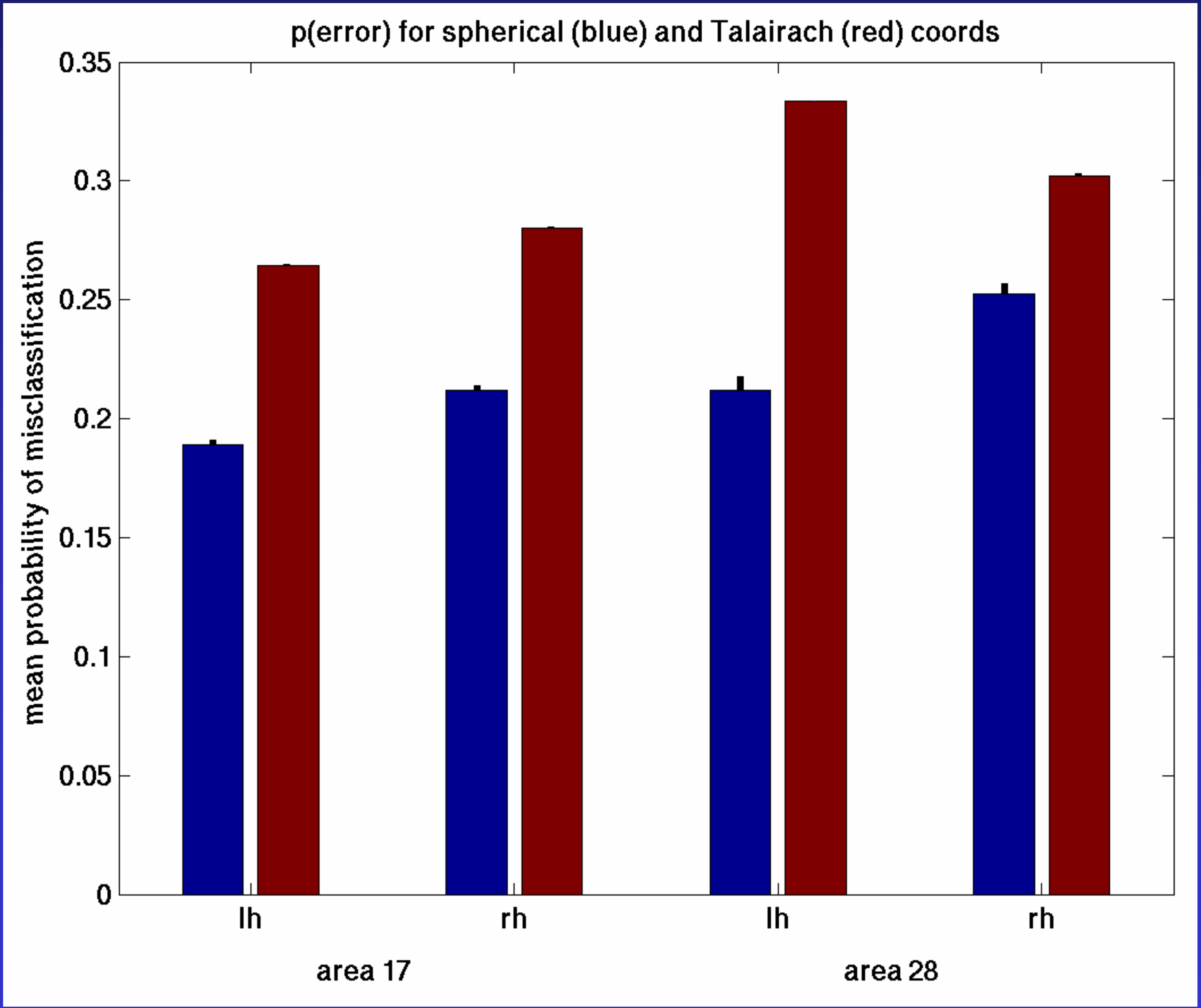
Tangential section
through layer II

Predicting Brodmann Areas from MRI

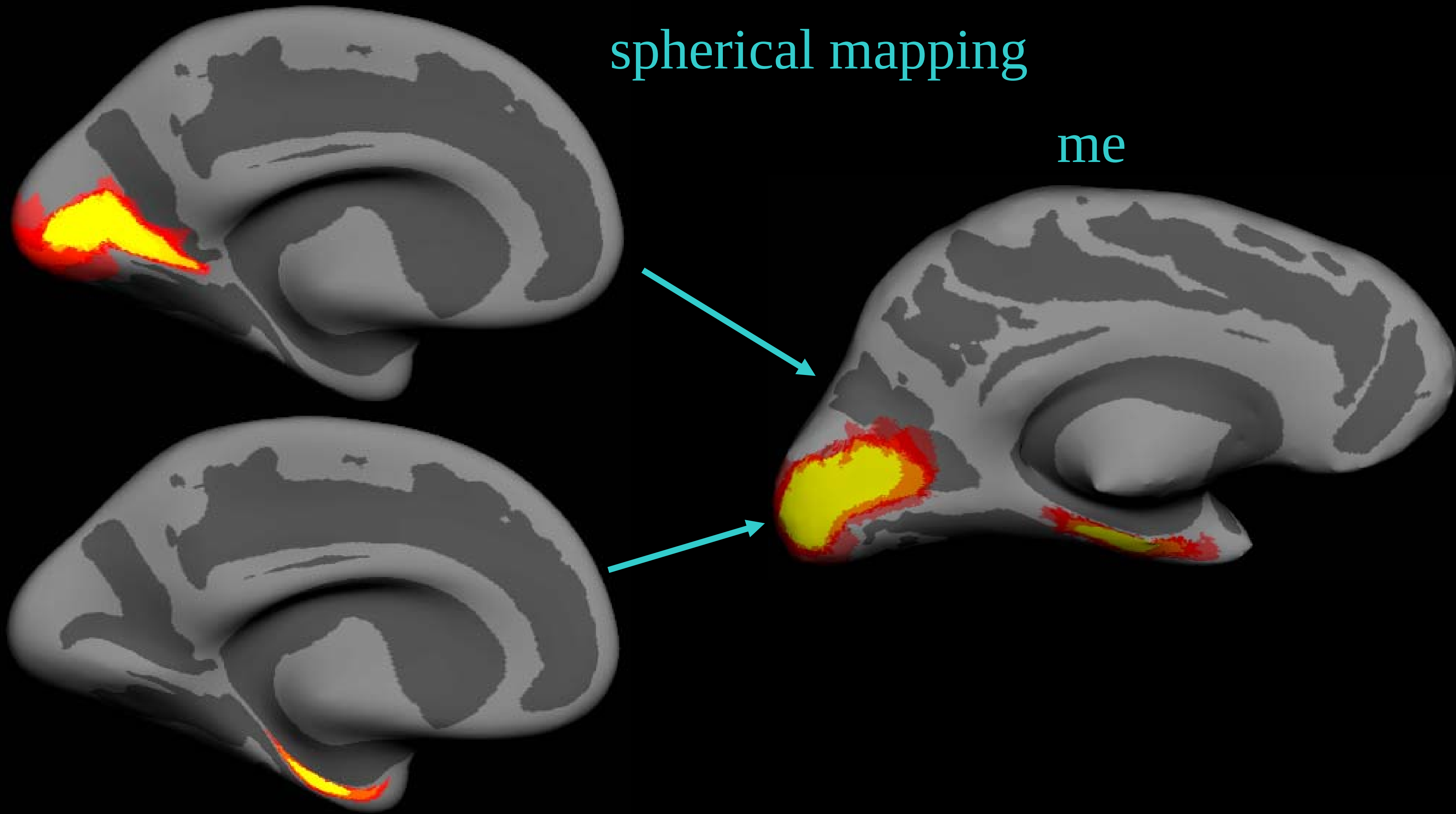
(only 5-6 hemispheres/area)



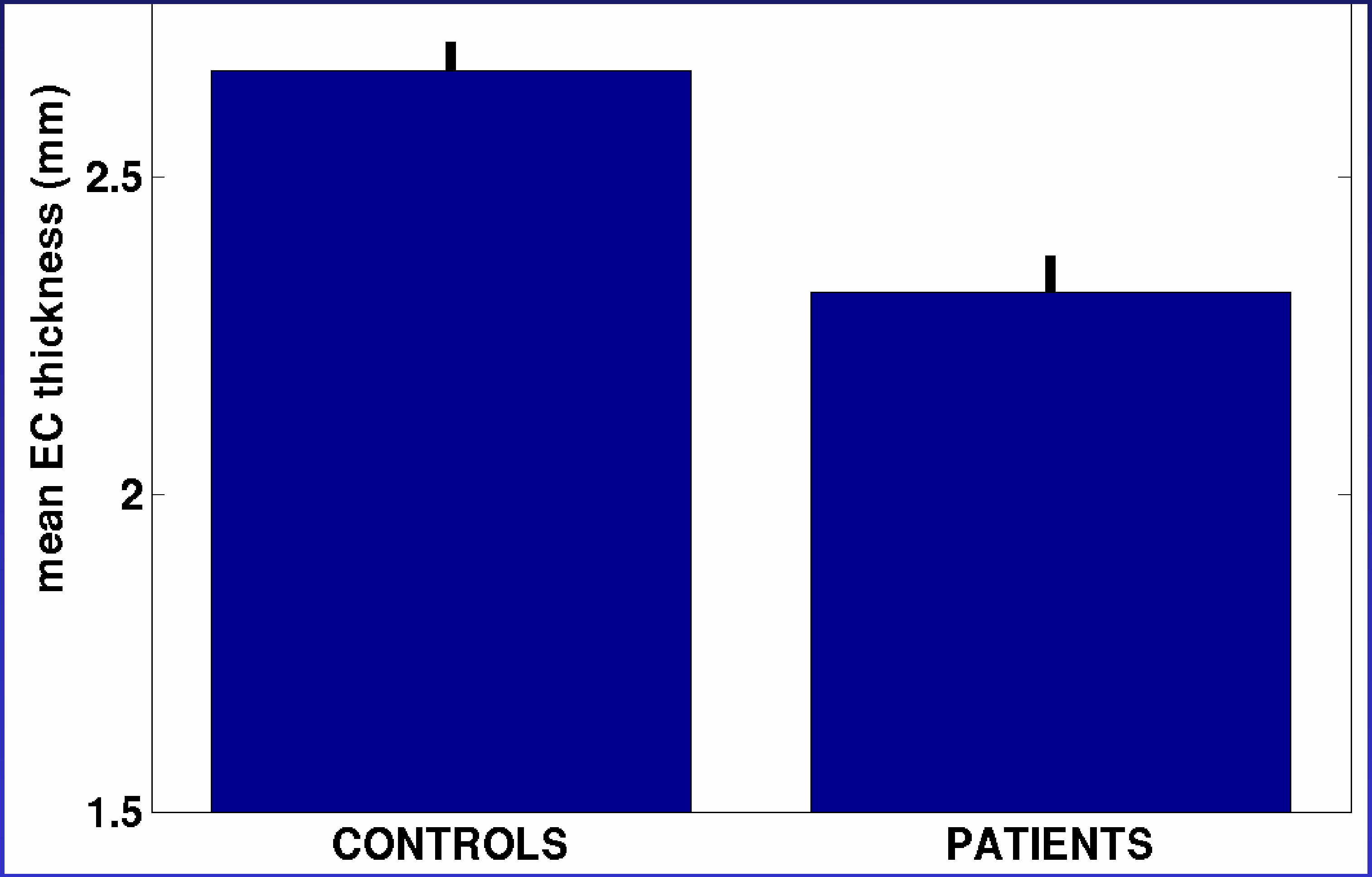
Comparing Coordinate Systems and Brodmann Areas



Making *in vivo* Predictions



Assessing Degeneration in AD



Thickness difference in cytoarchitecturally defined entorhinal cortex between 57 patients (22 CDR 1, 35 0.5) and 58 controls ($p<10^{-5}$).

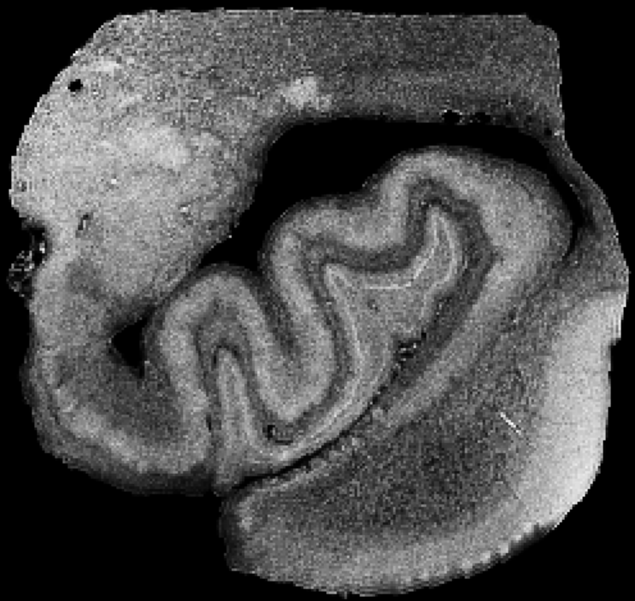
How to visualize additional areas/borders?

1. Increase SNR by building phased arrays (in collaboration with Larry Wald, Graham Wiggins and Siemens).

2. Determine borders with standard histology, and align histological images with MR (in collaboration with Gheorghe Postelnicu and Jean Augustinack).

3. MR Histology – make histological stains MR visible (in collaboration with Christian Farrar, Megan Blackwell, Jean Augustinack and Bruce Rosen).

Transferring Histological Information to MRI



MRI

Block Face

Nissl Stain

Joint work with Jean Augustinack, Matt Frosch, Gheorghe Postelnicu and Andre van der Kouwe

Entropy-based Rigid Registration

ML (Leventon and Grimson, 1998) similarity metric drawback:

-The model is specified by a pair of manually aligned images ➔ all histograms should coincide

-The metric is sensitive to the overlapping area of the 2 images

Entropy $$H(X) = \sum_{x} p_X(x) \log_2 (p_X(x))$$

Joint Entropy $$H(X,Y) = \sum_{x,y} p(x,y) \log_2 (p(x,y))$$

Mutual Information $$MI(X,Y) = H(X) + H(Y) - H(X,Y)$$

Use *Mutual Information (MI)* or *Joint Entropy (JE)* as similarity metric:

-No need to use prior manually aligned pair;

-Robust to change in direction of contrast

Drawbacks:

-Does not take spatial correlations in the image into account.

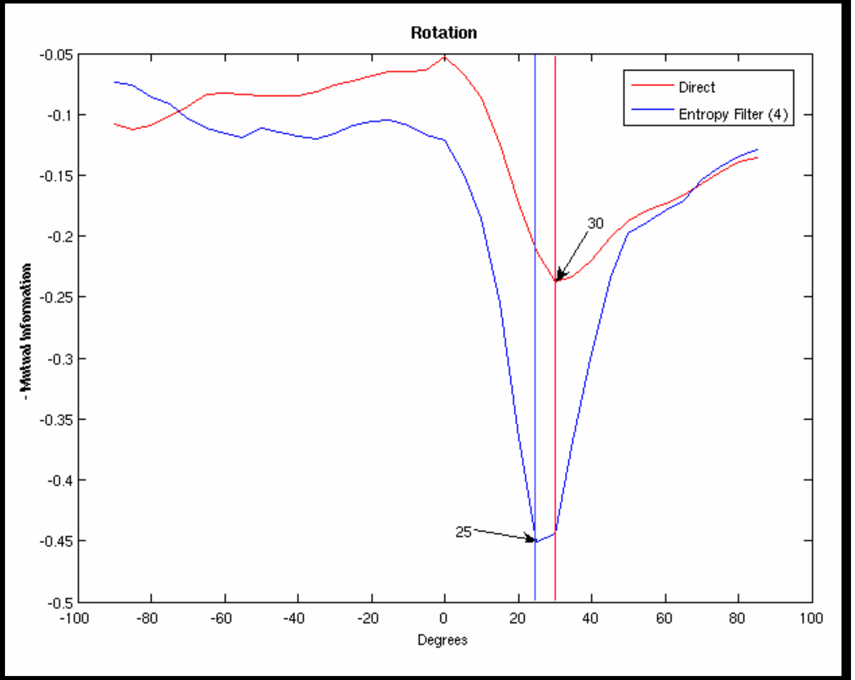
Proposed Solution

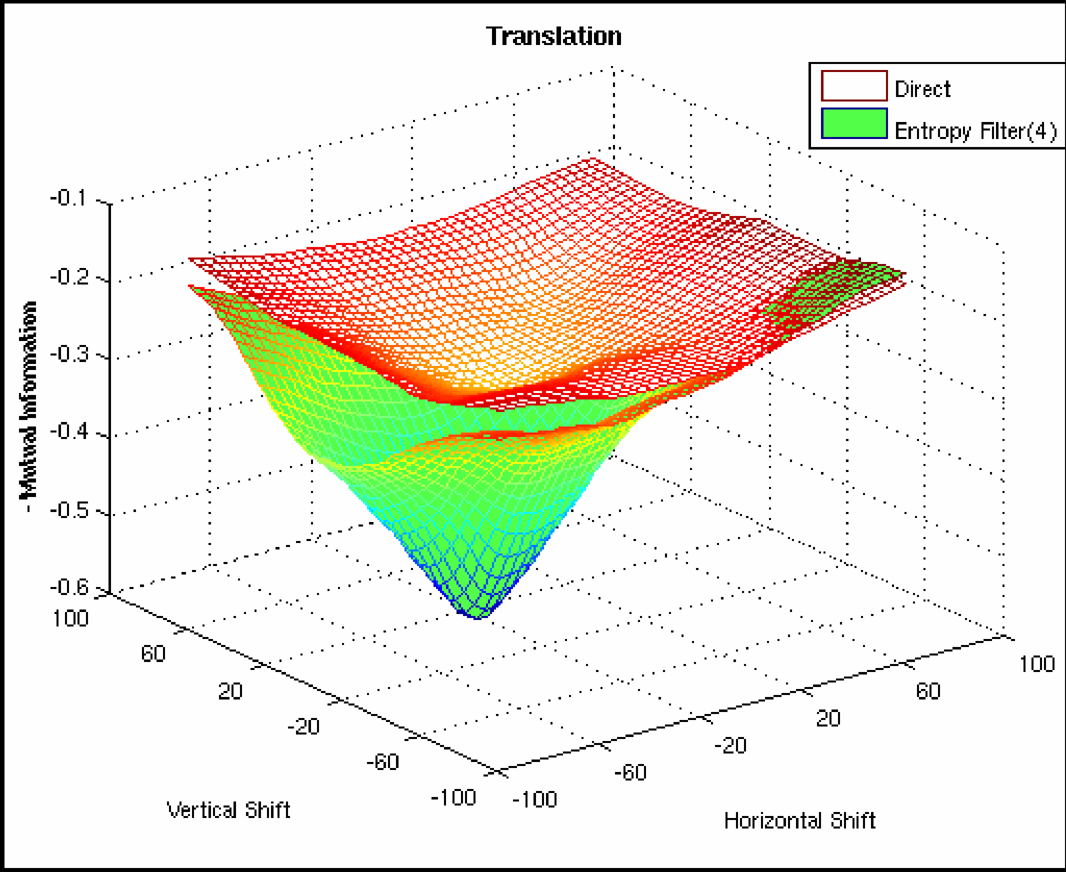
- Use MI or JE and consider a texture filter instead of the noisy histology slice

