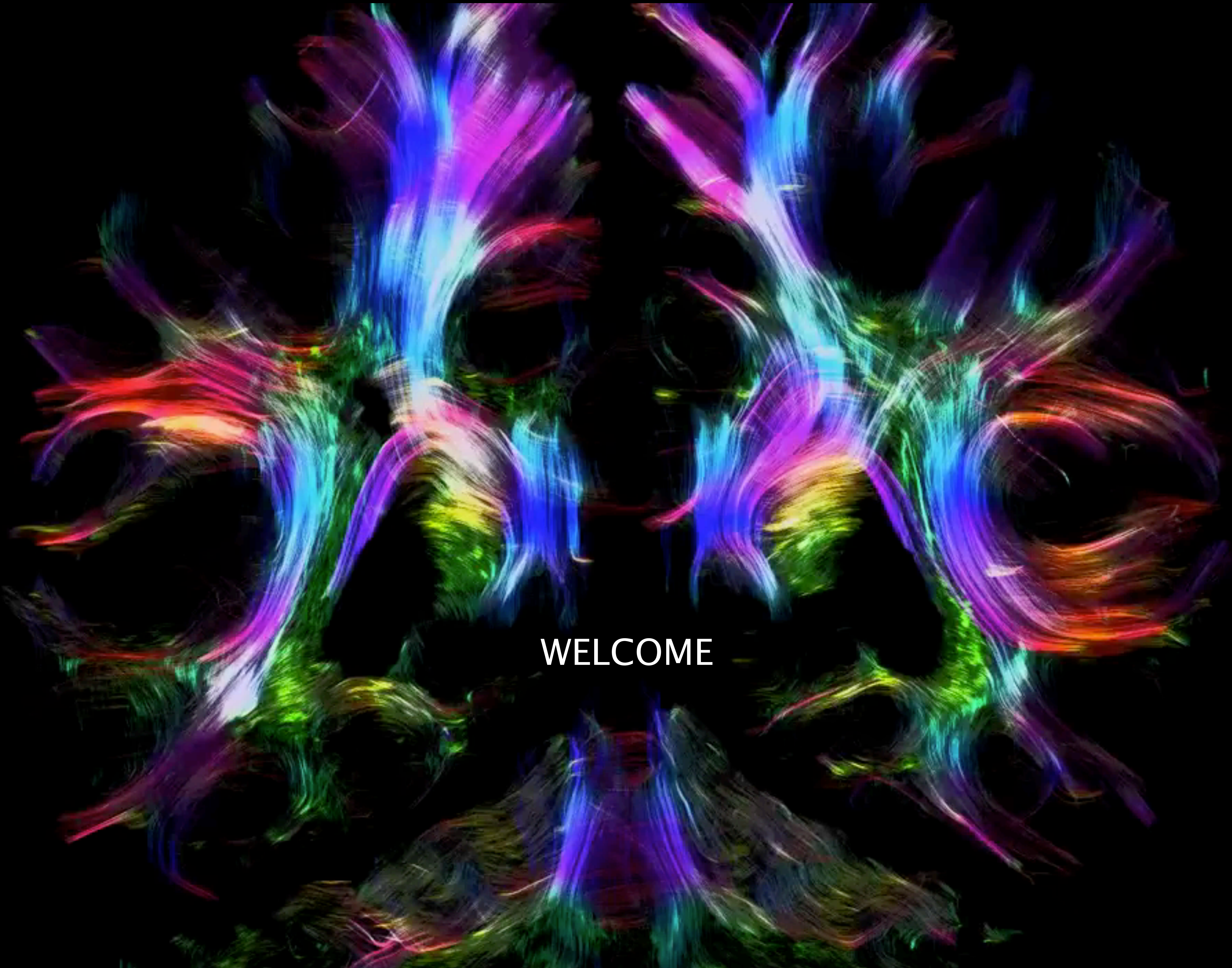

WELCOME

WELCOME + GENERAL ORGANIZATION

EVERY FRIDAY 10:30

NEURO – BT100

ROOM

boris.bernhardt@mcgill.ca

bratislav.misic@mcgill.ca

OVERALL OBJECTVIES

Read and evaluate research papers

Learn about neuroimaging + analytics

Discuss the work in class with your peers

Design an analysis and write a mock paper

REQUIREMENTS

Write 1/2 page critique (positive/negative) and suggestions for future work on each paper

Email this page to us BEFORE the class

Attend class

Be able to verbally summarize paper, understand the imaging methodology and analyses used

Discuss the paper with your peers

End of class: Write a mock paper using your own/open data

REQUIREMENTS

Materials/Slides stuff -

https://github.com/MICA-MNI/micaopen

MOCK PAPER

We will send you guidelines after the class:

1) Start thinking about it <u>now</u>

2) Discuss your ideas with your colleagues and with us

3) Prepare your paper draft (about 10 pages)

4) Submit full version on <u>Monday, October 29</u>

5) We give feedback by <u>Friday, November 2</u>

6) Submit the final version is <u>Monday, November 19</u>

7) Presentation and discussion of the work on the last day of class
   (November 30, 8 minutes talk+ 4 min Q&A)

MOCK PROPOSAL

GRADING

- COME TO THE CLASSES (EMAIL US IF YOU CANNOT MAKE IT)
- SUMMARY ASSIGNMENTS
- RESEARCH PAPER
- DISCUSSION

BRAIN CONNECTVIITY

BORIS BERNHARDT, PHD
MONTREAL NEUROLOGICAL INSTITUTE
MCGILL UNIVERSITY
lab: http://mica-mni.github.io
twitter: @BorisBernhardt

WHY STUDY CONNECTIVITY?

WHY STUDY CONNECTIVITY?

The cerebral cortex is composed of

100.000.000.000

neurons.

These neurons are interconnected by

100.000.000.000.000

synapses

WHY STUDY CONNECTIVITY?

The cerebral cortex is composed of

hundreds

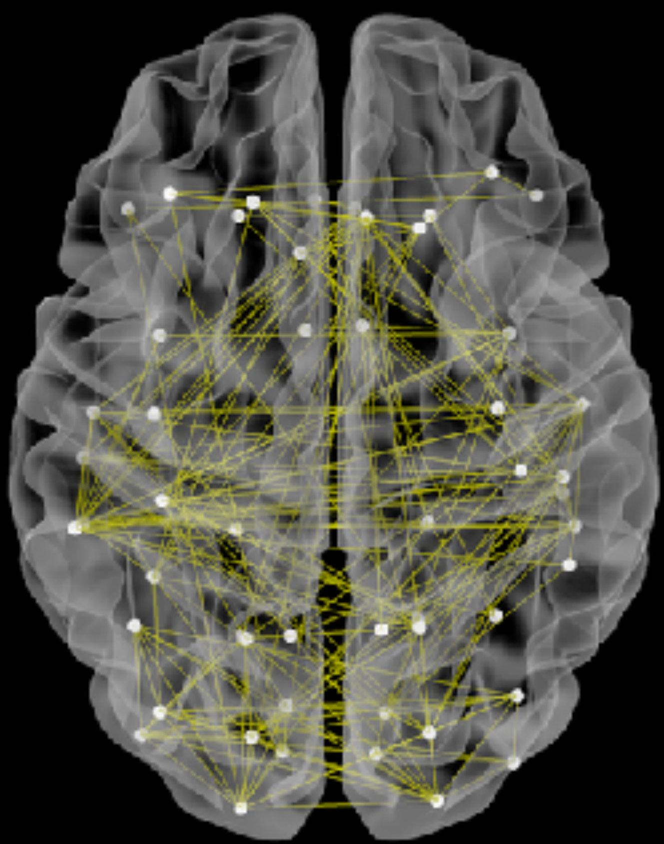
of regions.

These regions are interconnected by

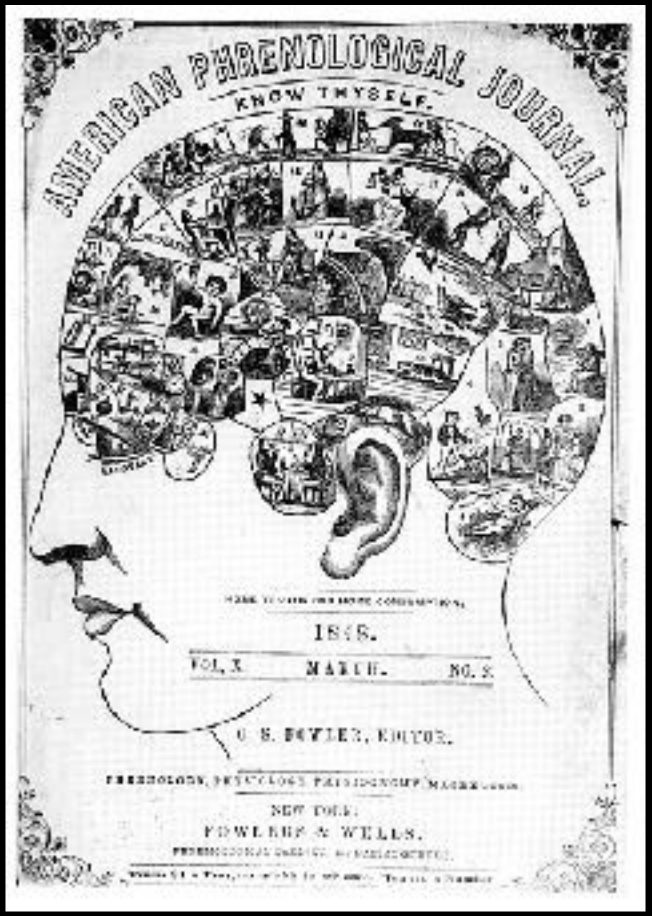
thousands

of white matter tracts.

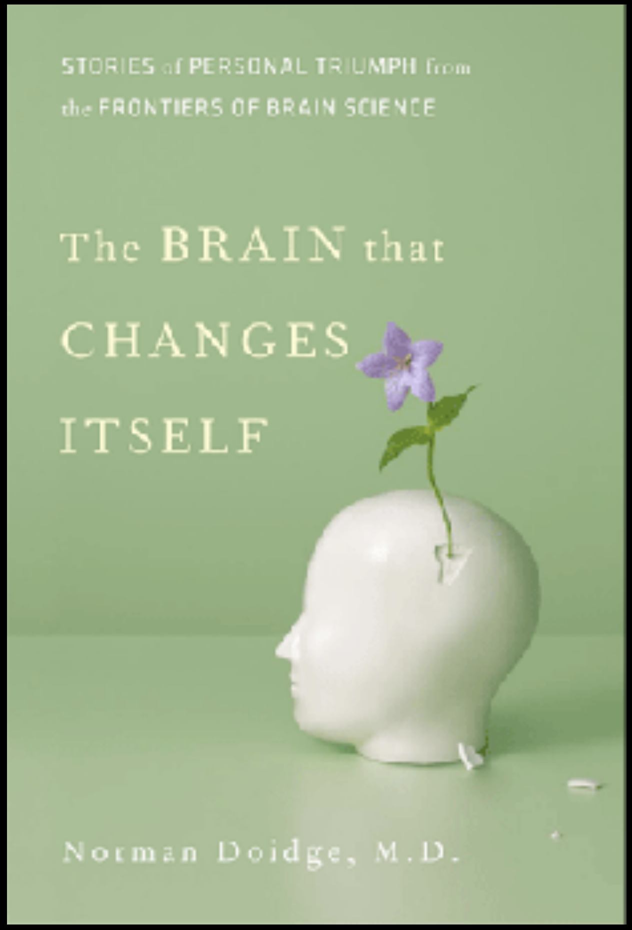
WHY STUDY CONNECTIVITY?



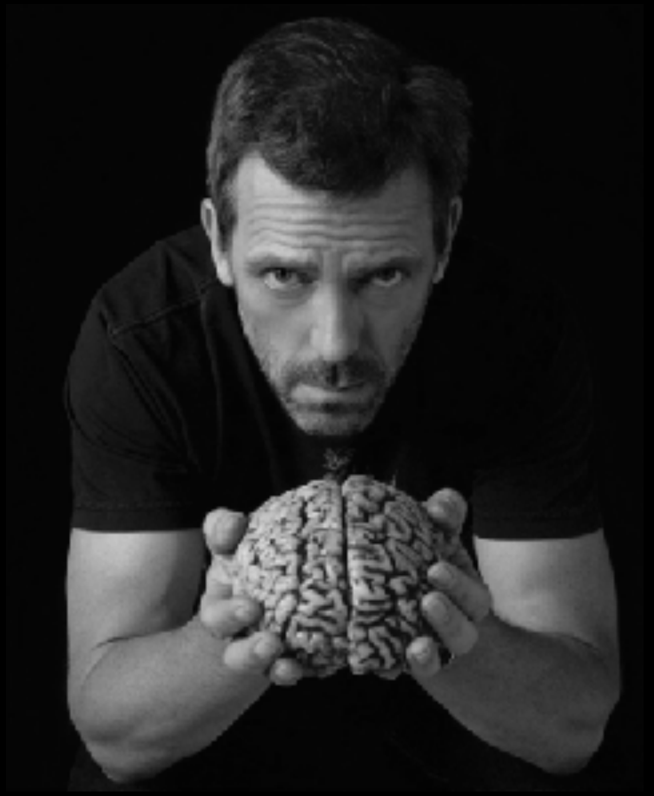
BRAIN ORGANIZATION



INDIVIDUAL DIFFERENCES



PLASTICITY



BRAIN DISORDERS

HOW TO MEASURE BRAIN CONNECTIVITY?

(ANIMAL) CONNECTIVITY

ANATOMICAL CONNECTIONS:
THE WIRING BETWEEN REGIONS

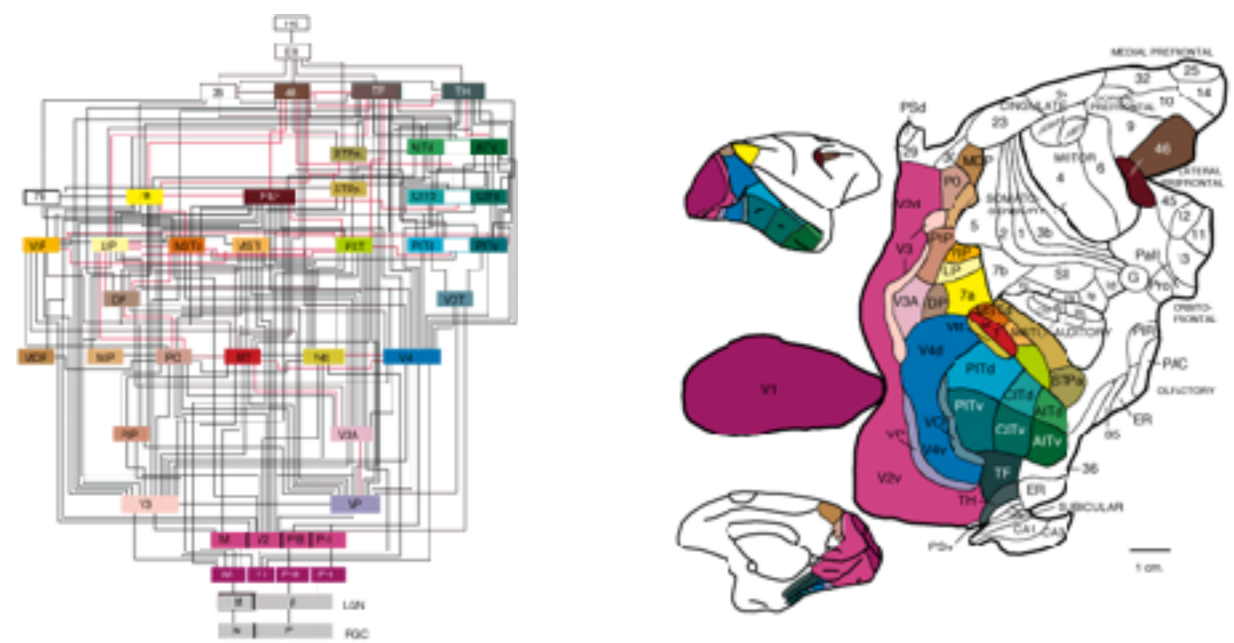
CLASSICALLY DERIVED FROM
TRACT-TRACER STUDIES

INVASIVE: ONLY IN ANIMALS

LABORIOUS + TIME CONSUMING

ACROSS SUBJECT AVERAGING
AND ANATOMICAL CORRESPONDENCE
ASSESSMENT CHALLENGING

Petrides & Pandya, 1999, EJN



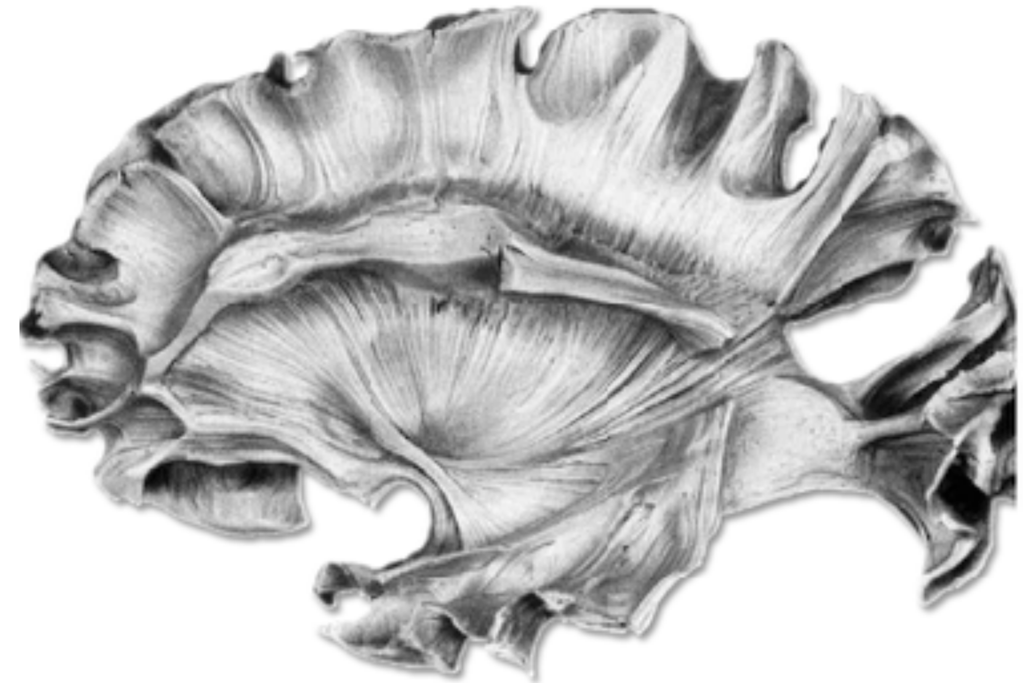
Felleman and Van Essen, 1991, Cerebral Cortex

