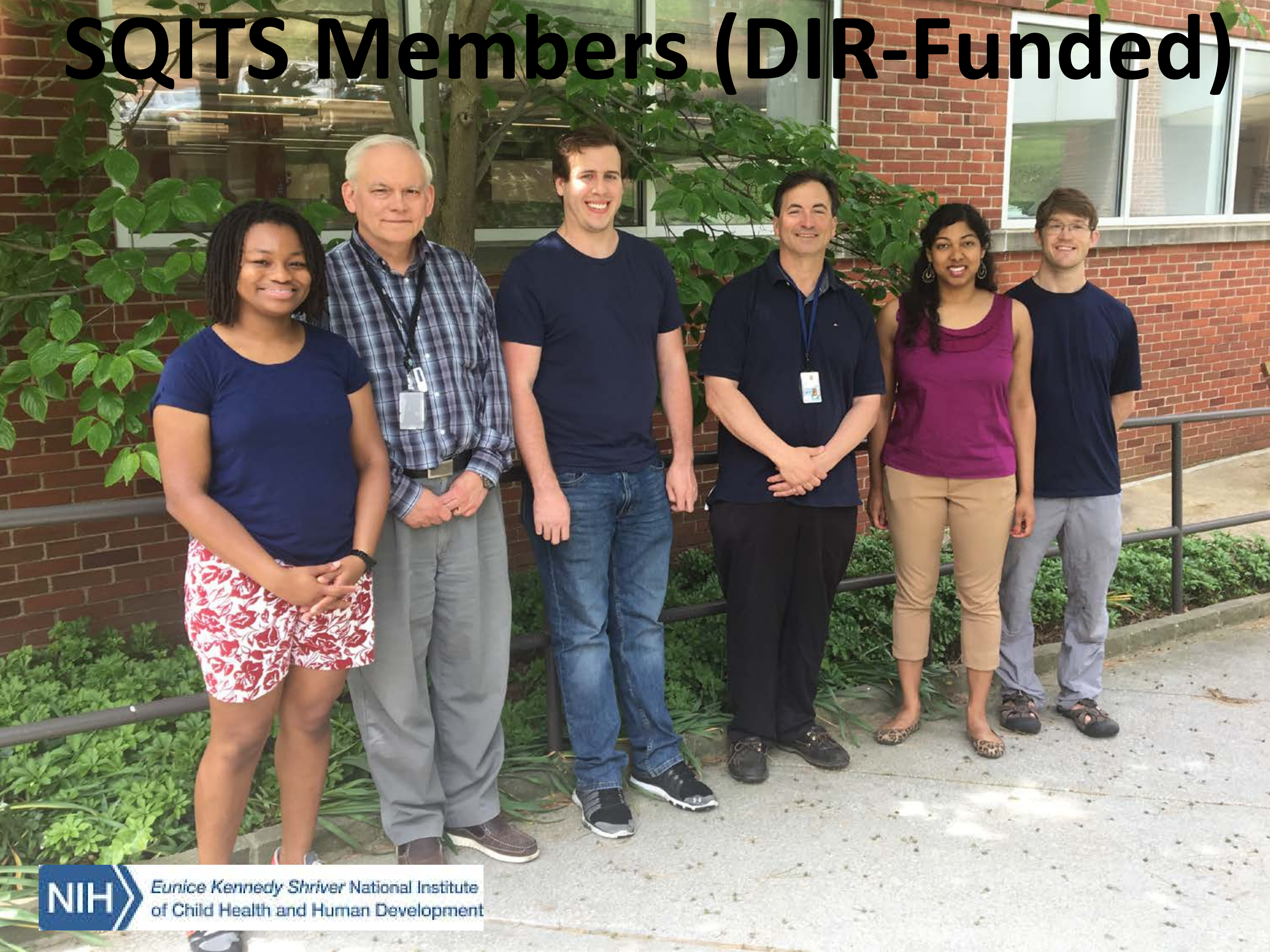
# Toward *In Vivo* Imaging of Cortical Architecture and Function

Peter Basser
Section on Quantitative Imaging and Tissue Sciences (SQITS), NICHD, NIH

Eunice Kennedy Shriver National Institute of Child Health and Human Development

# SQITS Members (DIR-Funded)



NIH *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

# Section Goals

- Discover fundamental structure/function relationships in the nervous system (and in ECM)
- Use this knowledge to invent, develop, and translate novel *in vivo* quantitative imaging ‘biomarkers’ to make key ‘invisible’ biological processes and features ‘visible’.

# New Developments--
# New Directions

Microdynamic Imaging

Functional Imaging

Microstructure Imaging

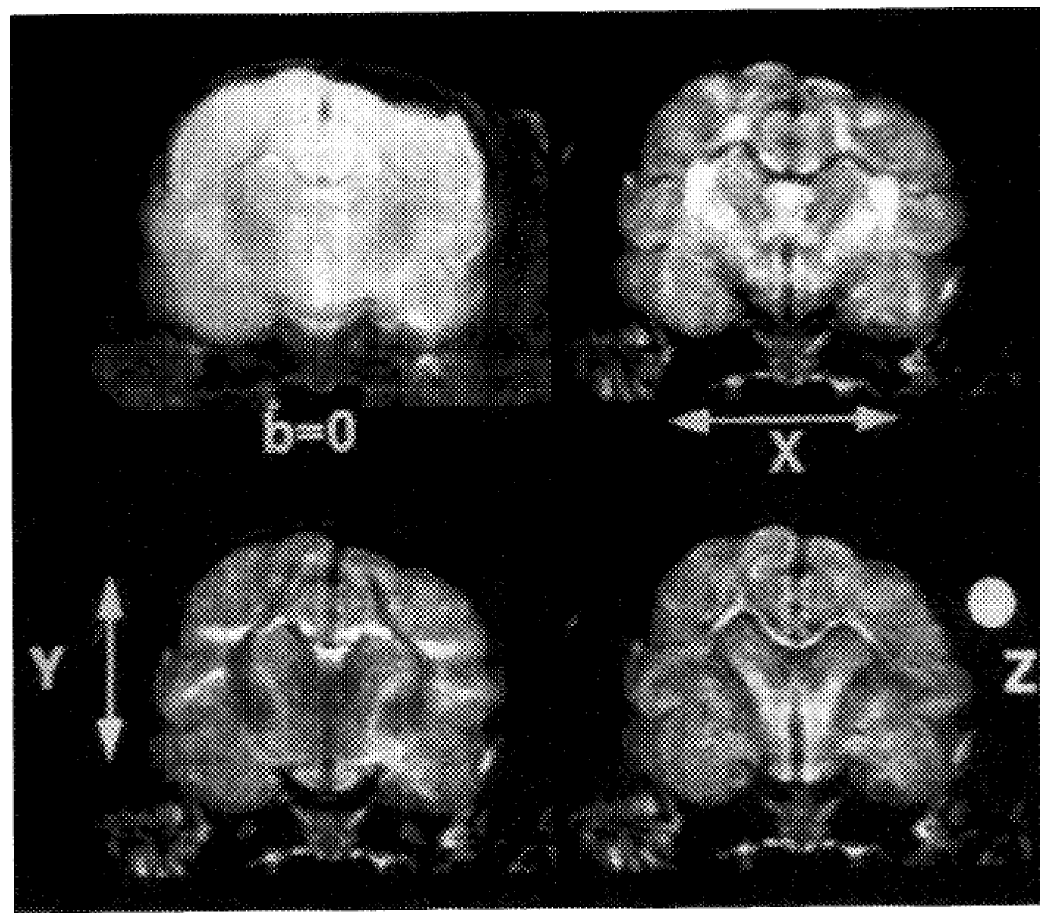
MAGNETIC RESONANCE IN MEDICINE 19, 321–326 (1991)

# Anisotropy in Diffusion-Weighted MRI*

MICHAEL E. MOSELEY, JOHN KUCHARCZYK, HALEH S. ASGARI,
AND DAVID NORMAN

*Department of Radiology, University of California, San Francisco, California 94143*

Received February 1, 1991



# MR Imaging of Anisotropically Restricted Diffusion of Water in the Nervous System: Technical, Anatomic, and Pathologic Considerations

Joseph V. Hajnal, Mark Doran, Alasdair S. Hall, Alan G. Collins, Angela Oatridge, Jacqueline M. Pennock, Ian R. Young, and Graeme M. Bydder

*Journal of Computer Assisted Tomography*
15(1):1–18, January/February

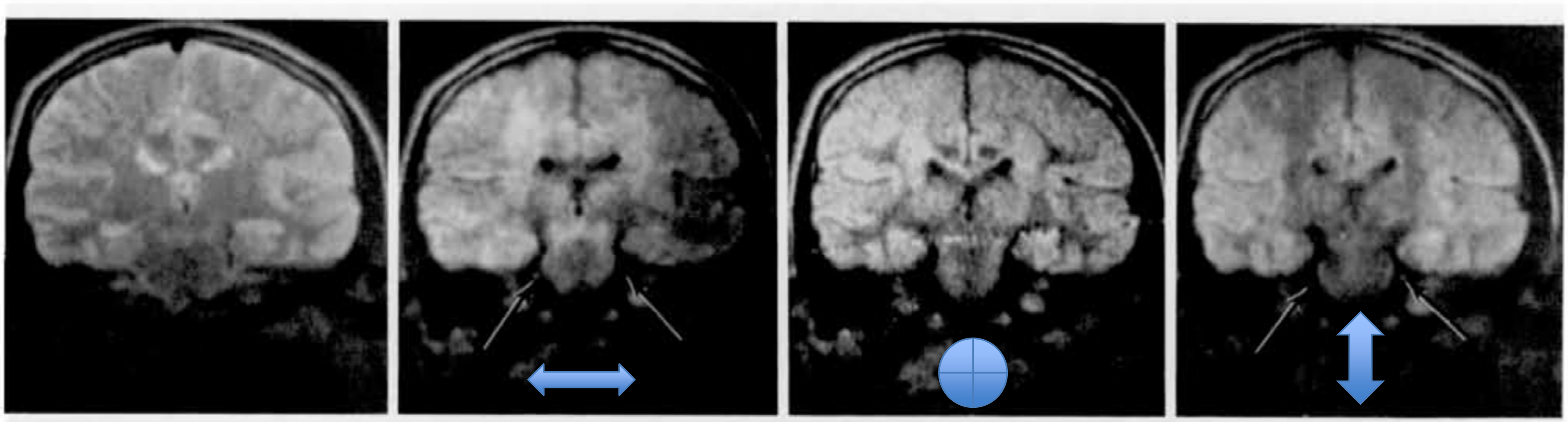
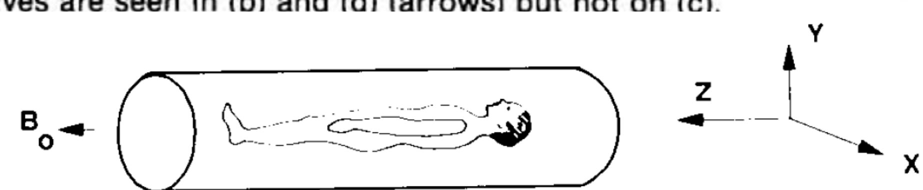
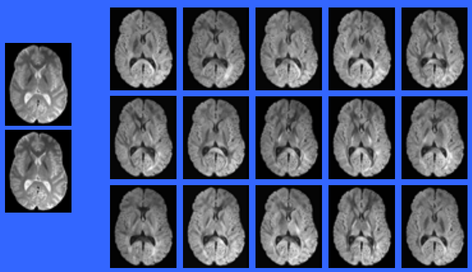




**FIG. 5.** Normal volunteer (male, 31 years old): 256 × 256 coronal SE ≈1,500/130 **(a)**, SE ≈1,500/130/1,0,0/44/550 **(b)**, SE ≈1,500/130/0,1,0/44/550 **(c)**, and SE ≈1,500/130/0,0,1/44/550 **(d)** images. Ascending and descending projection fibres are of higher signal intensity in (b) and (c) than in (d). Tracts that run anteroposteriorly appear low in signal intensity on (c) but higher on (b) and (d). The trigeminal nerves are seen in (b) and (d) (arrows) but not on (c).

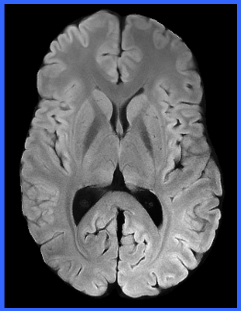


Basser, P.J., Mattiello, J., and LeBihan, D. (1994). Biophys. J. 66:259-267.
Pierpaoli, C., Jezzard, P., Basser, P.J., Barnett, A., and Chiro, G. (1996). Radiology 201:637-648.
https://www.youtube.com/watch?v=1_BeCeDak3w

# DTI "Pipeline"



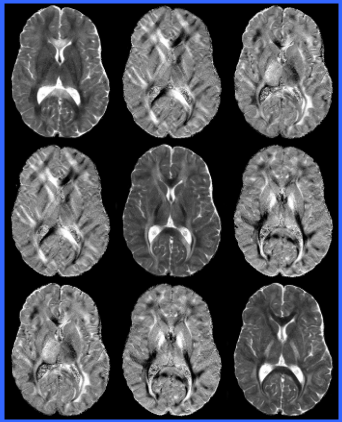
Non-Diffusion Weighted MRI, $A(\mathbf{0})$



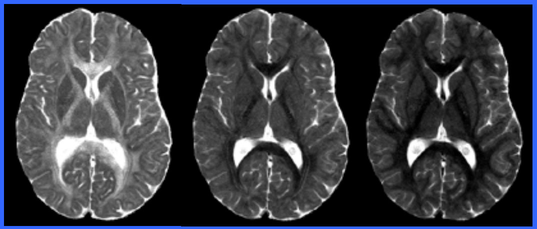
Estimate **D** from Diffusion Weighted MRIs using:

$$A(\mathbf{b}) = A(\mathbf{0})\exp(-\mathbf{b}:\mathbf{D})$$

**D** =

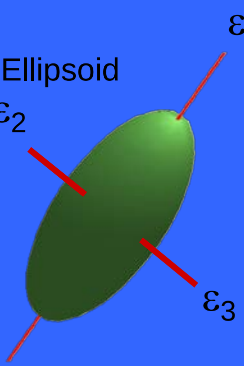


Diagonalize **D**



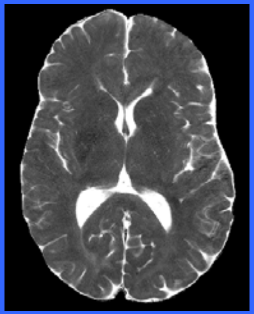
Three eigenvalues (principal diffusivities)

Diffusion Ellipsoid

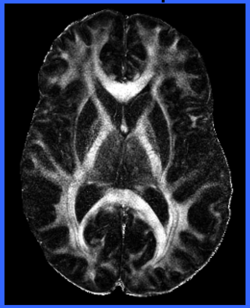



Three corresponding eigenvectors (principal directions)

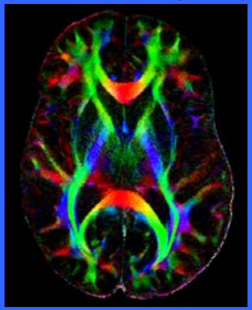
"Mean ADC" Map

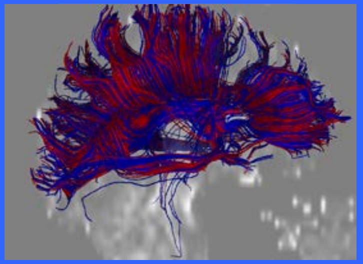


*FA* Map



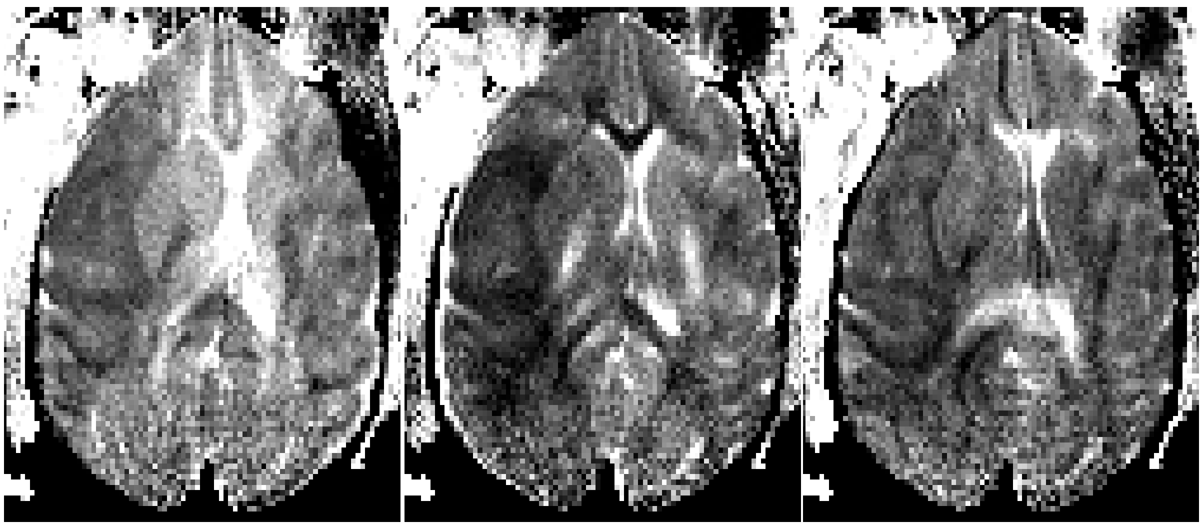
DEC Map





Ellipsoid Maps/Tracts

# Trace(**D**) delineates (disambiguates) infarcted areas better than individual ADCs in Ischemia



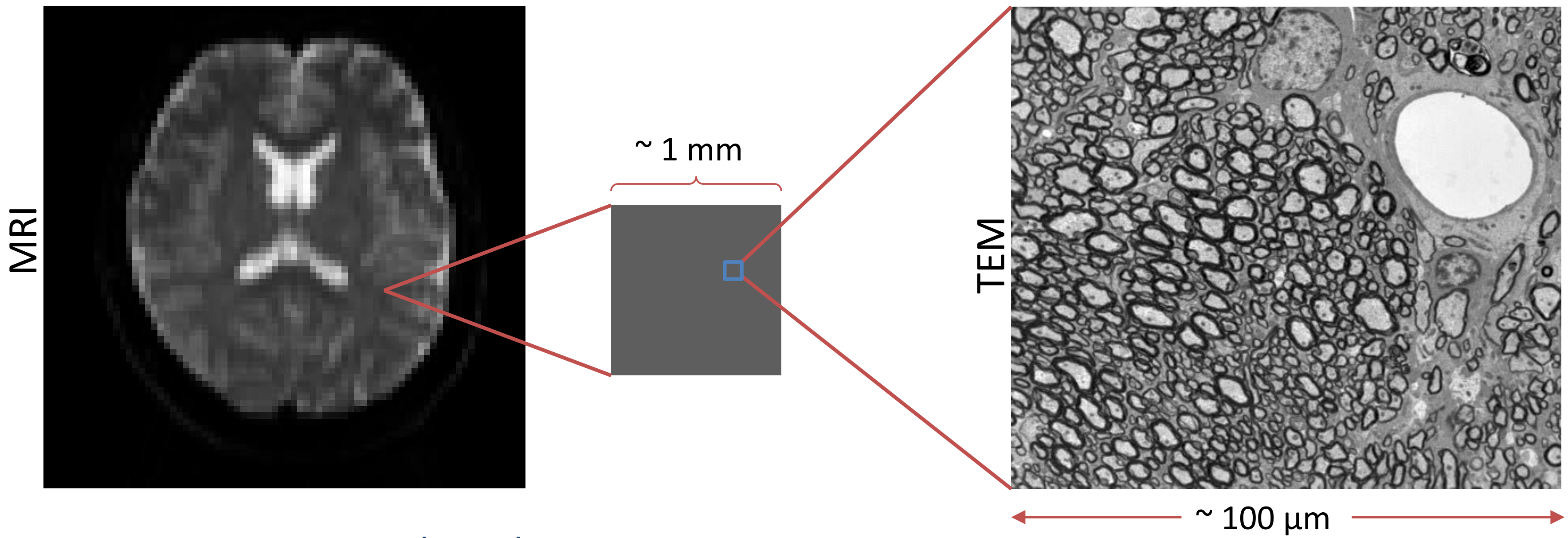
$D_{yy}$ $D_{zz}$ $D_{xx}$

$\langle D \rangle = \mathrm{Trace}(\mathbf{D})/3$

Experimental validation in cats first shown in
*van Gelderen P., et al. 1994. Magn. Reson. in Med. 31:154-163.*

“Trace ADC”, “Mean ADC” “Orientationally-averaged ADC”, “ADC”, “mADC” …

# “Drilling Down into the Voxel”: Image Resolution vs Length Scale Probed



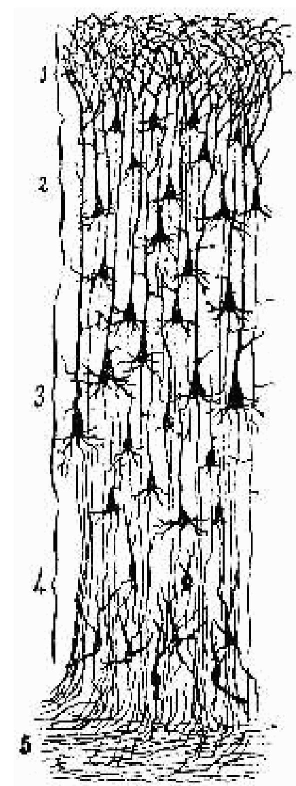

- Increase MRI voxel resolution.
- “*In Vivo* MRI Histology”: Use low-resolution *in vivo* MRI data and physical/mathematical models to obtain microscopic scale features that characterize the morphology, structure and/or architecture of cells and tissues.
    - Cell orientation
    - Cell shape
    - Cell size
    - Cell size distribution (e.g., axon diameter distribution or ADD)
    - Extracellular matrix (ECM) fraction
    - Intra-axonal fraction
    - Fractal dimension …

# Goal

To parcellate the human cortex (and other brain areas) *in vivo* in about 45 minutes.

Fig.1 Santiago Ramon y Cajal at work (From Cajal Institute; http://www.cajal.csic.es/).

