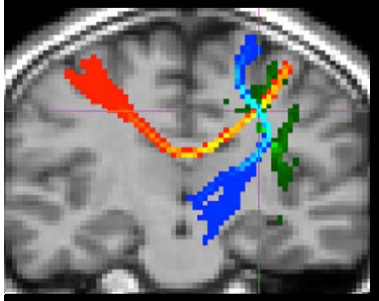
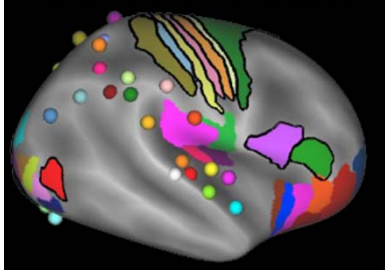
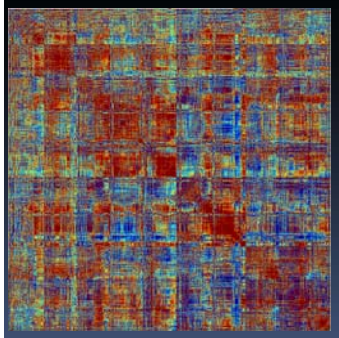
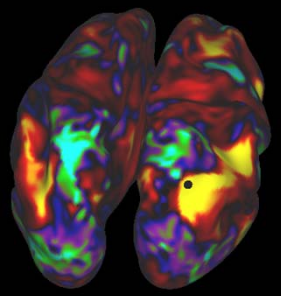
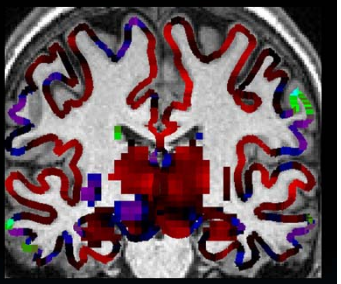
# Mapping the Human Brain

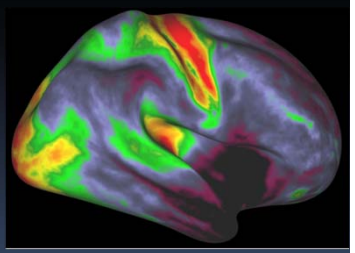












David C. Van Essen
Washington University in St. Louis

Capitol Hill Luncheon
June 5, 2013

Supported by the NIH Neuroscience Blueprint

# Big Questions

- What makes us think, love, talk, and ‘tick’?
- Why do each of us behave so differently?
- What goes wrong in devastating brain disorders?

  Alzheimer’s, autism, schizophrenia,…..

It’s the connections – the  wiring of the brain!

Physical wires (axons, dendrites)

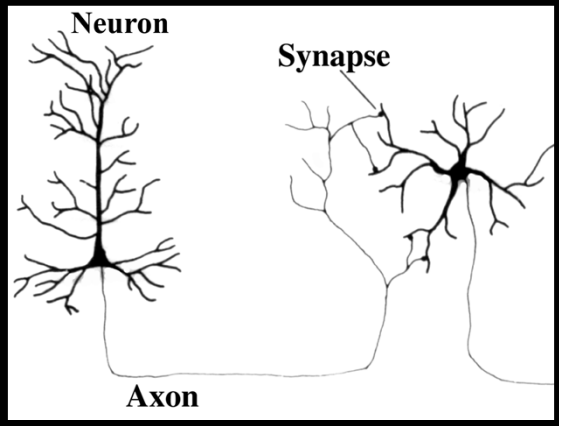
Strength of connections: “Functional connectivity”

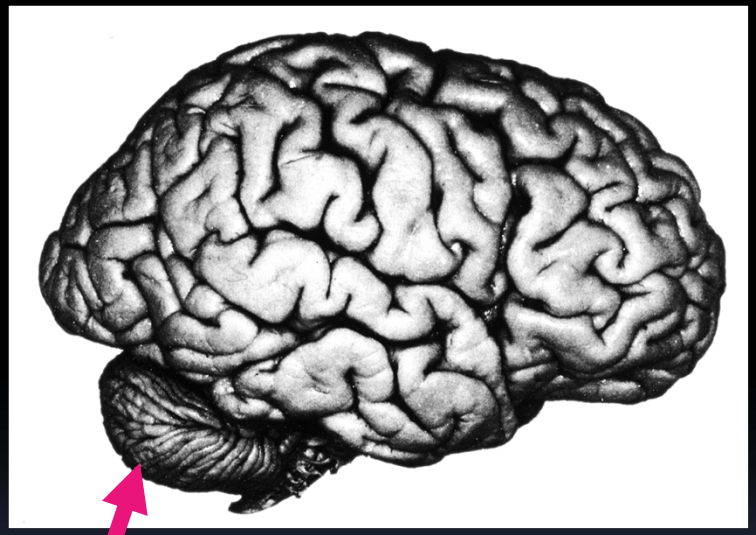
# Human Brain Parts List

Whole brain: 1500g; 86 billion neurons[1]

Cerebral cortex:

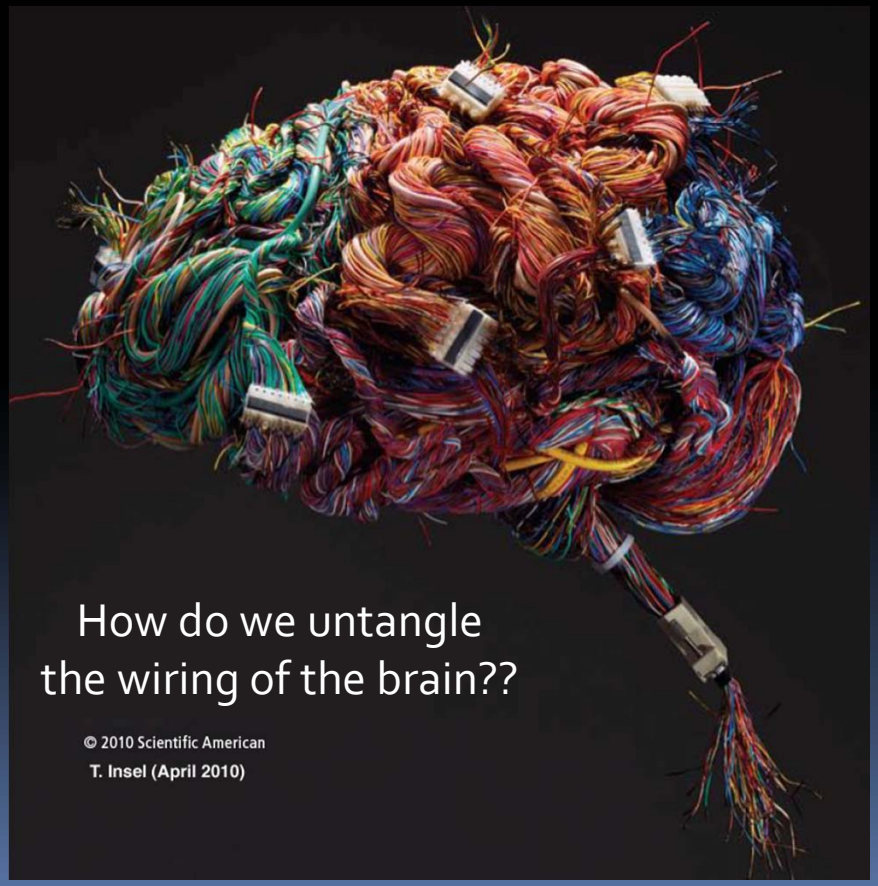
- ~80% of brain mass
- 16 billion neurons (~20%)
- 150 trillion synapses
- 100,000 miles of axons in white matter

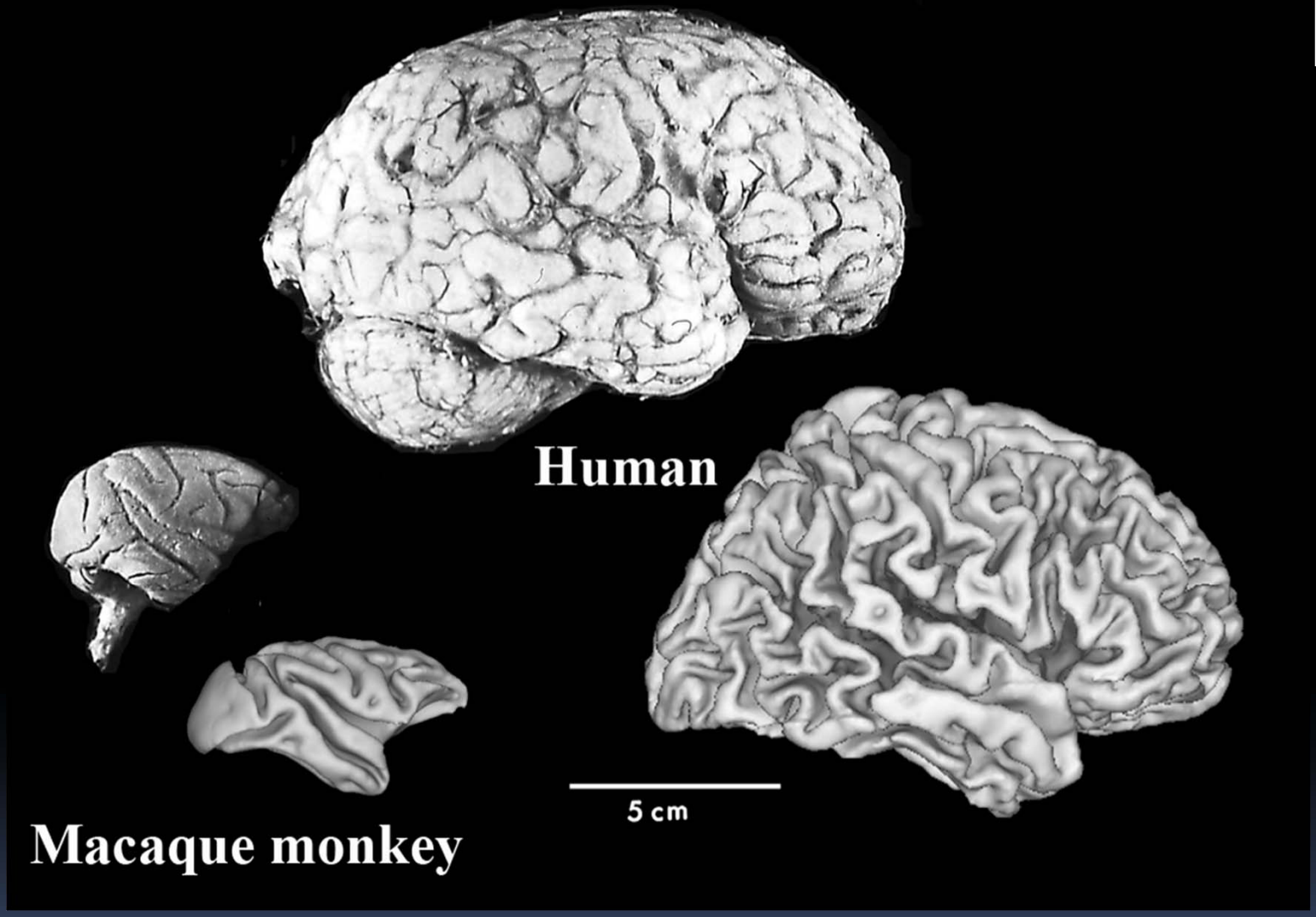


Cerebellum:

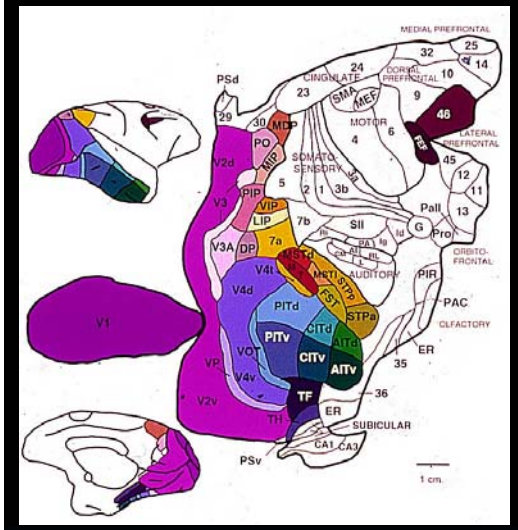
- 10% of brain mass
- 69 billion neurons (80%)





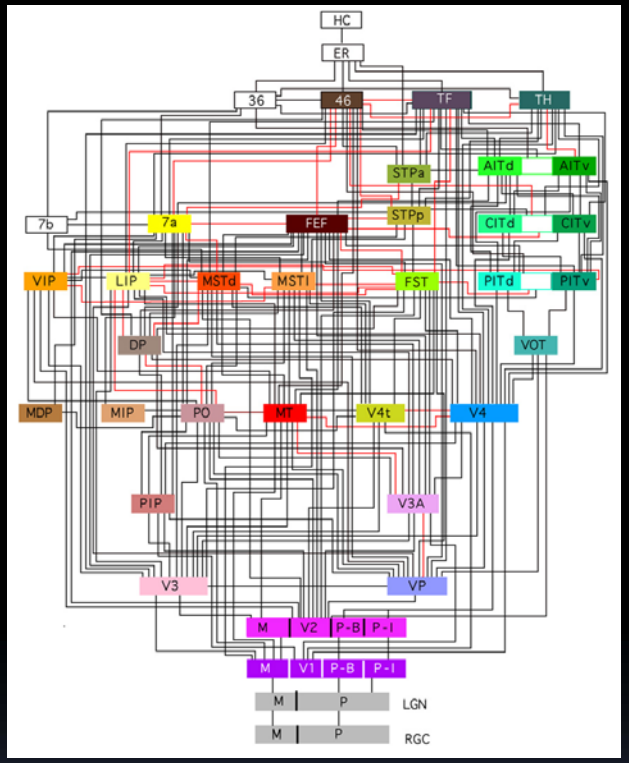

- Focus on human brain
- Invaluable information from animal models

# A view of primate cortex in 1991




(Felleman & Van Essen, 1991)

A cortical hierarchy




A binary connectivity matrix:

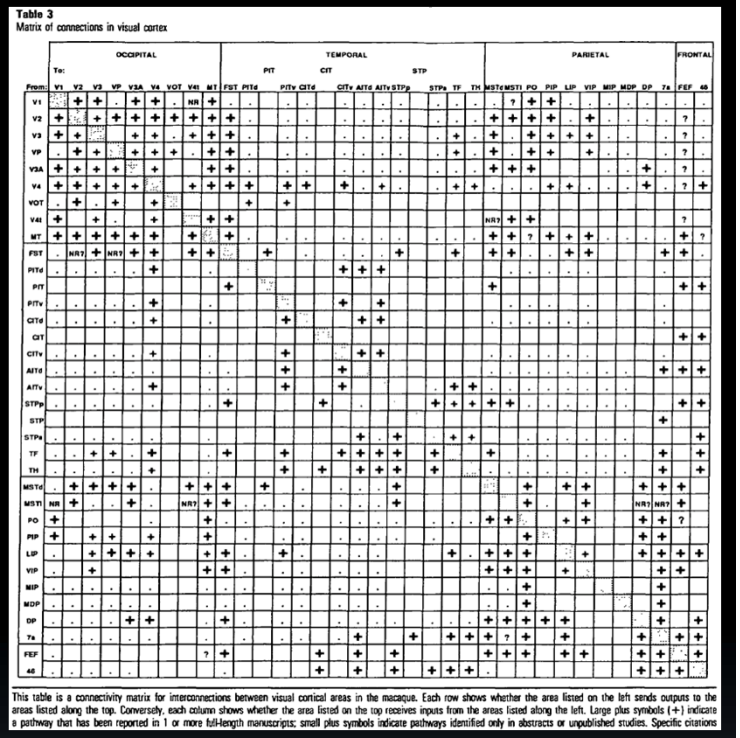


**Table 3**
Matrix of connections in visual cortex

| | OCCIPITAL | | | | | | | | TEMPORAL | | | | | | | | | | PARIETAL | | | | | | | FRONTAL | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | PIT | | | CIT | | | STP | | | | | | | | | | | | |
| From: / To: | V1 | V2 | V3 | VP | V3A | V4 | VOT | V4t | MT | FST | PITd | PITv | CITd | CITv | AITd | AITv | STPp | STPa | TF | TH | MSTd | MSTl | PO | PIP | LIP | VIP | MIP | MDP | DP | 7a | FEF | 46 |
| V1 | | + | + | . | + | + | . | NR | + | . | . | . | . | . | . | . | . | . | . | . | . | ? | + | + | . | . | . | . | . | . | . |
| V2 | + | | + | + | + | + | + | + | + | + | . | . | . | . | . | . | . | . | . | . | + | + | + | + | . | + | . | . | . | . | ? | . |
| V3 | + | + | | . | + | + | . | + | + | + | . | . | . | . | . | . | . | . | + | . | + | . | + | + | + | + | . | . | . | . | ? | . |
| VP | . | + | + | | . | + | + | . | + | + | . | . | . | . | . | . | . | . | + | . | + | . | + | . | + | . | . | . | . | . | ? | . |
| V3A | + | + | + | + | | . | . | . | + | + | . | . | . | . | . | . | . | . | . | . | + | + | . | . | . | . | . | + | . | ? | . |
| V4 | + | + | + | + | + | | . | + | + | + | + | + | + | + | . | + | . | . | + | + | . | . | . | + | + | . | . | . | + | . | ? | + |
| VOT | . | + | . | + | . | + | | . | + | . | + | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . |
| V4t | + | . | + | . | . | + | . | | + | + | . | . | . | . | . | . | . | . | . | . | NR? | + | + | . | . | . | . | . | . | . | ? | . |
| MT | + | + | + | + | + | + | . | + | | + | . | . | . | . | . | . | . | . | . | . | + | + | ? | + | + | . | . | . | . | . | + | ? |
| FST | . | NR? | + | NR? | + | + | . | + | + | | . | + | . | . | . | + | . | . | + | . | + | + | . | . | + | + | . | . | + | . | + | . |
| PITd | . | . | . | . | . | + | . | . | . | . | | . | + | + | + | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . |
| PIT | . | . | . | . | . | . | . | . | + | . | . | | . | . | . | . | . | . | . | . | + | . | . | . | . | . | . | . | . | . | + | + |
| PITv | . | . | . | . | . | + | . | . | . | . | . | . | | . | + | + | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . |
| CITd | . | . | . | . | . | + | . | . | . | . | + | . | . | | + | + | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . |
| CIT | . | . | . | . | . | . | . | . | . | . | . | . | . | . | | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | + | + |
| CITv | . | . | . | . | . | + | . | . | . | . | . | . | + | . | . | | . | . | . | . | . | . | . | . | . | . | . | . | . | . | + | + |
| AITd | . | . | . | . | . | . | . | . | . | . | . | . | . | . | + | . | | . | . | . | . | . | . | . | . | . | . | . | . | . | + | + |
| AITv | . | . | . | . | . | + | . | . | . | . | . | . | + | . | + | | . | . | + | + | . | . | . | . | . | . | . | . | . | . | + | + |
| STPp | . | . | . | . | . | . | . | . | + | . | . | . | . | . | . | . | | + | + | + | + | + | . | . | . | . | . | . | . | . | + | + |
| STP | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | | . | . | . | . | . | . | . | . | . | . | . | . | + | . |
| STPa | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | | + | . | . | . | . | . | . | . | . | . | . | . | + |
| TF | . | . | + | + | . | + | . | . | + | . | . | + | . | + | + | + | . | . | + | | . | . | + | . | . | . | . | . | . | . | + | + |
| TH | . | . | . | . | . | + | . | . | . | . | . | + | . | + | + | + | . | . | + | . | | . | . | . | . | . | . | . | . | . | + | + |
| MSTd | . | + | + | + | + | . | . | + | + | + | . | + | . | . | . | . | . | . | . | . | . | | + | + | . | + | + | . | + | + | + | . |
| MSTl | NR | + | . | . | + | . | . | NR? | + | + | . | . | . | . | . | . | . | . | . | . | . | . | | . | . | . | . | . | NR? | NR? | + | . |
| PO | + | . | . | . | . | . | . | + | + | . | . | . | . | . | . | . | . | . | . | . | + | + | . | | + | + | . | . | + | + | ? | . |
| PIP | + | . | + | + | . | . | . | + | . | . | . | . | . | . | . | . | . | . | . | . | . | + | . | . | | . | . | . | + | + | . | . |
| LIP | . | . | + | + | + | + | . | + | + | . | . | + | . | . | . | . | . | . | + | . | + | + | + | . | + | | . | . | + | + | + | + |
| VIP | . | . | + | . | . | . | . | + | + | . | . | . | . | . | . | . | . | . | . | . | + | + | + | . | . | + | | . | + | + | + | . |
| MIP | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | + | . | . | . | . | | . | + | . | . |
| MDP | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . | + | . | . | . | . | . | | + | . | . |
| DP | . | . | . | . | + | + | . | . | + | . | . | . | . | . | . | . | . | . | . | . | + | + | + | + | . | . | . | . | . | | + | . |
| 7a | . | . | . | . | . | . | . | . | . | . | . | . | . | . | + | . | . | . | + | . | ? | + | . | + | . | . | . | . | . | . | | + |
| FEF | . | . | . | . | . | . | . | . | ? | + | . | . | + | . | + | . | + | . | + | + | + | + | . | + | + | . | . | . | . | . | + | |
| 46 | . | . | . | . | . | . | . | . | . | . | . | . | + | . | + | . | + | + | + | . | . | . | . | . | . | . | . | . | . | . | + | + |

