

*Not so tangled -
the geometric structure of the brain*

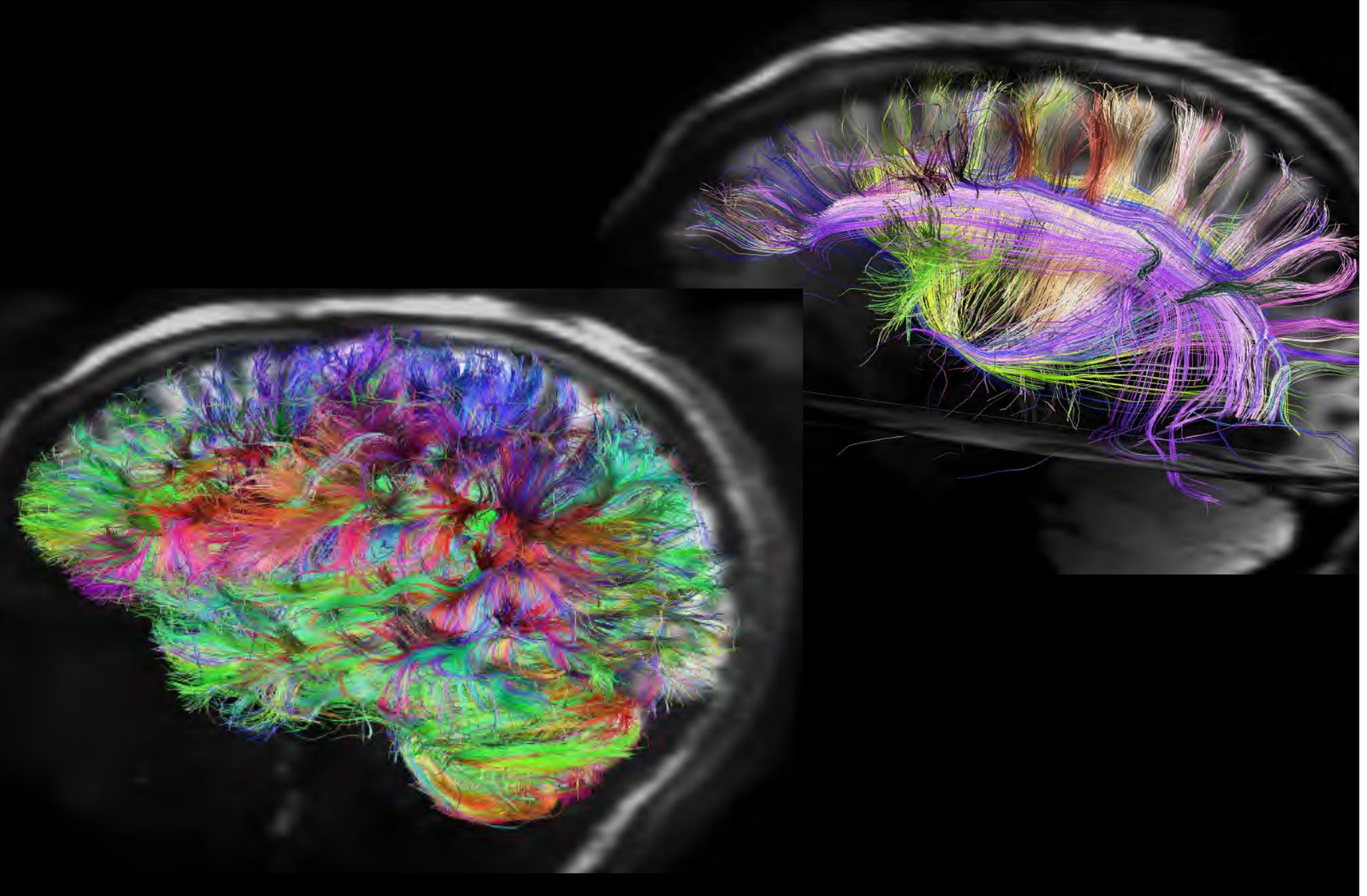
*Van J Wedeen, MD
MGH R&DIOLOGY*



*Ellen Grant
Doug Rosene
Patric Hagmann
Jon Kaas
W-Y Isaac Tseng
Tom Brady
Larry Wald
Ruopeng Wang
Bruce Rosen
Guangping Dai
Farzad Mortazawi
Jeremy Schmahmann
Jack Beliveau*



Promise of diffusion MRI - order from disorder

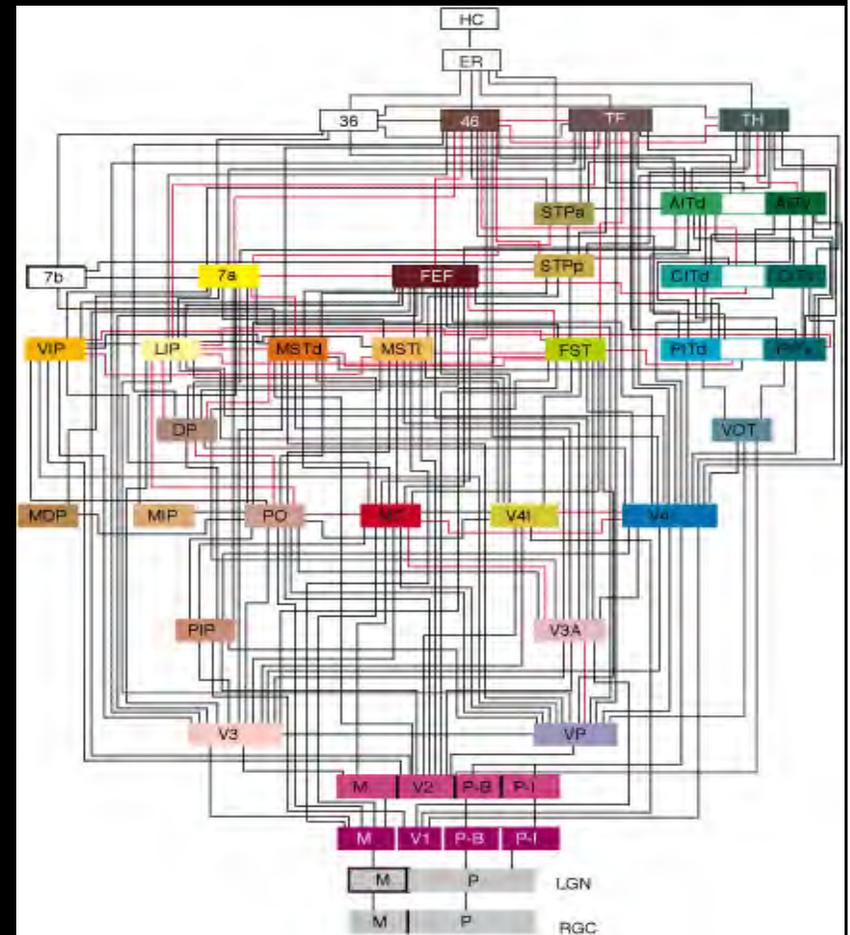


“It is intolerable that we do not have a knowledge of the connectivity of the human brain”

- Crick & Jones, 1993

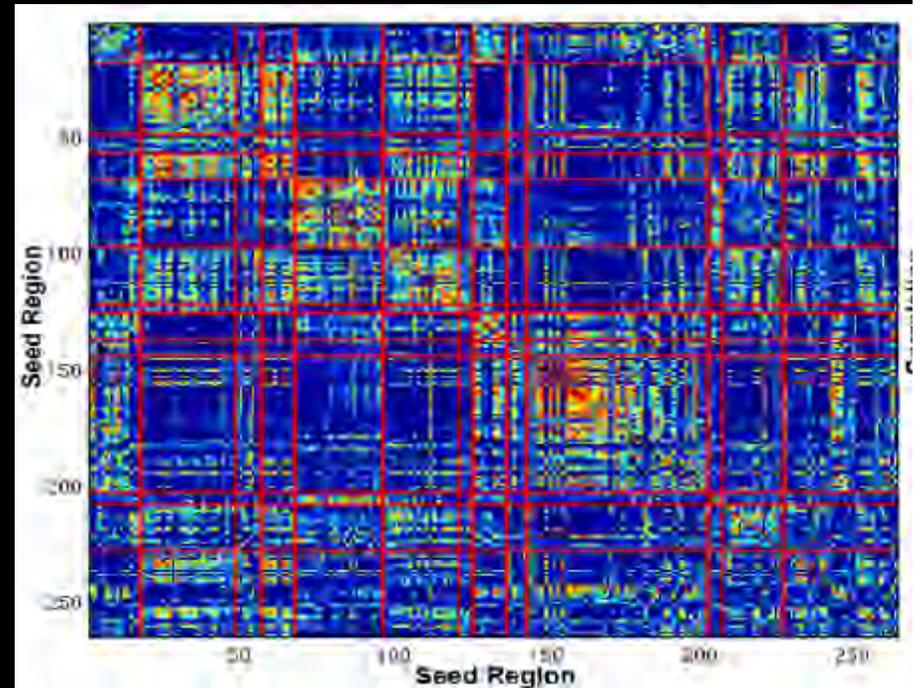
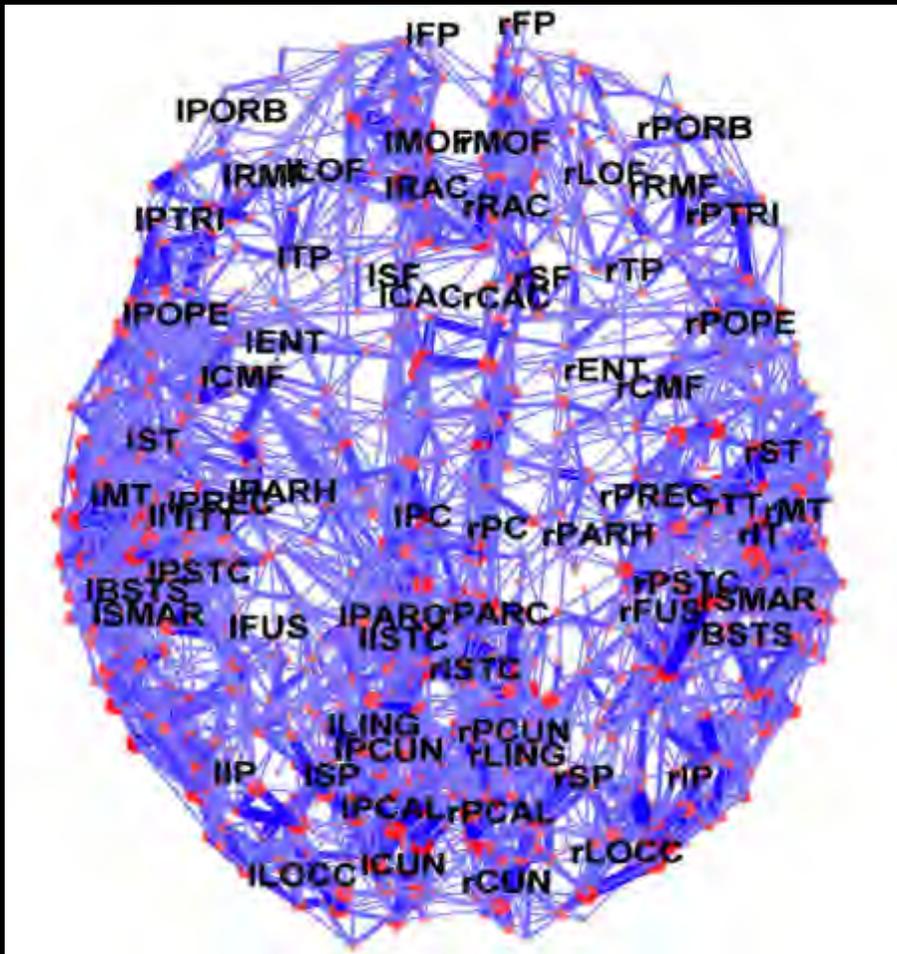
The NIH Human Connectome Project, a five year mission to build a “network map” of the connectivity within the brain, and facilitate research into disorders such as autism, Alzheimer's disease, and schizophrenia.

- Wikipedia



*Felleman & Van Essen, 1989
rhesus visual system*

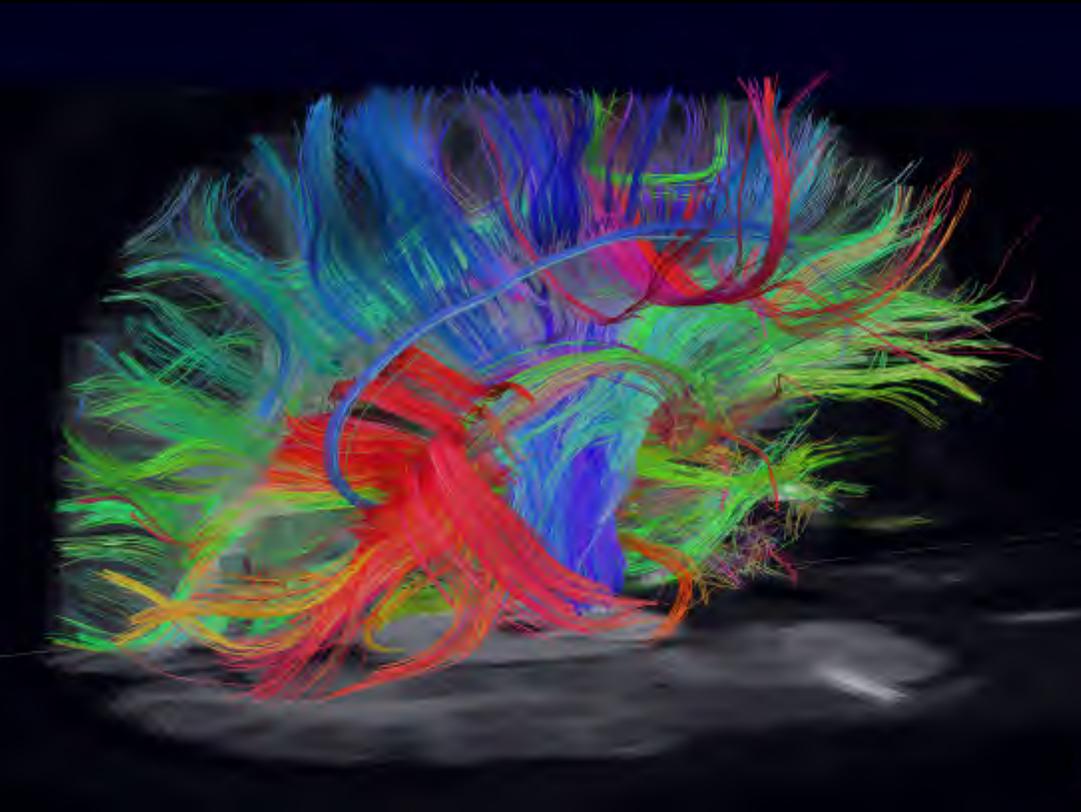
*The predominant network paradigm of the connectome derived from DSI is not entirely satisfying.
Does it help us understand coherence and plasticity, development and evolution*