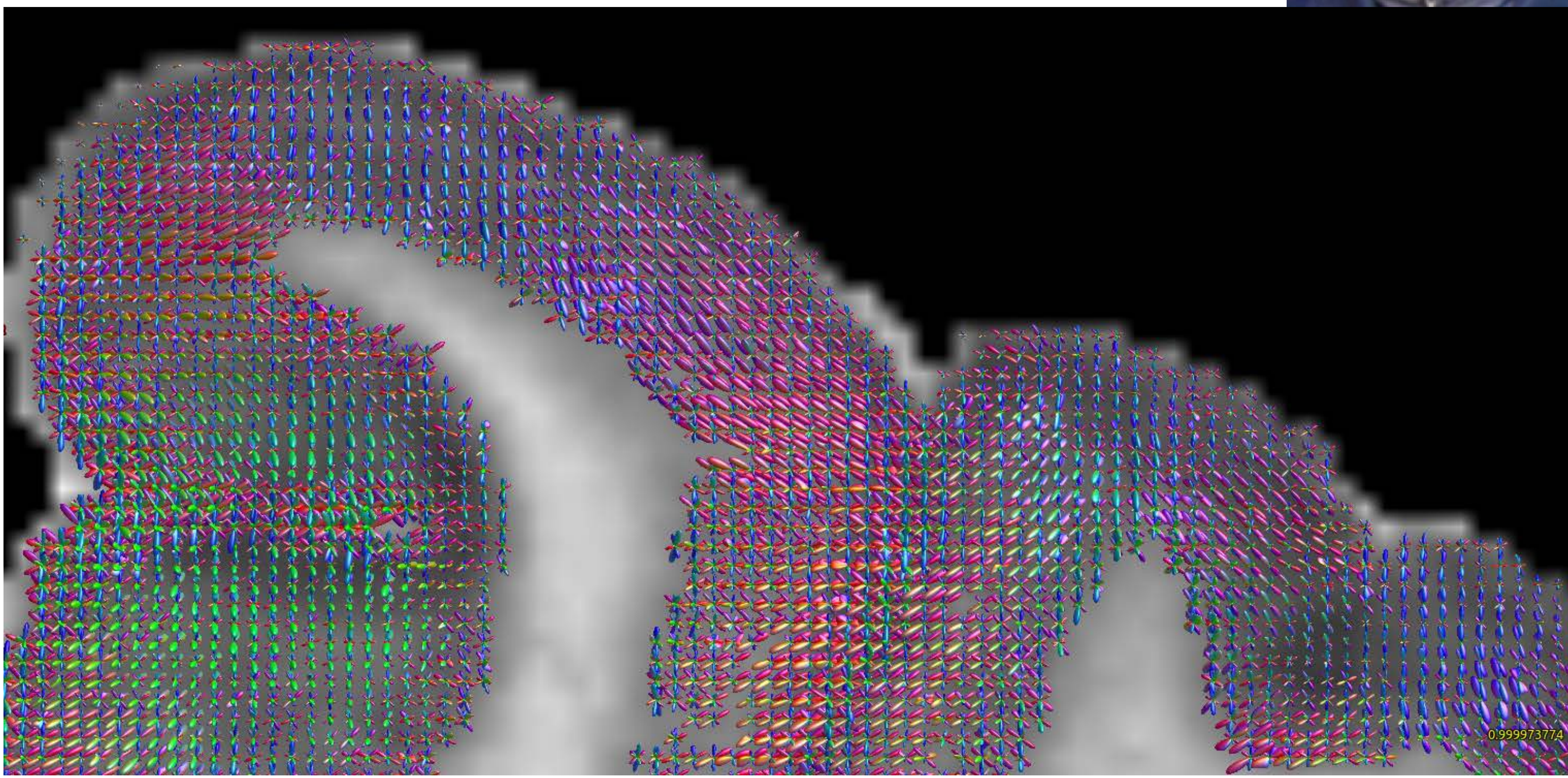
Cortical surface




Sub-cortical white matter

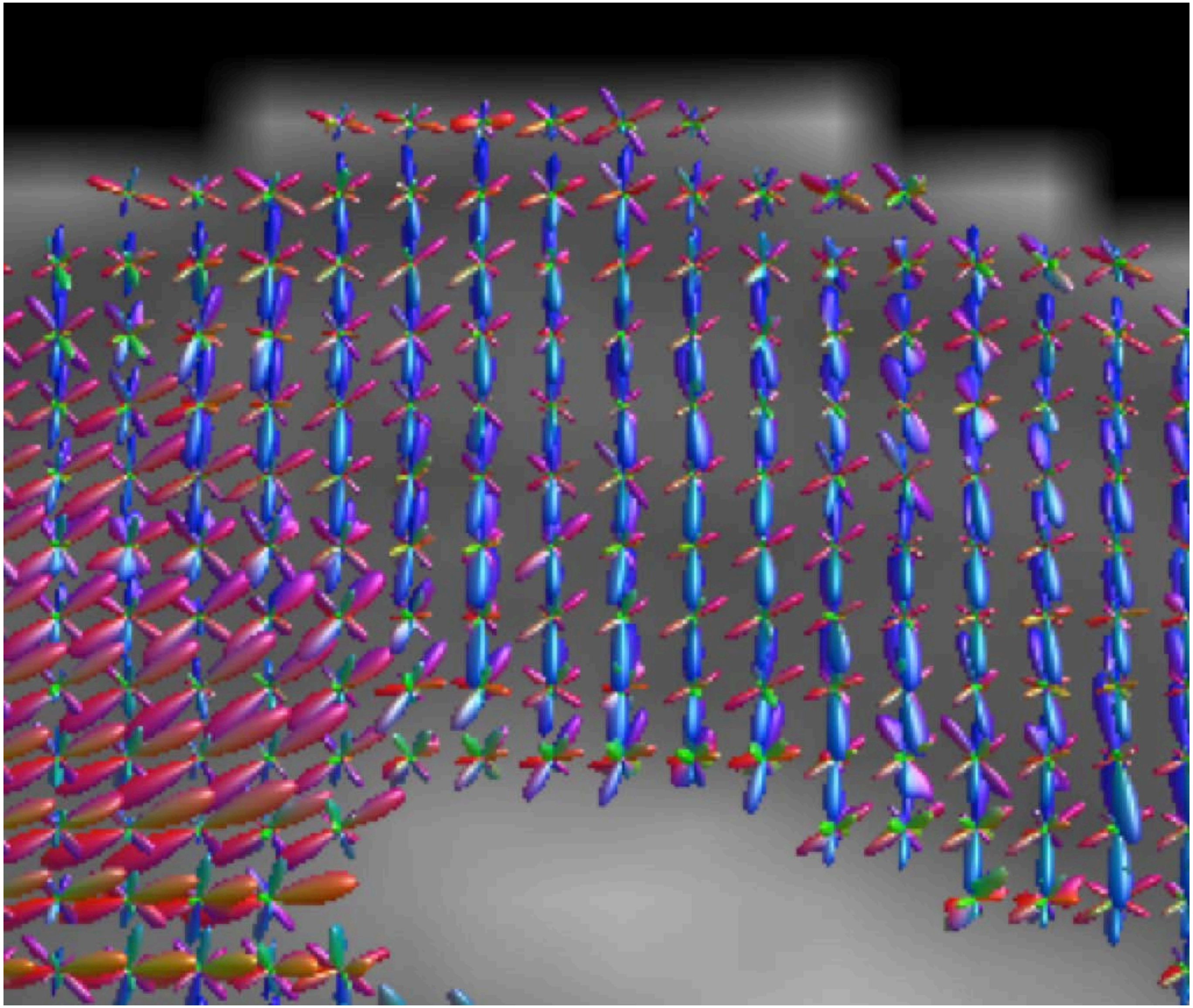
# Mean Apparent Propagator (MAP) MRI

Evren Özarslan

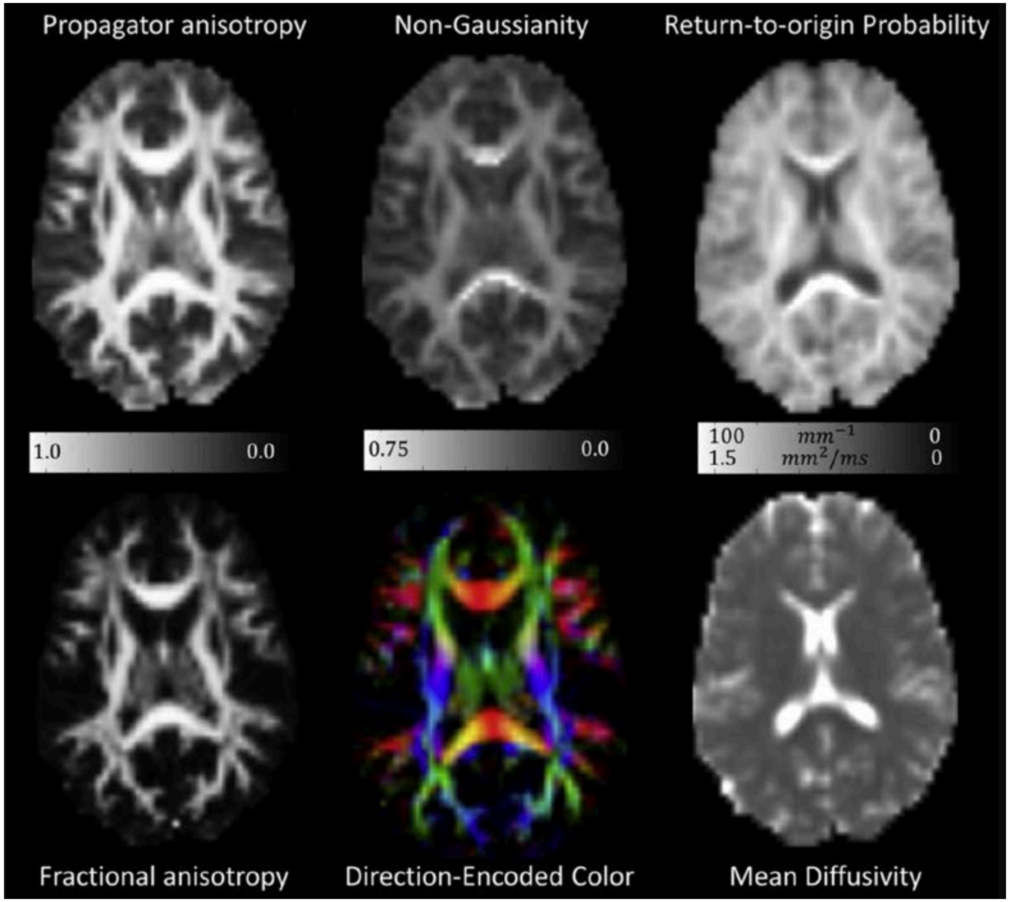



'glyphs' show size, shape and orientational features of the average propagator

# Mean Apparent Propagator (MAP) MRI



# Clinical Translation of Mean Apparent Propagator (MAP) MRI




Alexandru Avram

Avram AV, Sarlls JE, Barnett AS, Özarslan E, Thomas C, Irfanoglu MO, Hutchinson E, Pierpaoli C, Basser PJ. 2016. Clinical feasibility of using mean apparent propagator (MAP) MRI to characterize brain tissue microstructure. Neuroimage 127:422-34.

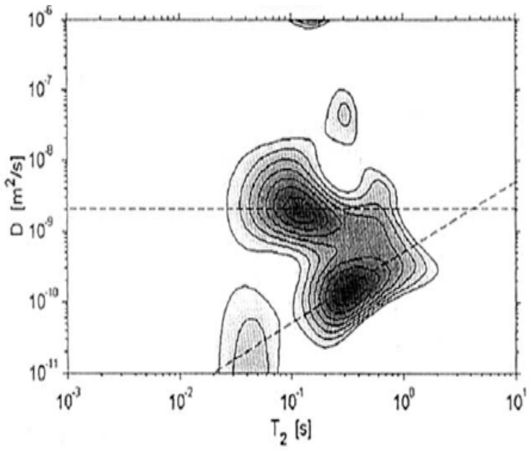
# Developing new MRI Contrasts: Multi-dimensional relaxometry-diffusometry *MRI*

- 2D NMR relaxometry/diffusometry methods have been used in porous media NMR applications.
- Because of vast data requirements and complexity in reconstructing 2D spectra, spectral MRI has been infeasible—nigh impossible.
- We have recently invented and developed $p(T_1,T_2)$, $p(\mathrm{mADC},T_2)$, $p(\mathrm{mADC},T_1)$, … MRI to reveal ‘invisible’ components and compartments within tissues and cells.

# Examples of 2D Correlation NMR Spectroscopy

**48,000 data points!**

Berea sandstone

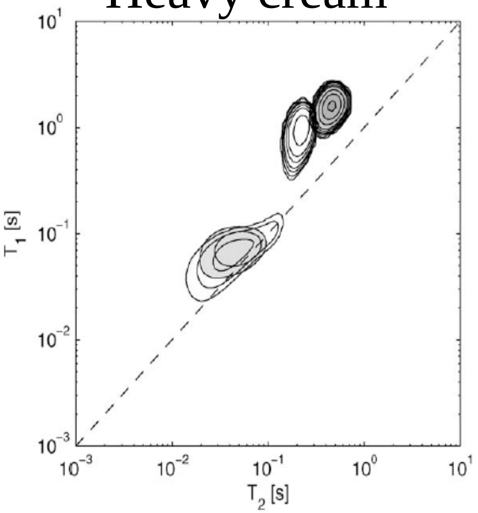



Hürlimann et al., 2003

*p*($T_2$,D) NMR

**240,000 data points!**

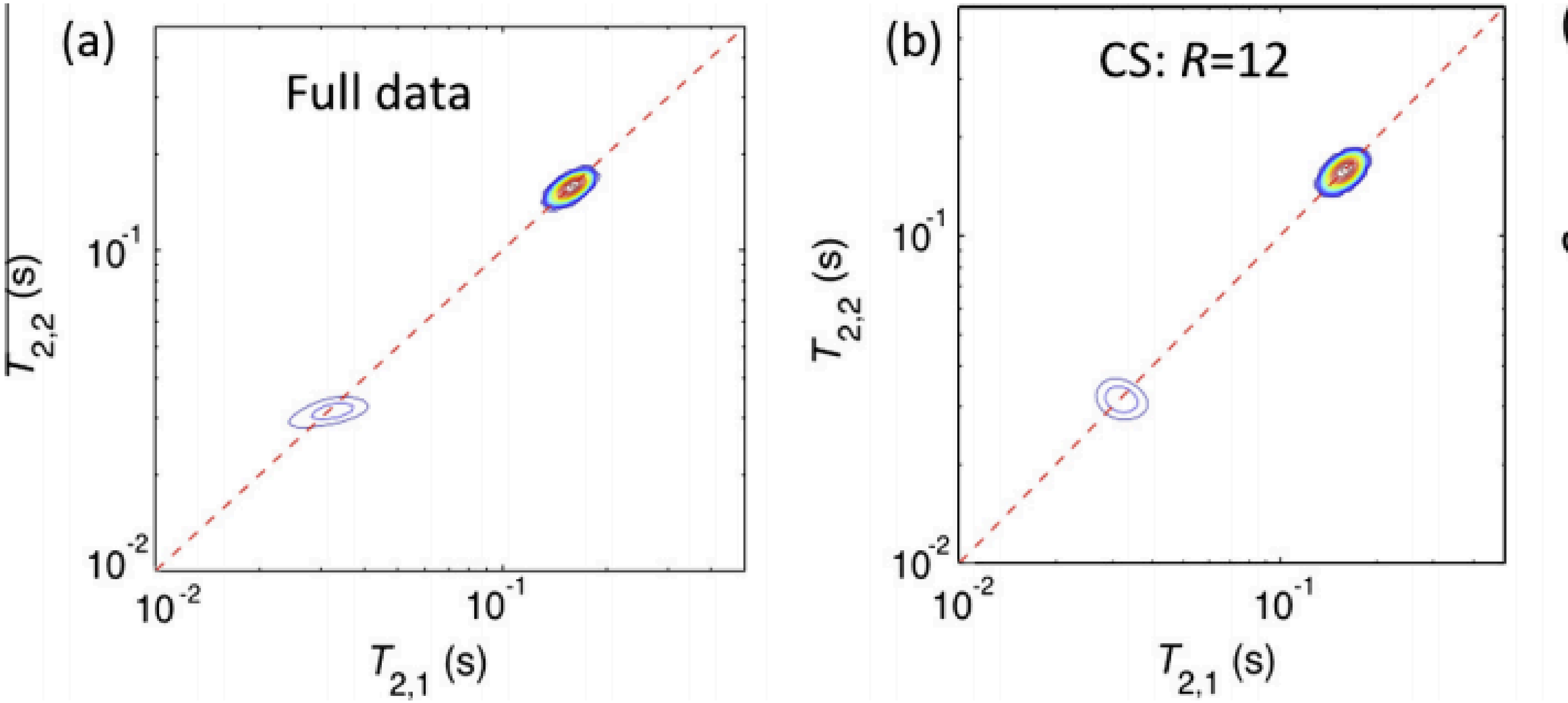
Heavy cream




Hürlimann et al., 2006

*p*($T_2$,$T_1$) NMR

# 2D Relaxometry with 'Compressed Sensing'




Efficient 2D MRI relaxometry using compressed sensing

Ruiliang Bai [a,b], Alexander Cloninger [c], Wojciech Czaja [d], Peter J. Basser [a,*]

Journal of Magnetic Resonance 255 (2015) 88–99

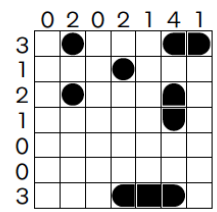

A *Milton Bradley*™ Game

# BATTLESHIPS

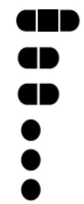
By Wei-Hwa Huang

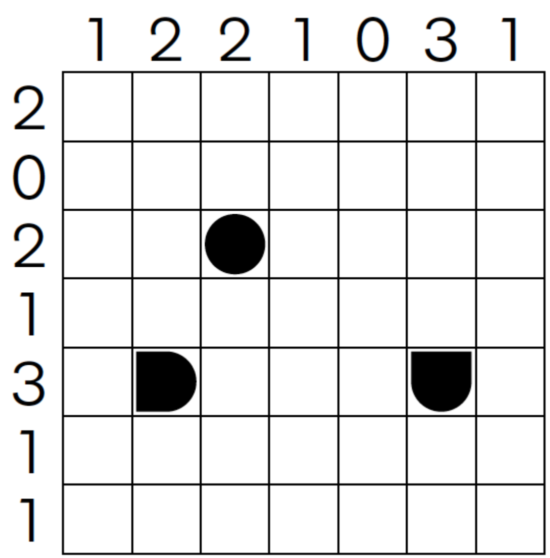
This is a puzzle version of the classic pencil-and-paper game. Place one cruiser (three grid cells, as shown), two destroyers (two cells) and three submarines (one cell) in the grid horizontally and vertically so that no two vessels touch, not even diagonally. The numbers at the side of the grid tell you how many cells in the corresponding rows and columns are occupied by vessels.

**Ex.**



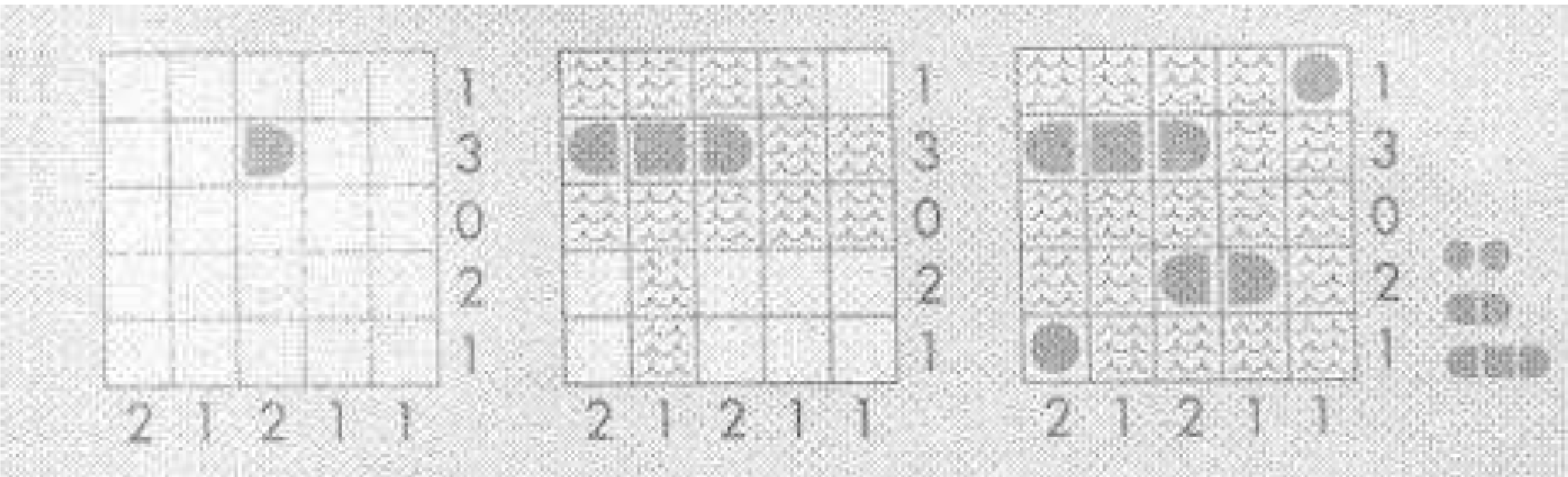

**Fleet**





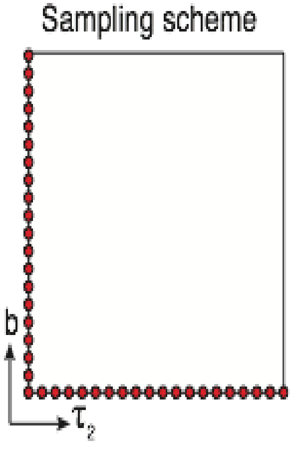

The New York Times, Puzzles, "A little variety" 03/06/16; Editor: Will Shortz

# Strategy changes when you know "opponent's" marginal distributions!




Rows and columns show partial sums from
which marginal distributions can be calculated

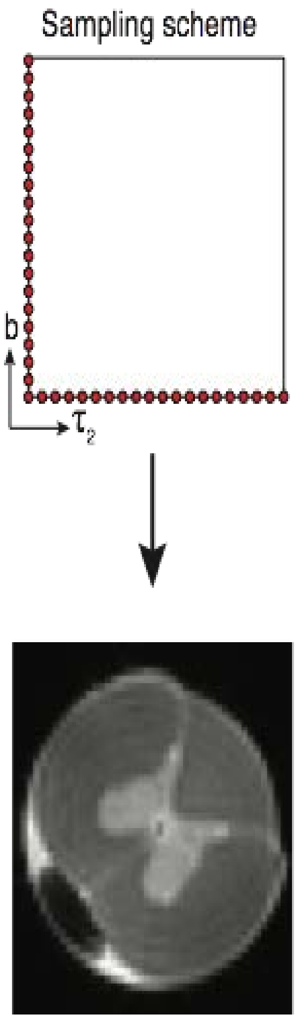
# Marginal Distribution Constrained Optimization (MADCO) for multispectral imaging




Dan Benjamini

Benjamini and Basser, Neuroimage, 2017; http://www.sciencedirect.com/science/article/pii/S1053811917307814

# MADCO for multispectral imaging




Benjamini and Basser, Neuroimage, 2017; http://www.sciencedirect.com/science/article/pii/S1053811917307814

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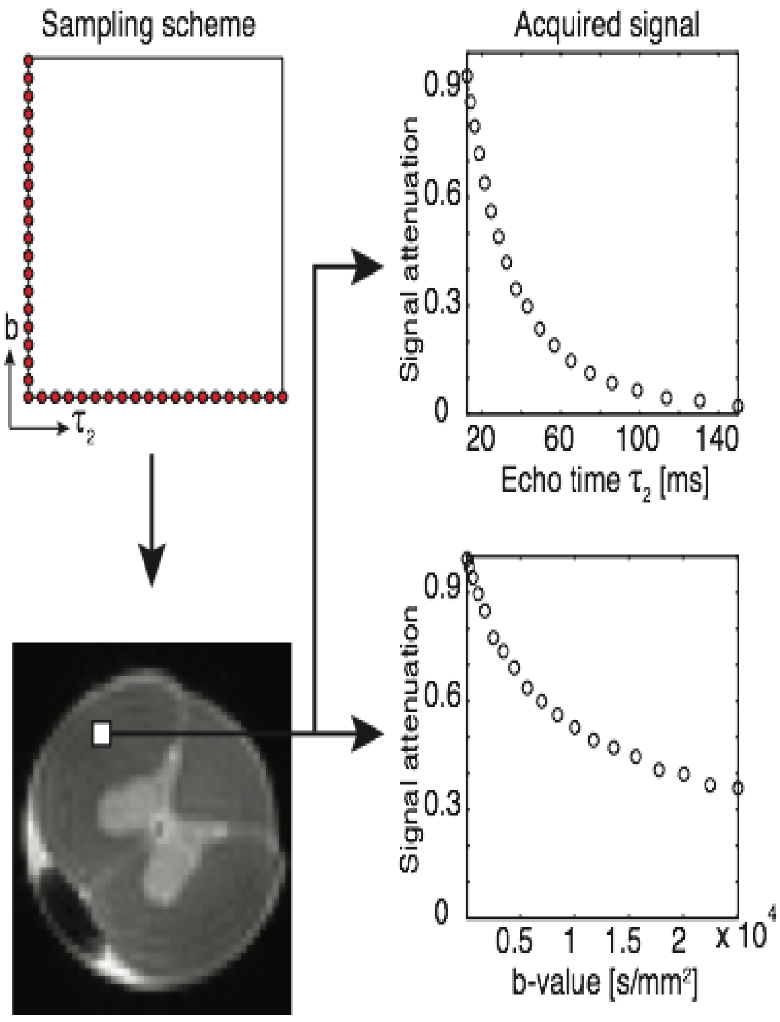


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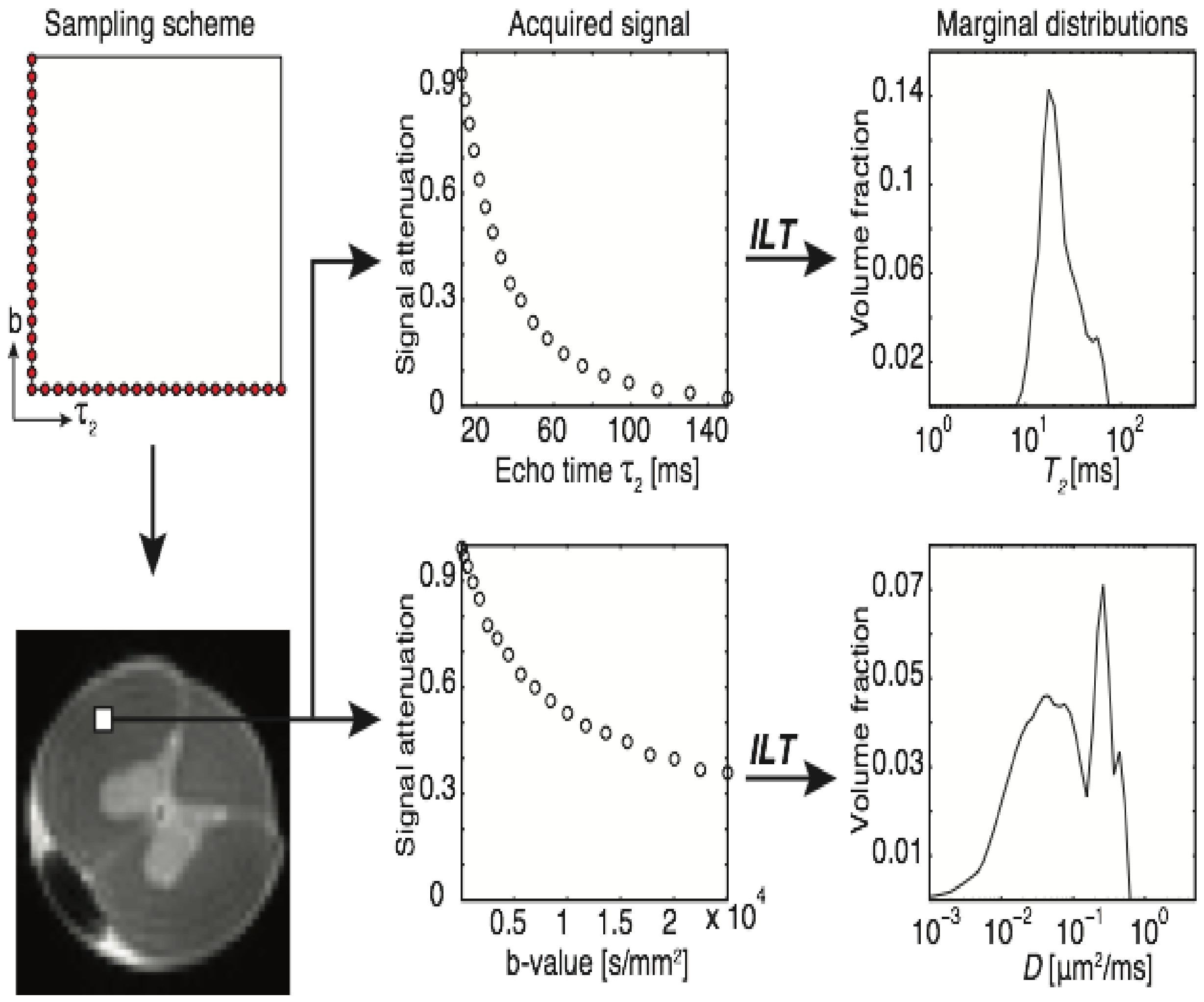
# MADCO for multispectral imaging