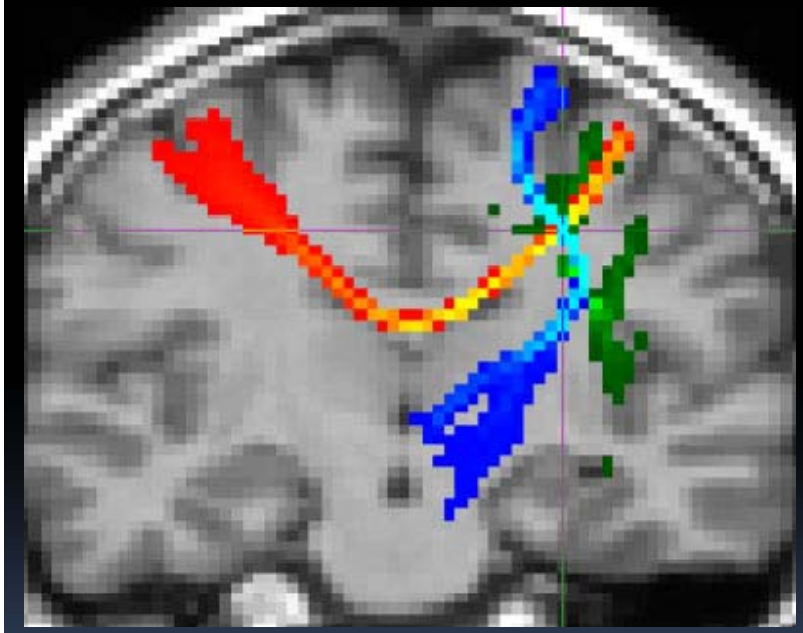
This table is a connectivity matrix for interconnections between visual cortical areas in the macaque. Each row shows whether the area listed on the left sends outputs to the areas listed along the top. Conversely, each column shows whether the area listed on the top receives inputs from the areas listed along the left. Large plus symbols (+) indicate a pathway that has been reported in 1 or more full-length manuscripts; small plus symbols indicate pathways identified only in abstracts or unpublished studies. Specific citations

- Dozens of visual cortical areas in the macaque;
- Hundreds of connections (pathways)
- Human brain circuits: very little known in 1991
- 1992–2012: an explosion of brain imaging and analysis methods!

# What's a connectome?

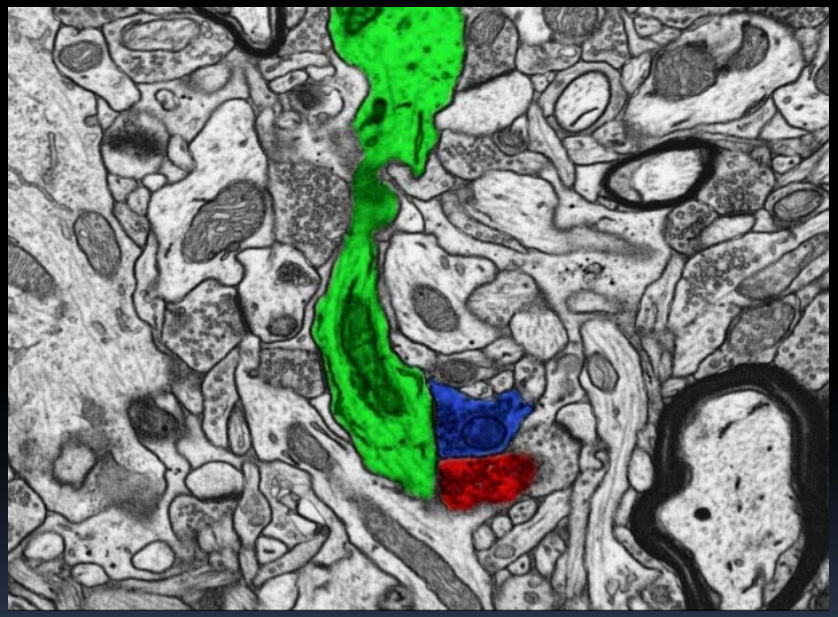
## A "comprehensive" map of neuronal connections

Macro-connectome
whole-brain, long-distance



Resolution: 1 – 2 mm 'voxels'

Micro-connectome
(every synapse, neuron, dendrite)



Volume reconstructed: <<1 $mm^3$ (to date)

## The Human Connectome Project:

A systematic study of the macro-connectome in 1,200 healthy adults

HUMAN Connectome PROJECT

Mapping structural and functional connections in the human brain

The “WU-Minn” HCP consortium

10 institutions:

- Washington University
- University of Minnesota
- Oxford University
- Saint Louis University
- University d’Annunzio
- Indiana University, Warwick University
- Ernst Strungmann Institute (Frankfurt)
- Radboud University (Nijmegen)
- Duke University

99 on HCP team (June, 2013)

*Supported by the NIH Neuroscience Blueprint*

# HCP objectives (2010 – 2015)

Improve the methods of data acquisition and analysis

- 2010 - 2012 and continuing

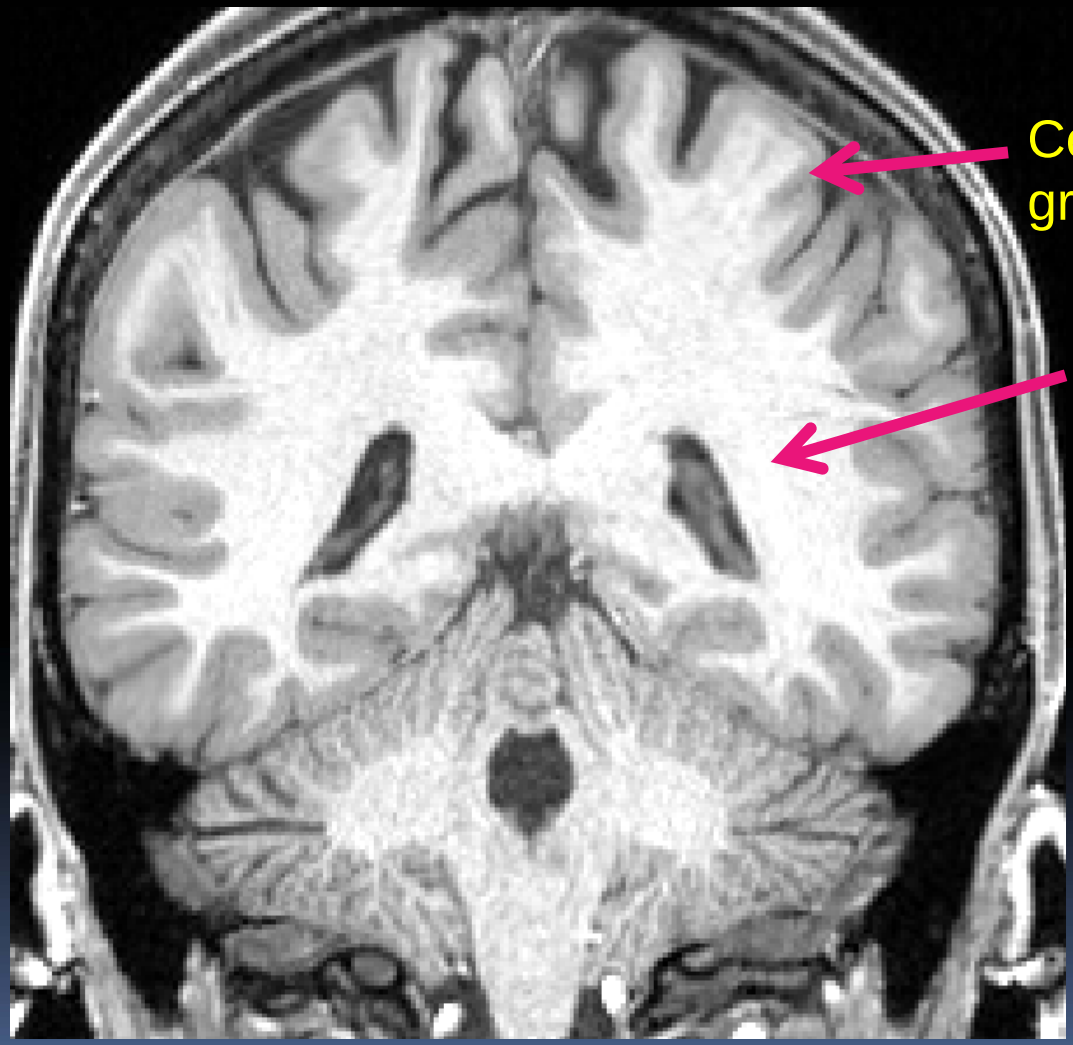
Study brain circuits in healthy adults (2012 - 2015)

- Twins and their non-twin siblings (1,200 total)
- Relate brain circuits to behavior

Share the data with the scientific community

- Promote discoveries, accelerate progress

# Structural Magnetic Resonance Imaging (MRI)

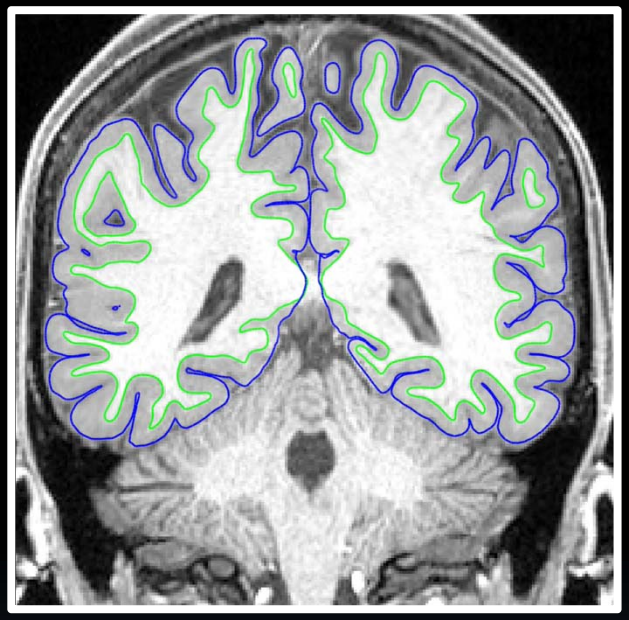


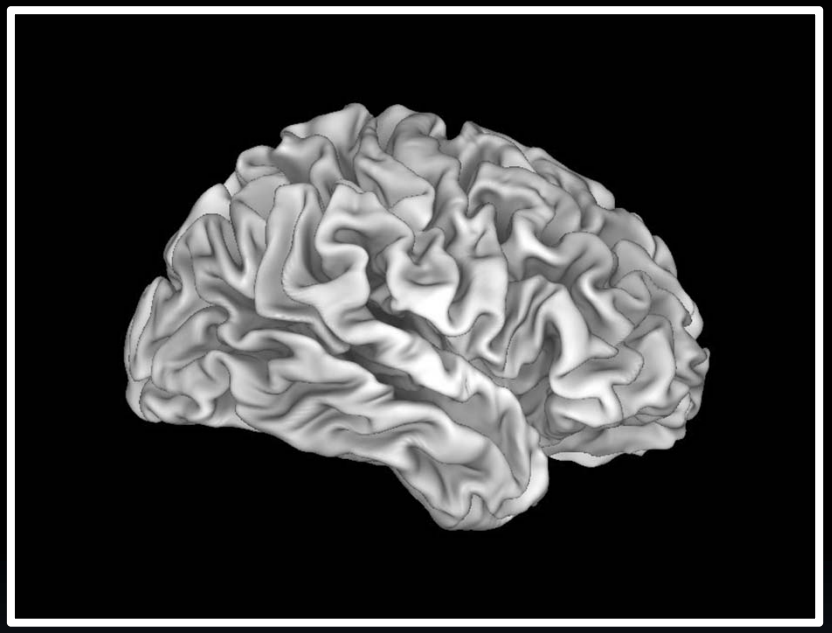
Cerebral cortex
gray matter

Subcortical
white matter
"myelin" = insulation
for faster signaling

High resolution scans (0.7 mm voxels)