Popular demand for brain imagery - two views of a human DSI

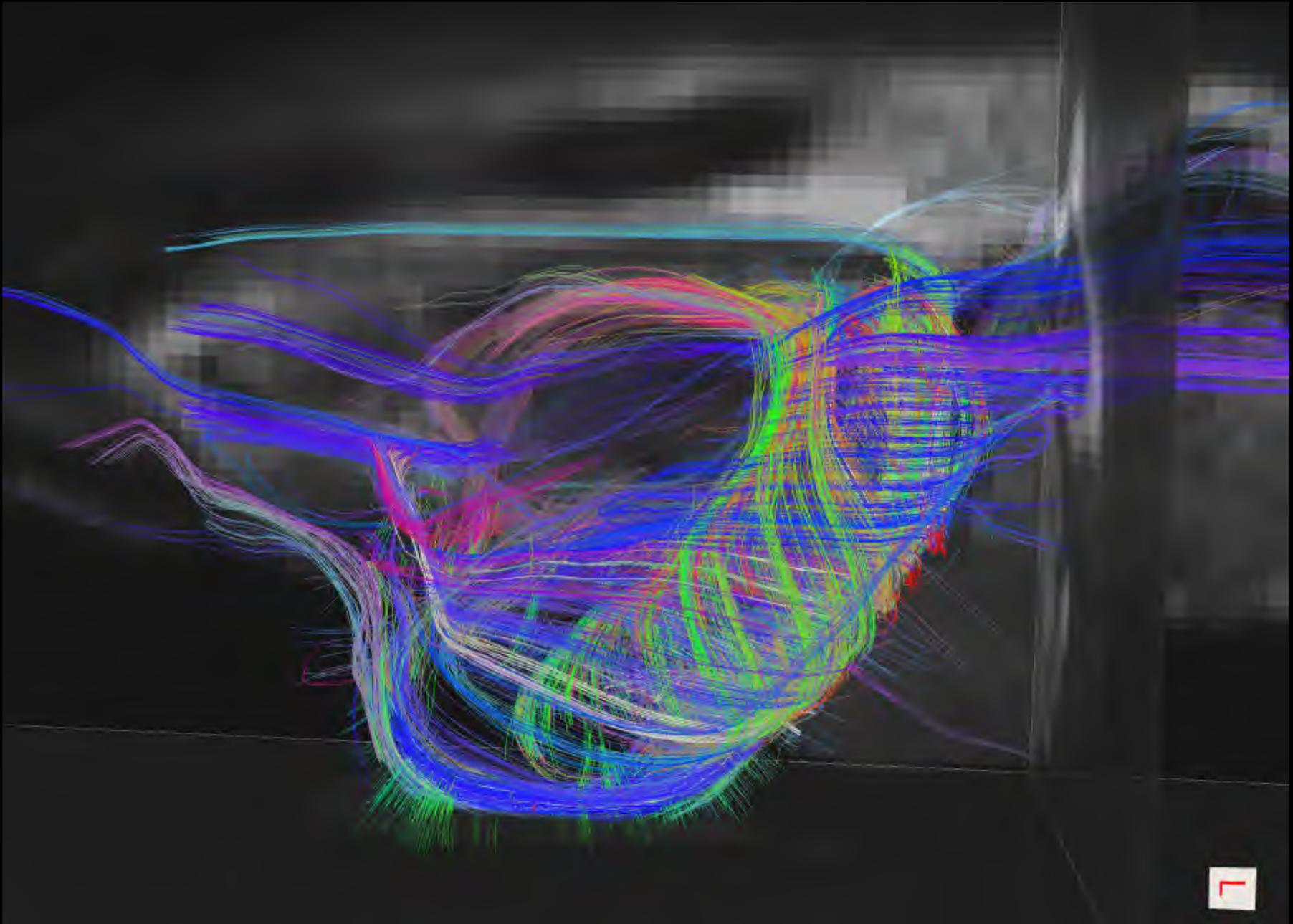
structure almost understandable

complex and a bit mysterious



Guess which one National Geographic decided to use?

Early evidence of geometric structure, owl monkey hippocampus 2005



Factoids of the net-centric world

Economic value of the Internet in 2011 ~ \$3 trillion

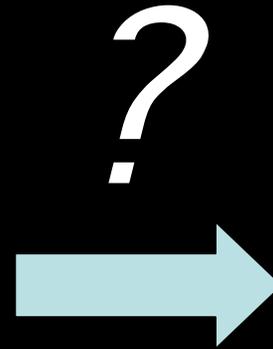
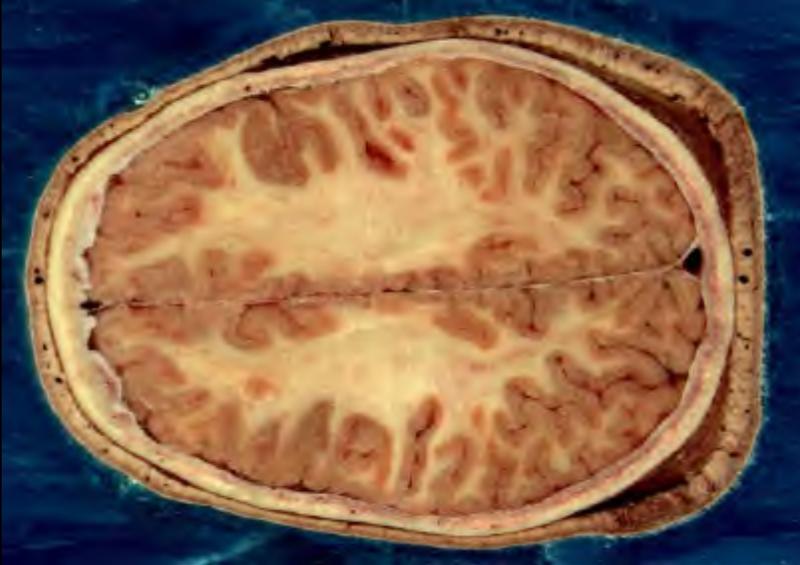
Google giga-hits

<i>Facebook</i>	<i>36</i>
<i><u>net*</u></i>	<i><u>25</u></i>
<i>US</i>	<i>25</i>
<i>health</i>	<i>15</i>
<i>Google</i>	<i>13</i>
<i>god</i>	<i>5</i>
<i>Apple</i>	<i>2</i>
<i>Obama</i>	<i>0.8</i>
<i>DNA</i>	<i>0.4</i>
<i>x-ray</i>	<i>0.2</i>

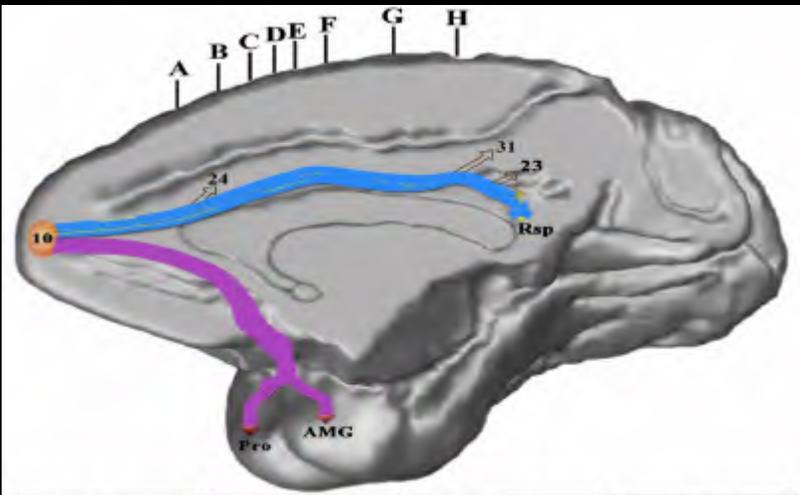
The proposition that the brain is the most complex thing in the universe has a mythic status.

Why the geometric structure of the brain pathways was undiscovered

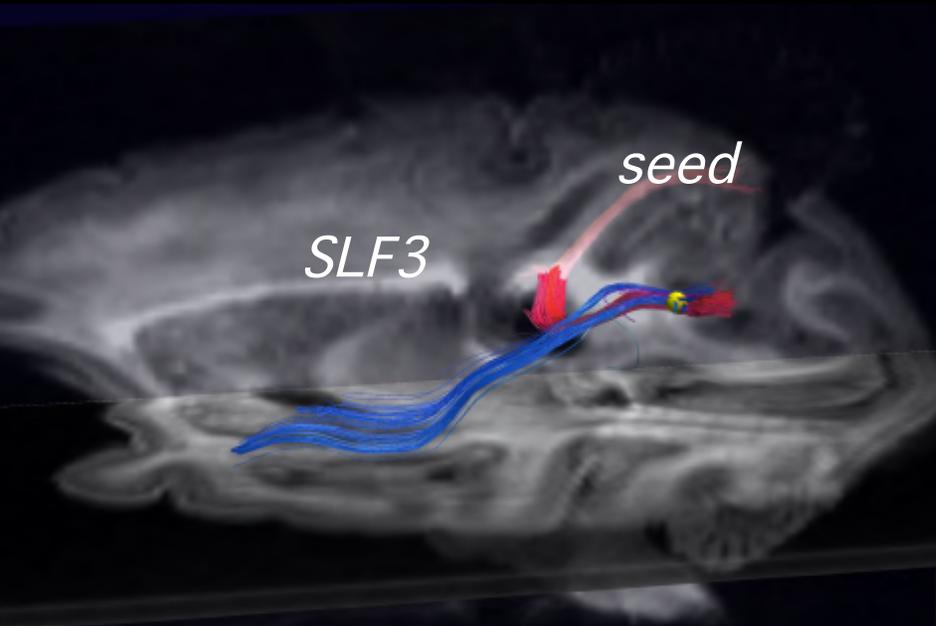
3D studies provide context but scant pathways



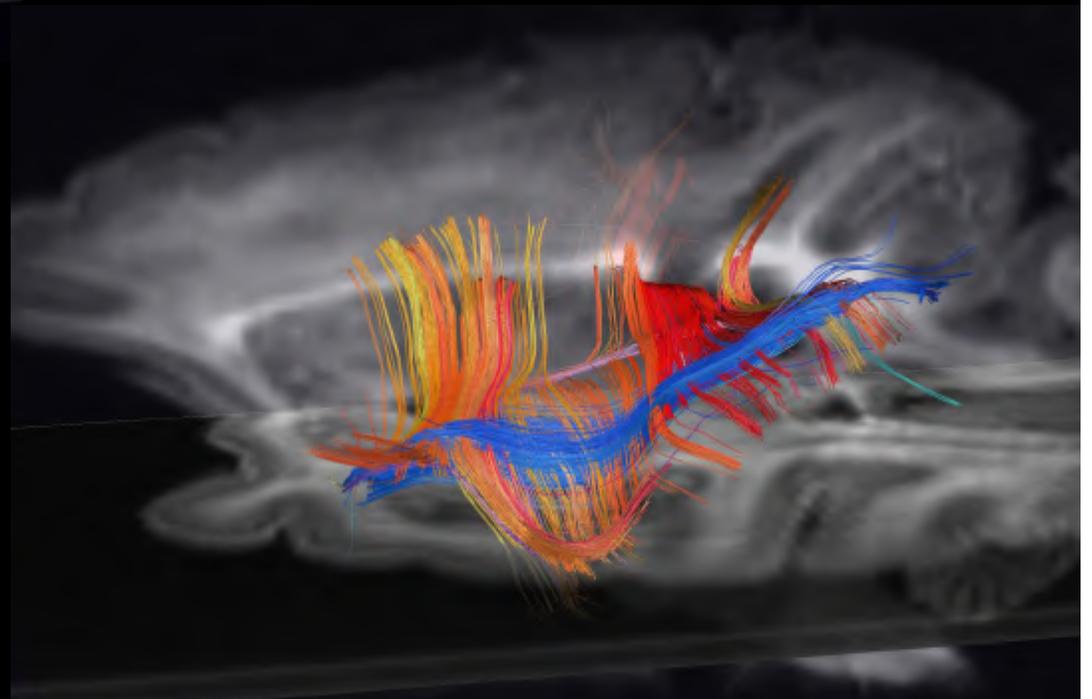
tracer studies provide pathways but scant context



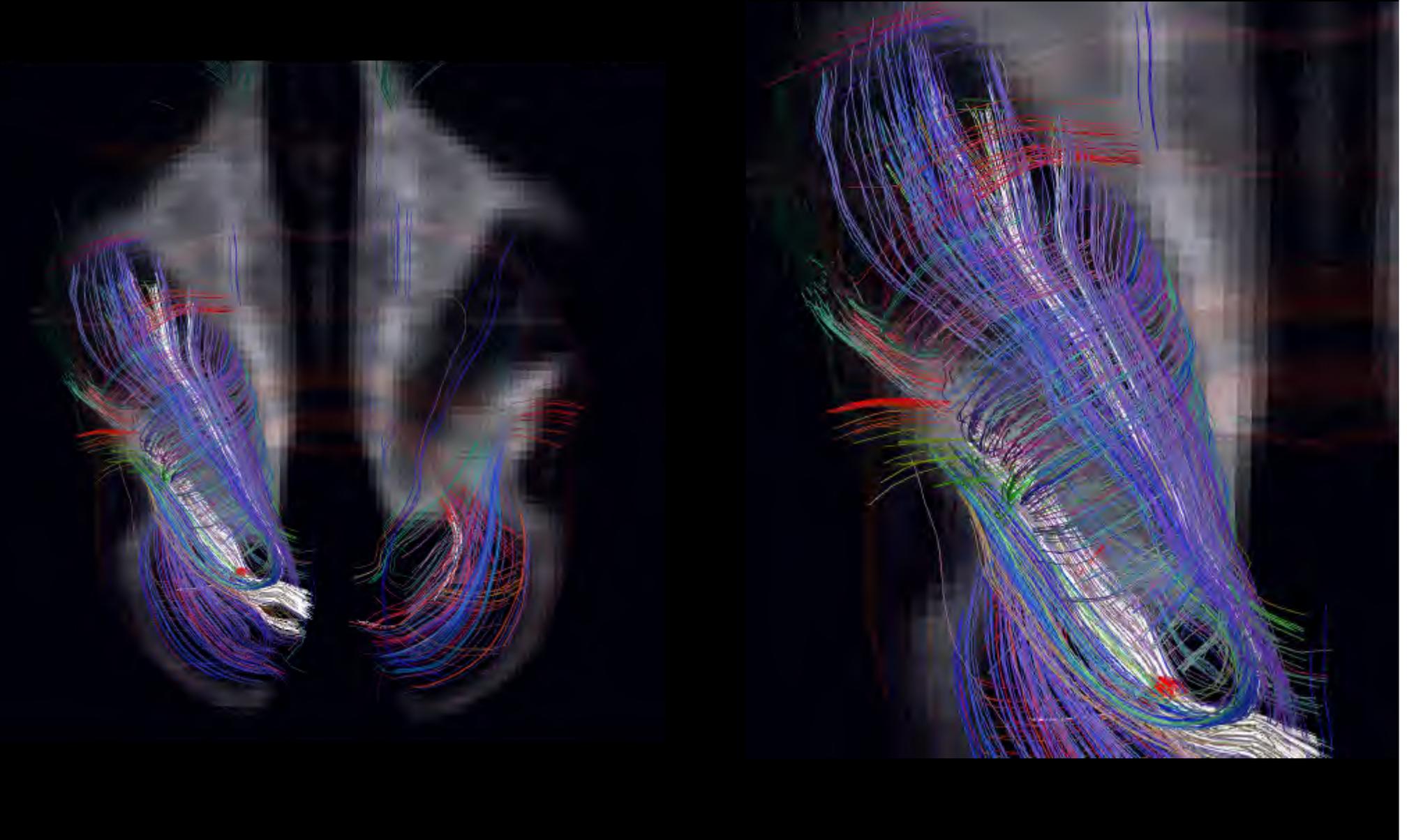
In tracer studies and their MRI analogs, paths appear to be isolated structures. Can we ask what other paths are near to a given path - its path neighborhood?