Entropy filter size r

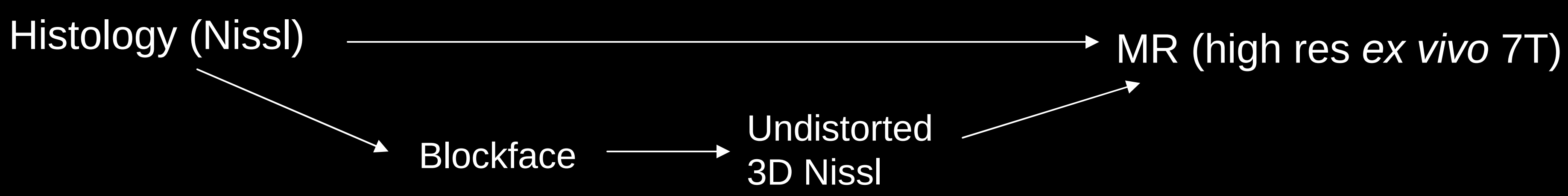
$$EF_r(i,j) = H\left(I(i \pm r, j \pm r)\right)$$

Probing Capture Regions (Mutual Information)





Histology Volume Reconstruction and Registration with MR data



Steps:

1. Reconstruct a 3D volume from the histology slices
   - Automatic rigid registration with the blockface pictures;
   - Correct mounting distortions (elastic warping)
2. Align histology volume to the MR
   - Rigid registration (3D)
   - In this case → also non-rigid (tubing problems and MR distortions)

Joint work with Jean Augustinack and Gheorghe Postelnicu

Overview of the MR->Histology Registration

Rigid Nissl

↓

Blockface

↓

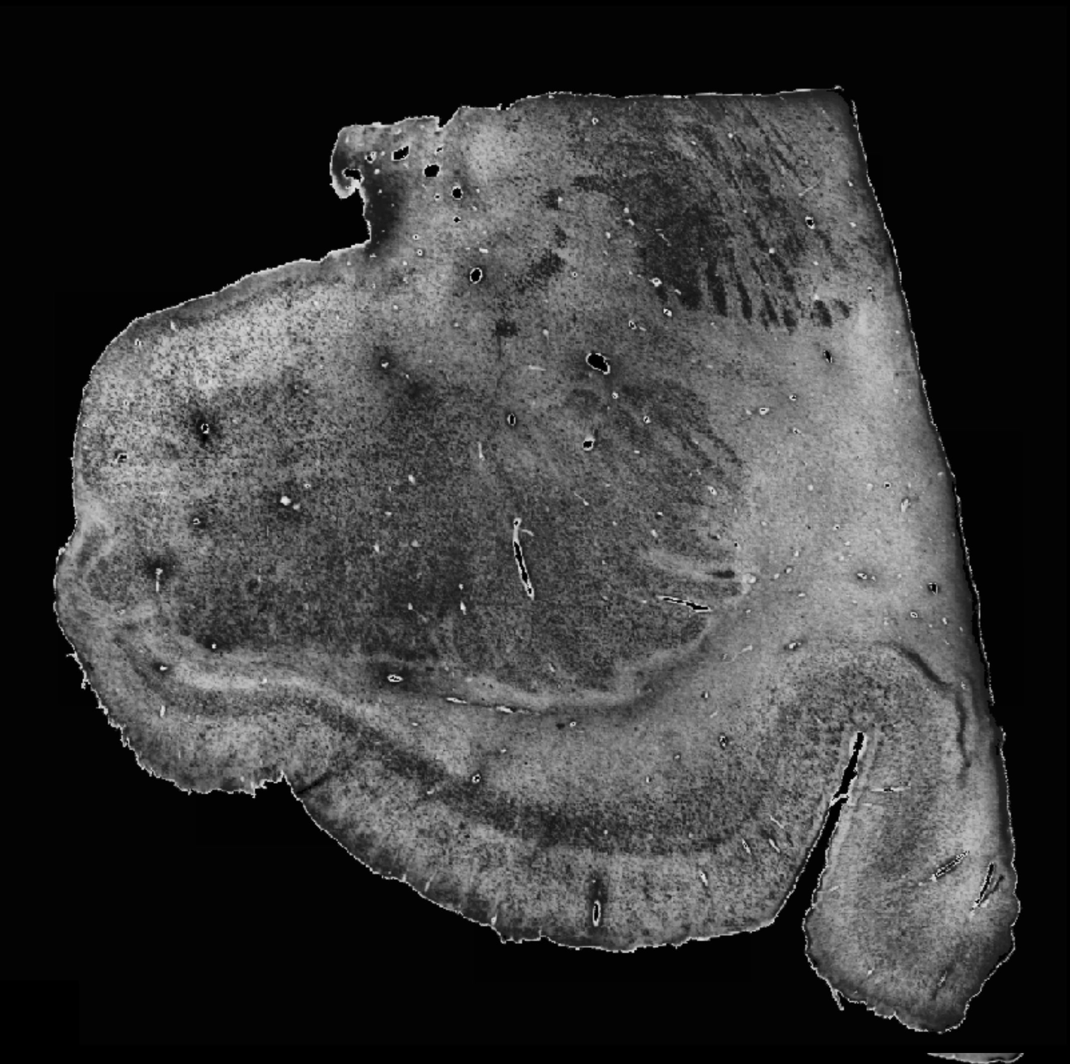
Unwarped Nissl

↓

Rigid MR

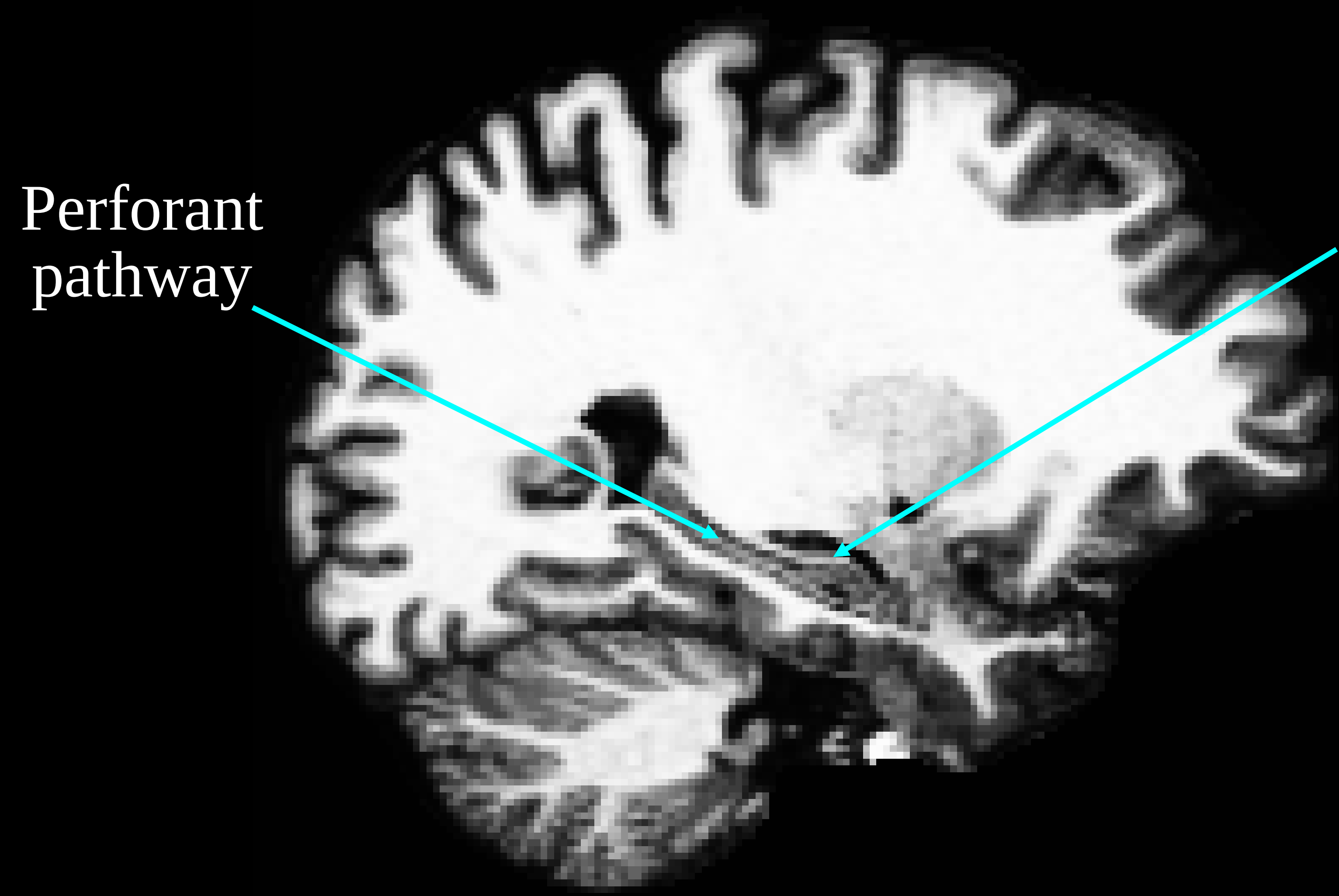
↓

Warped MR



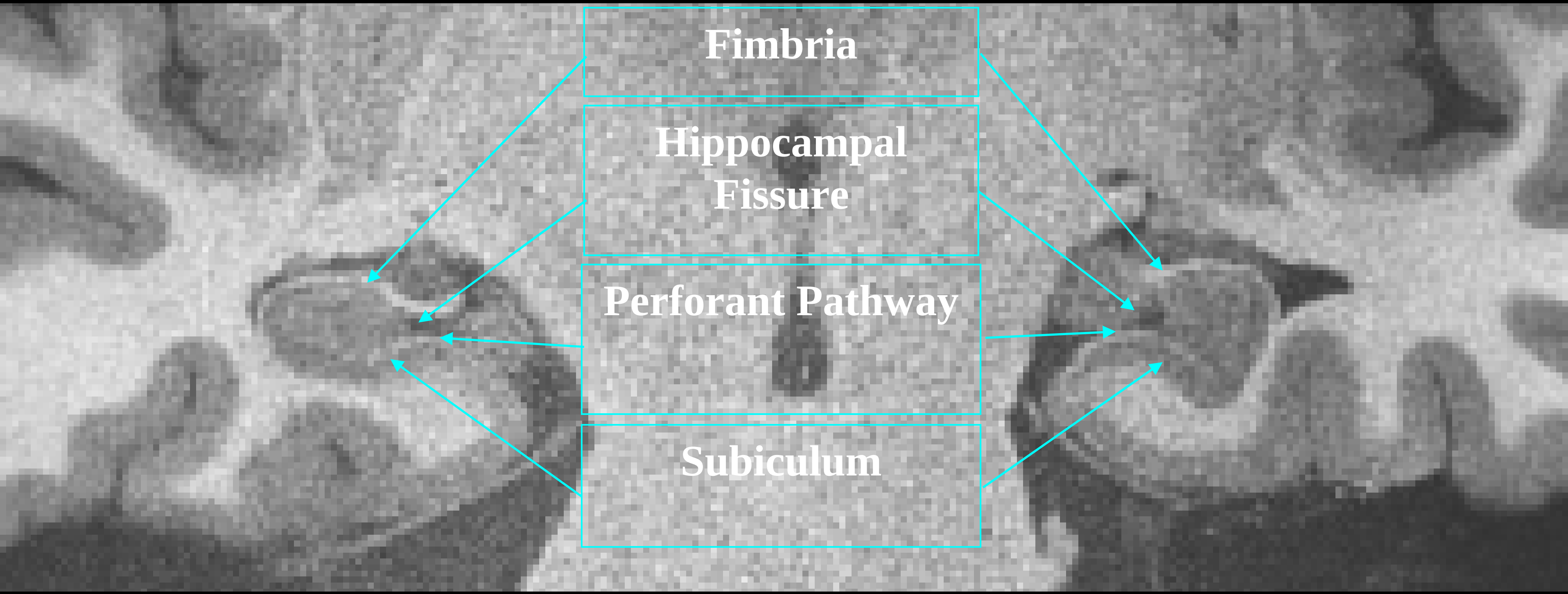
Joint work with Jean Augustinack and Gheorghe Postelnicu

High Resolution Hippocampal Modeling



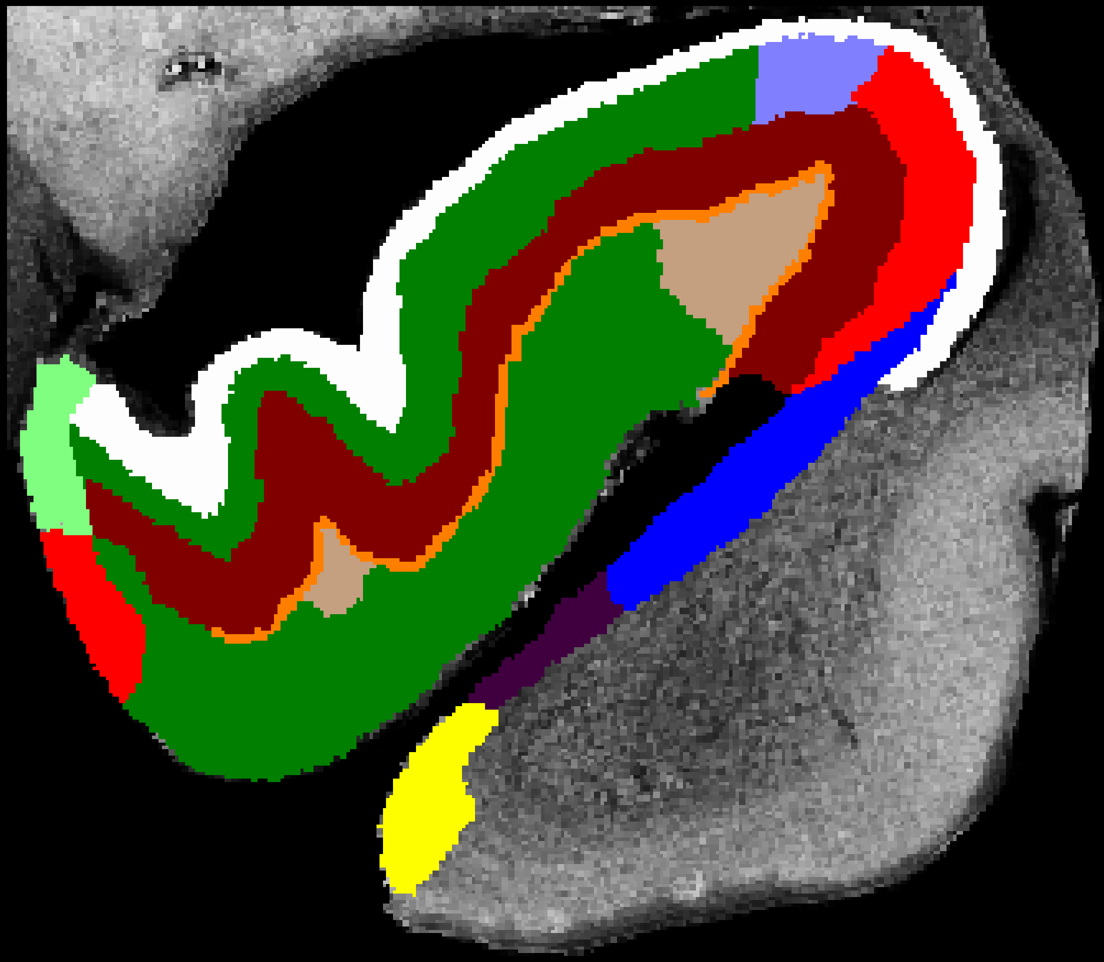
Even in standard 1mm MP-RAGE can discern hippocampal substructures (e.g. alveus, perforant pathway)