# Human cortical convolutions

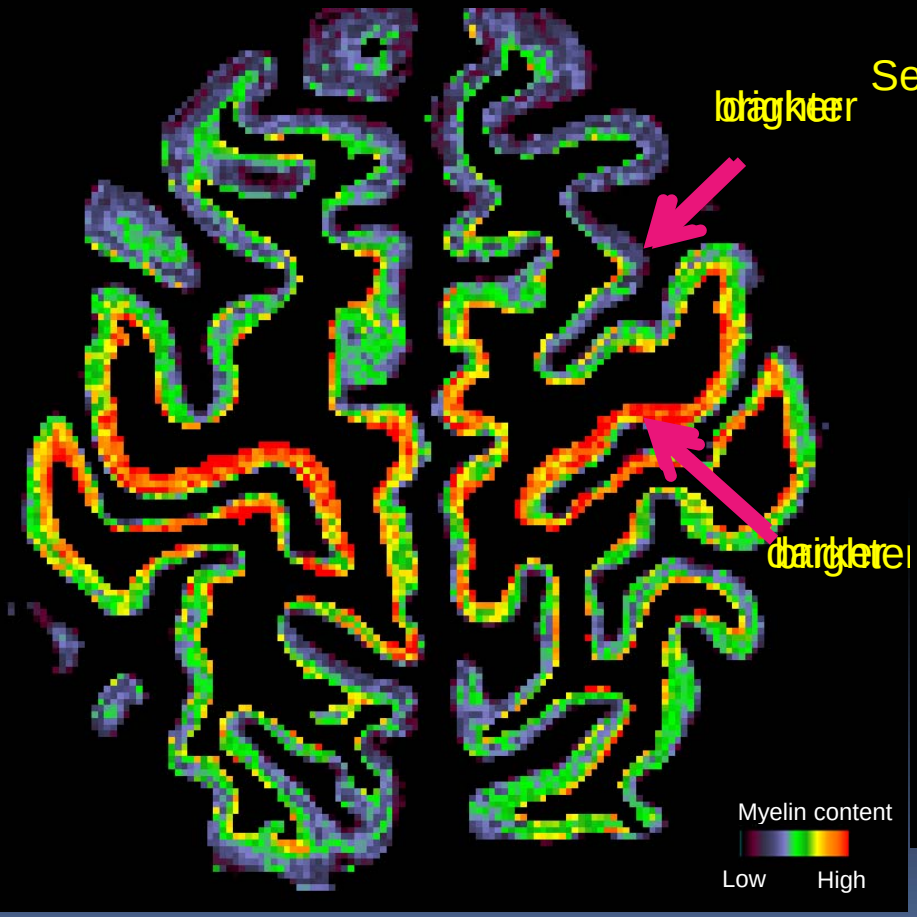




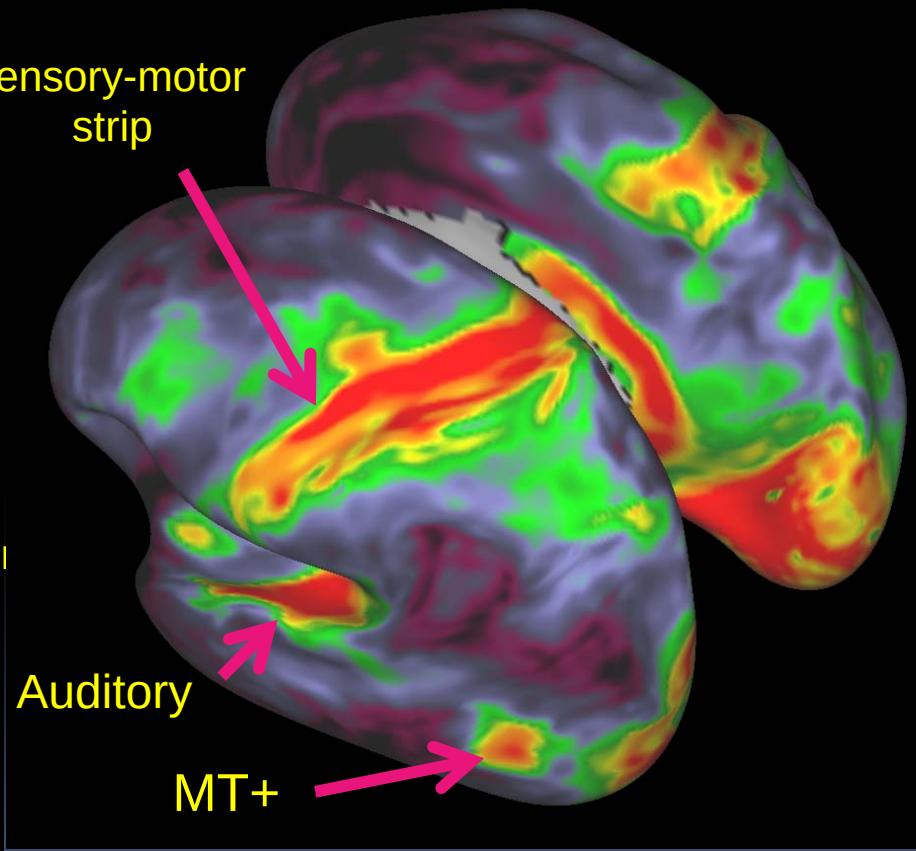
- Surface models capture the shape of cortical convolutions
- Surface inflation ‘smooths out the wrinkles’
- Depth maps reflect 3D shape features: “cortical brainprints”

# Myelin maps in cerebral cortex

Divide and conquer:
T1w/T2w ratio




Cortical myelin map
individual subject

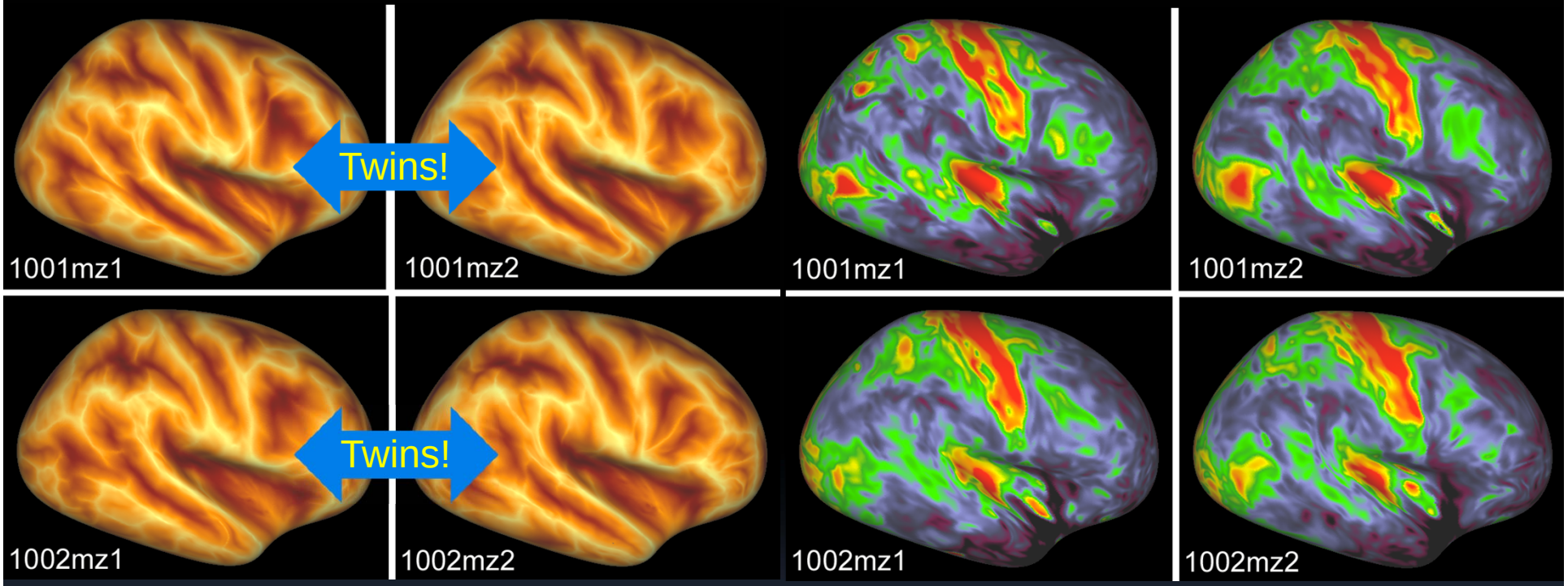



Glasser & Van Essen (2011)

# Individual variability in cortical convolutions

Two pairs of identical twins
Which are the twin pairs?