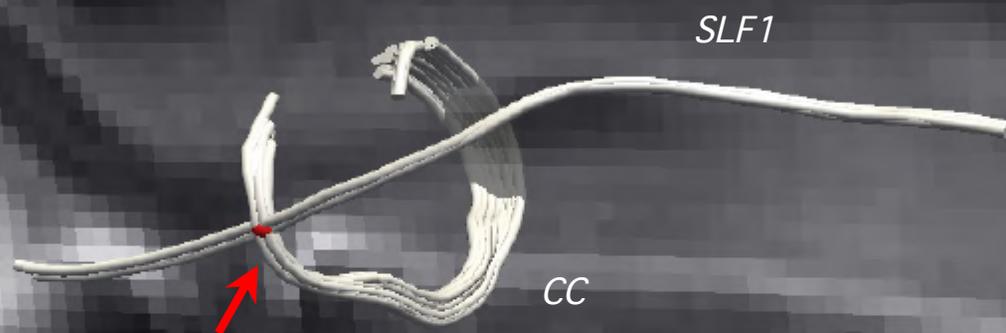
All paths crossing SLF3. Astonishingly, they all form a single 2D sheet



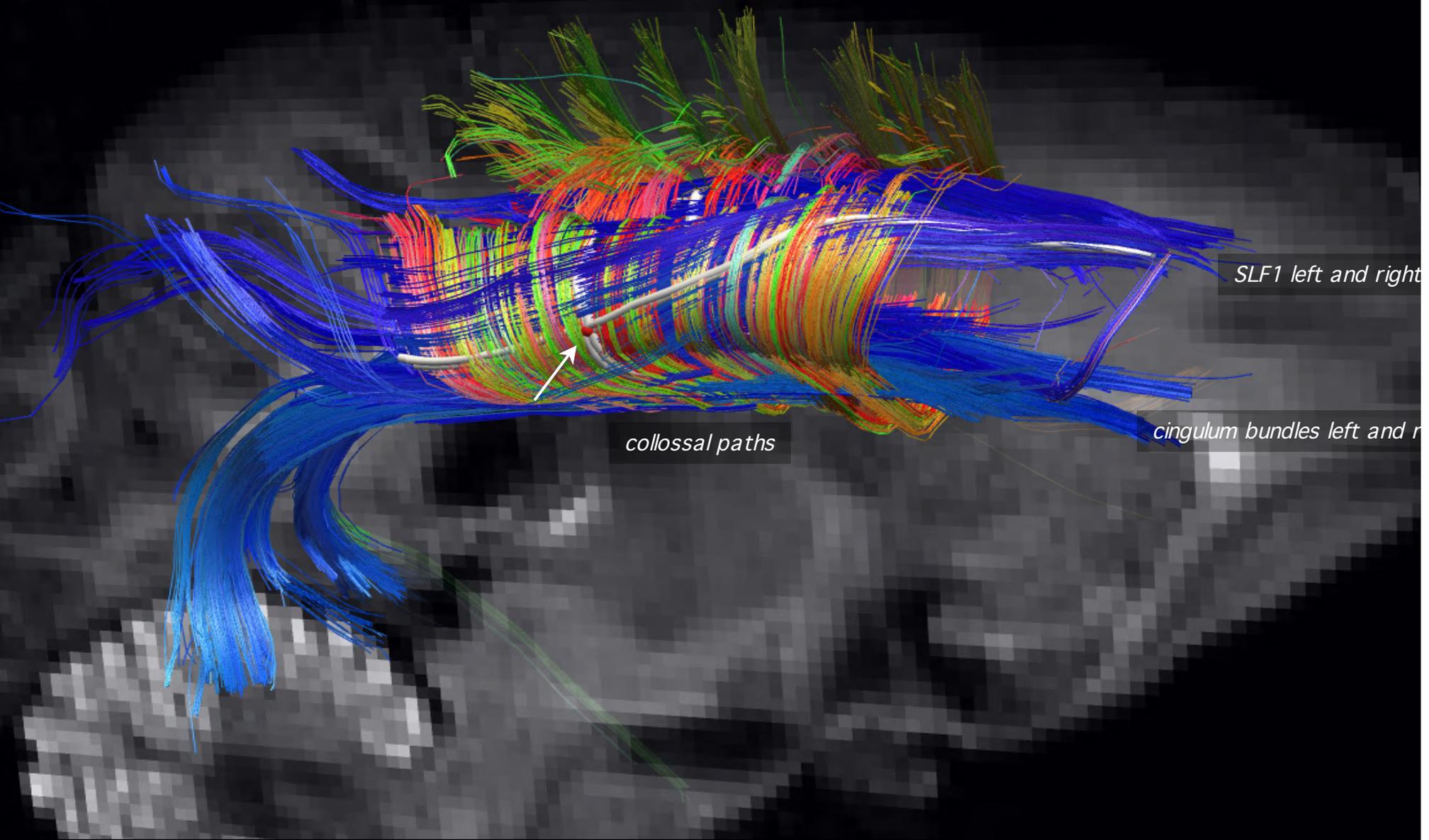
The "a ha!" moment, Sept 2009 - owl monkey Sylvian fissure



Rhesus, test voxel (red) and the paths through it (white)



Rhesus callosum and longitudinal pathways form a 2D sheet and grid

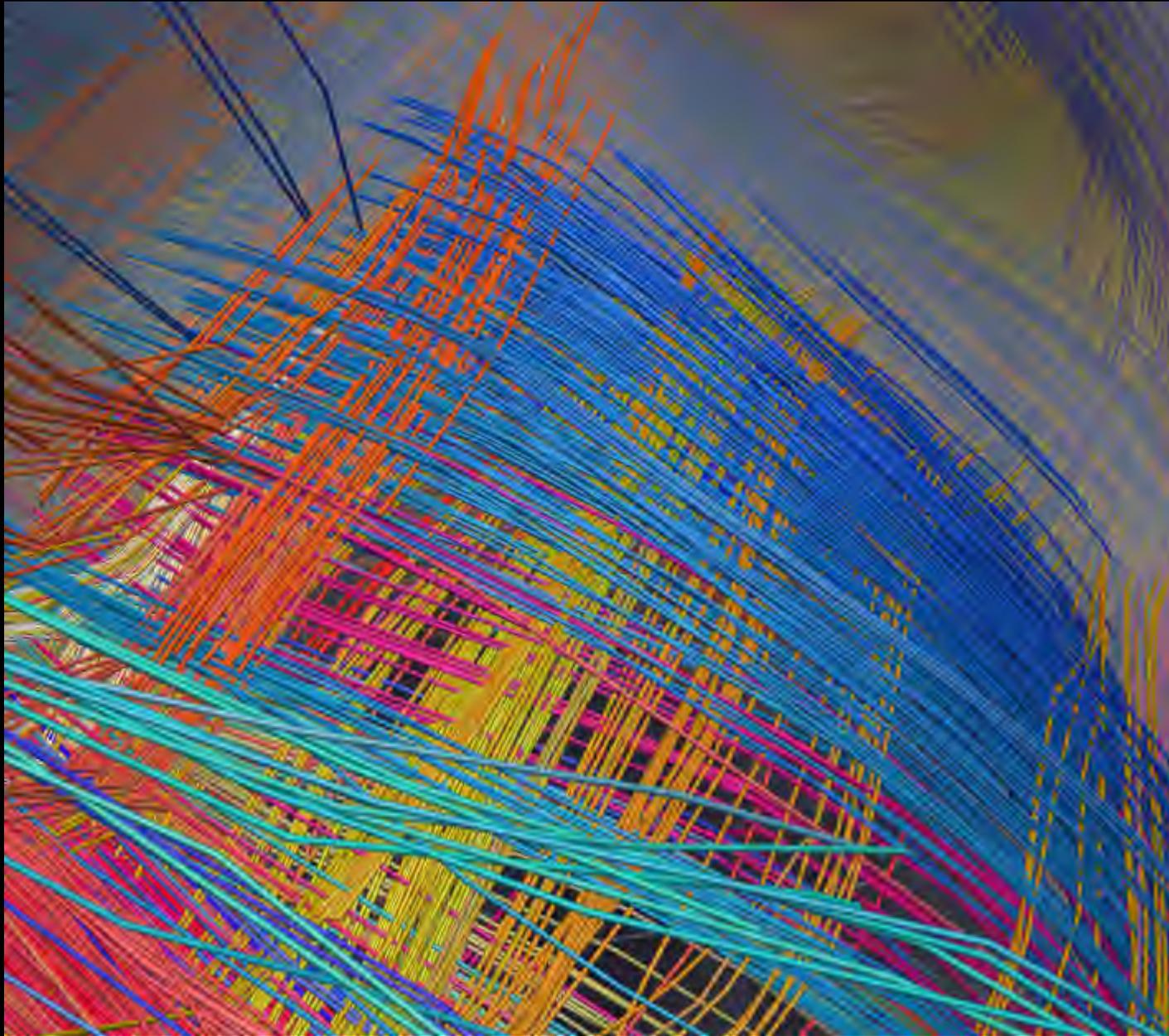


SLF1 left and right

colossal paths

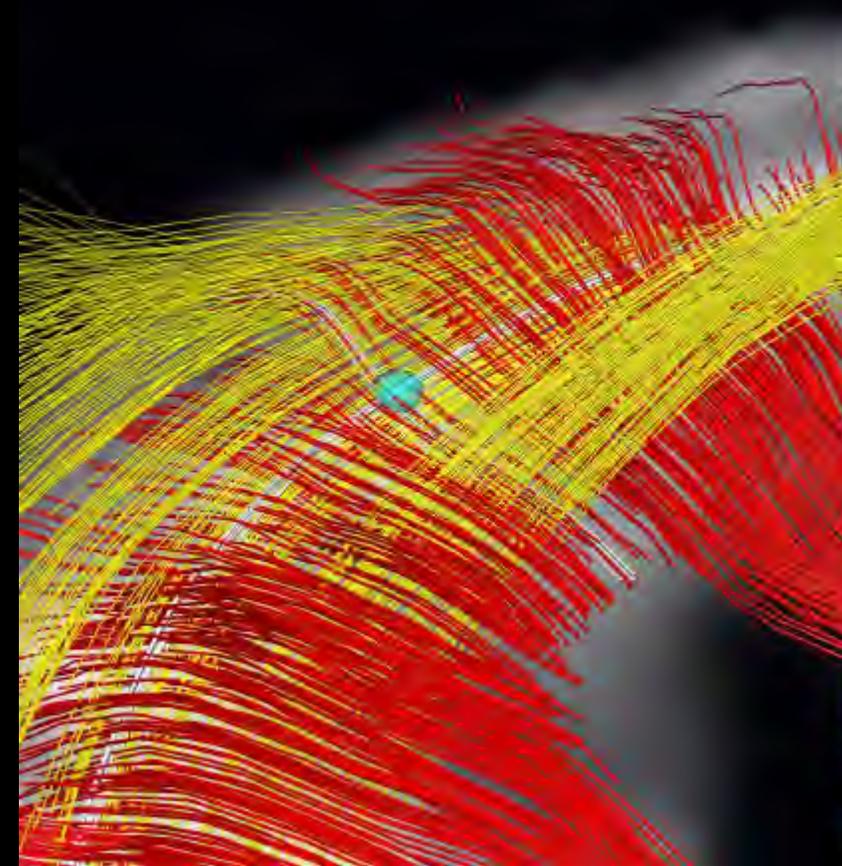
cingulum bundles left and right

*Crossing fiber pathways of the brain are interwoven, forming 2D sheets
This is overwhelmingly non-random*



*Myocardial fibers and sheets
not foliate or interwoven
Generic
prior probability ≈ 1*

*Brain path crossings:
foliate and interwoven
Highly exceptional:
prior probability ≈ 0 .*



Equivalent statements:

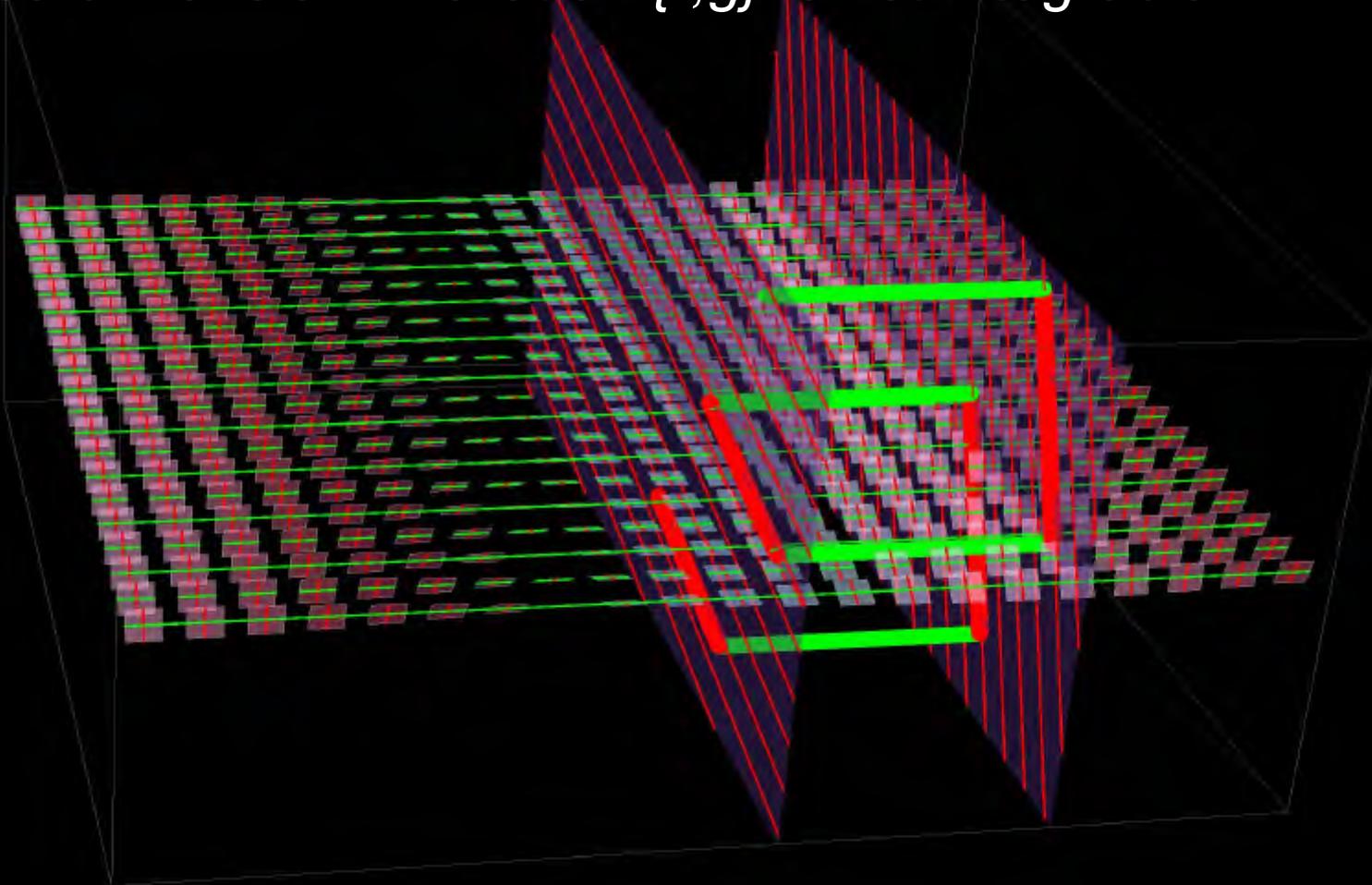
red and green are "not interwoven"