Stephan and Koetter, 2000, CoCoMac

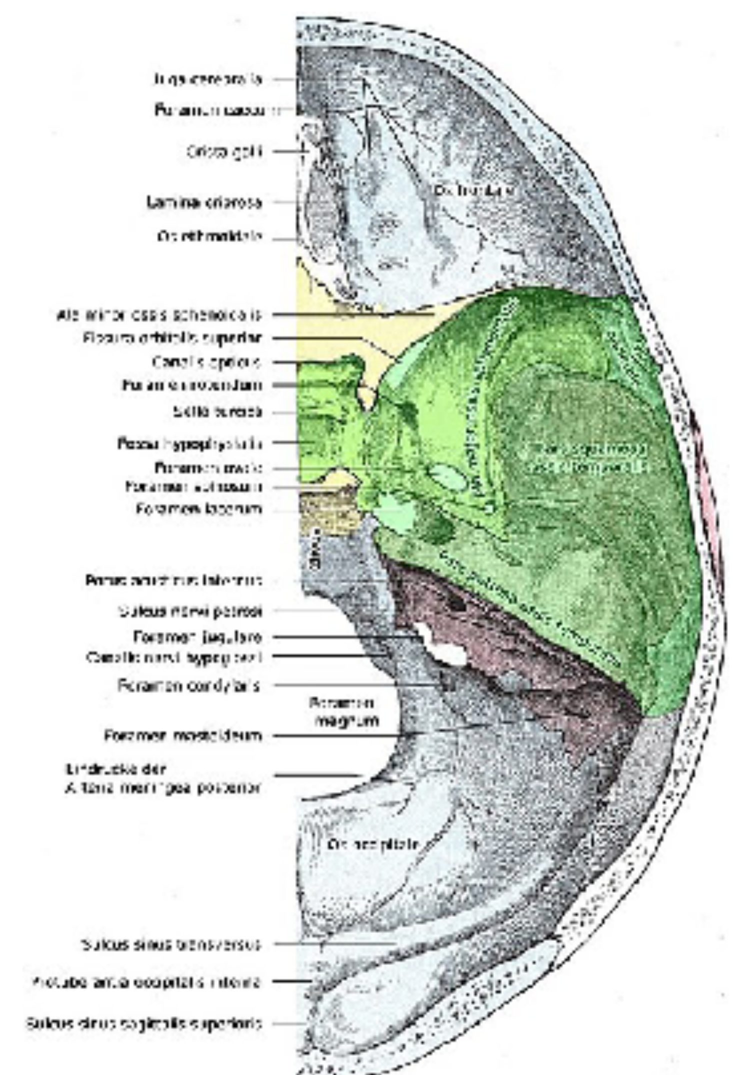
HUMAN CONNECTIVITY

POSTMORTEM DATA ON
COURSE OF CRANIAL NERVES

KLINGLER DISSECTION
TECHNIQUES FOR CEREBRAL
WHITE MATTER BUNDLES



Klingler 1956



HUMAN IN-VIVO CONNECTIVITY

MRI KEY MODALITY
TO APPROXIMATE BRAIN CONNECTIVITY

NON-INVASIVE

HIGH-RESOLUTION

WHOLE-BRAIN

3-DIMENSIONAL

FUNCTIONAL & STRUCTURAL CONNECTIVITY

MEASURING AND ANALYZING STRUCTURAL CONNECTIVITY: TENSORS, FODS, AND FIBERS

DIFFUSION MRI CONNECTIVITY

IDEA:
FOLLOW PATHWAYS
OF UNHINDERED WATER DIFFUSION

+
PROBES
WM CONNECTIVITY

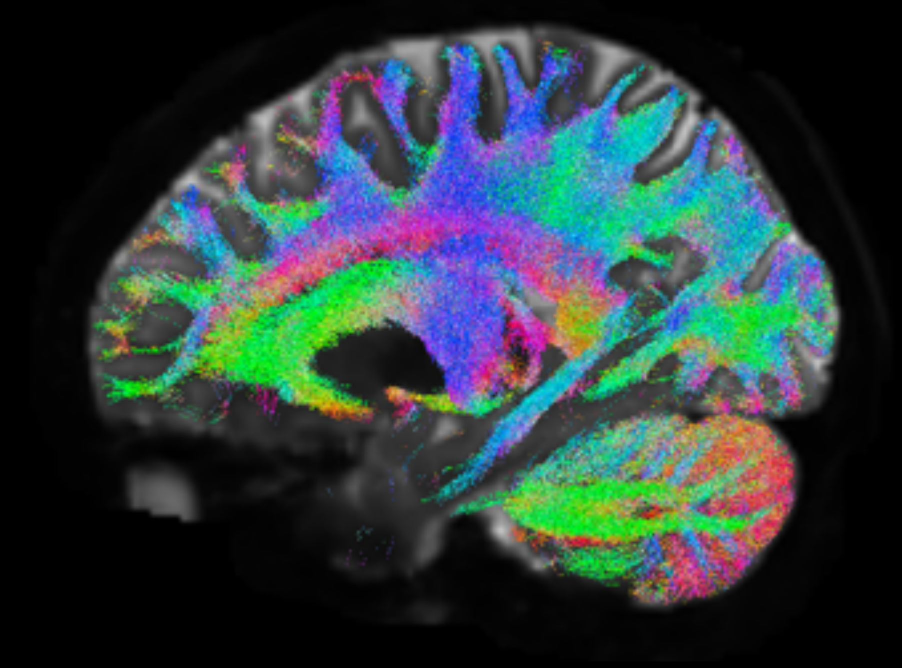
DIFFUSION PARAMETER
ANALYSIS CAN BE PERFORMED AS WELL

–

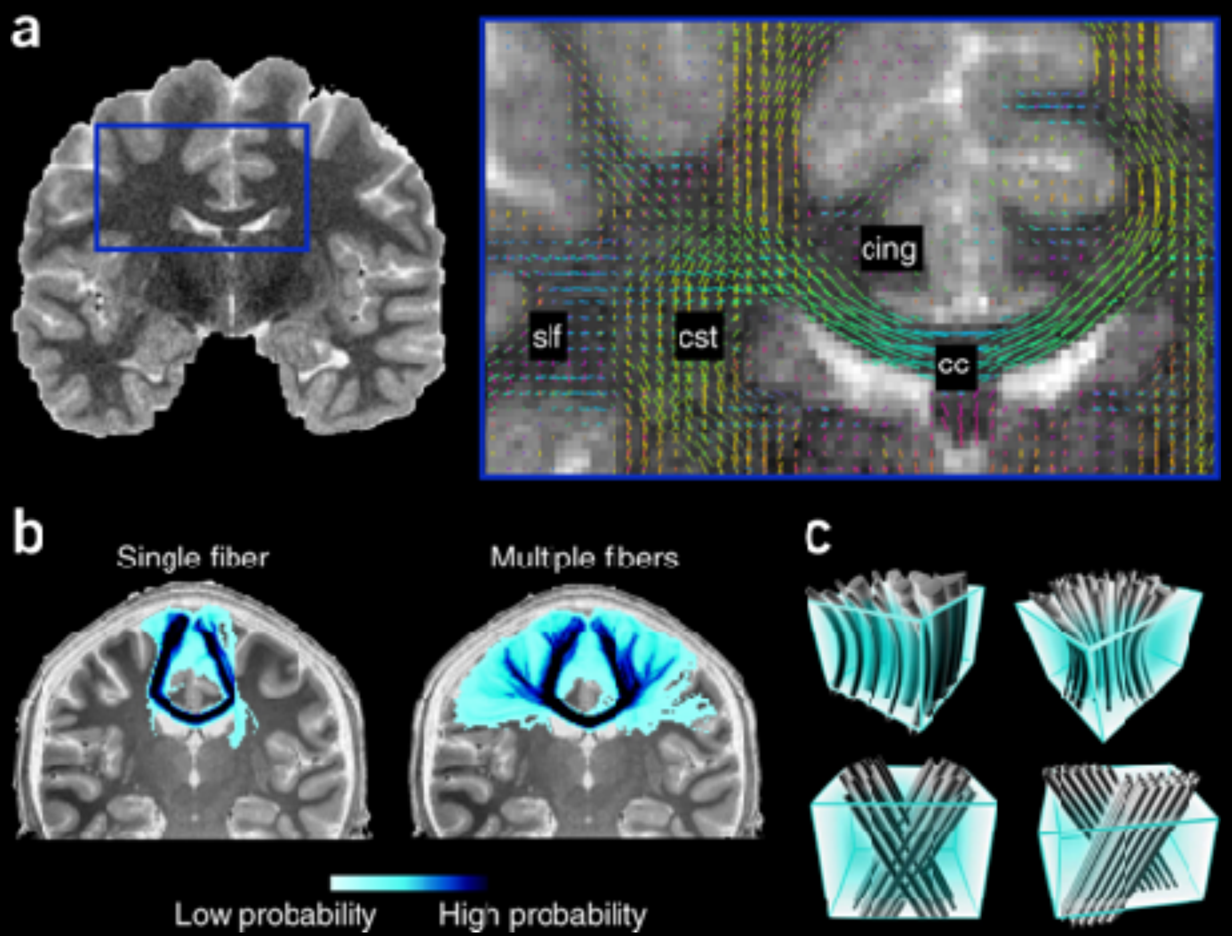
CHALLENGES IN REGIONS OF
FIBRE CROSSING AND UNCERTAINTY

DISTANCE BIAS

VALIDITY IN PATHOLOGICAL
REGION UNCLEAR

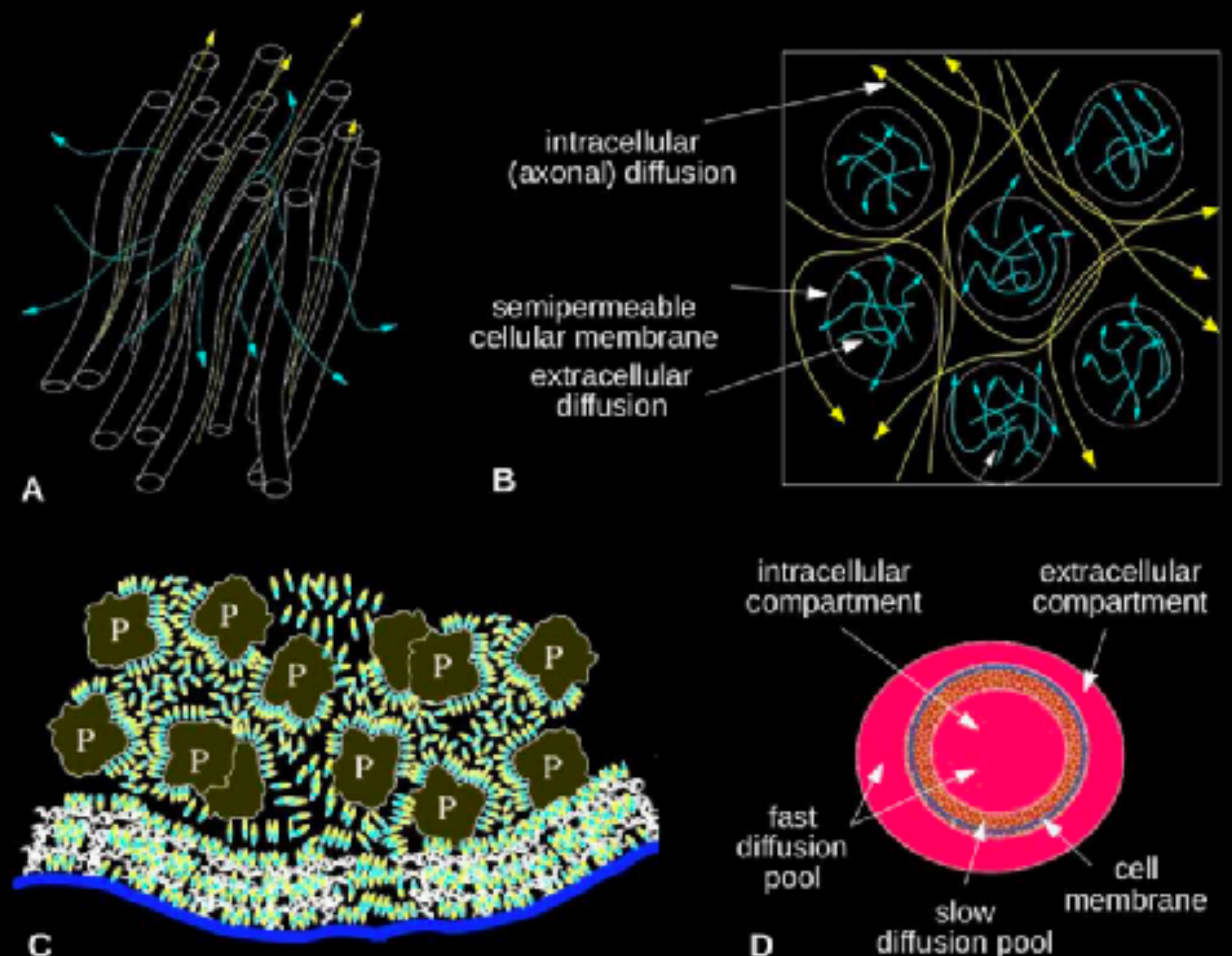


SINGLE SUBJECT (HCP)