High Resolution *in vivo* Hippocampal Imaging



3T MP-RAGE, 400μm isotropic, 8 channel phased-array, TE=4.54msec, TI=1sec, α=12º, NEX=4 (12.5 minutes/scan)

High Resolution Hippocampal Modeling



Joint work with Jean Augustinack, David Salat and Andre van der Kouwe

Inferring *in vivo* Structure

1. Compute linear transform that maximizes overlap with *in vivo* segmentation (Dice coefficient).

$$L = \arg\max \frac{\iiint_{\mathbf{r}} I(\mathbf{r}) \wedge H(L\mathbf{r})}{\iiint_{\mathbf{r}} I(\mathbf{r}) \vee H(L\mathbf{r})}$$

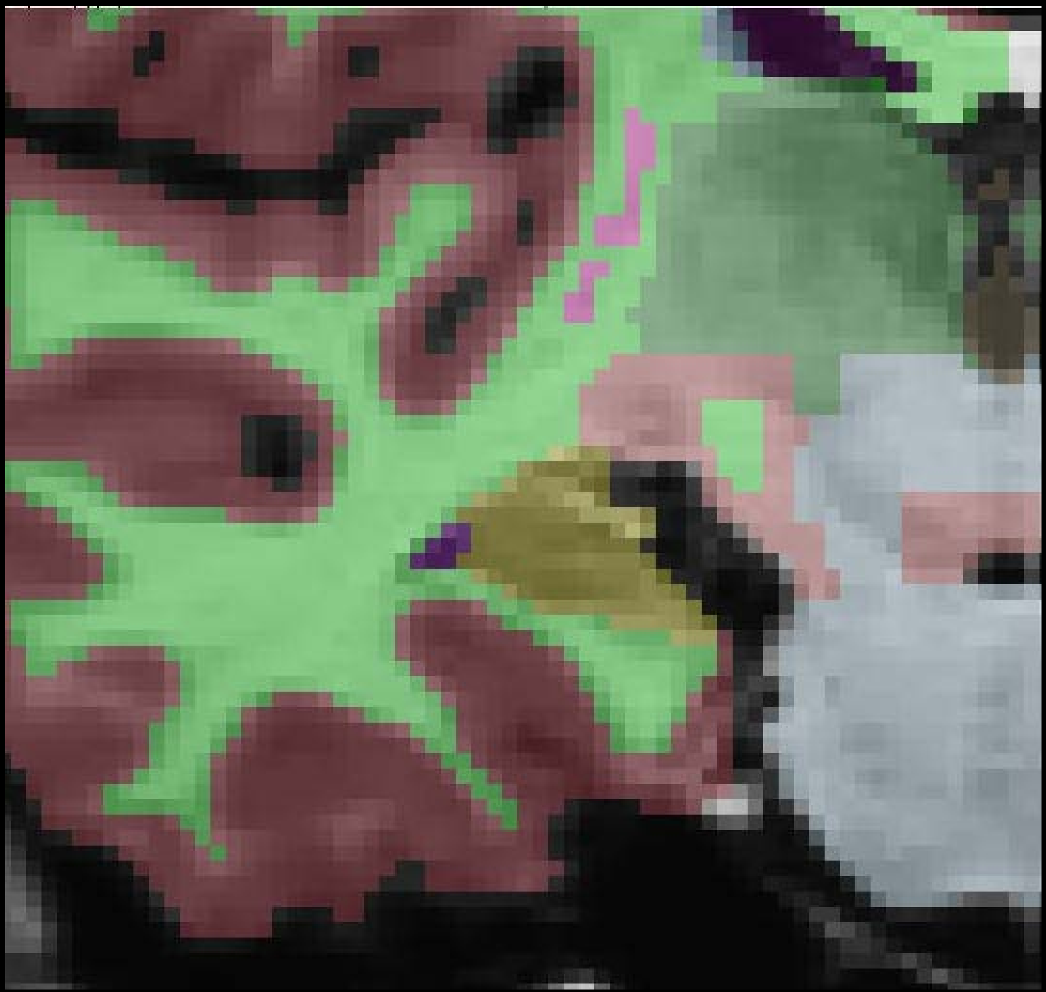
2. Compute nonlinear transform that maximizes overlap while minimizing metric distortion.