Benjamini and Basser, Neuroimage, 2017; http://www.sciencedirect.com/science/article/pii/S1053811917307814

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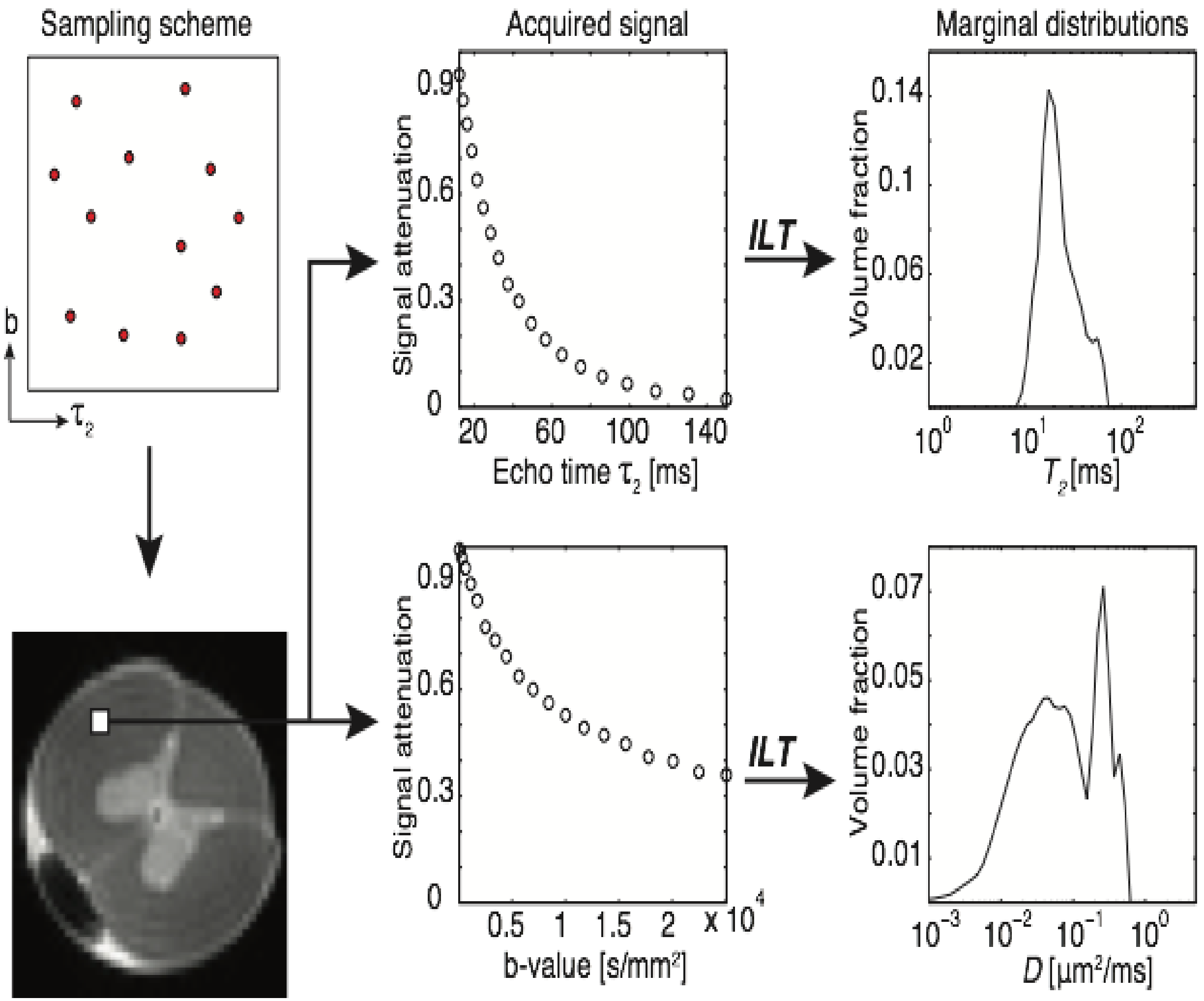


Benjamini and Basser, Neuroimage, 2017; http://www.sciencedirect.com/science/article/pii/S1053811917307814

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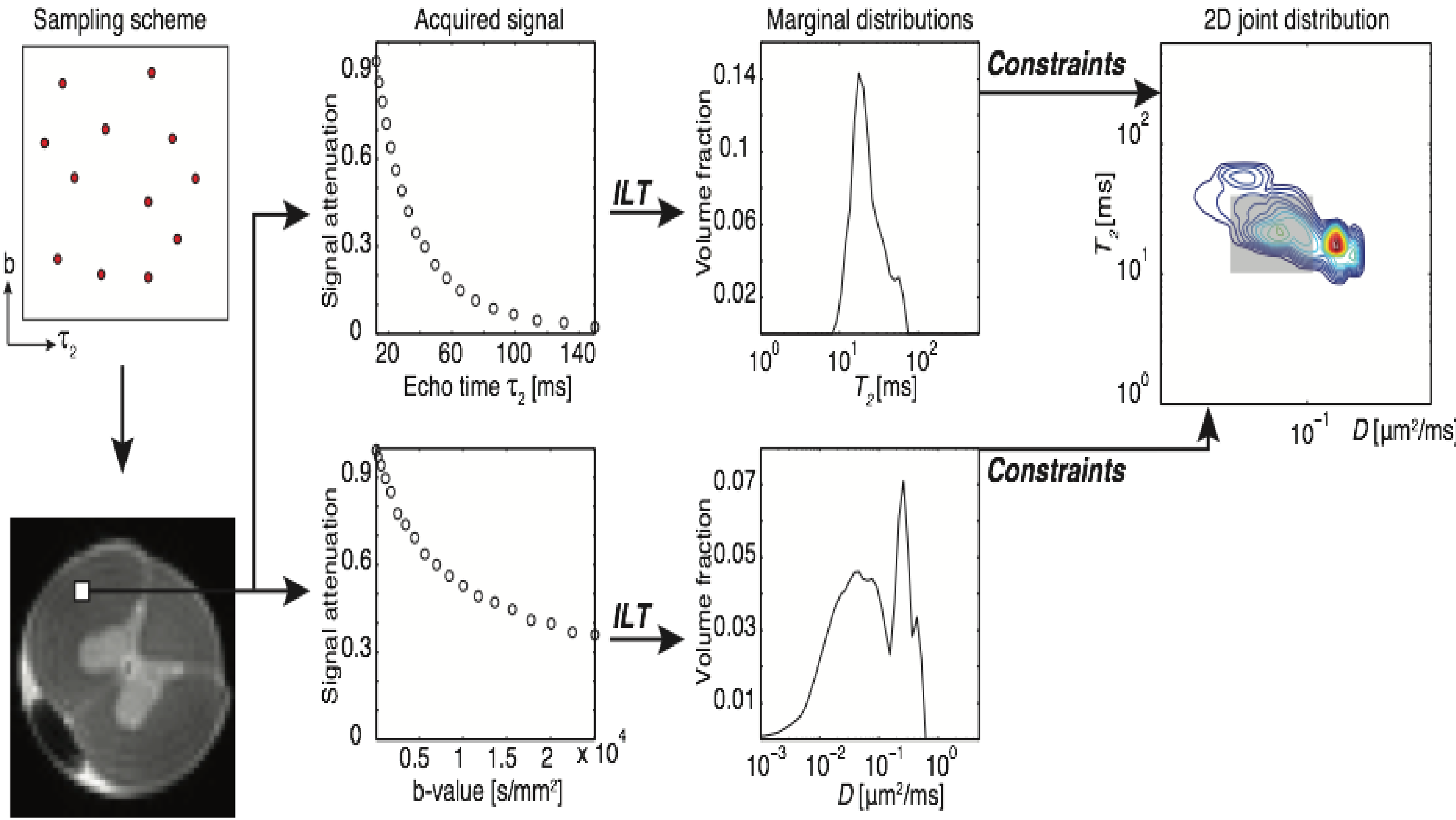


Benjamini and Basser, Neuroimage, 2017; http://www.sciencedirect.com/science/article/pii/S1053811917307814

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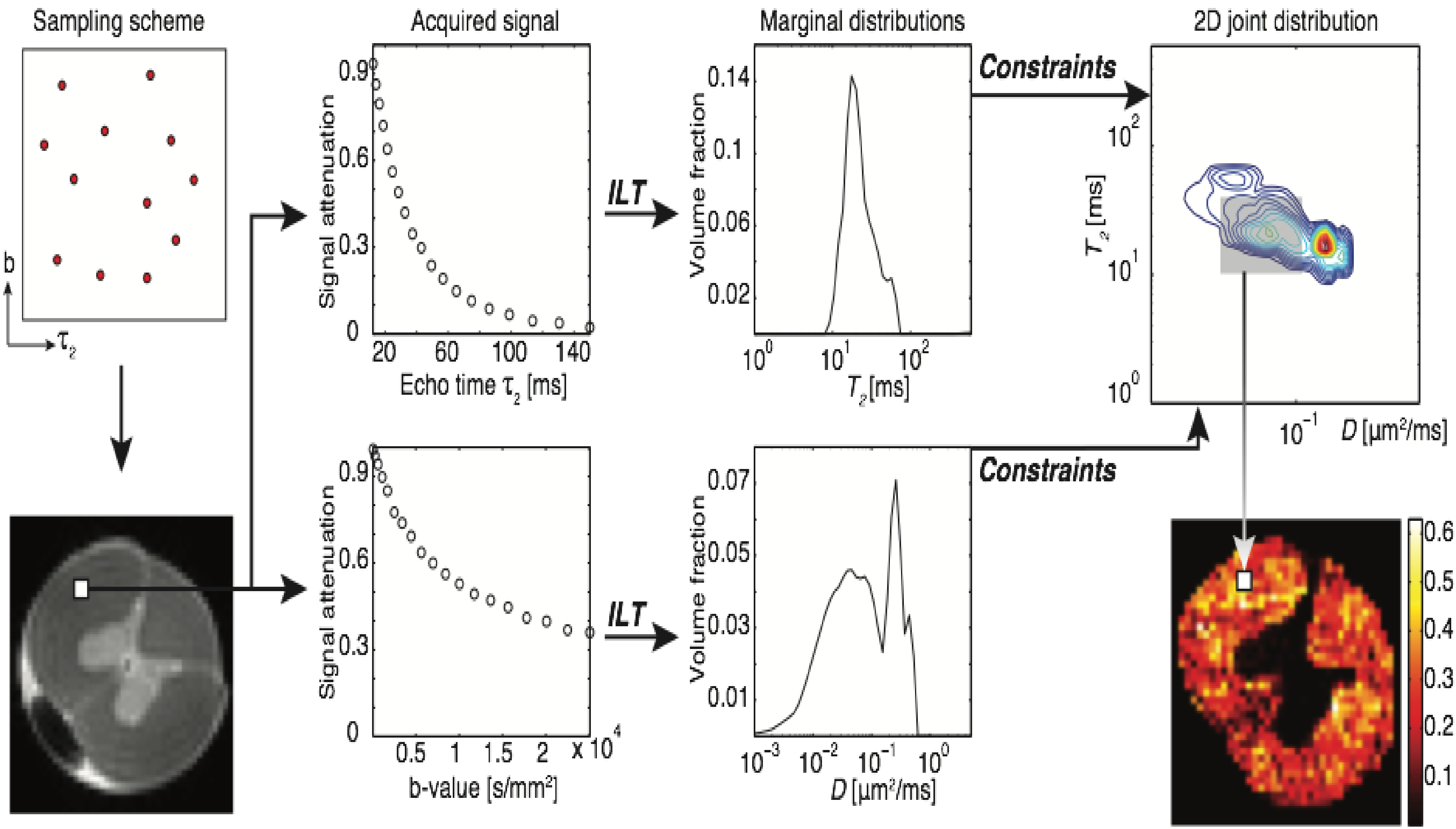
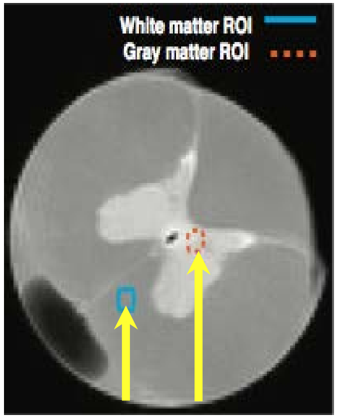
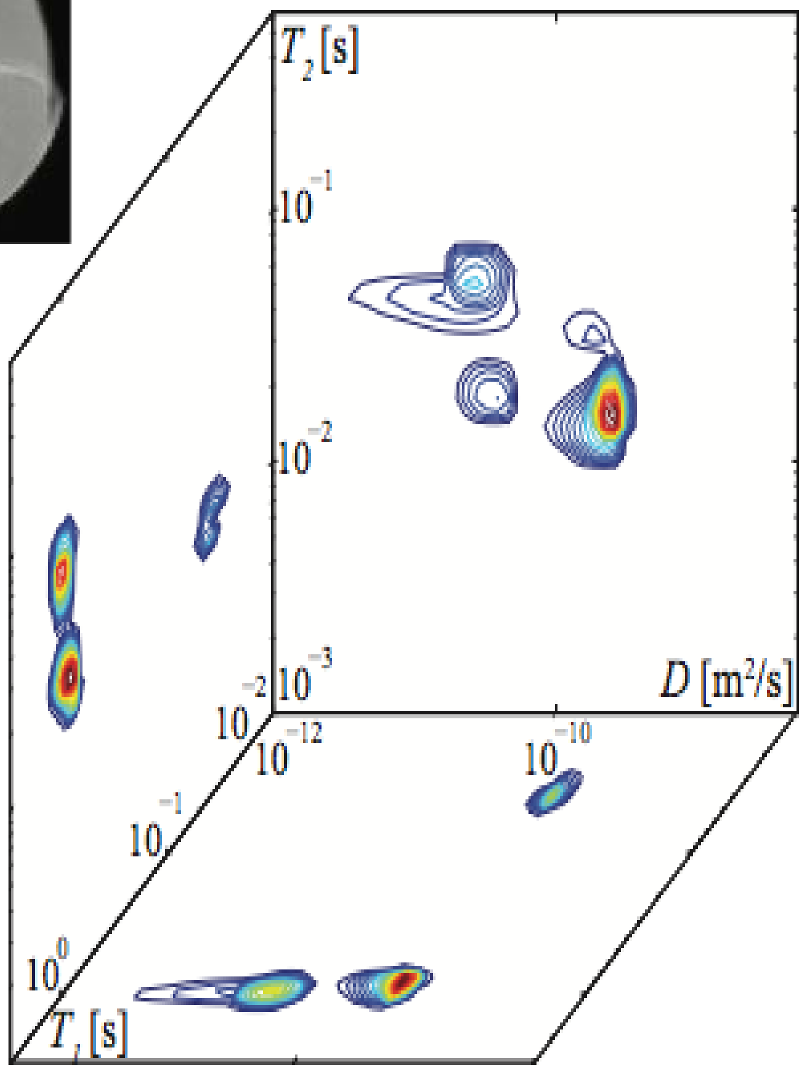



Benjamini and Basser, Neuroimage, 2017; http://www.sciencedirect.com/science/article/pii/S1053811917307814

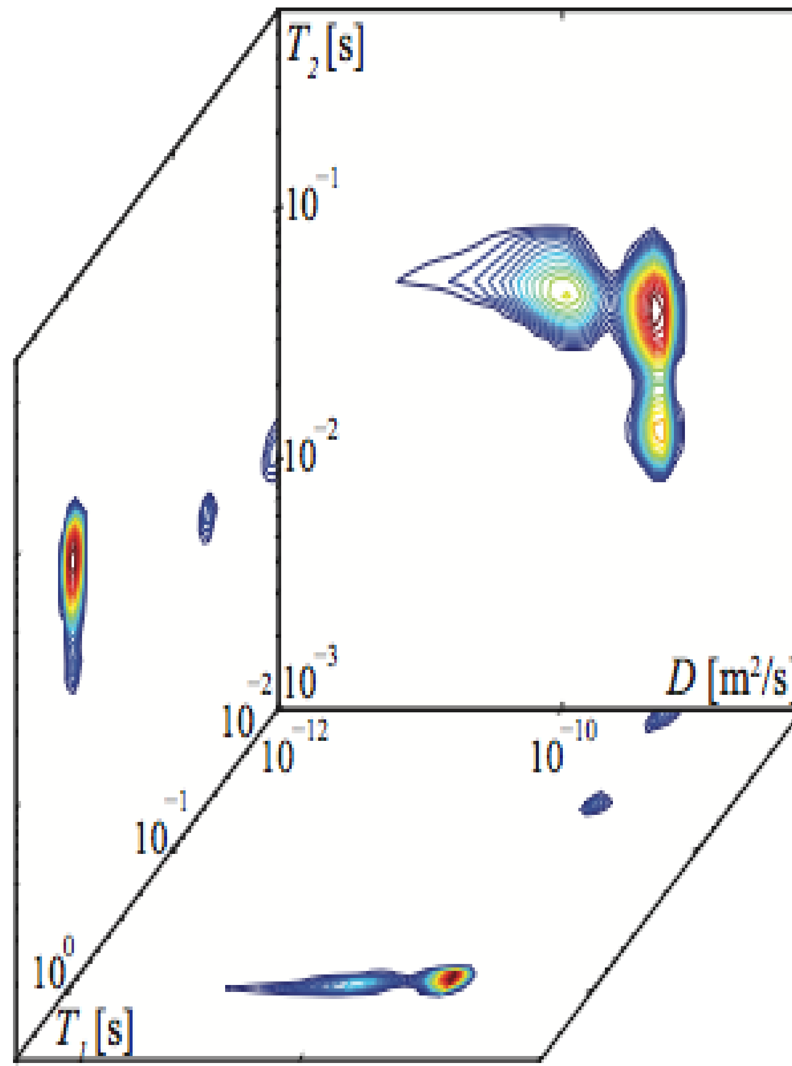
# MADCO: *ex vivo* ferret spinal cord




White Matter ROI




Gray Matter ROI

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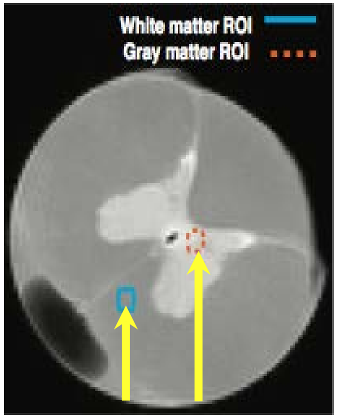
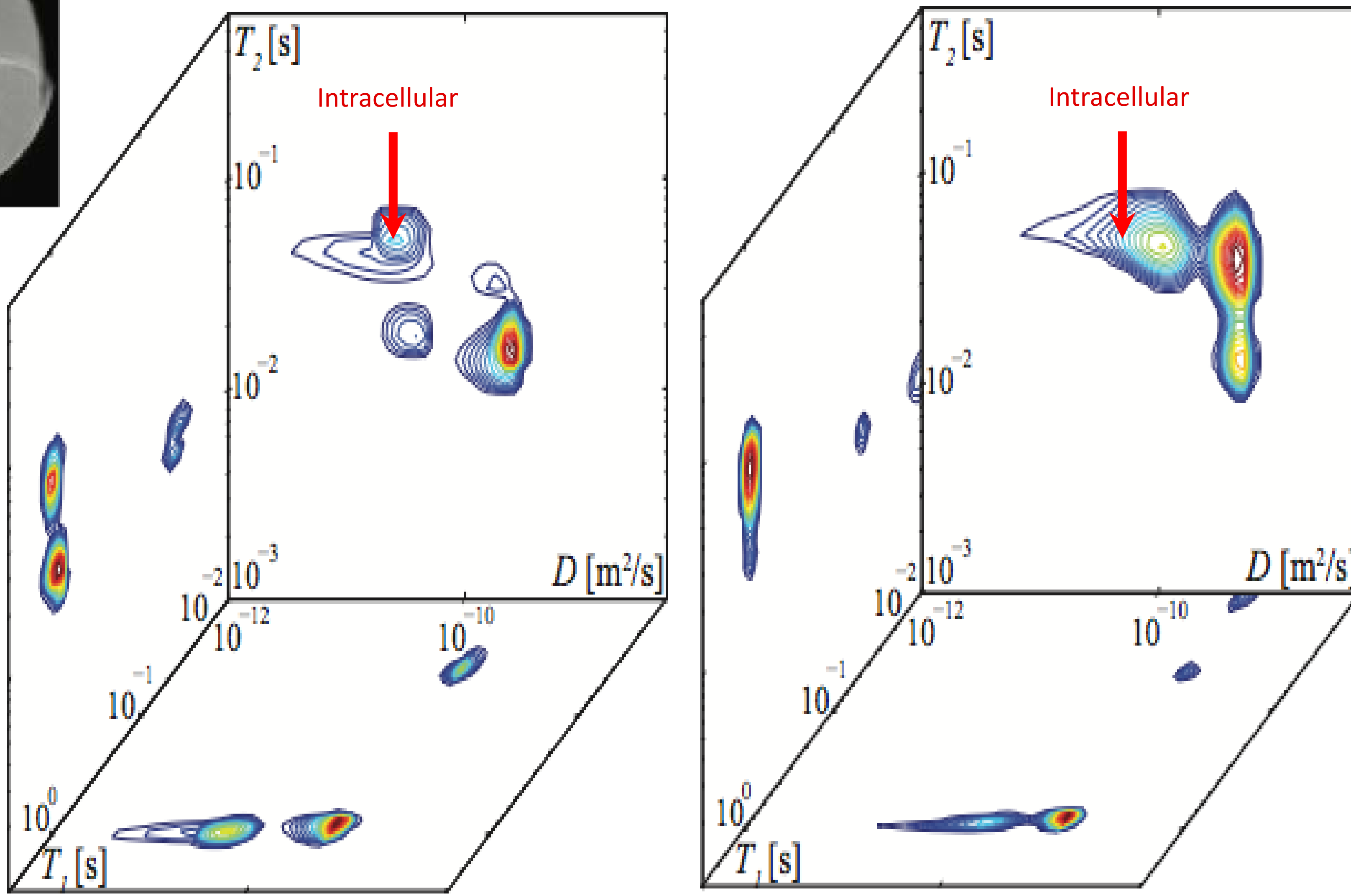



White Matter ROI

Gray Matter ROI

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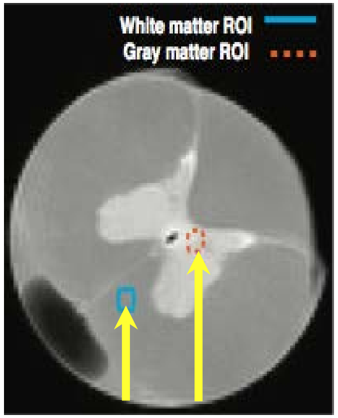


