New methods for measuring activity, connections and tissue properties in the living human brain

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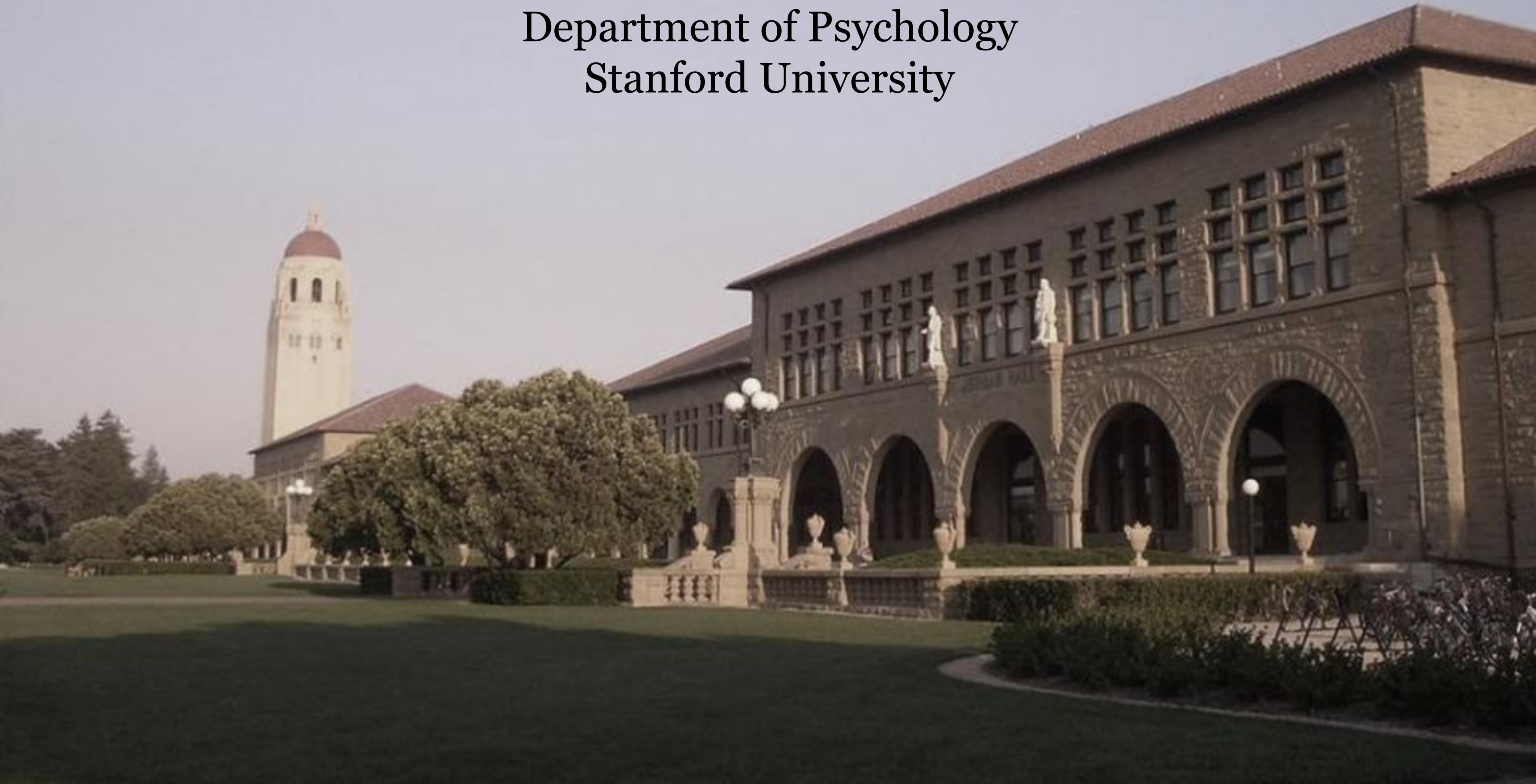
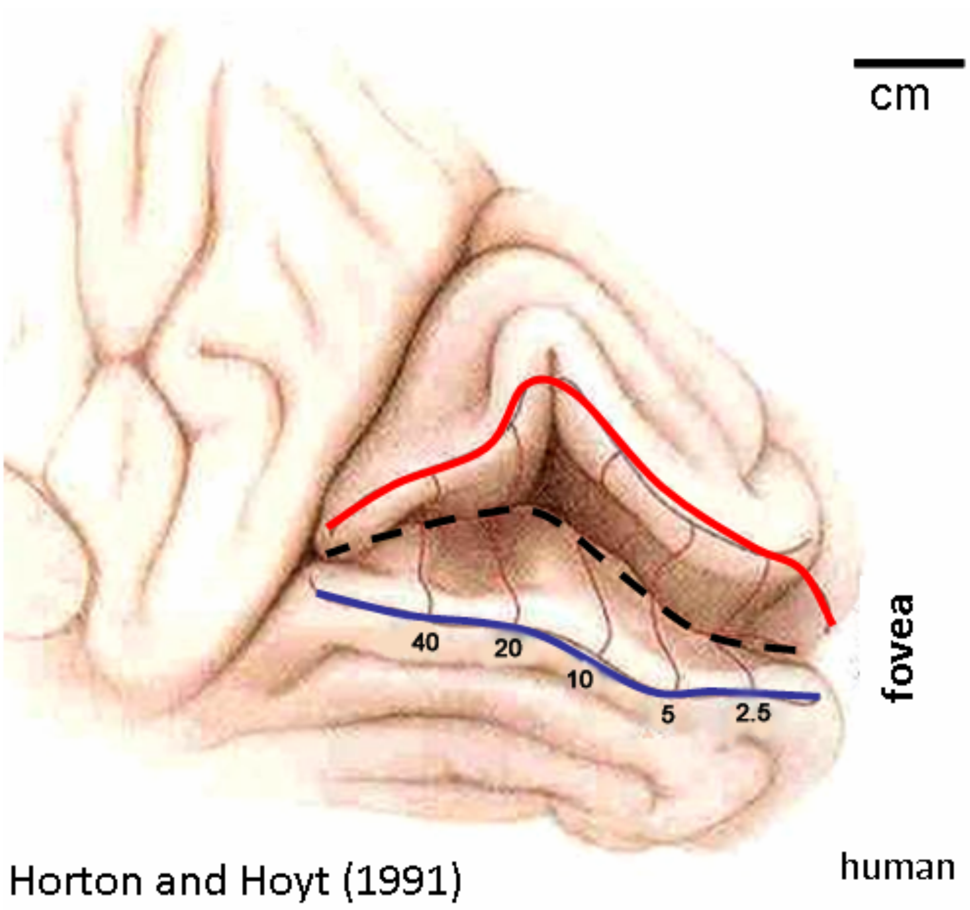
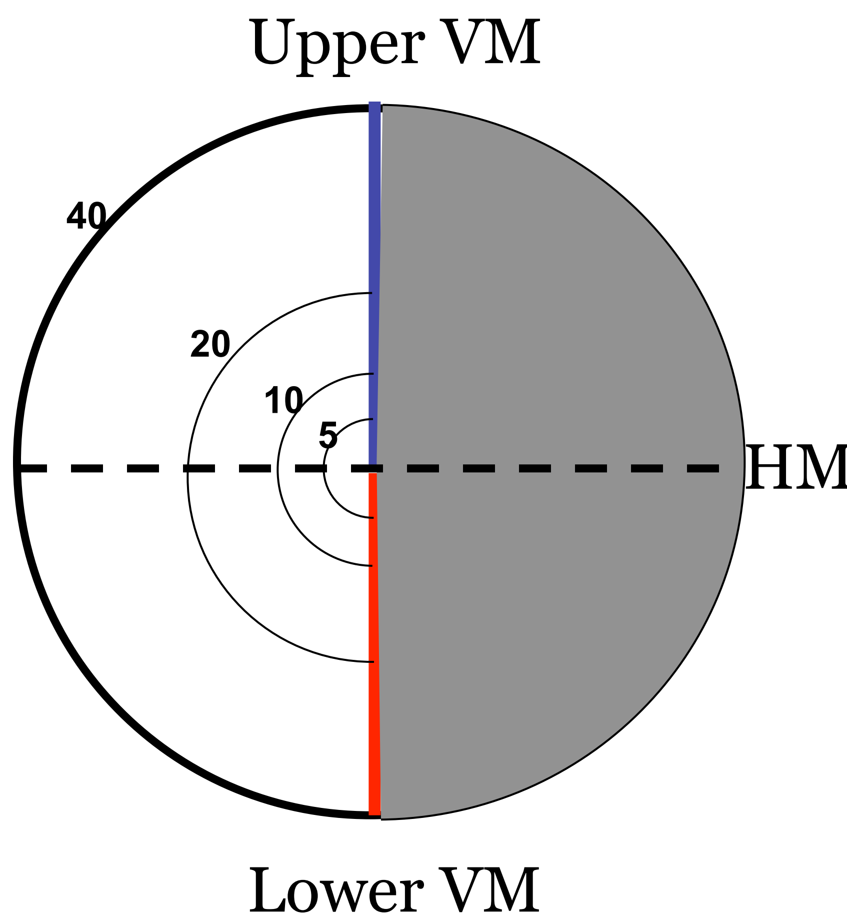


New methods for measuring activity, connections and tissue properties in the living human brain

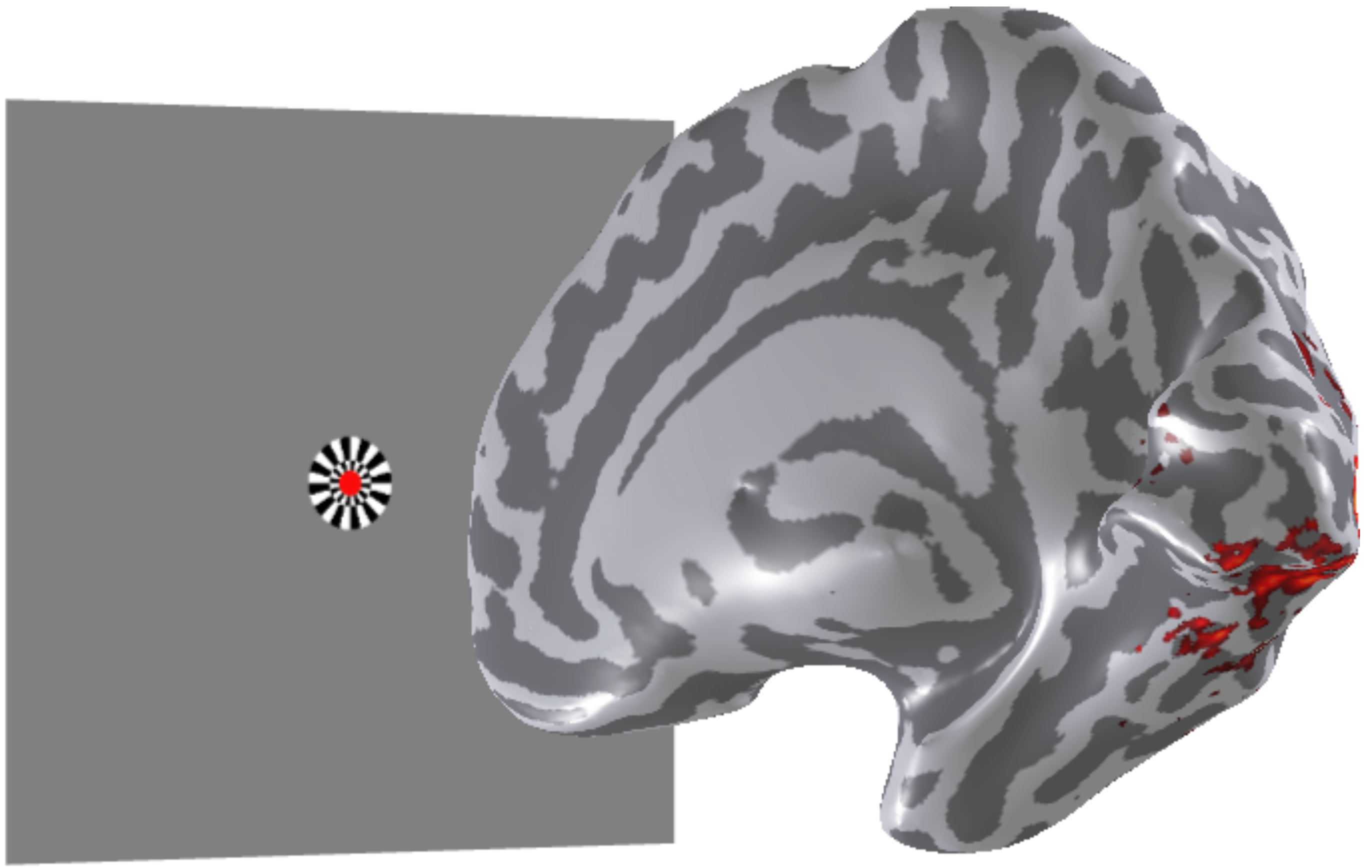
- Human visual field maps (Kay, Winawer, Dumoulin)
- White matter tracts for reading development (Yeatman)
- Quantitative MRI of brain tissue (Mezer)
- Project on Scientific Transparency