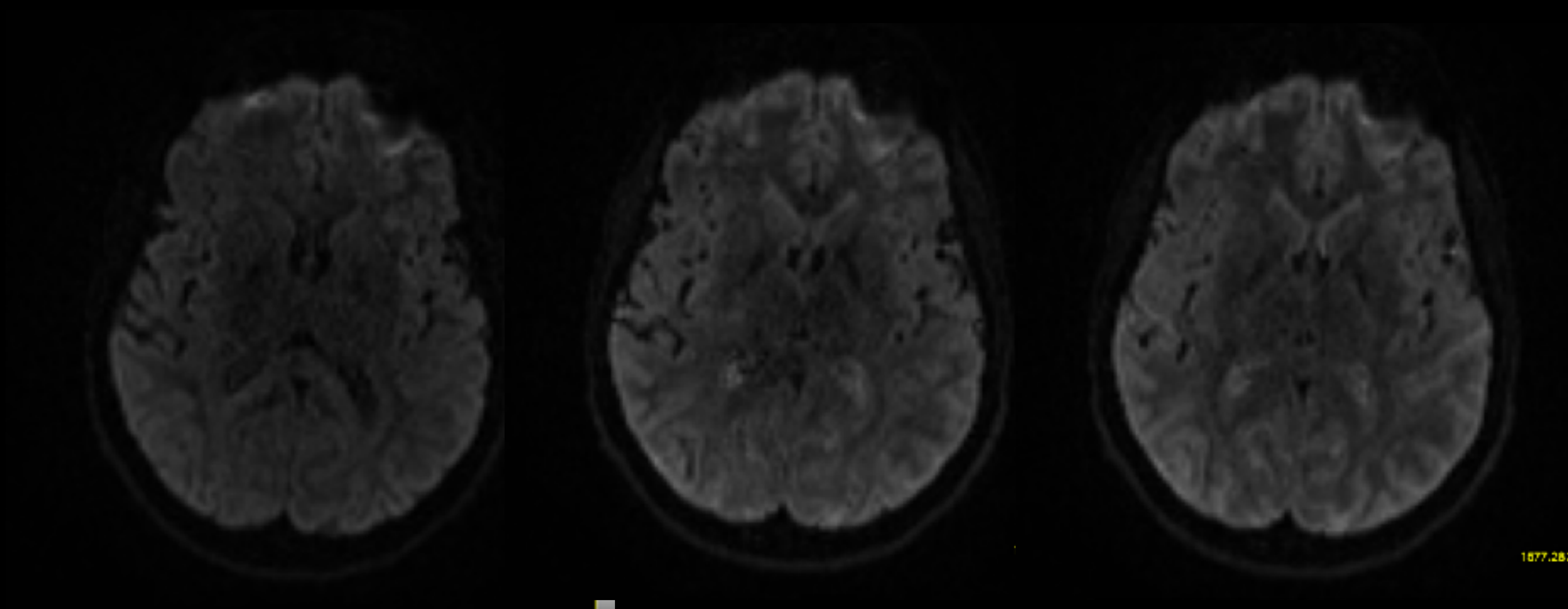


Jbabdi 2015 Nature Reviews Neuroscience

DIFFUSIVITY



RAW DIFFUSION-MRI DATA



DIFFUSION MRI PROCESSING

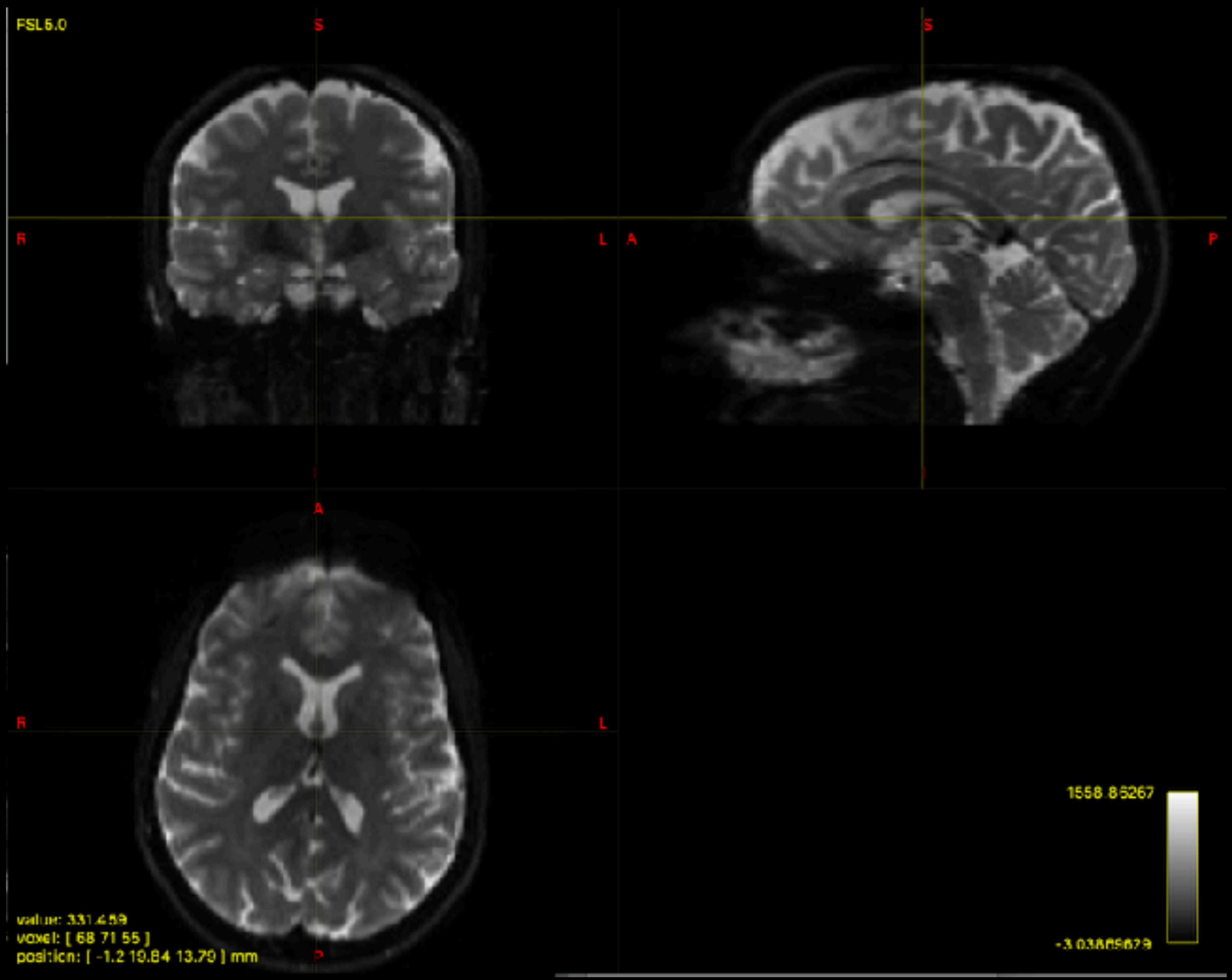
PREPROCESISNG/CORRECTION:
EDDY CURRENTS, MOTION, DISTORTION

COREGISTRATION

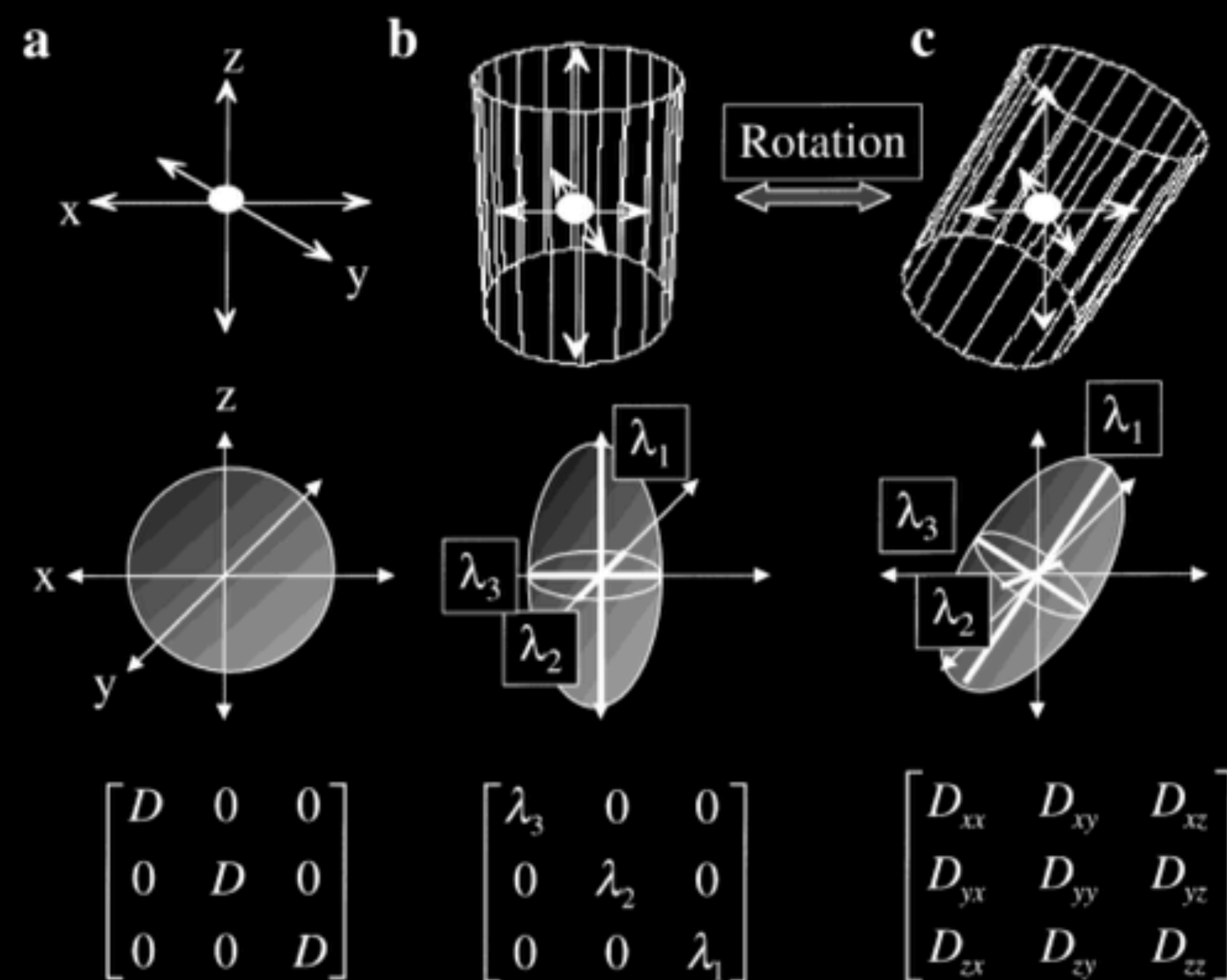
ESTIMATION OF FIBER ORIENTATIONS

TRACOGRAPHY AND CONNECTOME GENERATION

PROCESSED DATA: B0

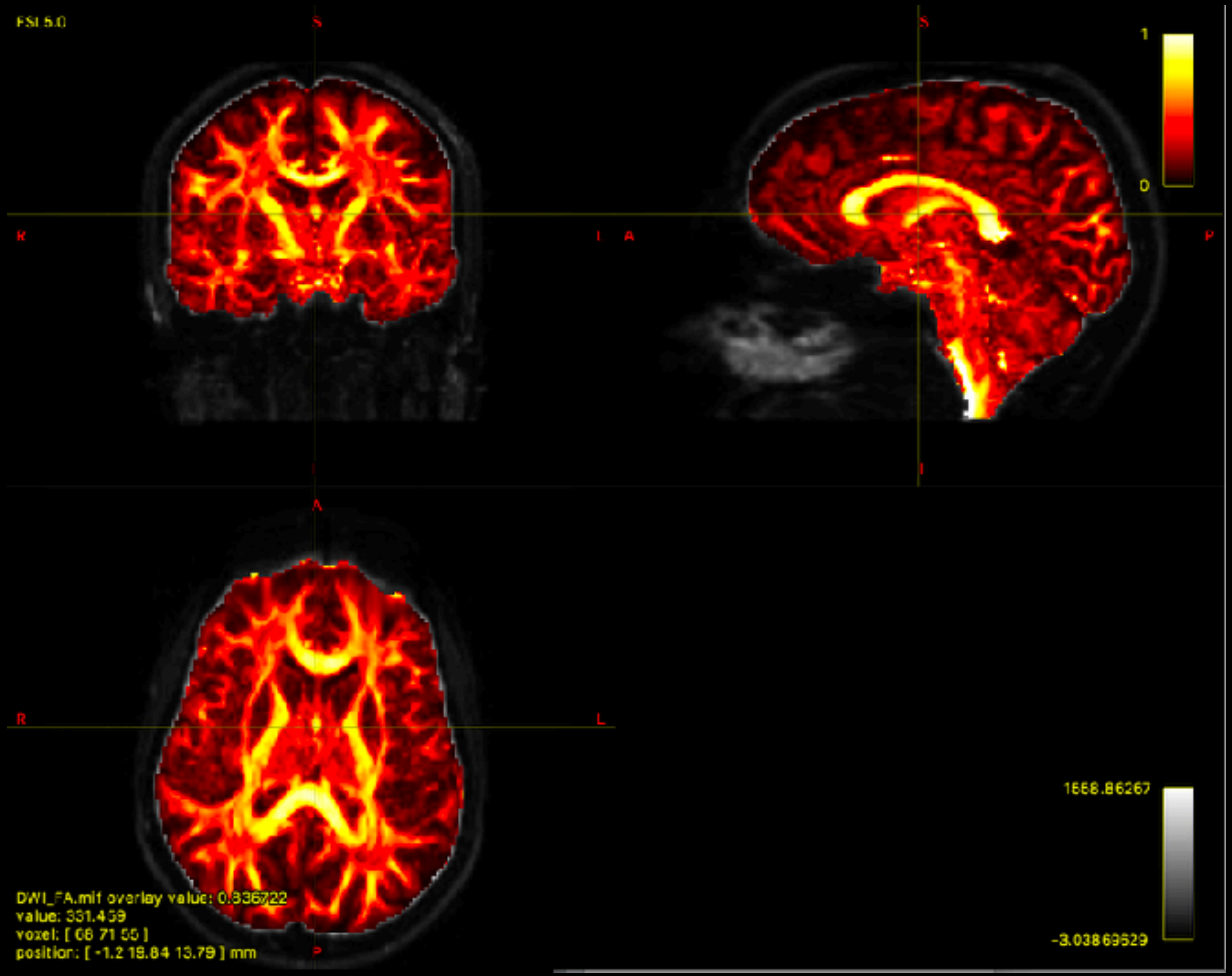


DIFFUSION MRI TENSOR MODEL

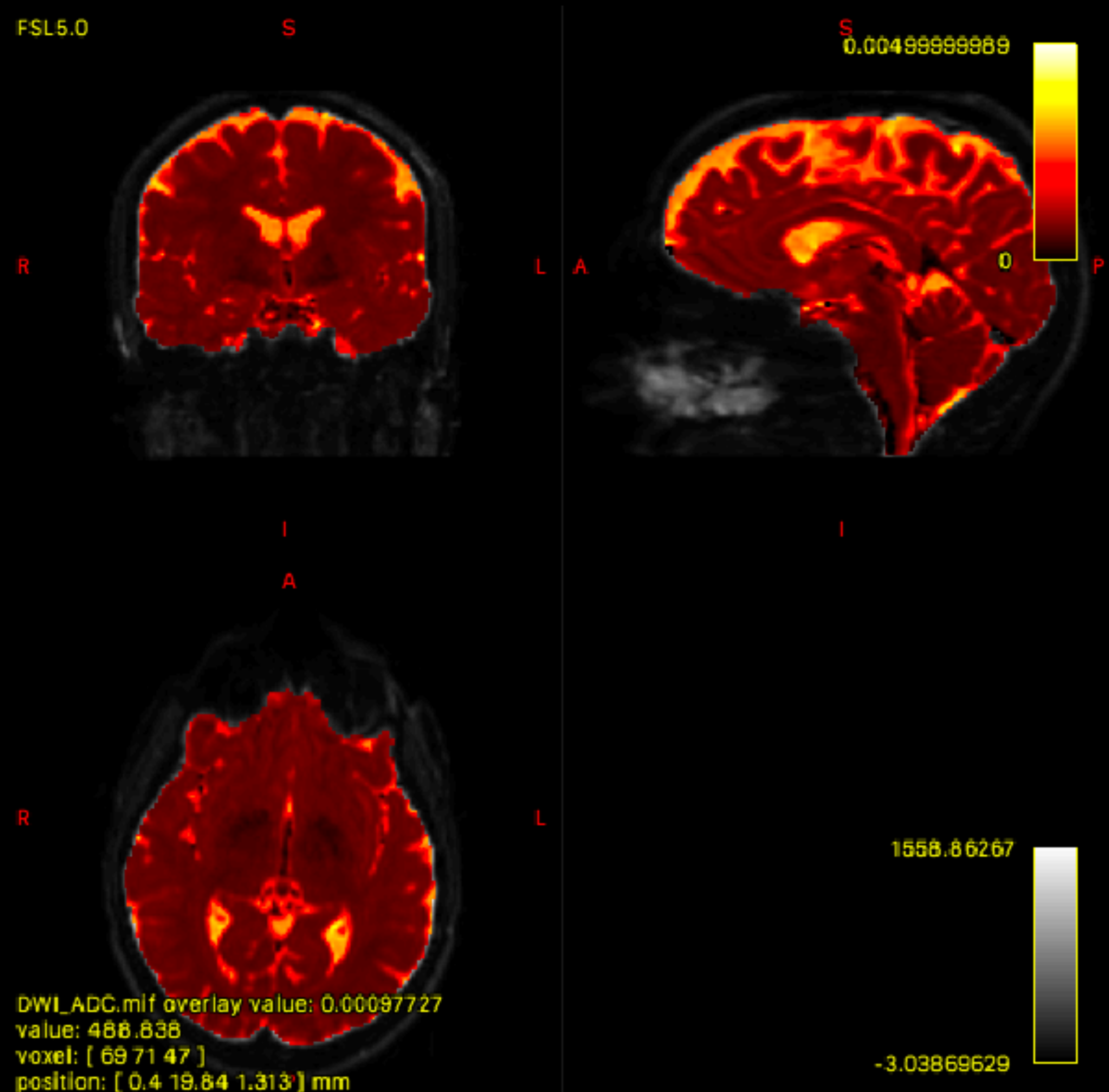


Mori et al 1997

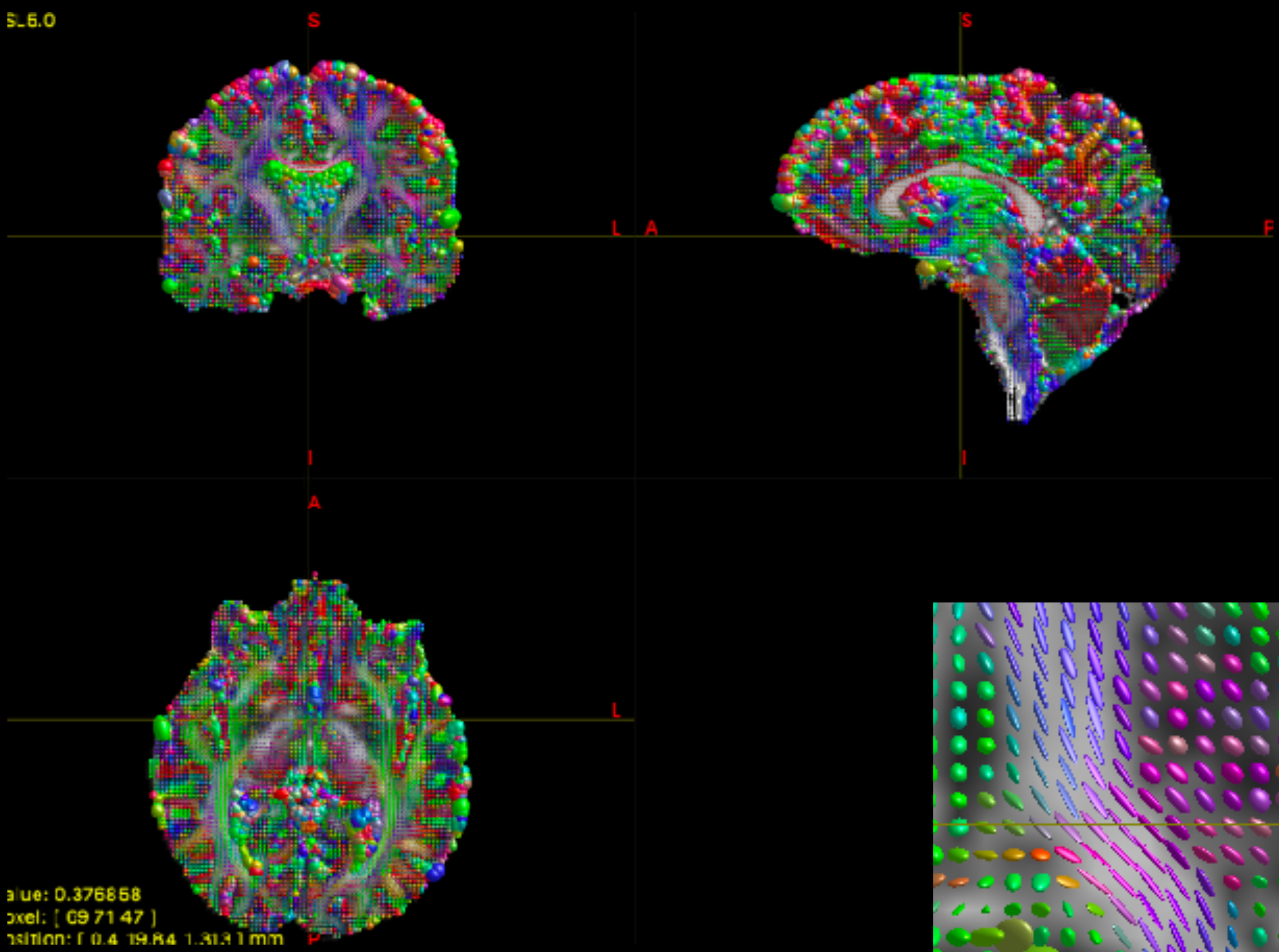
PROCESSED DATA: FA

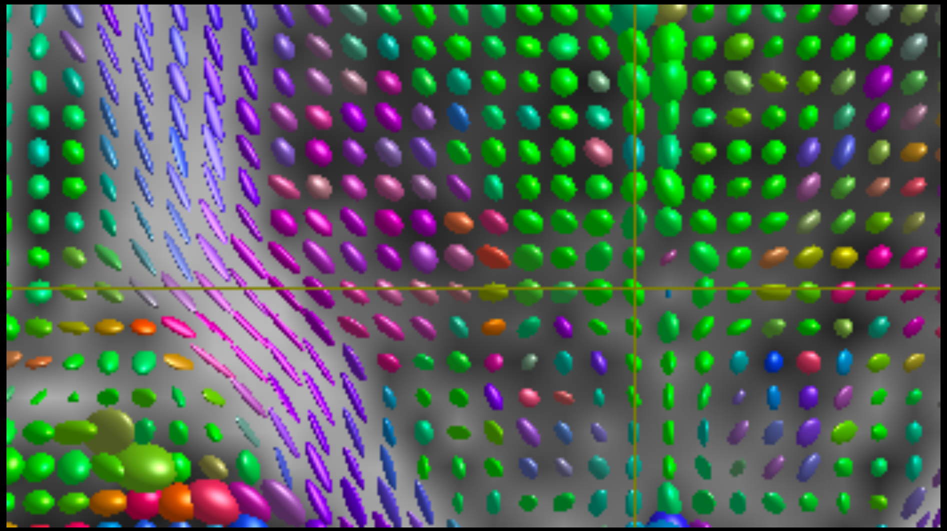


PROCESSED DATA: ADC/MD

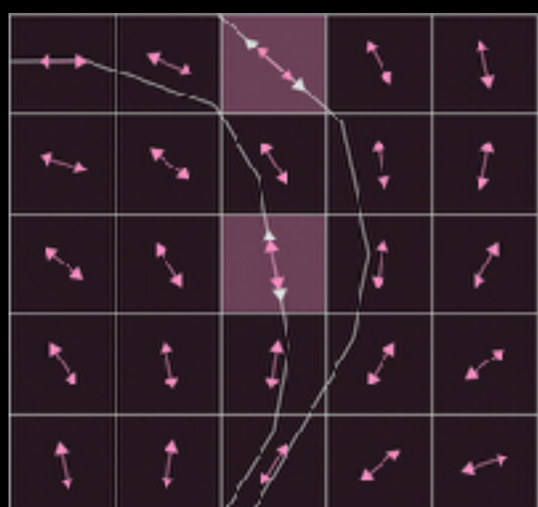


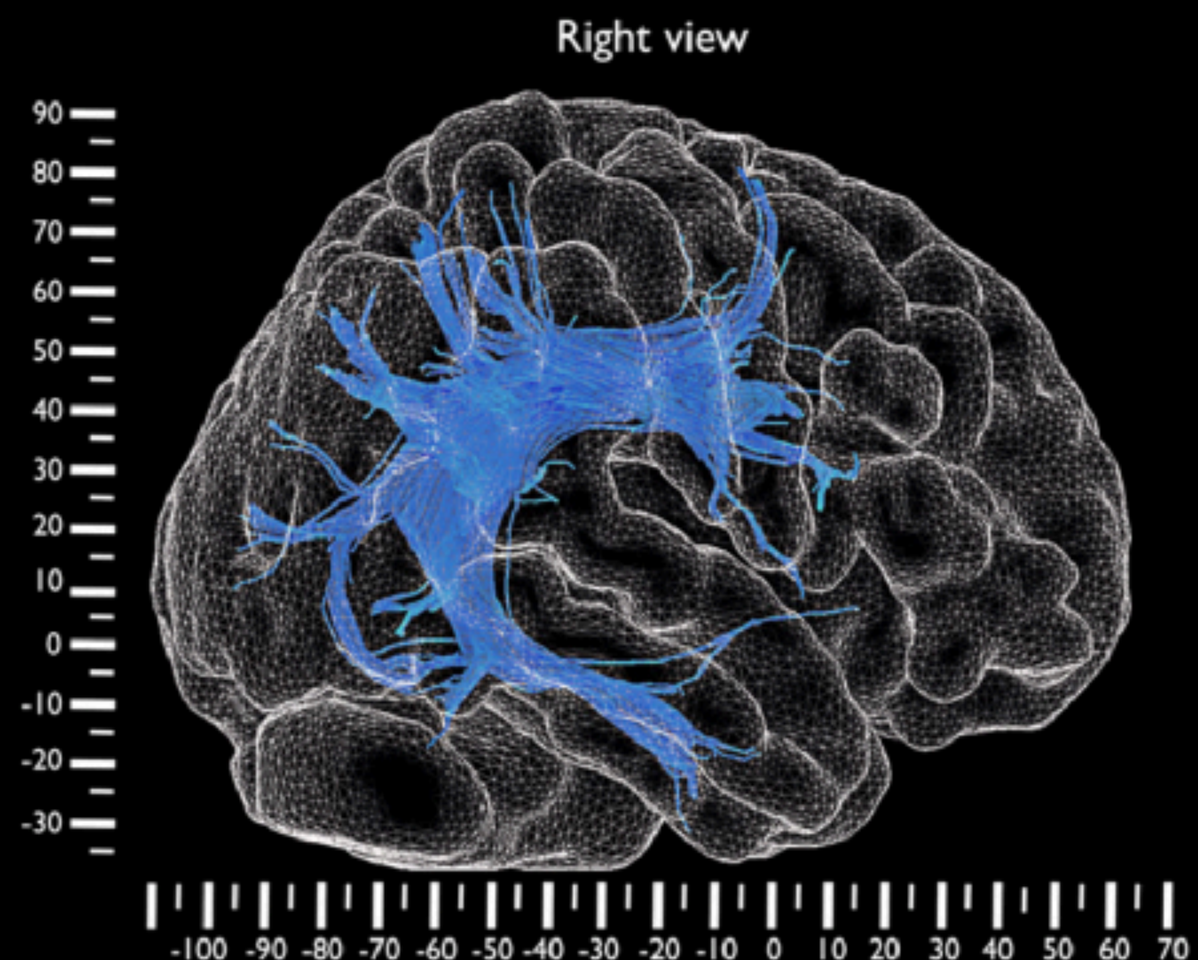
PROCESSED DATA: TENSORS





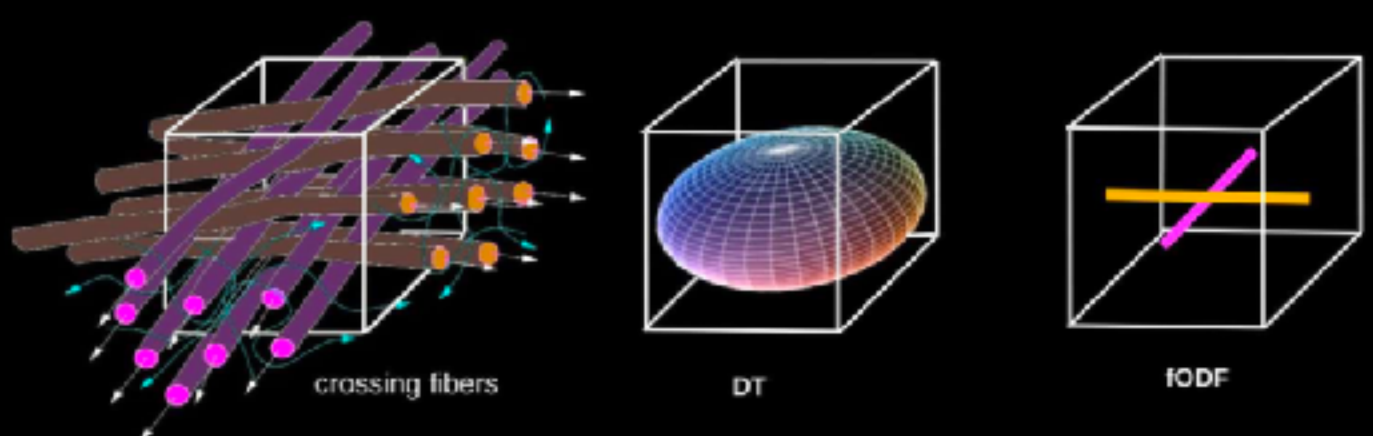
PROCESSED DATA: DETERMINISTIC TRACTOGRAPHY



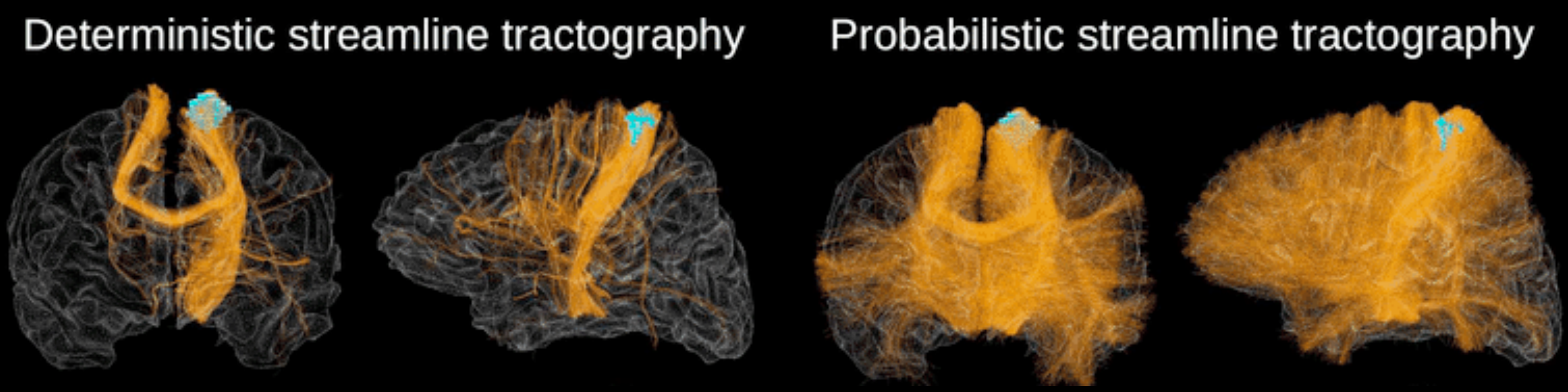


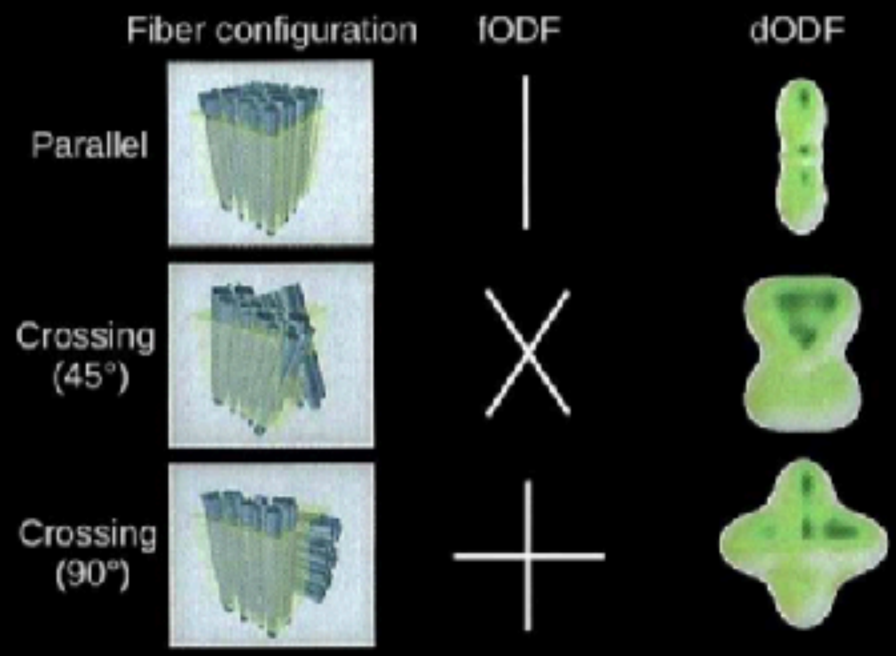
Catani et al 2008

LIMITATIONS OF THE TENSOR MODEL

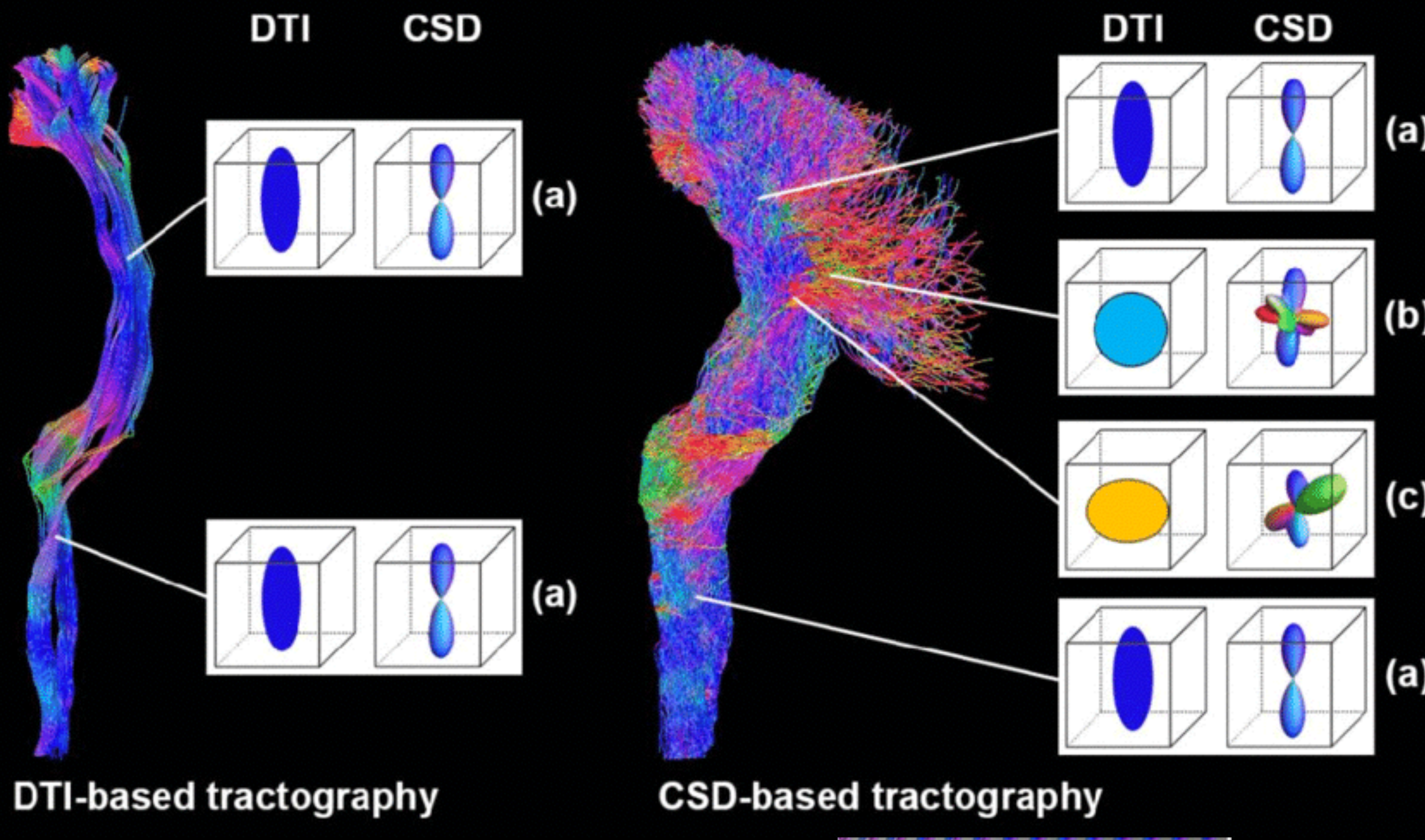


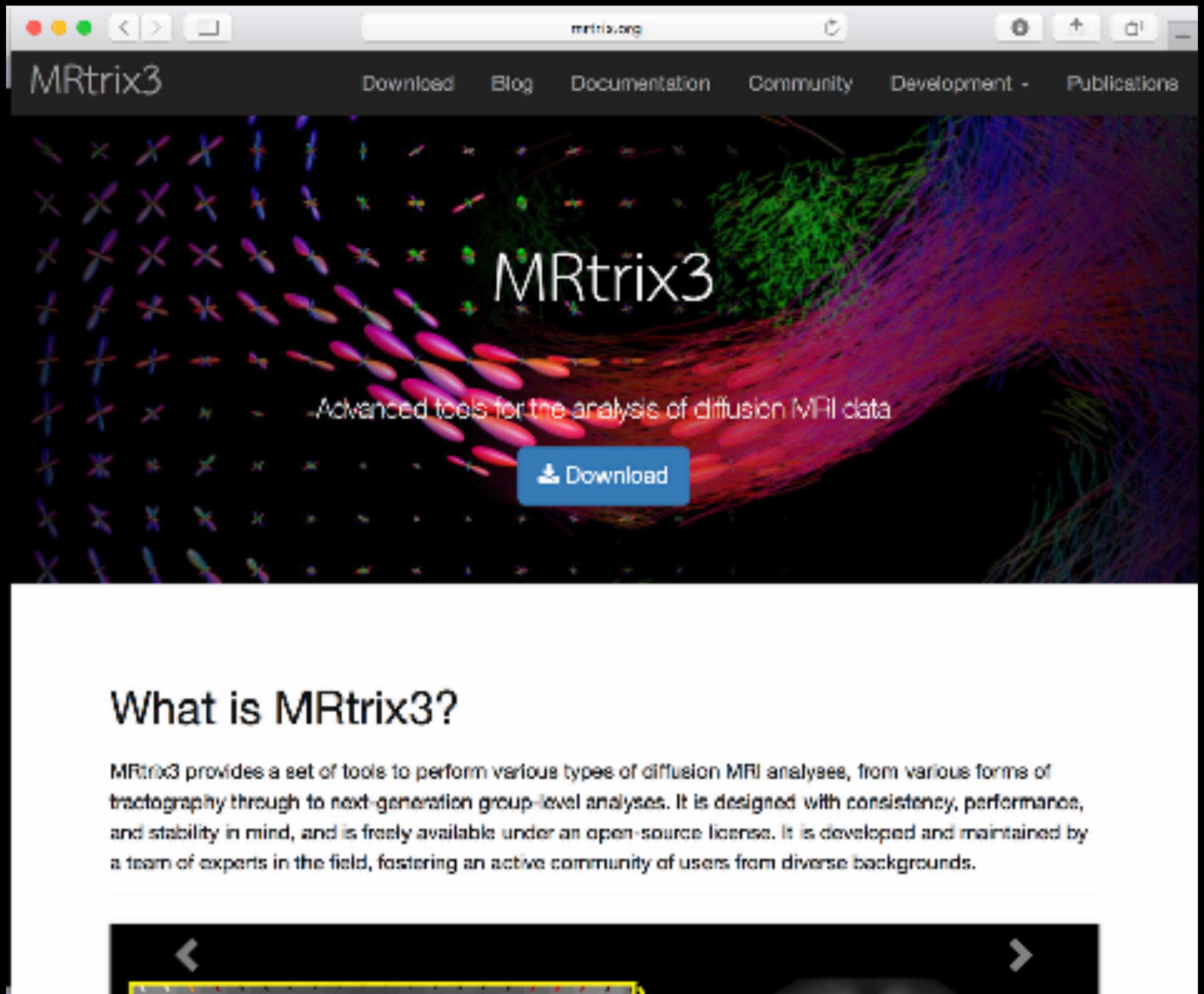
DIFFUSION MRI: MORE COMPLEX MODELS



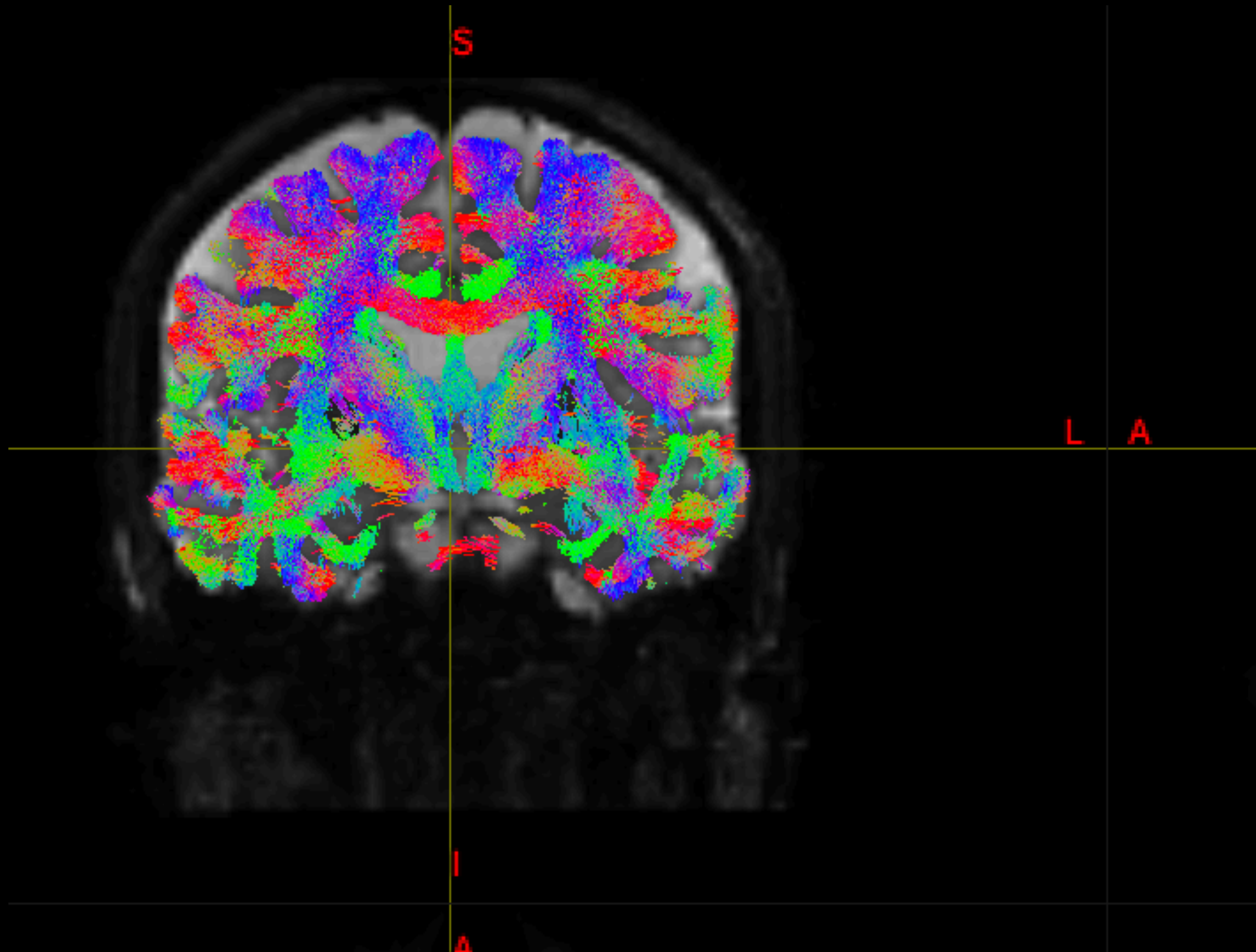


DIFFUSION MRI: MORE COMPLEX MODELS




mrtrix.org
MRtrix3
Download
Blog
Documentation
Community
Development
Publications
MRtrix3
Advanced tools for the analysis of diffusion MRI data
Download
What is MRtrix3?
MRtrix3 provides a set of tools to perform various types of diffusion MRI analyses, from various forms of tractography through to next-generation group-level analyses. It is designed with consistency, performance, and stability in mind, and is freely available under an open-source license. It is developed and maintained by a team of experts in the field, fostering an active community of users from diverse backgrounds.