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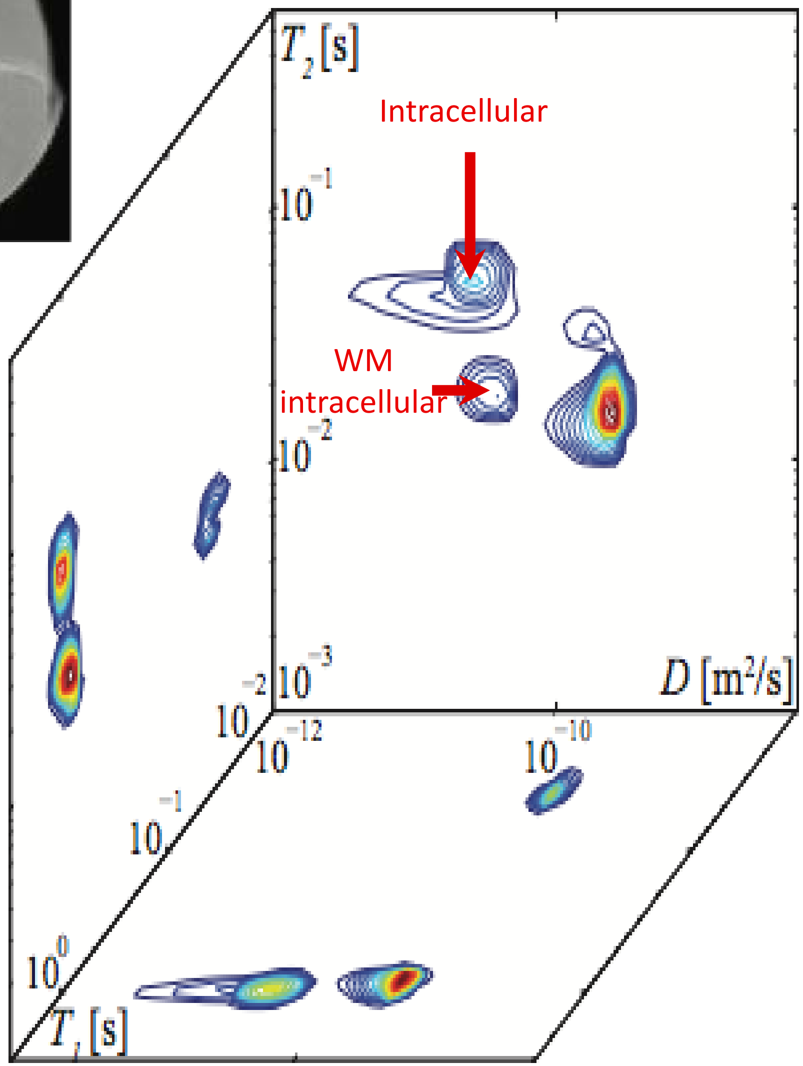


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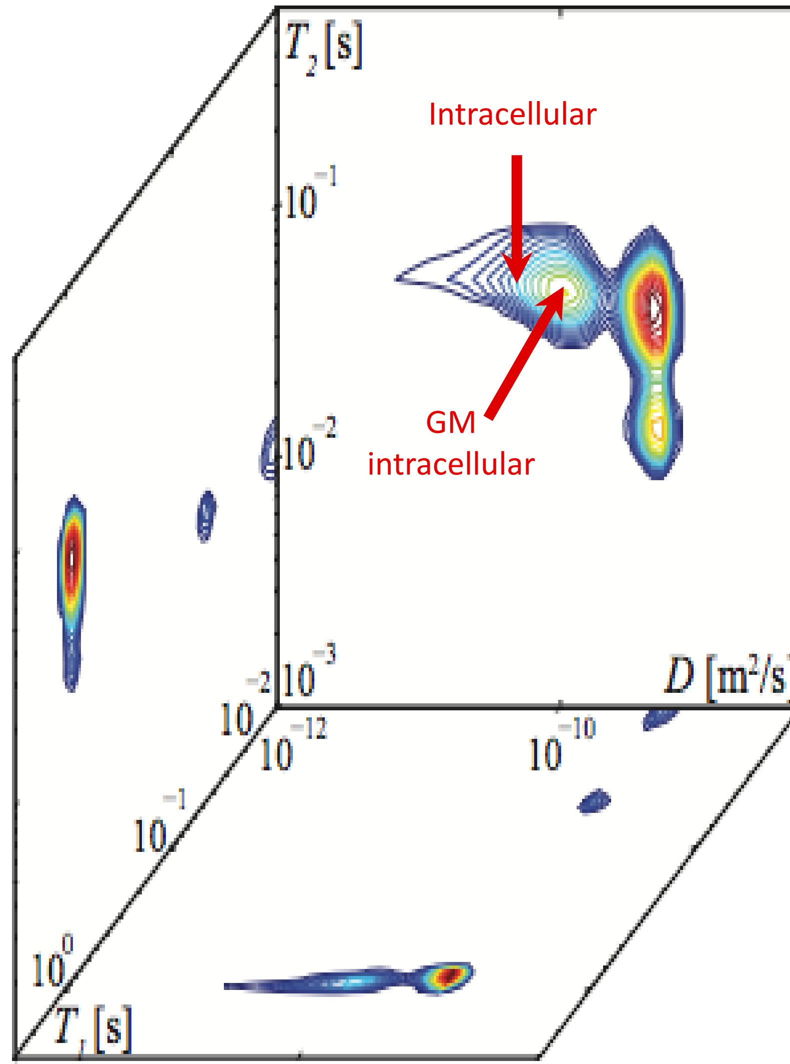


Benjamini and Basser, Neuroimage, 2017; http://www.sciencedirect.com/science/article/pii/S1053811917307814

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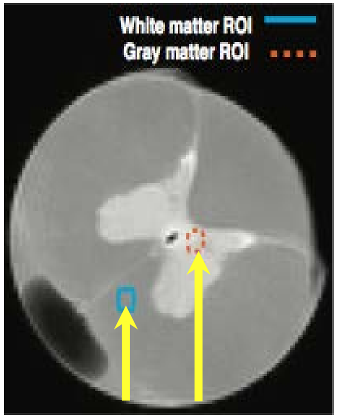


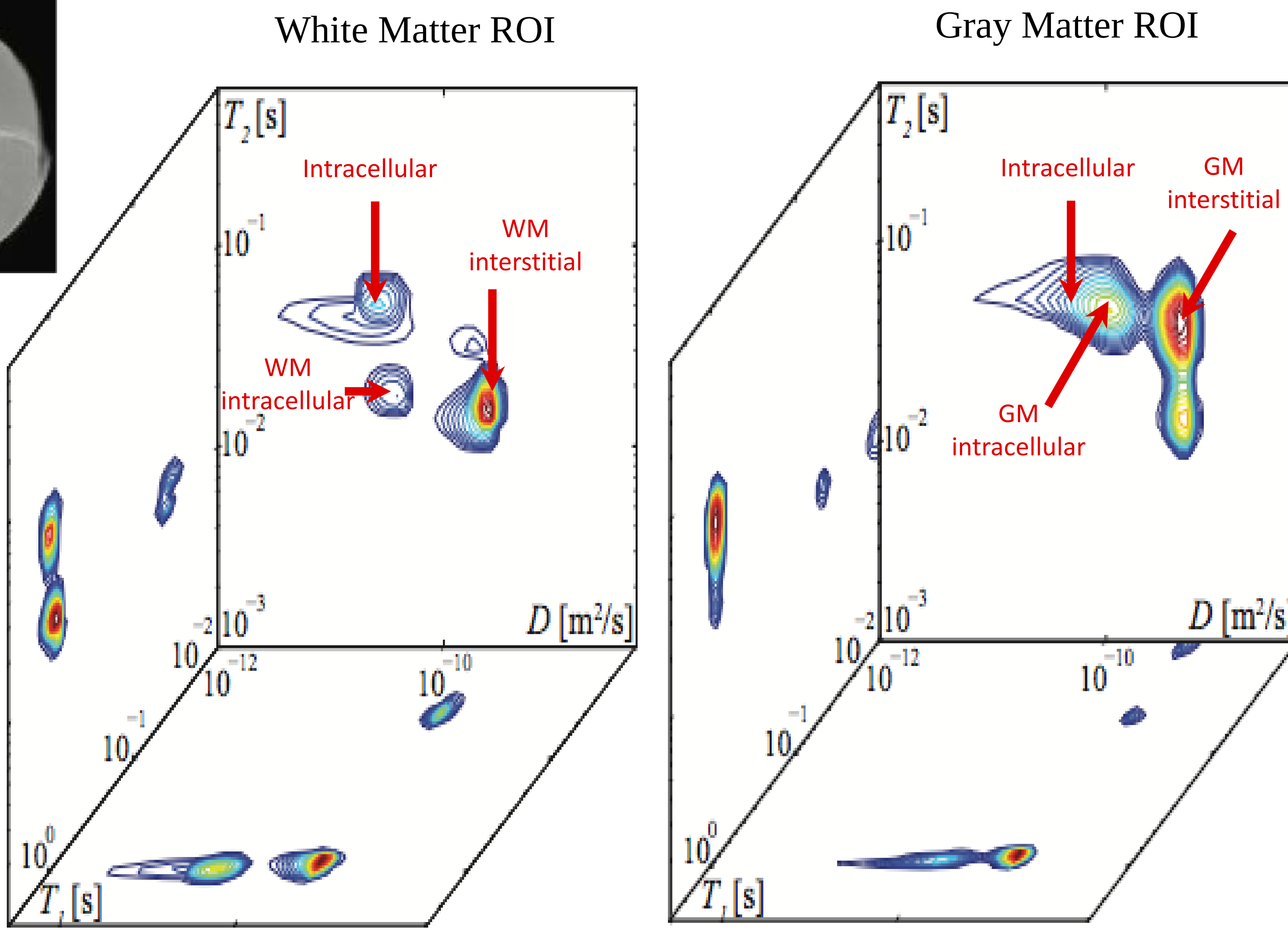


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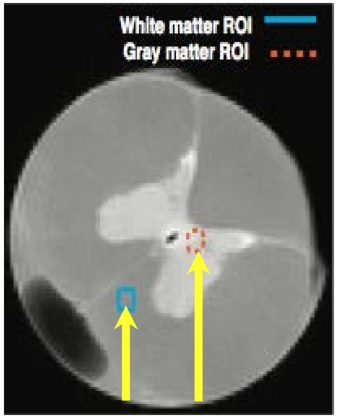
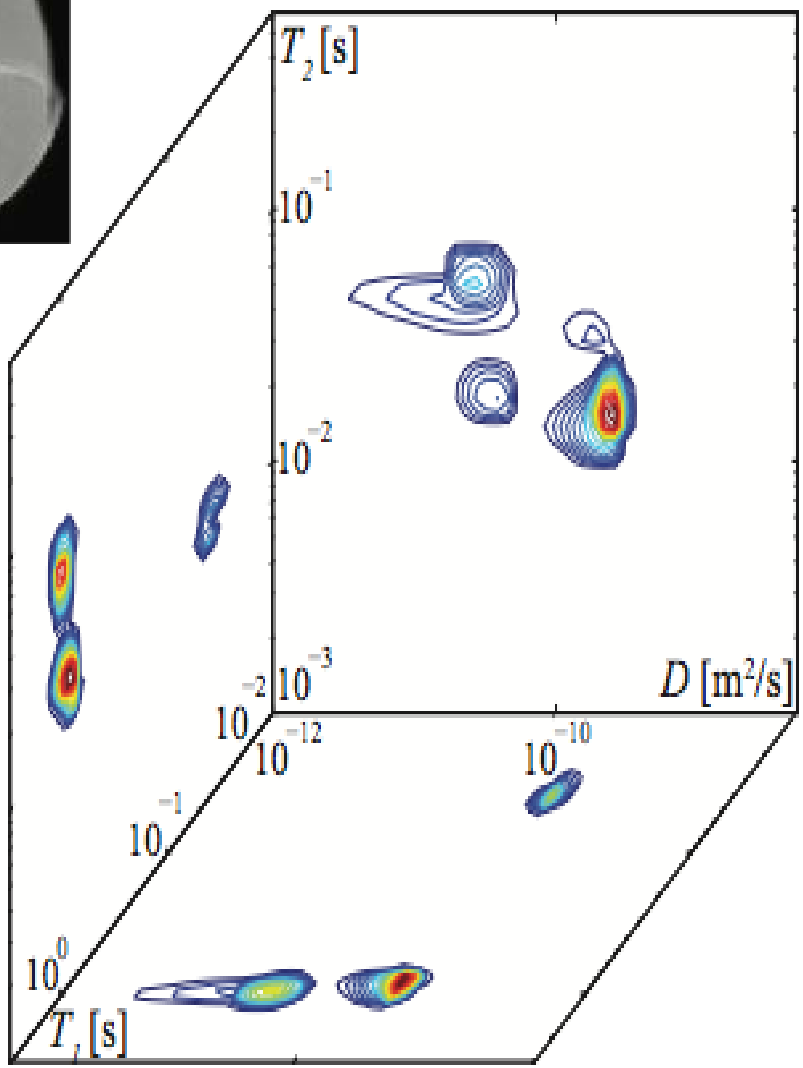
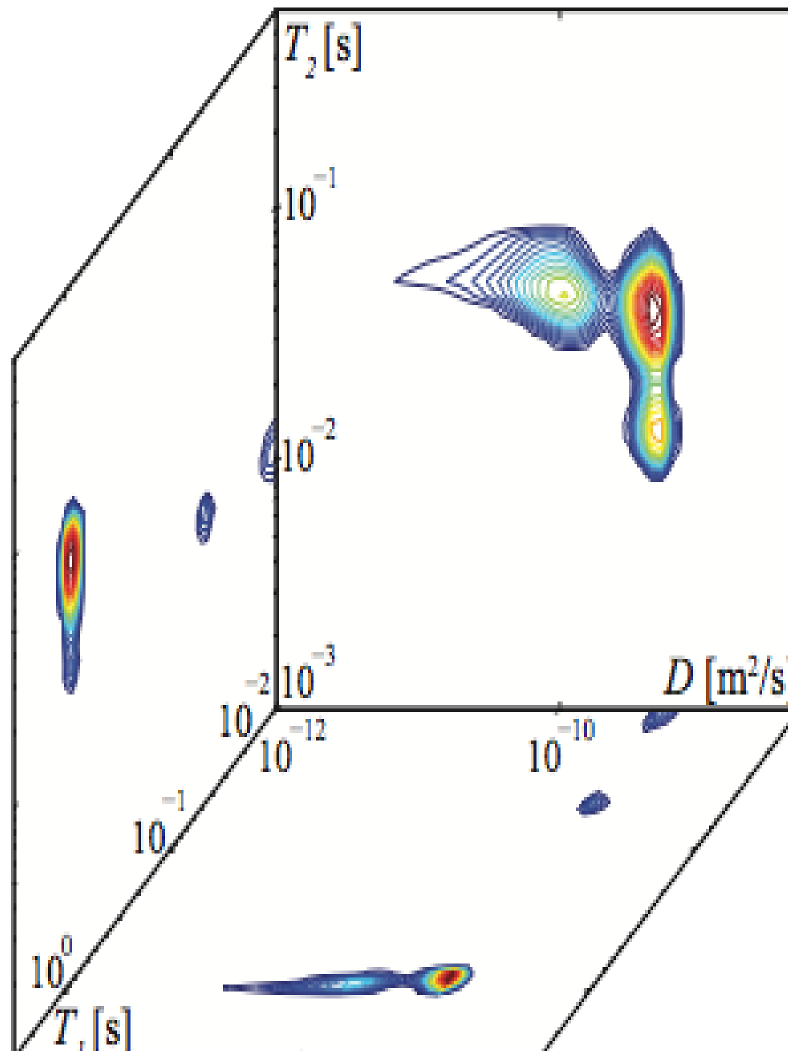



White Matter ROI

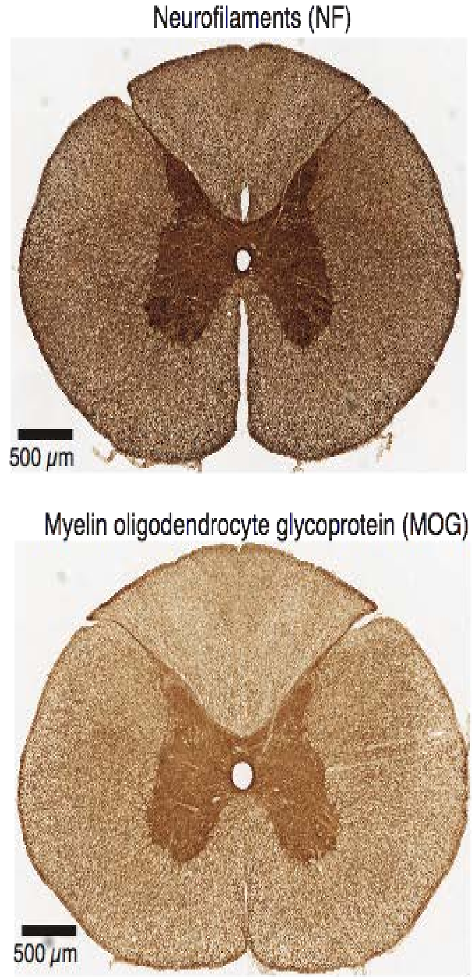



Gray Matter ROI




Benjamini and Basser, Neuroimage, 2017; http://www.sciencedirect.com/science/article/pii/S1053811917307814

# MRI / Immunohistochemistry Correlation

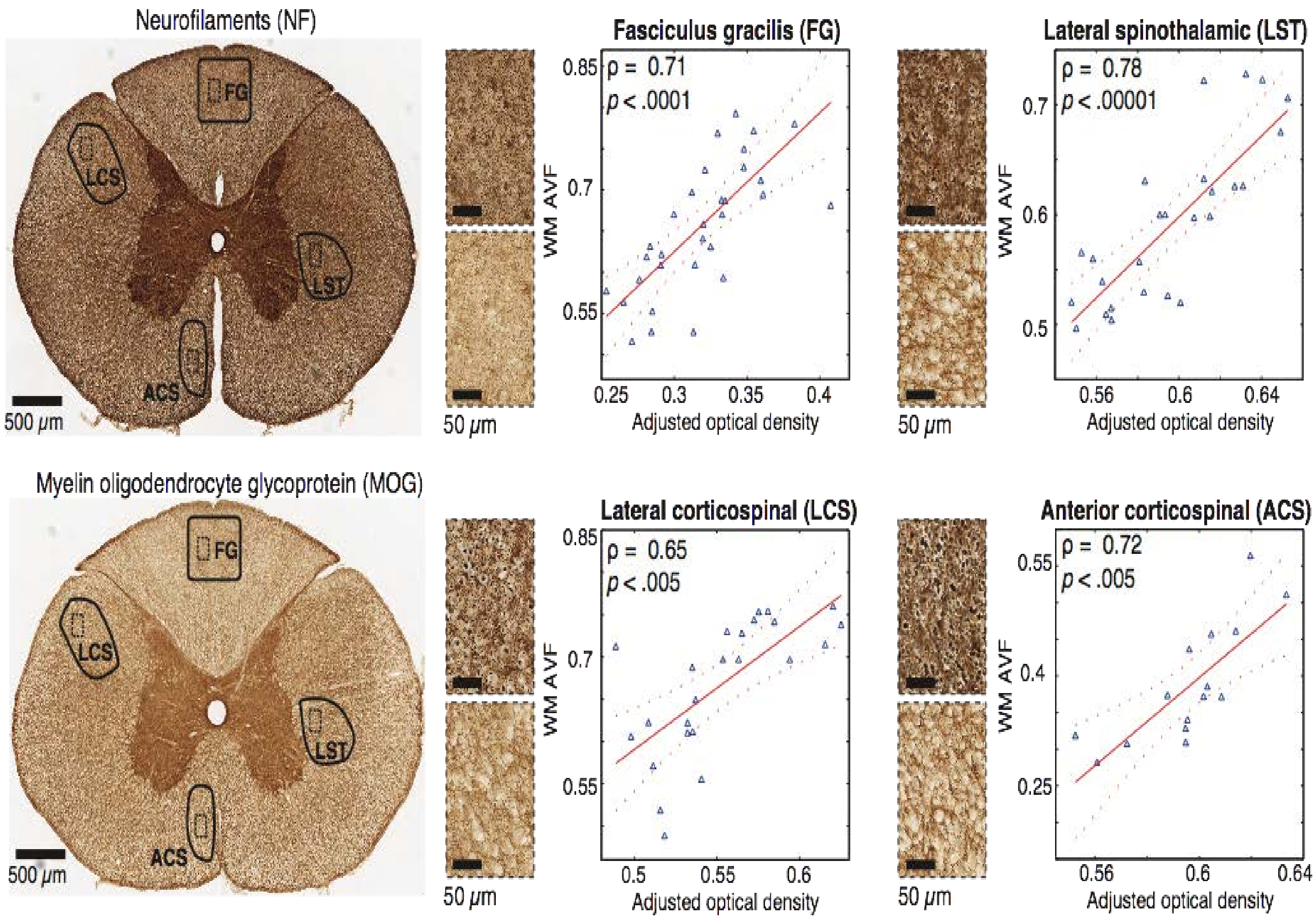



MRI and histology images are co-registered

Multivariate linear regression is used to correlate MRI and histology imaging data in ROIs (with optical density images used as the independent variables)

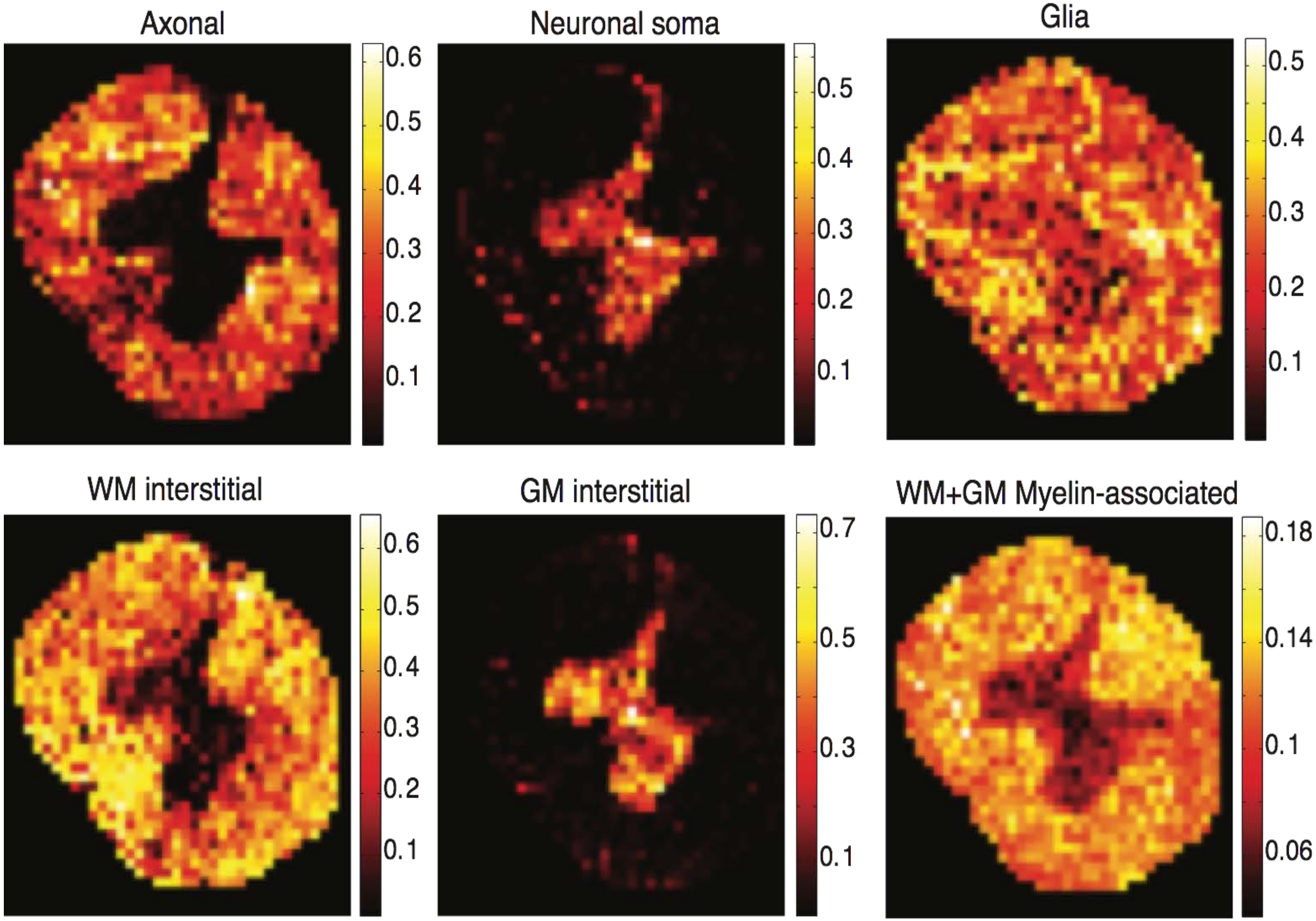
Benjamini and Basser, Neuroimage, 2017; http://www.sciencedirect.com/science/article/pii/S1053811917307814