any two points can be connected by a polygon in r and g

the only functions with $\{r,g\}$ -isosurfaces are constants

the commutator $[r,g] \neq 0$

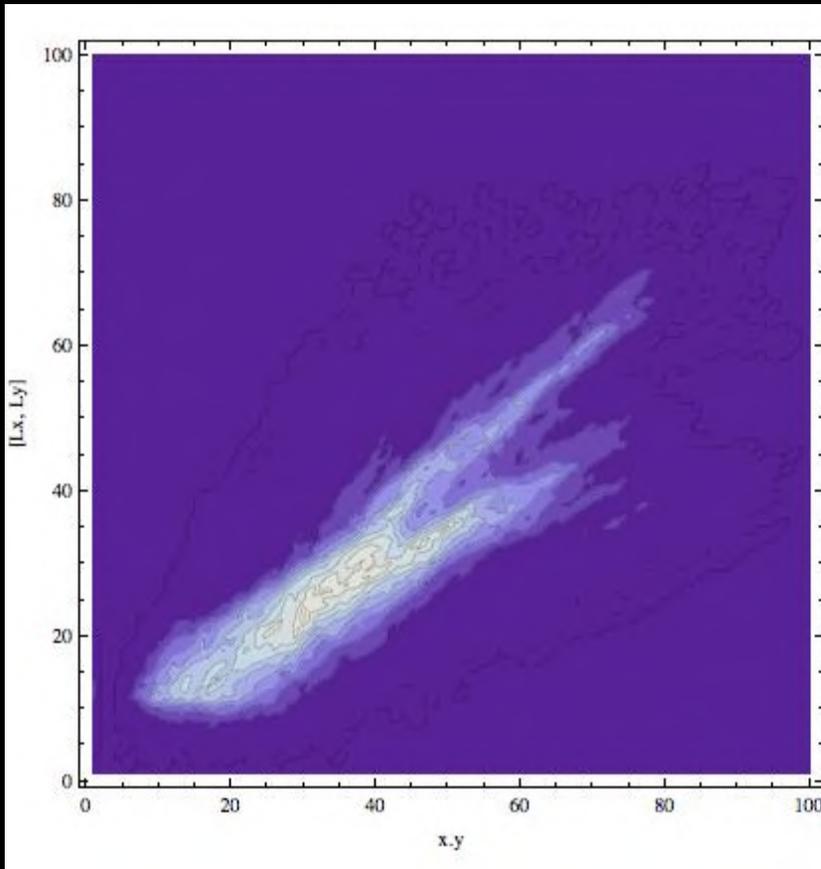
the co-dimension 1 foliation $\{r,g\}$ is not integrable



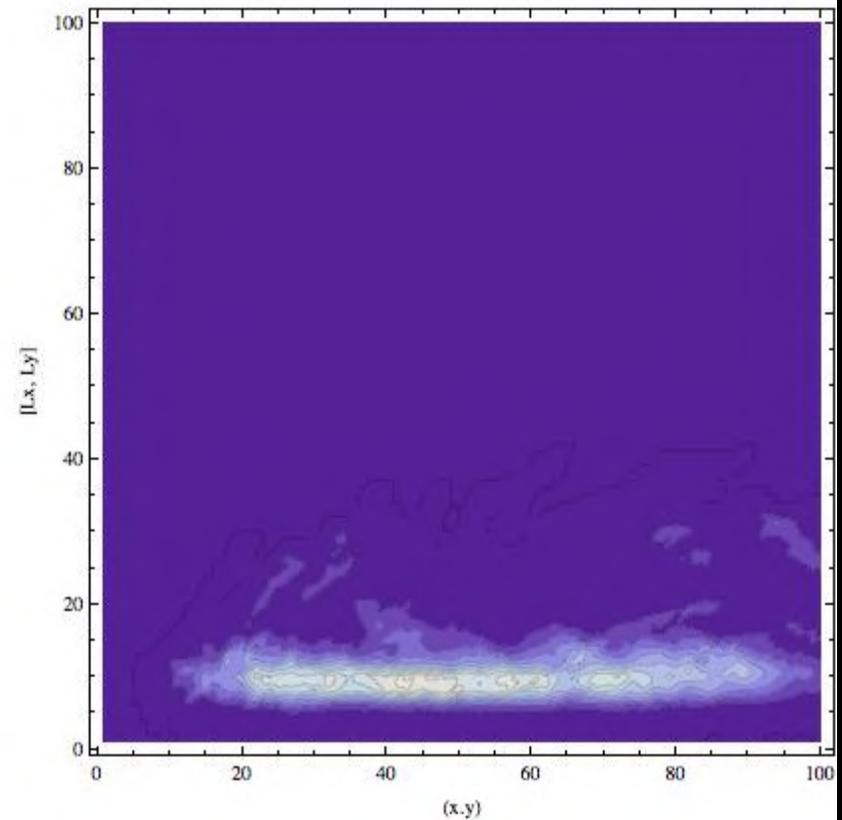
Tilt between fiber-sheets is described by a solid angle

*heart fibers and cracks
not interwoven*

*brain crossing fibers
interwoven*



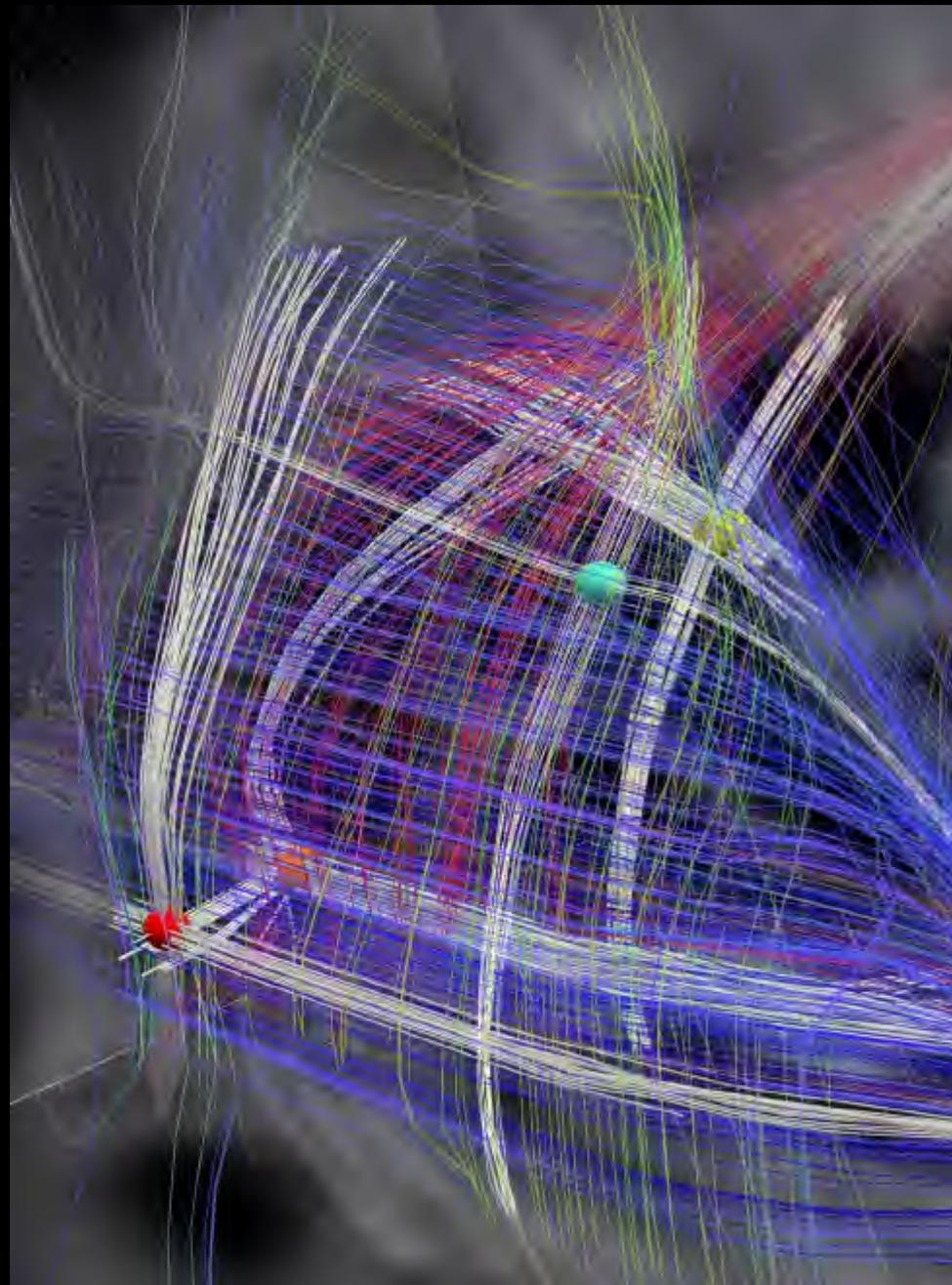
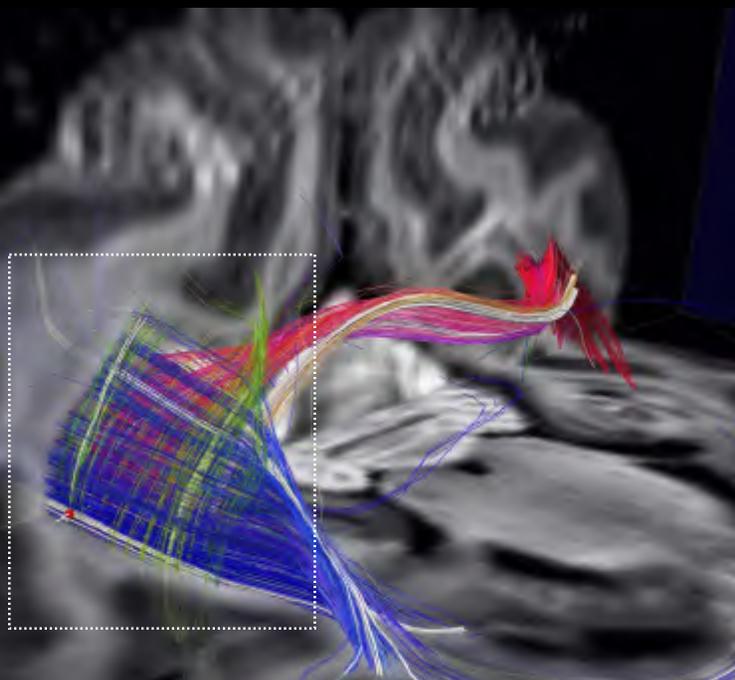
area