Primary visual cortex (V1) contains a visual field map

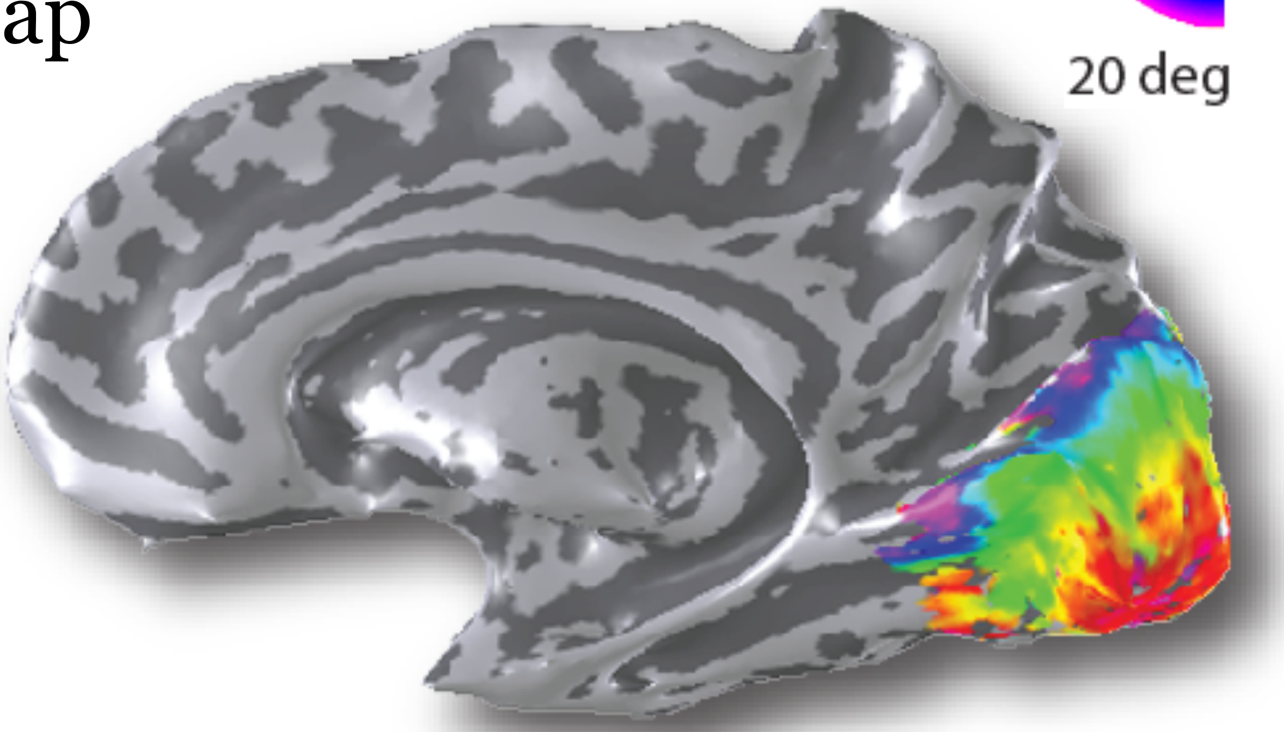


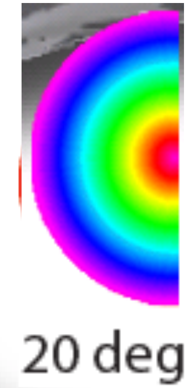


Human eccentricity mapping
(Engel et al., 1994,1997; Sereno; DeYoe; Others)

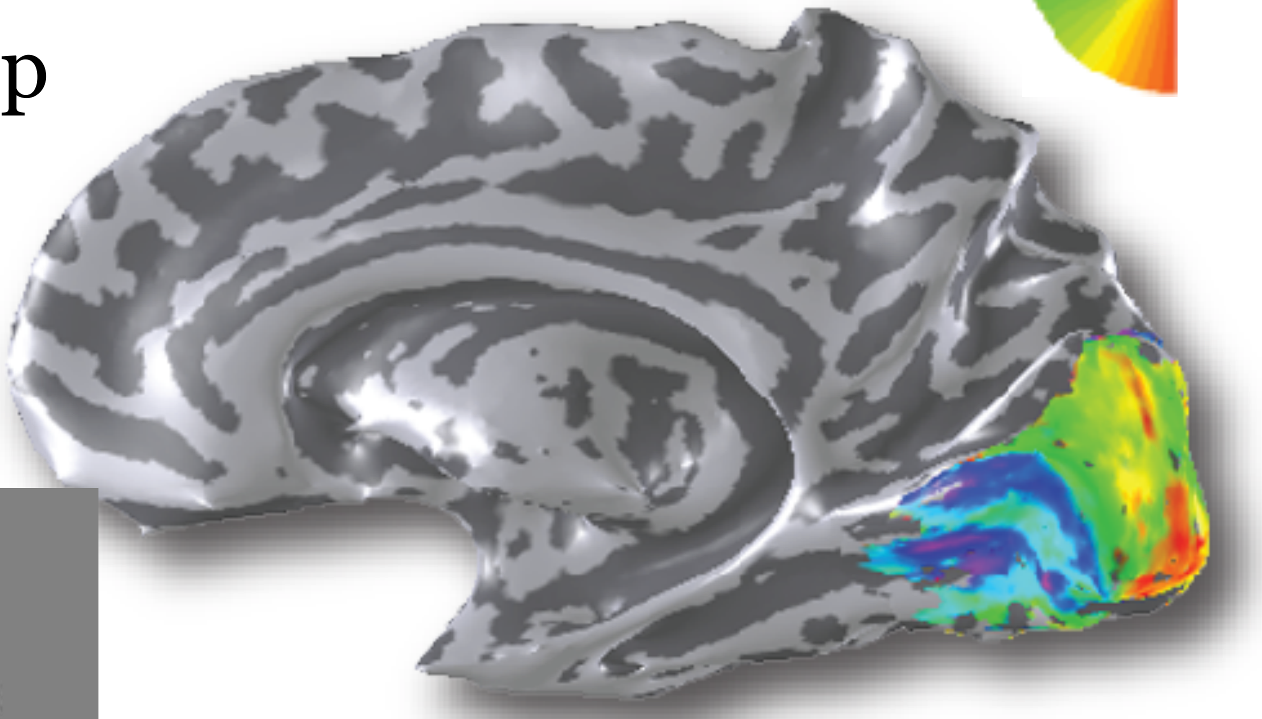


Pseudo-color representation of visual field map





Angular measurements sharply delineate visual field map boundaries

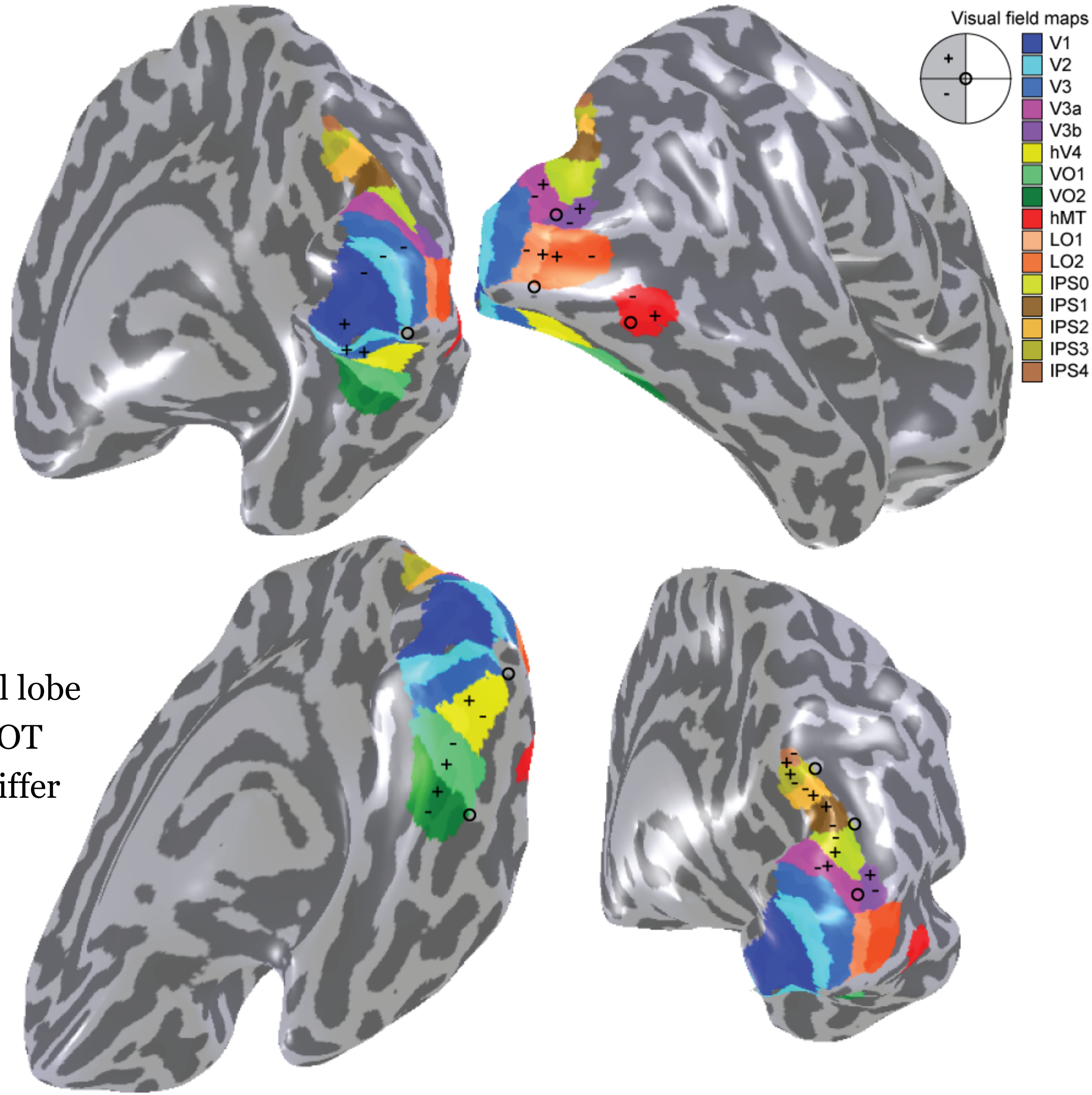


More than sixteen visual field maps

Wandell, Dumoulin, Brewer (2007)
Neuron

Wandell and Winawer (2011)
Vision Research

- Tile the entire occipital lobe
- Extend into IPS and VOT
- Response properties differ



Modeling human visual field map responses

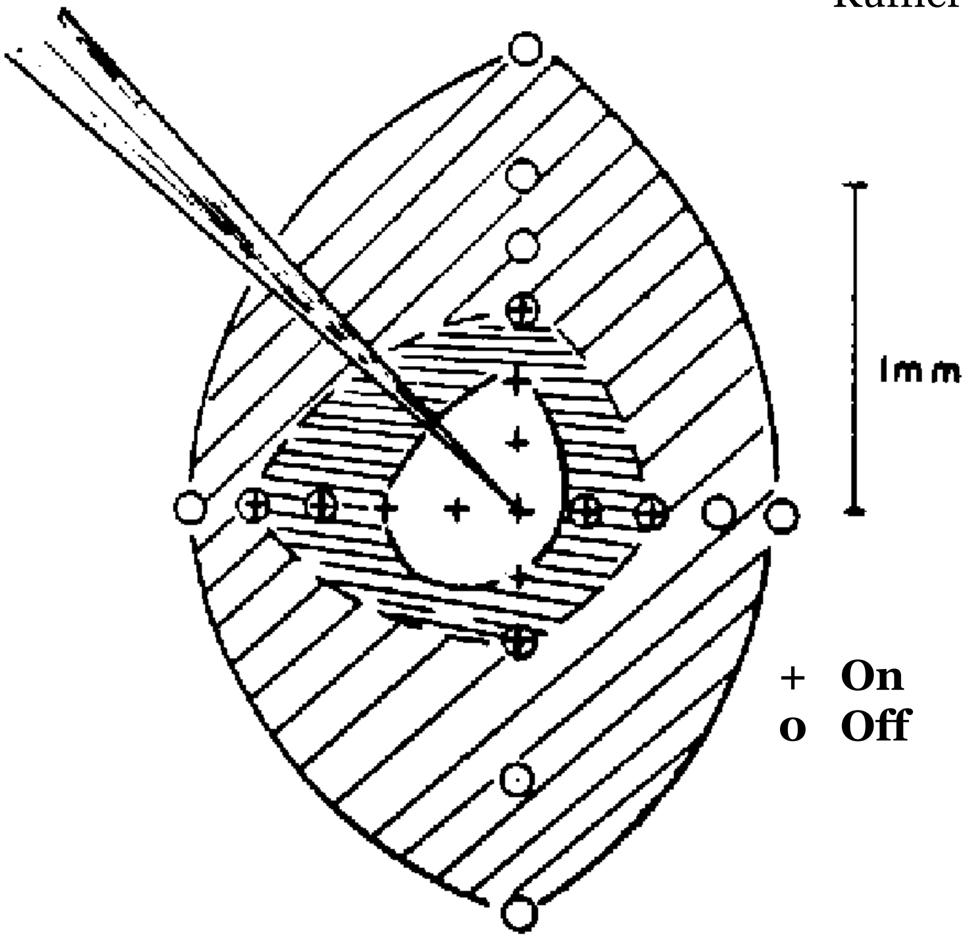
- Linear models of population receptive fields

The receptive field
A stimulus referred measurement

Kuffler

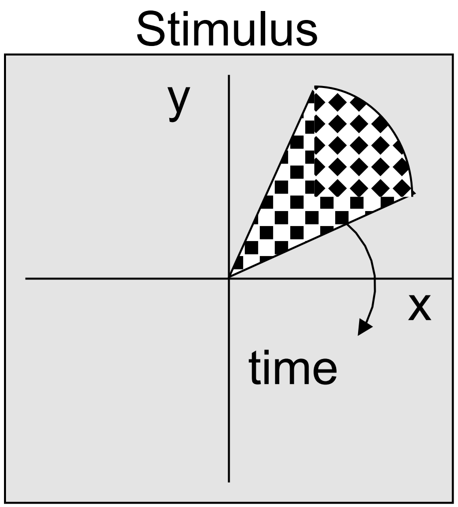
'Responses can be obtained in a given optic nerve fiber only upon illumination of a certain restricted region of the retina, termed the receptive field of the fiber (Hartline, 1936)'.