# MRI / Immunohistochemistry Correlation



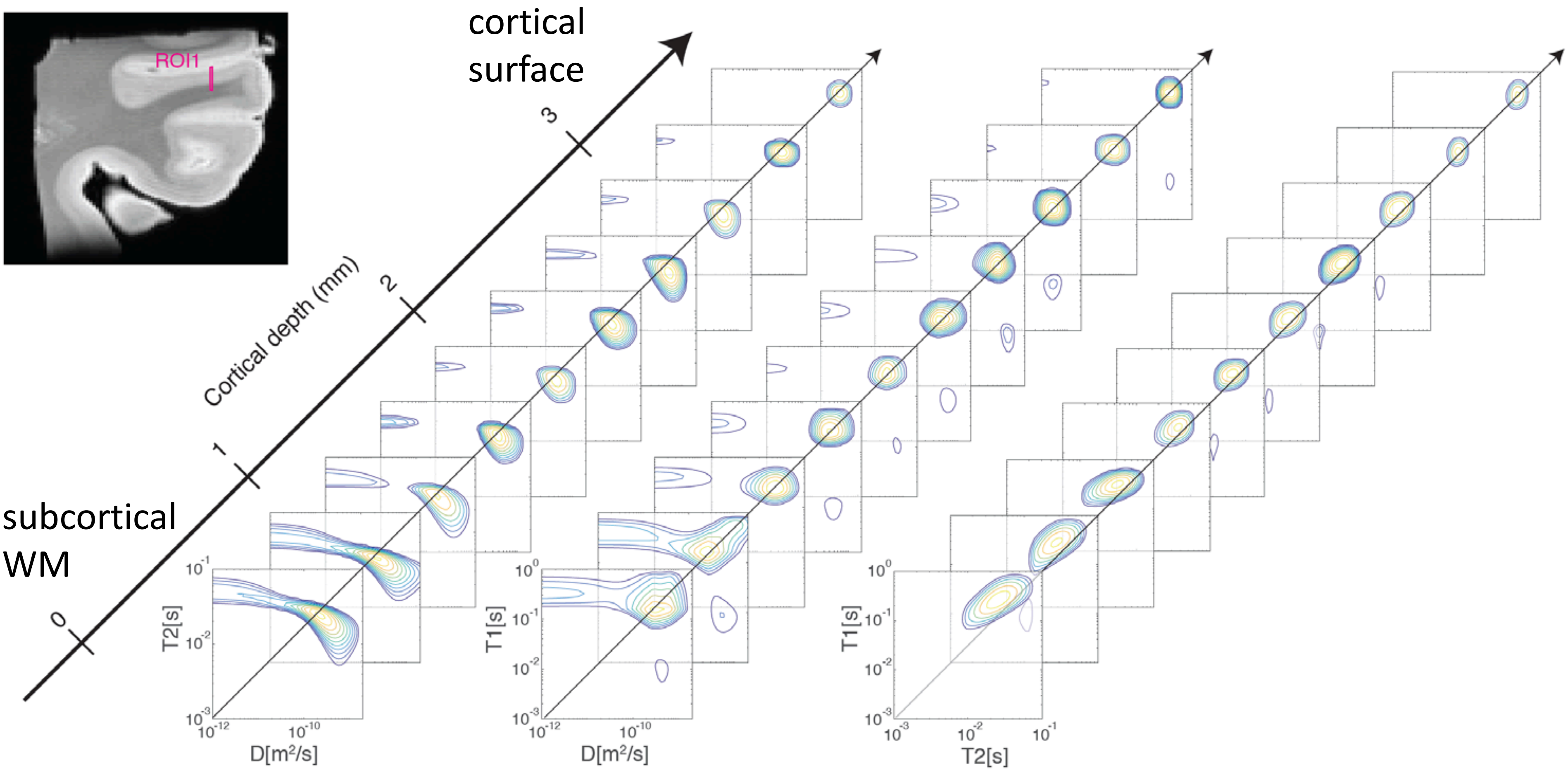

Benjamini and Basser, Neuroimage, 2017; http://www.sciencedirect.com/science/article/pii/S1053811917307814

# Apparent Volume Fraction MRI maps show distinct water microenvironments




Benjamini and Basser, Neuroimage, 2017; http://www.sciencedirect.com/science/article/pii/S1053811917307814

# Human Cortical Tissue Parcellation



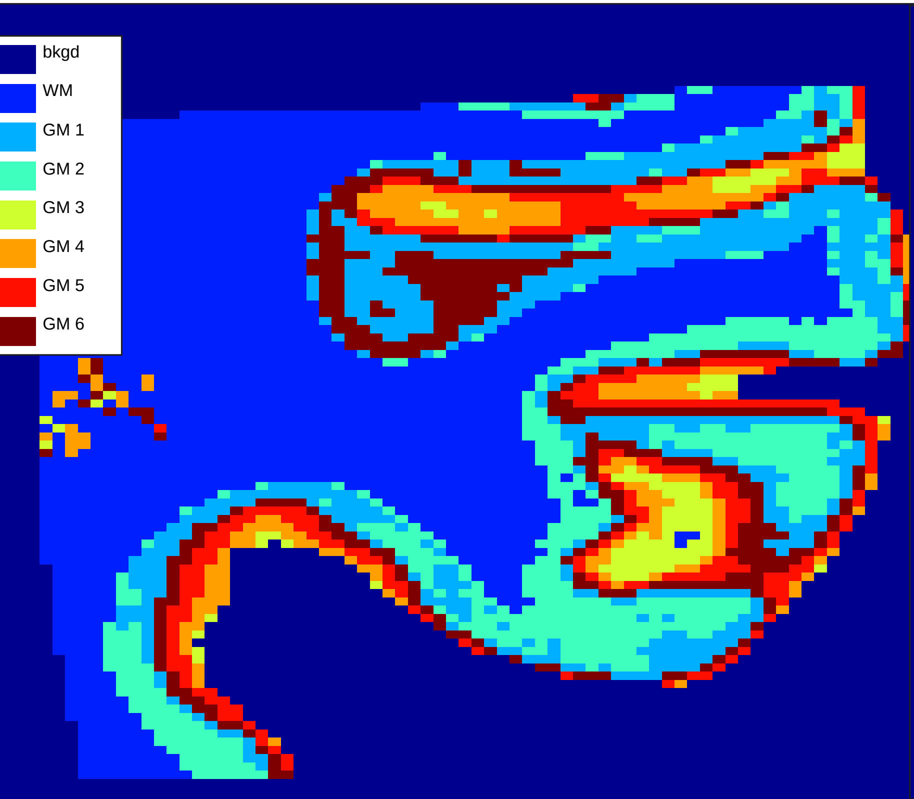

First 2D relaxometry/diffusometry MRI data obtained in human brain tissue (unpublished) in BA17 from CNRM Neuropathology colleagues Drs. Perl, Rhodes and Iacono

# Unsupervised Cortical Parcellation

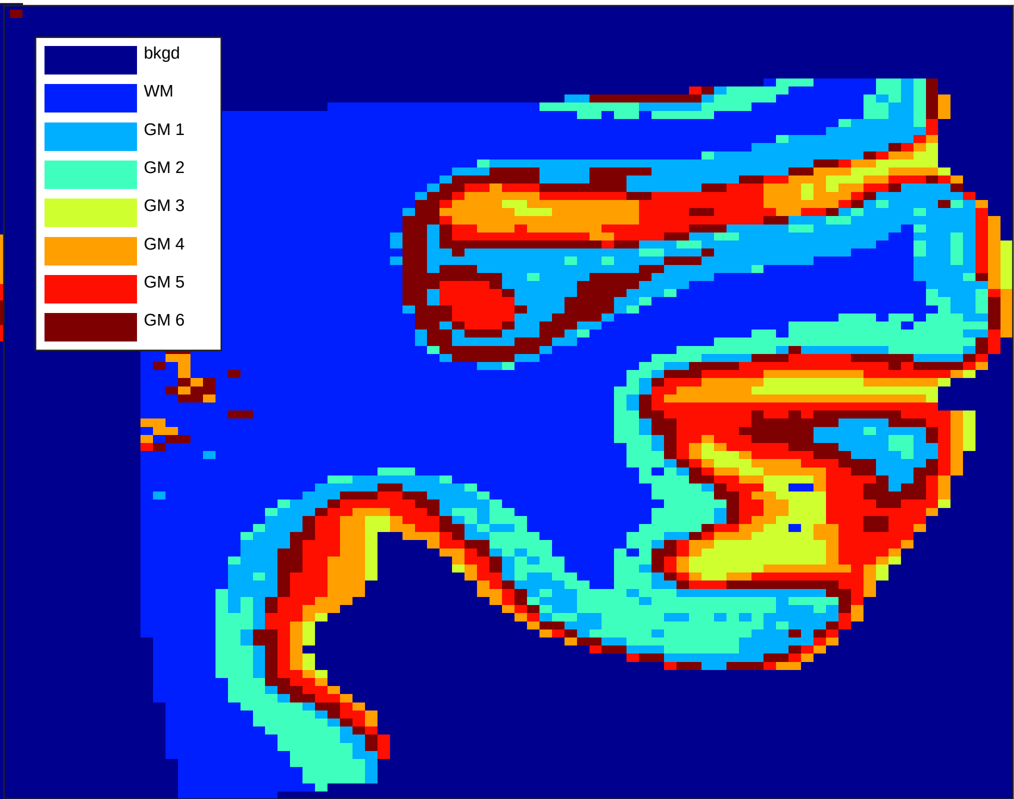
Segmentation of GM and WM
Clustering into 6 Cortical Layers
Clustering of Cortical Areas

Shinjini Kundu
Unpublished Data

3D segmented tissues, 2D Euclidean, slice 28




3D segmented tissues, 2D Euclidean, slice 29

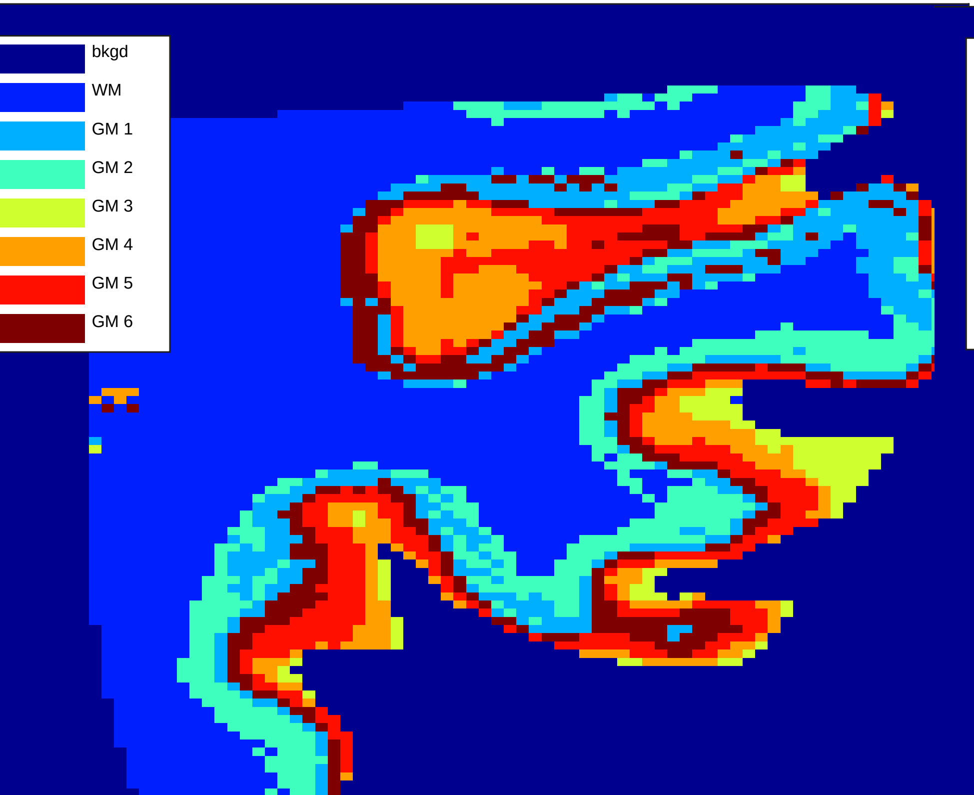


# Unsupervised Cortical Parcellation

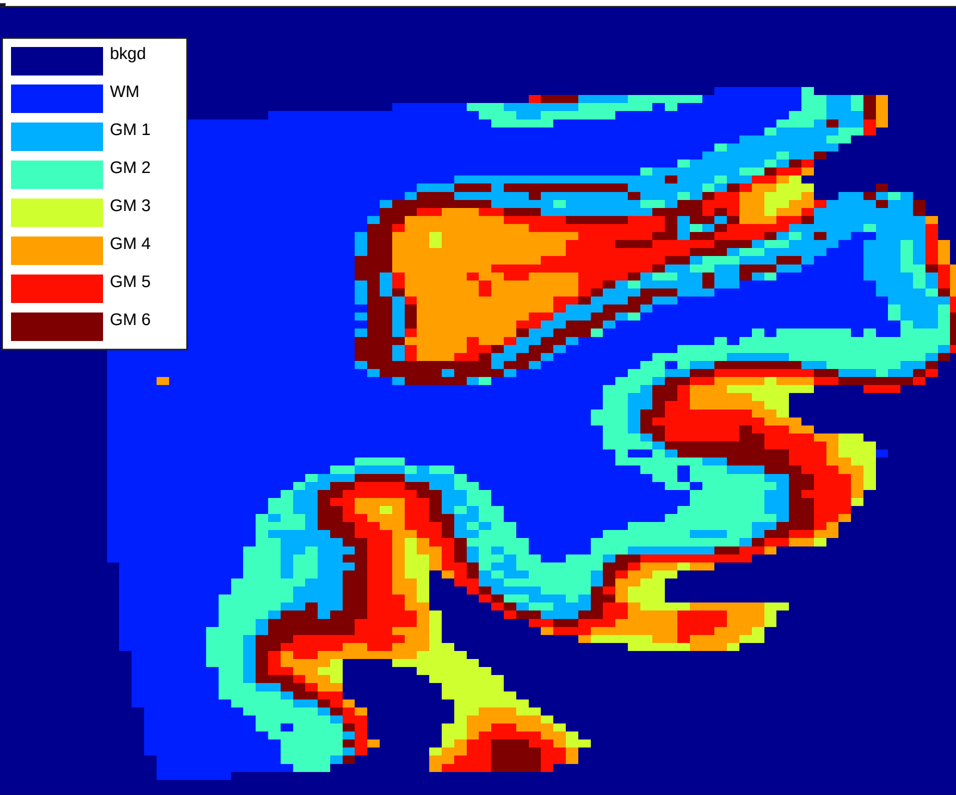
- Segmentation of GM and WM
- Clustering into 6 Cortical Layers
- Clustering of Cortical Areas

Shinjini Kundu
Unpublished Data

3D segmented tissues, 2D Euclidean, slice 32




3D segmented tissues, 2D Euclidean, slice 33

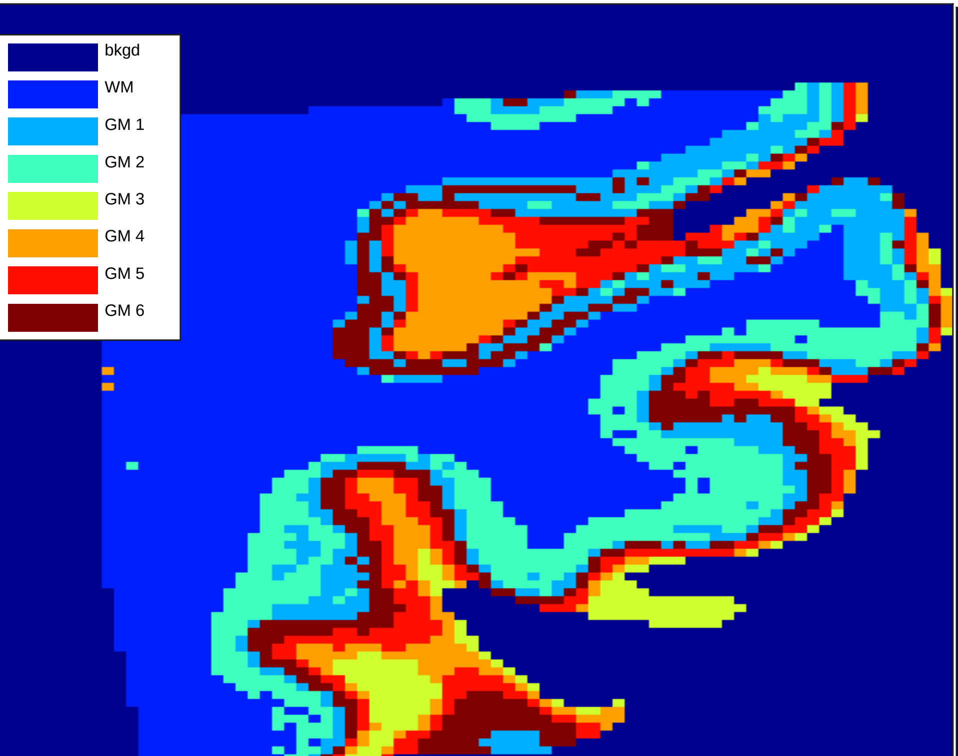


# Unsupervised Cortical Parcellation

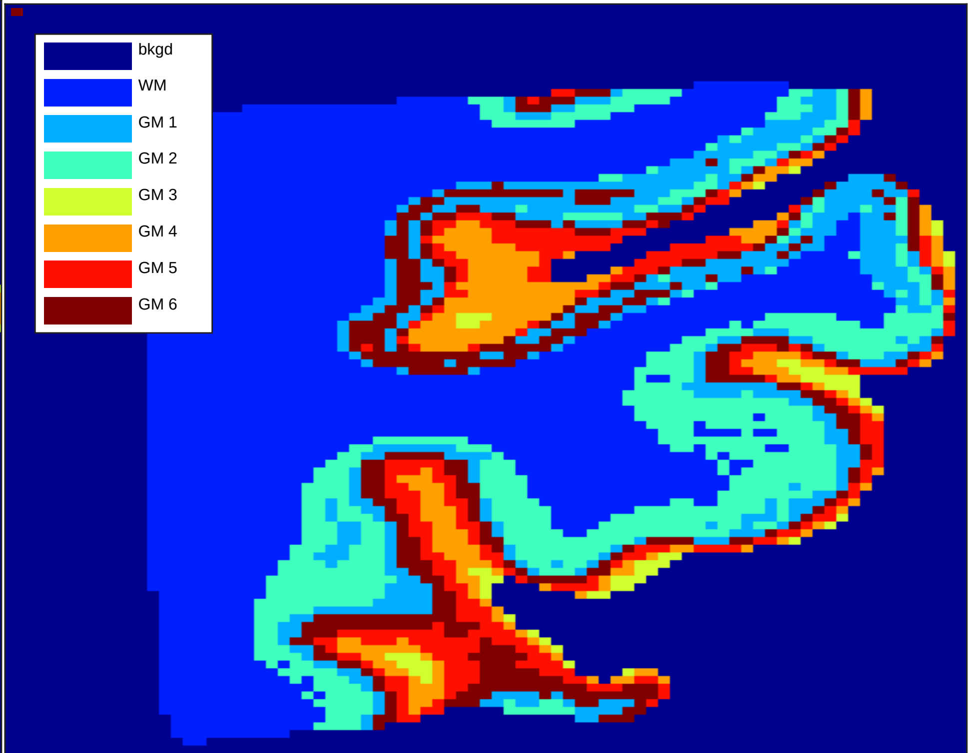
- Segmentation of GM and WM
- Clustering into 6 Cortical Layers
- Clustering of Cortical Areas

Shinjini Kundu
Unpublished data

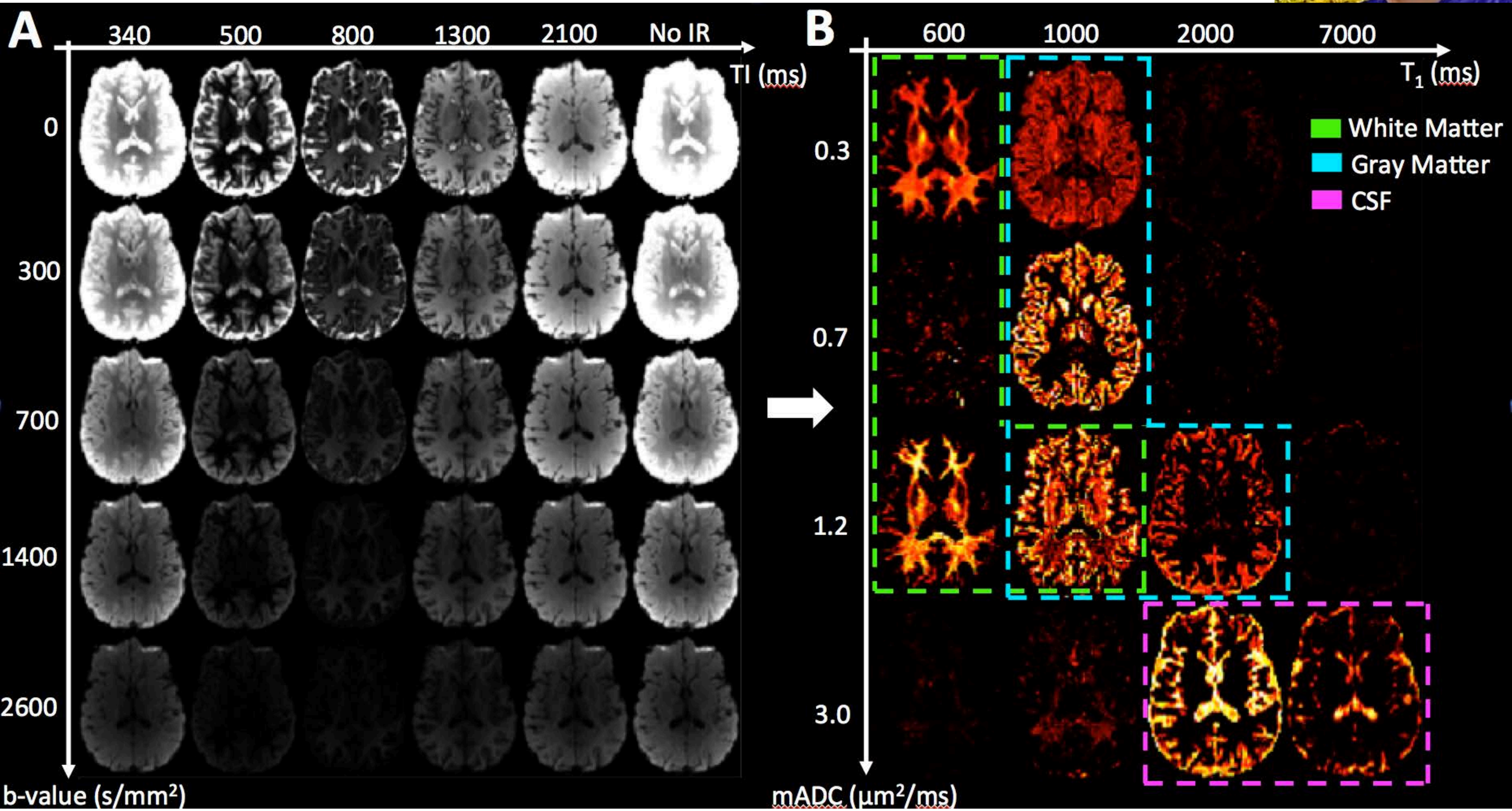
3D segmented tissues, 2D Euclidean, slice 34




3D segmented tissues, 2D Euclidean, slice 35

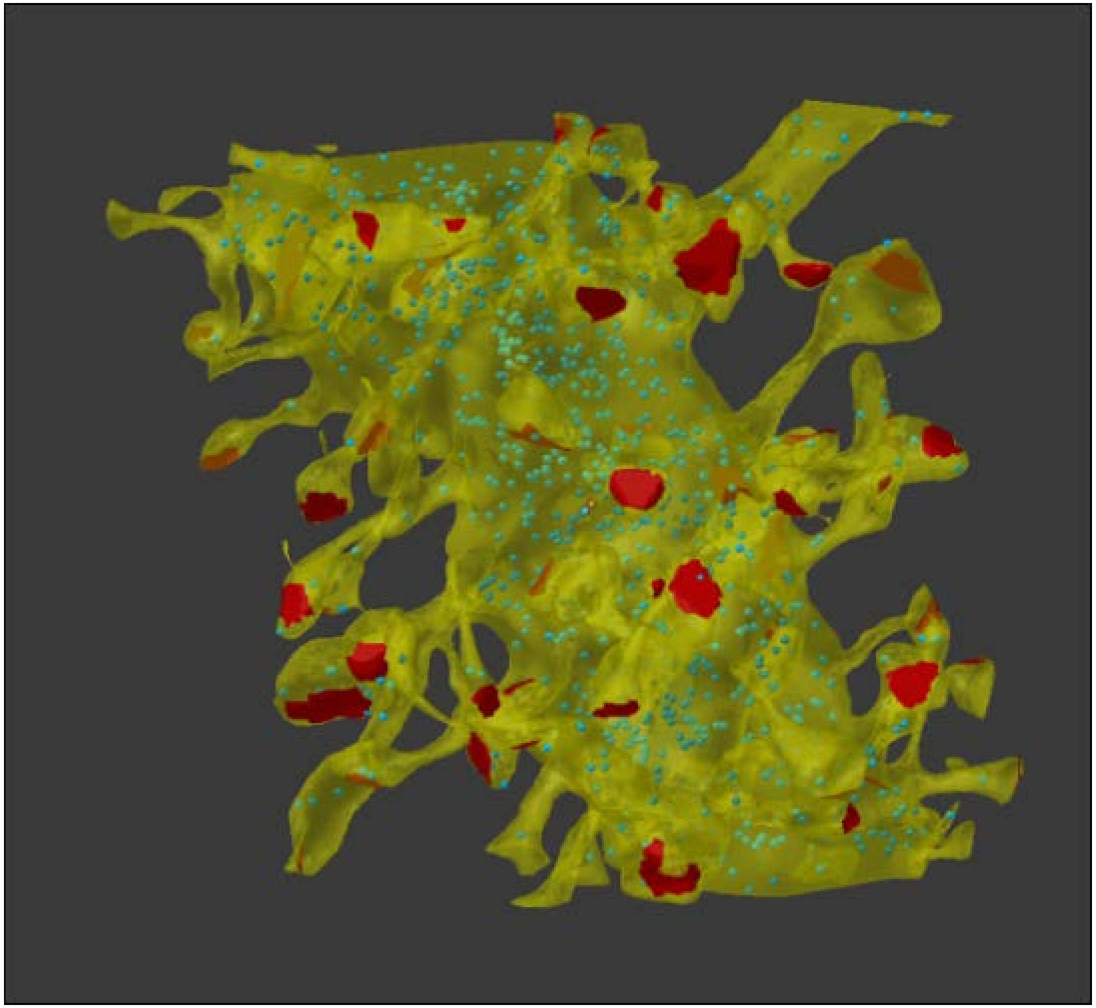


# Clinical $p(T_1,\text{mADC})$ Mapping




A.V. Avram, J.E. Sarlls, and P.J. Basser, *Estimating intravoxel joint T1-mean diffusivity probability distributions using a clinical MRI scanner* (in preparation)

# *DiffSim* Monte-Carlo Modeling Framework



Adam
Bernstein

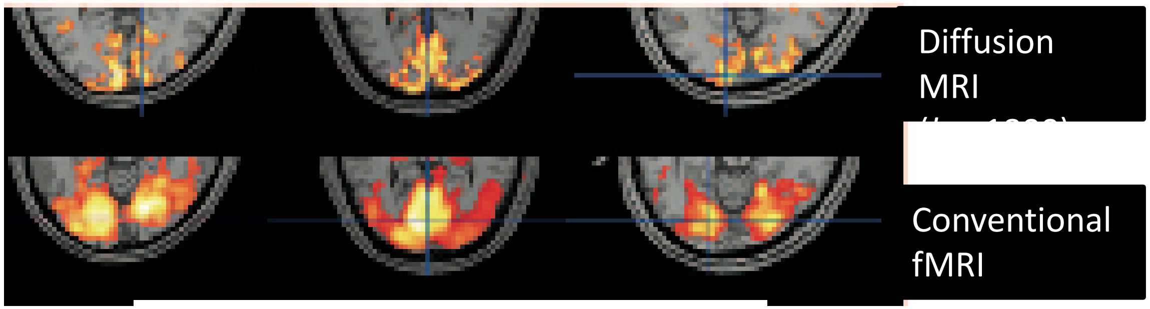
AS Bernstein; B Regner; GT Baxter; E Özarslan; PJ Basser; TJ Sejnowski; LR Frank, *Insights into double pulsed field gradient experiments in non-ideal geometries using Monte-Carlo simulations*, submitted, JMR 2018

# Explore Novel Functional MRI (fMRI) Mechanisms and Image Contrasts

Can we discover new mechanisms that are more direct, sensitive, and specific than conventional Blood Oxygen Level Dependent (BOLD) fMRI?