area

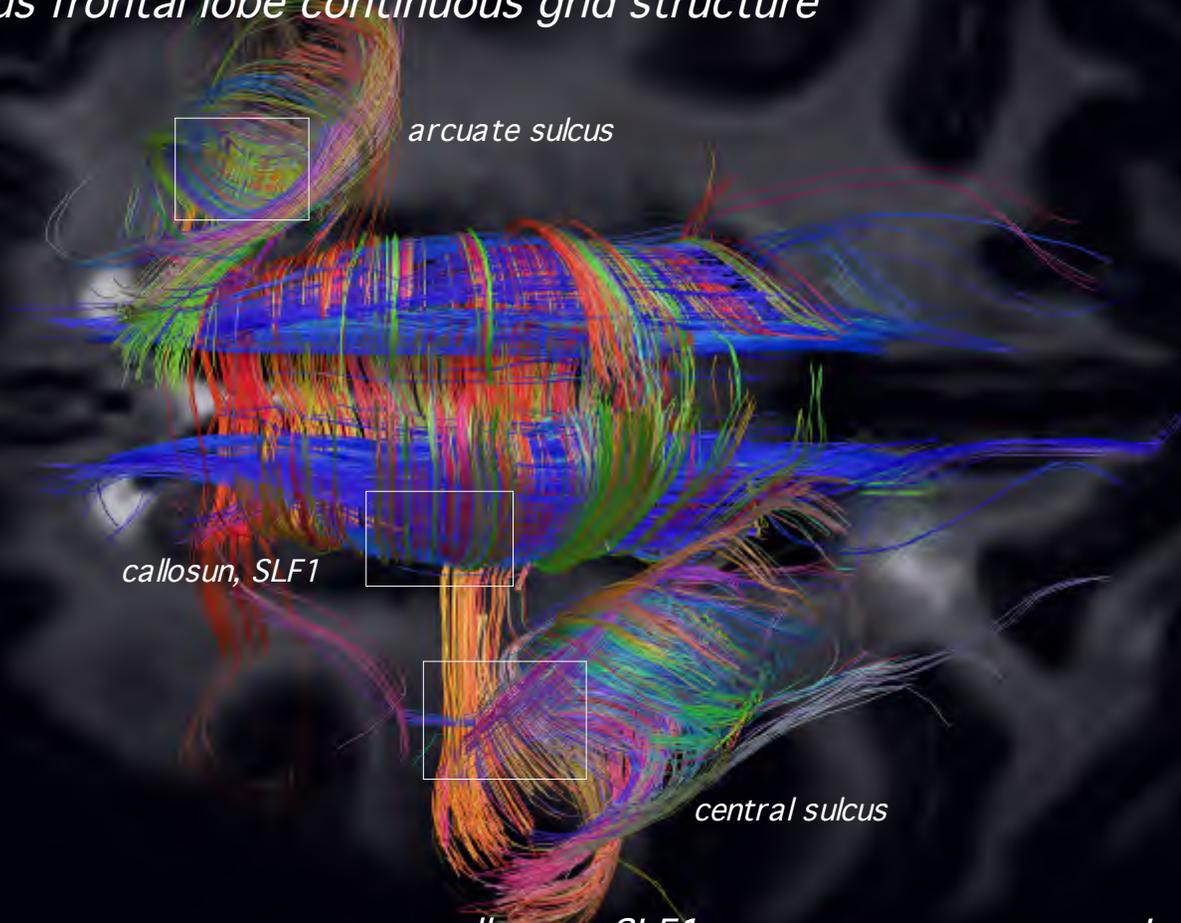
gap

*Grid structure is 3D
occipital white matter rhesus*



fiber pathways in rhesus frontal lobe continuous grid structure

rostral



arcuate sulcus

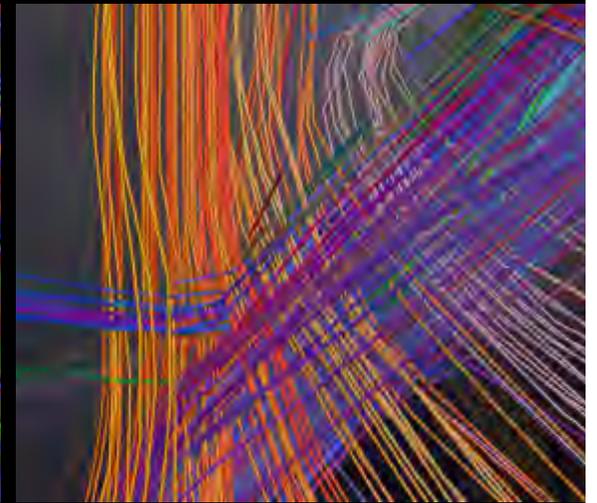
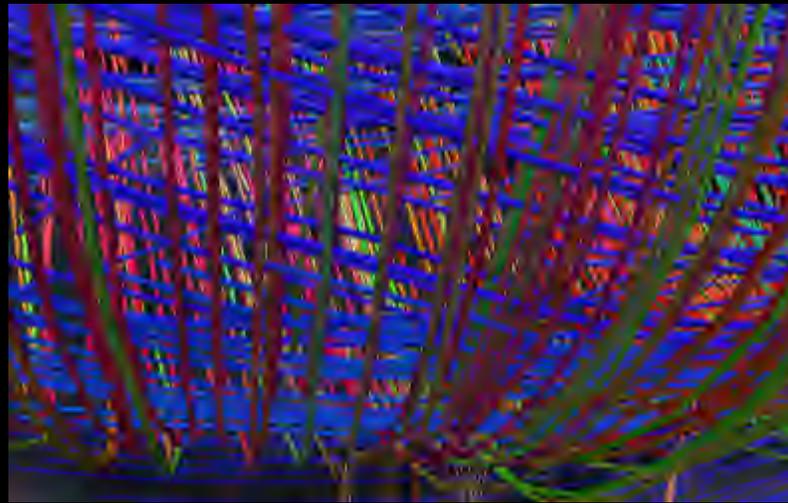
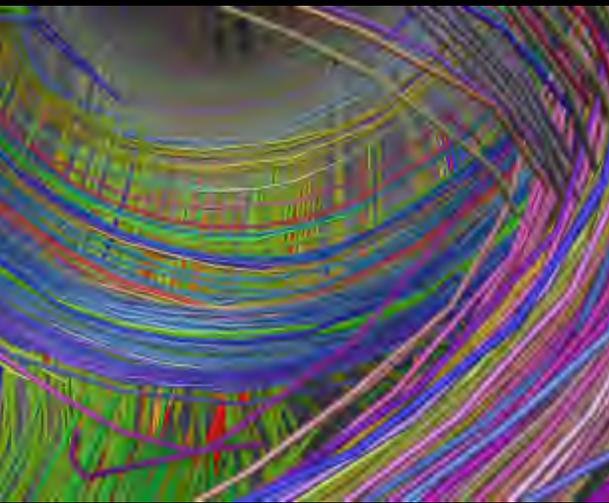
callosun, SLF1

central sulcus

R arcuate sulcus

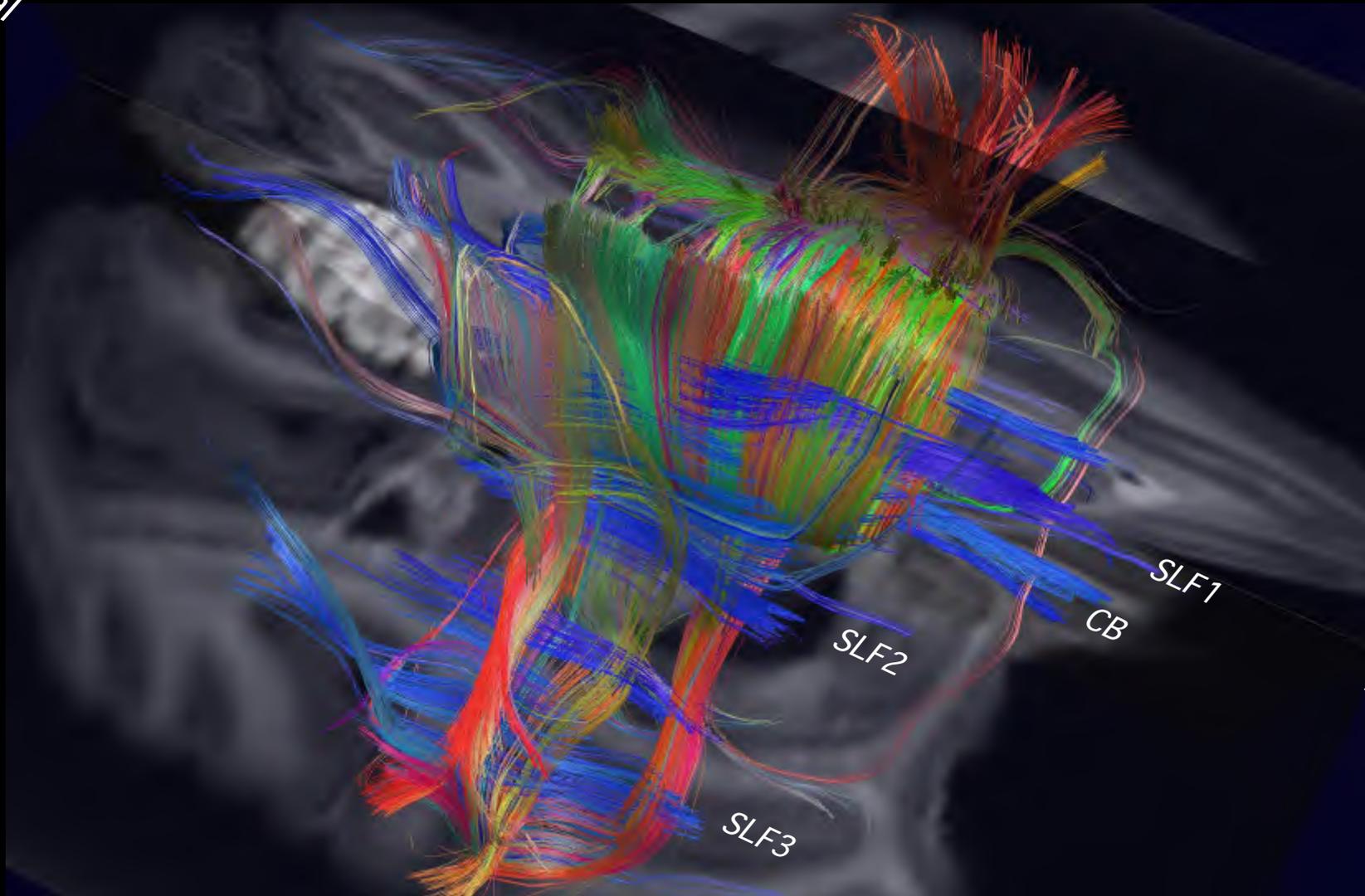
corpus callosum, SLF1

L central sulcus



Rhesus; association pathways are local condensations of a single continuous grid

caudal



rostral

Rhesus

stral

caud

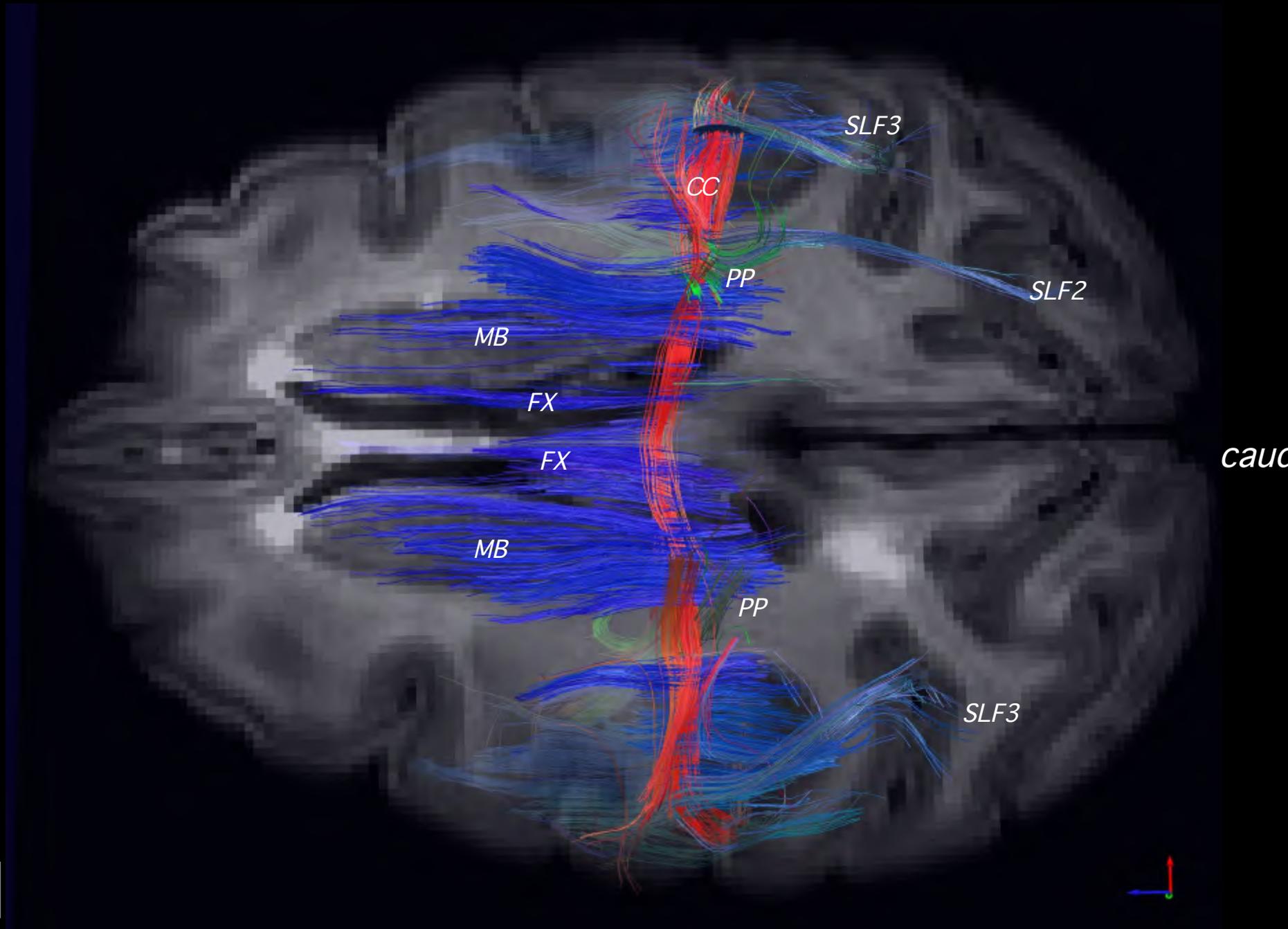
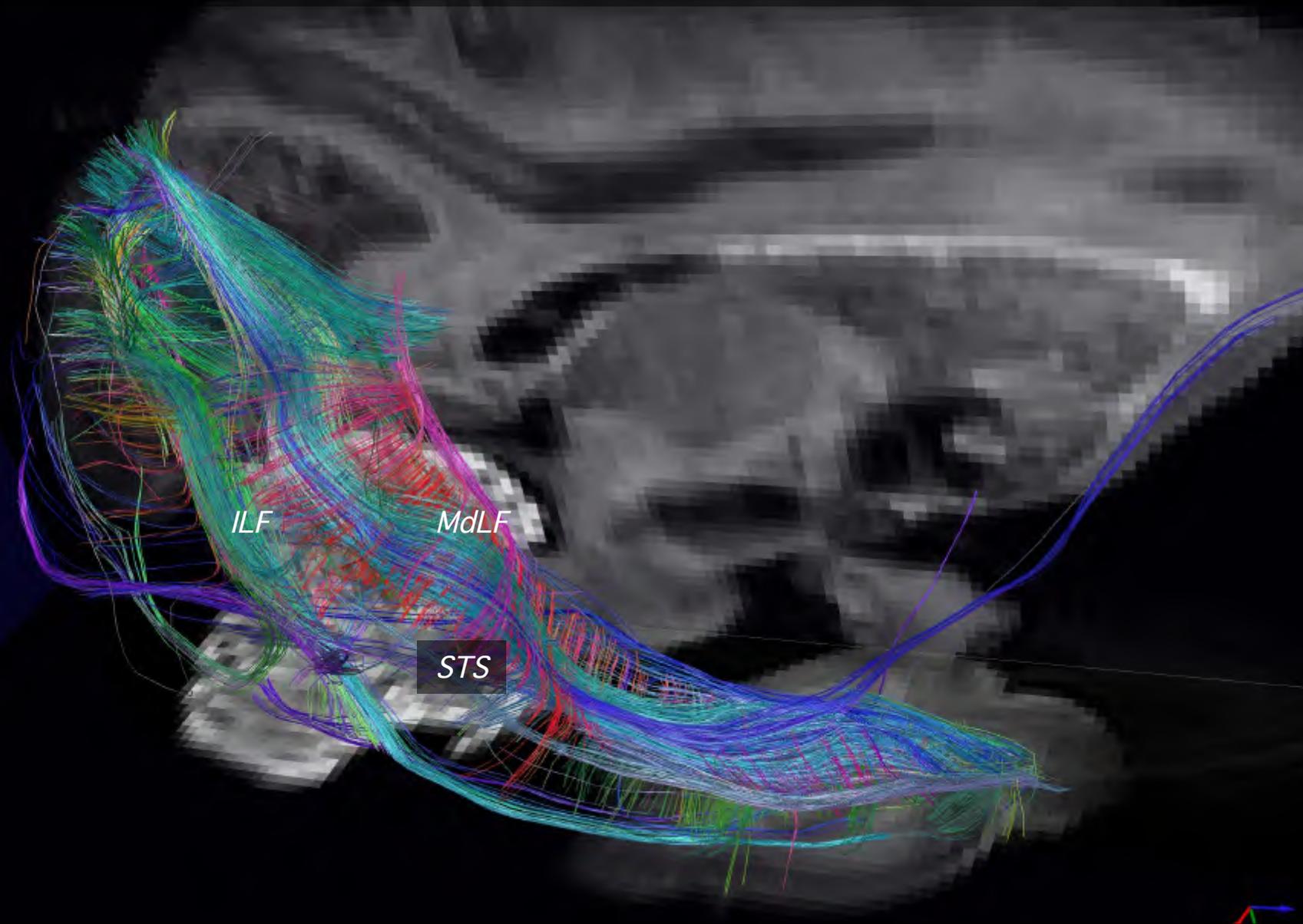
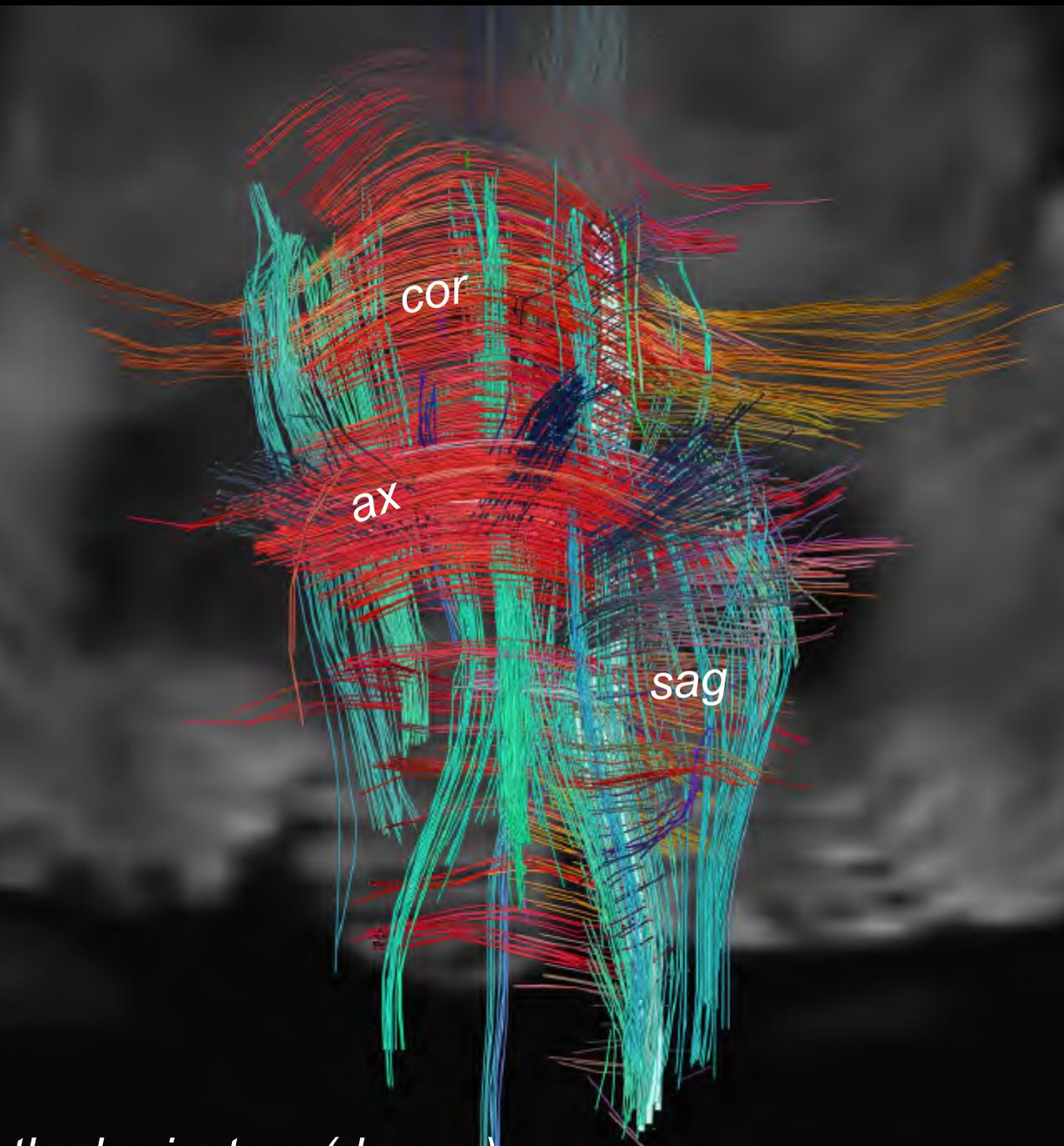