$$J = \lambda_d J_d + \lambda_P J_P + \lambda_B J_B + J_S$$

High res *ex vivo* model morphed into register with *in vivo* data

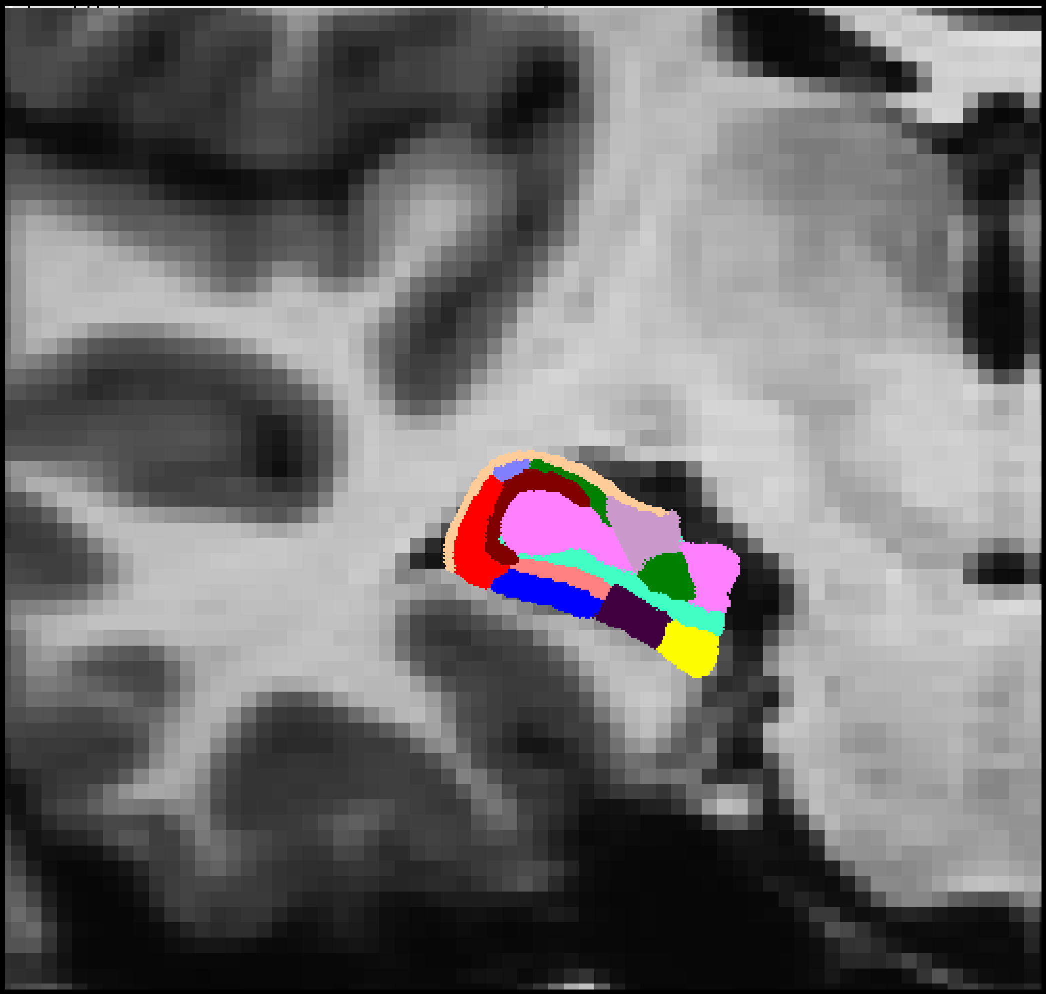
1mm MP-RAGE

High res *ex vivo* model morphed into register with *in vivo* data



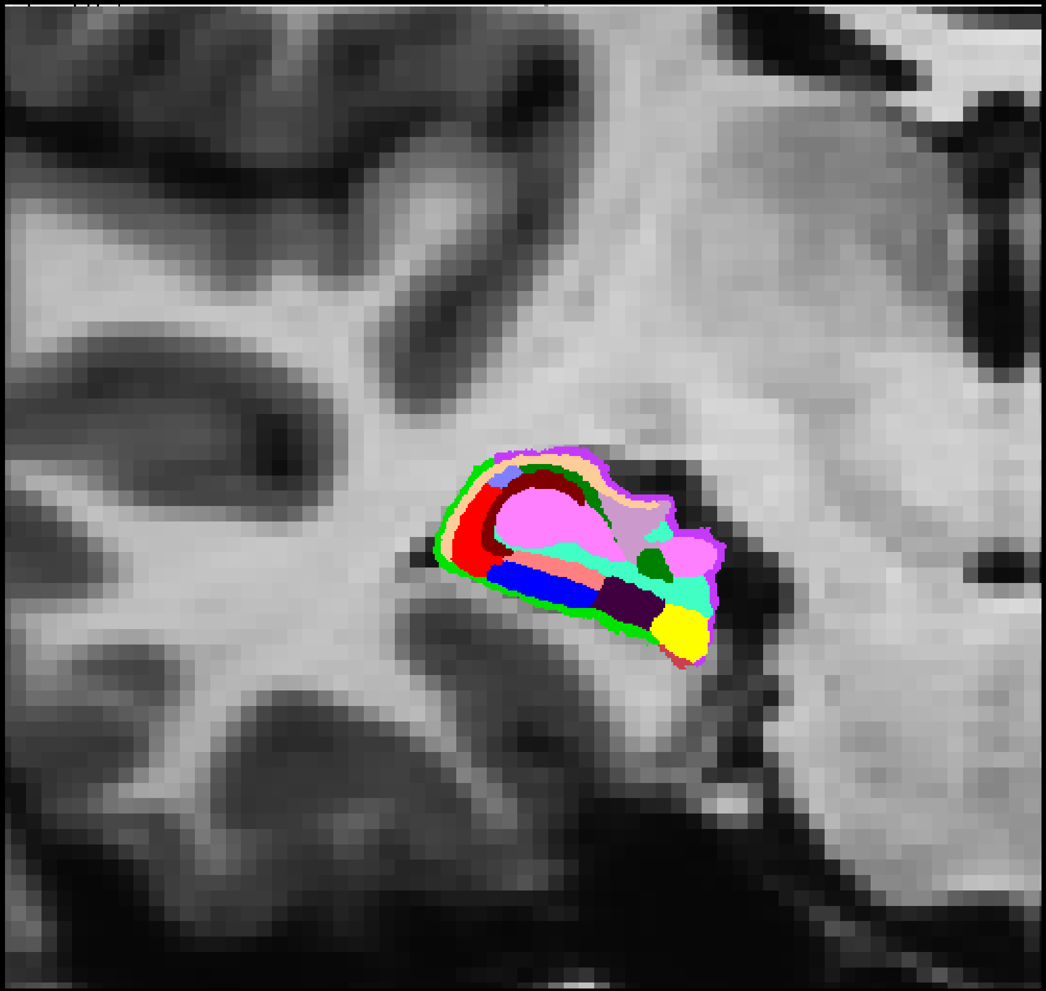
Whole-Brain Segmentation

High res *ex vivo* model morphed into register with *in vivo* data



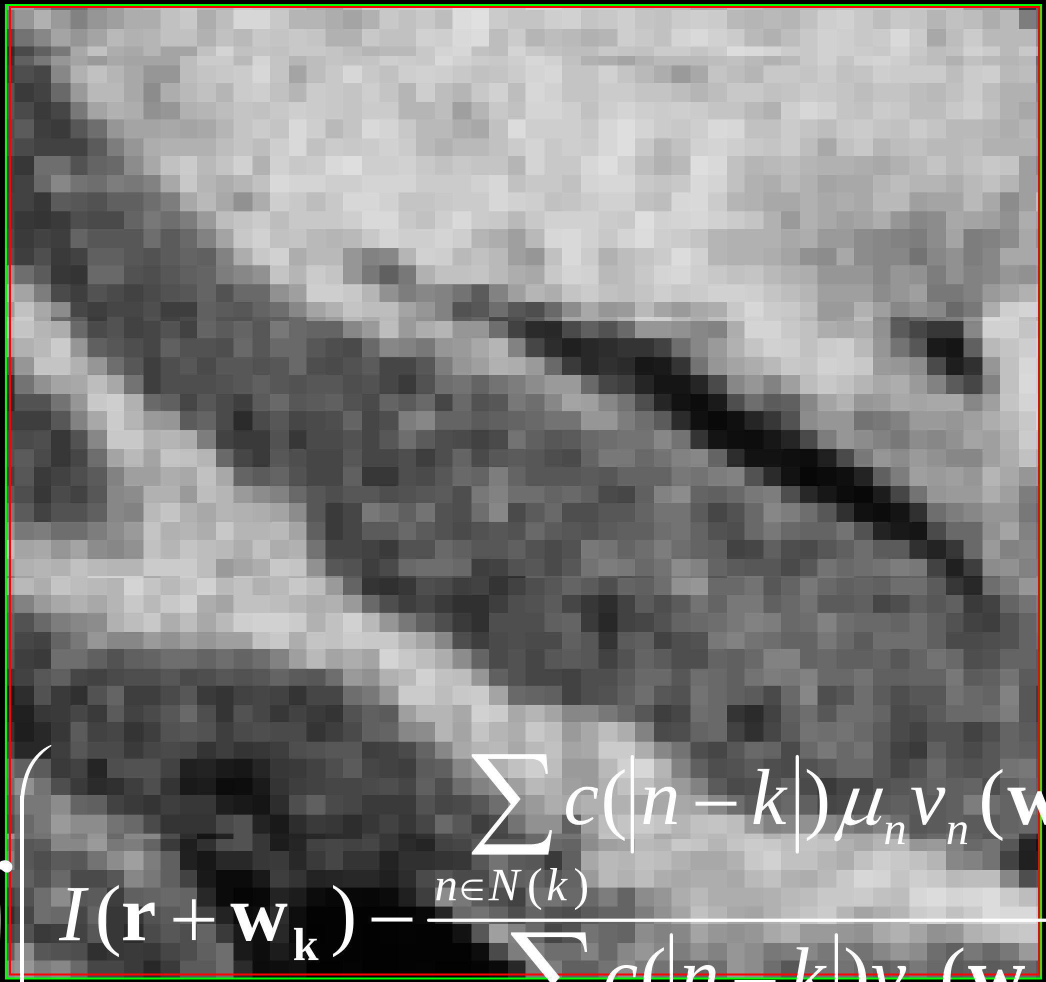
Linear Registration

High res *ex vivo* model morphed into register with *in vivo* data



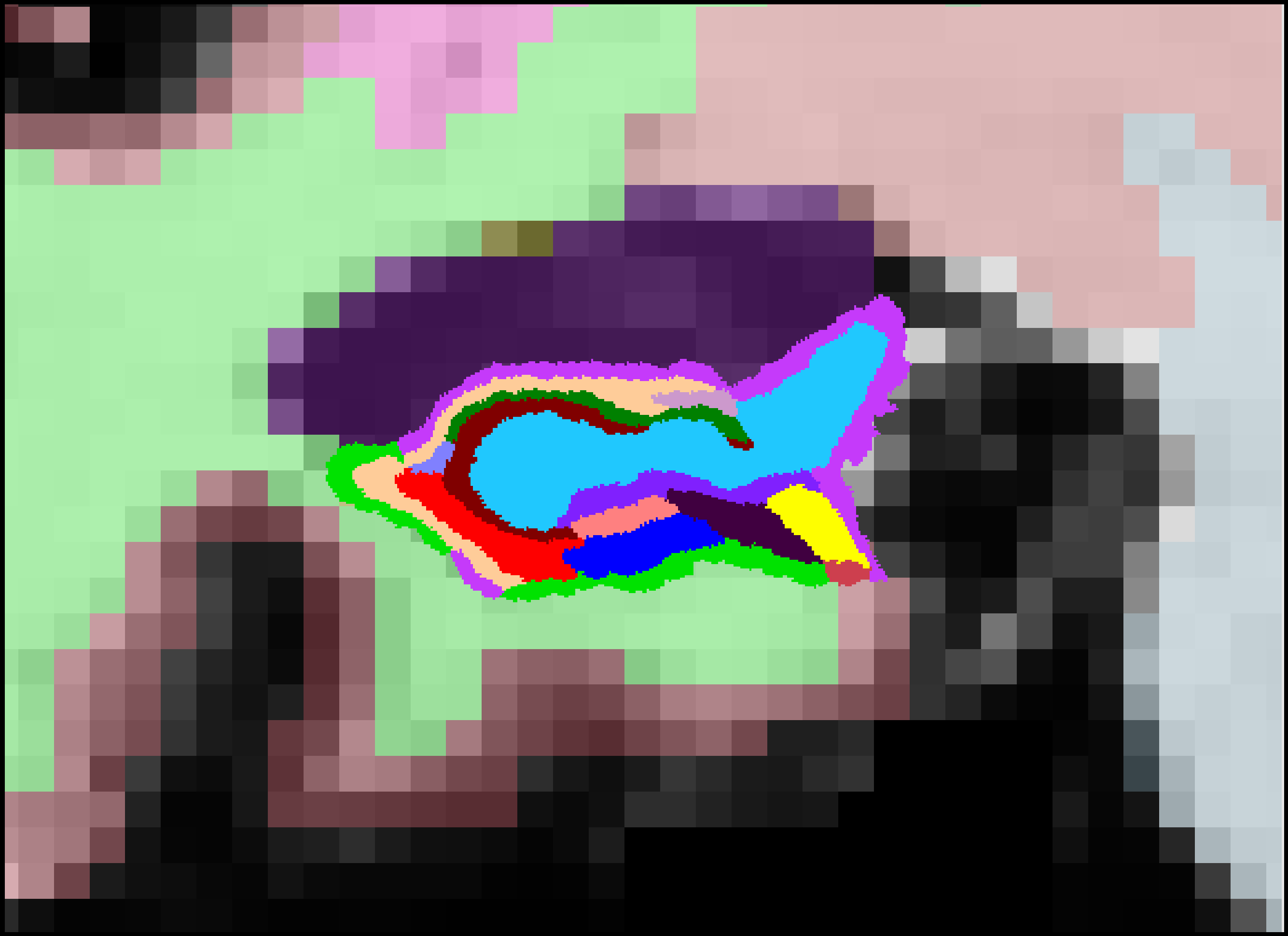
Nonlinear Registration

Using Intensity Information

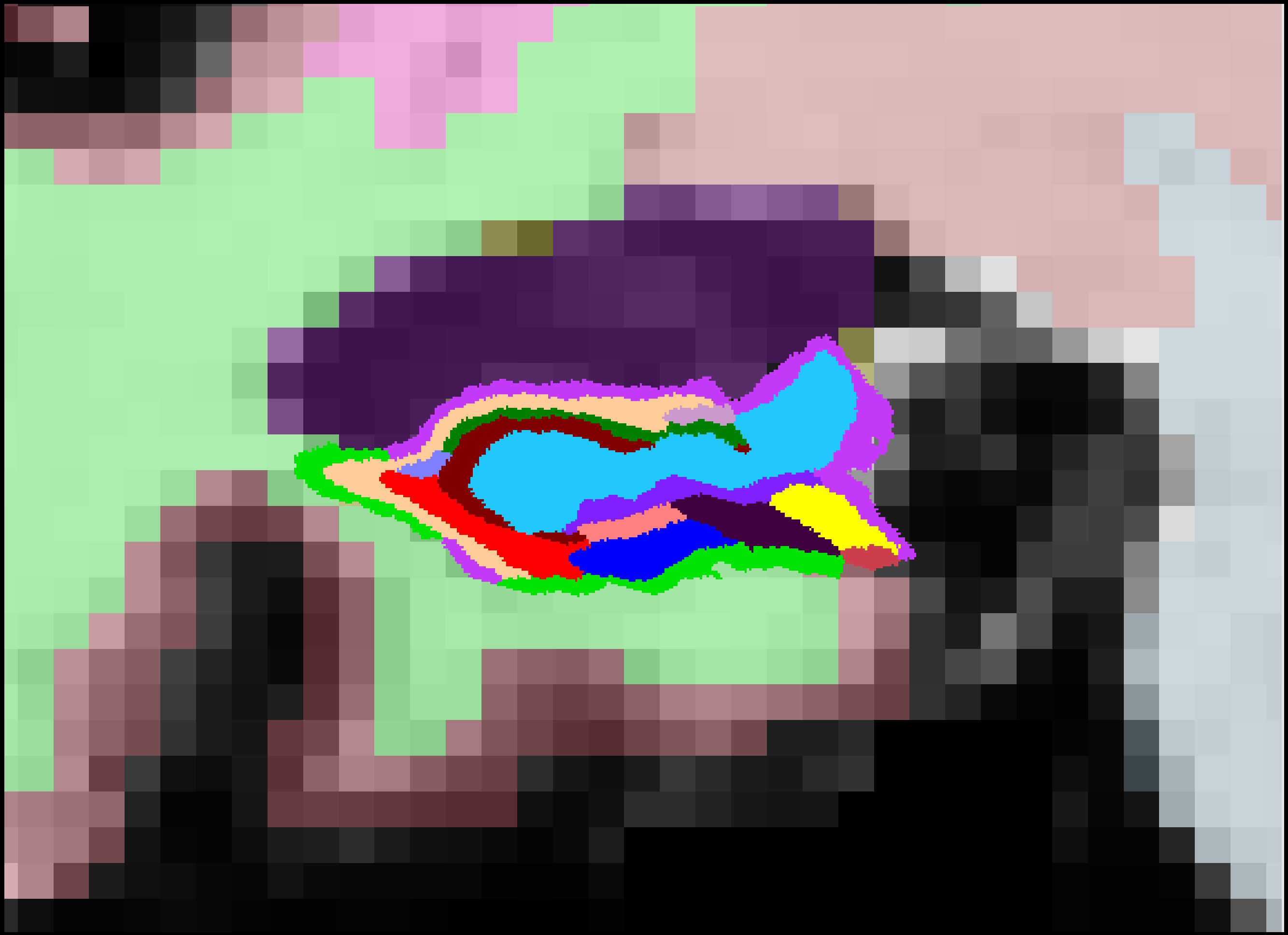


$$J_P = \iiint_k \left(I(\mathbf{r}+\mathbf{w_k}) - \frac{\sum_{n \in N(k)} c(|n-k|)\mu_n v_n(\mathbf{w_k})}{\sum_{n \in N(k)} c(|n-k|) v_n(\mathbf{w_k})} \right)^2 d\mathbf{k}$$

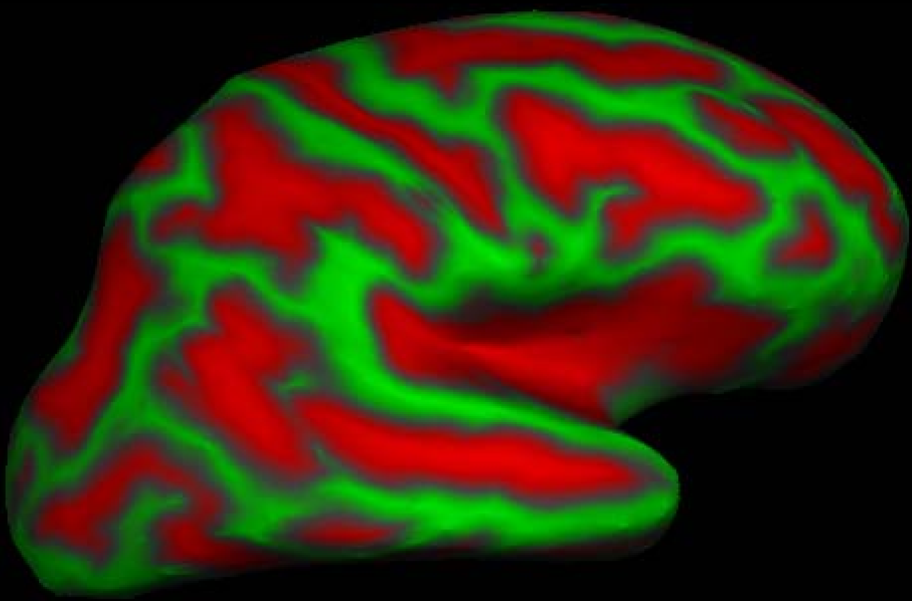
Preliminary Results: Initial



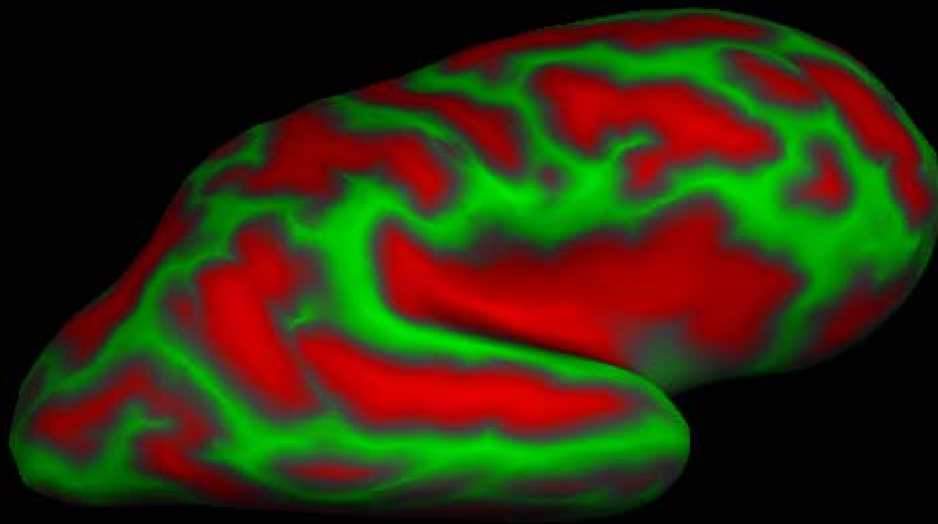
Preliminary Results: Deformed



Direct Validation: *in vivo* and *ex vivo* scans of same subject



in vivo



ex vivo

Thanks to Xiao Han for helping generate these results

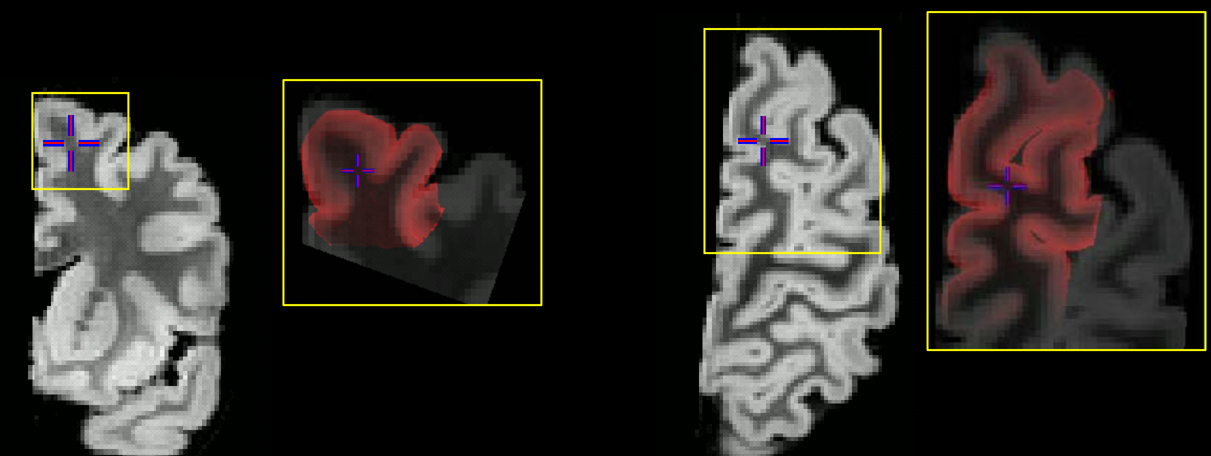
Hippocampal Labeling: Direct Validation

Outline of subiculum

Thanks to Xiao Han for helping generate these results

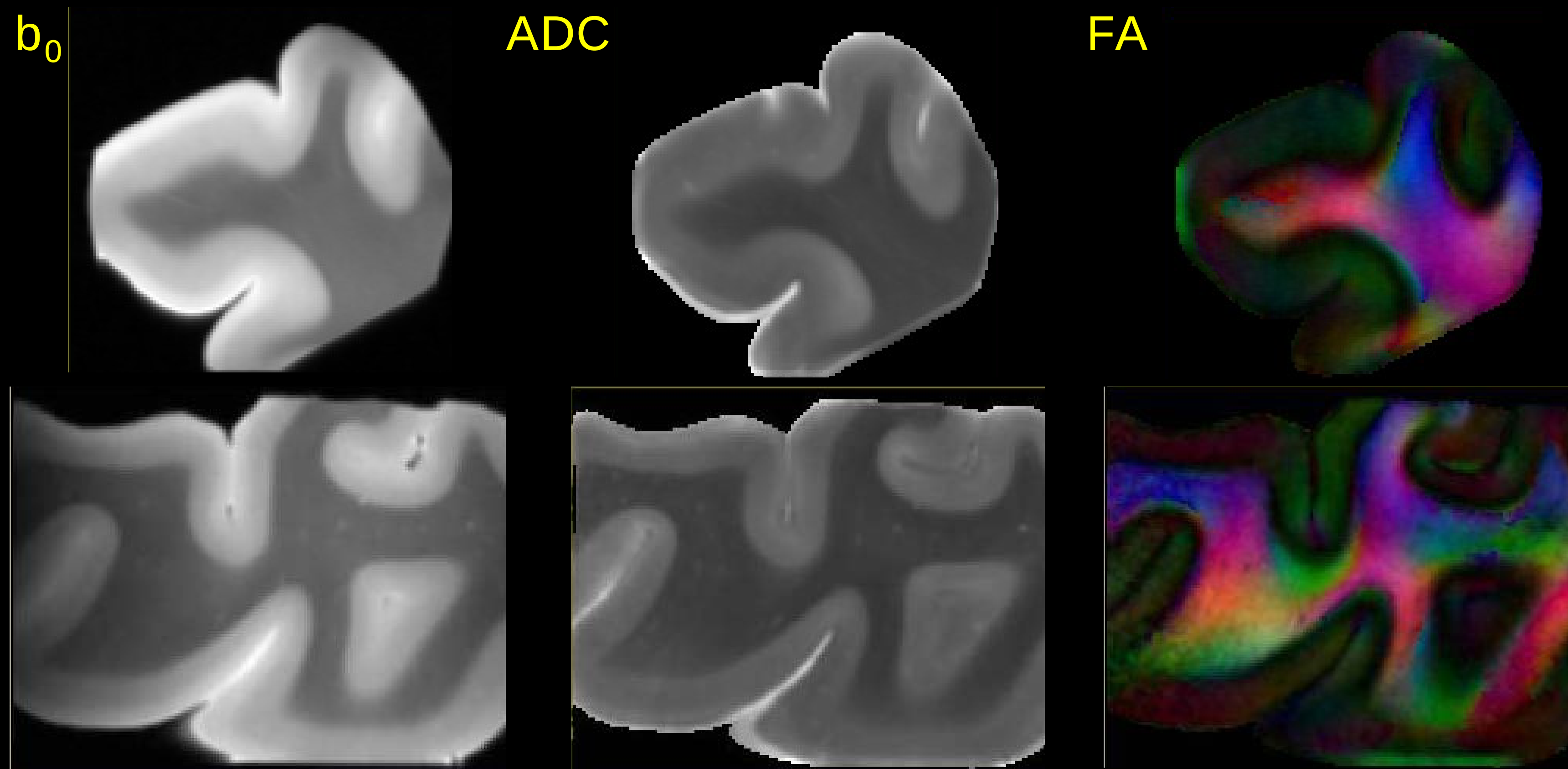
Ex vivo DTI studies in human cortex

- Normal adult male premotor cortex
- Cut from an entire fixed hemisphere
- $225\mu m$ isotropic resolution
- $b=4{,}000\ smm^{-2}$