TUTORIAL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DIFFUSION MRI CONNECTIVITY

IDEA:
FOLLOW PATHWAYS
OF UNHINDERED WATER DIFFUSION

\+
PROBES
WM CONNECTIVITY

DIFFUSION PARAMETER
ANALYSIS CAN BE PERFORMED AS WELL

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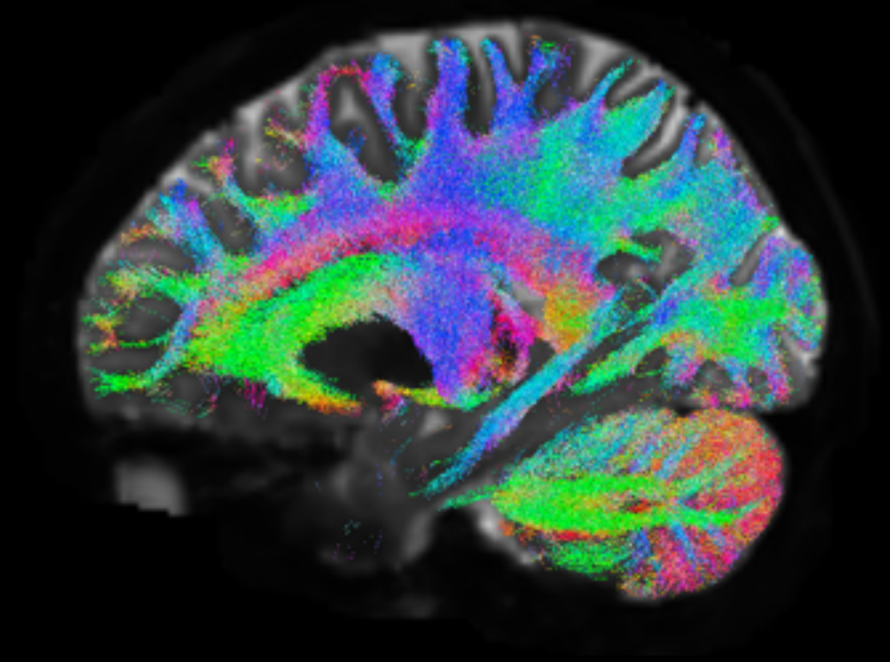
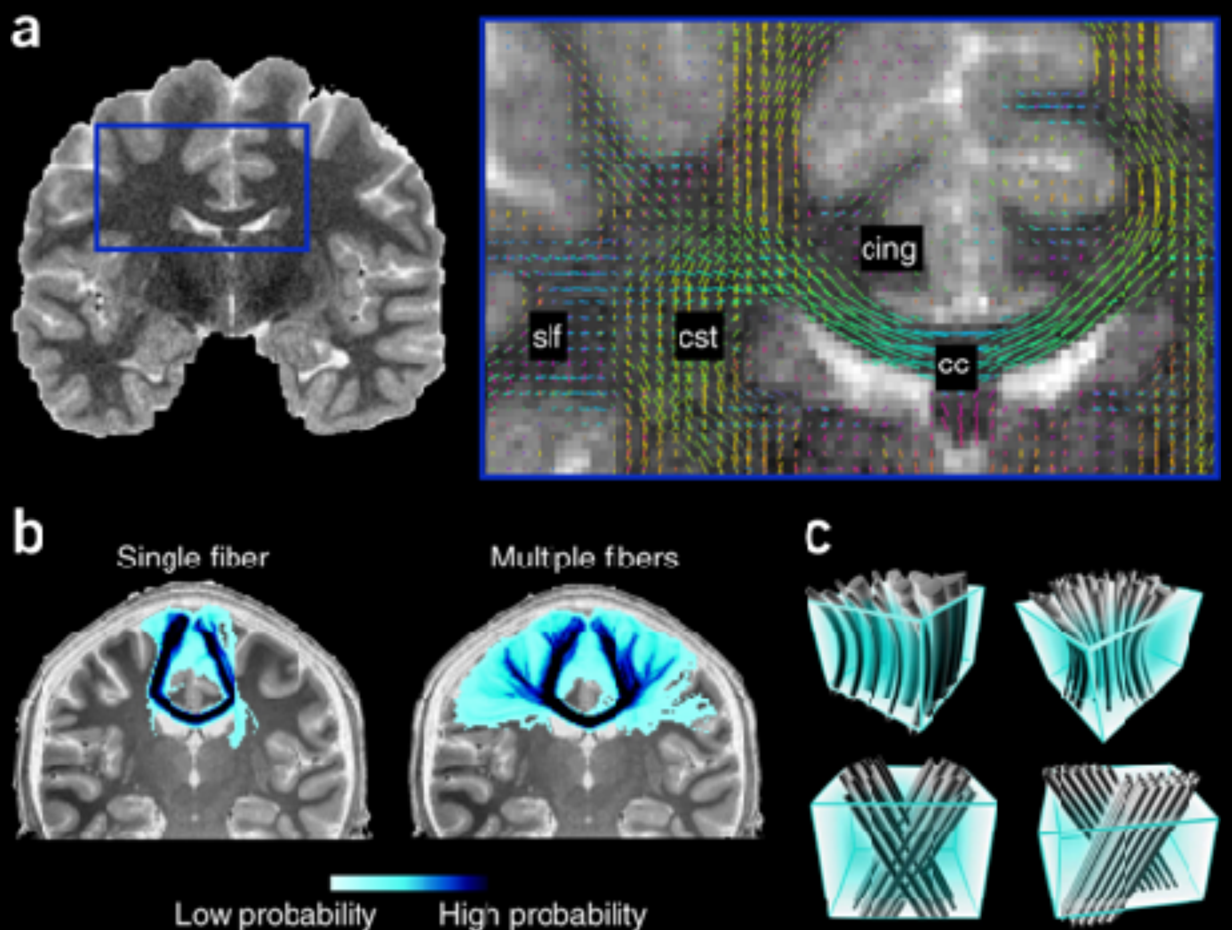


SINGLE SUBJECT (HCP)



Jbabdi 2015 Nature Reviews Neuroscience

MEASURING AND ANALYZING FUNCTIONAL CONNECTIVITY: SEEDS, COMPONENTS, GRADIENTS

RESTING-STATE fMRI CONNECTIVITY

IDEA:
CORRELATE SPONTANEOUS BRAIN ACTIVITY

+
COST-EFFECTIVE, REPRODUCIBLE

INDIVIDUALIZED

REGIONAL AND INTER-REGIONAL

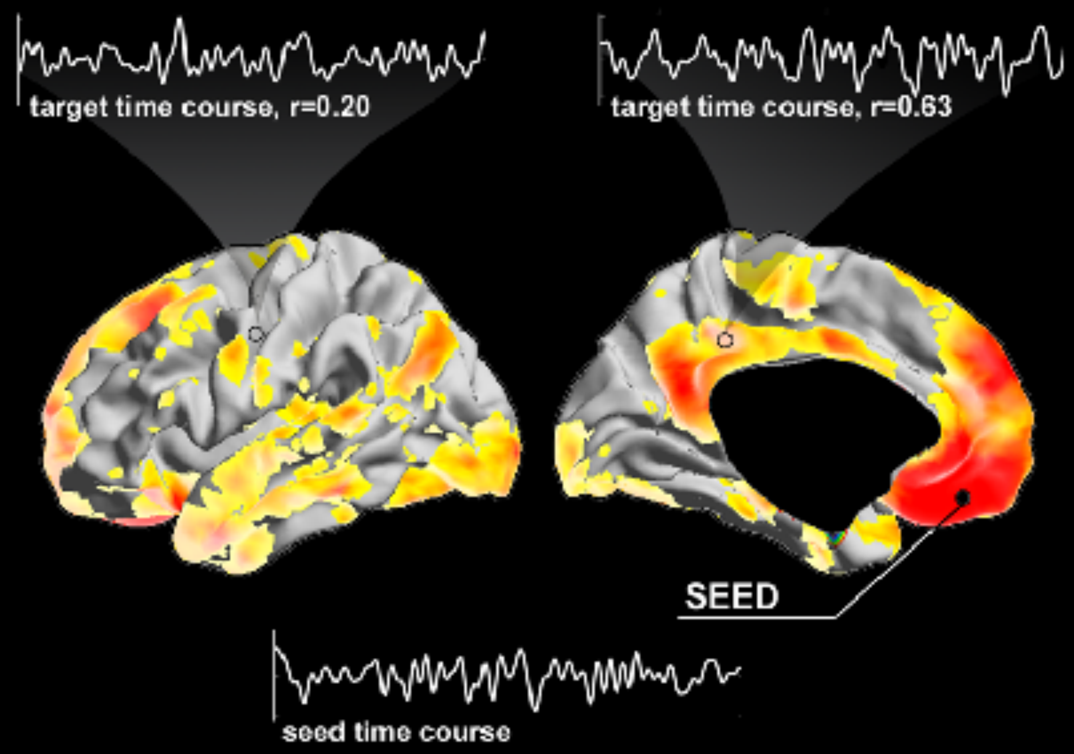
SEEDING FROM GM

CORRELATION WITH MENTAL STATES & INDUCTION

–
EFFECTS OF PHYSIOLOGY + MOTION

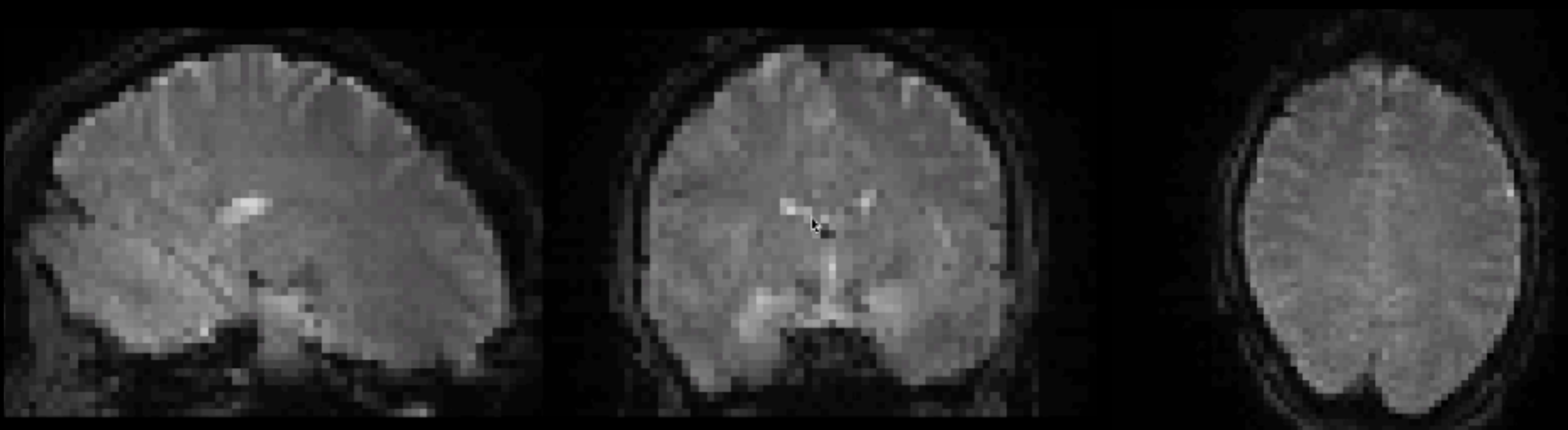
INDIRECT CONNECTIONS

CORRELATION WITH MENTAL STATES & INDUCTION



+

RAW RESTING-STATE FMRI DATA



FUNCTIONAL MRI PROCESSING

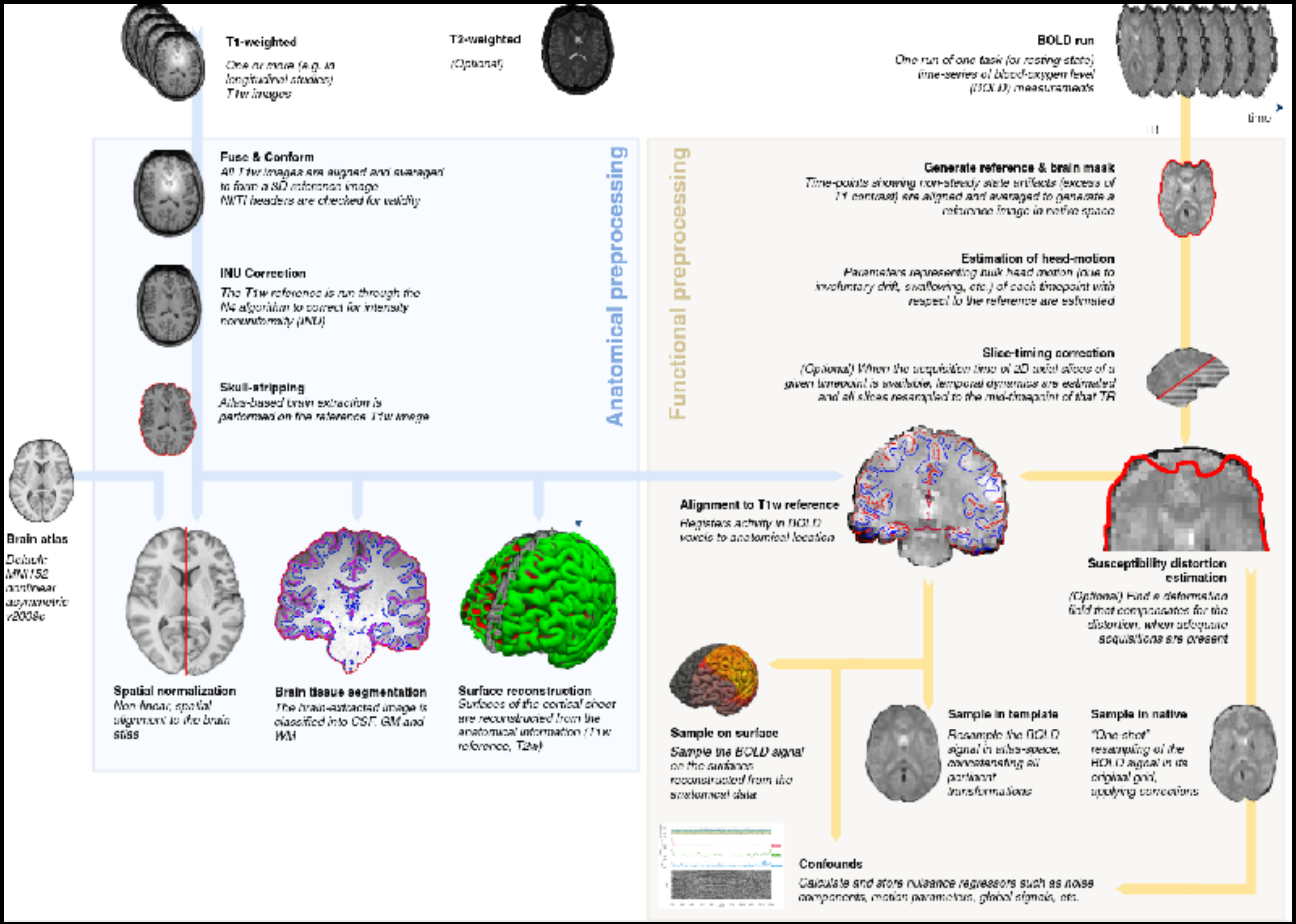
PREPROCESISNG/CORRECTION:
SLICE TIME, MOTION, DISTORTION

COREGISTRATION

CONFOUND CORRECTION AND FILTERING

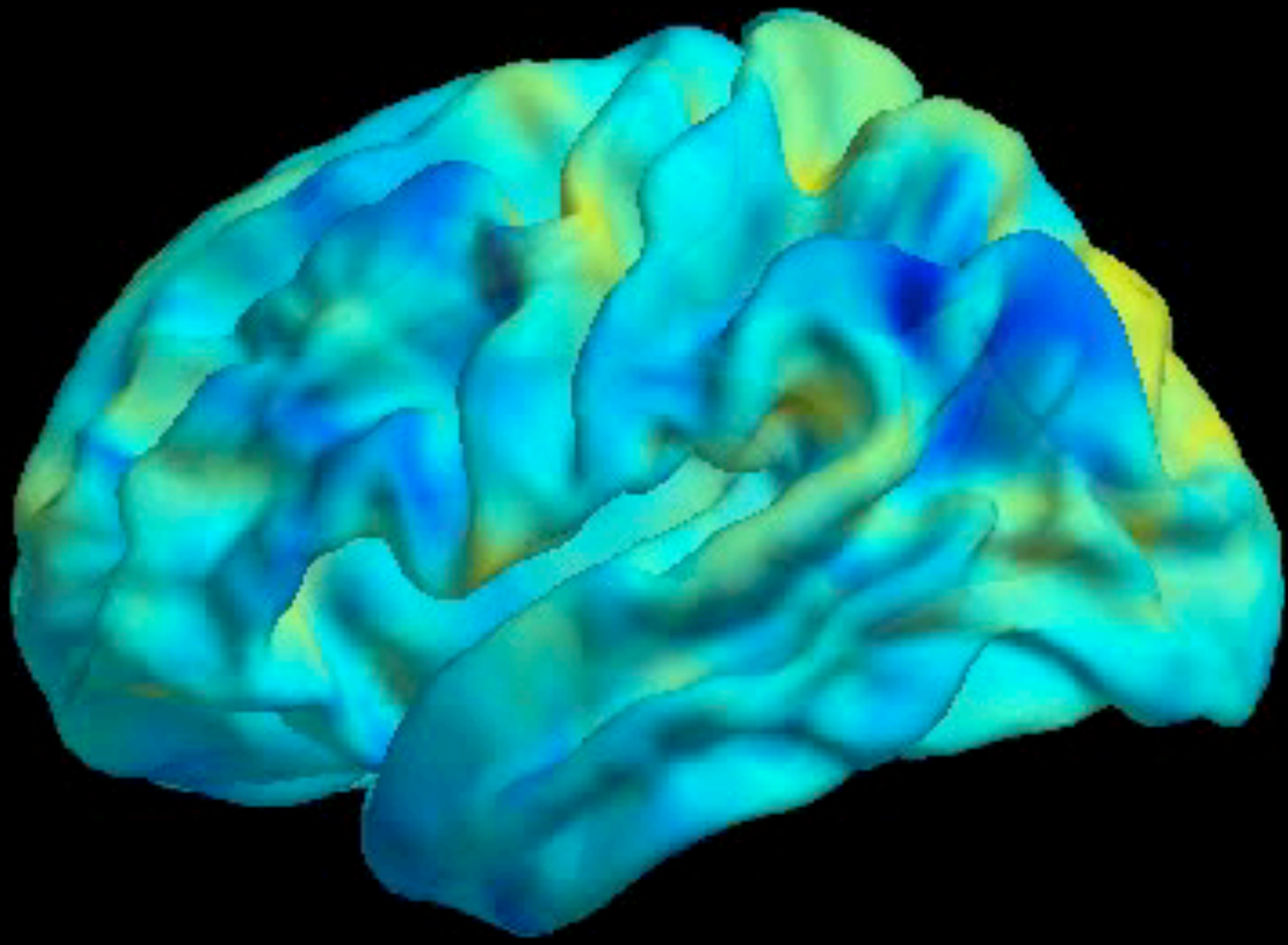
FUNCTIONAL CONNECTION AND CONNECTOME GENERATION