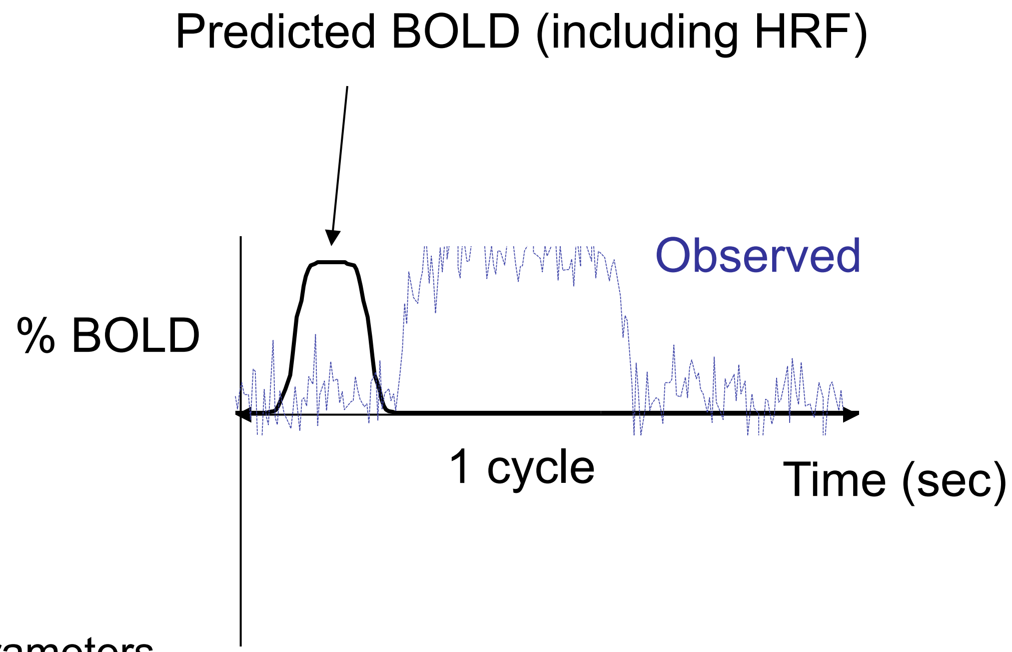
- Functional description
- Stimulus-referred

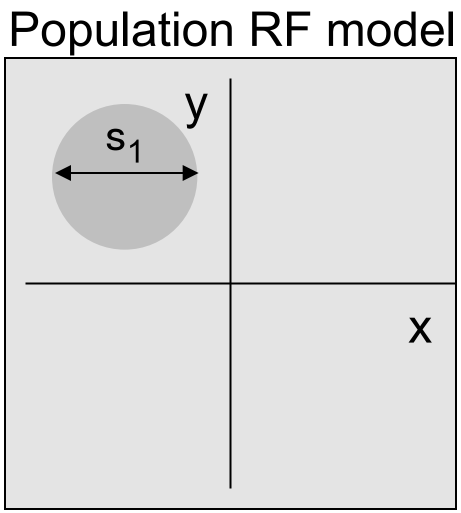


Kuffler, 1953

Population RF estimation
(Dumoulin and Wandell, 2008)





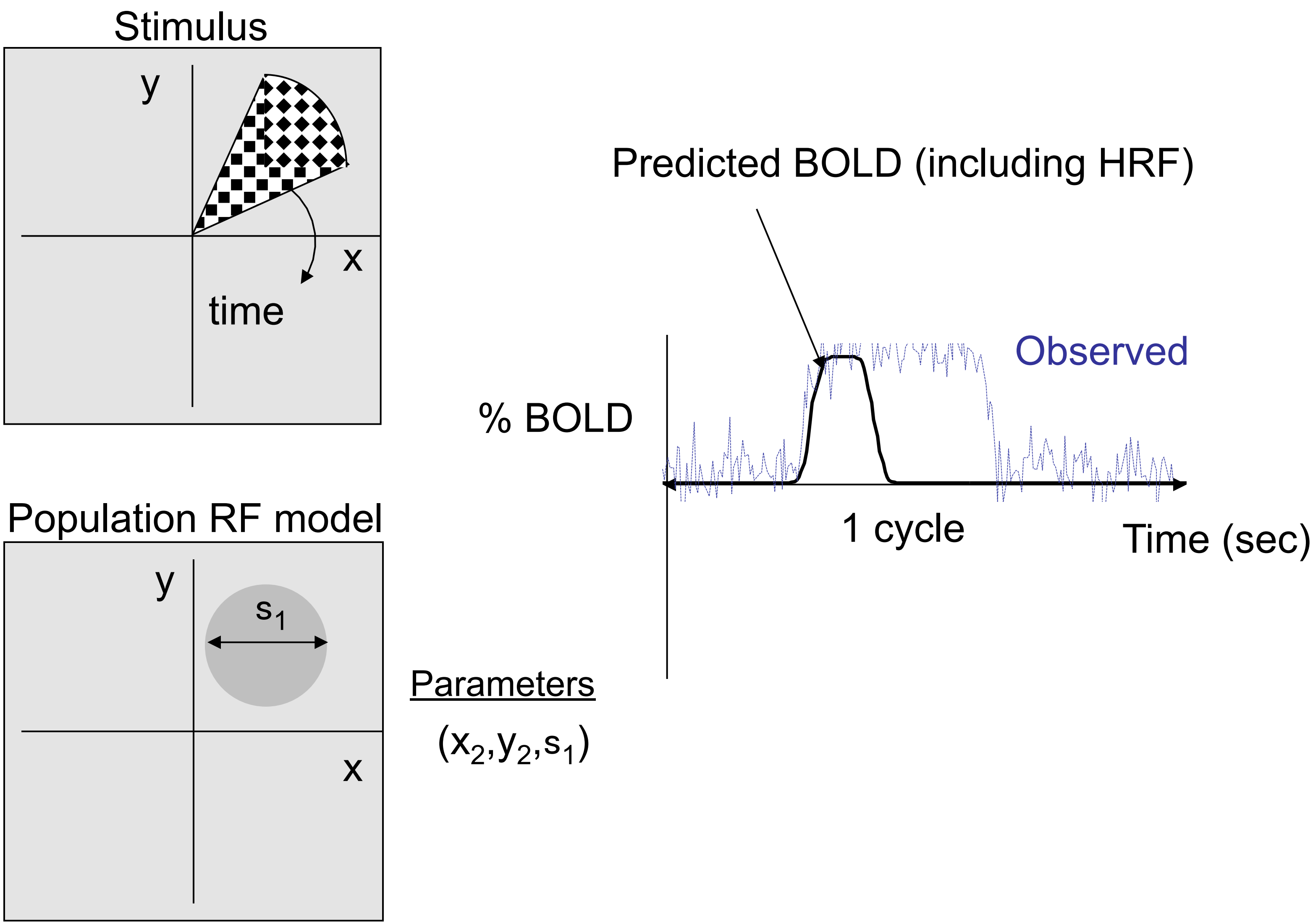


Parameters

(x_1, y_1, s_1)

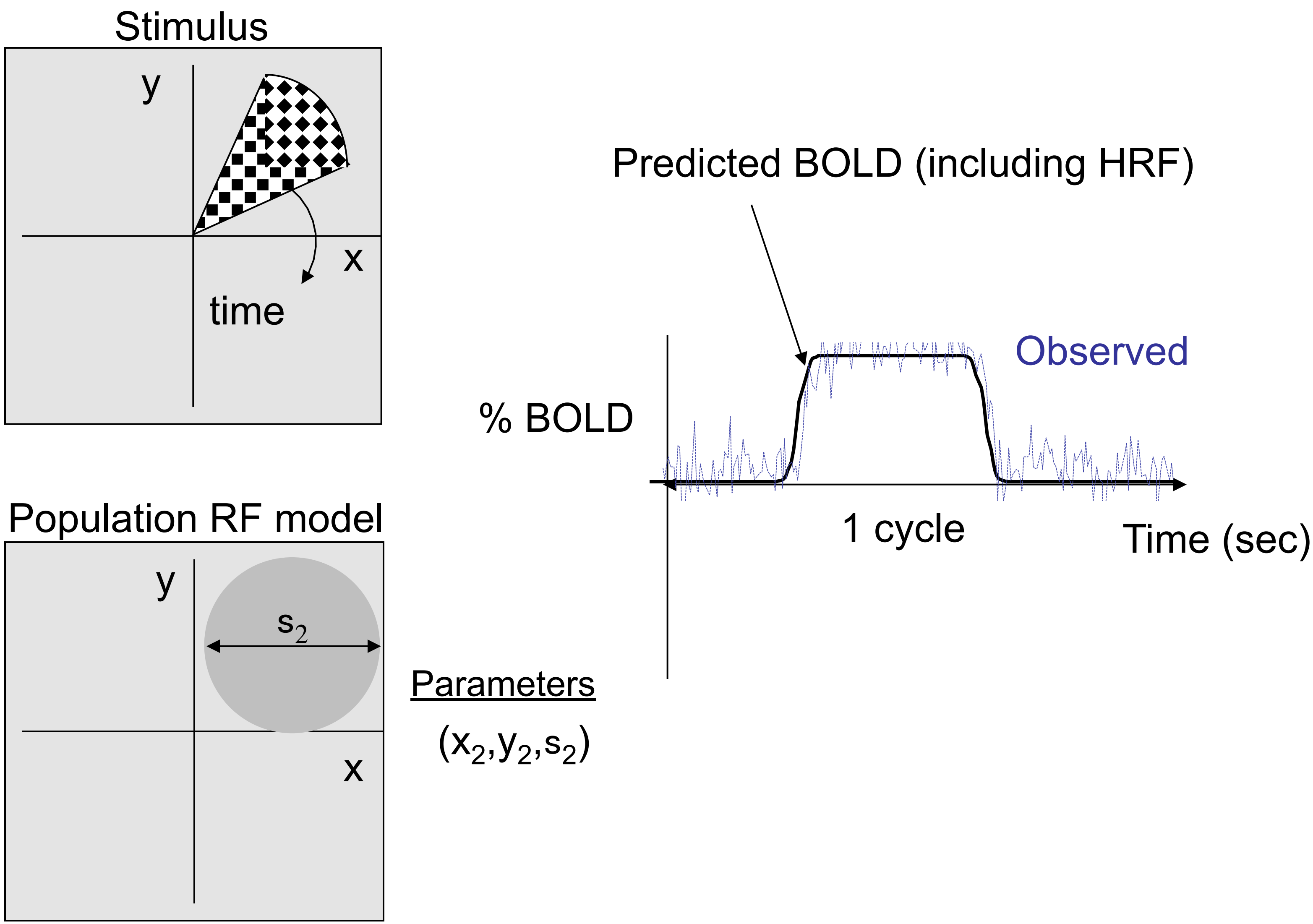
(Dumoulin and Wandell, 2008)

Population RF estimation



(Dumoulin and Wandell, 2008)

Population RF estimation

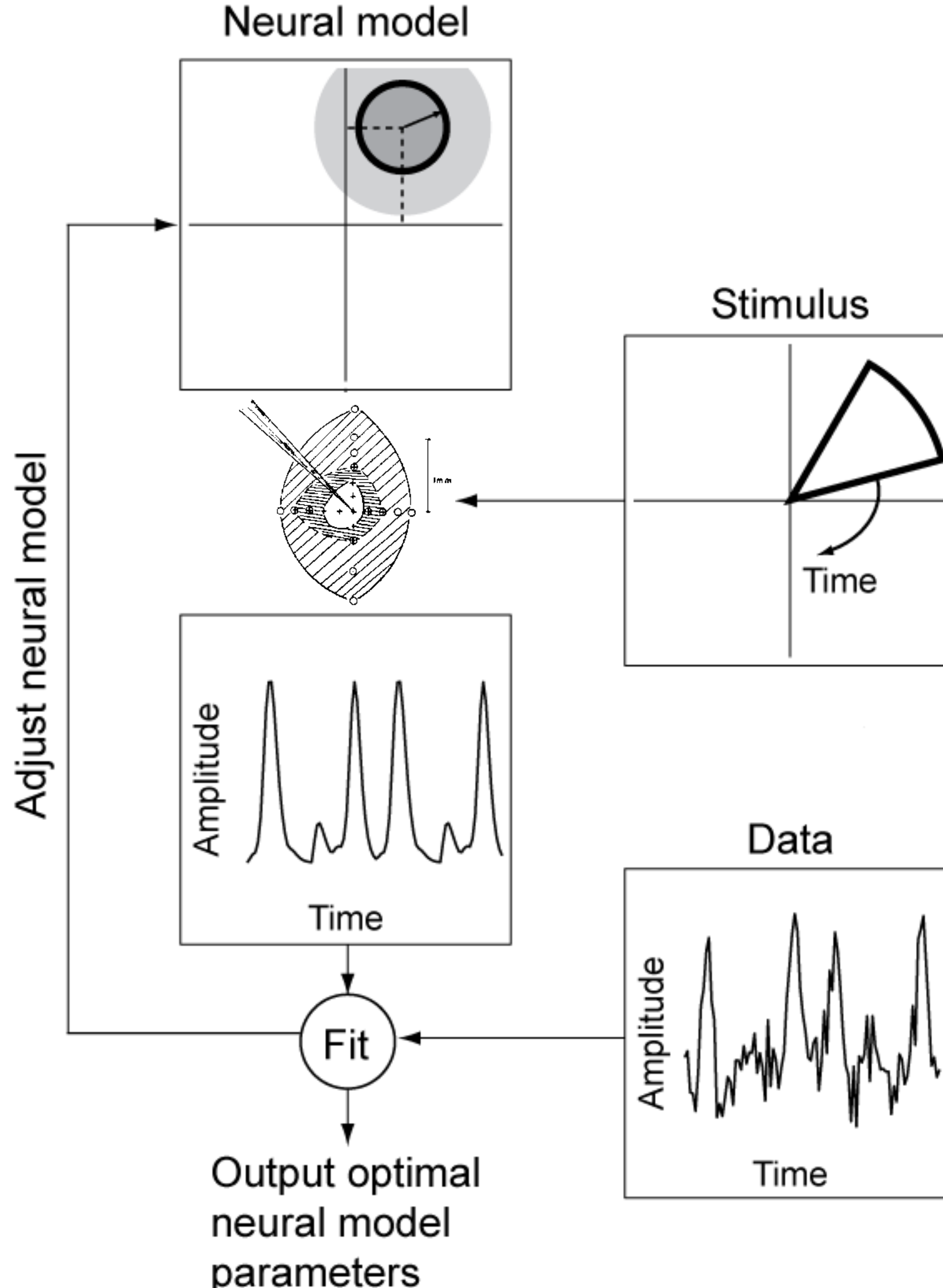


Population receptive field estimates in human visual cortex.
Dumoulin and Wandell,
NeuroImage, Vol 39, Issue 2, 15, 2008