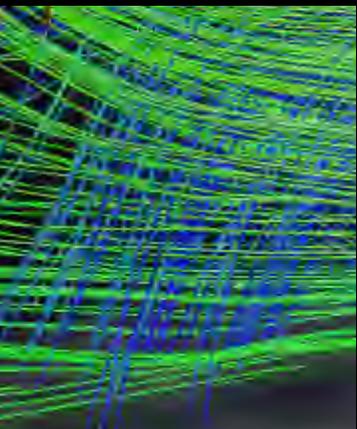
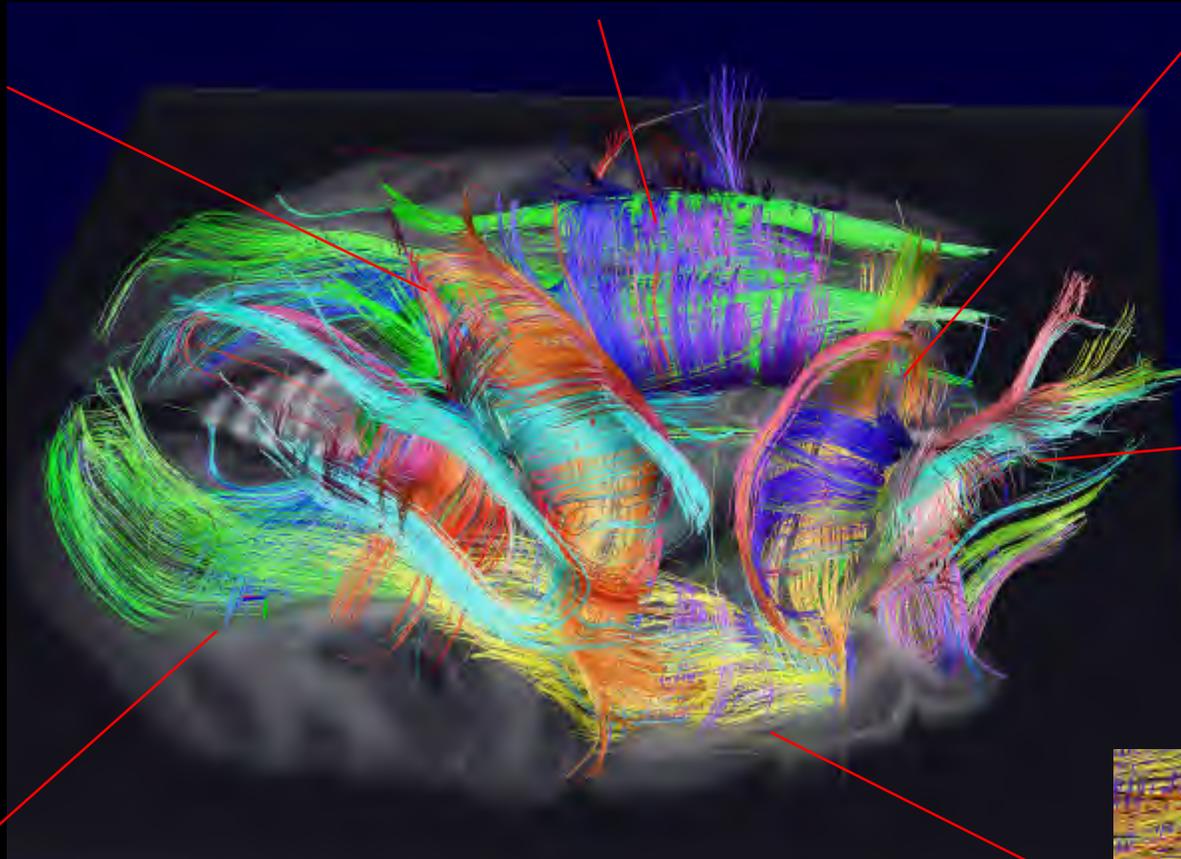
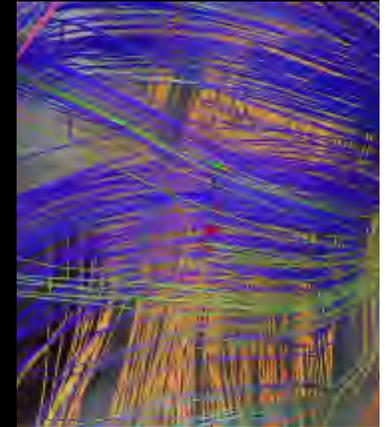
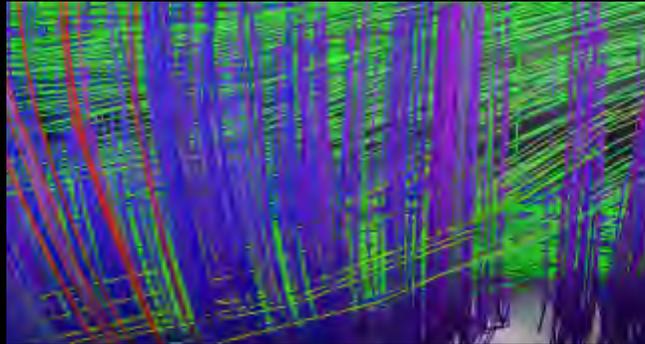
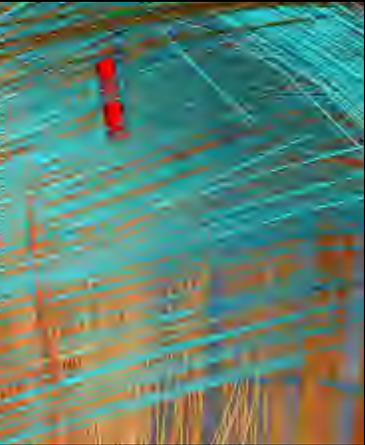
Fig. 3c

Rhesus temporal lobe transverse - longitudinal grid structure



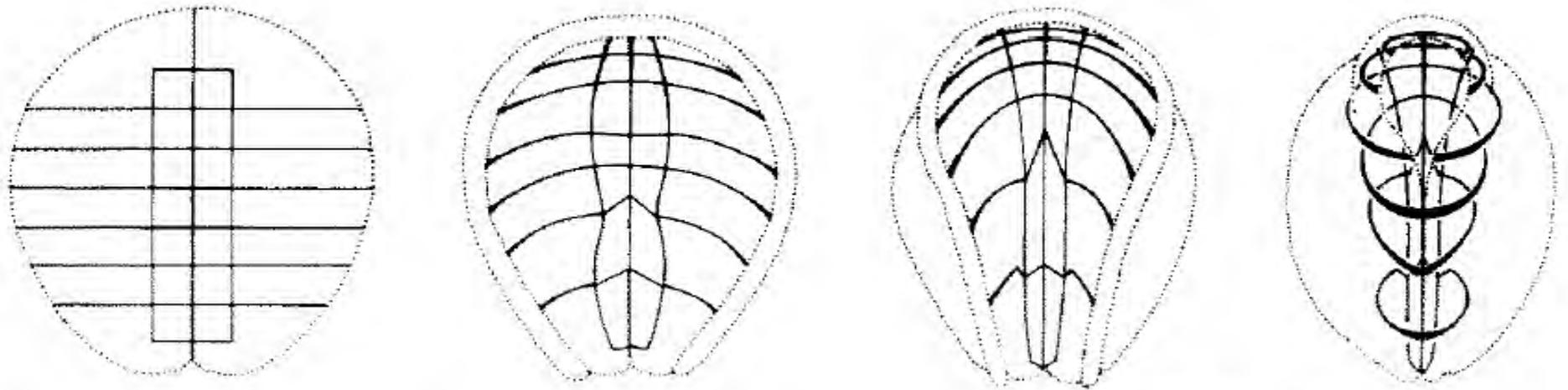


Grid structure in the brainstem (rhesus)



Rhesus pieces

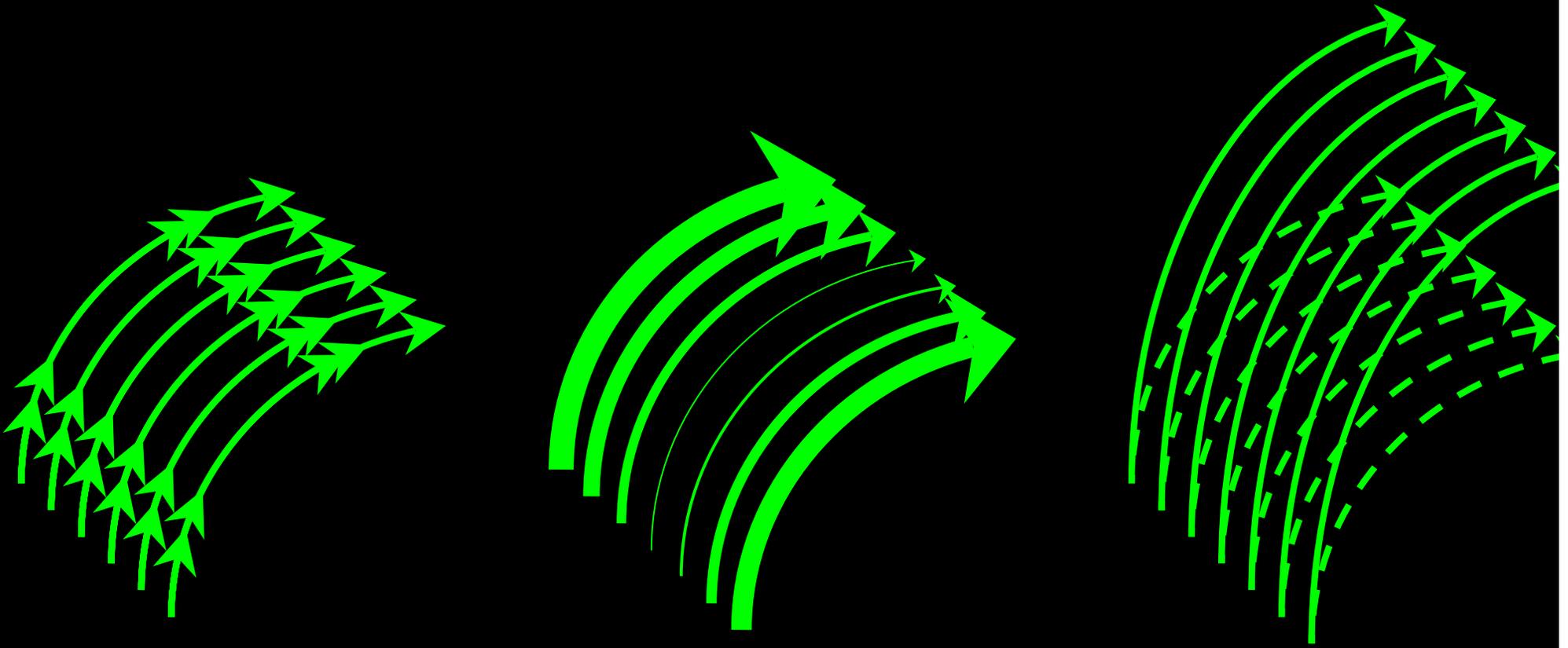
CNS pathways morphogenesis: begin as a grid, then roll up to achieve its adult configuration



Burnside & Jacobsen, 19

The structure and function of the brain must change gradually and together for learning and plasticity, development and evolution.