Myelin maps also vary, even in twins




Cortical folding is highly variable, but also heritable

# functional MRI (fMRI)

fMRI signal reflects brain activity (over past several seconds)

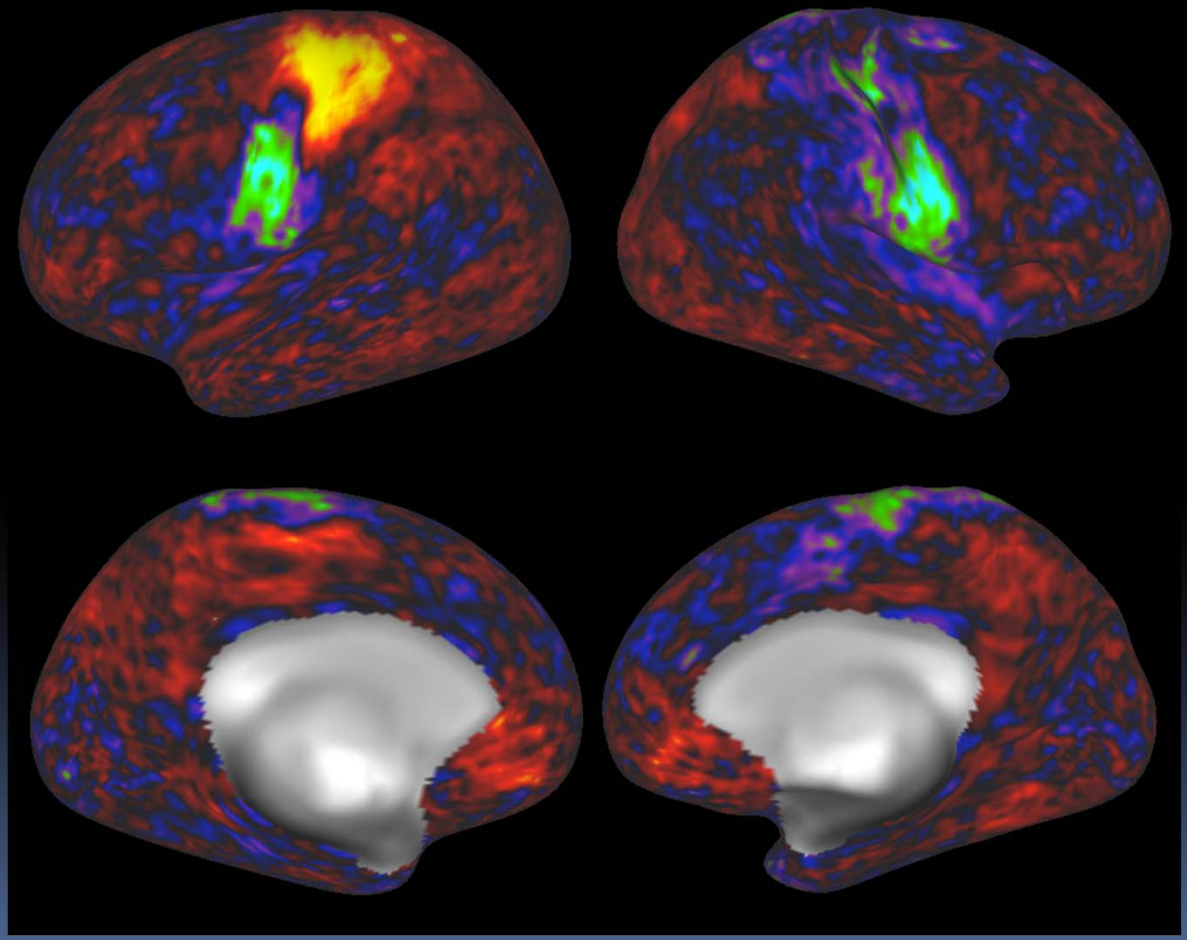
Task-fMRI: compare fMRI signals during a task to a baseline (at rest, or a ‘simpler’ task)

Differences in activity reflect functional specialization

# Task-fMRI activations

Move right hand

deactivation activation

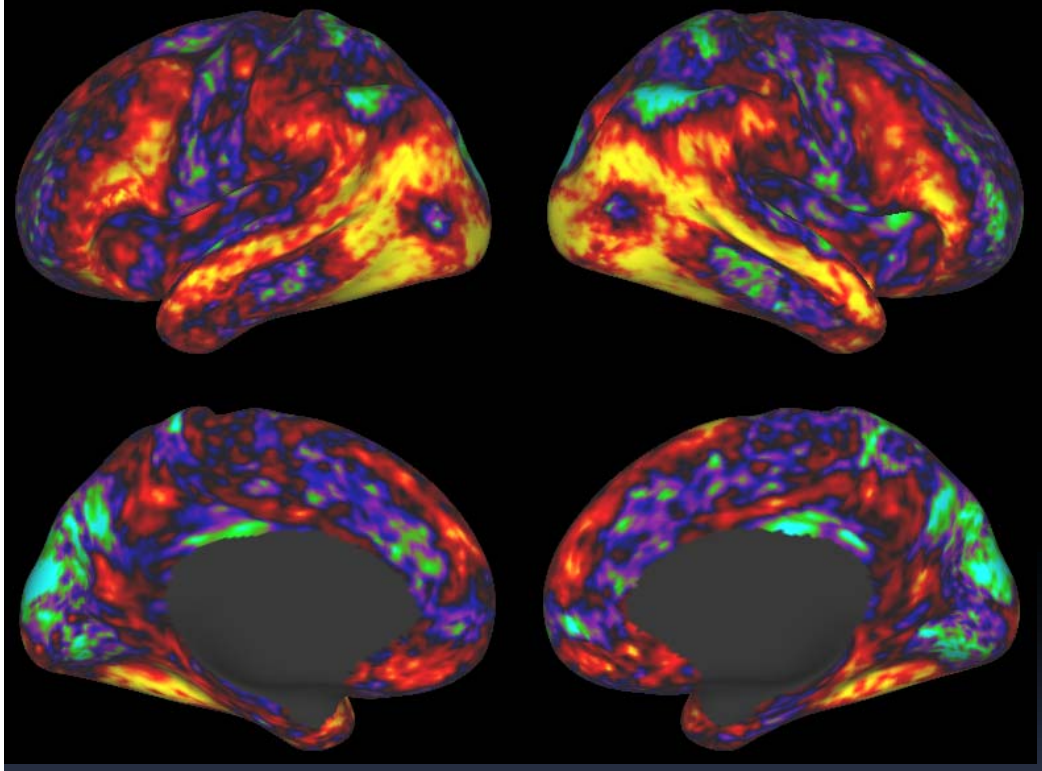


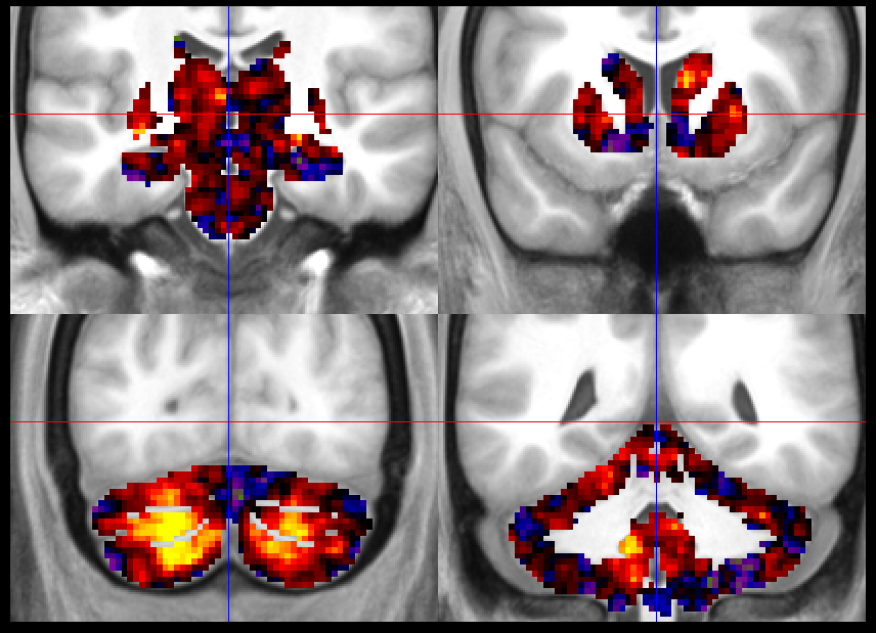
Activation in left hemisphere, central sulcus

# Task-fMRI activations

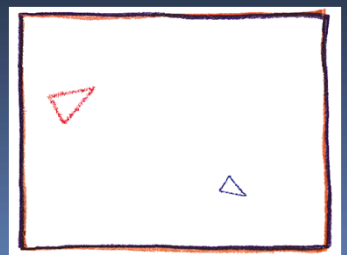
‘social interaction’ vs. random movement

deactivation activation

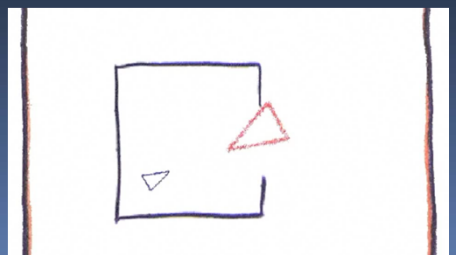




Random motion



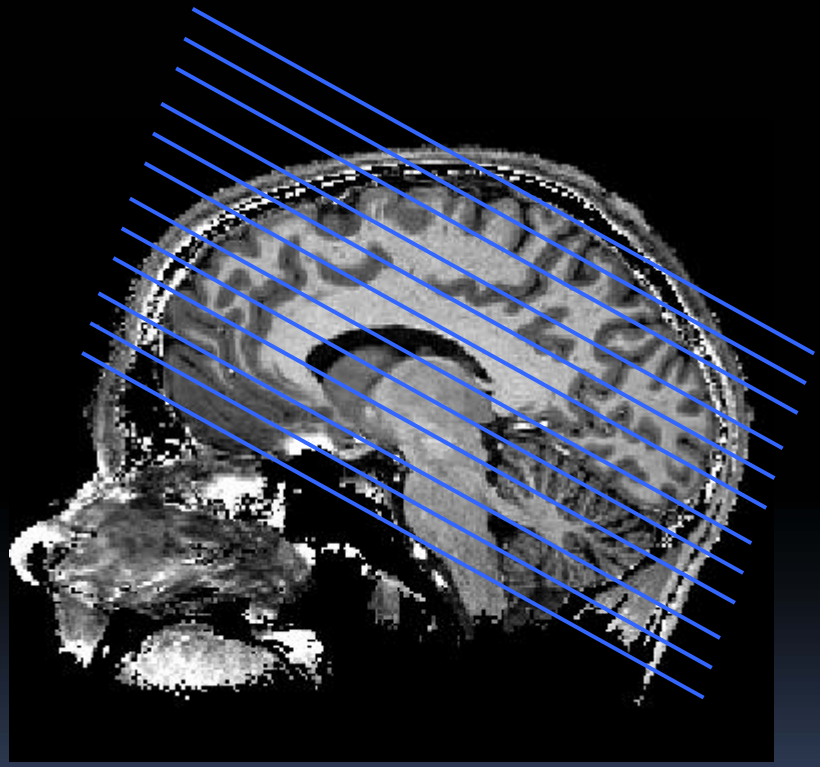
“Coaxing”



A complex brain network engaged in social cognition!