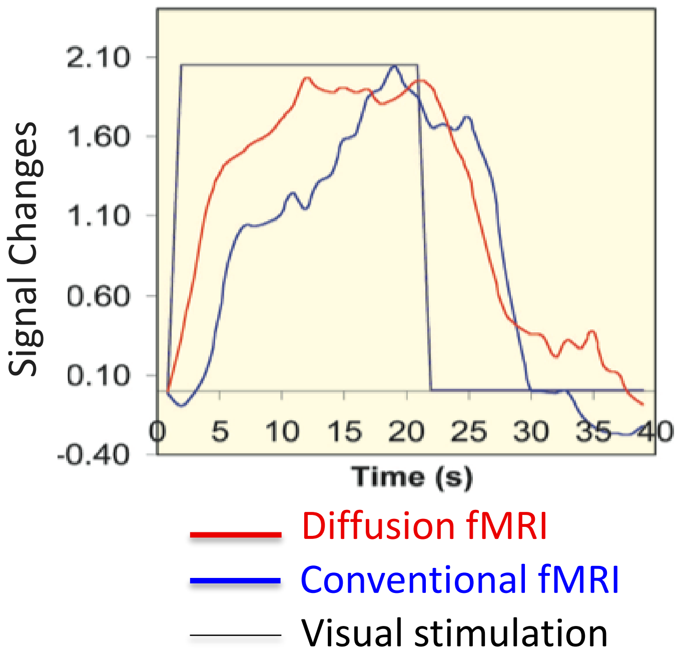
# ‘Direct’ fMRI via measuring changes in water diffusion?

➢ Claim: Functional diffusion MRI (fDMRI) detects microstructural changes associated with neuronal activity




fDMRI vs conventional BOLD fMRI during *in vivo* (human) visual stimulation.

------ D. Le Bihan, et al., *PNAS*, 2006

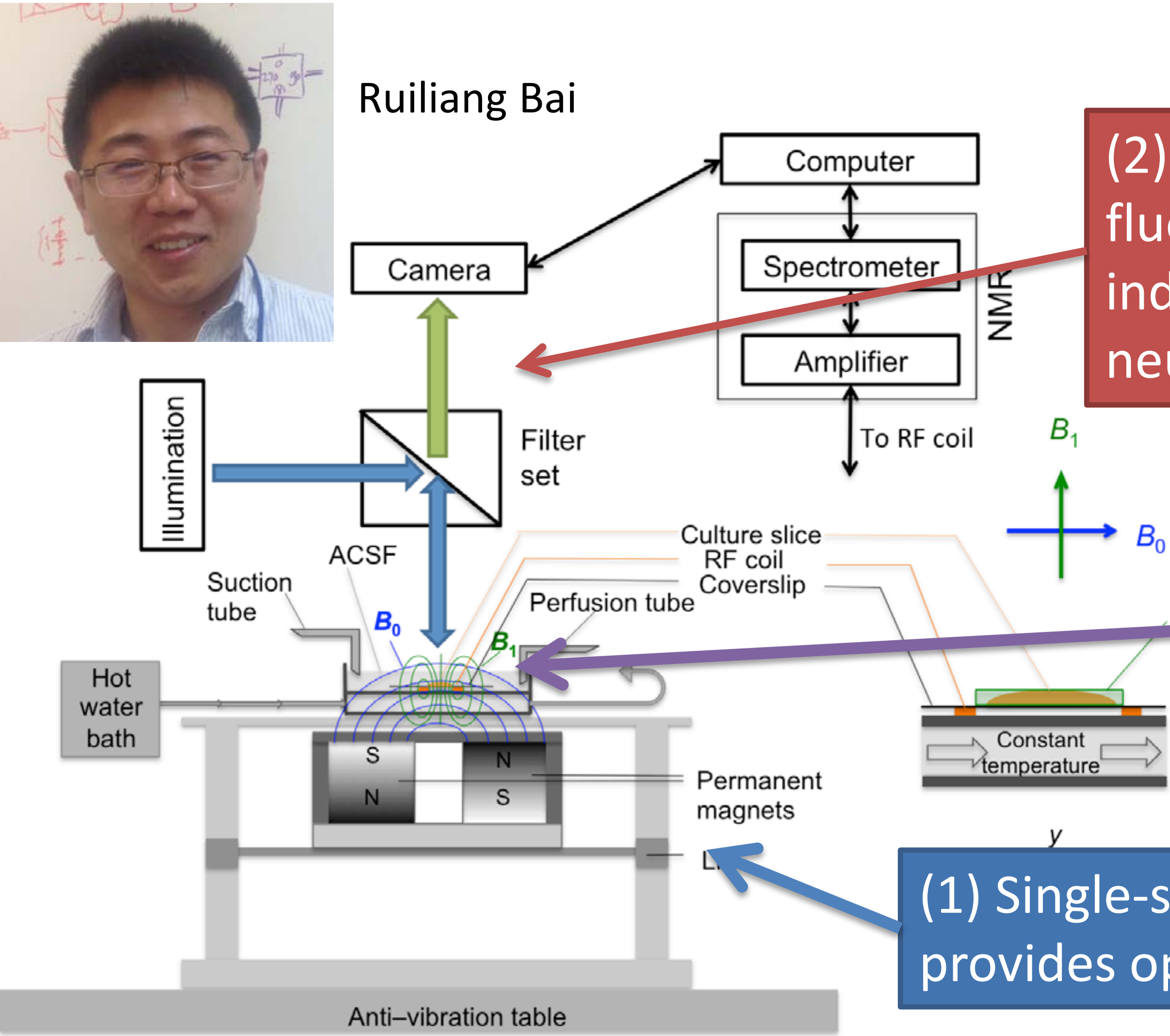



Authors reported fDMRI:

- Is more selective and accurate in localizing active brain areas
- Possesses faster temporal response
- Is more directly correlated with neuronal activity

# A novel fMRI test system providing simultaneous calcium fluorescence imaging and MR acquisition in neuronal tissue and cell cultures

Ruiliang Bai




(2) Intracellular calcium fluorescence imaging provides independent measurement of neuronal activity

(3) Organotypic cortical culture (OCC) is a well-established, avascular biological model of neuronal activity

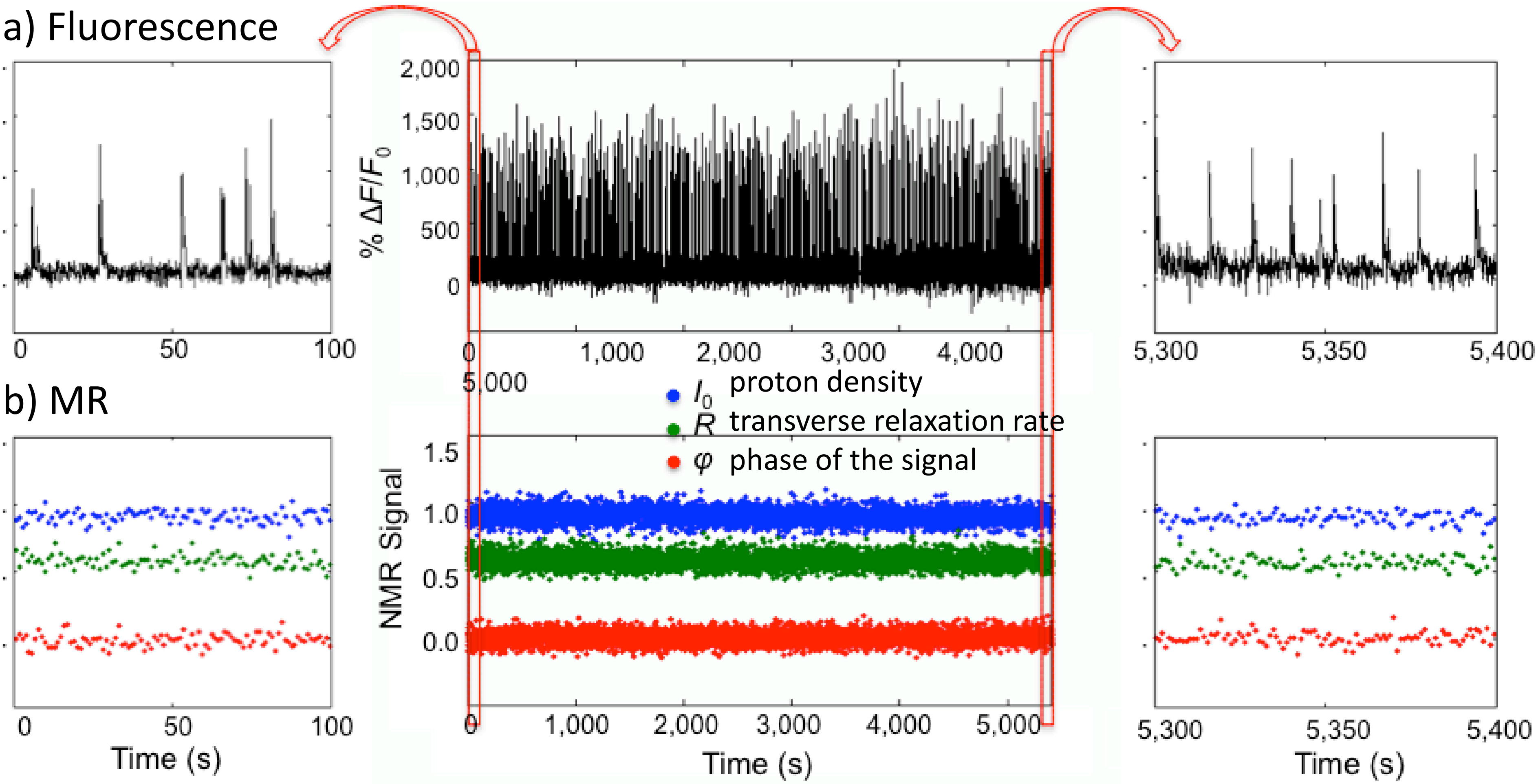
(1) Single-sided MR “profiler” provides open access to specimen

**R. Bai**, et al. *NMB*, 2015

# Stability of MR and Calcium Recordings: no systematic artifacts

(a) Fluorescence

(b) MR




1.5-hour recording:

- Both MR and optical recordings are stable for several hours.
- Number of neurons showing spontaneous activity decreases after several hours.

•

------**R. Bai**, et al. *NBM,* 2015

# Summary of Findings

## Pathological Perturbations

- **1. Excitation:** Kainate or Extracellular $K^+$
- **2. Inhibition Block:** Picrotoxin
- **3. "Stroke":** No oxygen/glucose

**Prolonged depolarization & Influx of $Ca^{2+}$ (calcium imaging)**

**cell swelling (~ 1 µm) via two-photo microscopy**

**"Slowed down" water diffusion / Increase of slow diffusion fraction**

## Normal Neuronal Activity

- **1. Neuronal Spike suppression:** Tetrodotoxin
- **2. MR diffusion signal near neuronal spikes**

**NO prolonged depolarization or continuous influx of $Ca^{2+}$**

**Negligible cell configuration change**

**NO changes in diffusion MR**

Bai R, Stewart CV, Plenz D, and Basser PJ. 2016. Assessing the sensitivity of diffusion MRI to detect neuronal activity directly. Proc Natl Acad Sci USA 113(12):E1728-E1737

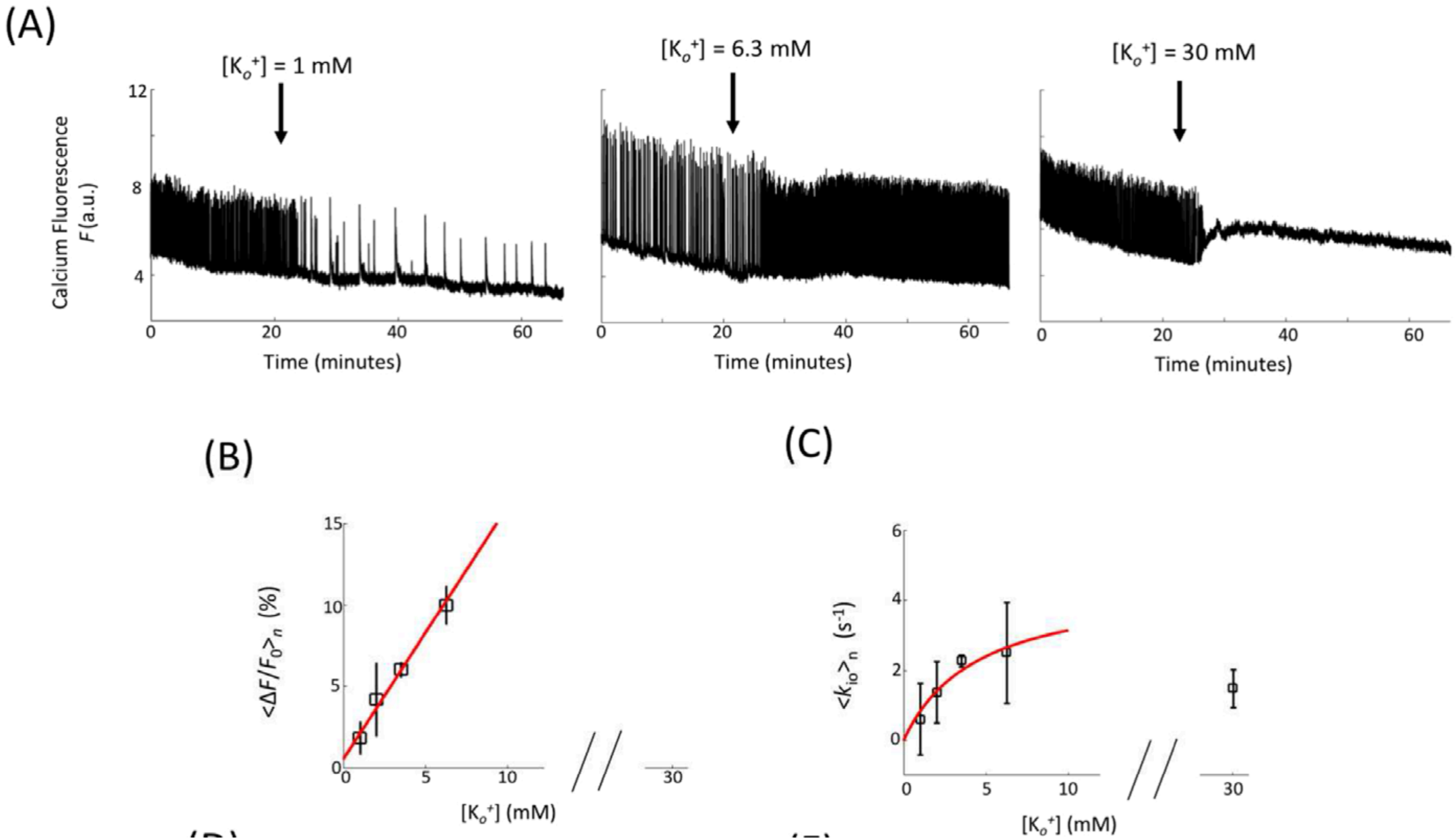
# Transmembrane Water Cycling Has Active and Passive Contributions!

$$k_{io} = k_{io}(\mathrm{a}) + k_{io}(\mathrm{p}),$$

Active Passive

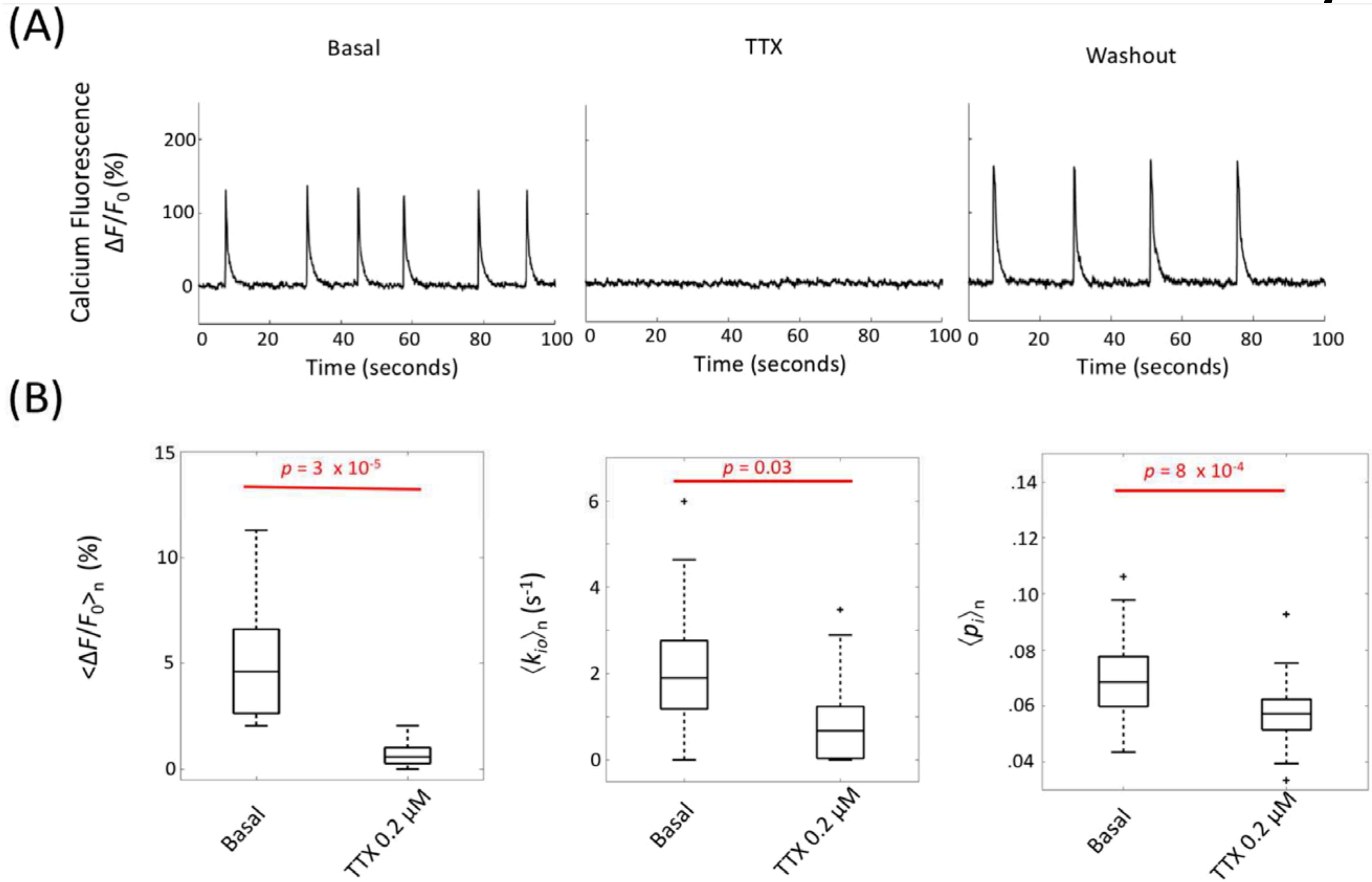
Bai R, Springer CS, Plenz D, and Basser PJ. 2018. Fast, Na+/K+ pump driven, steady-state transcytolemmal water exchange in neuronal tissue: A study of rat brain cortical cultures. Magn Reson Med 79:3207–3217. doi:10.1002/mrm.26980.

# *Active* Transmembrane Water Cycling and its Relation to Neuronal Activity




Bai R, Springer Jr, CS , Plenz D, Basser PJ, *Brain Active Trans-Membrane Water Cycling Measured by MR Is Associated with Neuronal Activity*, MRM, (in press, 2018)

# *Active* Transmembrane Water Cycling and its Relation to Neuronal Activity




Bai R, Springer Jr, CS , Plenz D, Basser PJ, *Brain Active Trans-Membrane Water Cycling Measured by MR Is Associated with Neuronal Activity*, MRM, (in press, 2018)

# *Active* Transmembrane Water Cycling and its Relation to Neuronal Activity

Can this finding lead to a novel fMRI method?

Can water cycling be measured, monitored, and mapped without using contrast agents?

# Summary

Our Brain Parcellation and Functional MRI (fMRI) research address significant, fundamental problems, and NICHD mission-critical challenges.

Our novel MRI ‘stains’ and ‘contrasts’ that are making ‘invisible’ processes and cell and tissue components ‘visible’, are grounded in recent scientific and technological breakthroughs in our laboratory.