This requires connectivity to be continuous and homogeneous

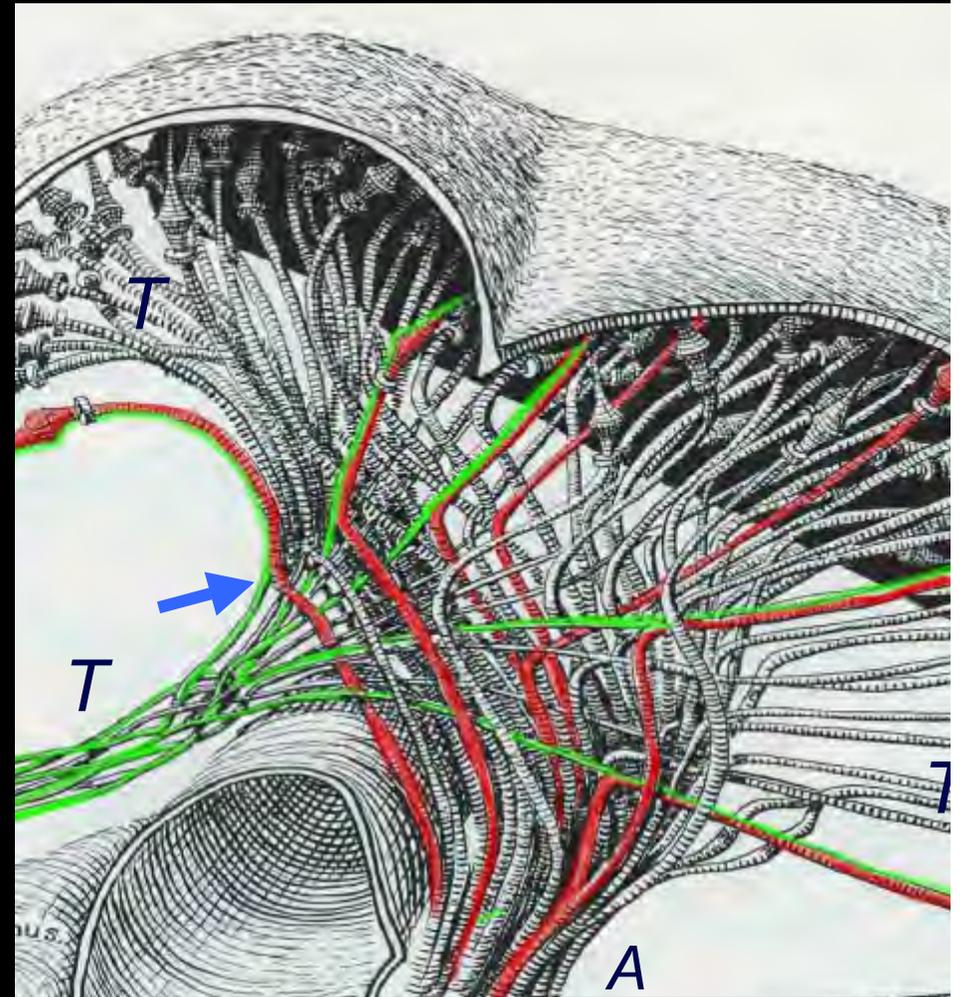
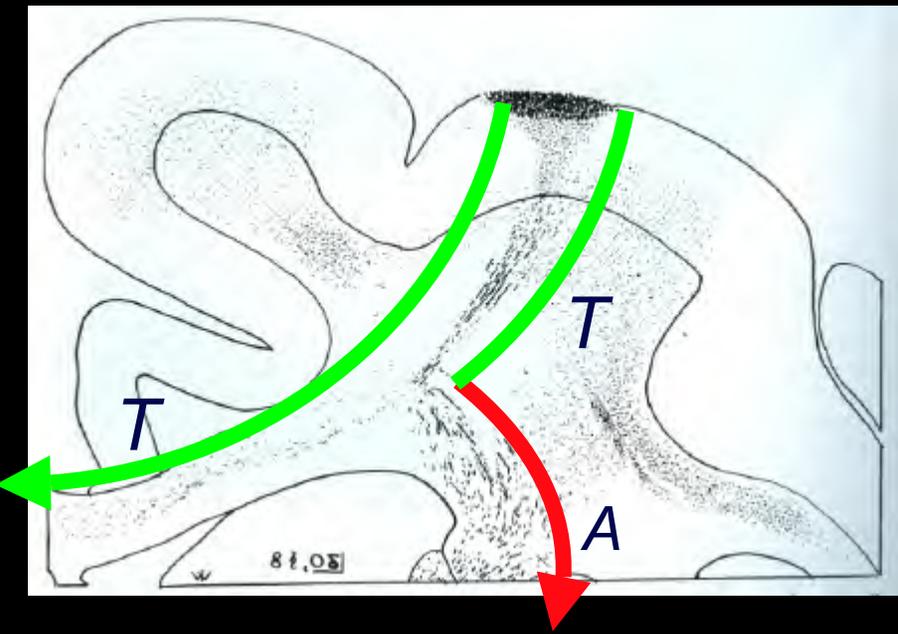


functional coherence

plasticity

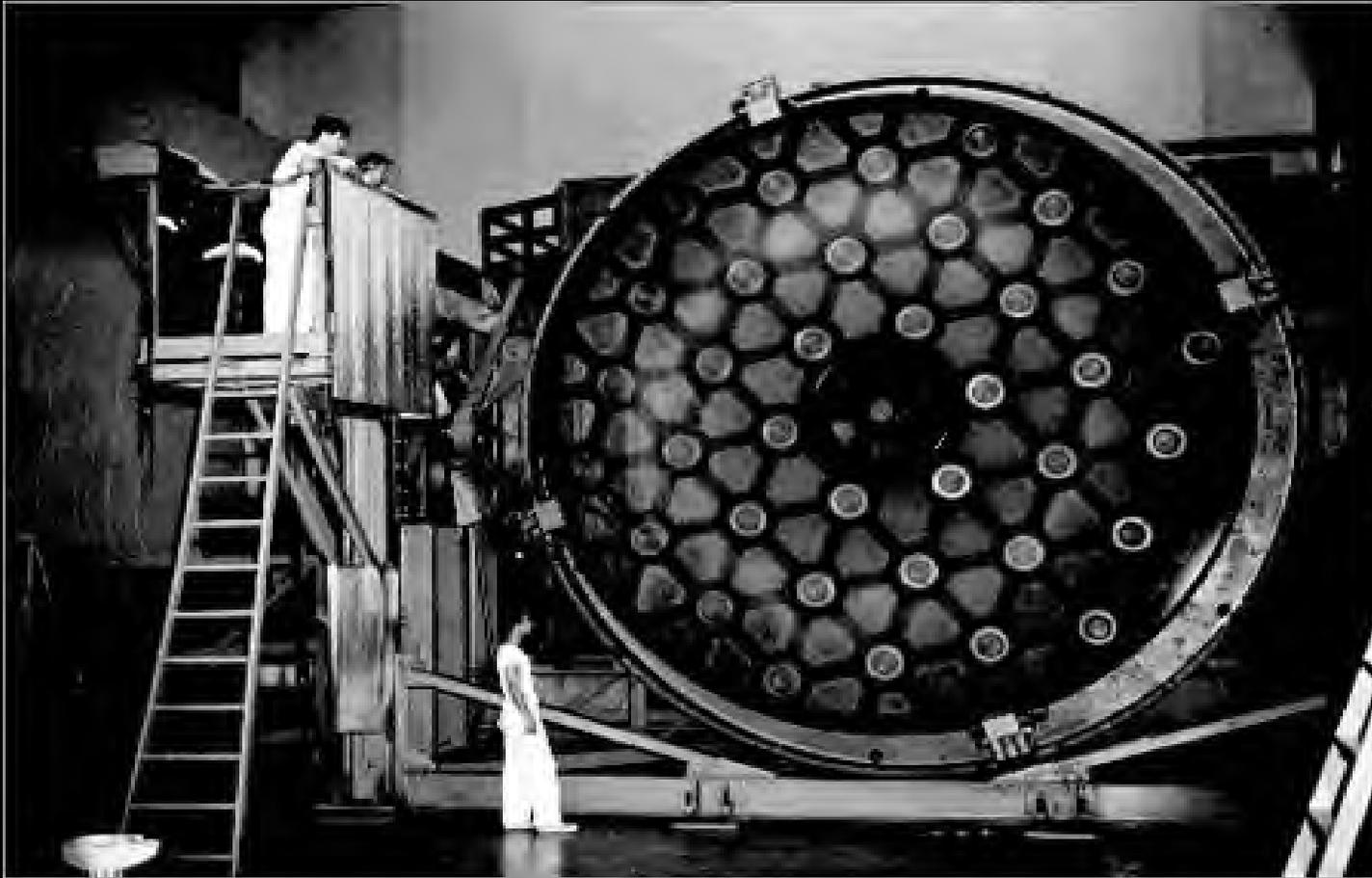
evolution

*Grid structure reduces axon path-finding to a 6 letter code -
Up, Down, Left, Right, Front, Back*



Wendell Krieg 1953 - Corticospinal axons sharply turn from effective transverse T to axial A

In astronomy, the way to sensitivity and resolution is mirror diameter



Corning 200" mirror for the Hale Telescope at Mt Palomar

In diffusion MRI, the way to boost signal-to-noise and resolution of micro-structure is gradient strength

MGH-UCLA HCP

Immediate goal: map human connectivity

Long-term goal: objective mental health care

The logo for the Human Connectome Project features a central bright yellow and white light source. From this source, numerous colorful lines radiate outwards, creating a sense of dynamic energy and connectivity. The lines are composed of small, overlapping circles or dots in shades of red, orange, yellow, green, and blue. The overall effect is a complex, multi-colored web of connections.

Human
Connectome
Project

NIH Blueprint

for Neuroscience Research

The ultimate diffusion machine...

7x the gradient strength.

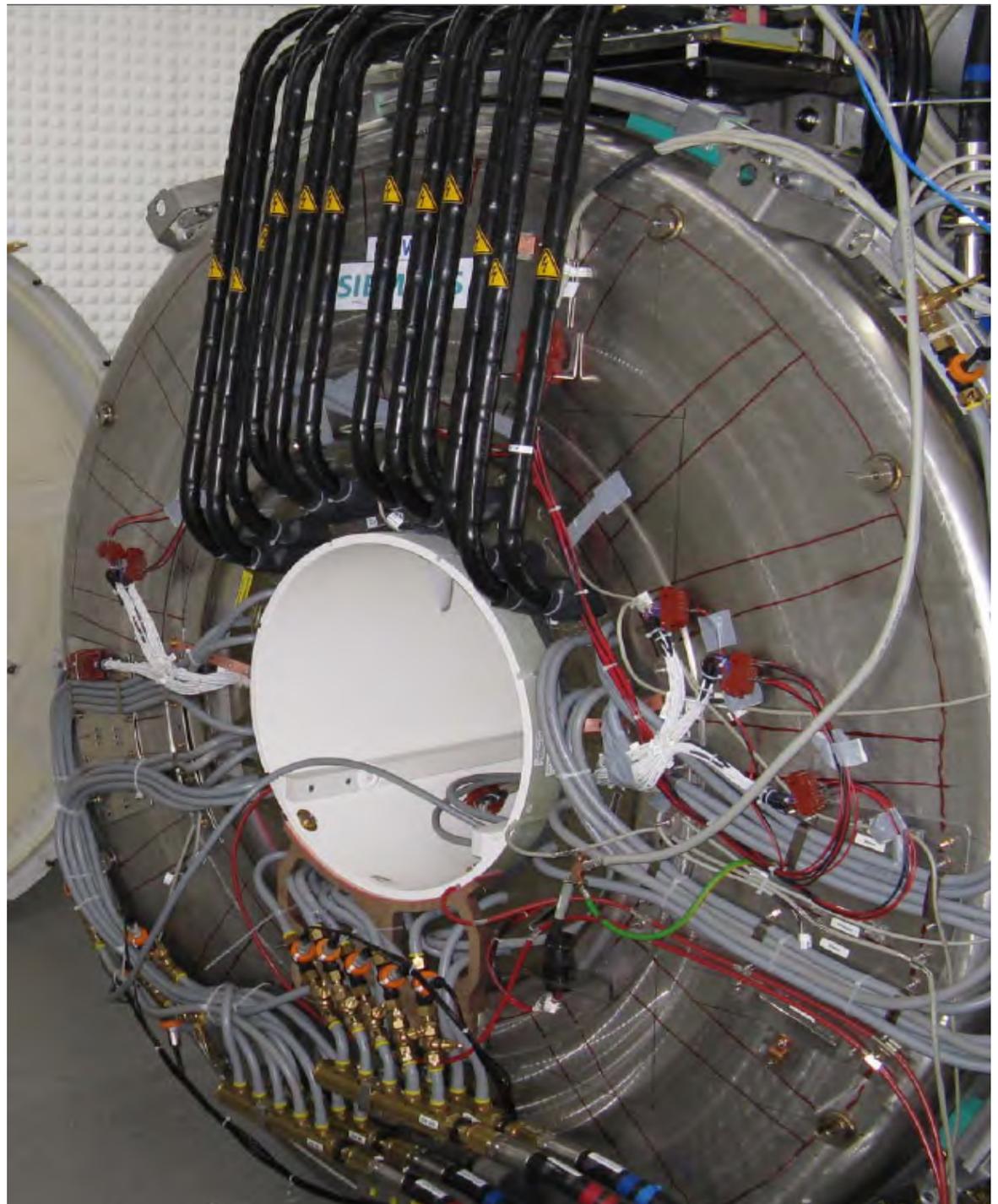
$$G_{\max} = 300\text{mT/m}$$

$$\text{Slew} = 200 \text{ T/m/s}$$

4x the encoding speed.