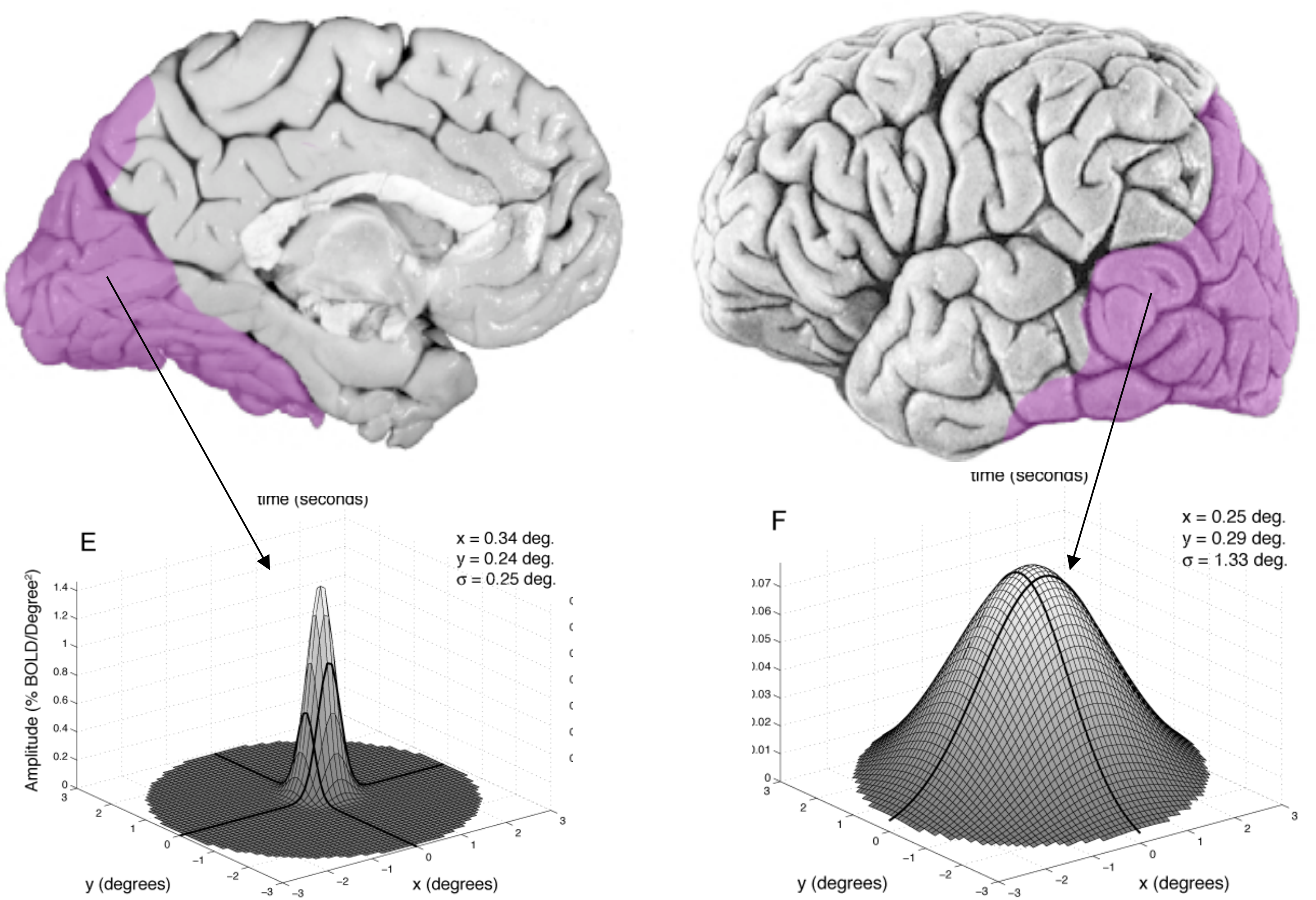
- Prediction: Weighted linear summation of over a portion of the visual field

- Spatial weights are Gaussian

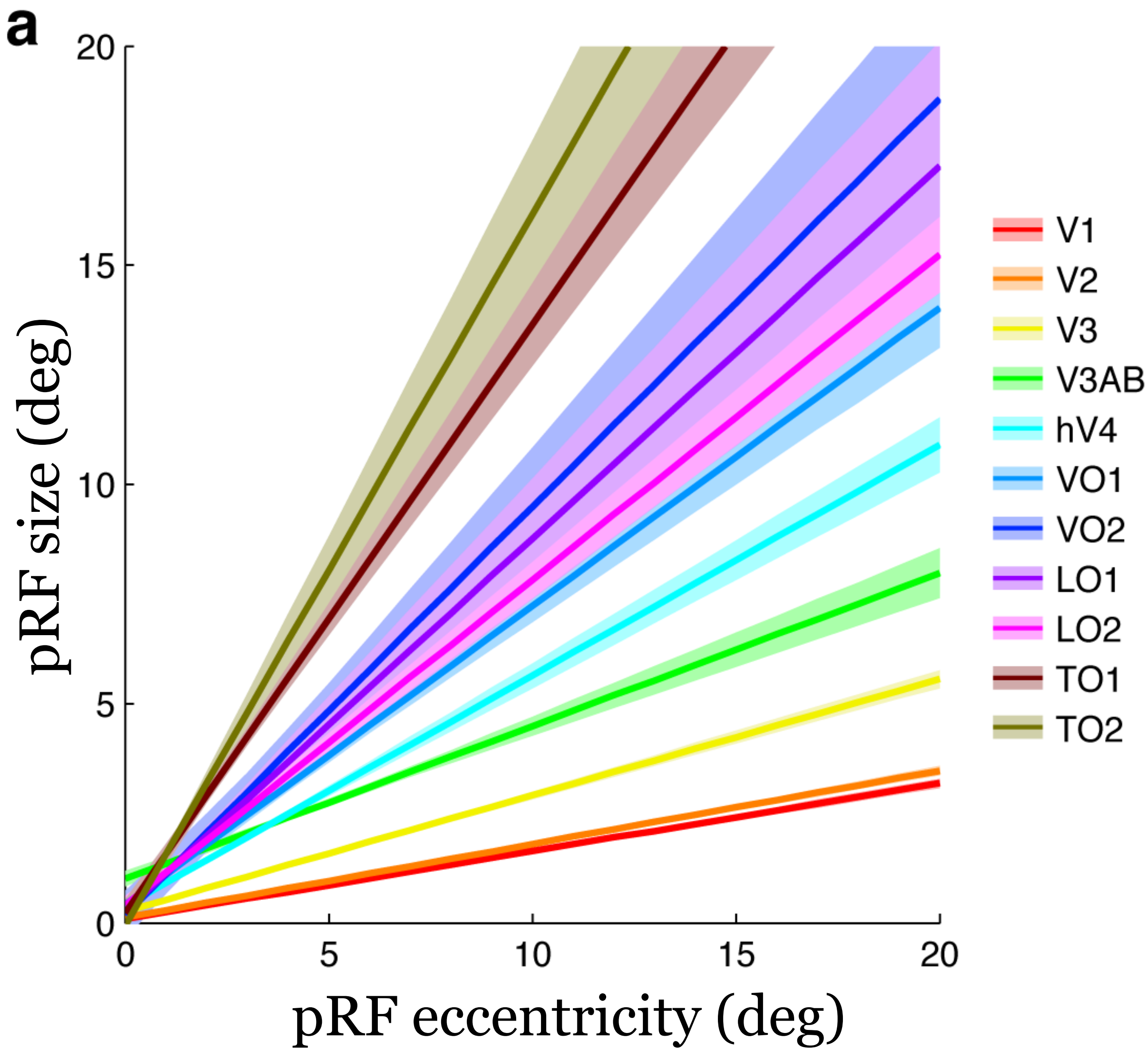
- Model estimates Gaussian center (x,y) and size ([illegible])



Population receptive field vary significantly across human visual cortex



Population RF size increases with eccentricity within each map

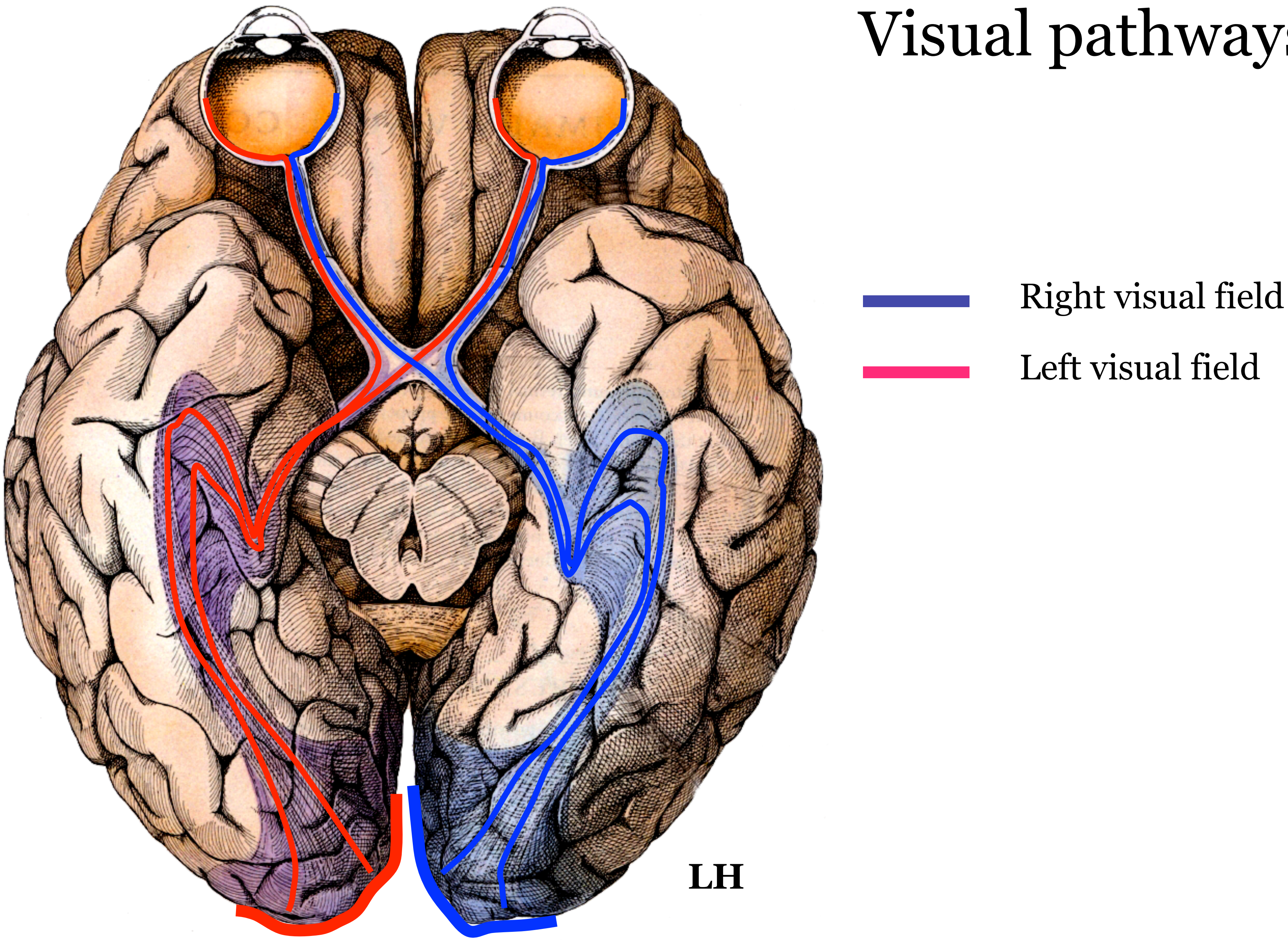


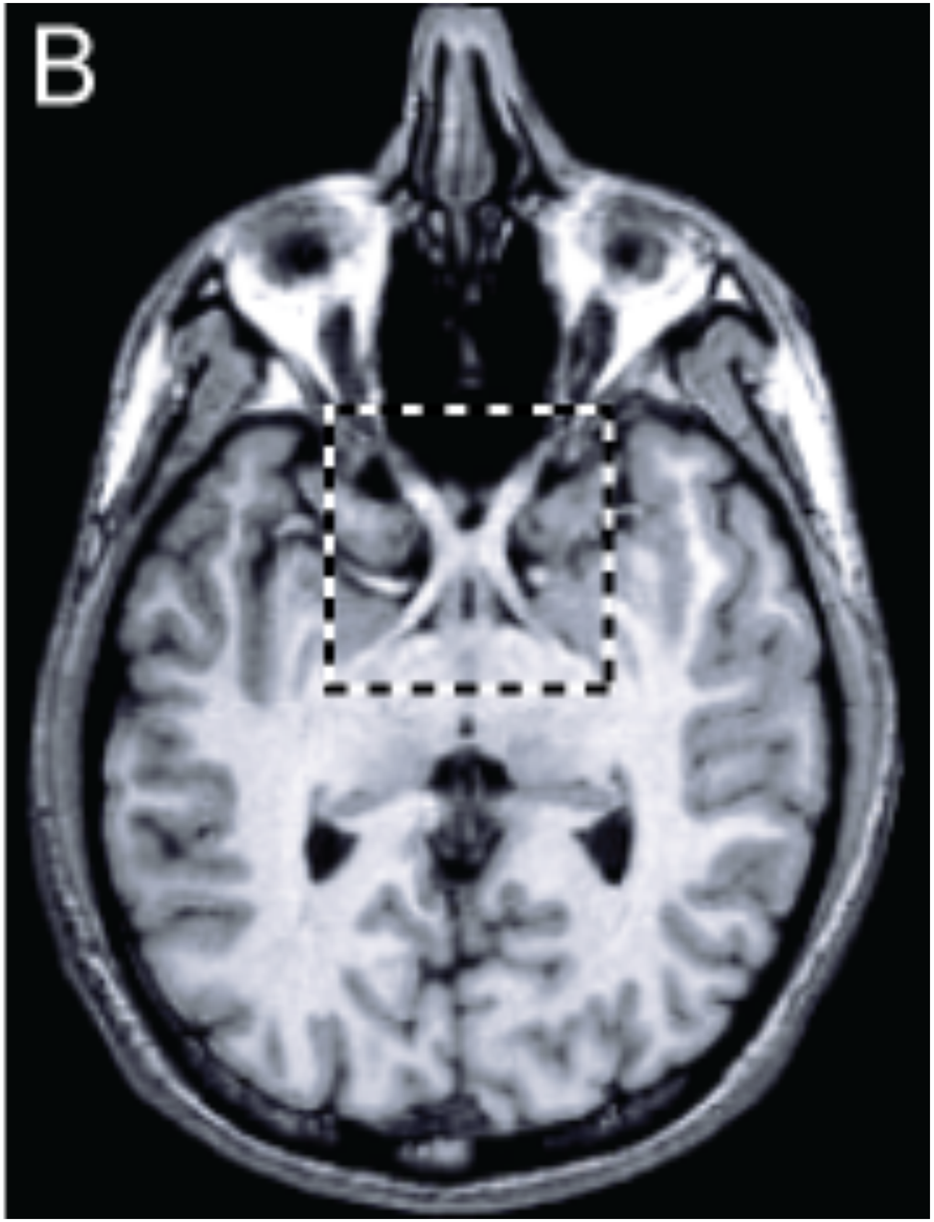
Neurological surprises

The case of the missing chiasm

Plasticity and stability of the visual system in human achiasma.