PREPROCESSING ZOO

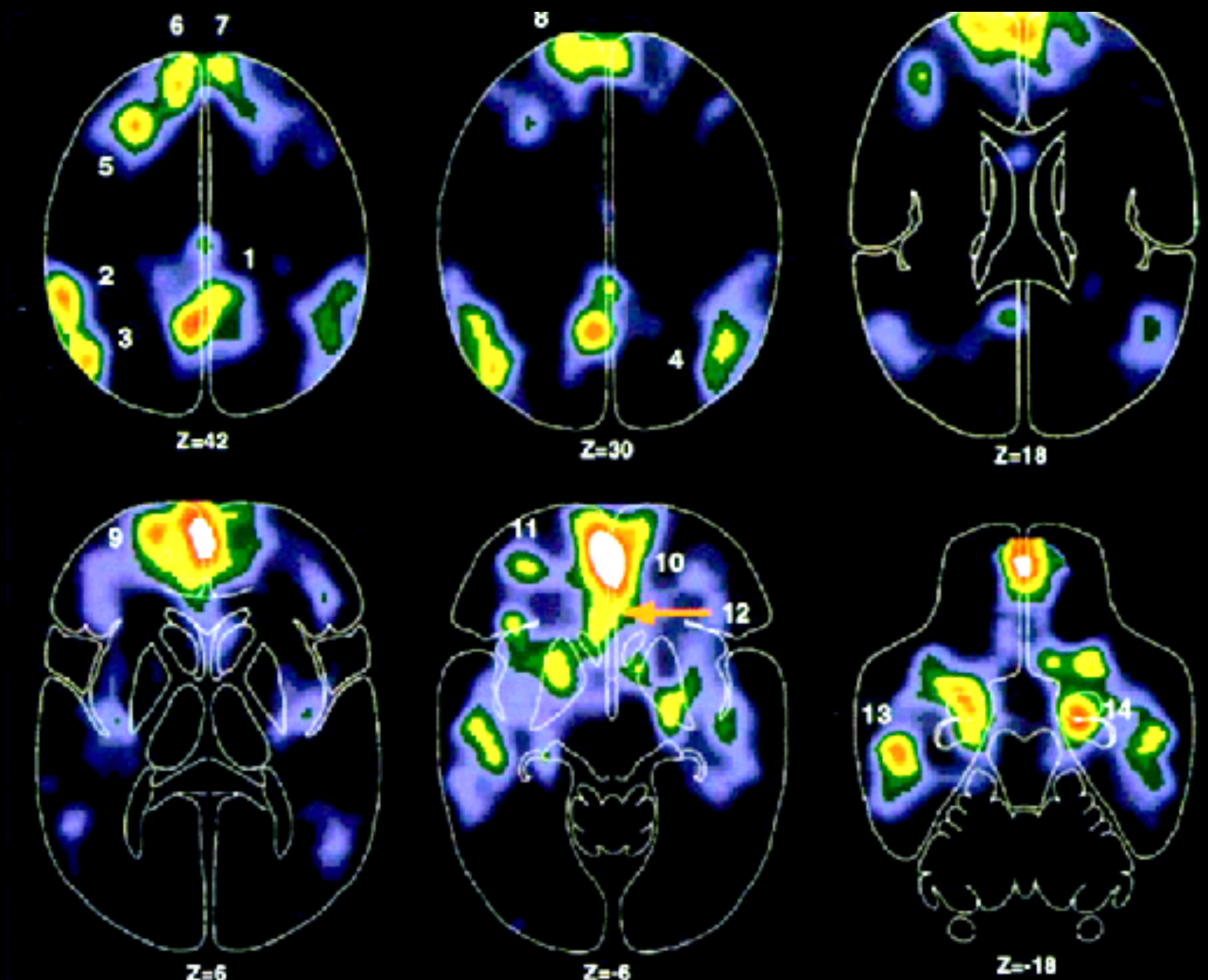


eg via. https://fmriprep.readthedocs.io, Esteban et al. 2018 bioarxivX

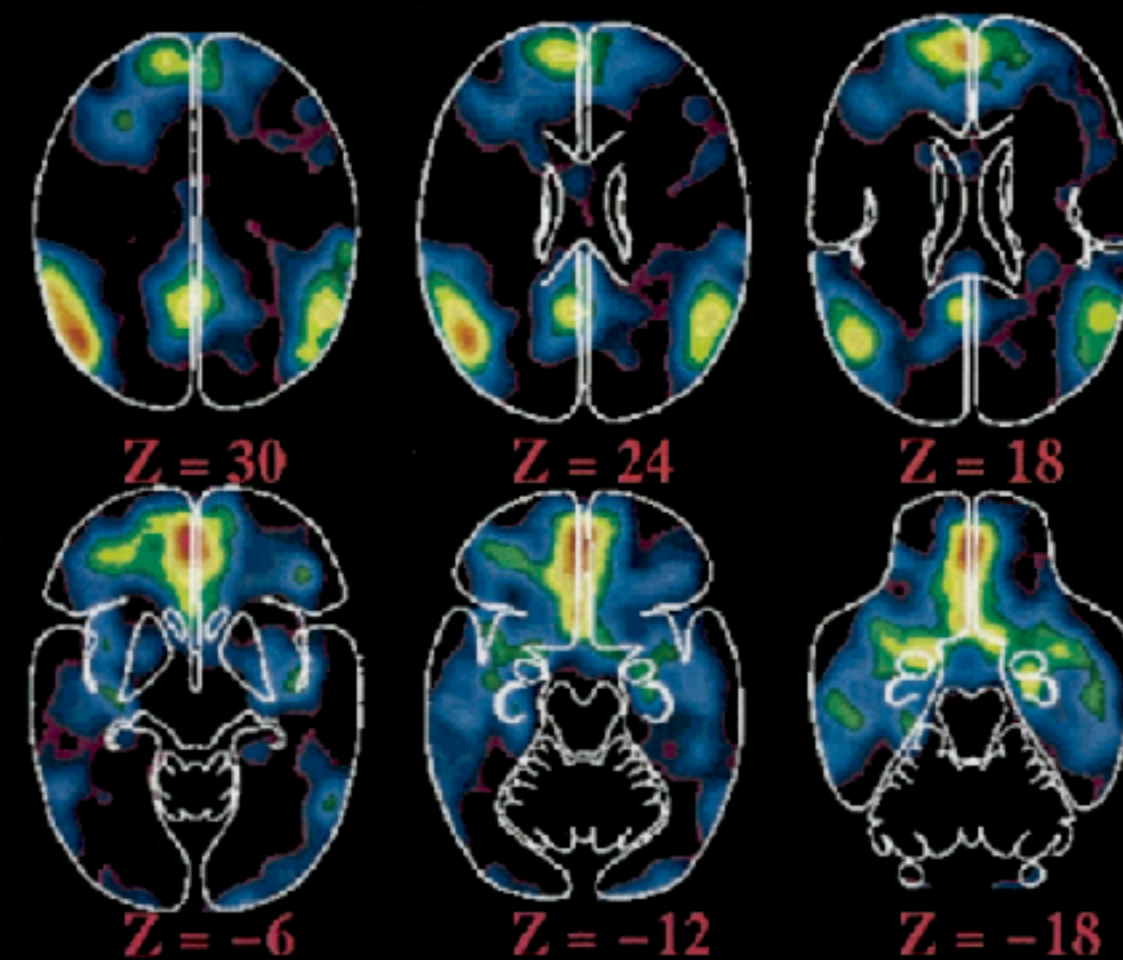
THE RESTING BRAIN: RELIABLY OSCILLATING



DISCOVERY OF DMN: ACTIVATIONS AND DEACTIVATIONS

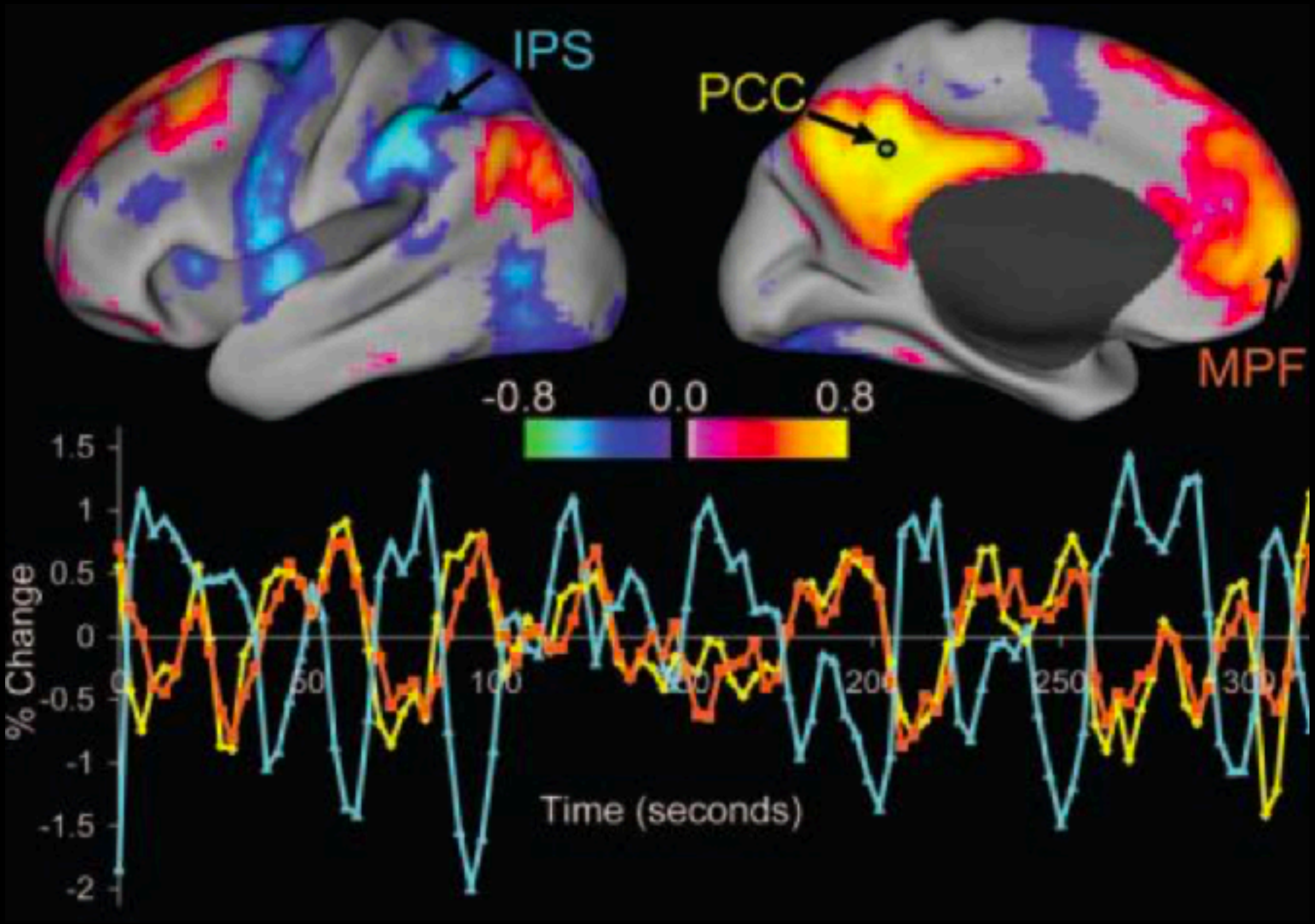


Schulman 1997 J Cog Neuro



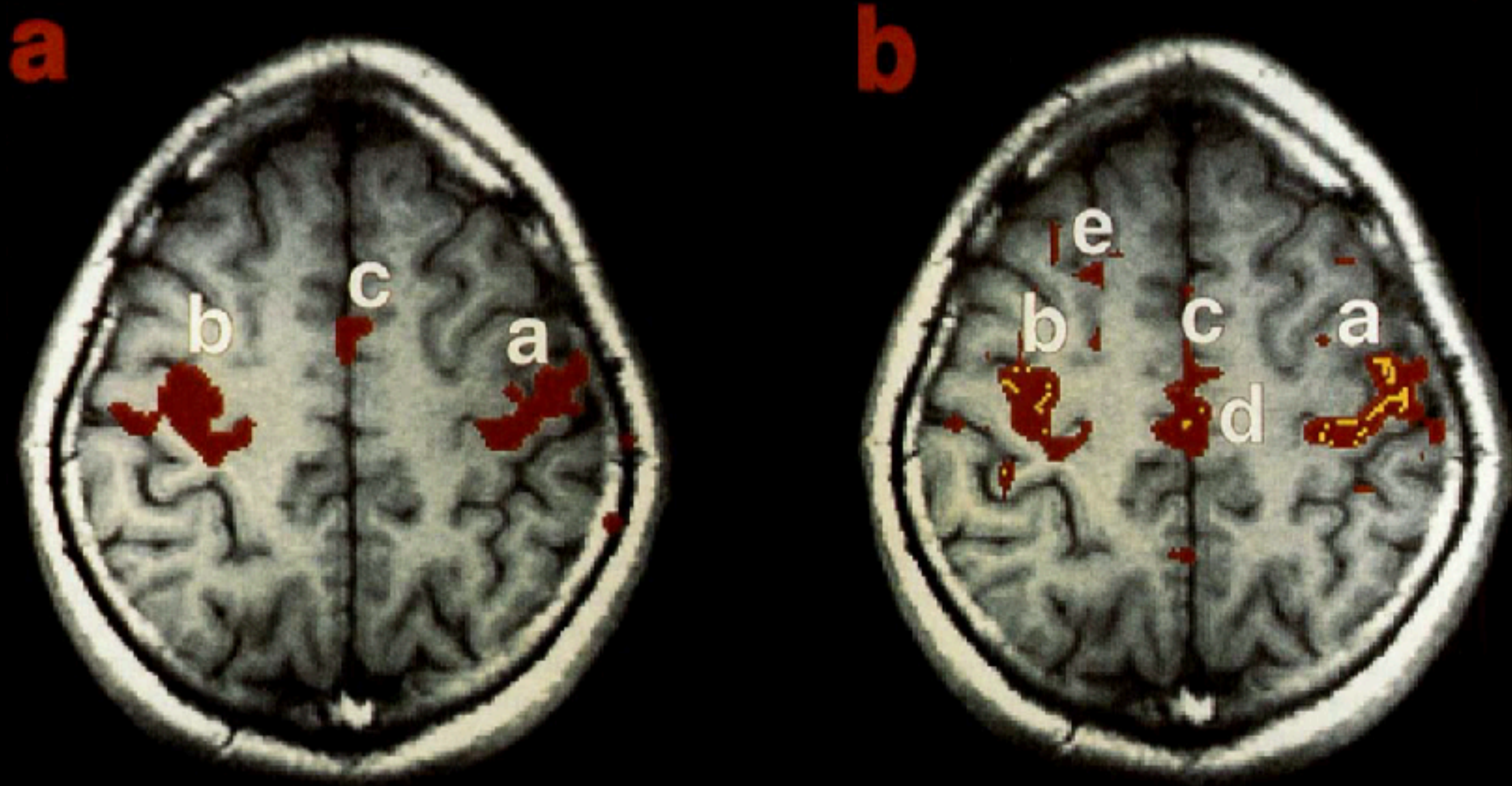
Raichle 2003 PNAS

SEED BASED CONNNECTIVITY: IDEA



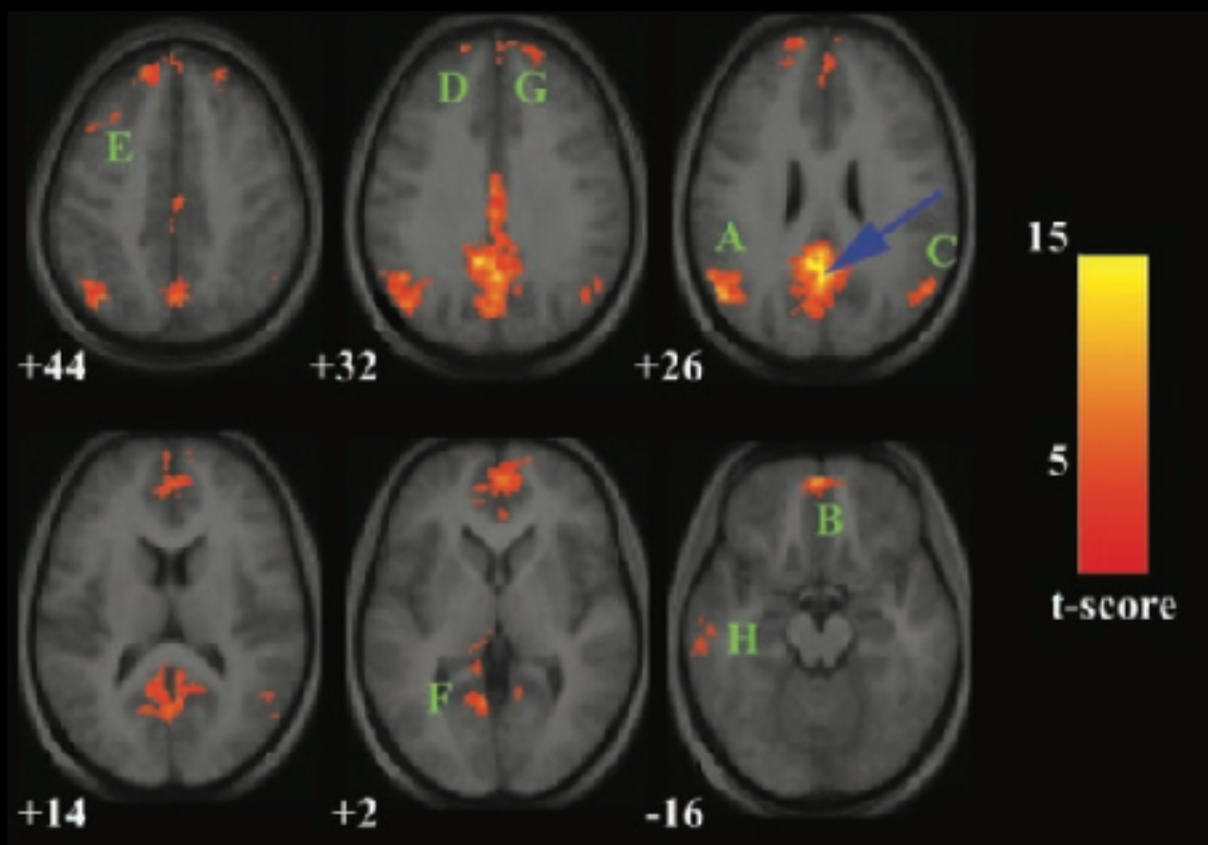
Fox 2005 PNAS

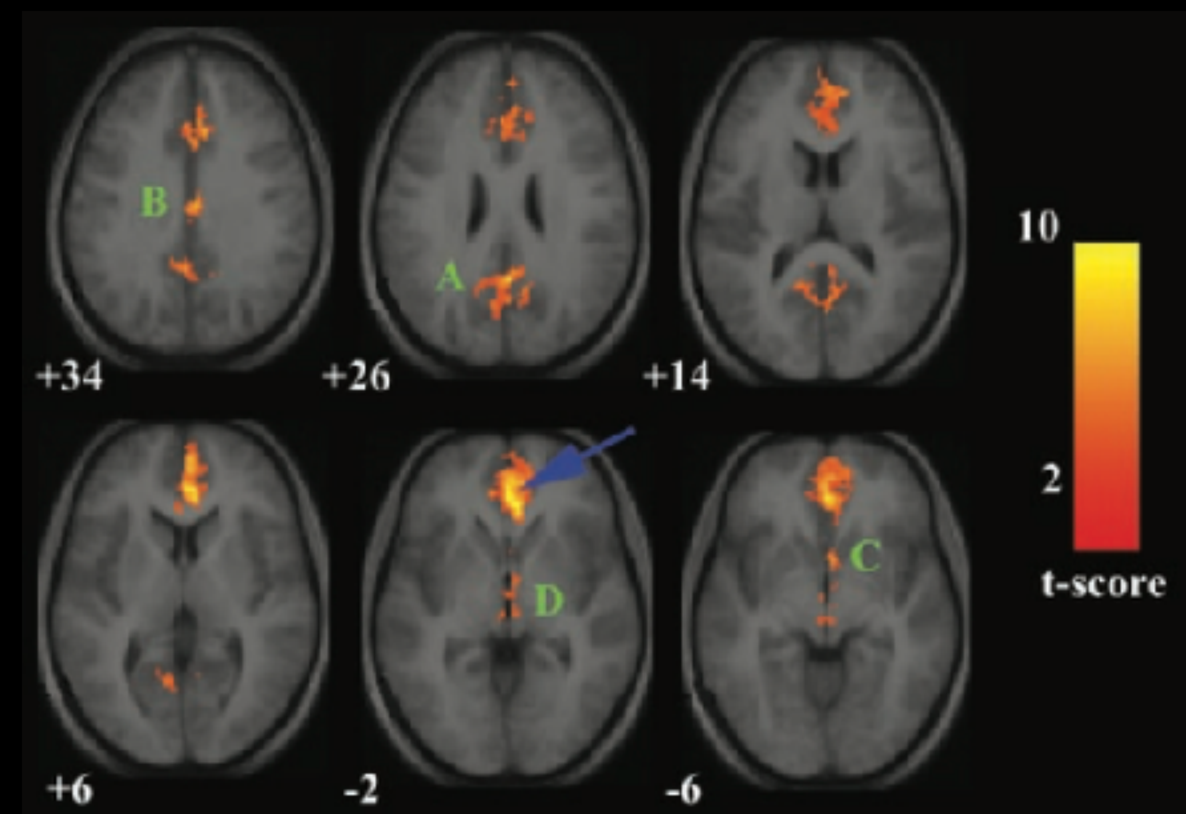
THE CLASSIC FUNCTIONAL CONNECTIVITY ANALYSIS