de Crespigny, D'Arceuil, MGH

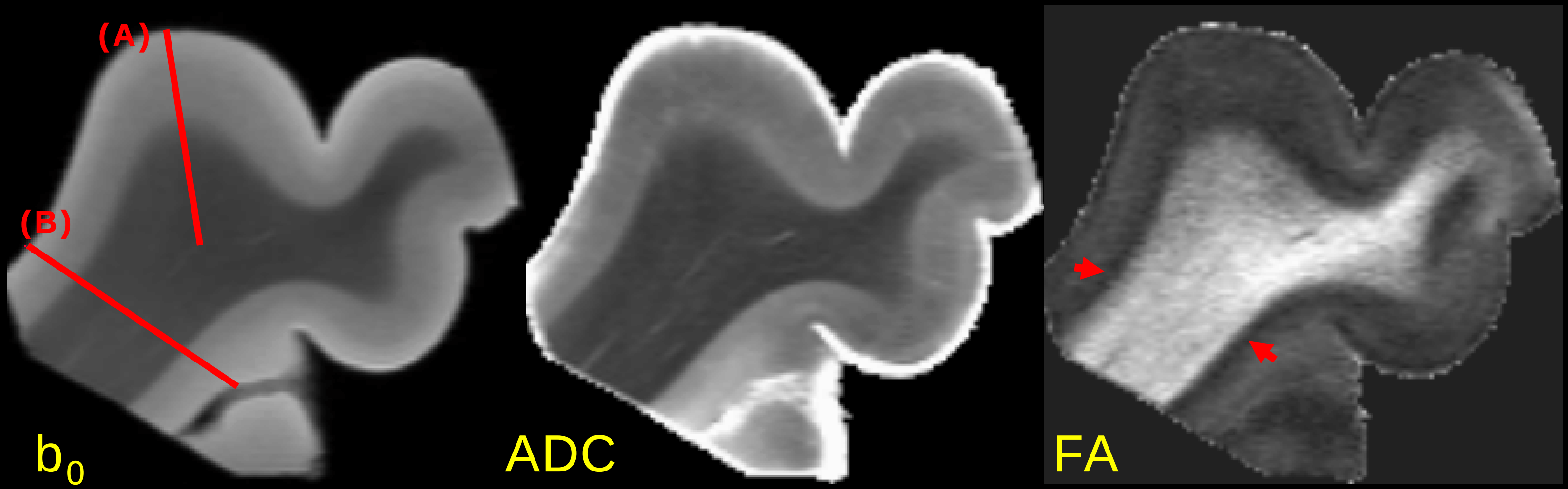
Ex vivo normal human cortex

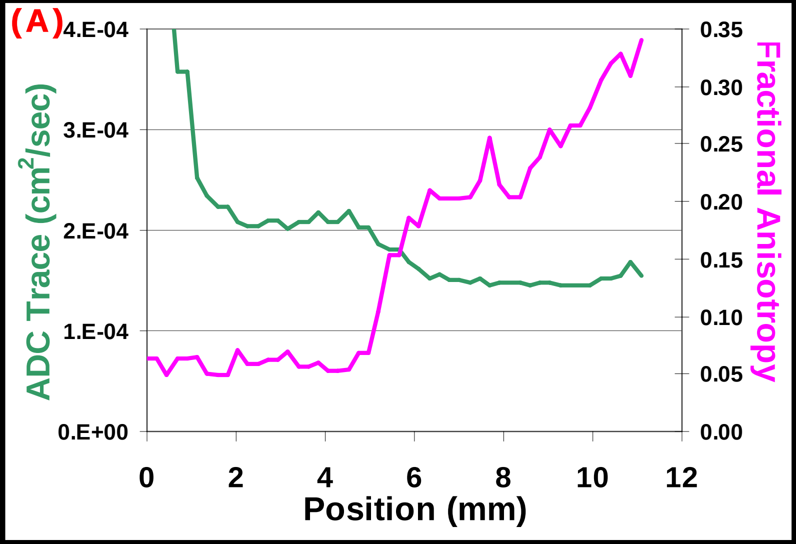


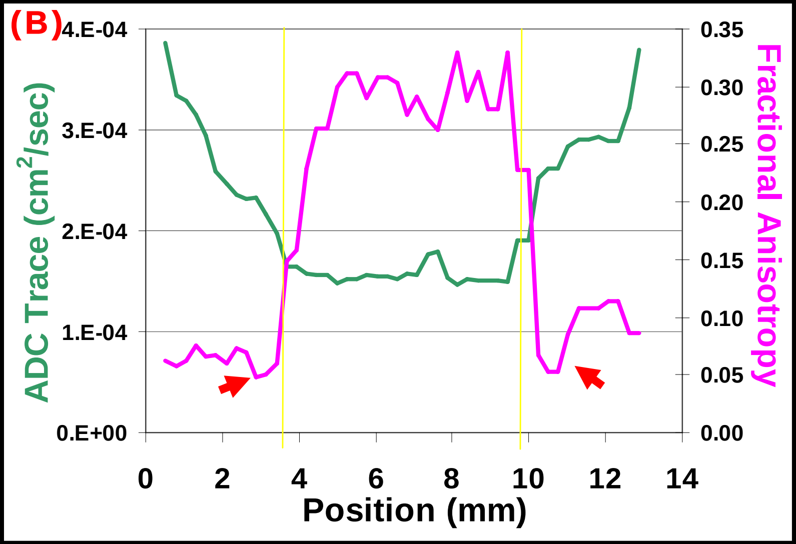
	FA	ADC $\times 10^{-3} cm^2 s^{-1}$
White Matter	0.3±0.05 (0.15 – 0.45)	0.154±0.004
Gray Matter	0.09±0.01	0.249±0.018
G-W Interface	0.05±0.01	0.256±0.014

de Crespigny, D'Arceuil MGH, 2005

Ex vivo normal human cortex

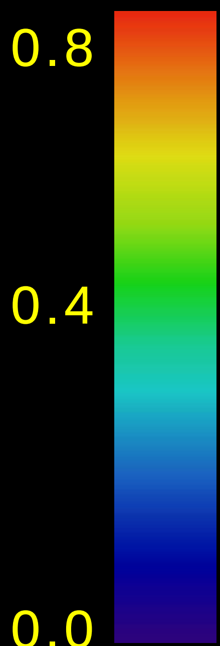


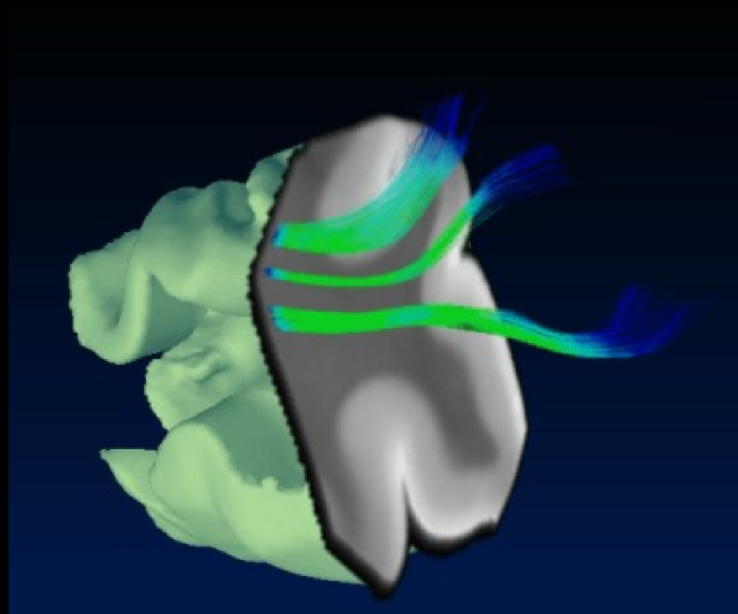


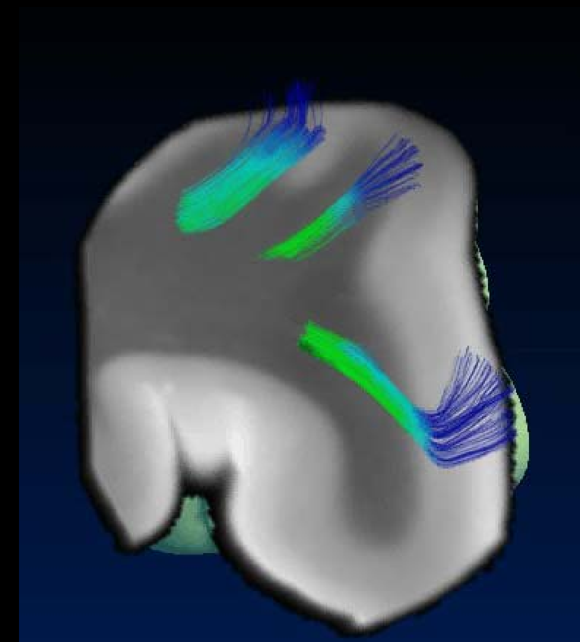


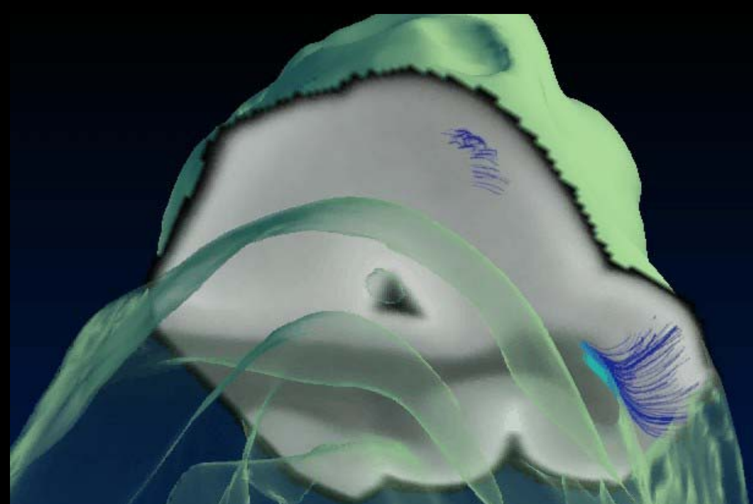
de Crespigny, D'Arceuil MGH

DTI Tractography in the cortex (250um isotropic)







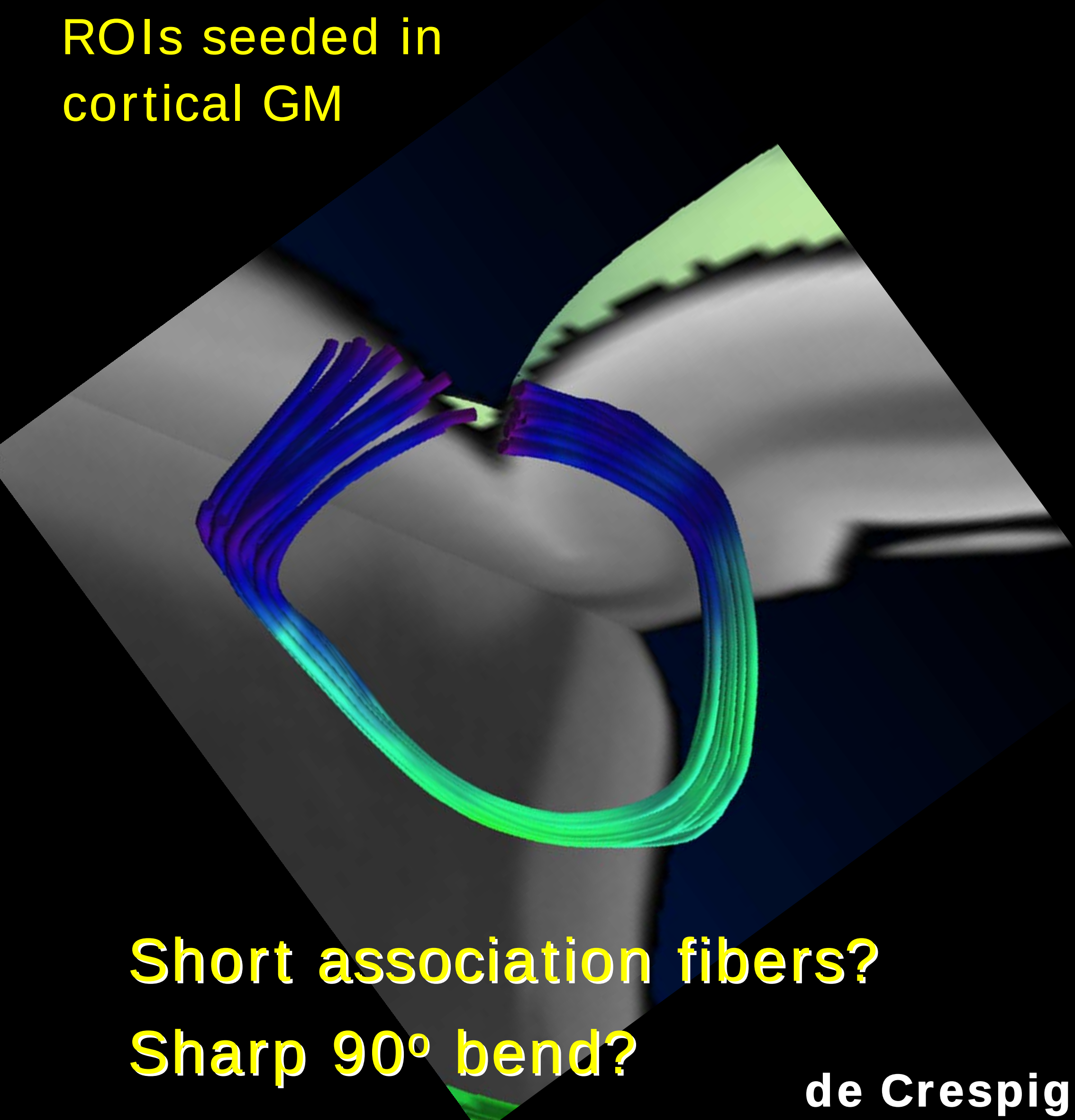


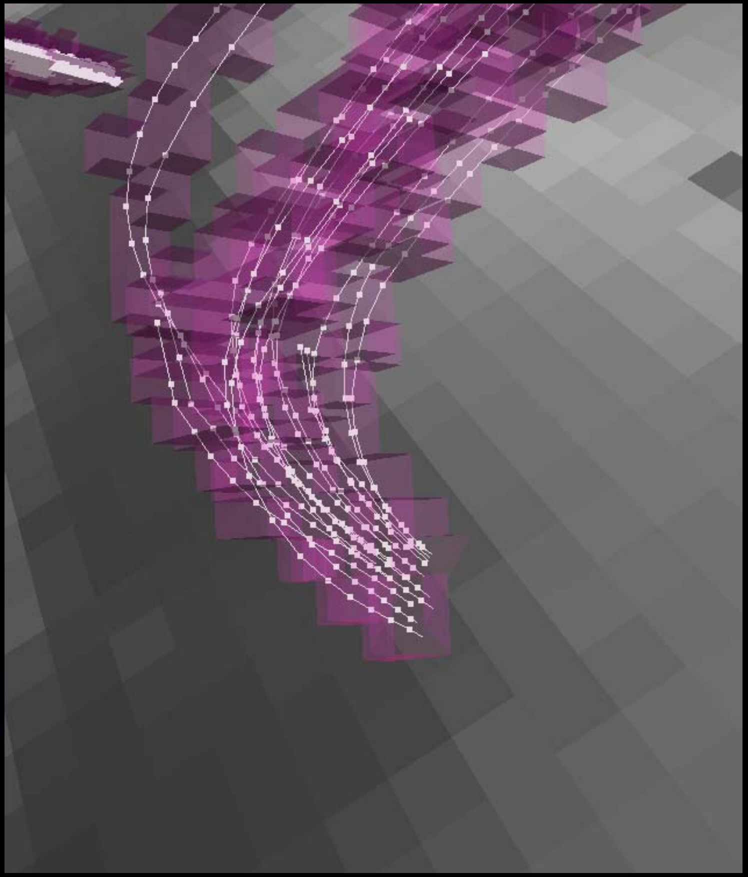
ROIs seeded in white matter tract

de Crespigny, D'Arceuil, Concha MGH

DTI Tractography in the cortex

ROIs seeded in cortical GM





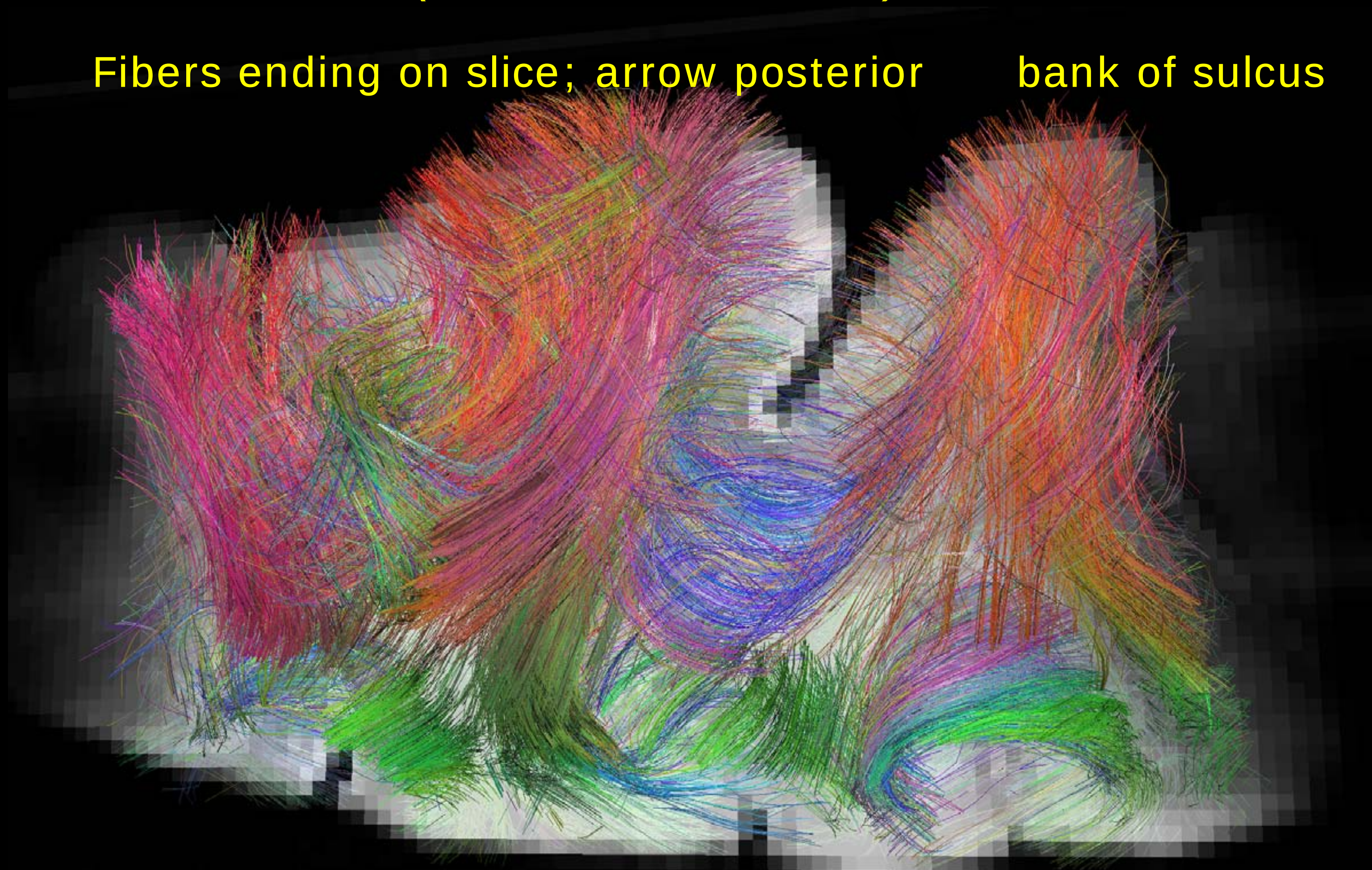
Turn into the cortex is smooth, FA is low here