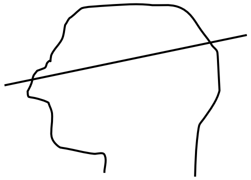
Visual pathways

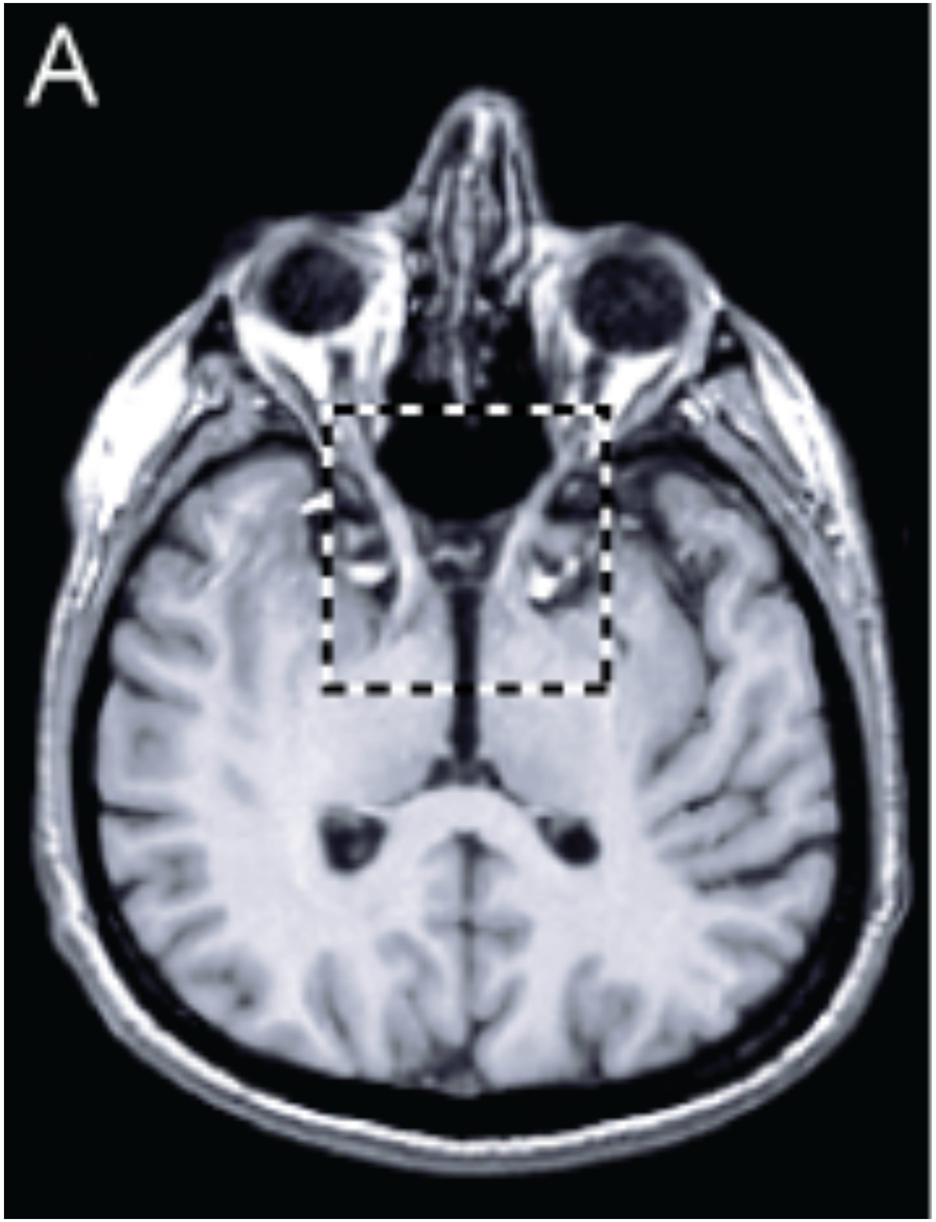




Conventional
optic chiasm

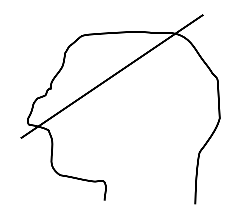
Control



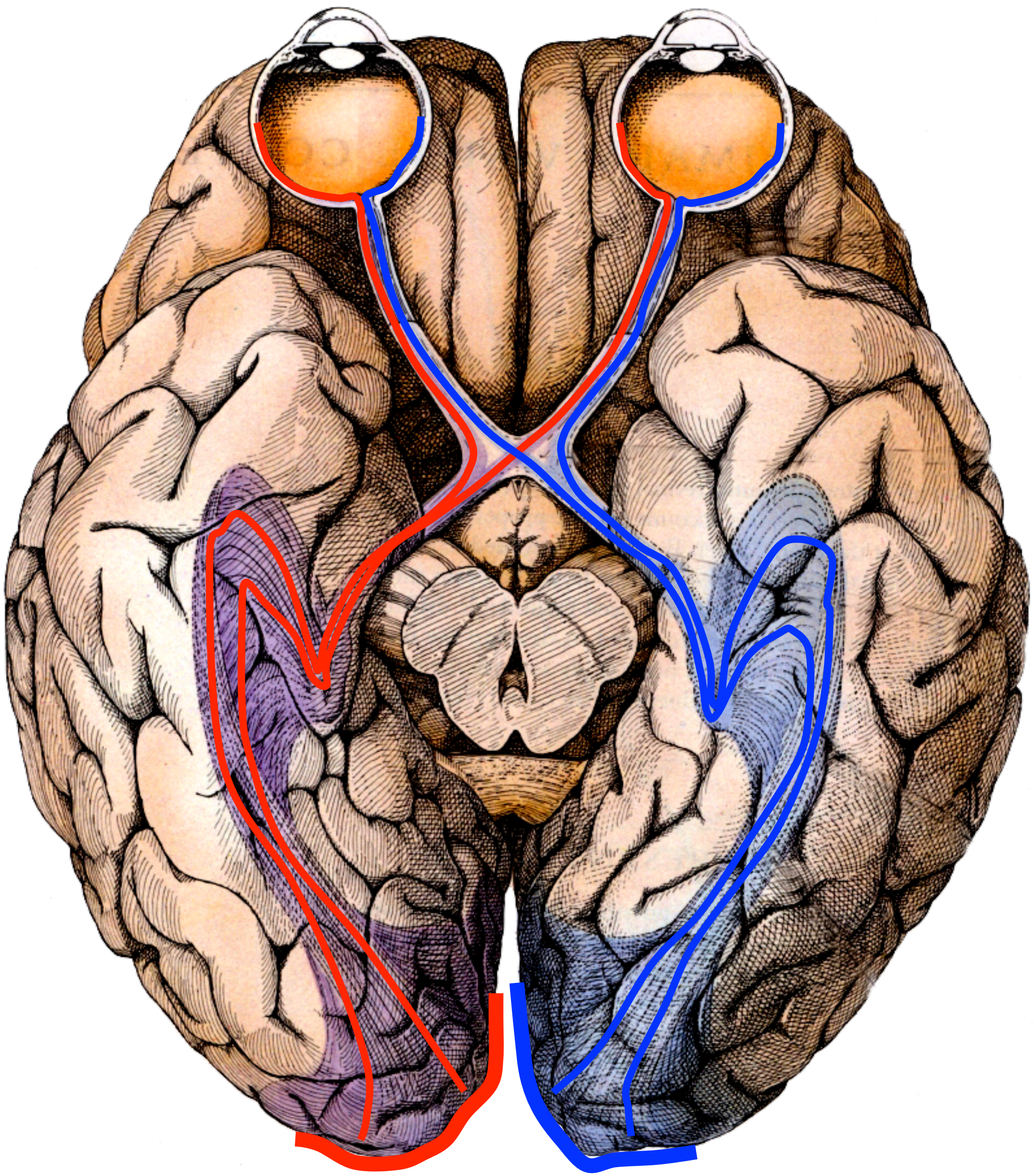


Missing optic chiasm

Achiasma



Normal

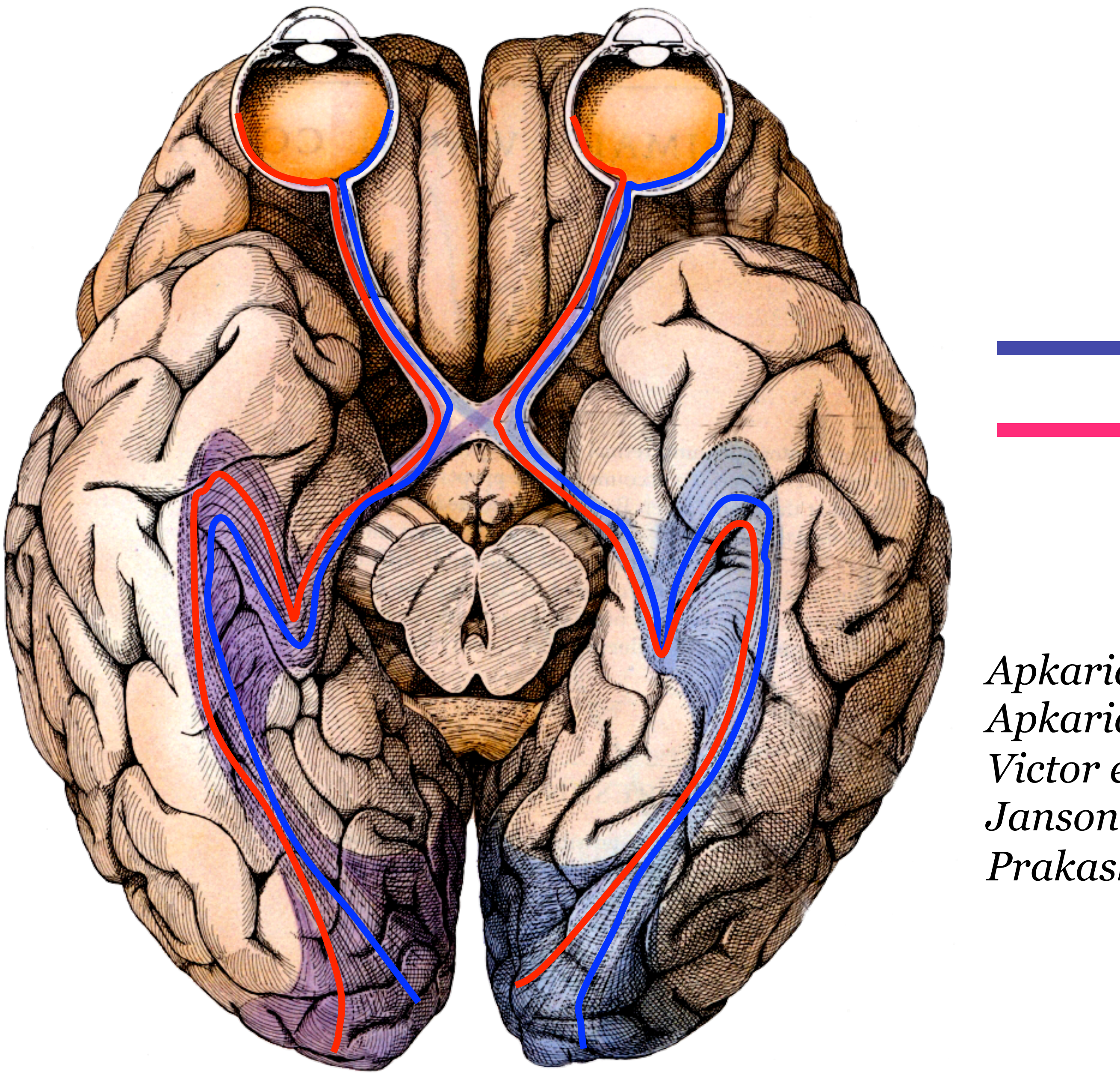


Right visual field

Left visual field

Molecular guidance at chiasm mediated by Ephrin-B2 and EphB1 (Williams et al., 2003, Neuron)

Achiasmic

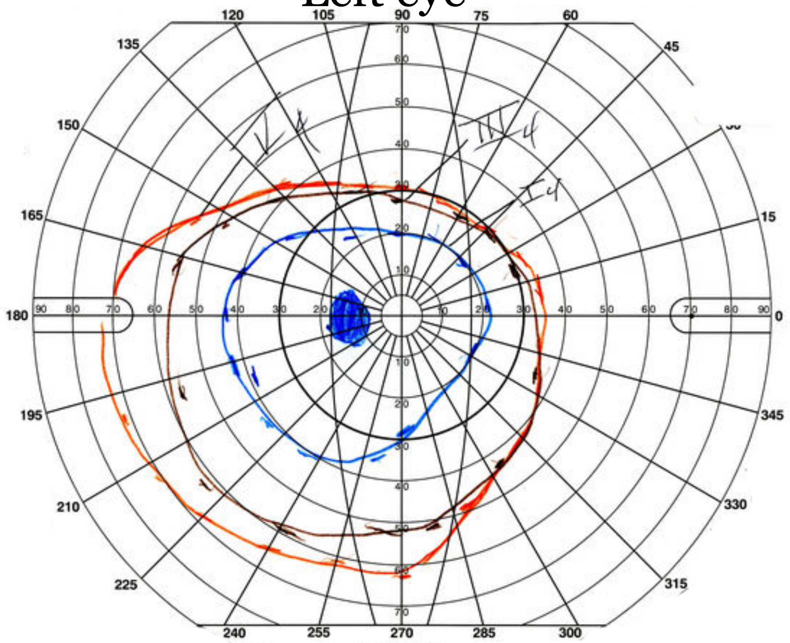


Apkarian et al., E.J.N. 1994
Apkarian et al., Brain, 1995
Victor et al., Cer. Cortex, 2000
Jansonius et al., JNO, 2001
Prakash et al., JNO, 2009

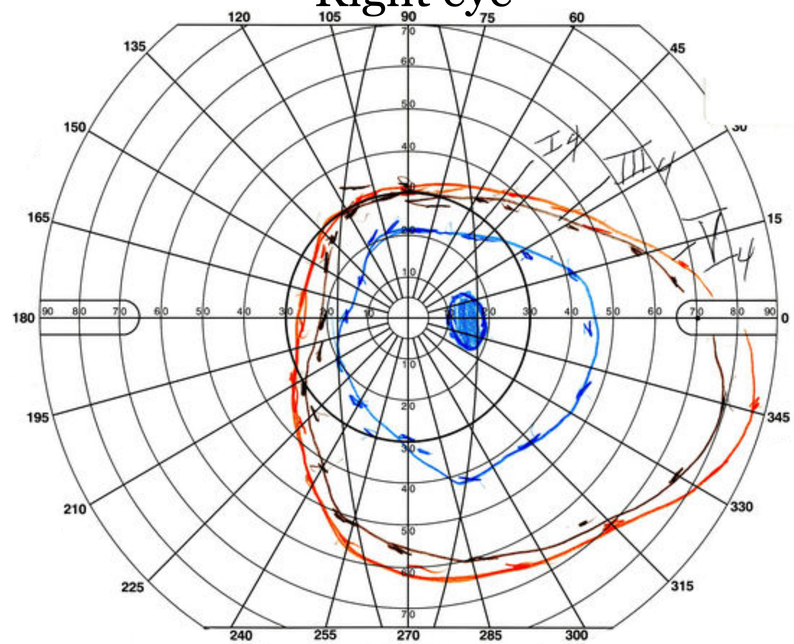
Subject AC2 characteristics

- Slight decrease in visual acuity
- Slightly reduced peripheral visual fields
- No stereopsis
- Prominent infantile and see-saw nystagmus (resolved)