Biswal 1995 MRM

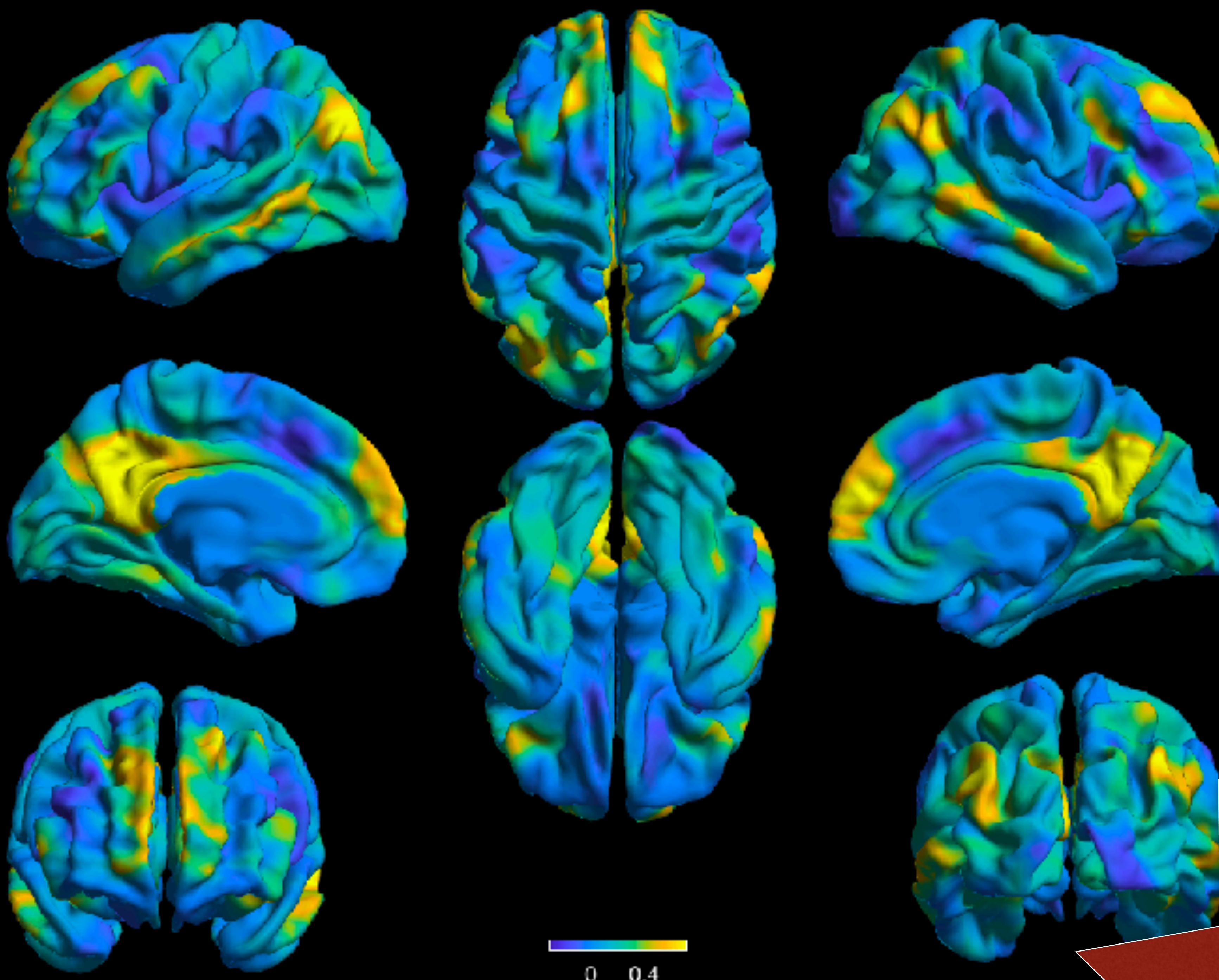
THE CLASSIC DMN CONNECTIVITY STUDY





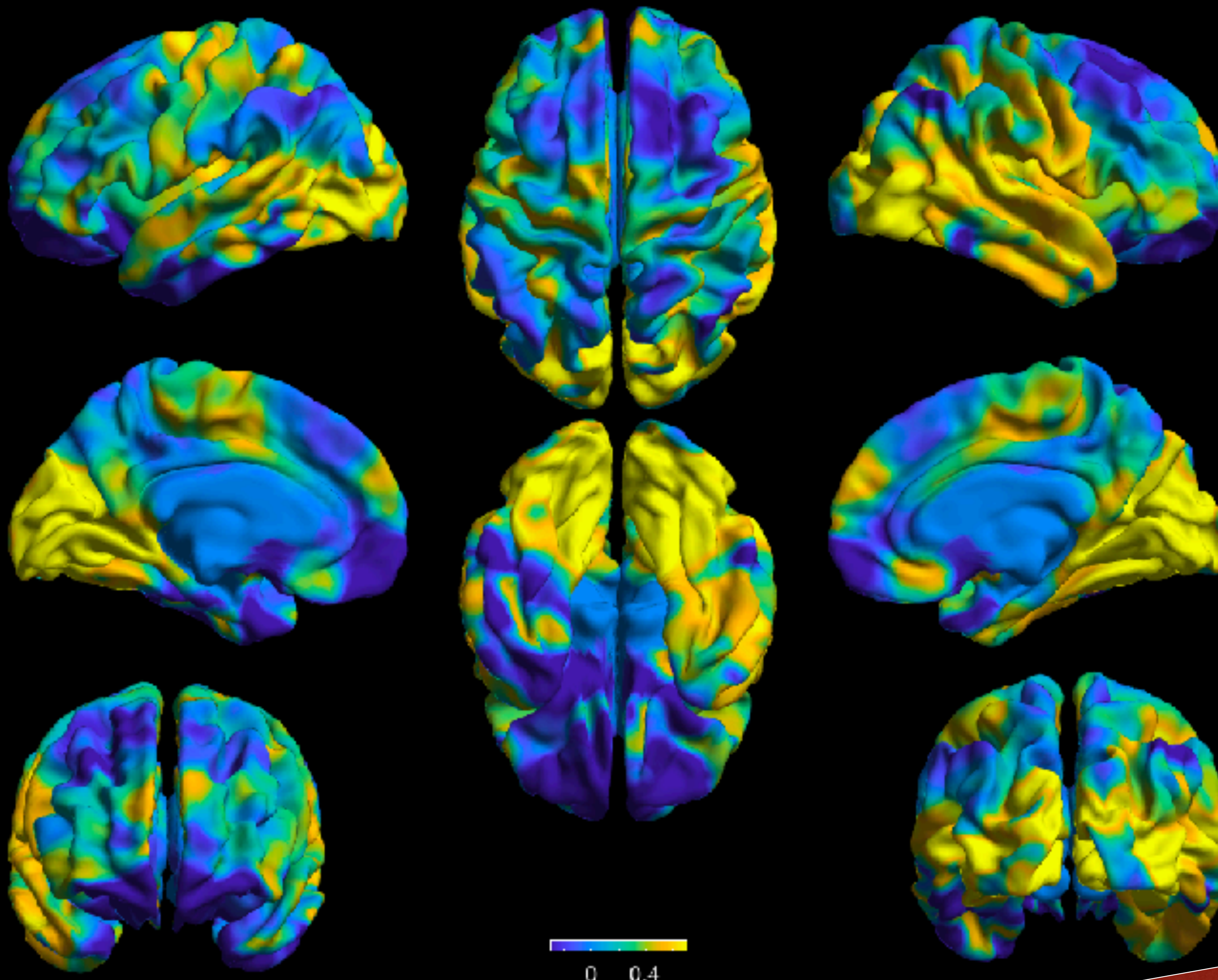
Grecius et al. 2003 PNAS

SINGLE SEED ANALYSIS: PRECUNEUS/PCC



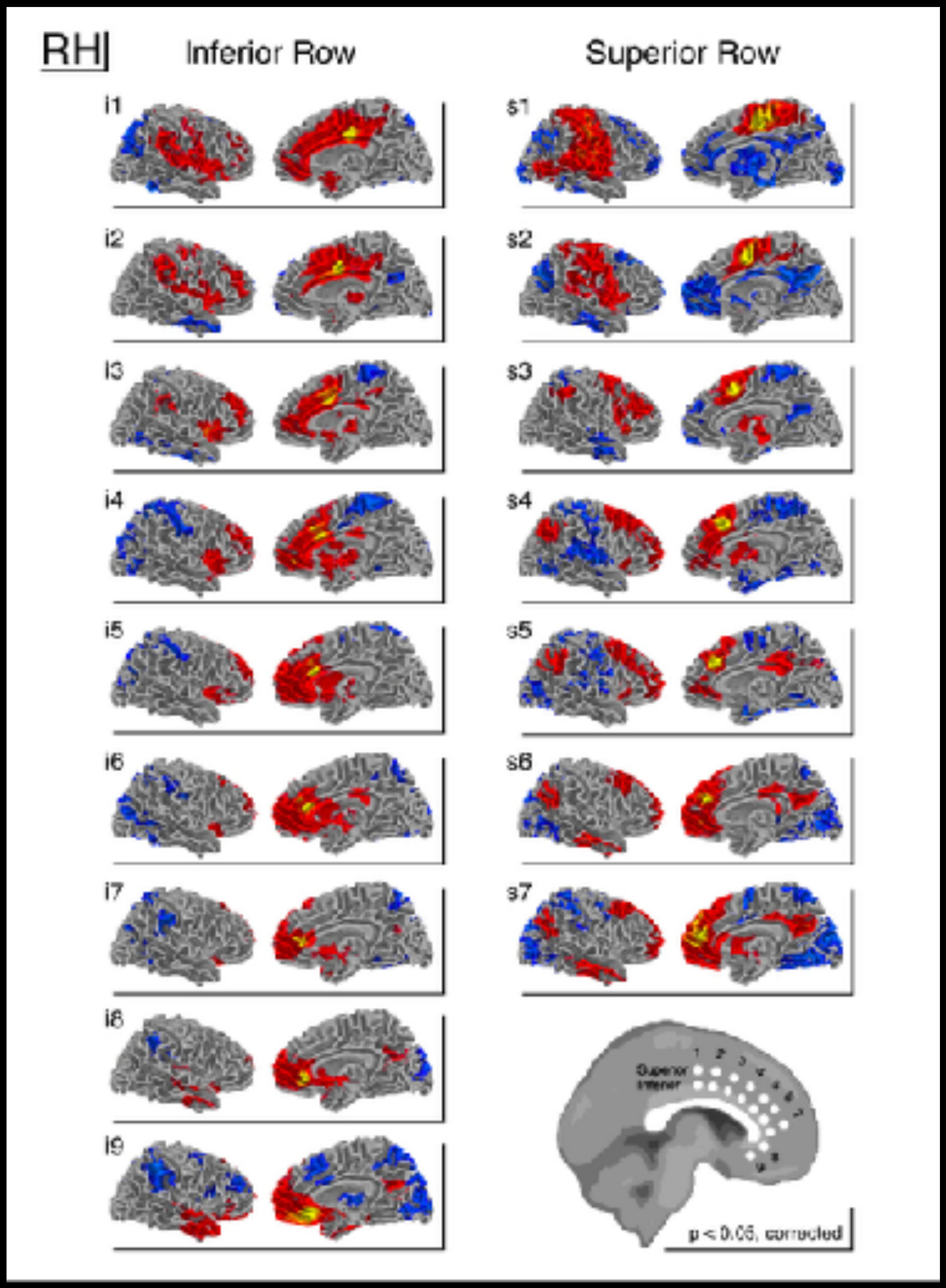
TUTORIAL

SINGLE SEED ANALYSIS: VISUAL CORTEX

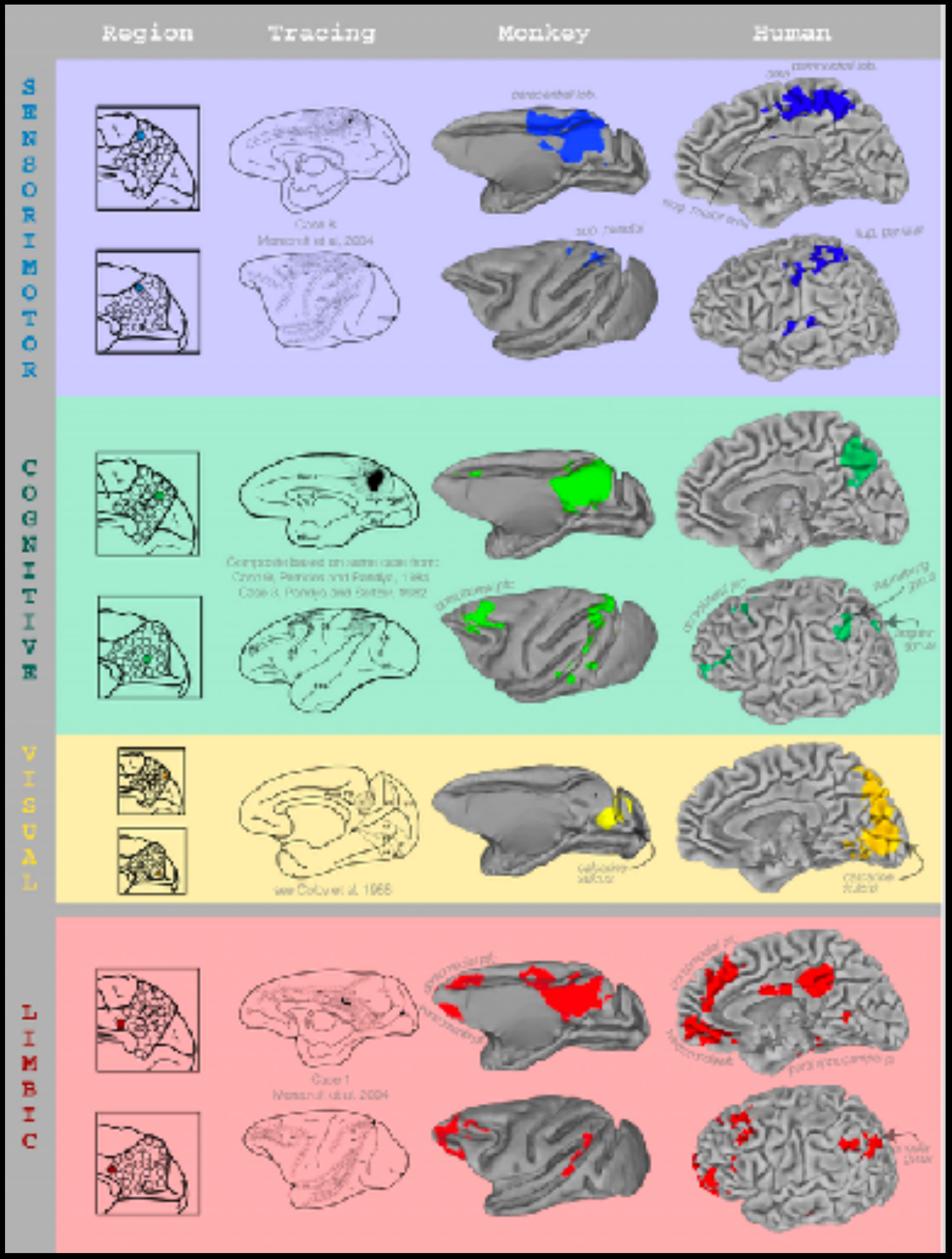


TUTORIAL

SYSTEMATIC SEEDING

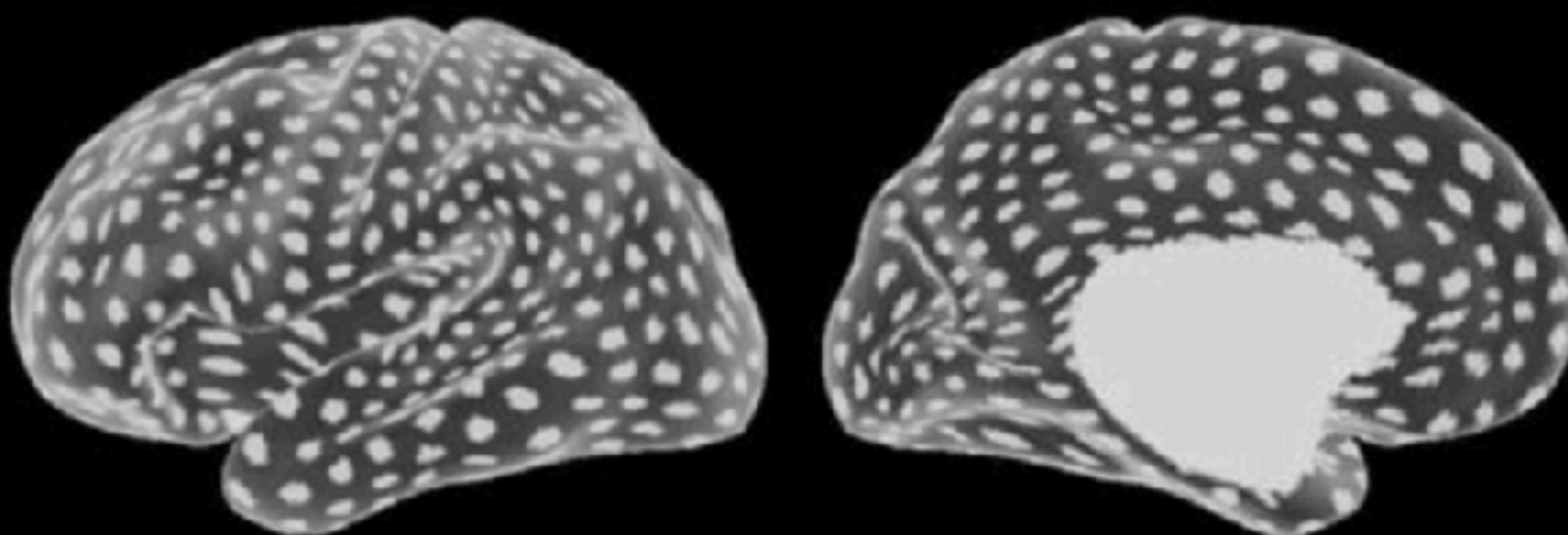


Margulies et al 2007 NIMG



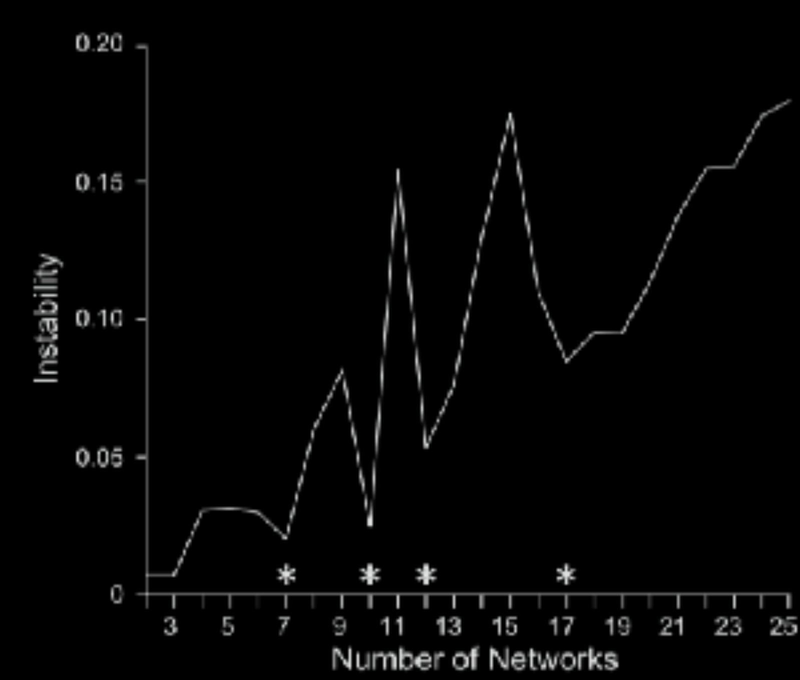
Margulies et al 2009 PNAS

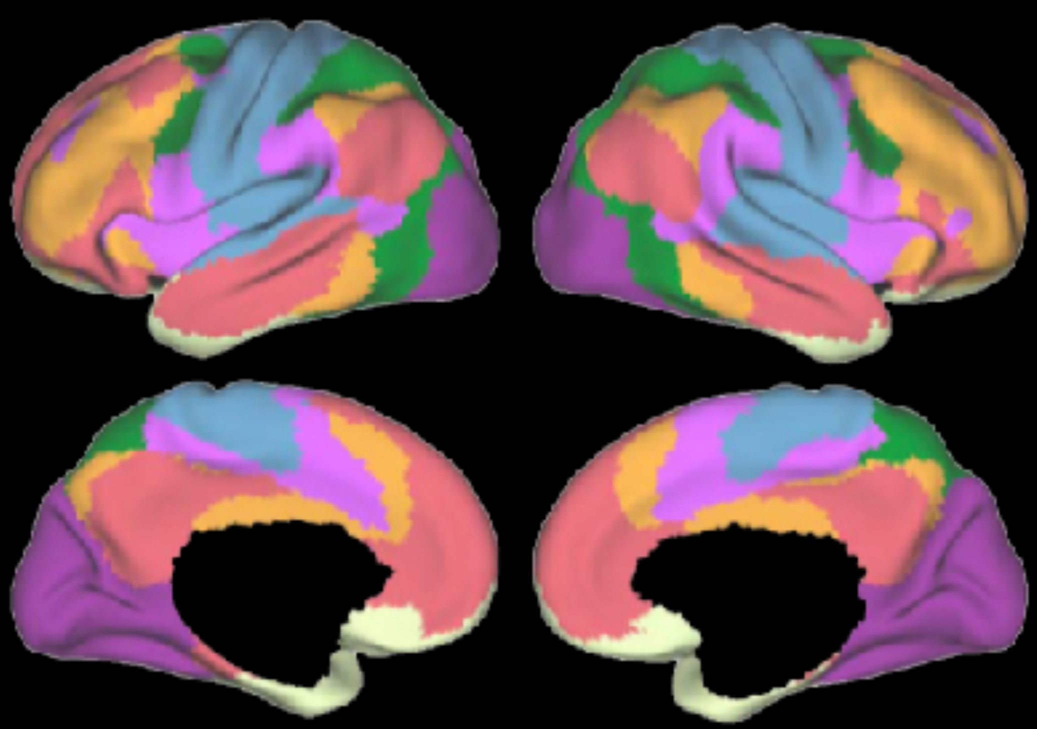
GRADIENT DETECTION TECHNIQUES



Yeo et al. 2011 JNeurophysiol

WHOLE BRAIN NETWORK ANALYSES: COMMUNITY DETECTION

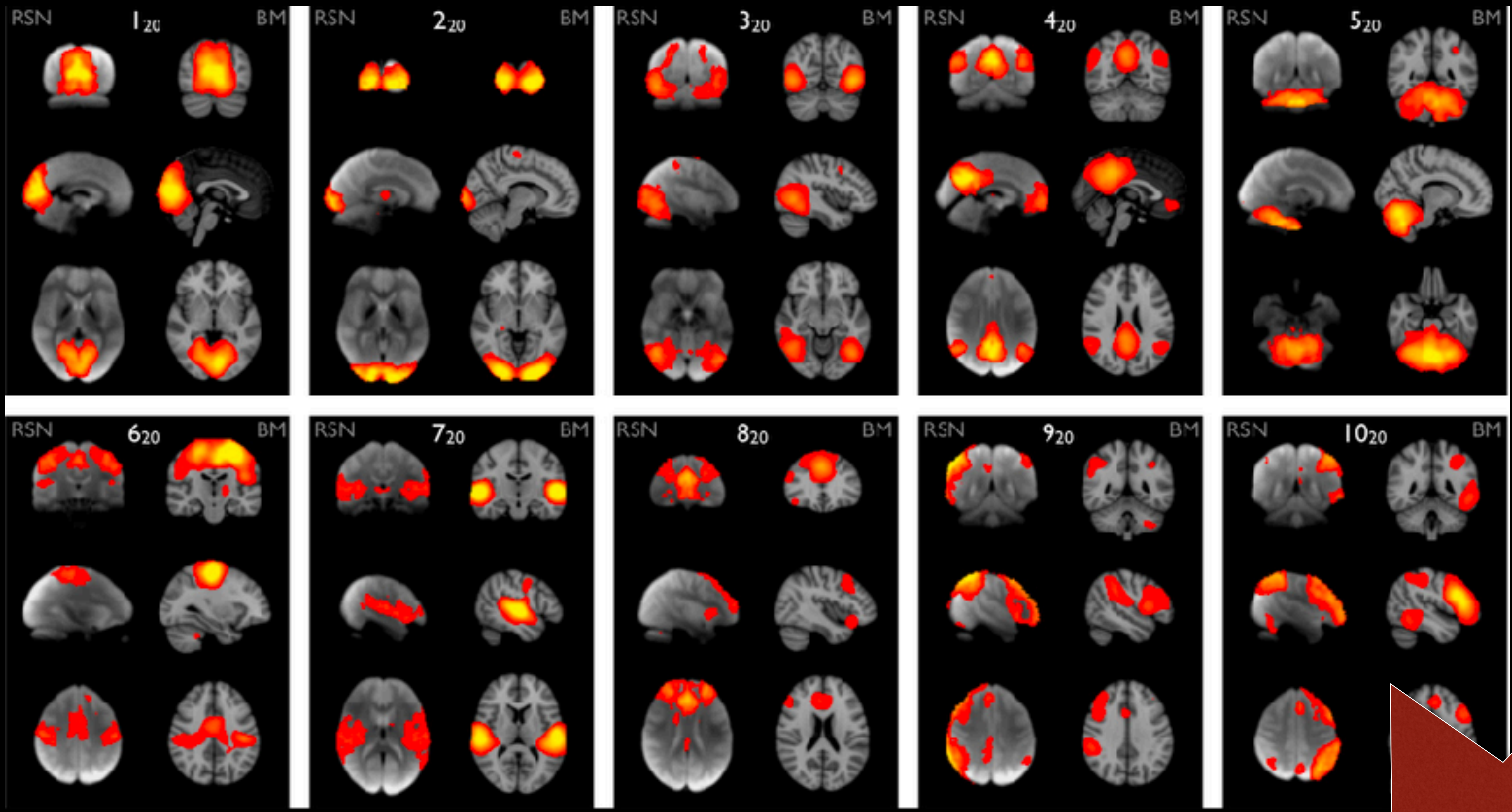




Yeo et al (2011) JNeurophysiol

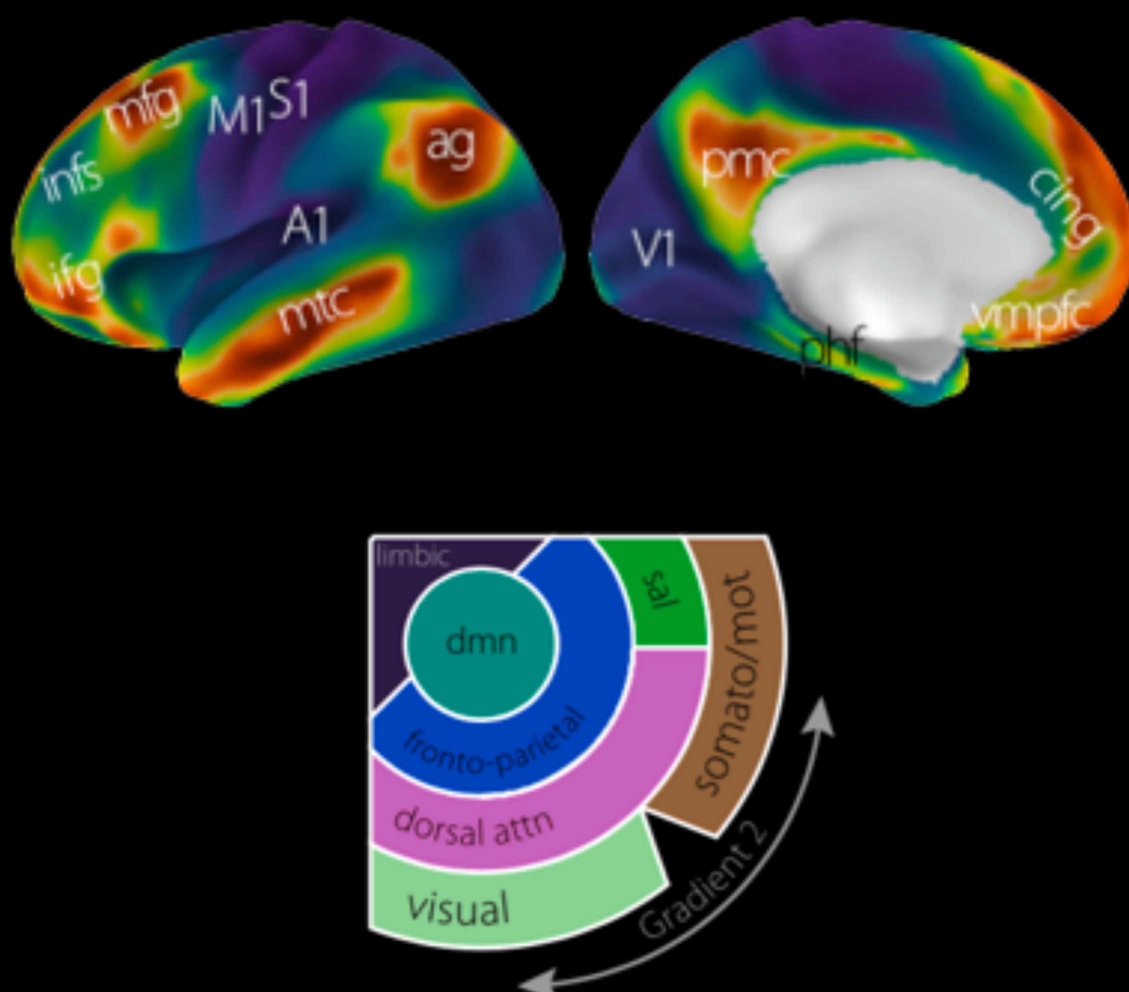
WEEK 6

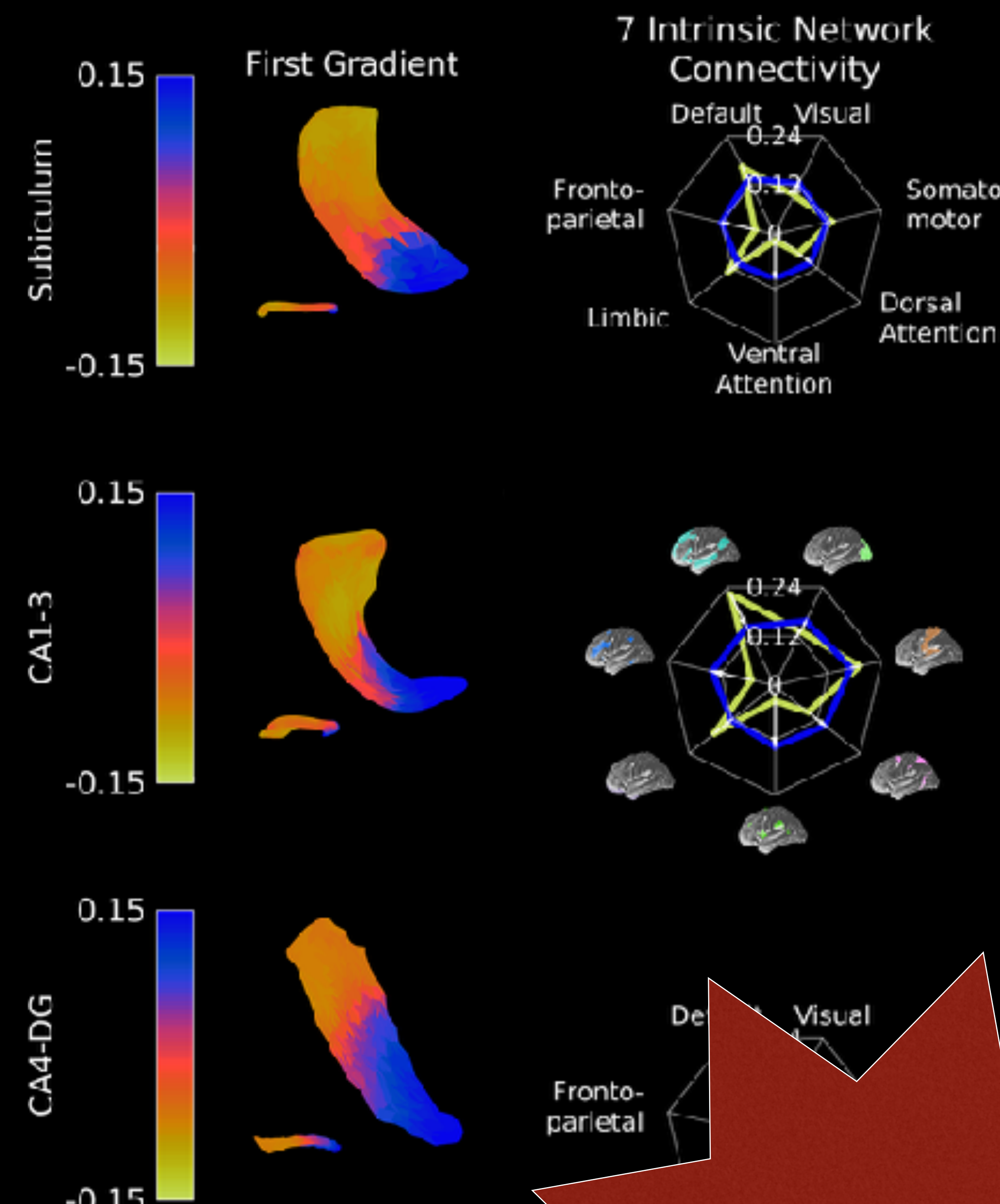
WHOLE BRAIN NETWORK ANALYSES: ICA



Smith et al. 2009 PNAS

WEEK 4





Margulies et al. 2016 PNAS,

Vos de Wael et al.