# Collaborators

CNRM
CENTER FOR NEUROSCIENCE AND REGENERATIVE MEDICINE

## "Blackboard"
Dan Benjamini
Sinisa Pajevic (CIT, NIH)
Shinjini Kundu (JHU)
Evren Özarslan (LU, Sweden)

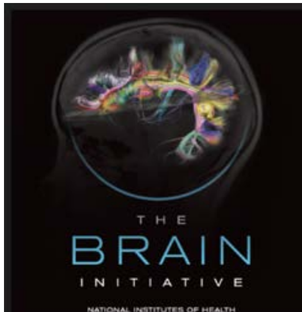
## "Bench"
Michal Komlosh (CNRM)
Nathan Williamson
Rea Ravin (Celoptics)
Ruiliang Bai (ZIINT, PRC)
Ferenc Horkay

## "Biological Models"
Dietmar Plenz (NIMH)
Beth Hutchinson (NIBIB/CNRM)
Charles Springer (UO)
Bernard Dardzinski (USUHS)
Neuropathology Core (CNRM)
Frank Ye (NIMH)

## "Bedside"
Alexandru Avram (NIBIB)
Joelle Sarlls (NINDS/NMRF)
Adam Bernstein (UA)
Carlo Pierpaoli (NIBIB)

http://science.nichd.nih.gov/confluence/display/sqits/home

NIH *Eunice Kennedy Shriver* National Institute of Child Health and Human Development



# Thank You!

# Non-DIR Funded Section Members

NIH
National Institute of Biomedical Imaging and Bioengineering

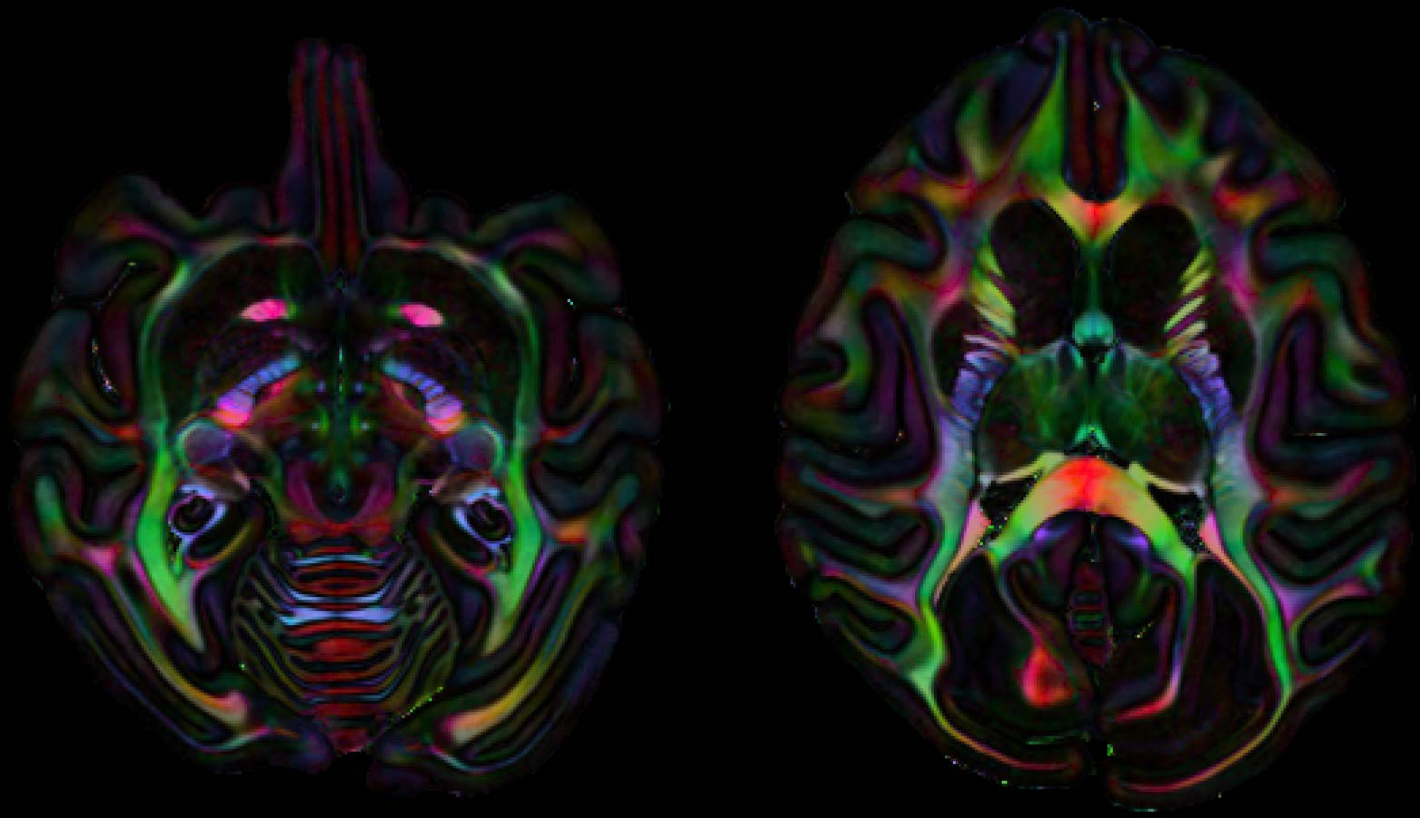
CNRM
CENTER FOR NEUROSCIENCE AND REGENERATIVE MEDICINE

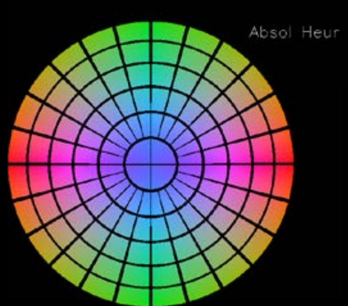
THE BRAIN INITIATIVE
NATIONAL INSTITUTES OF HEALTH

# SQITS' Recent Highlights

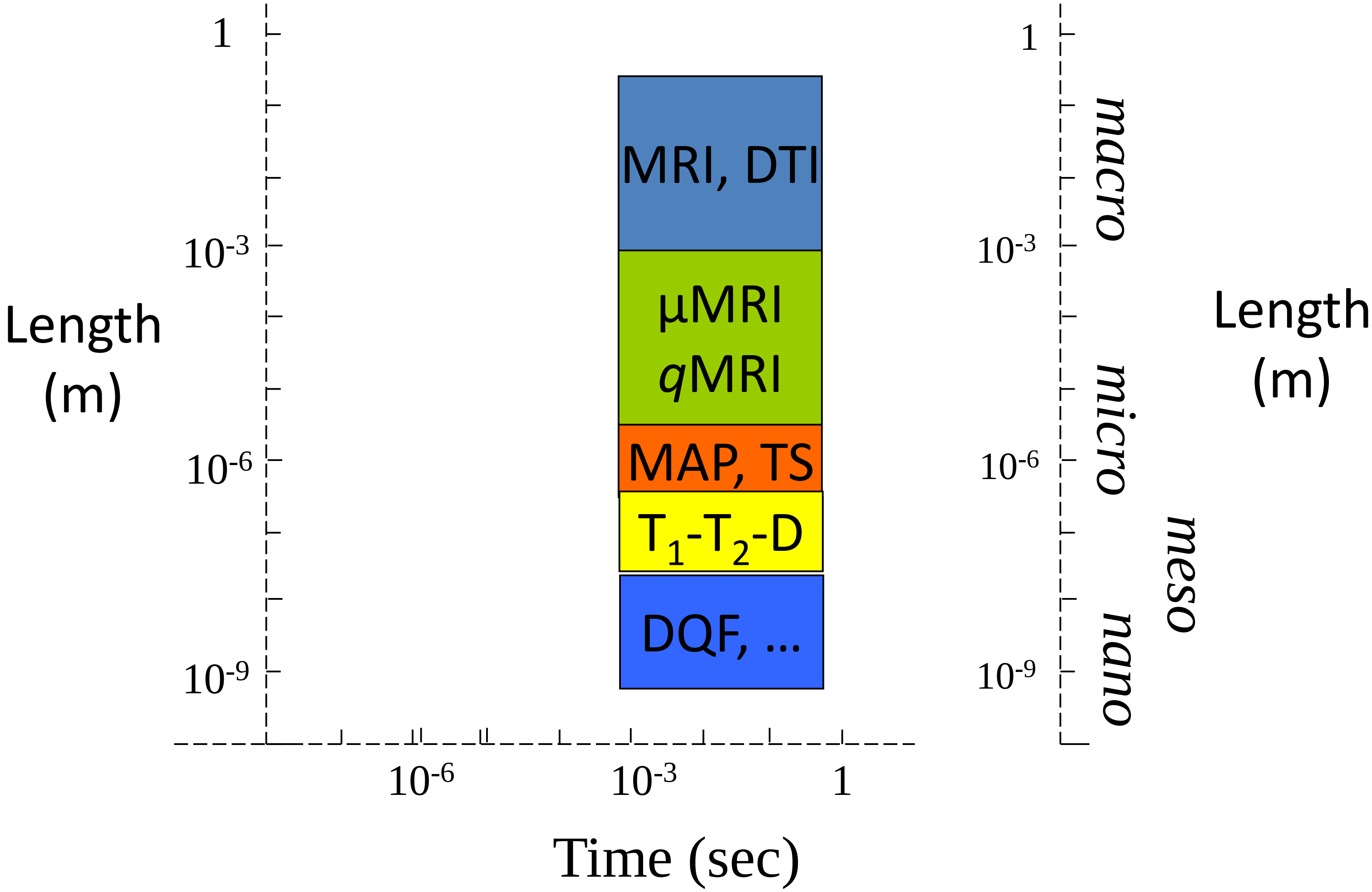
- Developed new 'stains' and 'contrasts' for brain microimaging (μMRI)
- Pioneered compressed sensing for 2D diffusometry/relaxometry MR
- Invented, implemented, and tested MADCO ('Battleship') method
- Invented and developed 2D diffusometry/relaxometry/exchange *MRI*
- Demonstrated their clinical feasibility
- Successfully translated MAP-MRI clinically
- Designed, built, and tested novel tandem MR/fluorescence microscope
- Used it to evaluate validity of functional diffusion MRI (fDMRI)
- Discovered evidence of active water cycling in neurons
- Discovered active water cycling increases during neuronal excitation
- Proposed active water cycling as a potential fMRI mechanism
- Developed quantitative collagen MRI method for ECM applications
- Developed novel biomimetic cartilage model
- Rolled out TORTOISE v.3 for quantitative diffusion MRI applications

# High-Resolution White Matter Mapping

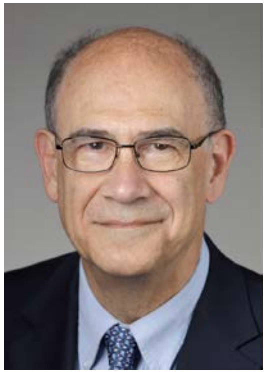




# Probing Different Length Scales
# "from Macro to Nano"



# R24 BRAIN Initiative "DREAM TEAM"



Mark Hallett, NINDS
Motor Control

Sini Pajevic, CIT
Comp. Neuroscience

Doug Fields, NICHD
Glial Biology

Zhen Ni, NINDS
Motor Control

Adam Bernstein
Michael Curry
Giorgio Leodori
Joelle Sarlls
Amber Simmons

Alexandru Avram, NIBIB
Clin. MRI, modeling

Richard Coppola, NIMH
MEG

NIH *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

NIH National Institute of Biomedical Imaging and Bioengineering
*Creating Biomedical Technologies to Improve Health*

# R24 BRAIN Initiative: Measuring the "Latency Connectome"

CellPress

Neuron
Perspective

## Glial Regulation of the Neuronal Connectome through Local and Long-Distant Communication

R. Douglas Fields,[1,*] Dong Ho Woo,[1] and Peter J. Basser[2]
[1]Nervous System Development and Plasticity Section, The Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, MD 20892, USA
[2]Section on Tissue Biophysics and Biomimetics, Program on Pediatric Imaging and Tissue Sciences, The Eunice Kennedy Shriver National Institute of Child Health and Human Development, NIH, Bethesda, MD 20892, USA

Neuron, 2015 Apr 22;86(2):374-86. doi: 10.1016/j.neuron.2015.01.014

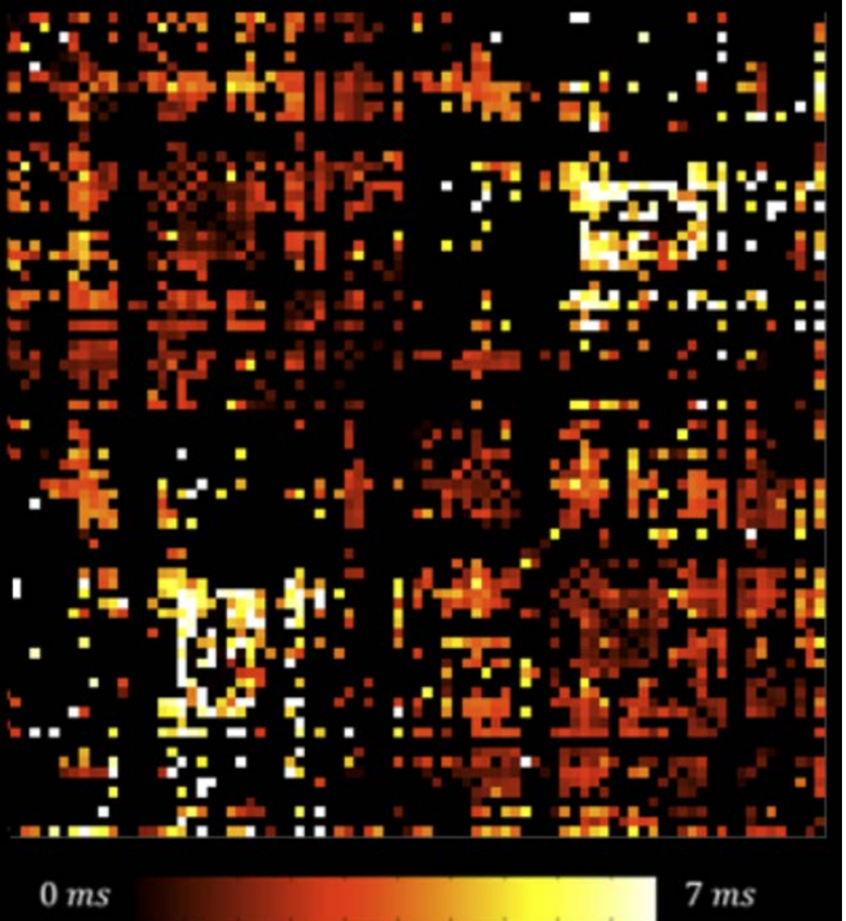
# Latency Maps in Telecom Applications

http://ipnetwork.bgtmo.ip.att.net/pws/network_delay.html

**Current Overall Average:** **35 ms**

| CITY PAIRS | Atl | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Austin | 25 | Aus | | | | | | | | | | | | | | | | | | | | | | | |
| Cambridge | 29 | 54 | Cam | | | | | | | | | | | | | | | | | | | | | | |
| Chicago | 26 | 33 | 26 | Chi | | | | | | | | | | | | | | | | | | | | | |
| Cleveland | 19 | 40 | 20 | 8 | Cle | | | | | | | | | | | | | | | | | | | | |
| Dallas | 18 | 11 | 46 | 22 | 29 | Dal | | | | | | | | | | | | | | | | | | | |
| Denver | 38 | 31 | 48 | 21 | 28 | 21 | Den | | | | | | | | | | | | | | | | | | |
| Detroit | 22 | 43 | 24 | 8 | 4 | 33 | 28 | Det | | | | | | | | | | | | | | | | | |
| Houston | 20 | 6 | 49 | 28 | 34 | 6 | 26 | 38 | Hou | | | | | | | | | | | | | | | | |
| Indianapolis | 27 | 47 | 28 | 6 | 8 | 37 | 27 | 13 | 42 | Ind | | | | | | | | | | | | | | | |
| Kansas City | 27 | 21 | 32 | 13 | 19 | 10 | 15 | 19 | 16 | 18 | Kan | | | | | | | | | | | | | | |
| Los Angeles | 50 | 40 | 79 | 62 | 68 | 32 | 41 | 69 | 35 | 67 | 42 | LA | | | | | | | | | | | | | |
| Madison | 45 | 39 | 42 | 6 | 32 | 29 | 36 | 32 | 34 | 11 | 18 | 67 | Mad | | | | | | | | | | | | |
| Nashville | 8 | 29 | 31 | 18 | 11 | 19 | 39 | 15 | 24 | 19 | 18 | 50 | 27 | Nas | | | | | | | | | | | |
| New Orleans | 13 | 13 | 42 | 38 | 31 | 13 | 33 | 34 | 8 | 39 | 23 | 43 | 41 | 21 | NO | | | | | | | | | | |
| New York | 24 | 49 | 6 | 21 | 15 | 41 | 42 | 19 | 44 | 27 | 27 | 82 | 37 | 26 | 36 | NY | | | | | | | | | |
| Orlando | 11 | 27 | 40 | 36 | 30 | 27 | 48 | 33 | 22 | 37 | 37 | 59 | 45 | 19 | 15 | 35 | Orl | | | | | | | | |
| Philadelphia | 22 | 47 | 10 | 19 | 11 | 40 | 39 | 15 | 41 | 19 | 25 | 79 | 35 | 22 | 34 | 4 | 33 | Pa | | | | | | | |
| Phoenix | 42 | 30 | 68 | 44 | 51 | 23 | 43 | 54 | 25 | 59 | 32 | 11 | 50 | 40 | 32 | 63 | 46 | 62 | Phx | | | | | | |
| San Antonio | 25 | 10 | 54 | 36 | 37 | 8 | 28 | 40 | 5 | 41 | 18 | 31 | 36 | 26 | 12 | 48 | 26 | 48 | 20 | SA | | | | | |
| San Diego | 46 | 37 | 75 | 51 | 58 | 29 | 45 | 61 | 32 | 56 | 39 | 4 | 57 | 47 | 39 | 69 | 56 | 69 | 8 | 27 | SD | | | | |
| San Francisco | 60 | 51 | 78 | 51 | 58 | 44 | 30 | 58 | 46 | 56 | 45 | 11 | 65 | 62 | 53 | 72 | 68 | 69 | 22 | 41 | 15 | SF | | | |
| St. Louis | 20 | 31 | 27 | 9 | 17 | 20 | 21 | 17 | 25 | 15 | 6 | 52 | 15 | 12 | 32 | 22 | 30 | 20 | 42 | 27 | 49 | 50 | StL | | |
| Seattle | 73 | 65 | 73 | 47 | 54 | 54 | 34 | 54 | 59 | 53 | 49 | 35 | 72 | 65 | 67 | 68 | 81 | 65 | 45 | 62 | 38 | 24 | 57 | Sea | |
| Washington | 19 | 44 | 11 | 22 | 14 | 32 | 42 | 18 | 39 | 22 | 22 | 68 | 32 | 25 | 31 | 6 | 30 | 3 | 53 | 43 | 60 | 72 | 17 | 69 | Was |

Mean Latency Matrix

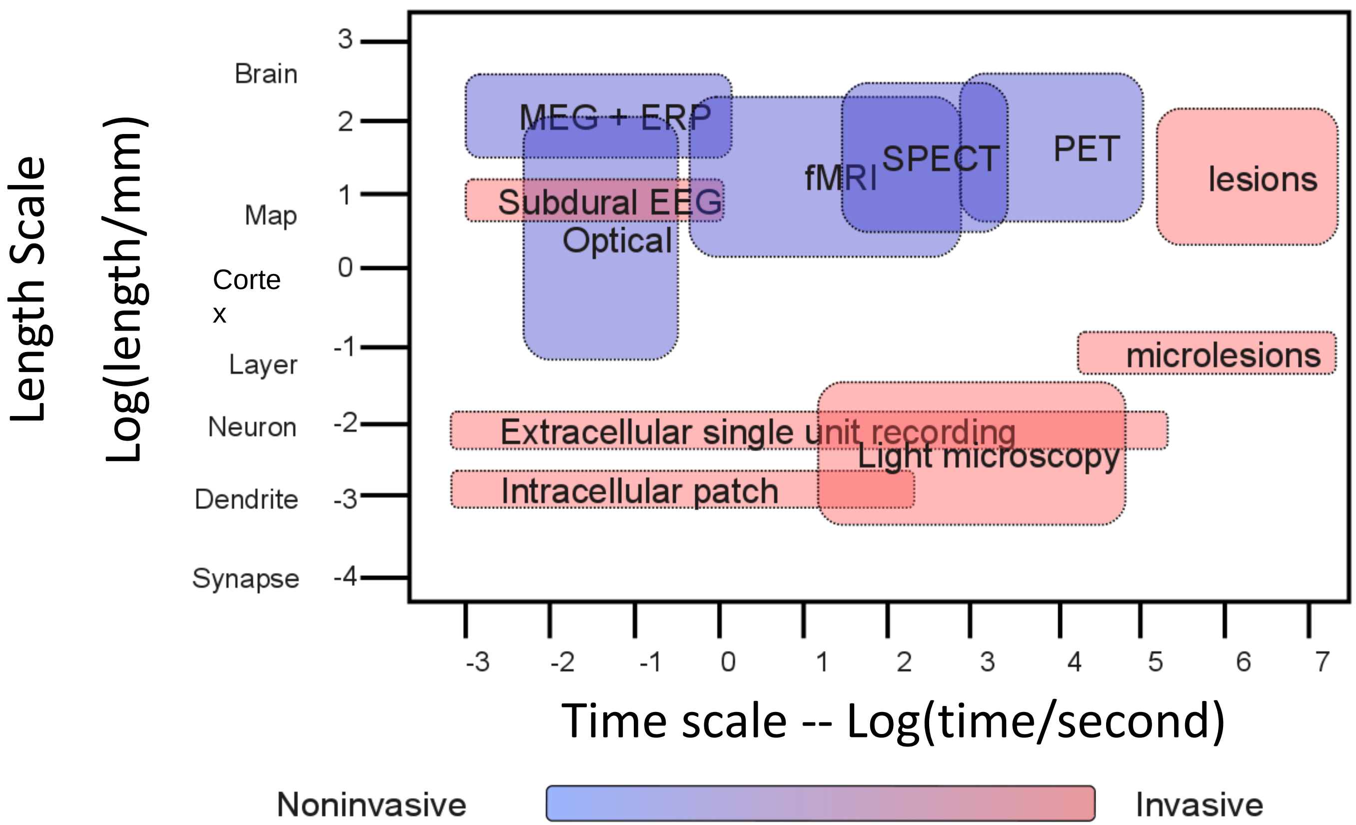



# Mean Latency Matrix

- The estimated mean latencies along all white matter pathways are collated into a Mean Latency Matrix (MLM)
- The MLM may provide important clinical and biological information about large scale brain network dynamics at the *millisecond* time-scale

Avram and Basser, Proc. ISMRM 22 (2014)

# Length and Time Scales of Different Neurophysiological and Functional Imaging Methods



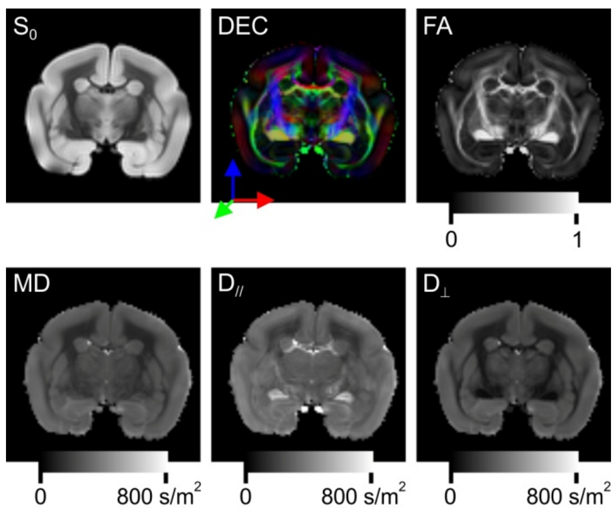

*GLOSSARY:*
*Optical:* near-infrared spectroscopy
*EEG:* electro-encephalography;
*MEG:* magneto-encephalography
*PET:* positron emission tomography
*SPECT:* single-photon emission computed tomography

**Whole Brain Functional MRI (BOLD fMRI):**

- spatial resolution: 1 – 5 mm
- temporal resolution: 1 – 1000 sec.
- does not provide a direct measure of neural excitation