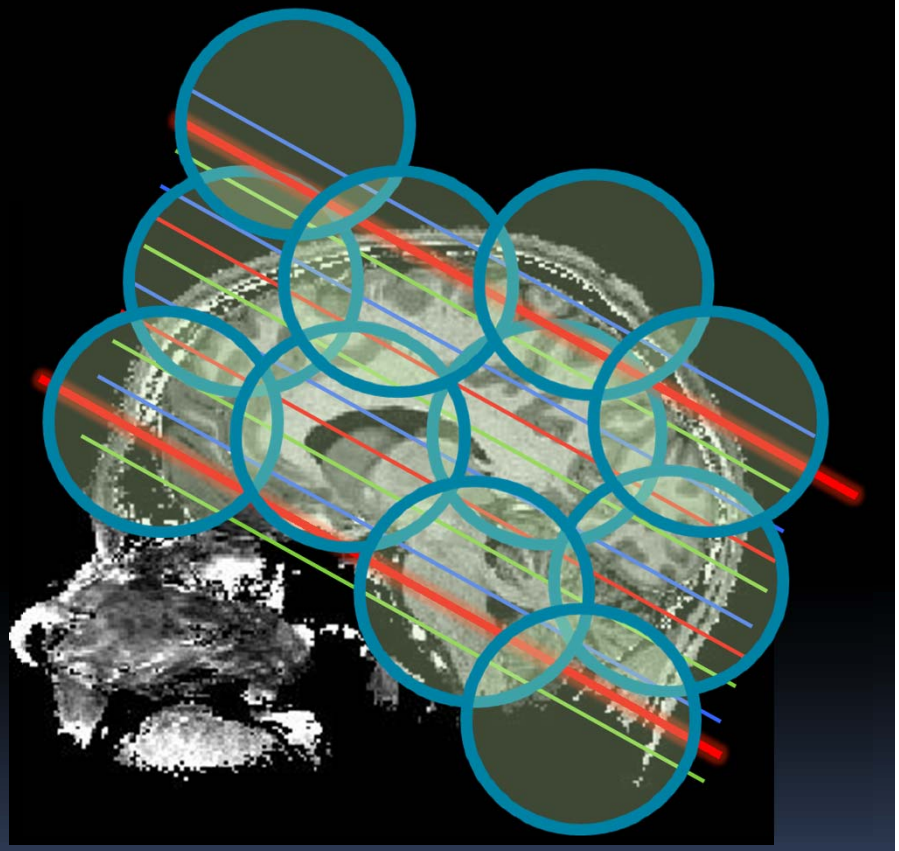
# Conventional fMRI

Whole Brain:
several seconds to scan



# “Multi-band” Brain Imaging

- Excite *multiple* slices simultaneously
- Each “coil” around the head picks up signals from nearby brain slices
- Computer algorithms decipher the original pattern



- Yields more data & better data!

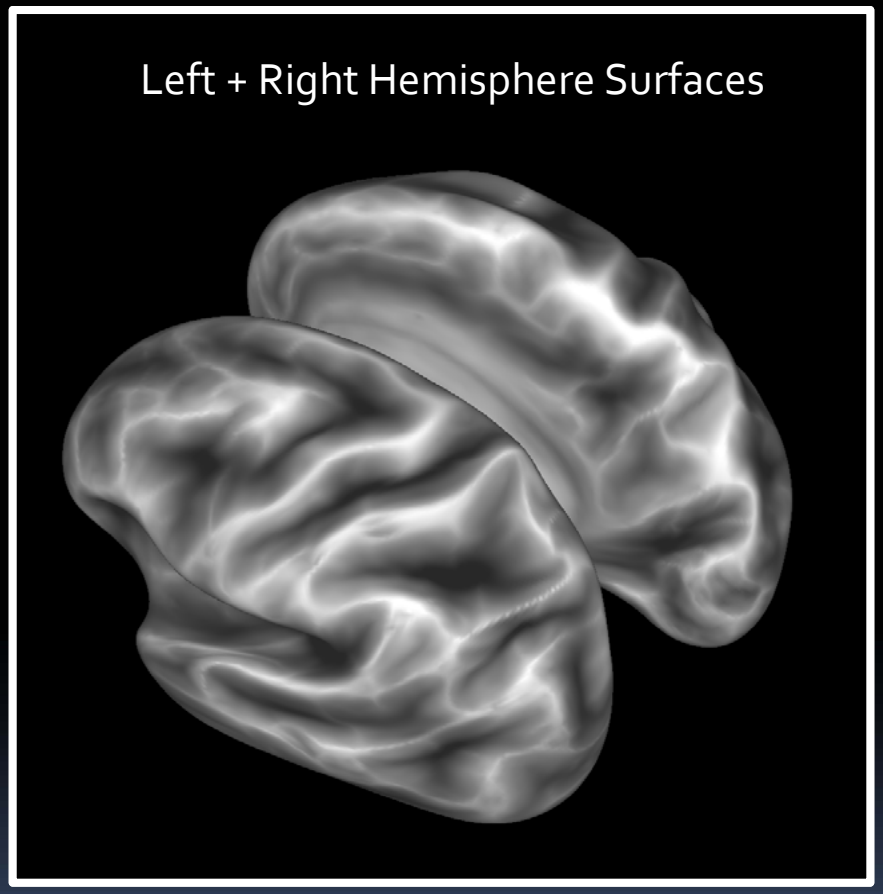
Moeller et al. (2010)

# Functional Connectivity

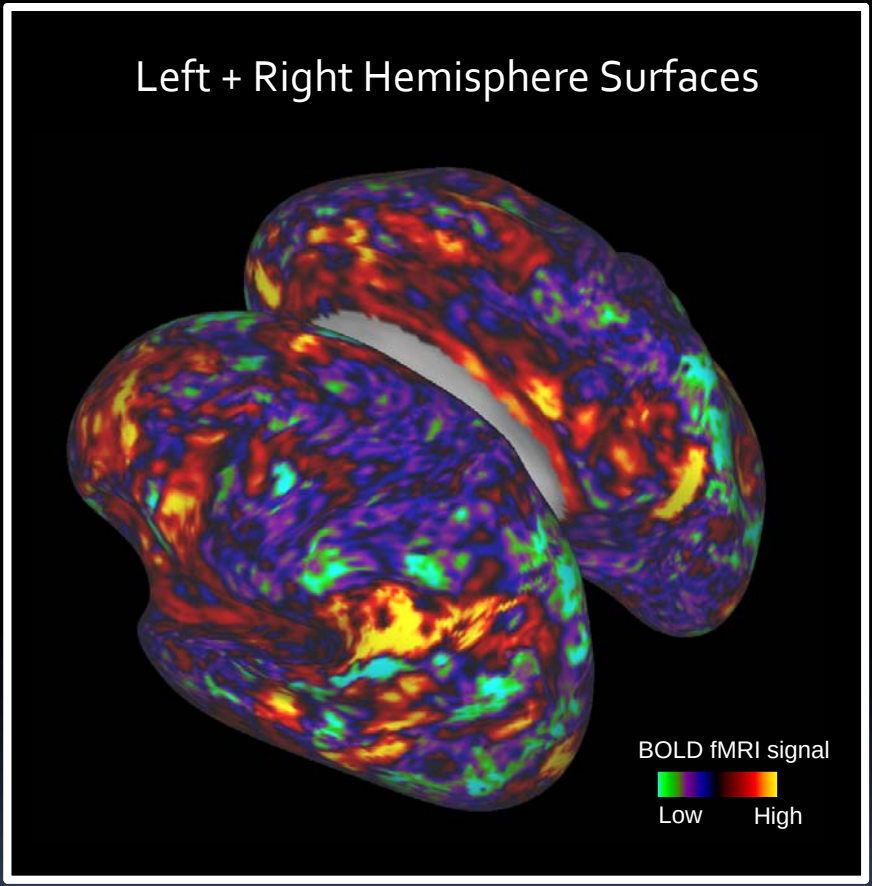
The brain is very active when ‘doing nothing’

“Resting-state” fMRI reveals functional connectivity (regions that are active together are ‘wired together’)

# Anatomical substrate for fMRI visualization

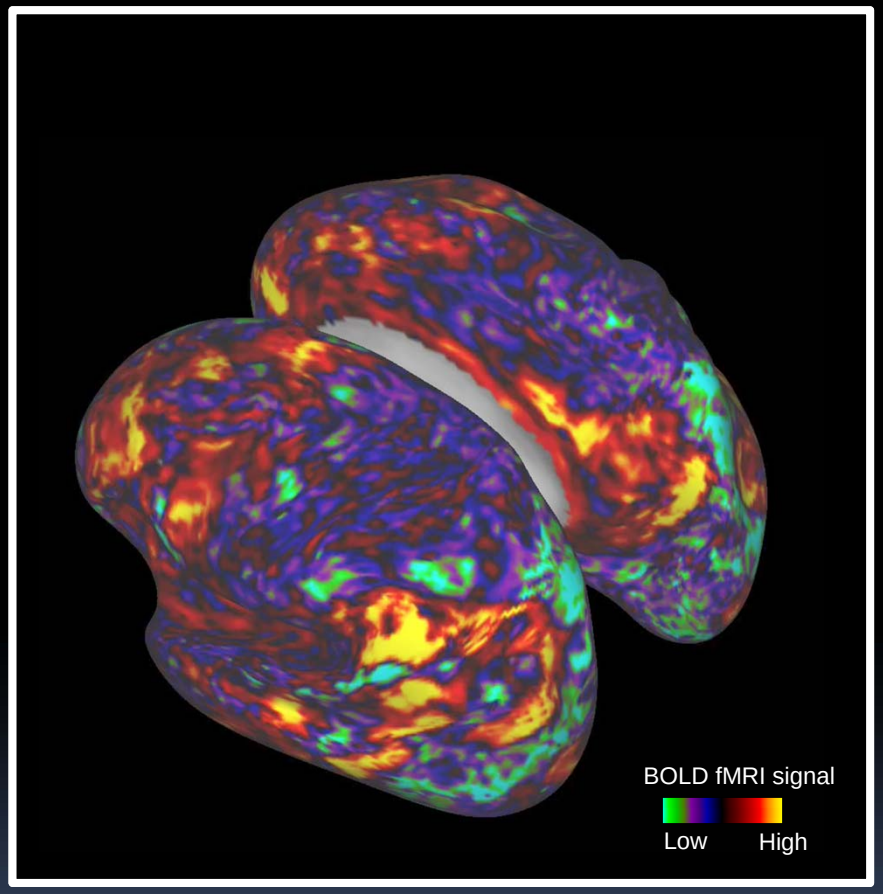


# One moment in one subject's life in the MRI scanner




Glasser et al. (HCP unpublished)