WEEK 9

RESTING-STATE fMRI CONNECTIVITY

IDEA:
CORRELATE SPONTANEOUS BRAIN ACTIVITY

+
COST-EFFECTIVE, REPRODUCIBLE

INDIVIDUALIZED

REGIONAL AND INTER-REGIONAL

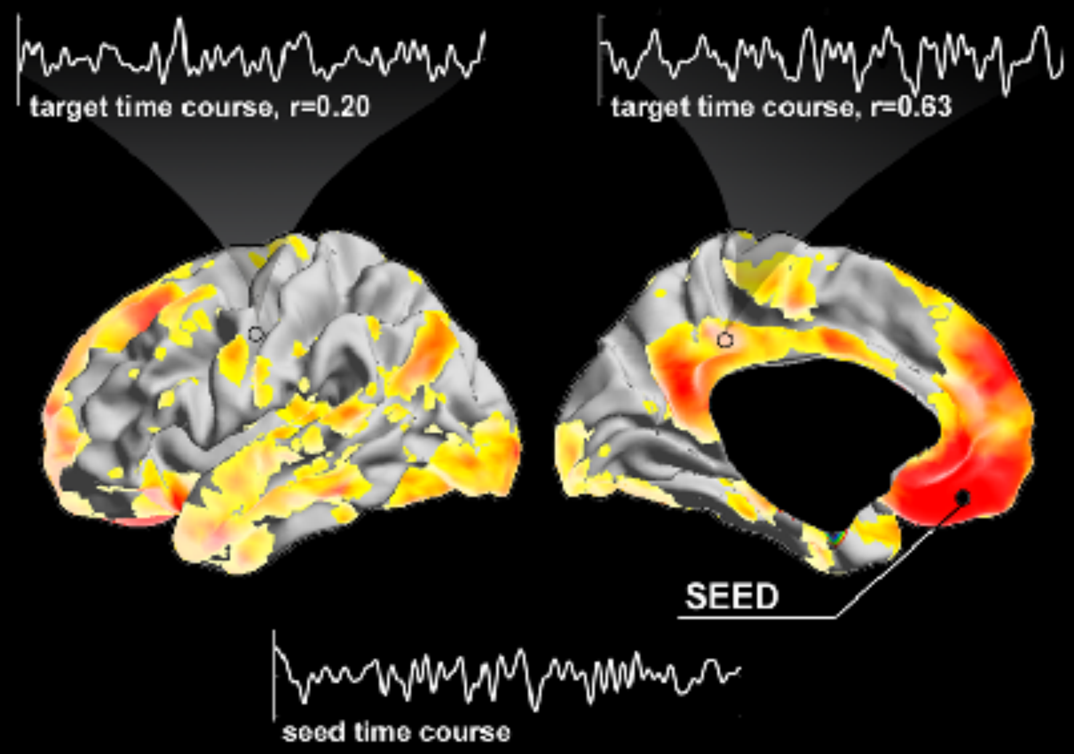
SEEDING FROM GM

CORRELATION WITH MENTAL STATES & INDUCTION

–
EFFECTS OF PHYSIOLOGY + MOTION

INDIRECT CONNECTIONS

CORRELATION WITH MENTAL STATES & INDUCTION



STRUCTURAL COVARIANCE ANALYSIS
COVARIANCE, MATURATION, MICROSTRUCTURAL SIMILARITY

MRI COVARIANCE ANALYSIS

IDEA:
CORRELATE MORPHOLOGICAL INDICES ACROSS SUBJECTS

+

COST-EFFECTIVE, REPRODUCIBLE

DIRECT SEEDING FROM GREY MATTER POSSIBLE

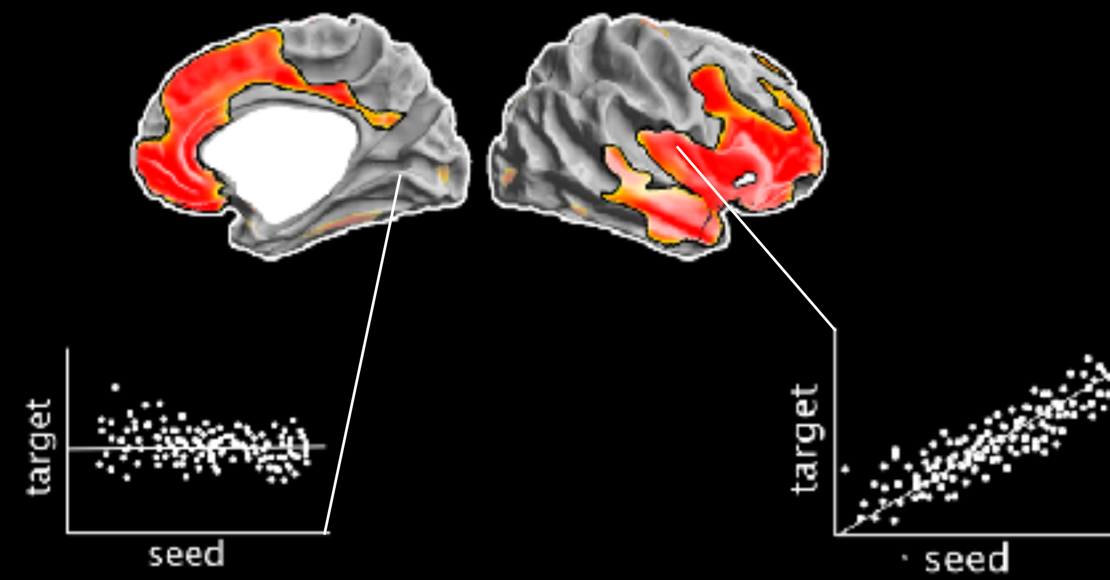
SIMPLE PREPROCESSING AND MODELLING

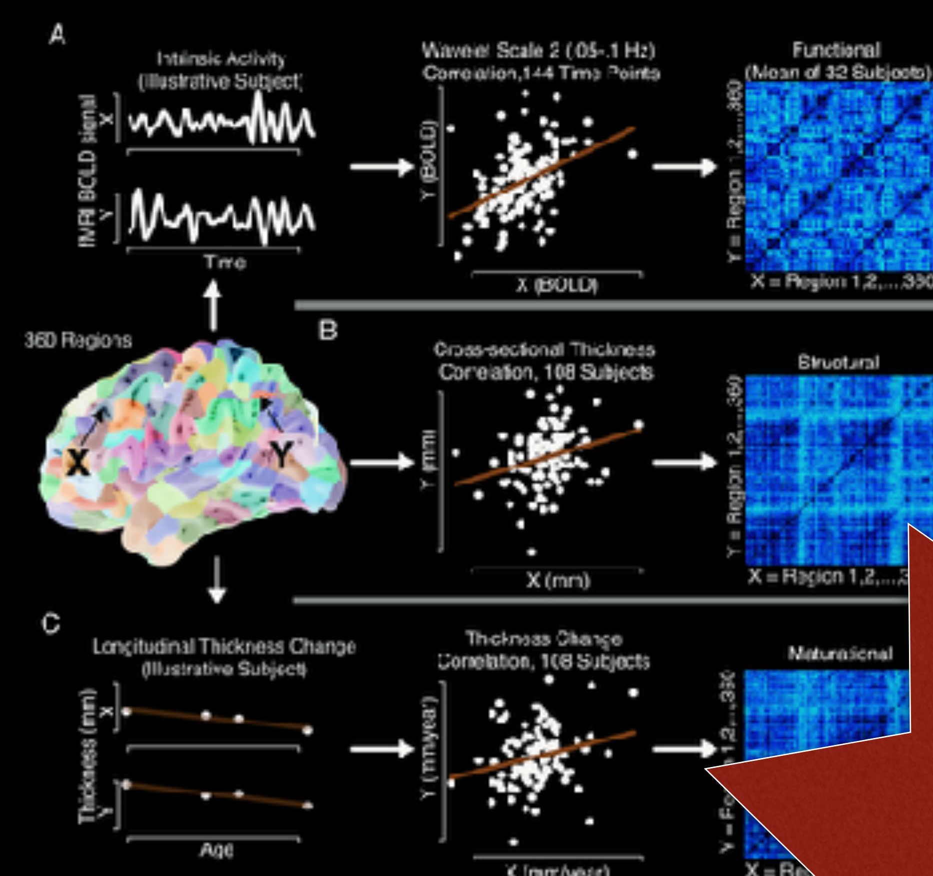
–

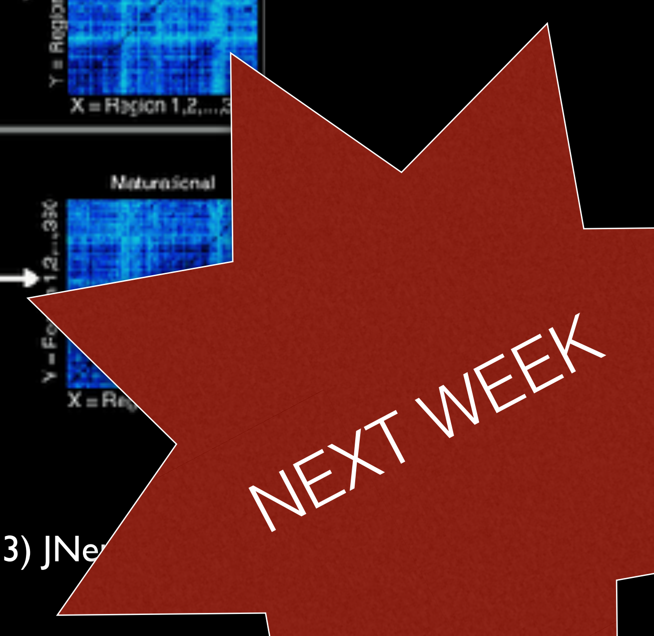
ONLY GROUP-WISE

RELATES RATHER TO PROCESSES THAN TO STATES

NO DIRECT WM CONNECTIVITY MEASUREMENT



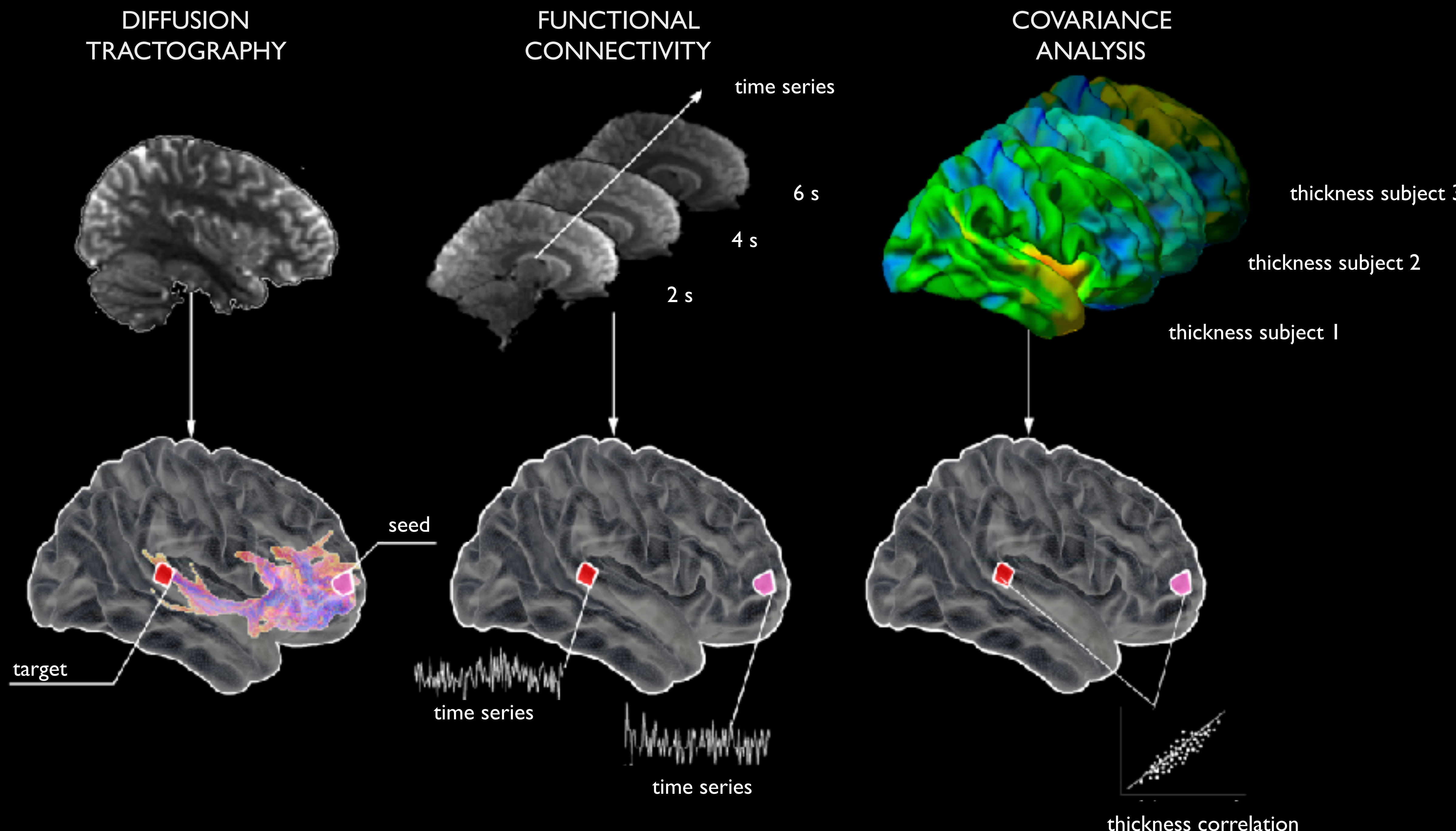




Alexander-Bloch, Bullmore, Giedd (2013) JNe

CONNECTOME GENERATION

INTER-REGIONAL CONNECTIVITY ANALYSIS

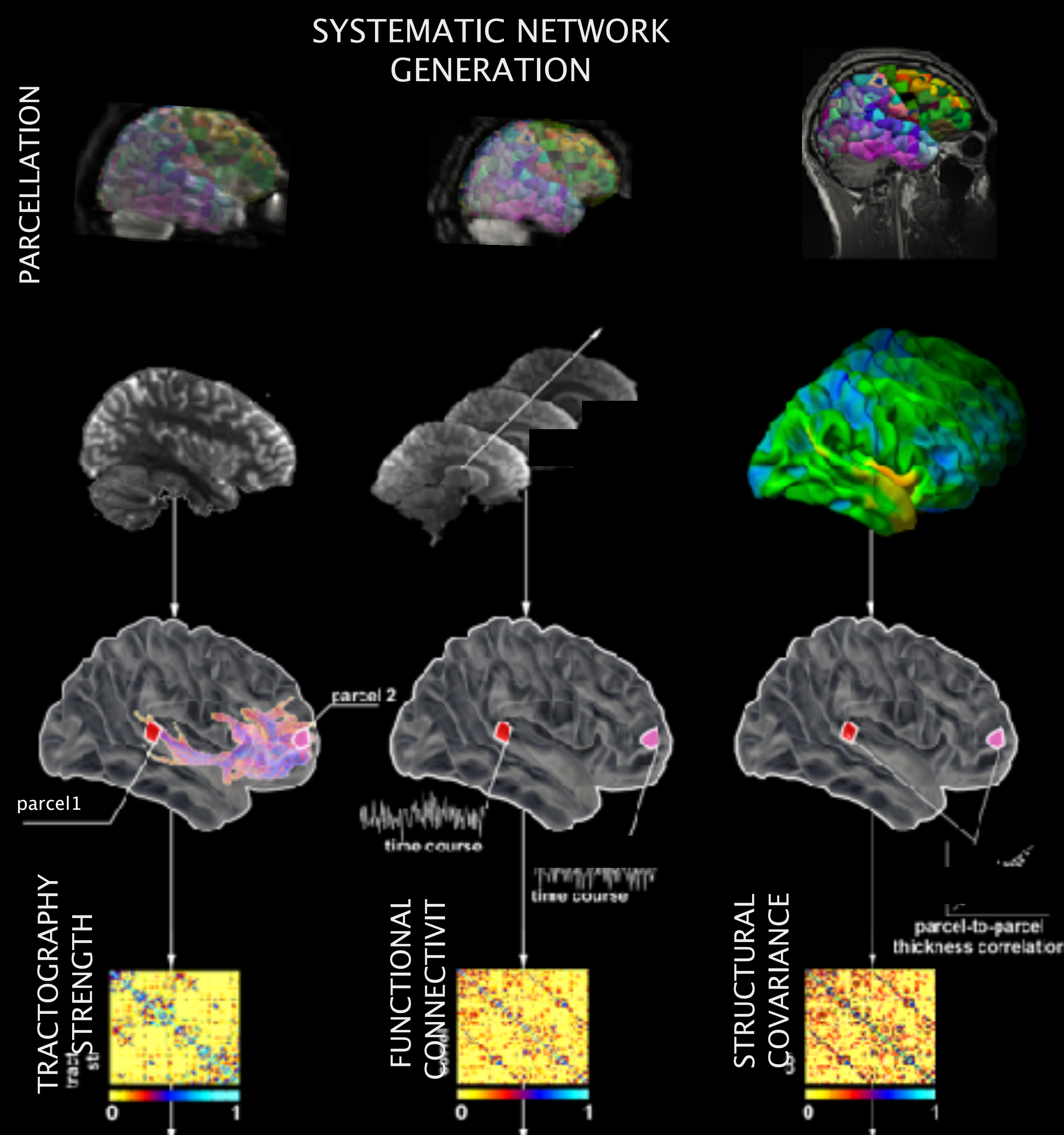


Mori et al. (1999) Ann Neu
Behrens et al. (2007) NIMG

Friston (1994) HBM
Smith (2012) NIMG

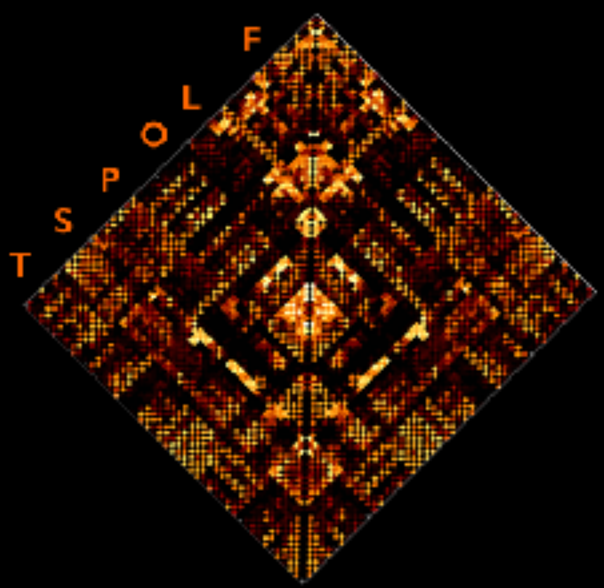
Lerch et al. (2006) NIMG
Alexander-Bloch et al. (2013) NRN

CONNECTOME ANALYSIS

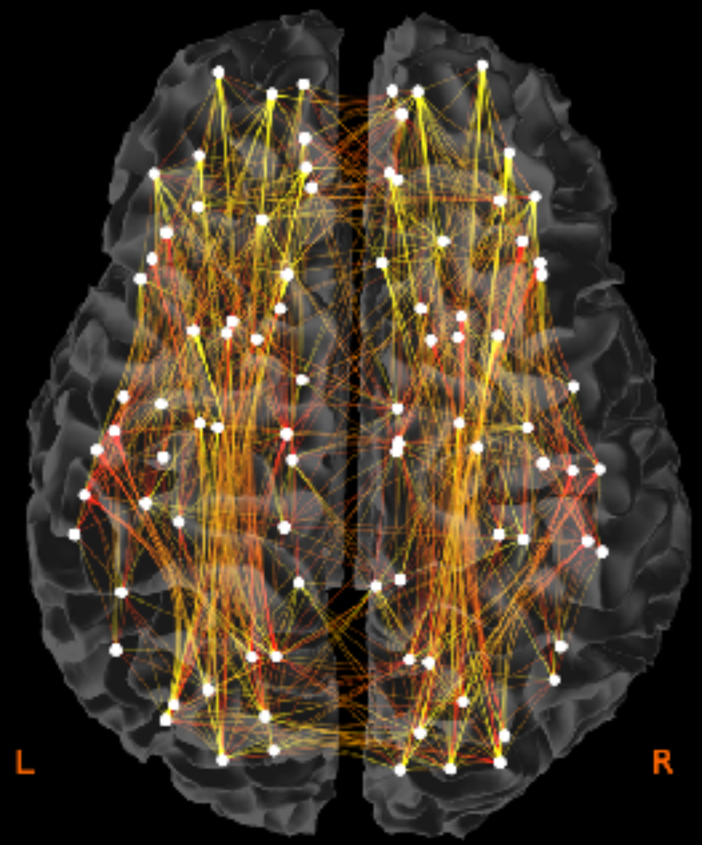


Bullmore and Sporns (2009) NRN, Watts and Strogatz (1998) Nature

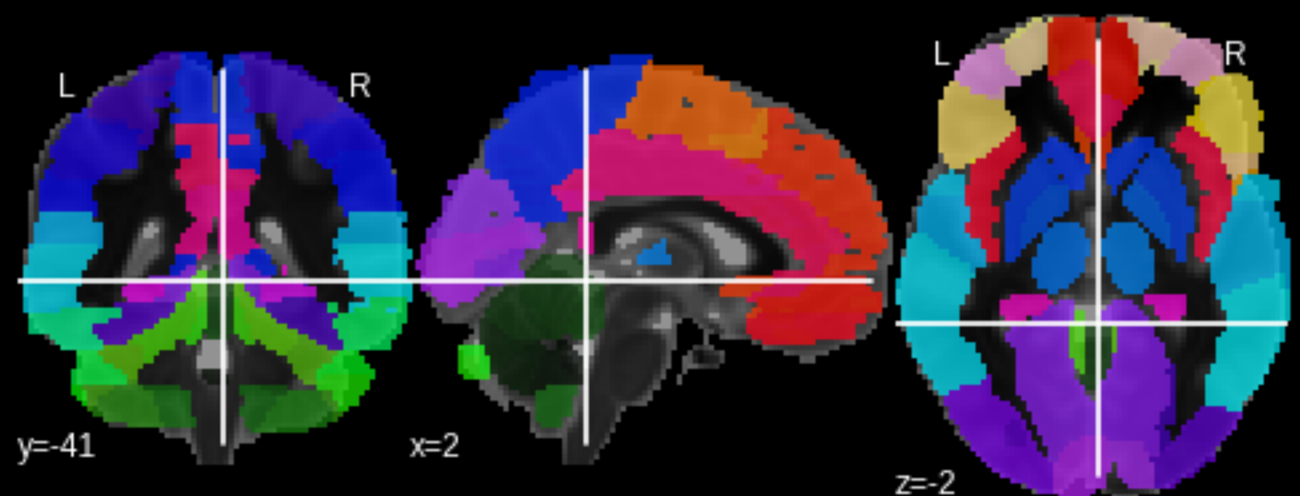
MATRICES AND GRAPHS



CONTROLS



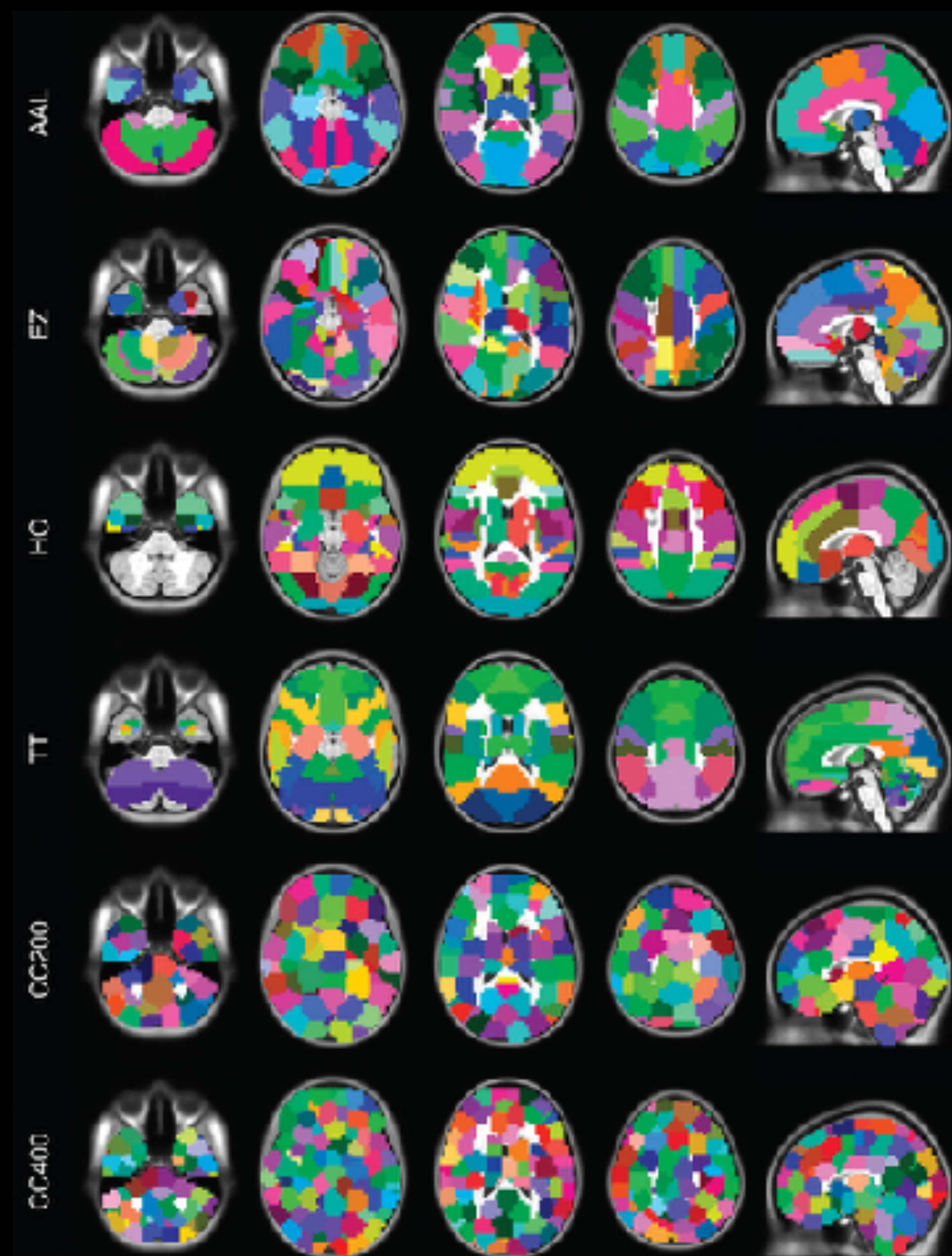
DEFINITION OF REGION



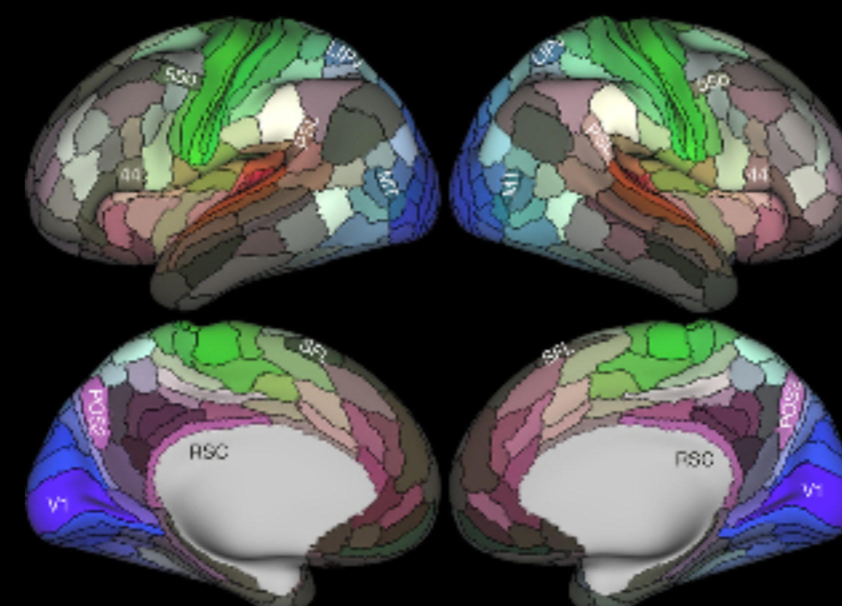
Tzuorio-Mazoyer et al (2002) Neuroimage

DEFINITION OF REGION

Fan et al (2016) Cerebral Cortex



Craddock et al (2013) Nature Methods



Glasser et al (2016) Nature

INTERIM SUMMARY

NEUROIMAGING TECHNIQUES MAP
FUNCTIONAL AND STRUCTURAL CONNECTIONS

COMPLEMENTARY TECHNIQUES:
DIFFUSION MRI TRACTOGRAPHY, RESTING-STATE FMRI CORRELATIONS, STRUCTURAL COVARIANCE

CONNECTOMES:
MATRICES GENERATED FROM SYSTEMATIC ROI-TO-ROI CONNECTIVITY ANALYSES

INFLUENCE OF PARCELLATION ON FINDINGS:
AAL78, CRADDOCK200, GLASSER360, …

CRADDOCK

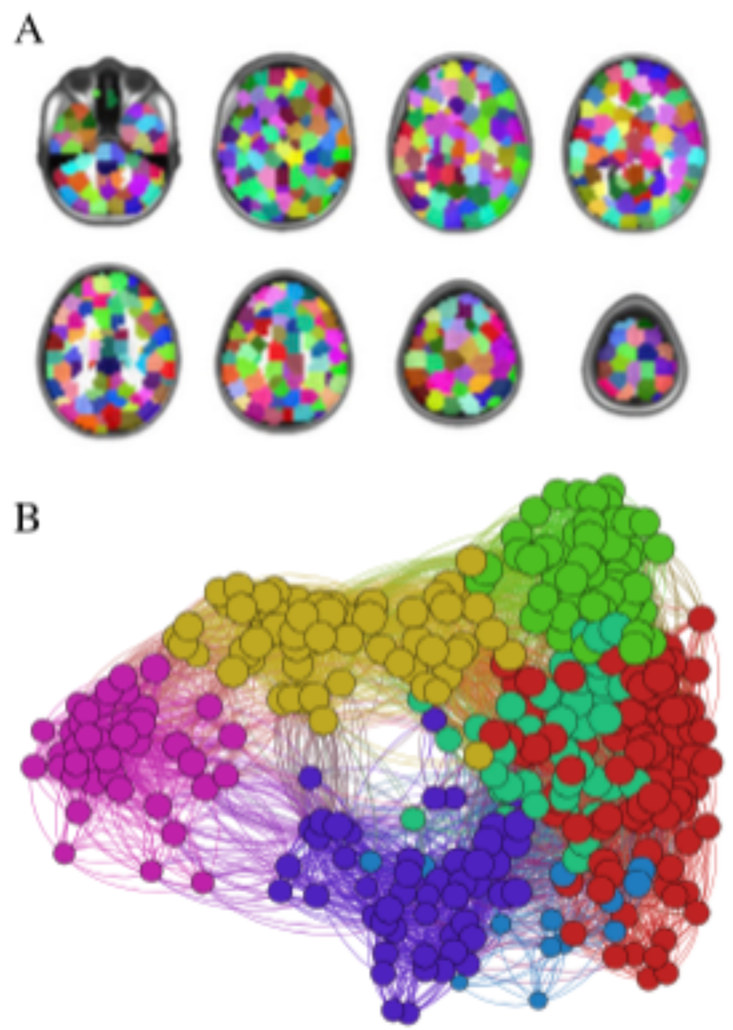


Figure 1 Parcellation of the brain into functionally homogenous brain regions (A) and the resulting connectome (B). Community detection identifies seven different modules, which are indicated by the color of the nodes in B.