# Old and New Diffusion MRI "Stains"

## DTI

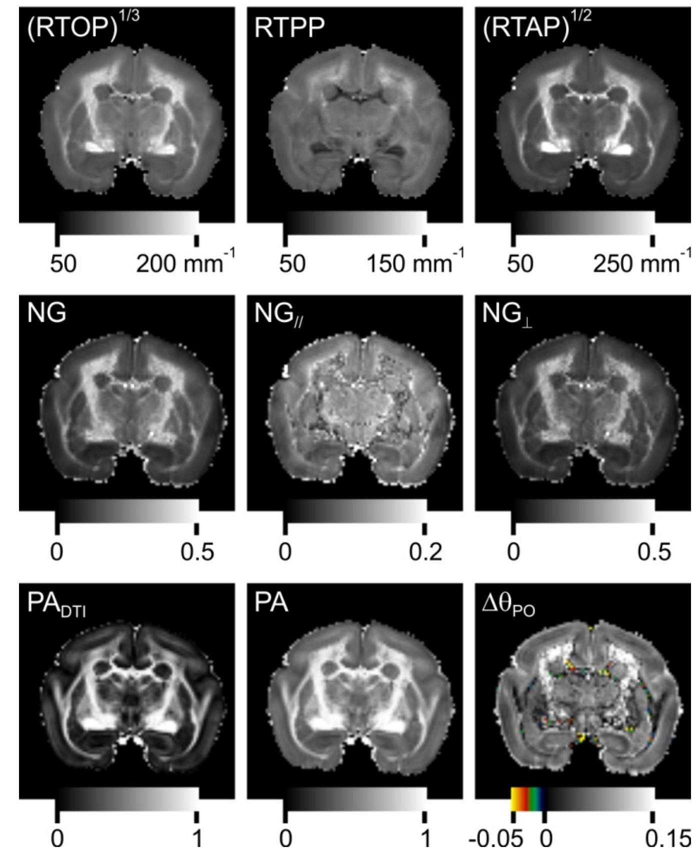



## MAP MRI

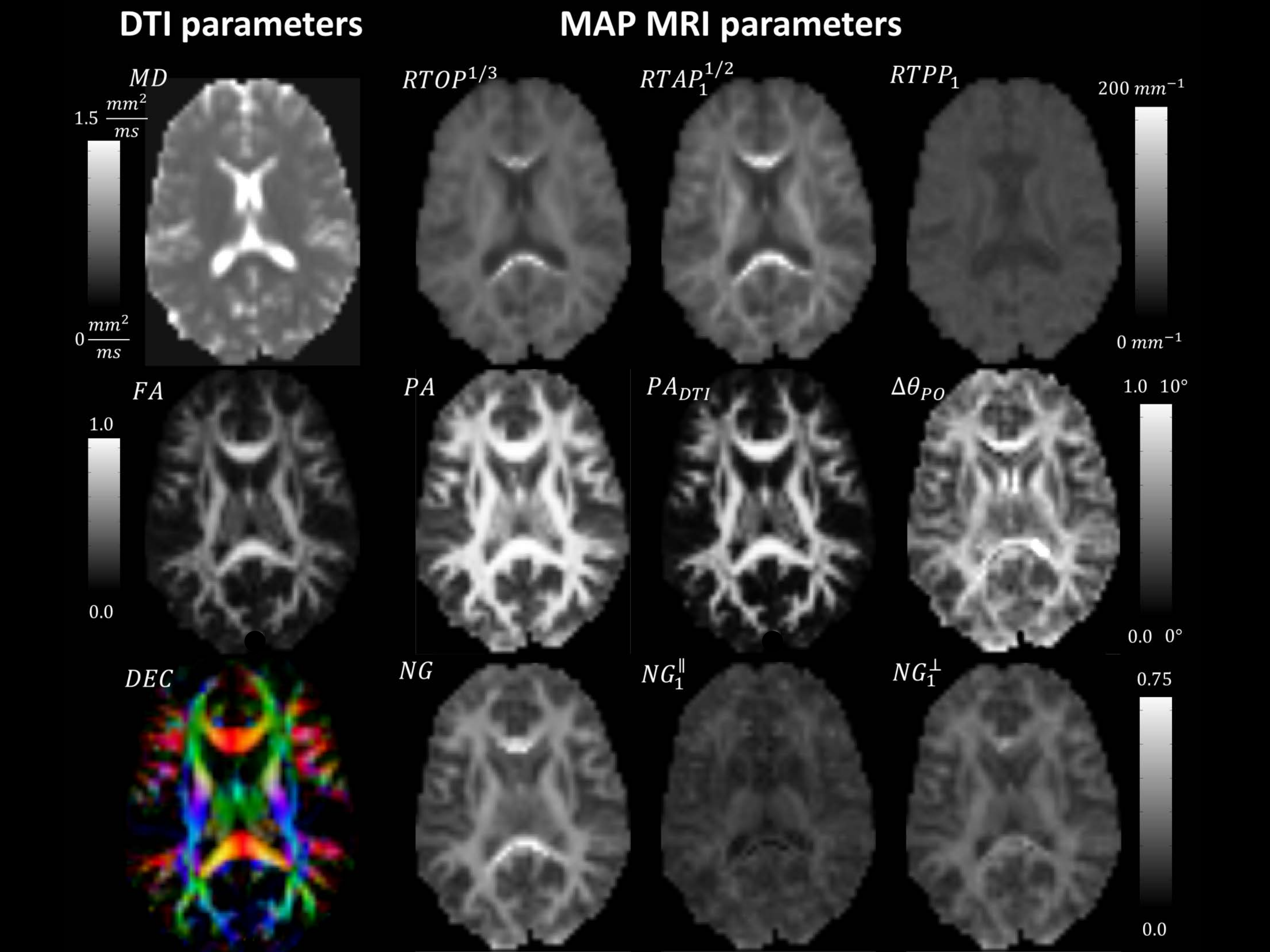
Zero displacement probabilities

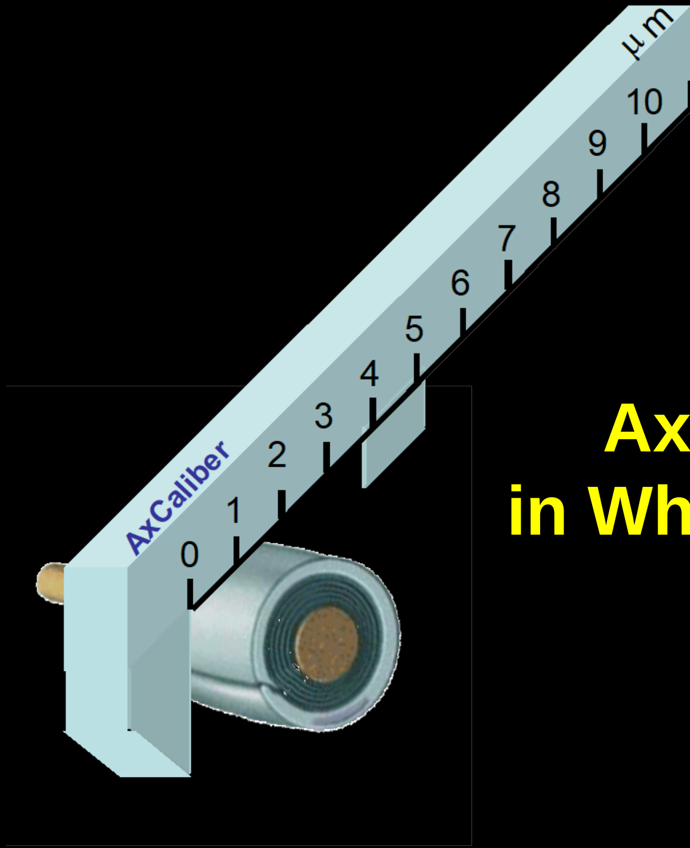
Non-Gaussianity

Average Propagator Anisotropy




Özarslan E, Koay CG, Shepherd TM, Komlosh ME, Irfanoglu MO, Pierpaoli C, and Basser PJ. (2013) Mean Apparent Propagator (MAP) MRI: a novel diffusion imaging method for mapping tissue microstructure. Neuroimage 78:16-32


DTI parameters
MAP MRI parameters
MD
1.5 $\frac{mm^2}{ms}$
0 $\frac{mm^2}{ms}$
$RTOP^{1/3}$
$RTAP_1^{1/2}$
$RTPP_1$
200 $mm^{-1}$
0 $mm^{-1}$
FA
1.0
0.0
PA
$PA_{DTI}$
$\Delta\theta_{PO}$
1.0 10°
0.0 0°
DEC
NG
$NG_1^{\parallel}$
$NG_1^{\perp}$
0.75
0.0



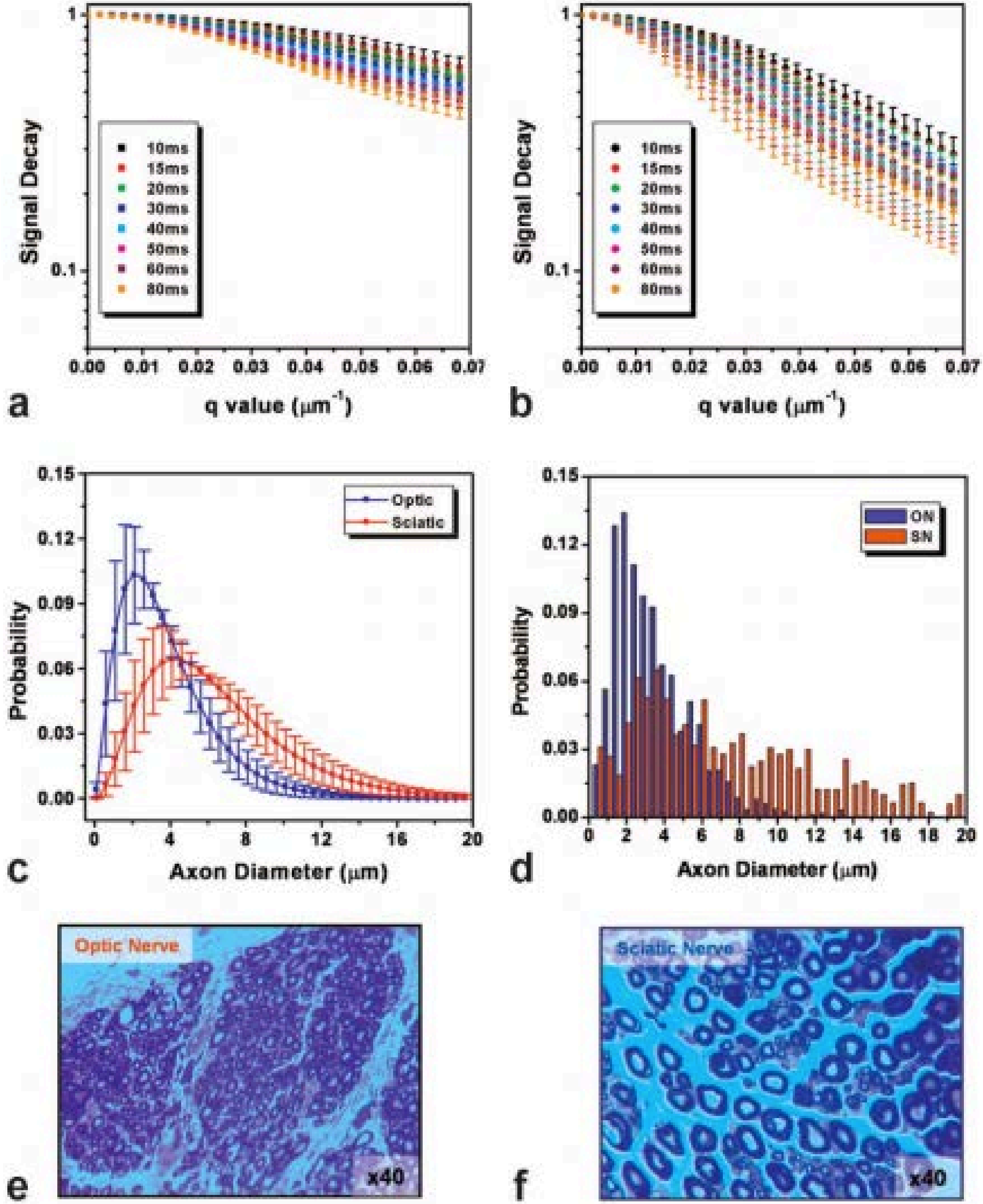

# *AxCaliber MRI*: A Method to Measure the Axon Diameter Distribution (ADD) in White Matter from Diffusion MRI Data

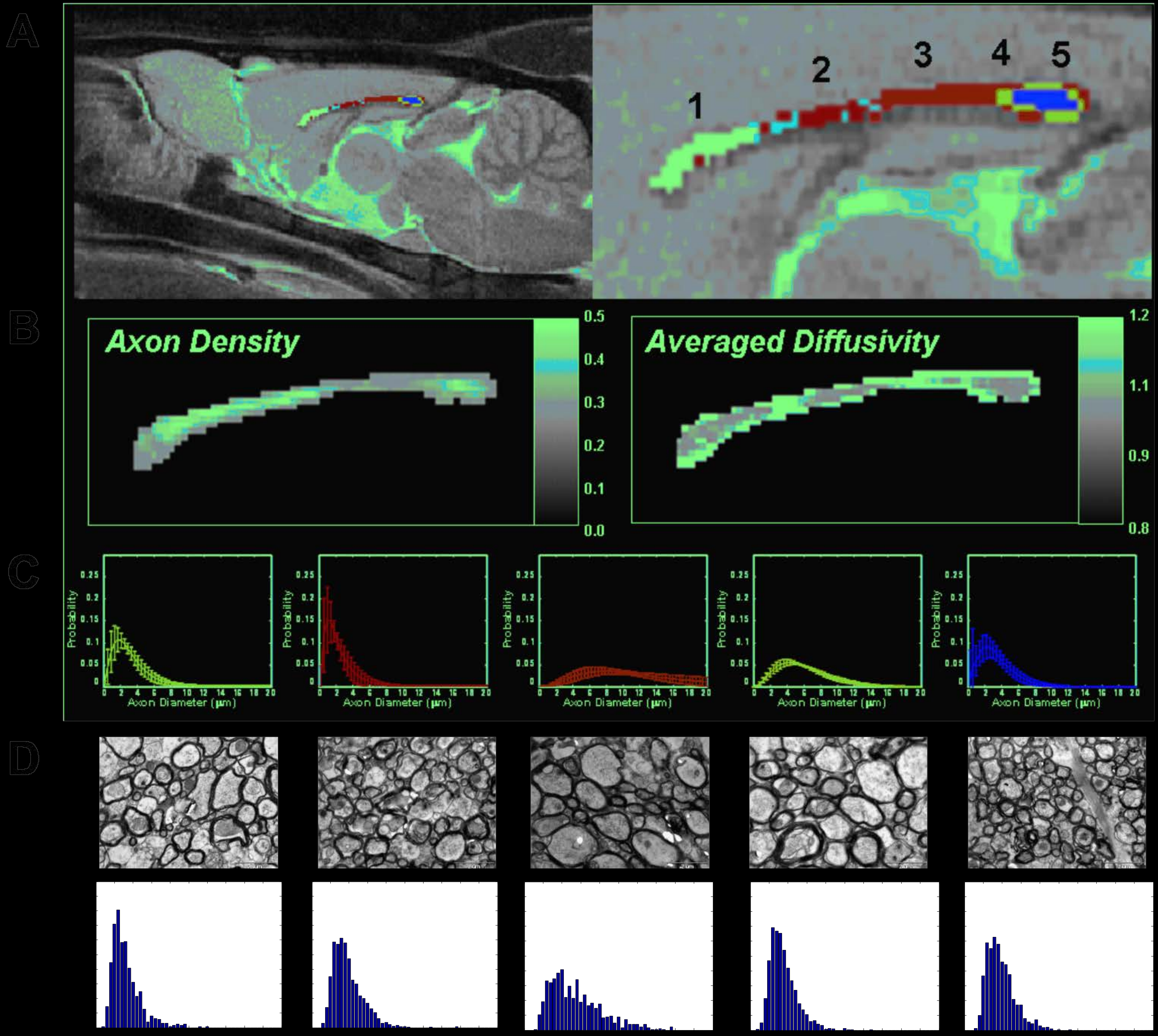
**Y. Assaf, D. Barazany, T. Blumenfeld,**
**G. Levine, Y. Yovel, P.J. Basser**

**Department of Neurobiology**
**The George S. Wise Faculty of Life Sciences**
**Tel Aviv University**

NIH *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

# AxCaliber MR Validation: Optic and Sciatic Nerve

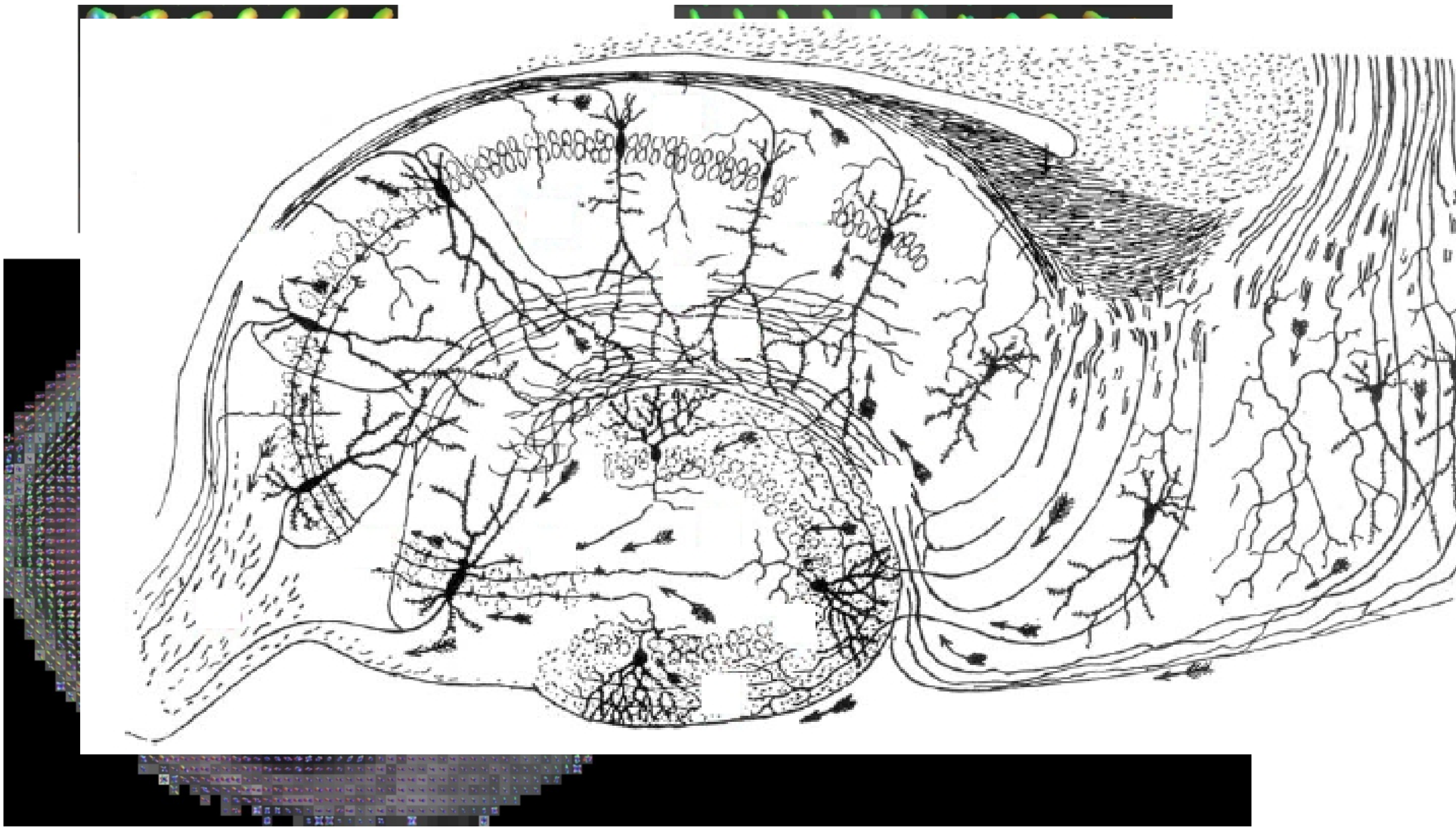



Barazany D, et al., Brain, 2009

# Anisotropic Diffusion: Apparent Propagators Reconstructed in Human Hippocampus

*Ramón y Cajal, 1911. Histologie Du Systeme Nerveux De L'Homme Et Des Vertebretes. A. Maloine, Paris.*



r radial
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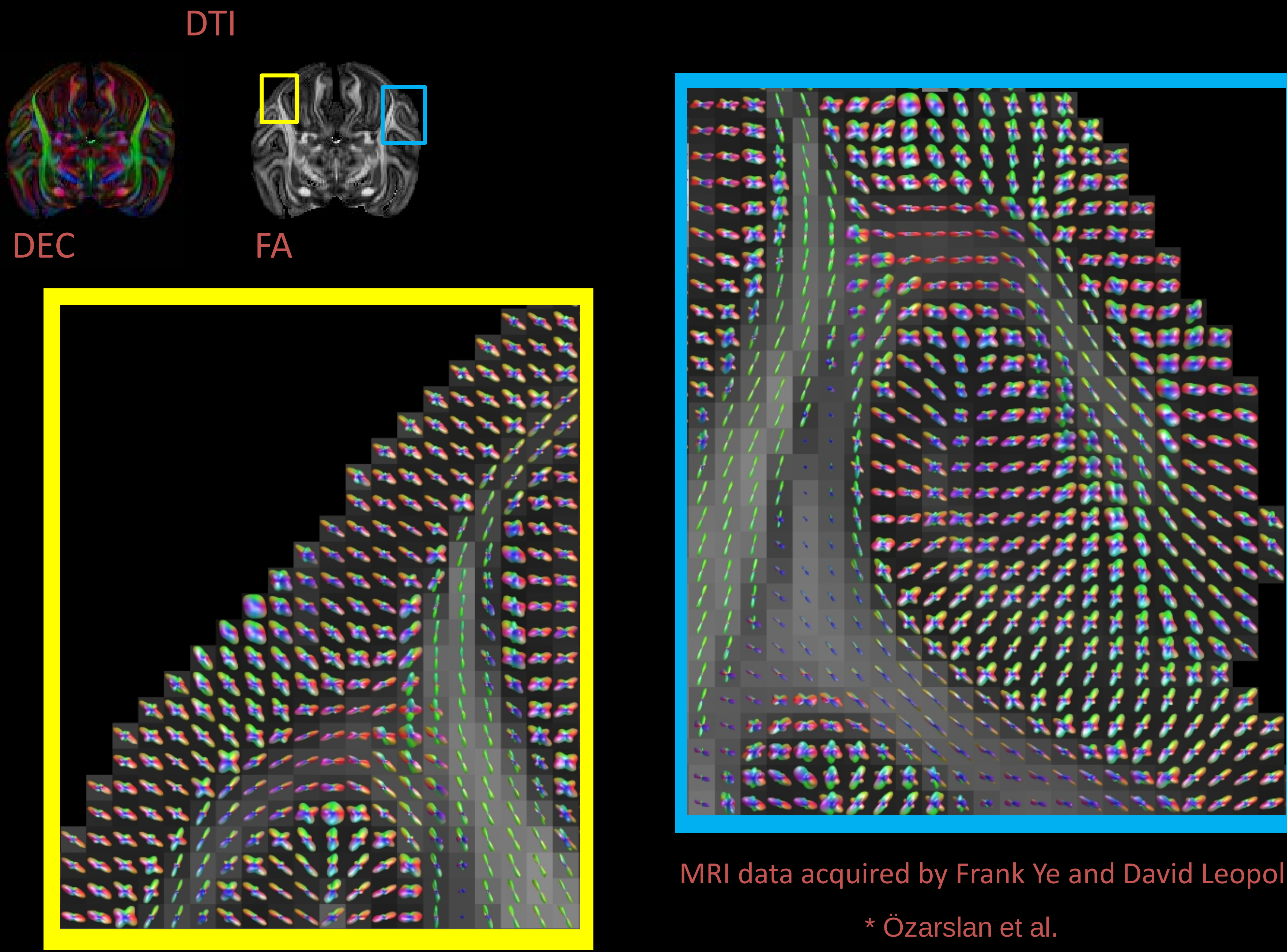
human

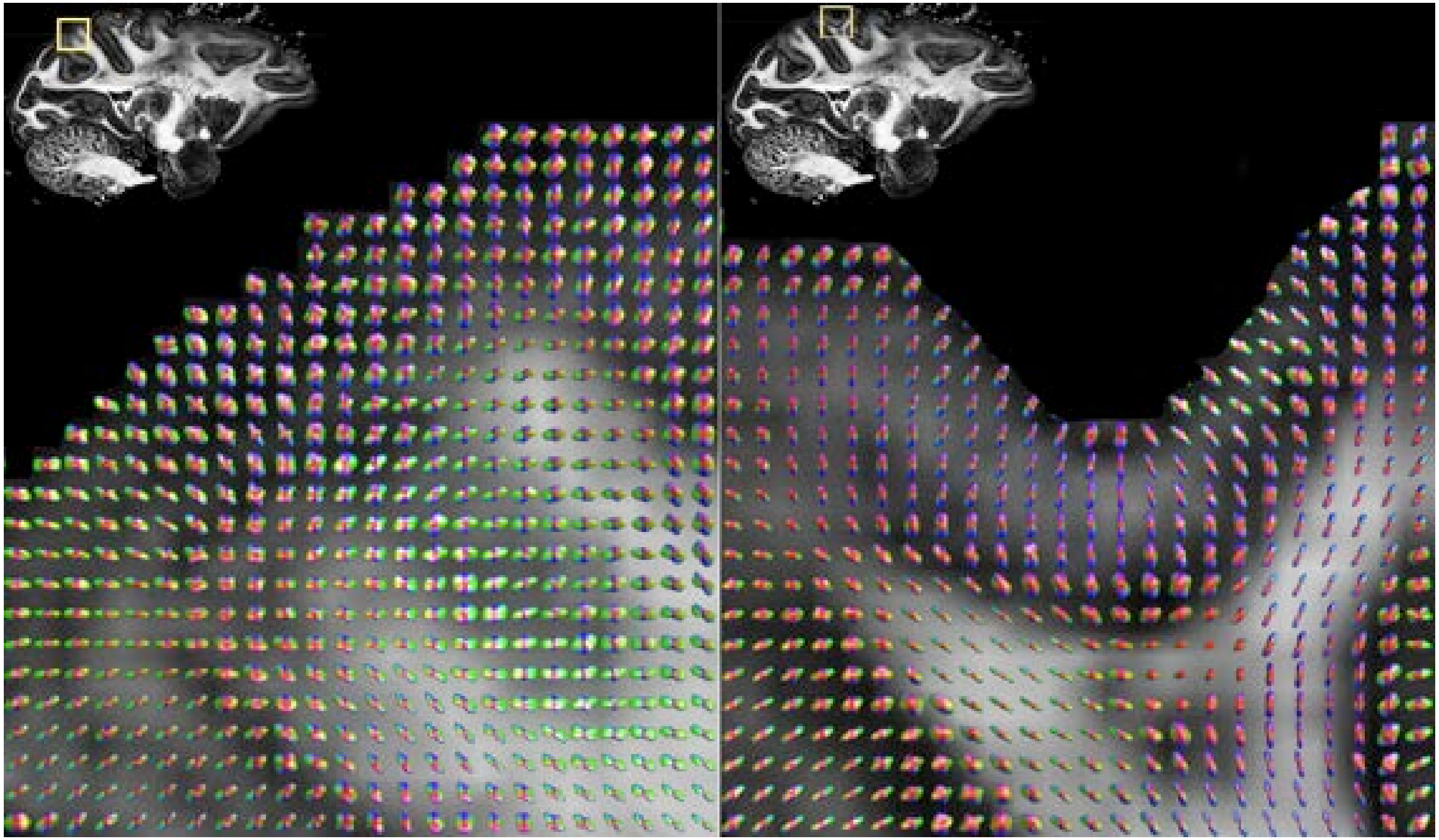
# Apparent Propagators Reconstructed in Macaque Brain




MRI data acquired by Frank Ye and David Leopold

* Özarslan et al.

# Toward Cortical Parcellation via MAP-MRI



Evren Özarslan and Okan Irfanoglu