Short association fibers?
Sharp 90^{o} bend?

de Crespigny, D'Arceuil, Concha MGH

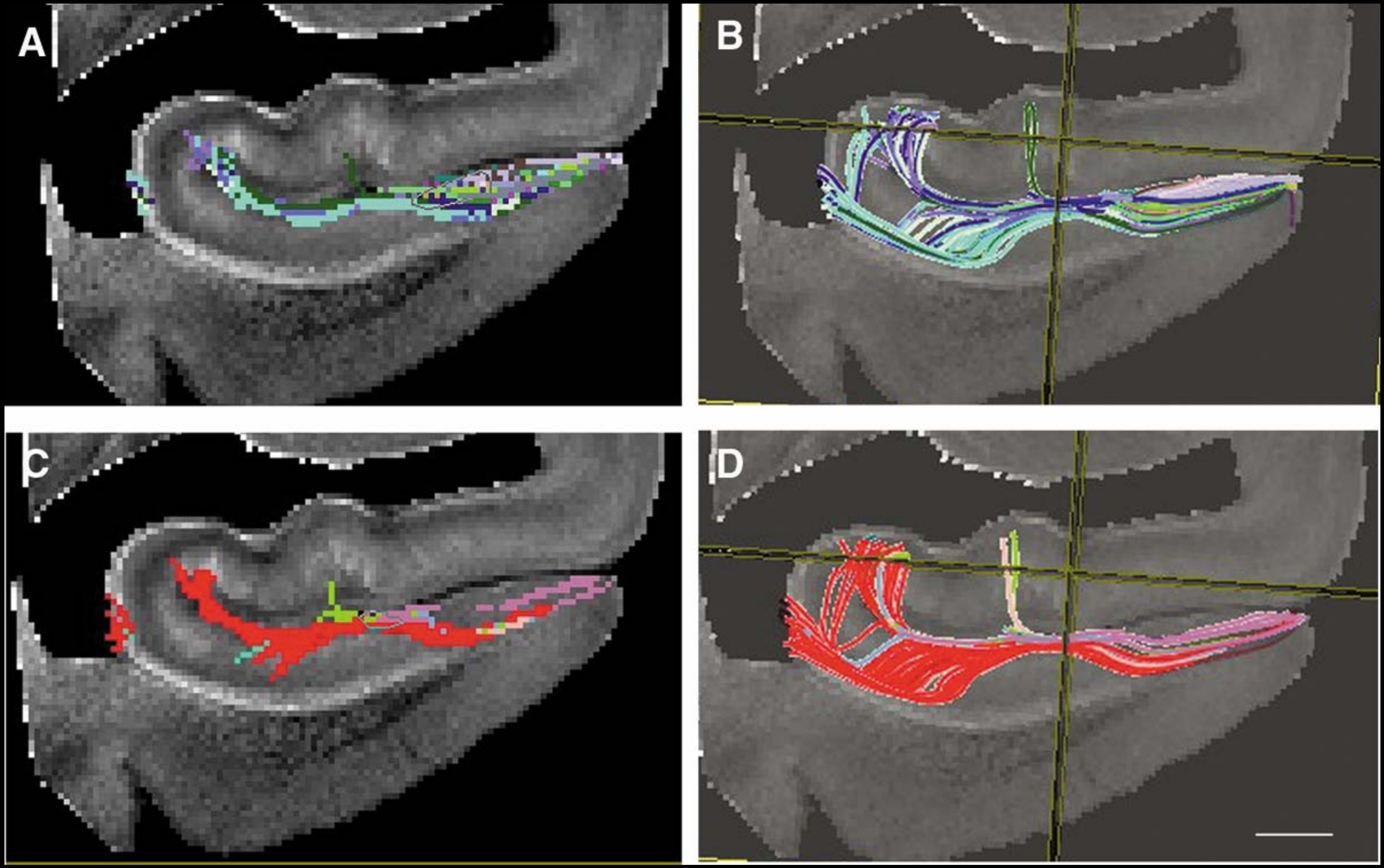
DSI Tractography in human cortex

DSI in fixed cortex: 4.7T, 3D EPI, 450μm, 1 NEX, 9 hours, b=40,000, 514drns, (truncated 11^3 cube)



de Crespigny, D'Arceuil, Wang, Wedeen, MGH

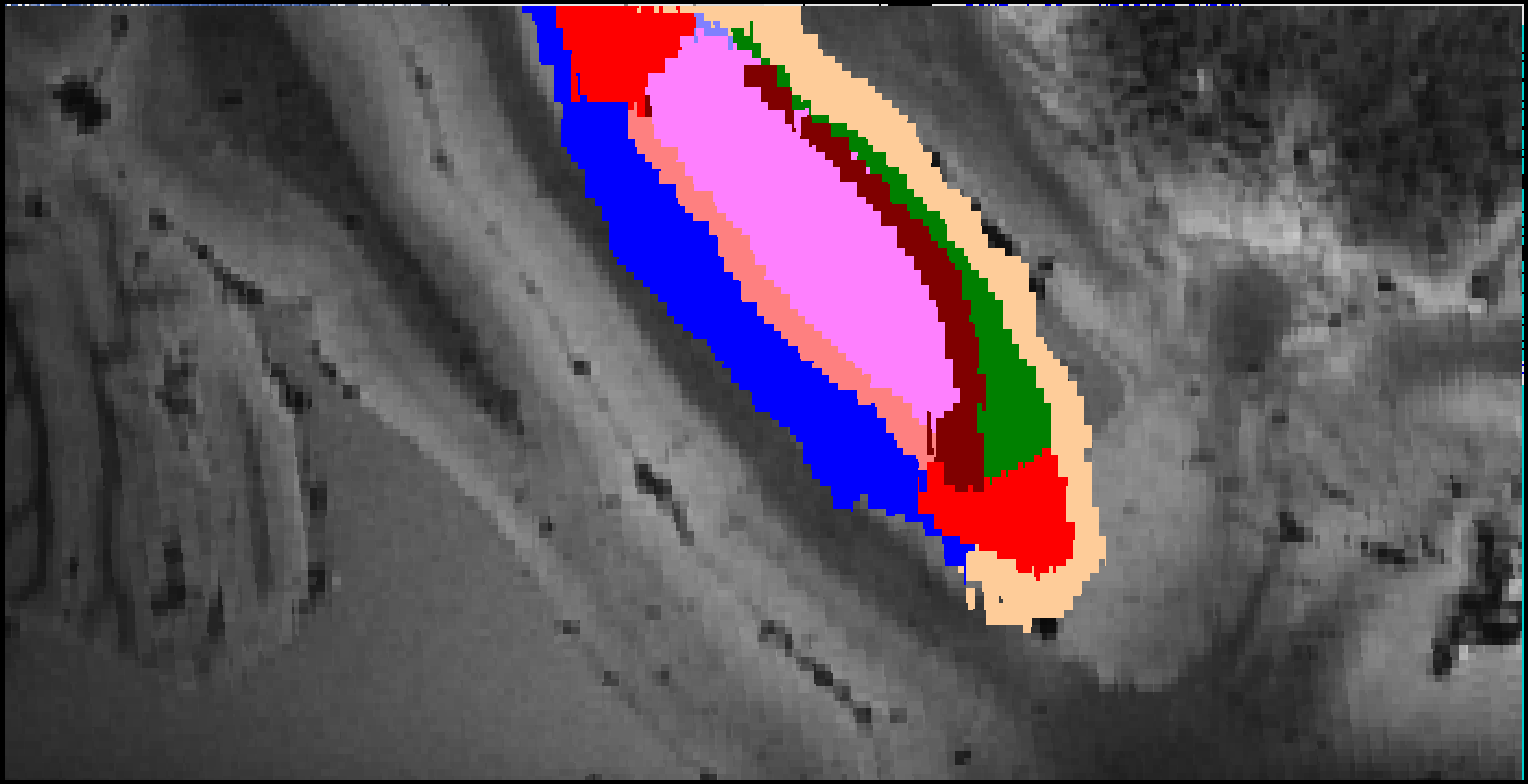
Modeling Fiber Tracts in the Hippocampus



Priors for Tractography?

Joint work with Jean Augustinack and Alex de Crespigny

Hippocampal Labeling: Direct Validation



In vivo labeling mapped to ex vivo scan (200μm)

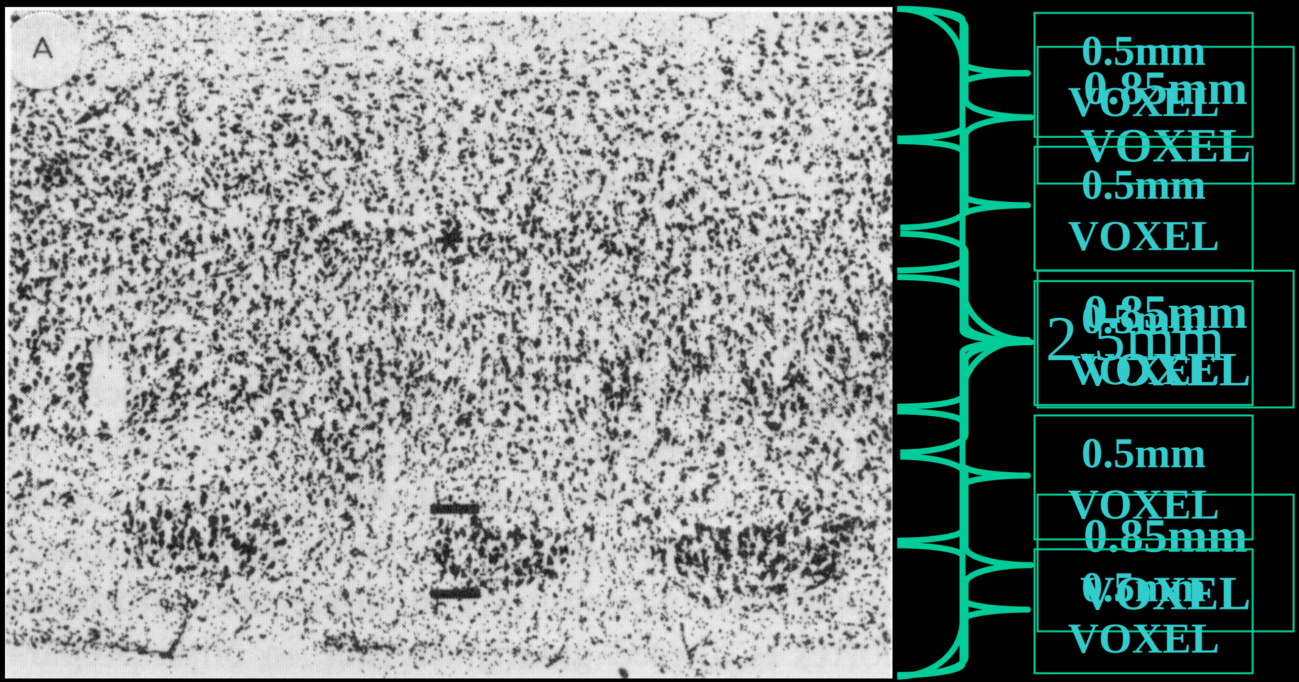
Thanks to Xiao Han for helping generate these results

in vivo Imaging of Laminar Structure

Can we detect laminar structure in the distribution of intensities across the cortical ribbon?

Imaging Markers of the Underlying Meyelo- and Cytoarchitecture

Entorhinal Cortex



The laminar distribution of cell types and degree of myelin should be detectible *in vivo*!

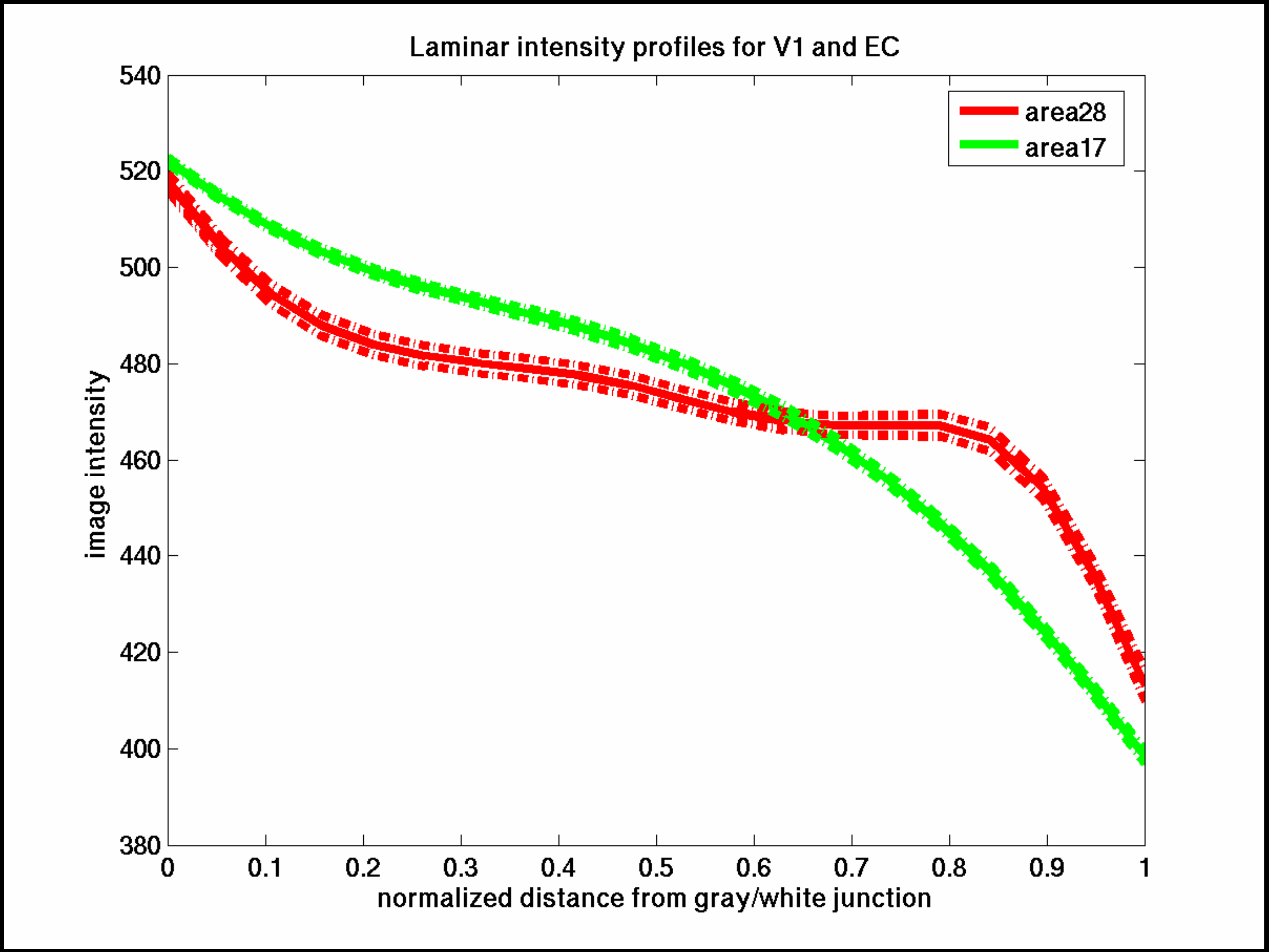
Imaging Temporal Visual Cortex

Are there structural differences between functionally defined regions and the surrounding cortex?

Specifically, can we use signal intensity and/or T1 as a surrogate marker for degree of myelination?