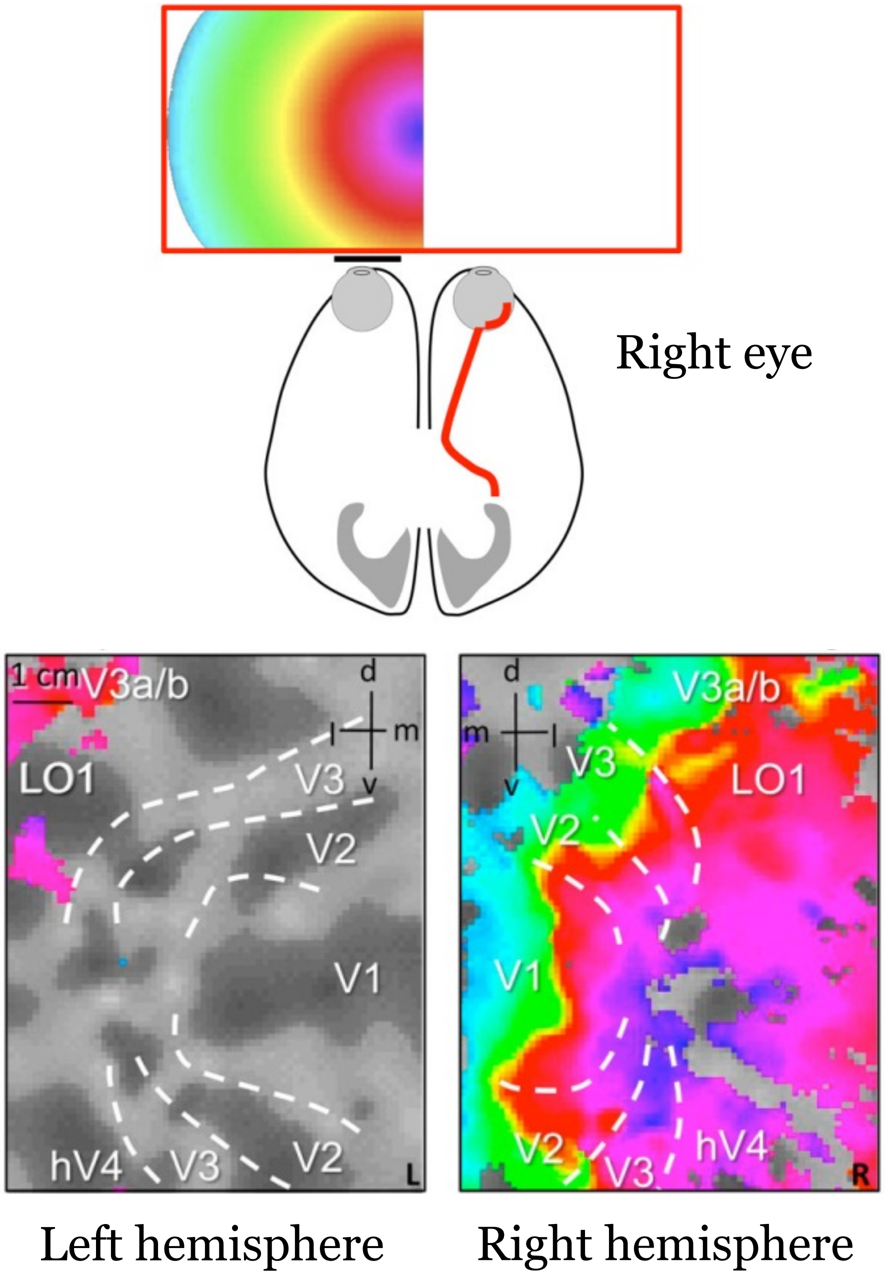
Left eye



Right eye



Right and left hemifield maps are overlaid in both hemispheres



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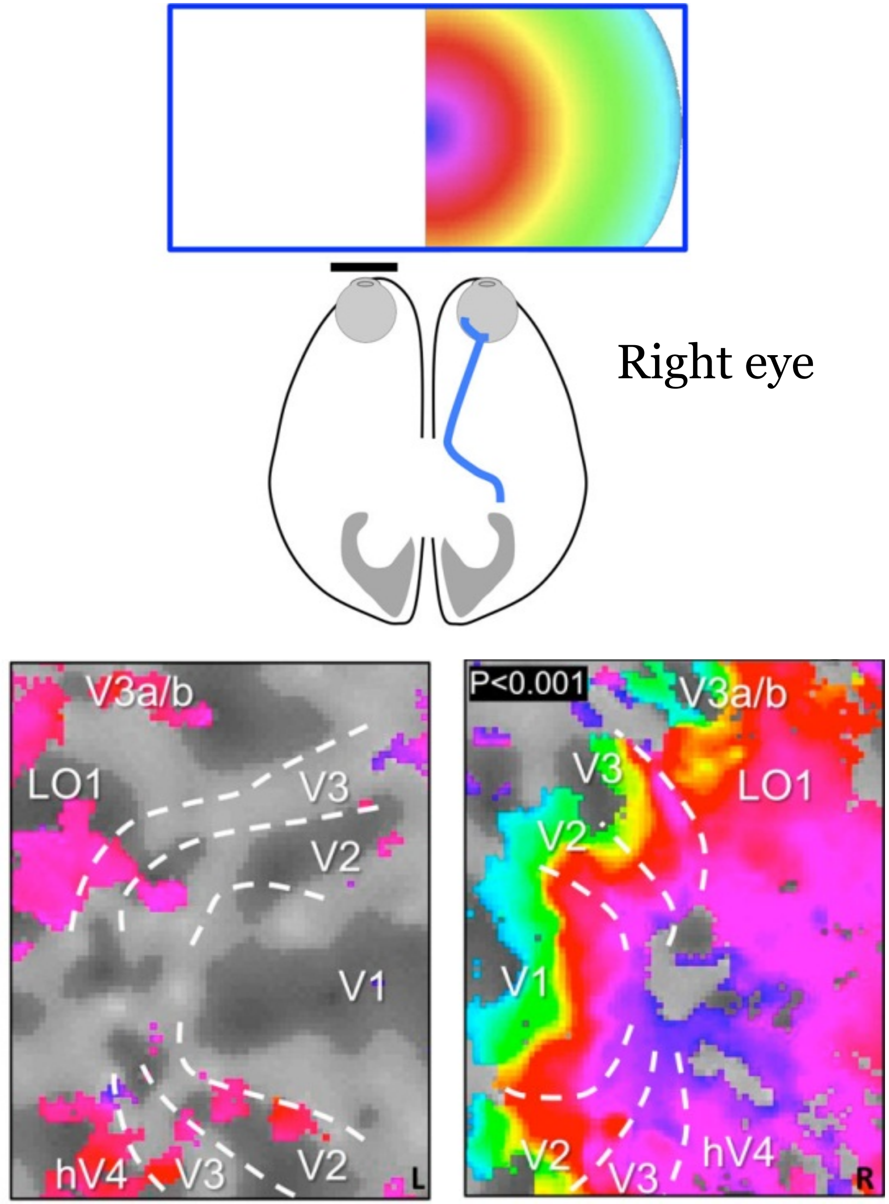
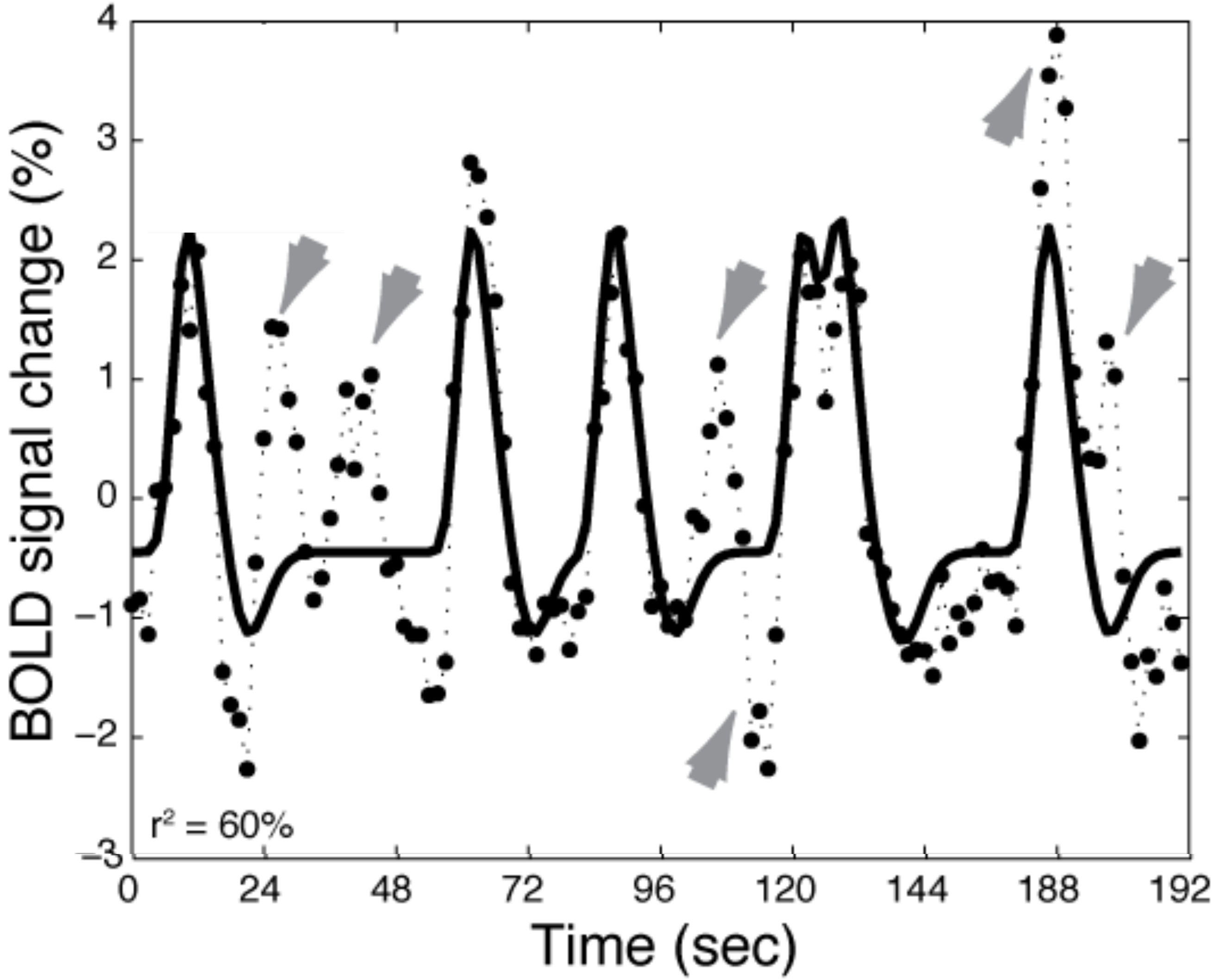
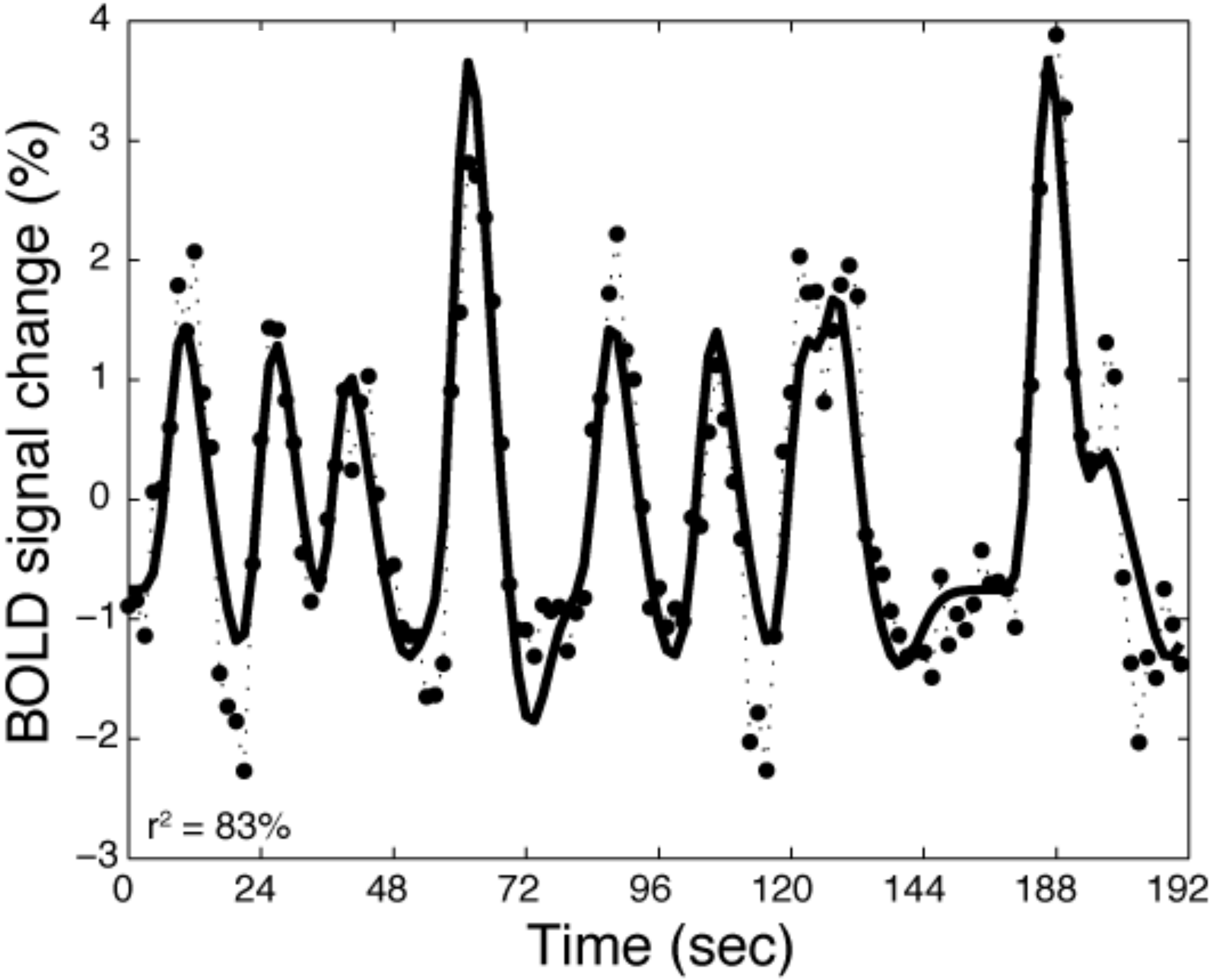


Left hemisphere Right hemisphere

Modeling the time course (1 Gaussian)

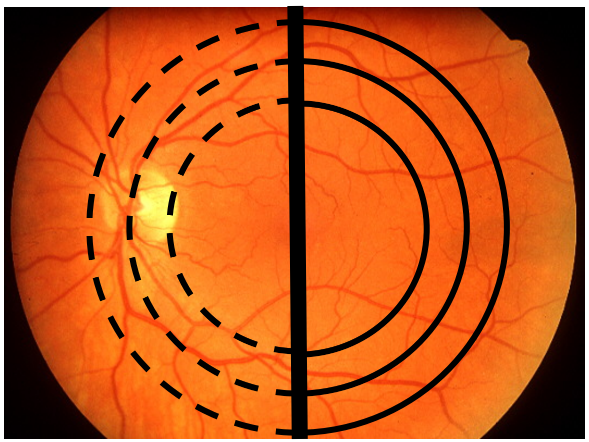


Modeling the time course (2 Gaussians)