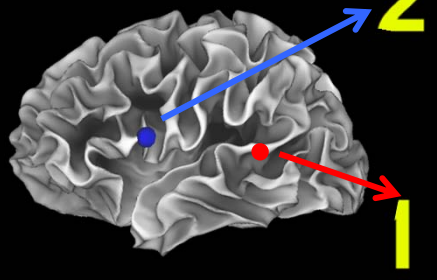
# 10 seconds ‘at rest’ in scanner

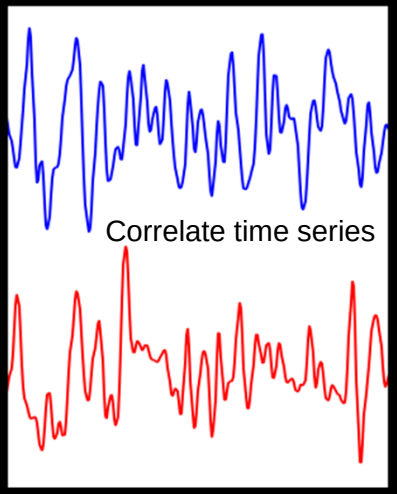


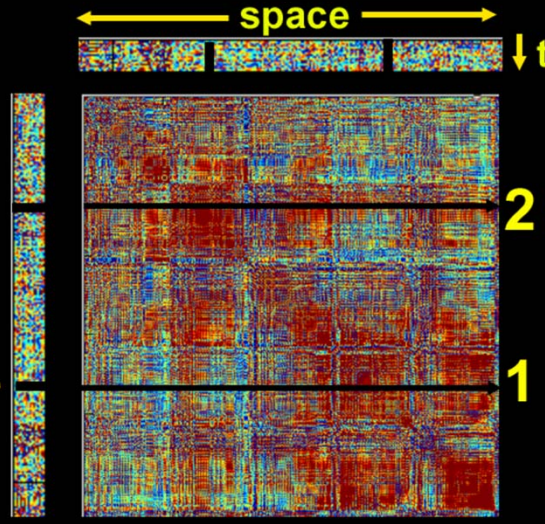

- Outstanding data quality!!
- Viewing the brain at rest, but in action

# Functional connectivity from resting-state fMRI

fMRI time course (locations 1, 2)

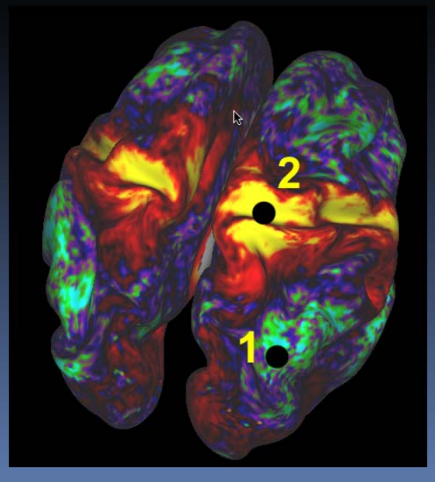


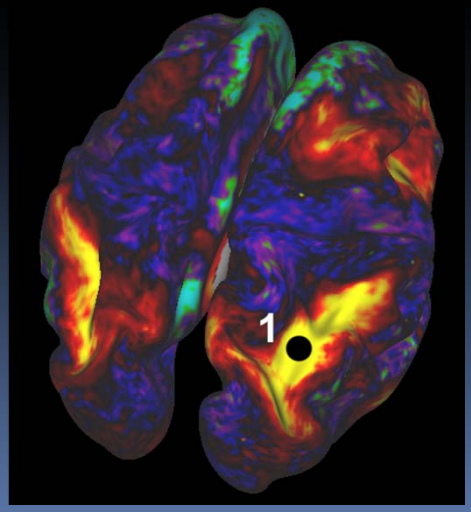




Functional connectivity matrix (‘dense connectome’)

Functional connectivity map (location 2)



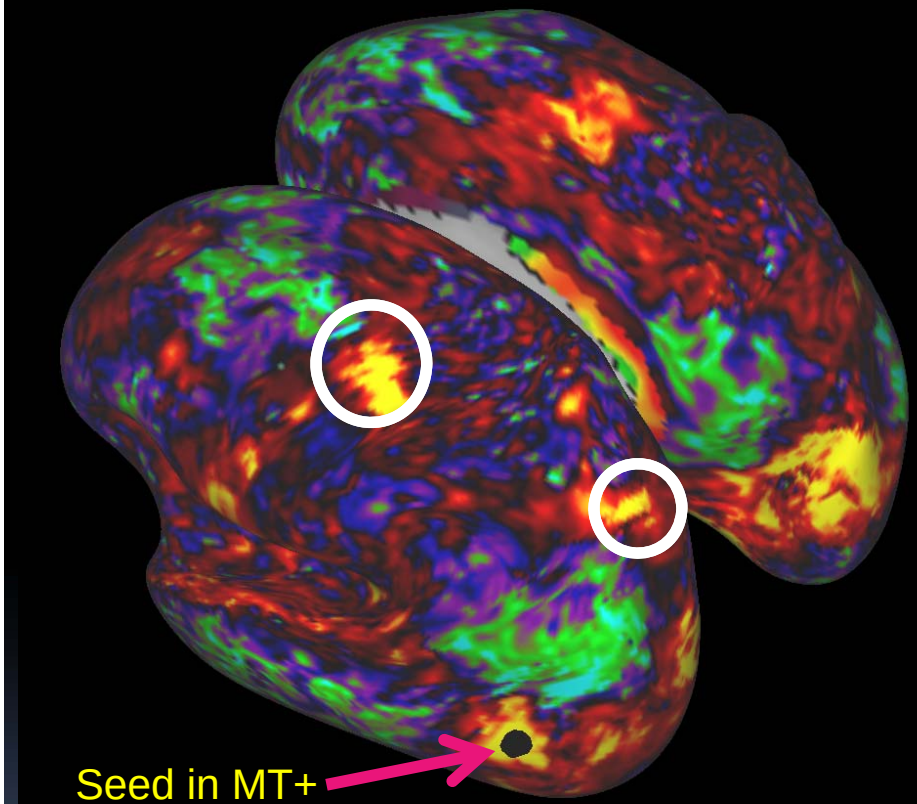



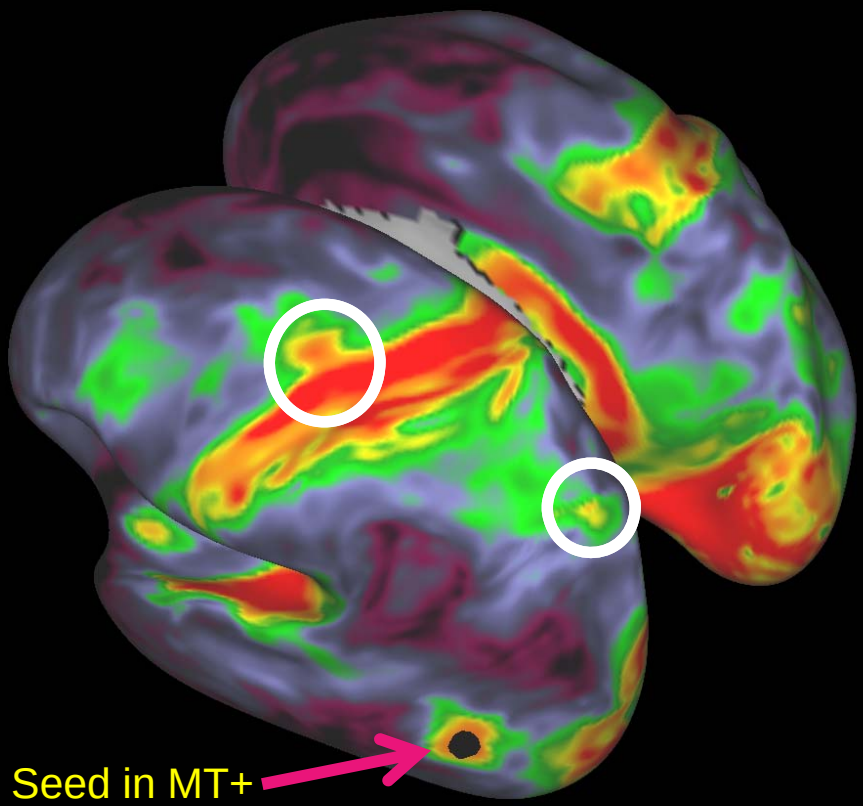

Functional connectivity map (location 1)

Correlation

Low High

# Comparing functional connectivity and myelin maps



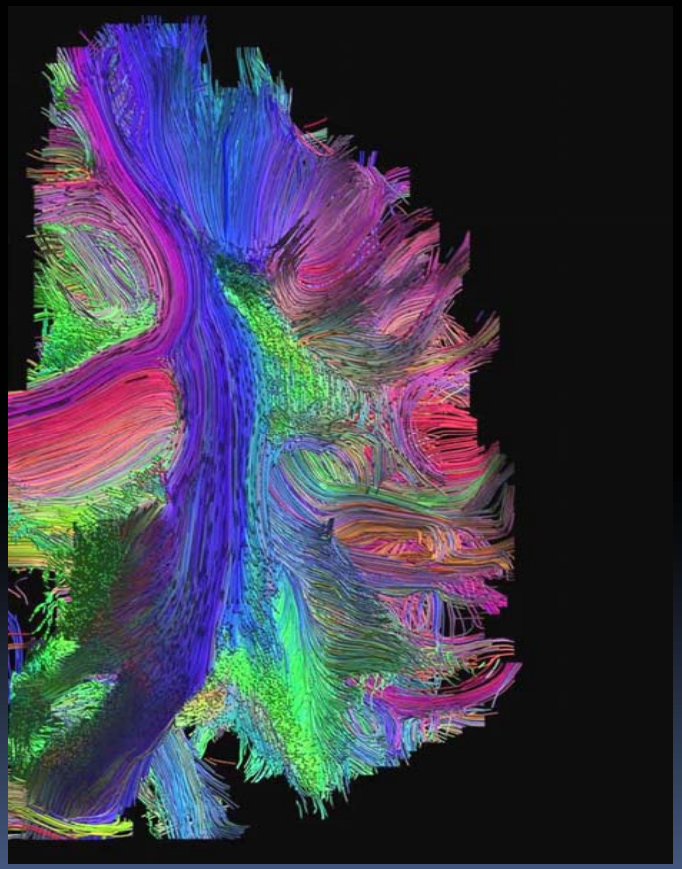

Myelin and functional connectivity hotspots colocalize

Glasser et al. (HCP unpublished)

# Structural Connectivity

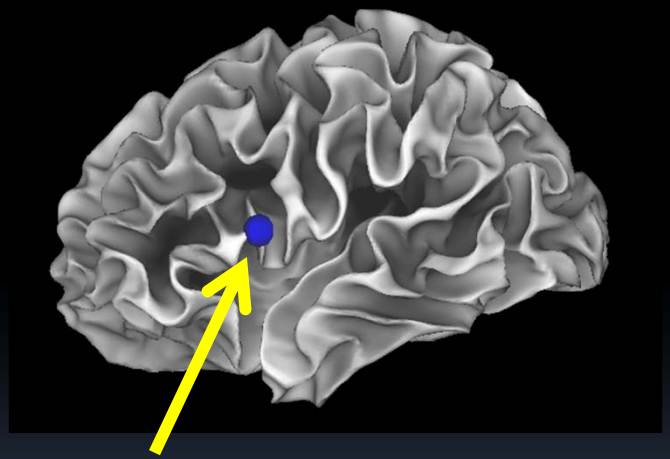
Fiber bundles in white matter (brain dissection)