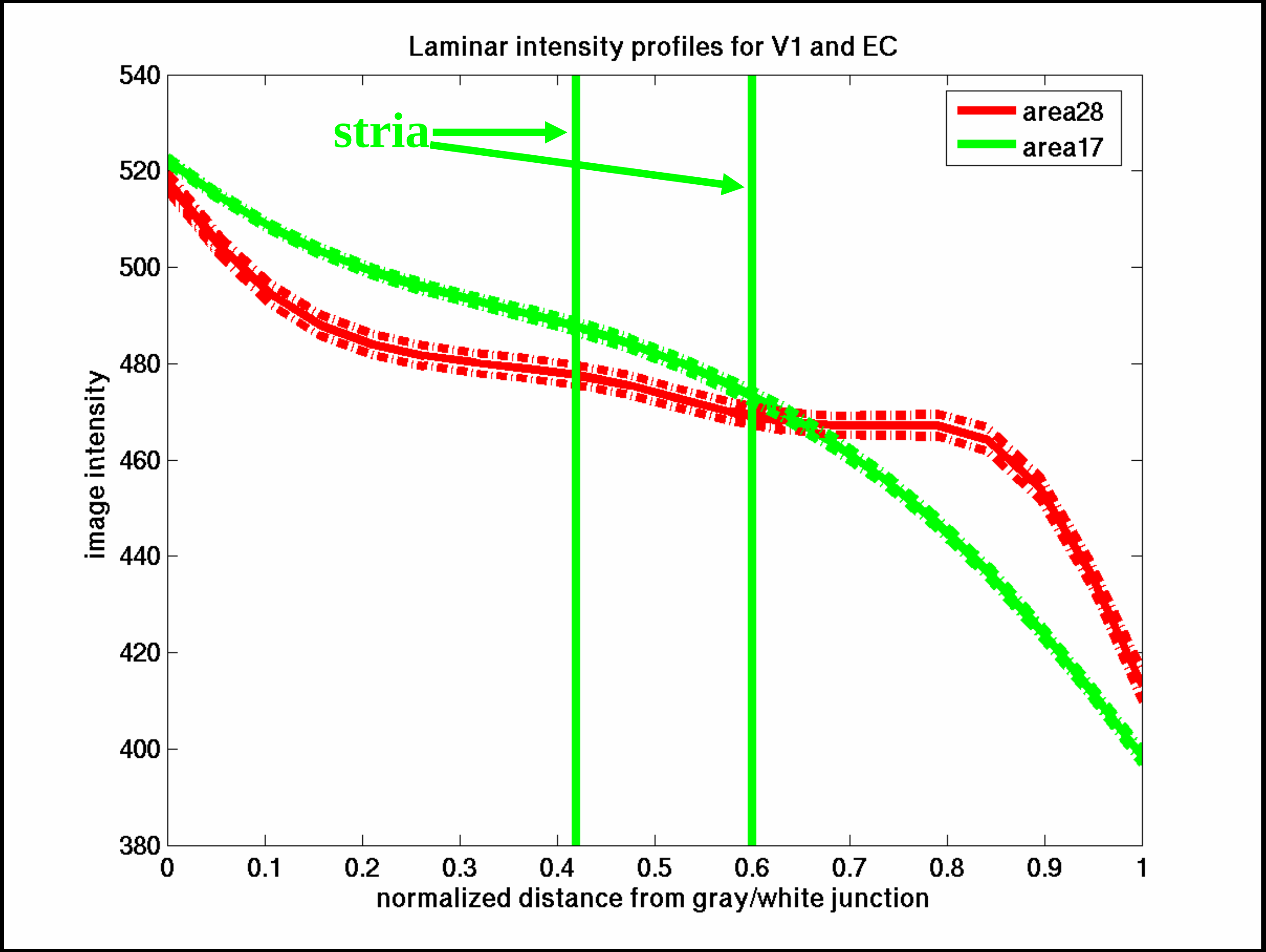
Joint work with Nancy Kanwisher, Becca Schwarzlose, Xiao Han and Doug Greve

Using Laminar Intensity Profiles



Intensity profiles across cortical ribbon in 500mm mp-rage (NEX=4)

Using Laminar Intensity Profiles



Intensity profiles across cortical ribbon in 500mm mp-rage (NEX=4)

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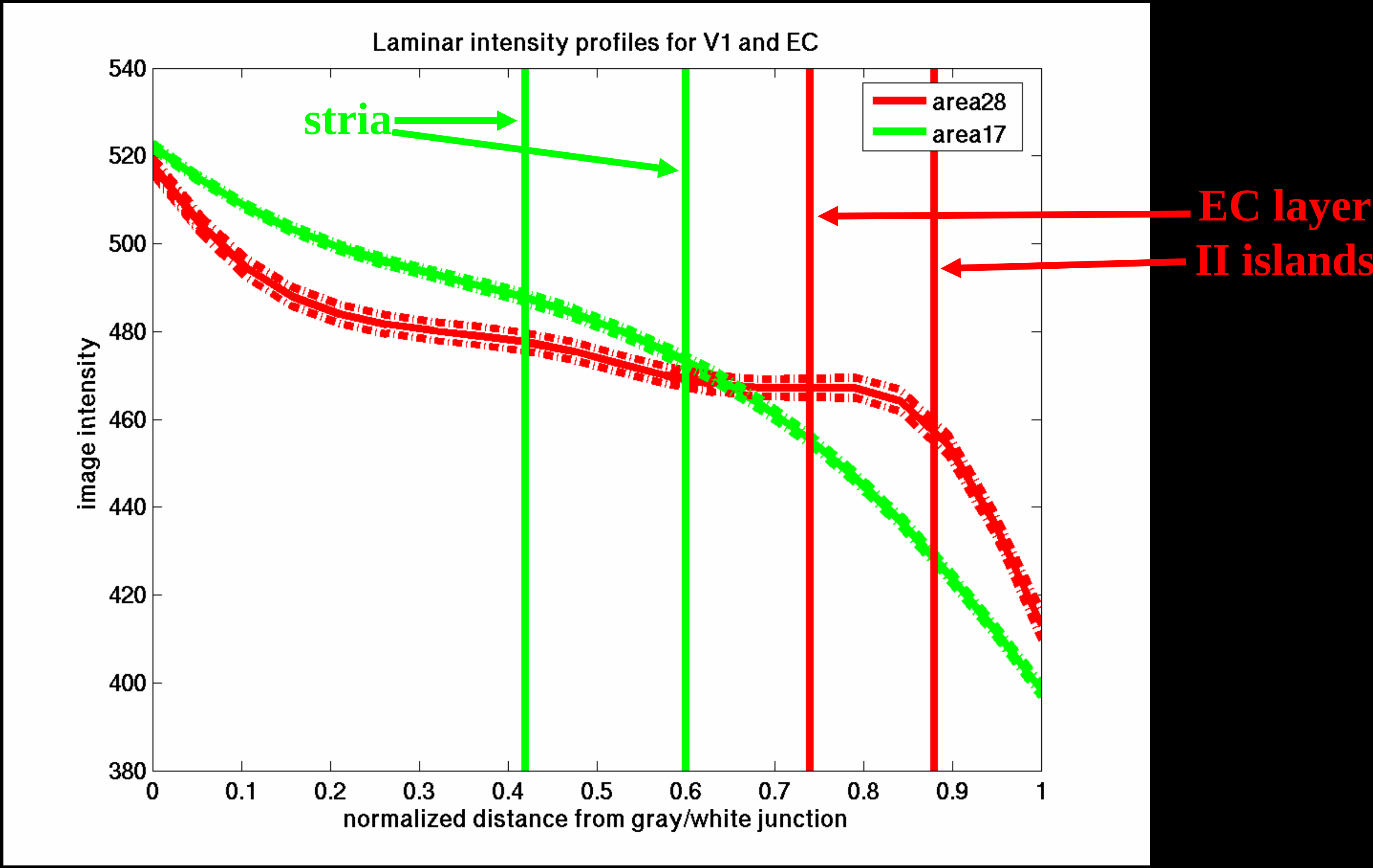

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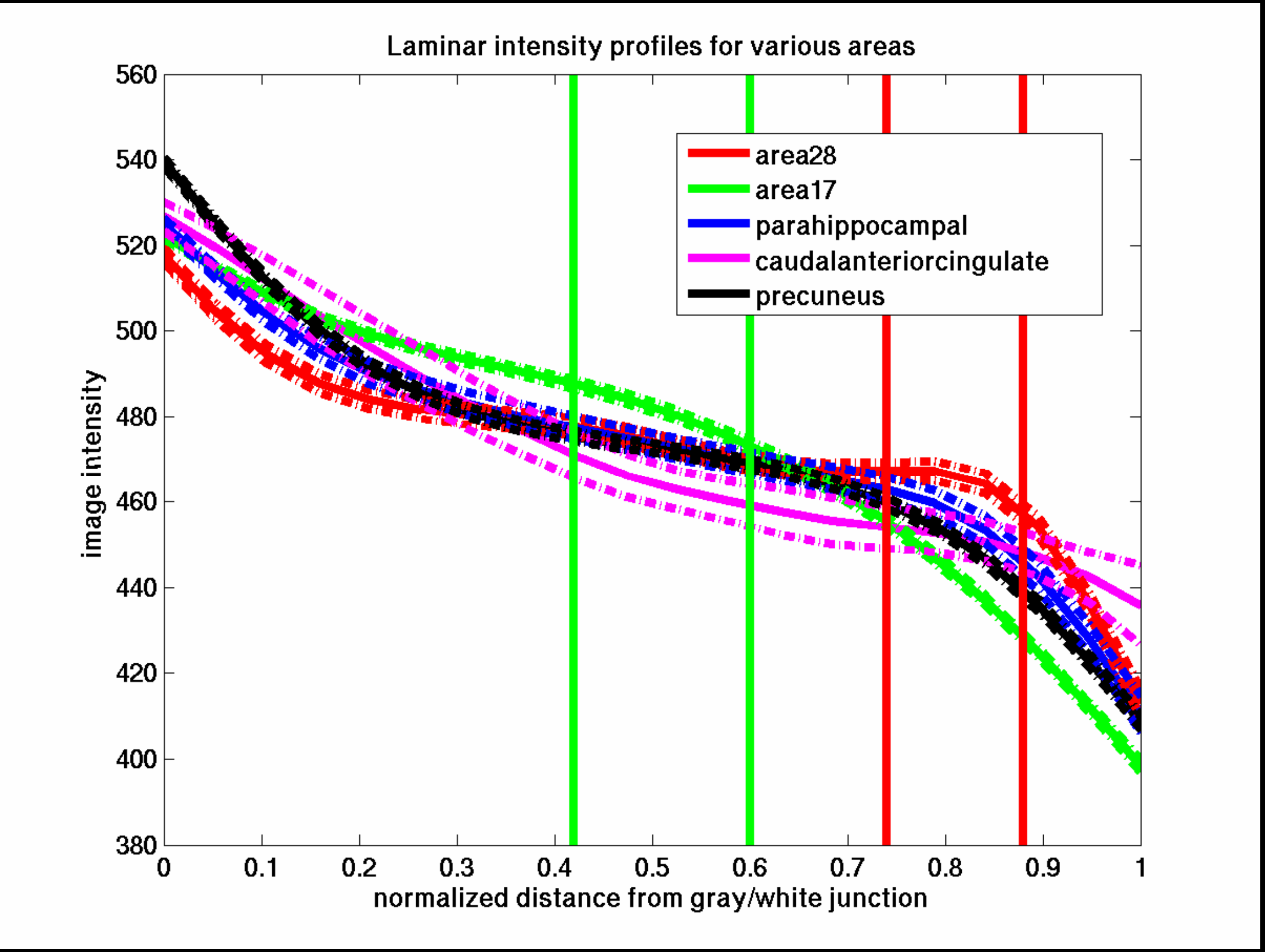
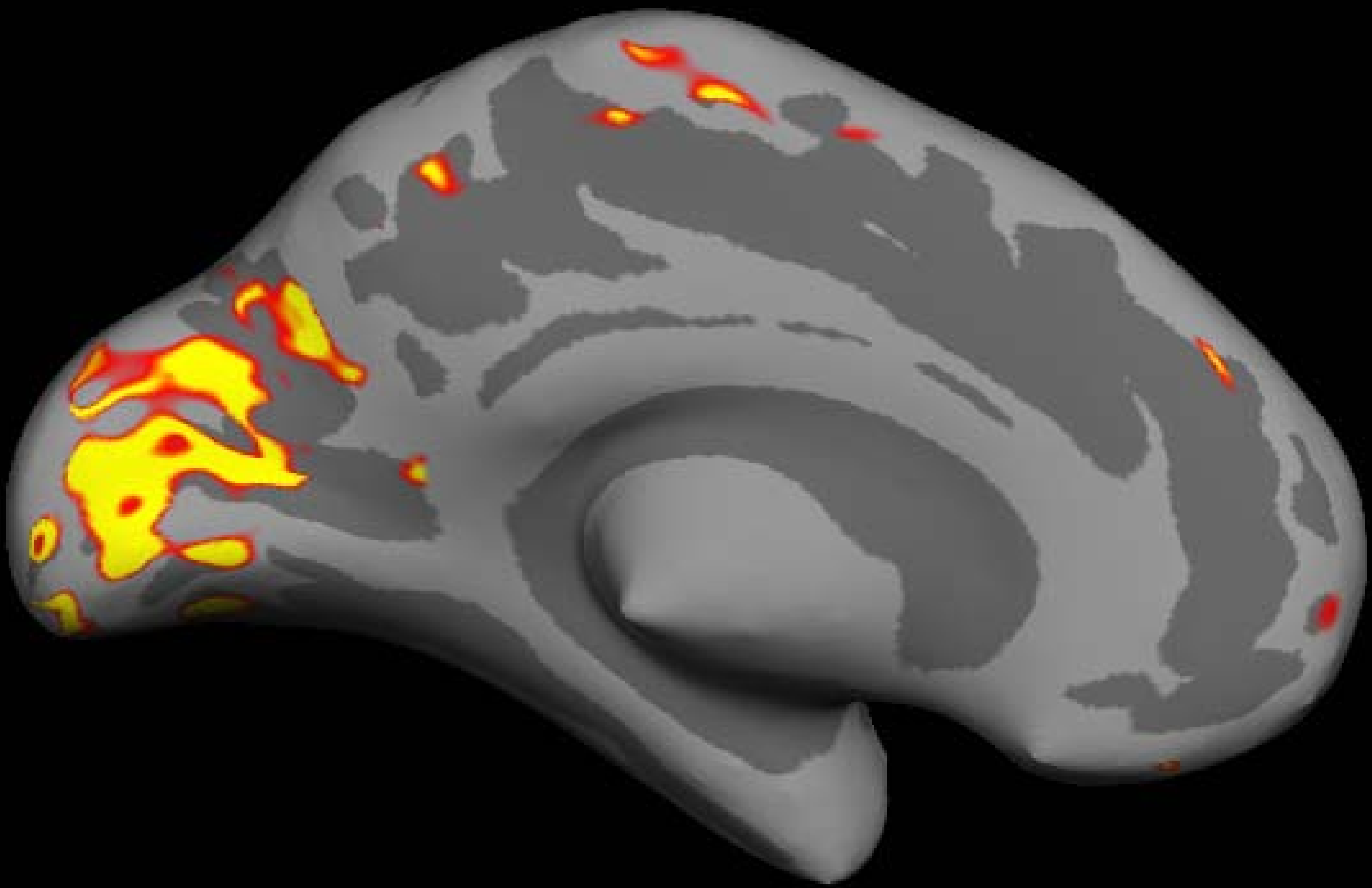


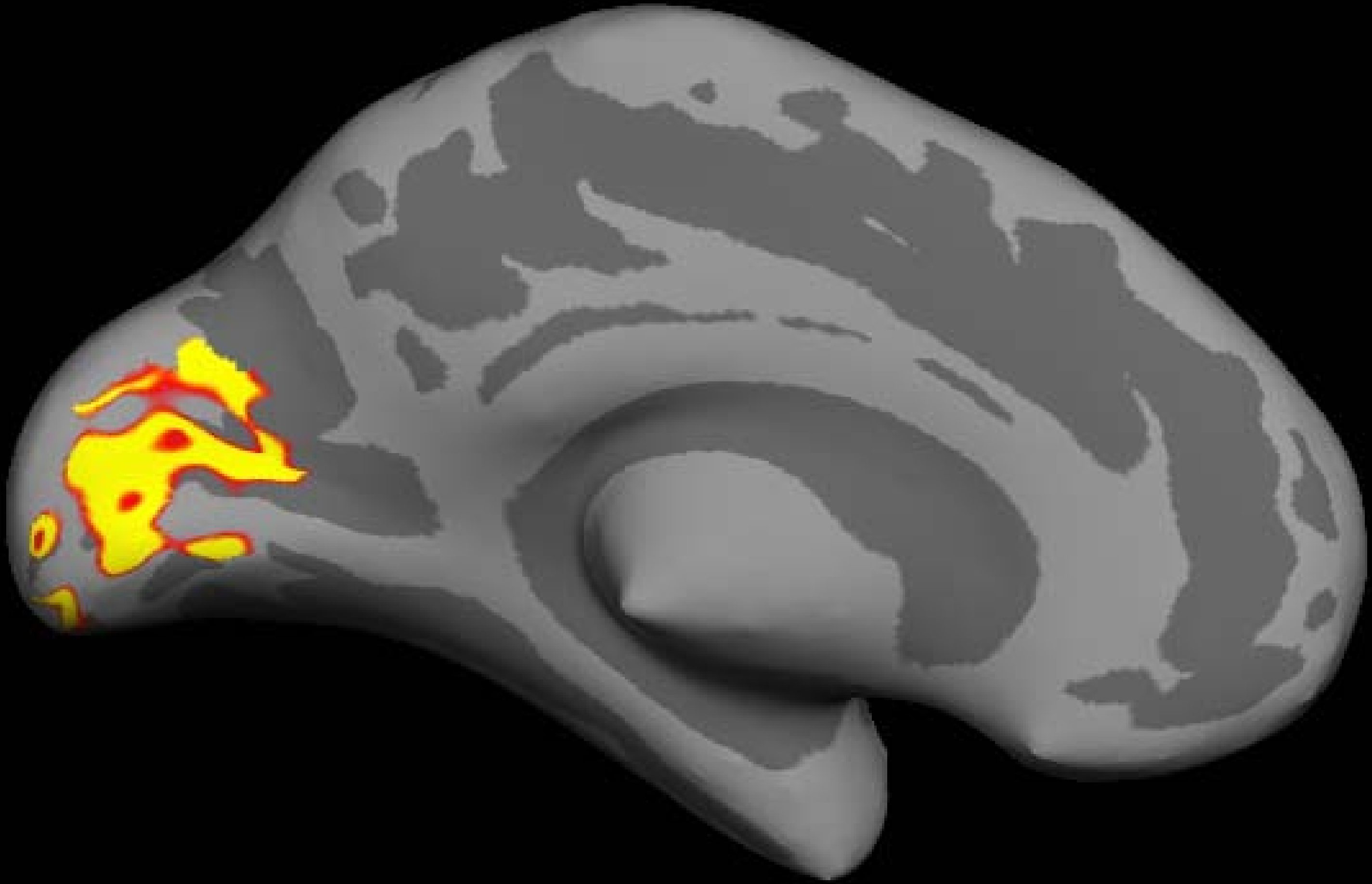
Intensity profiles across cortical ribbon in 500mm mp-rage (NEX=4)