Achiasmic - Folded representation

Right retina

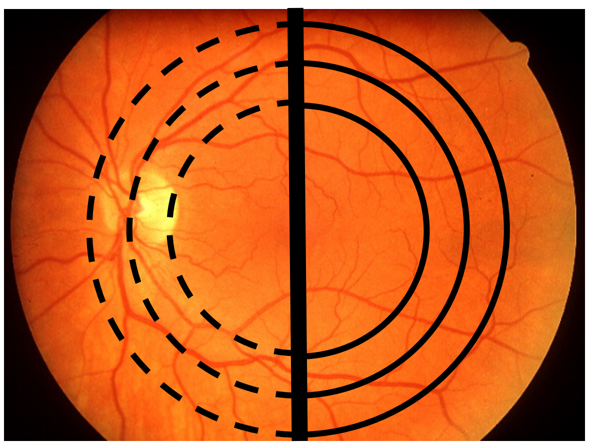


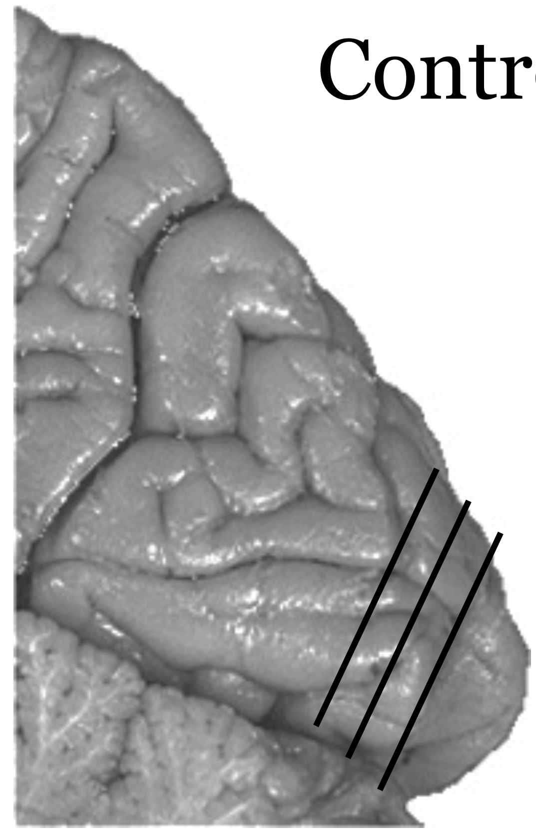
Control

V1

Achiasmic - Folded representation

Right retina

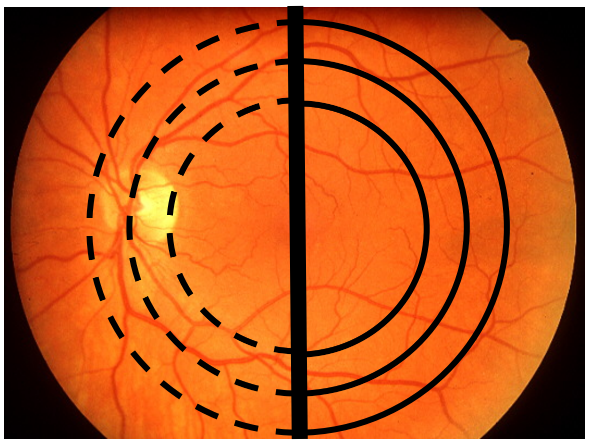


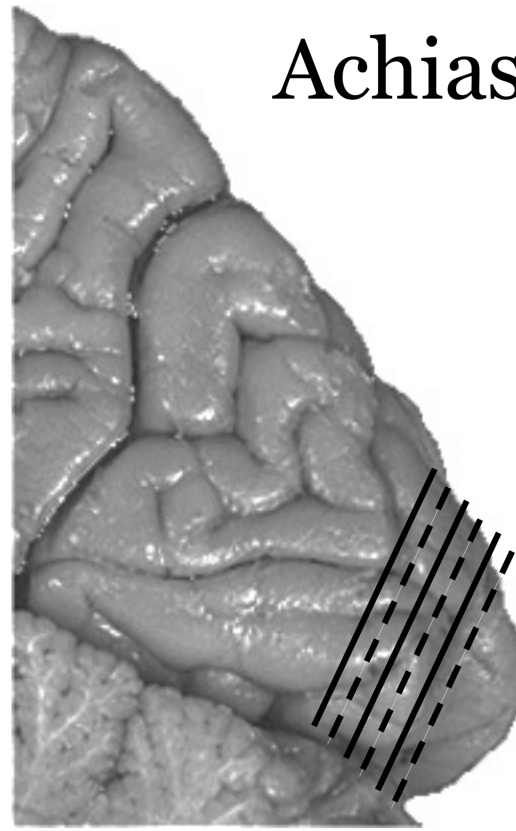


V1

Achiasmic - Folded representation

Right retina



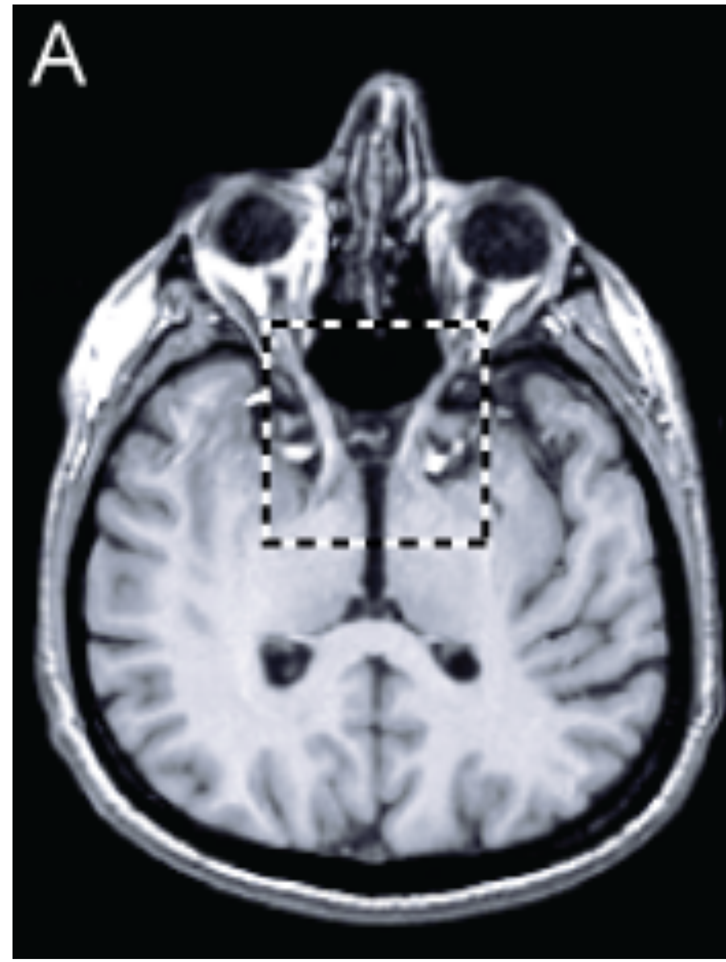


V1

(No evidence of an inserted map, re: Muckli et al.)

Summary – the system view

1. A genetic defect that disrupts crossing at the chiasm signaling causes a developmental reorganization in visual cortex.
2. **Despite the profoundly disrupted V1 maps, the rest of the brain figures out what to do.**



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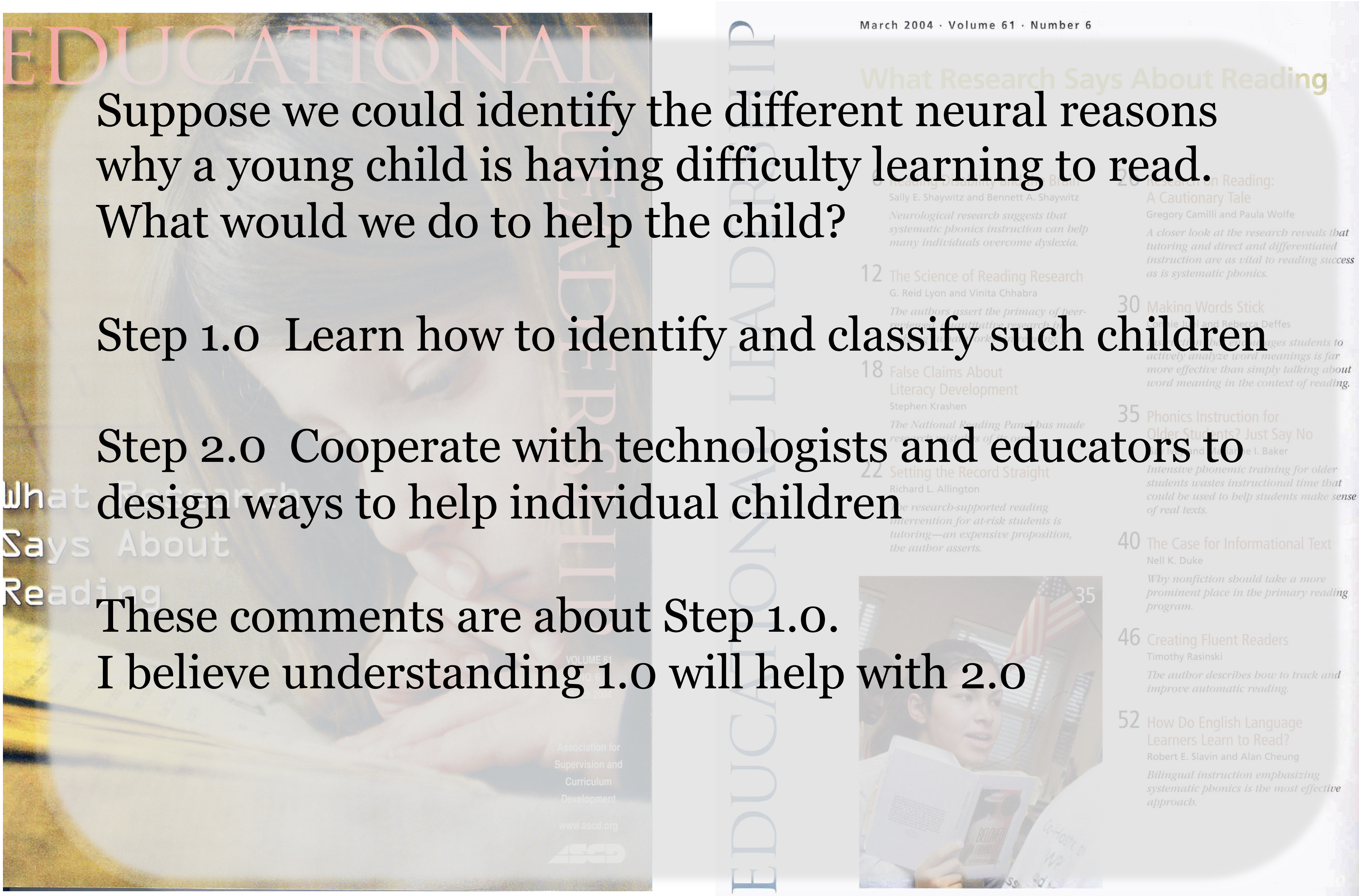
Seeing words

- Identify the reading circuitry in the developing child's brain
- Use this knowledge to predict reading outcomes and guide education



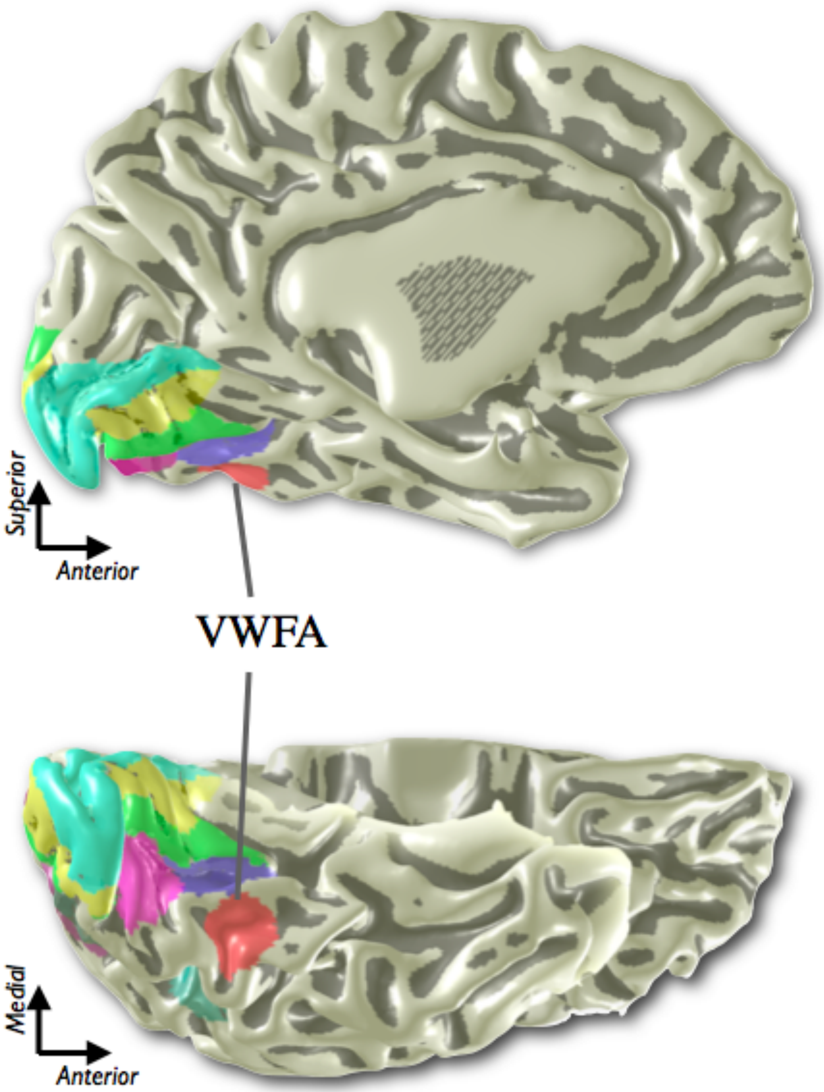
Suppose we could identify the different neural reasons why a young child is having difficulty learning to read. What would we do to help the child?