(thru simultaneous
multi-slice imaging)

64 channel brain array

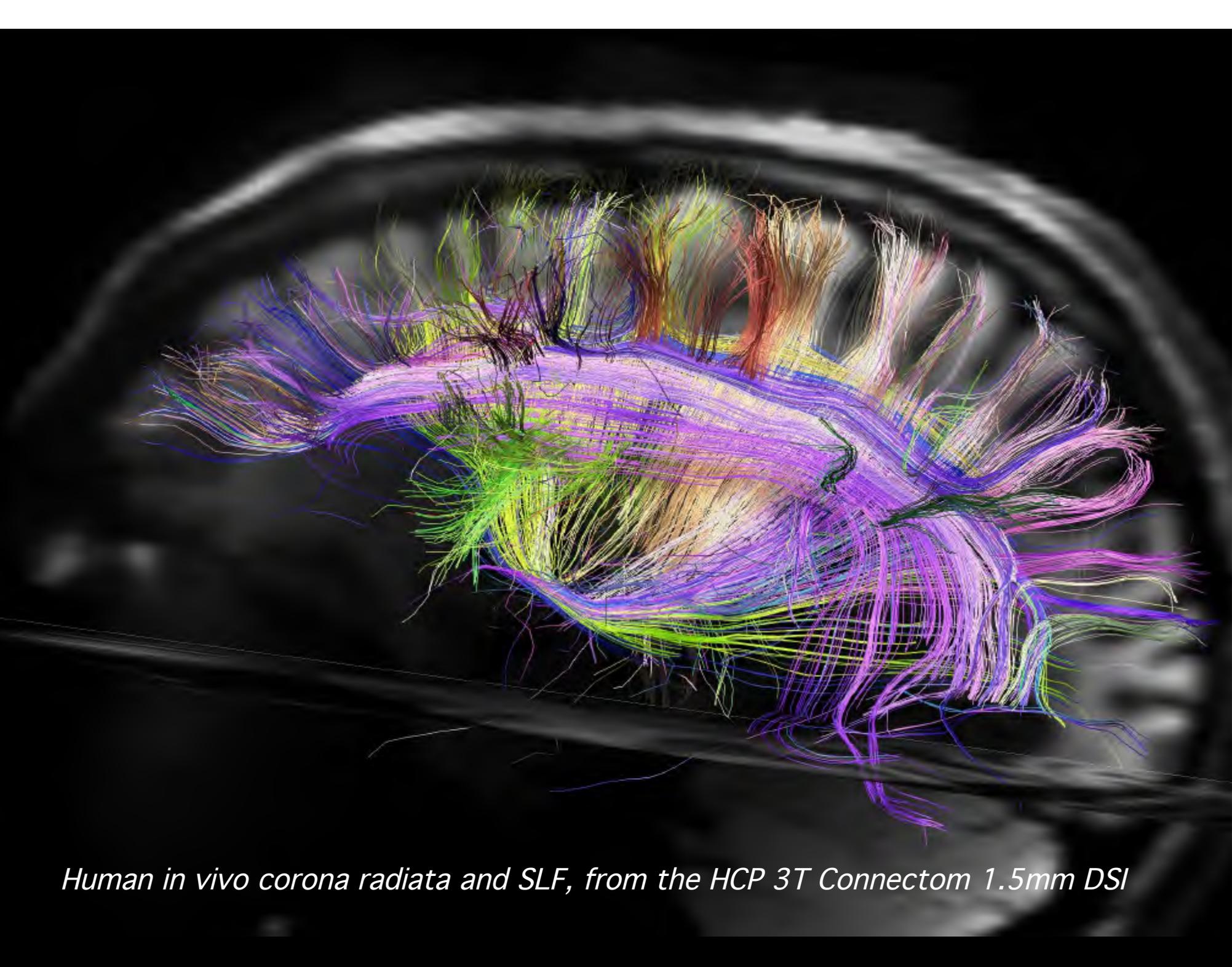


Expect nearly 10x increase in sensitivity for high b value diffusion

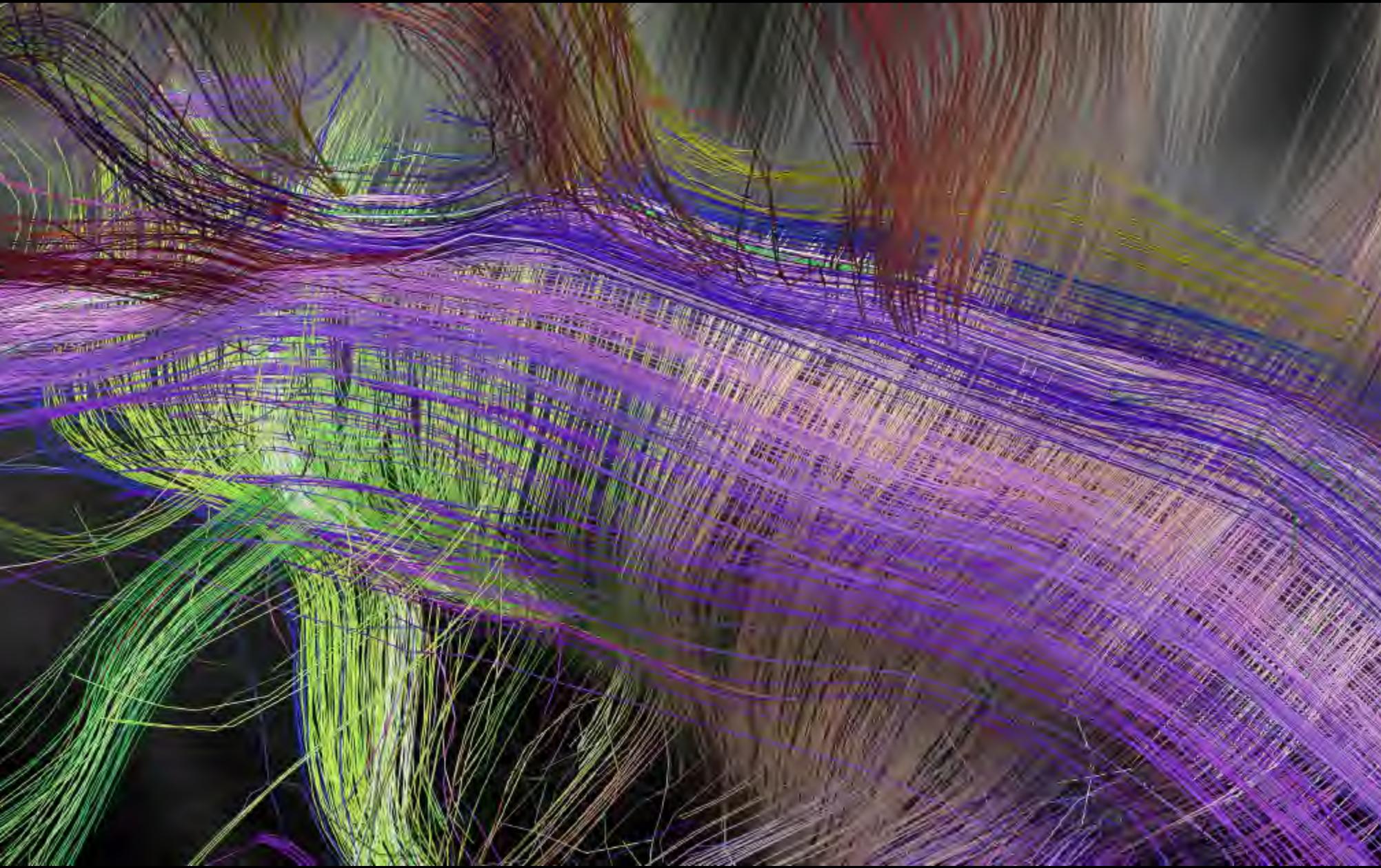
3T Connectom scanner, 24 megawatts

Los Angeles class nuclear submarine, 26 megawatts





Human in vivo corona radiata and SLF, from the HCP 3T Connectom 1.5mm DSI

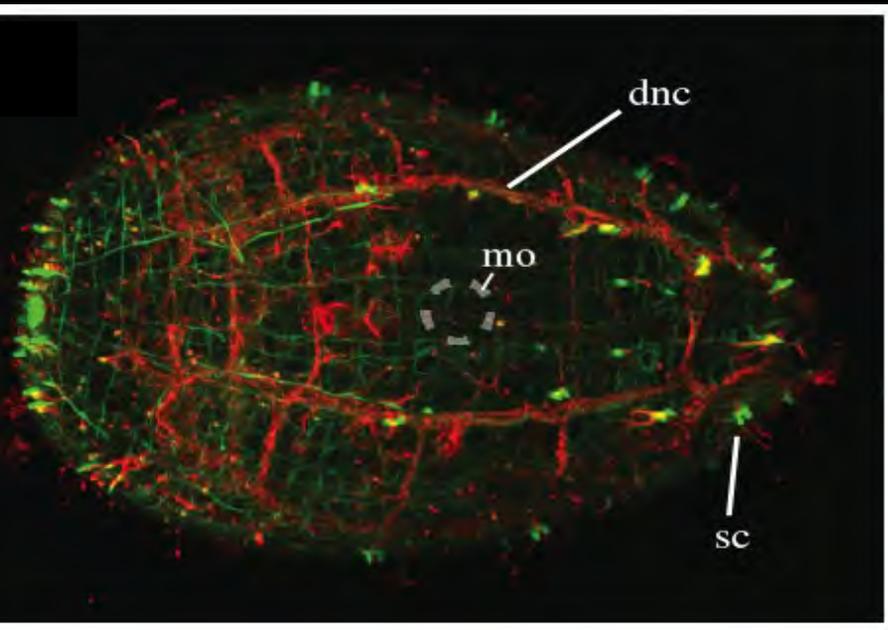


human corona in vivo deta

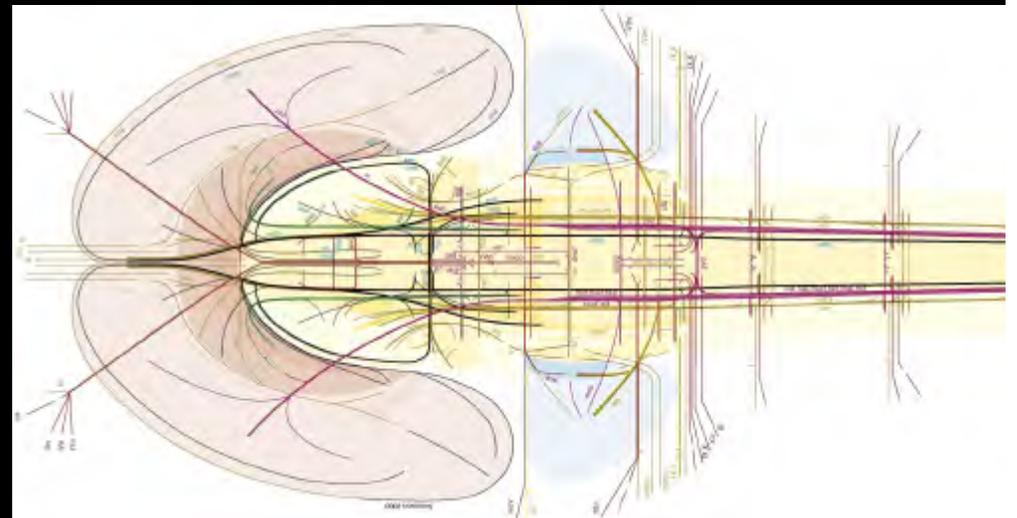
<u>Great Observatory</u>	<u>\$\$\$</u>
Large Hadron Collider	\$10 billion
Hubble Telescope	\$6 billion
National Ignition Facility	\$5 billion?
Human Genome Project	\$3 billion
Mars Curiosity Rover	\$2.5 billion
EU Extremely Large Telescope	\$1.5 billion
3T Connectom	\$0.01 billion (on time, on budget)
(7T Connectom	\$0.03 billion, in development)

Having a brain is an aspect of being a bilaterian

Juvenile acoelomate worm

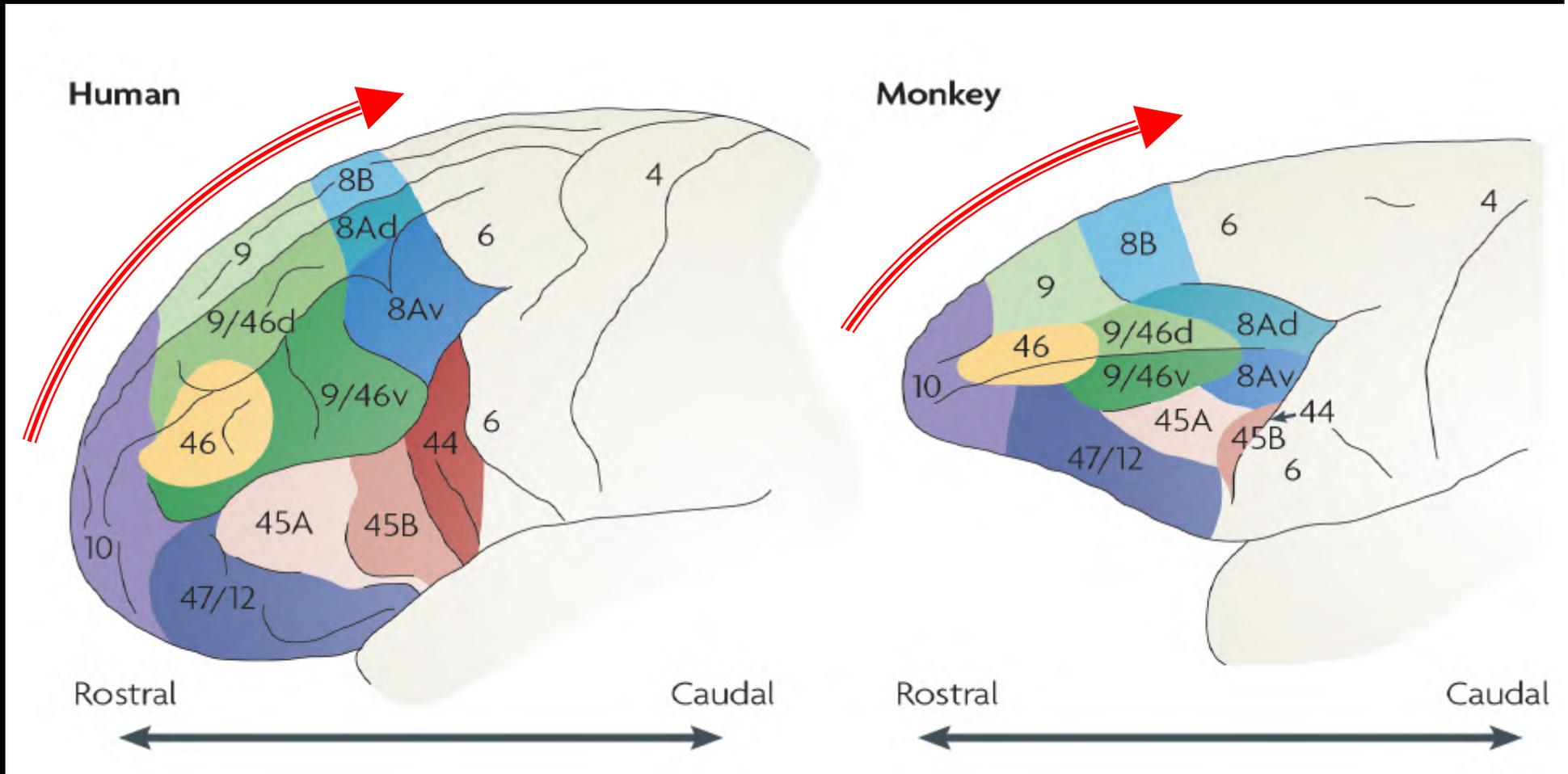


nervous system of a typical mammal - the rat



Specialization and hierarchy of cortical function follow the grid structure of connectivity

Cortical areas are arranged like a checkerboard, hierarchic from front to back



Geometric theory of mind and brain

*placazoan (pre-bilaterian pancake animal) -
breaking symmetry to forage*



*human -
abstraction and the future*



Concluding remarks -

The structure of the brain -

The fiber structure of the brain is a coordinate system. It reveals the relation of the brain its development, and to every other brain. Its order is expressed by differential topology.

The operation of the brain -

The fiber pathways of the brain are components within a single 3D continuum. This continuous structure allows functional coherence and plasticity, brain development and evolution.

The meaning of the brain -

The brain is an aspect of the bilaterian plan, to augment the breaking of the symmetries of space and time.

One should expect the condition of existing in time to endow every aspect of perception, thought, and experience.