"Diffusion imaging" reveals fiber trajectories in white matter



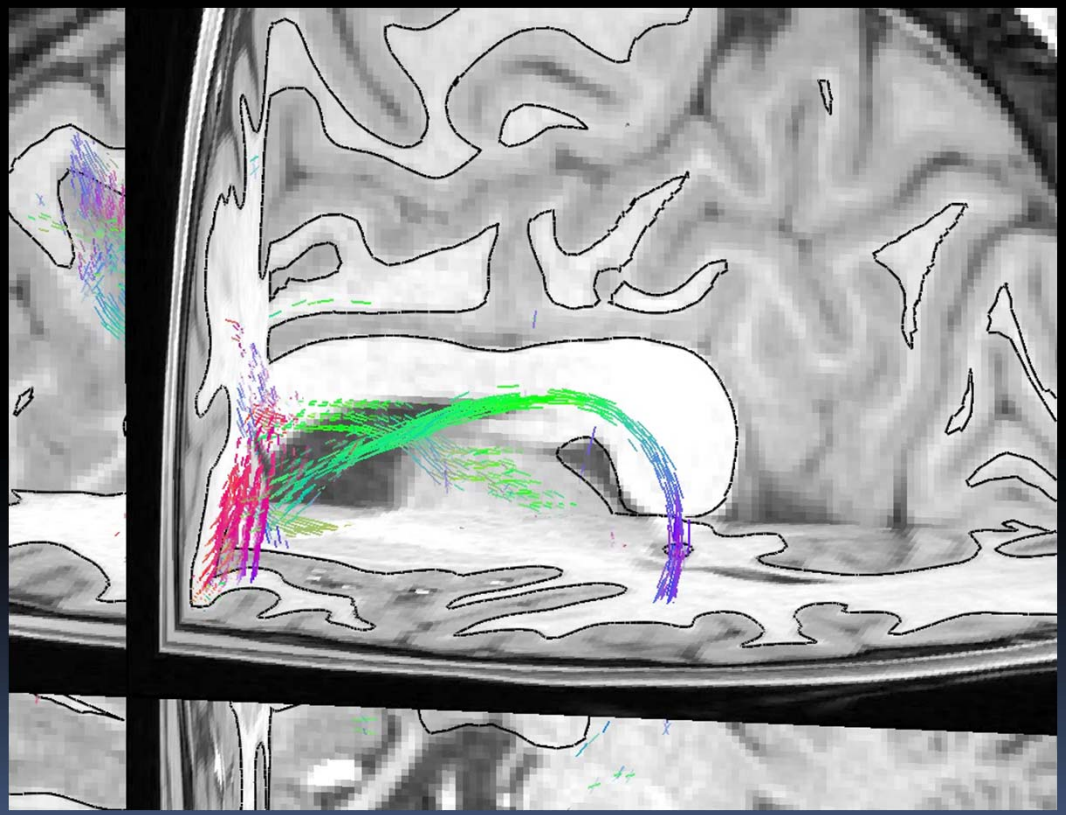
7T DWI Data (CMRR)
Thompson, P. (UCLA), Lenglet C., Sapiro, G. et al. CMRR

# Visualizing trajectories through white matter



"Seed" location (left hemisphere)

Trajectory through white matter



Oxford: Jbabdi, Sotiropoulos
WashU: Harwell, Coalson, Glasser

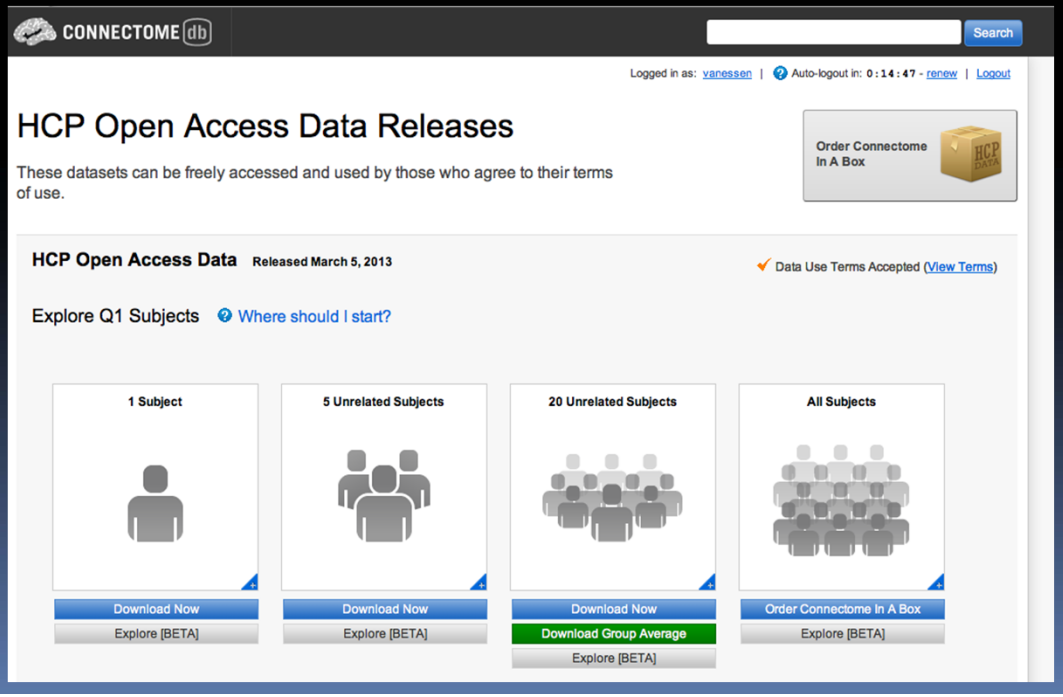
# Sharing HCP Data

March, 2013: First quarterly data release (68 subjects)

June 11, 2013: Second quarterly release (another 68 subjects)

- Unprocessed and processed data available
- Enthusiastic response from scientific community

https://db.humanconnectome.org/



# Concluding Comments

- Understanding human brain circuitry in health and disease: a grand challenge for the 21st century!
- The Human Connectome Project will elucidate brain connectivity and its variability in healthy adults.
- A ‘complete’ connectome (macro- plus micro-) is well outside our grasp
- Future studies of diseases, development, and aging will aid in diagnosis and treatment.
- Further methodological improvements are needed!

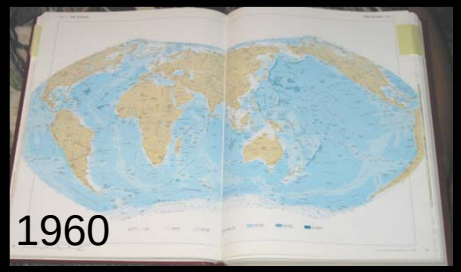
# Revolutions in Cartography

## EARTH

### Classical maps

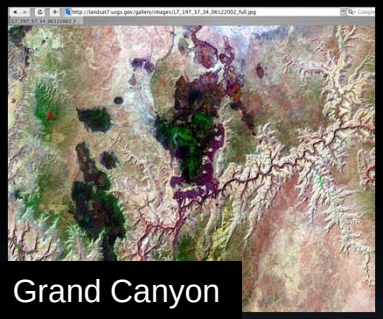
1630

### Book atlases

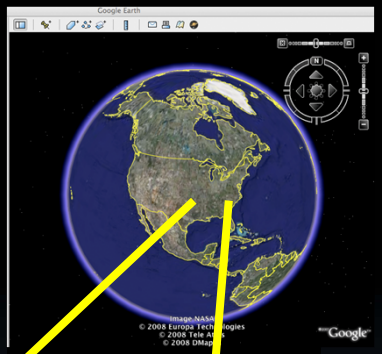


1960

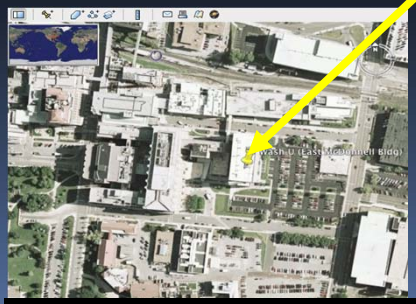
### Satellite imagery



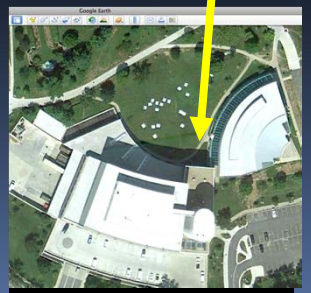
Grand Canyon



Google Earth



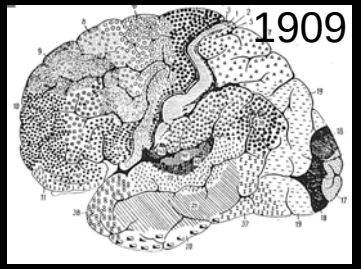
Washington University



NIH (Natcher)

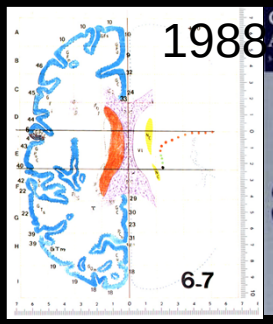
## BRAIN

### Classical maps



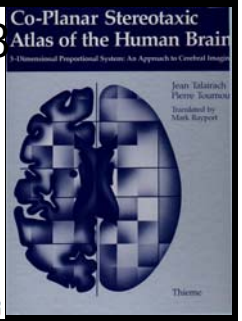
1909

### Talairach atlas



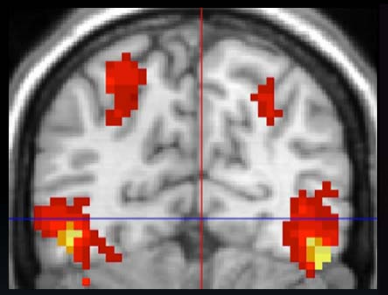
1988

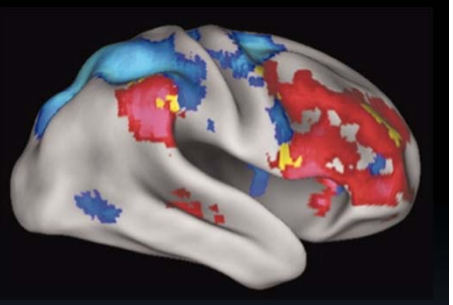
6-7



Co-Planar Stereotaxic Atlas of the Human Brain

### ~2005: MRI; volumes + surfaces





### 2011 and beyond Connectomics