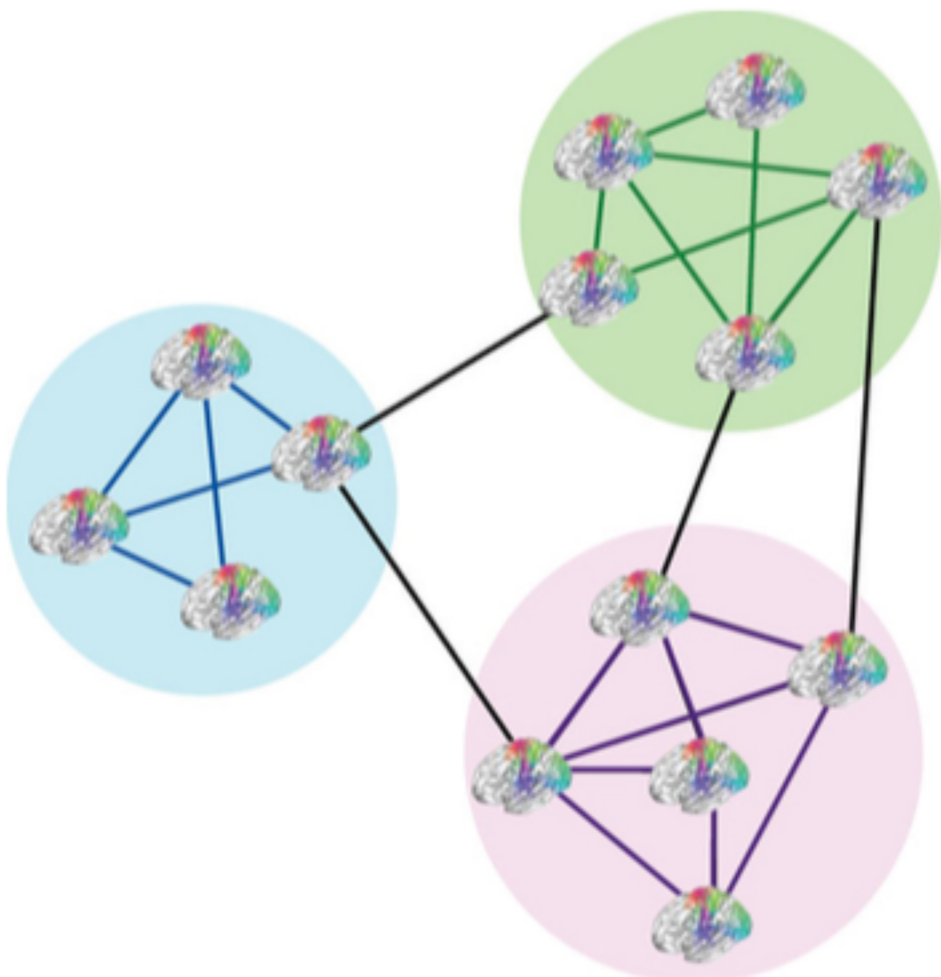


Figure 2 Identifying communities based on neurophenotypes. Brain glyphs provide succinct representations of whole brain functional connectivity [85].

JBABDI

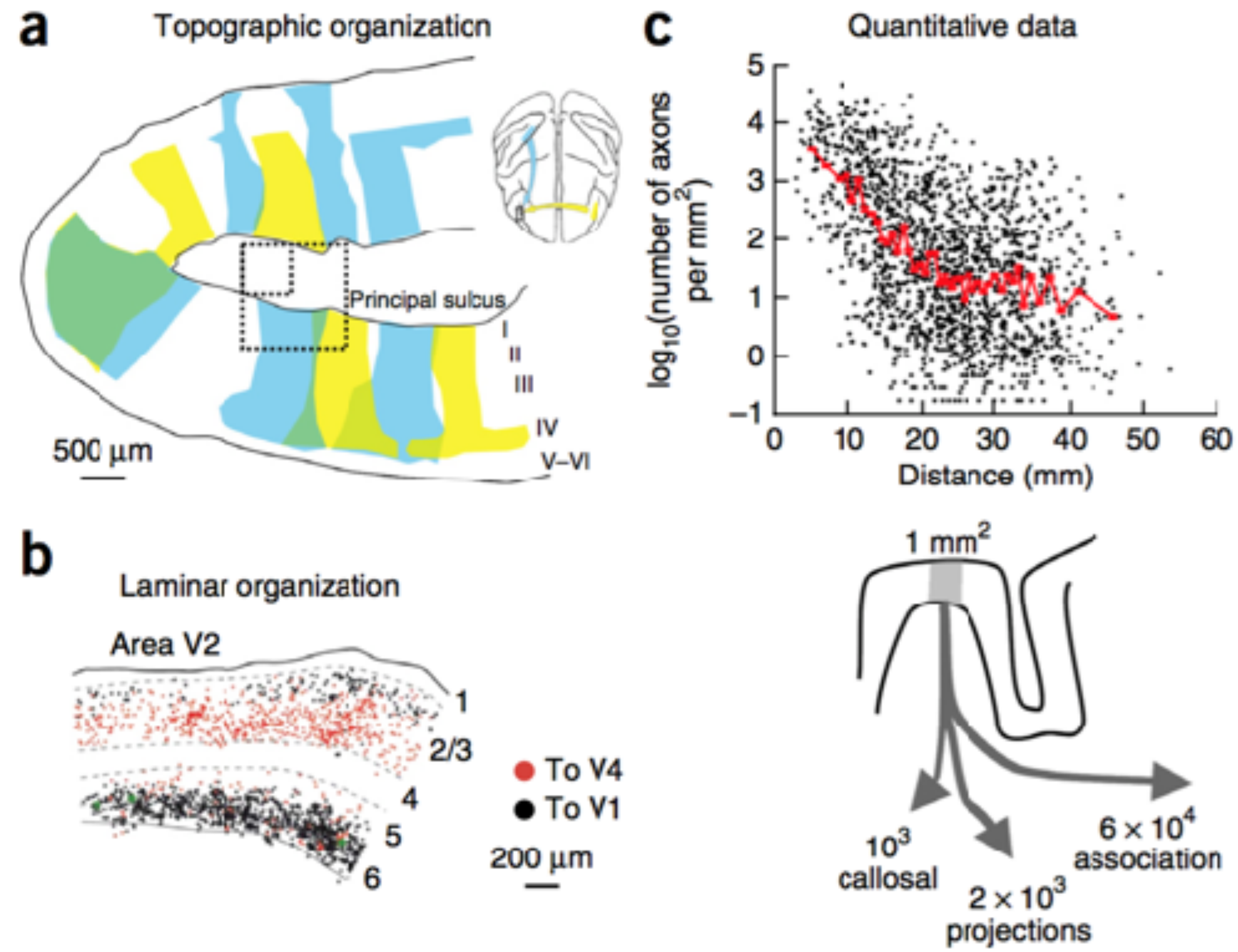


Figure 1 Examples of complex white-matter organization in monkey brains. (**a**) Topographic organization of afferent ipsilateral and contralateral connections to the principal sulcus in the macaque brain showing columnar interdigitation. Typical 1-mm and 0.5-mm isotropic voxels are shown as dashed boxes, indicating the resolution needed to reveal such macro-scale organization (modified with permission from ref. 9). (**b**) Laminar pattern of efferent connections from visual area V2. Cells connecting to V1 sit primarily in superficial and deep layers, whereas those connecting to V4 originate from layer 2/3. No labeled cells are found in layer 4 (modified with permission from ref. 115). (**c**) Top, estimate of the number of efferent ipsilateral association axons from 1 mm^2 of cortex as a function of the distance between source and target regions. Bottom, estimate of the number of axons from 1 mm^2 of cortex forming different categories of fiber tracts. Estimates are based on ref. 1 and data from http://core-nets.org.

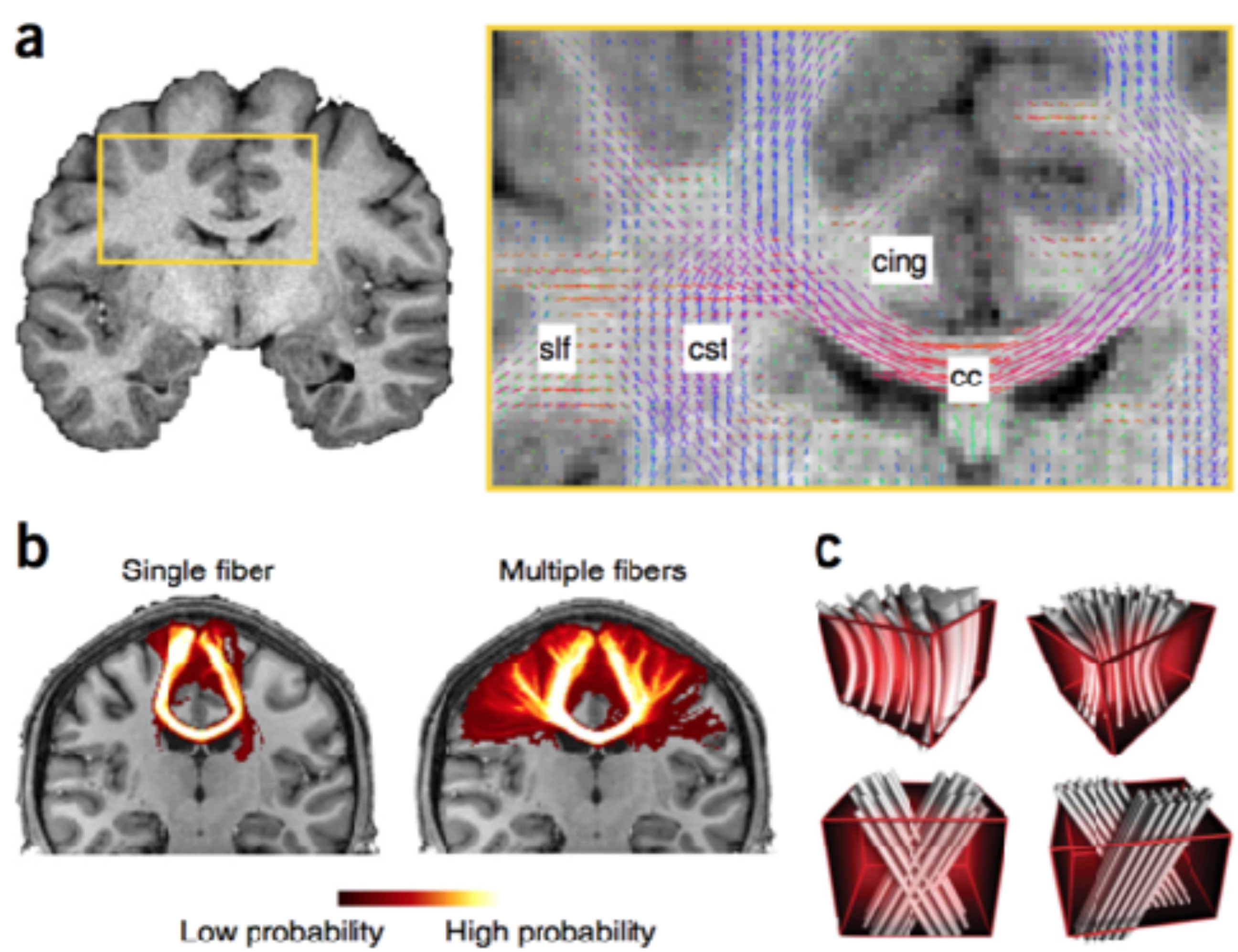


Figure 2 Diffusion MRI and tractography. (**a**) A coronal section through a human brain (left) and estimated fiber orientations from diffusion MRI data (right). Voxel-wise fibers are color-coded according to their orientation (red = left-right, green = anterior-posterior, blue = ventral-dorsal). Major fiber bundles can be visualized on the orientation maps (cing = cingulum bundle, cc = corpus callosum, cst = cortico-spinal tract, slf = superior longitudinal fasciculus). Note the many voxels with multiple orientation estimates (crossing fibers) allowing the major bundles to cross each other. Tractography algorithms use this type of local orientation estimates to infer long trajectories of white matter bundles. Data are from the Human Connectome Project[65,116]. (**b**) Probabilistic tractography of the corpus callosum pathways consists of constructing a spatial histogram that represents the likelihood that streamlines, through the diffusion field, pass through any voxel of the brain. The scenario of a single fiber orientation in a voxel is not always representative of the underlying anatomy. Crossings of fiber bundles are very common in white matter. The figure shows probability maps arising from the body of the corpus callosum when modeling multiple versus single fiber orientations. Ignoring fiber crossings gives rise to many false negatives (the lateral callosal projections are missing), but also false positives (paths merging with the internal capsule). (**c**) Ambiguities in modeling voxel-wise fiber orientations. Four different putative voxel-wise patterns of axonal organization can give rise to the same diffusion scatter pattern when averaged over a voxel. Top left, bending fibers; top right, 'kissing' fibers; bottom left, inter-digitated fibers; bottom right, 'touching' fibers. Simple crossing fiber modeling cannot distinguish these cases, which may lead to false positive and false negative connections. Figure reproduced with permission from ref. 117.

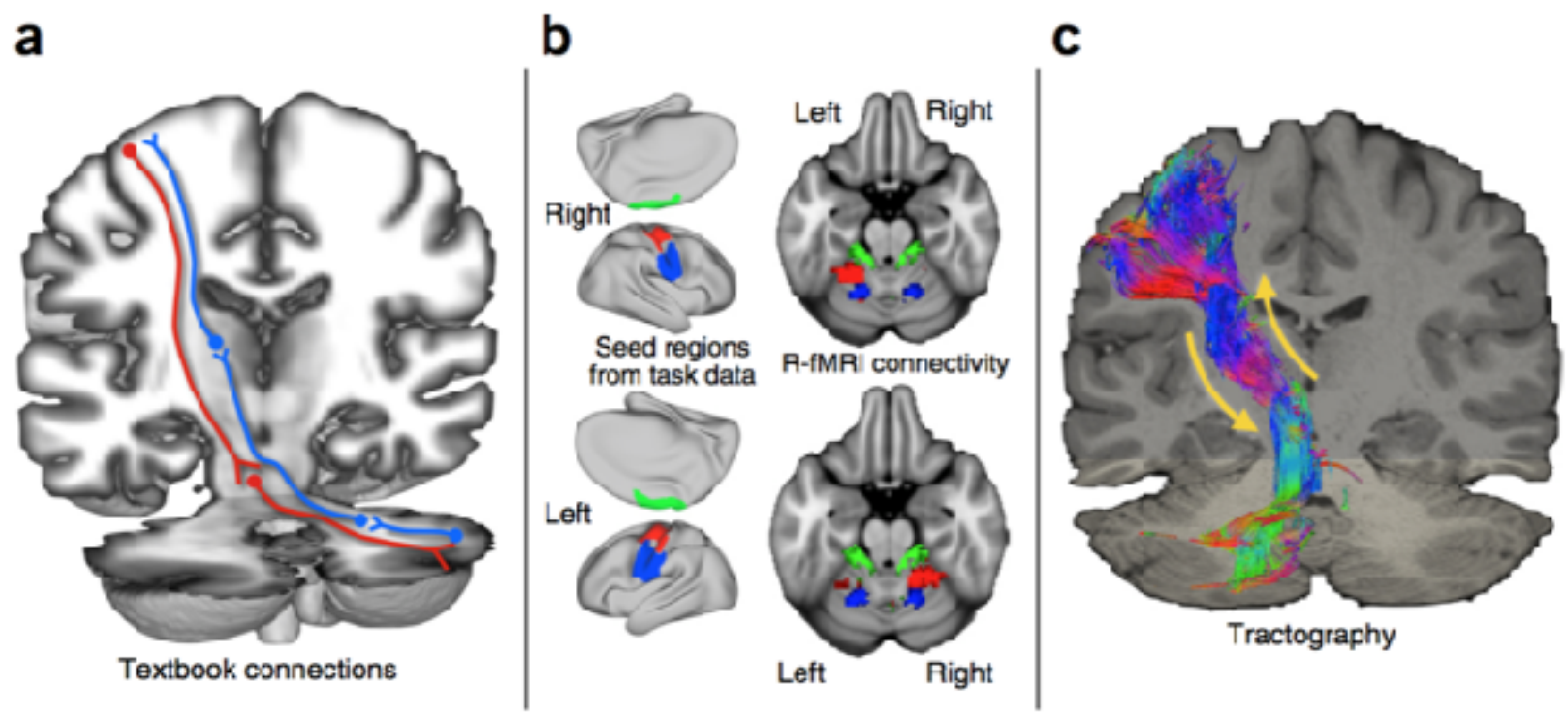


Figure 3 Textbook and estimated cortico-cerebellar connections using functional and diffusion MRI. (**a**) Multi-synaptic efferent (blue) and afferent (red) cerebellar connections decussate at the level of the pons. (**b**) Resting-state functional connectivity of motor cortical regions to cerebellum (foot, hand and face area as green, red and blue, respectively). The somatotopic organization is evident, but notice that, except for the hand area, homolog seed areas in the right and left hemisphere may yield almost identical connectivity results. (**c**) Diffusion MRI tractography streamlines when seeding from the hand area of the primary motor cortex. Tractography reconstructs the correct paths, but fails to decussate at the pons as a result of the smoothness constraints used in tracking algorithms.

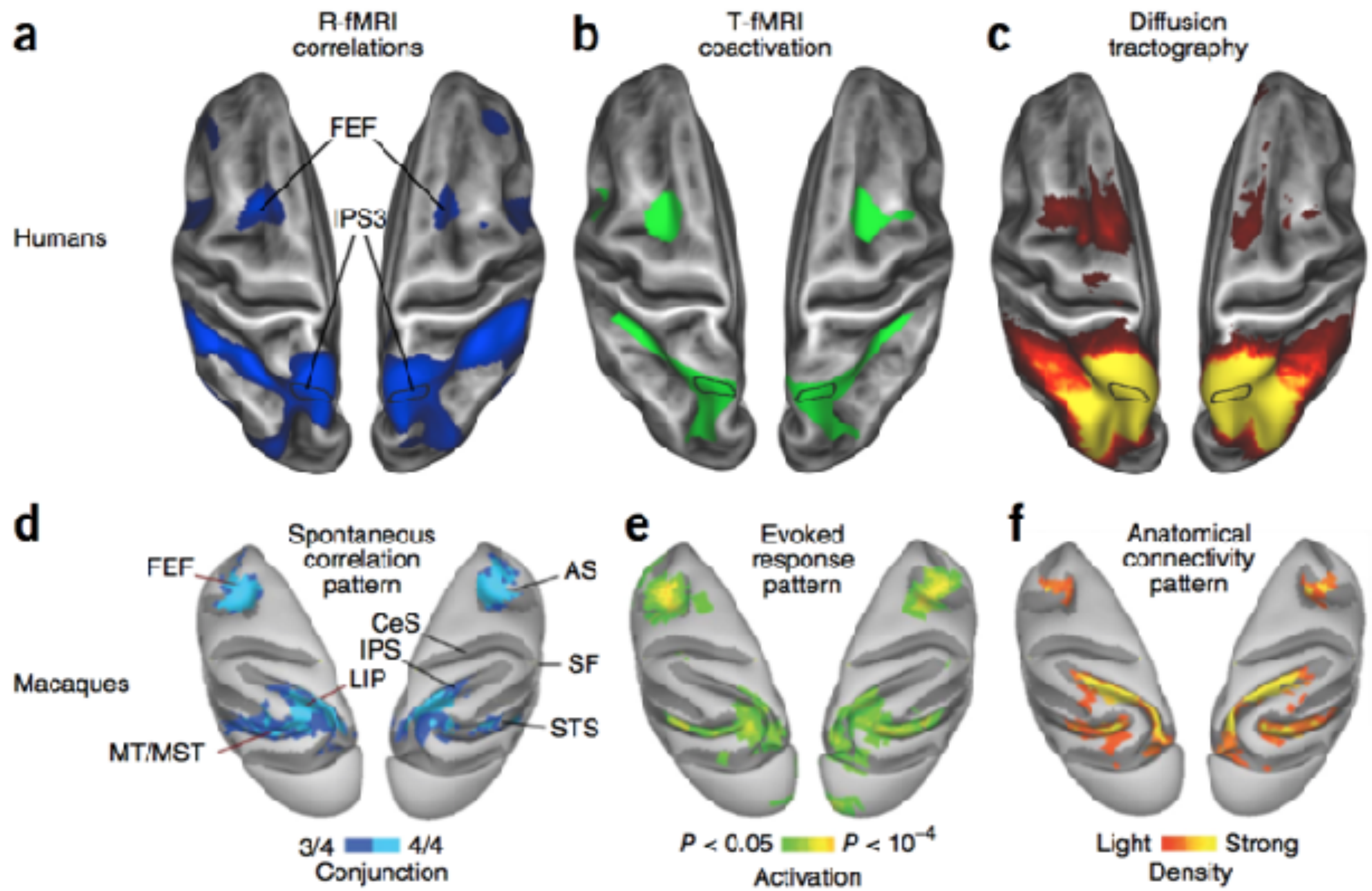


Figure 4 Agreement between functional and structural connectivity in measuring connections in human and macaques. (**a**–**c**) Connectivity maps for area IPS3 obtained from data acquired for the Human Connectome Project[65] (average connectivity of 40 unrelated subjects). (**a**) Functional connectivity using correlations of R-fMRI time series. (**b**) Functional connectivity using correlations of activations across multiple tasks (7 tasks and 42 contrasts). (**c**) Structural connectivity using diffusion MRI and probabilistic tractography. (**d**) Map of voxels exhibiting BOLD correlations in spontaneous activity amongst at least three of four regions of the oculomotor system in the anesthetized macaque (dorsal views, AS: arcuate sulcus, CeS: central sulcus, FEF: frontal eye fields, IPS: intraparietal sulcus, LIP: lateral intraparietal area, MT: middle temporal area, SF: sylvian fissure, STS: superior temporal sulcus). (**e**) Activation pattern evoked by performance of a saccadic eye movement task (average of two monkeys). (**f**) Density of cells labeled by retrograde tracer injections into LIP (average of three monkeys). Images in **d**–**f** are adapted with permission from ref. 63.

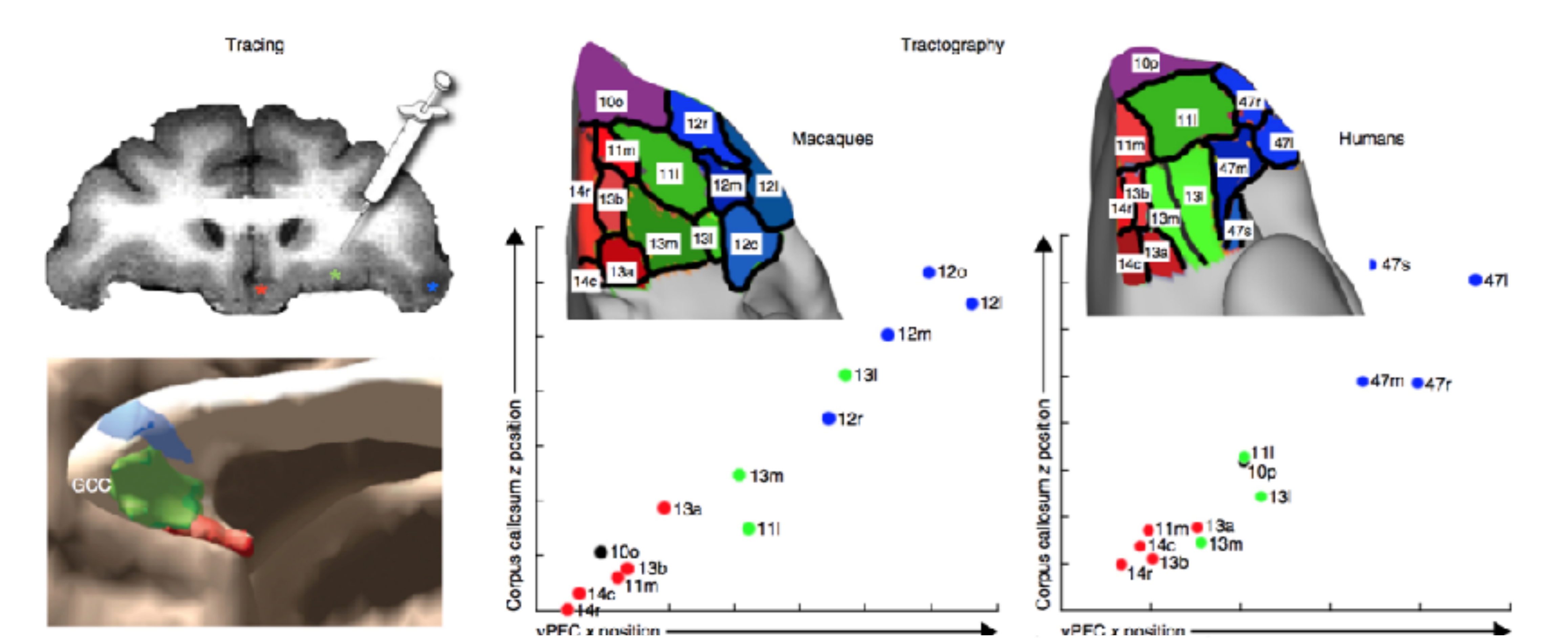


Figure 5 Testing generic organization principles using tractography. Injection of tracers into three locations of the macaque vPFC reveals that the medial-lateral position of the injection sites in the vPFC dictates the relative position of the corresponding pathways in the genu of the corpus callosum (GCC). Tractography is then utilized to test and confirm that this pattern is generalizable to the entire vPFC, both in macaques and humans. The scatter plots show the positions of the centers of gravity of the vPFC seed regions plotted against the centers of gravity of the pathways. It is clear that the *x* position (medial-lateral) of the seed regions correlates significantly with the *z* position (ventral-dorsal) of the corpus callosum projections. The insets show subdivisions of the vPFC into 13 regions according to ref. 105 for macaques and ref. 104 for humans. The regions are colored in red, green and blue according to their approximate medial-dorsal positions for ease of visualization. Figure adapted with permission from refs. 26,69.

neuro

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CIHR IRSC

NSERC CRSNG

CLAE LCCE Canadian League Against Epilepsy