Finding V1 (BA 17)

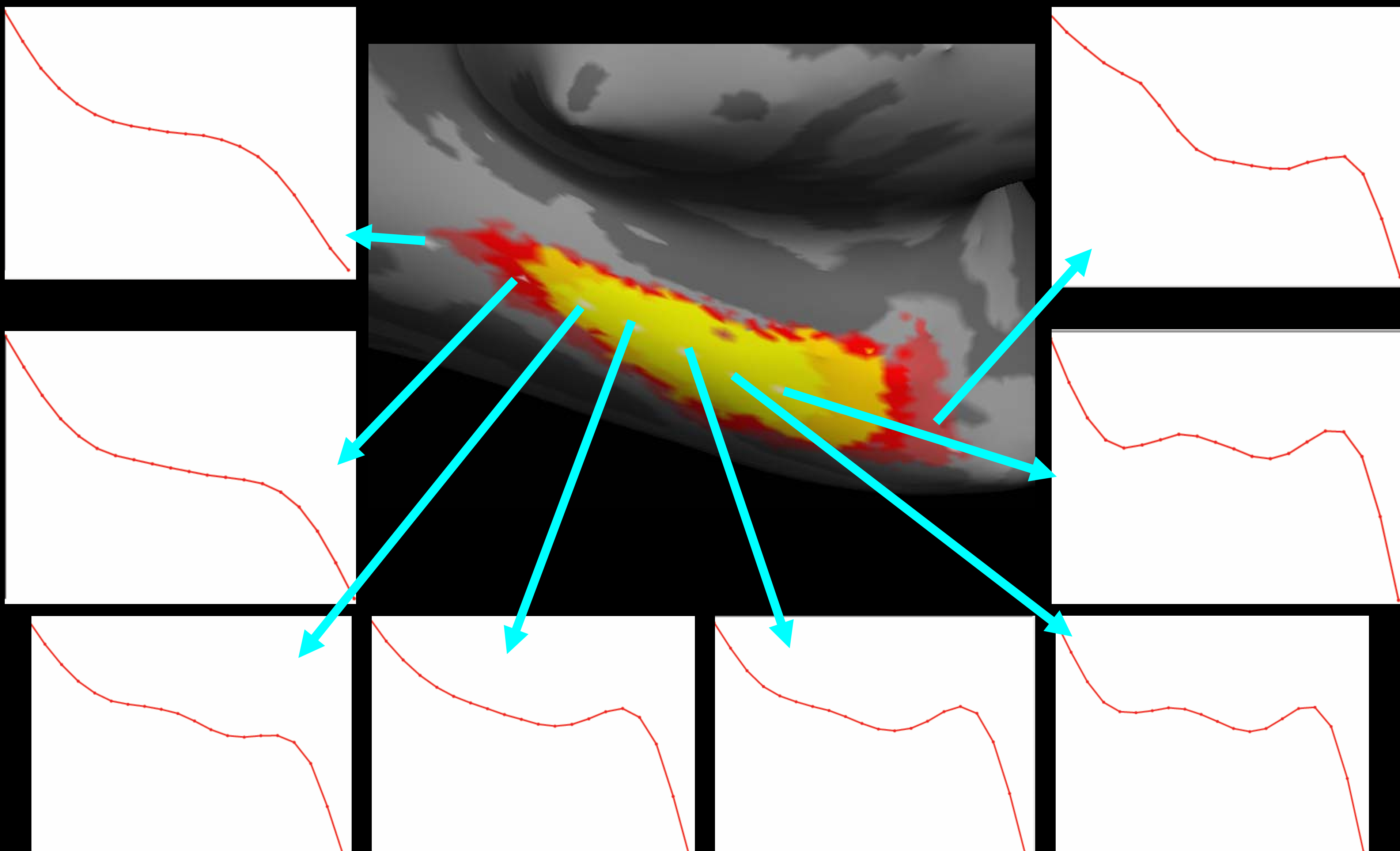


Likelihood

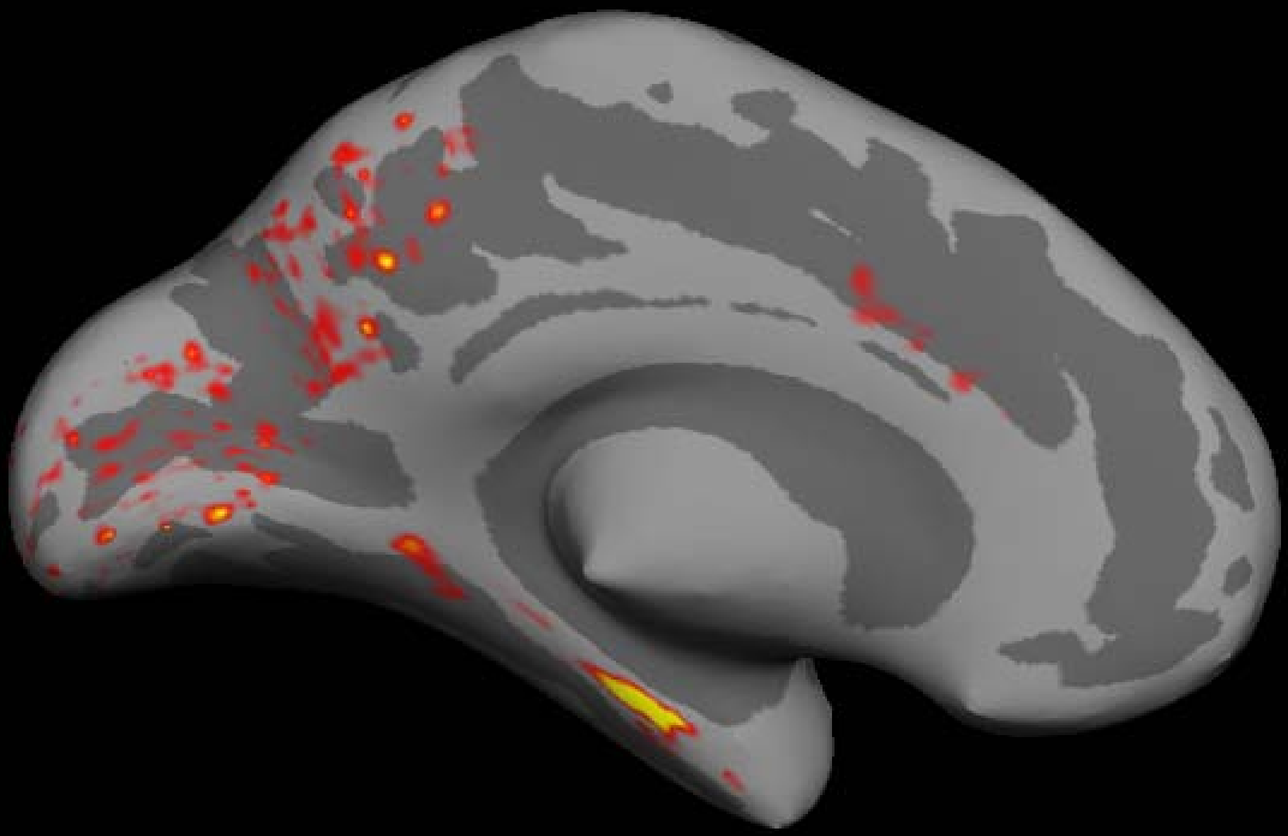
Finding V1 (BA 17)



How Selective are Profiles?

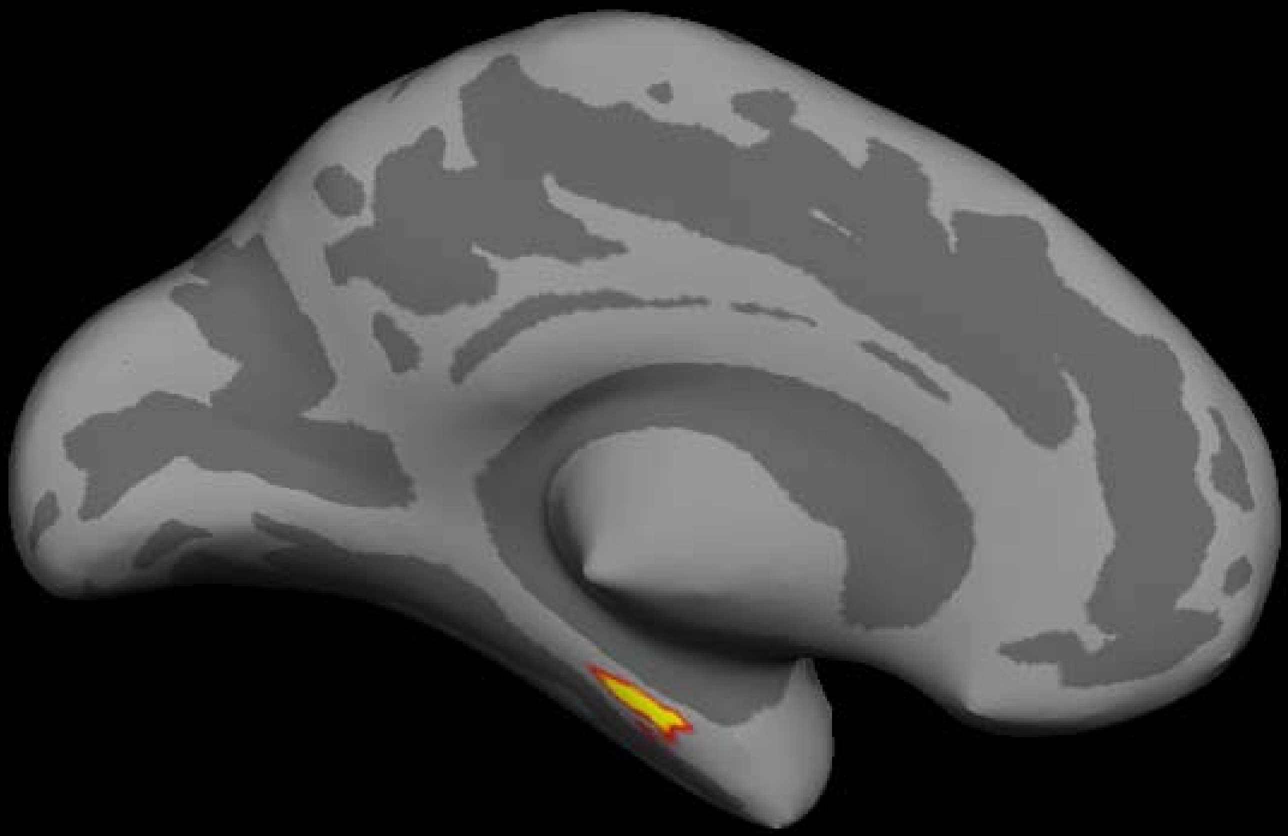


Finding Entorhinal Cortex (BA 28)



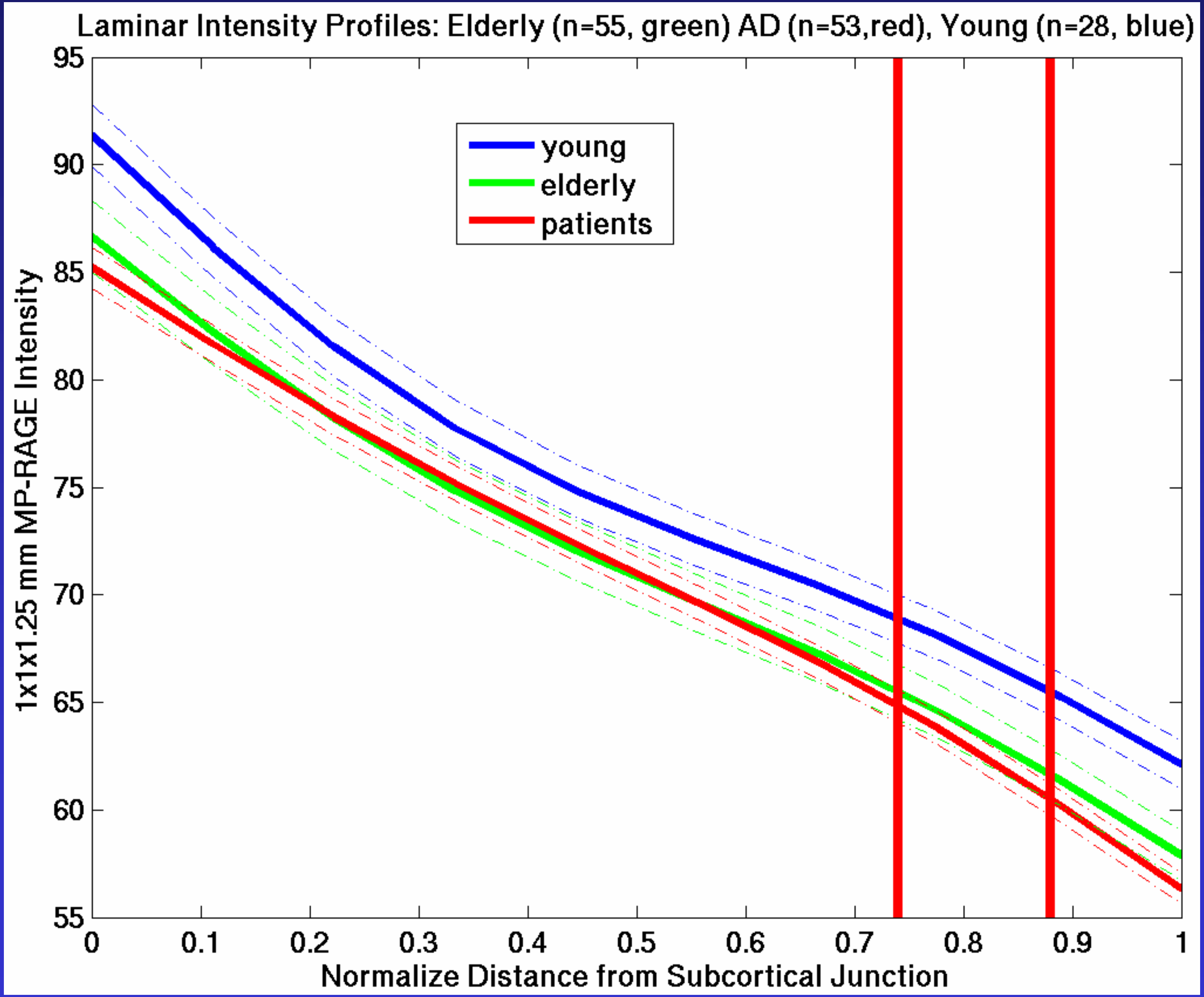
Correlation of EC intensity profile across a different hemisphere

Finding Entorhinal Cortex (BA 28)



Posterior density of EC (product with prior)

Young, Elderly and AD EC Profiles (not normalized, 1mm isotropic)



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Niranjini Rajendran
Brad Dickerson
Gheorghe Postelnicu
Brian T Quinn

Oxford University

Mark Jenkinson

Siemens

Andreas Potthast

MGH

Bruce Rosen
Diana Rosas
Larry Wald
Graham Wiggins
Chris Wiggins
Megan Blackwell
Xiao Han
Christian Farrar
Alex de Crespigny
Matthew Frosch
Brad Hyman

Boston Univeristy

Eric Schwartz
Jon Polimeni
Oliver Hinds

UC San Diego

Anders Dale
Marty Sereno

MIT

John Fisher
Nancy Kanwiser
Becca Schwarzlose
Polina Golland
Peng Yu
Florent Ségonne

HMS/MEEI

Jennifer Melcher
Irina Sigalovsky

MIND

National Center for Research Resources