Step 1.0 Learn how to identify and classify such children

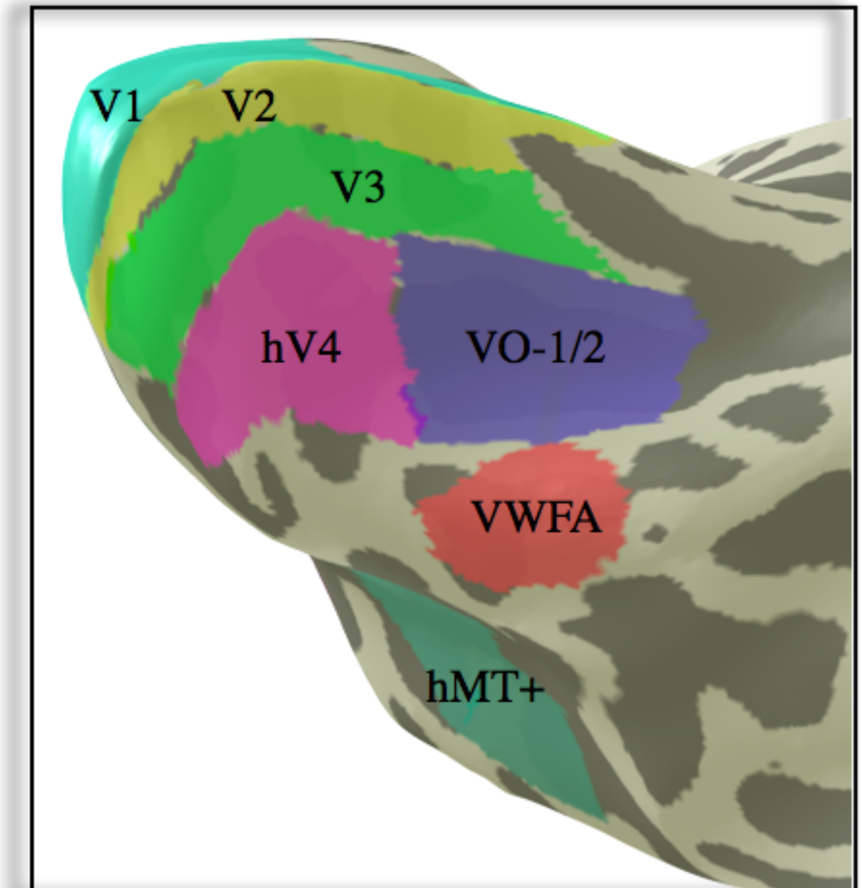
Step 2.0 Cooperate with technologists and educators to design ways to help individual children

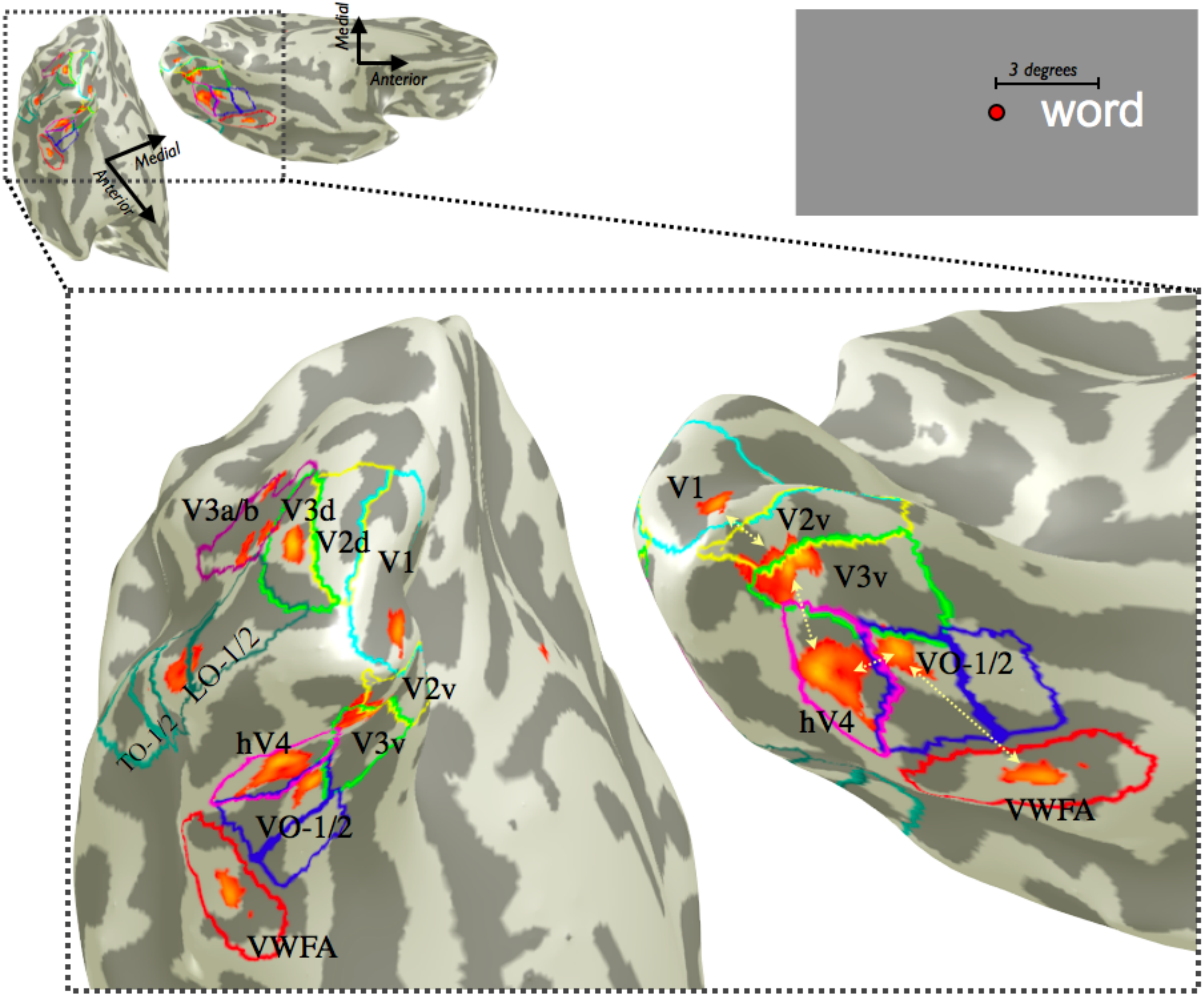
These comments are about Step 1.0.
I believe understanding 1.0 will help with 2.0

Locating reading circuits and maps



VWFA - essential for reading, but not unique to reading

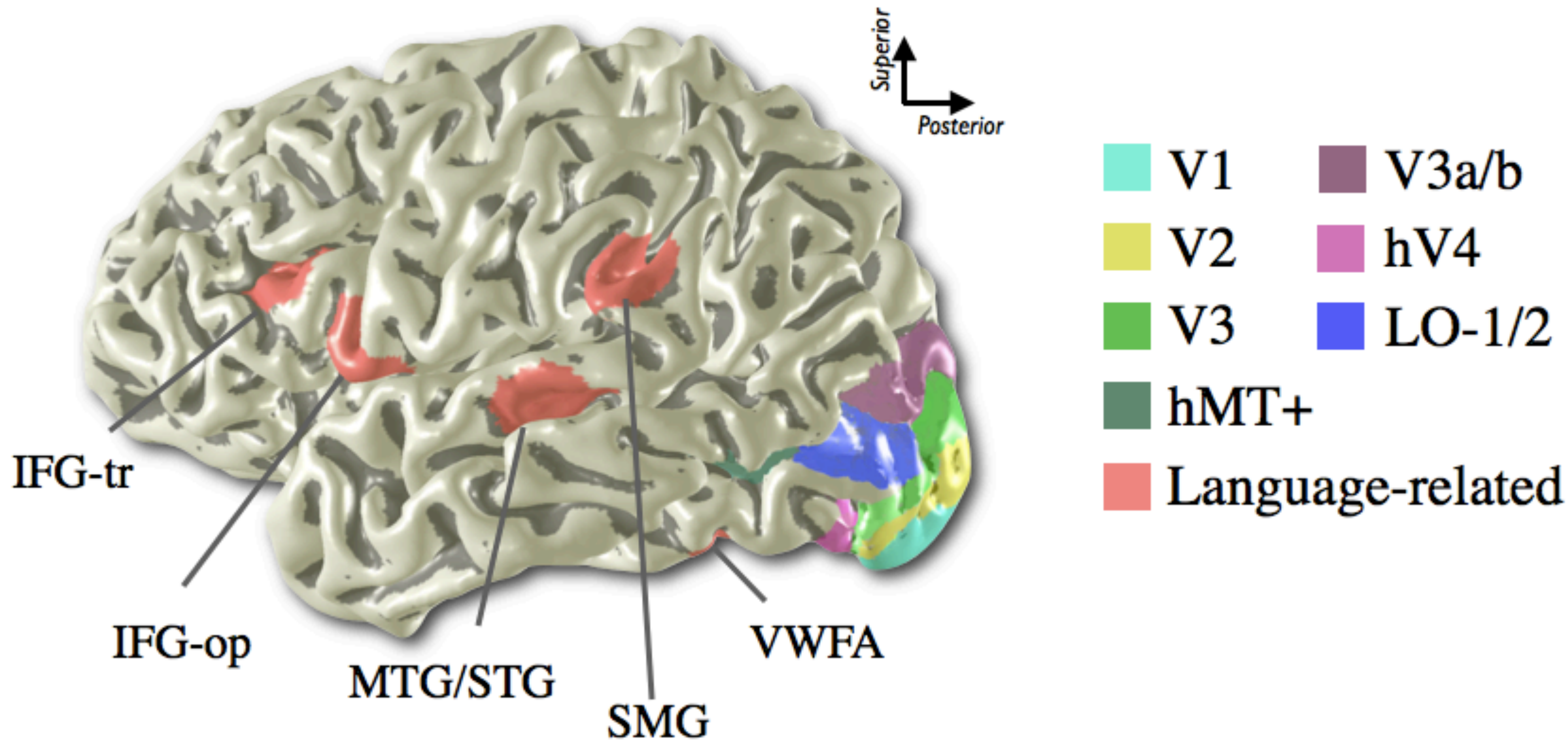




Medial
Anterior
Medial
Anterior
3 degrees
word
V3a/b
V3d
V2d
V1
LO-1/2
TO-1/2
V2v
hV4
V3v
VO-1/2
VWFA
V1
V2v
V3v
VO-1/2
hV4
VWFA

The cortical reading network

Learning to See Words
B.A. Wandell, A. Rauschecker and
J. Yeatman (2012).
Annual Review of Psychology Vol. 63, pp.31-53.

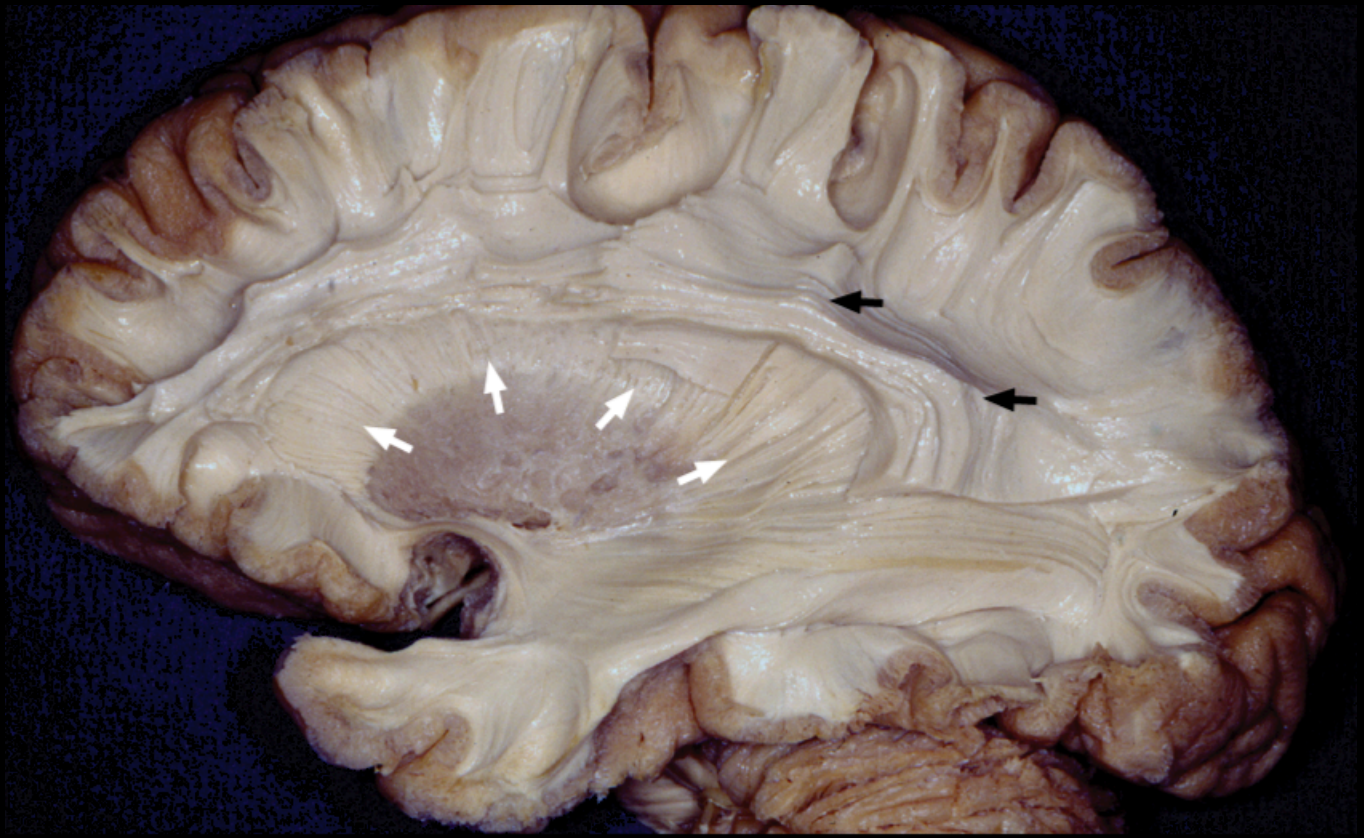


Diffusion weighted terminology

- Apparent diffusion coefficients
- Parallel and perpendicular diffusivity
- Diffusion images

Human fascicles (tracts)

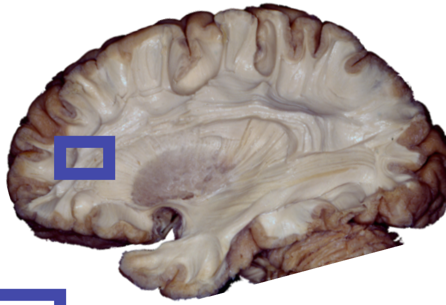
- There are many long-range connections
- These connections are not passive – they change their properties in response to use
- A system with active wires



Courtesy Professor Ugur Ture

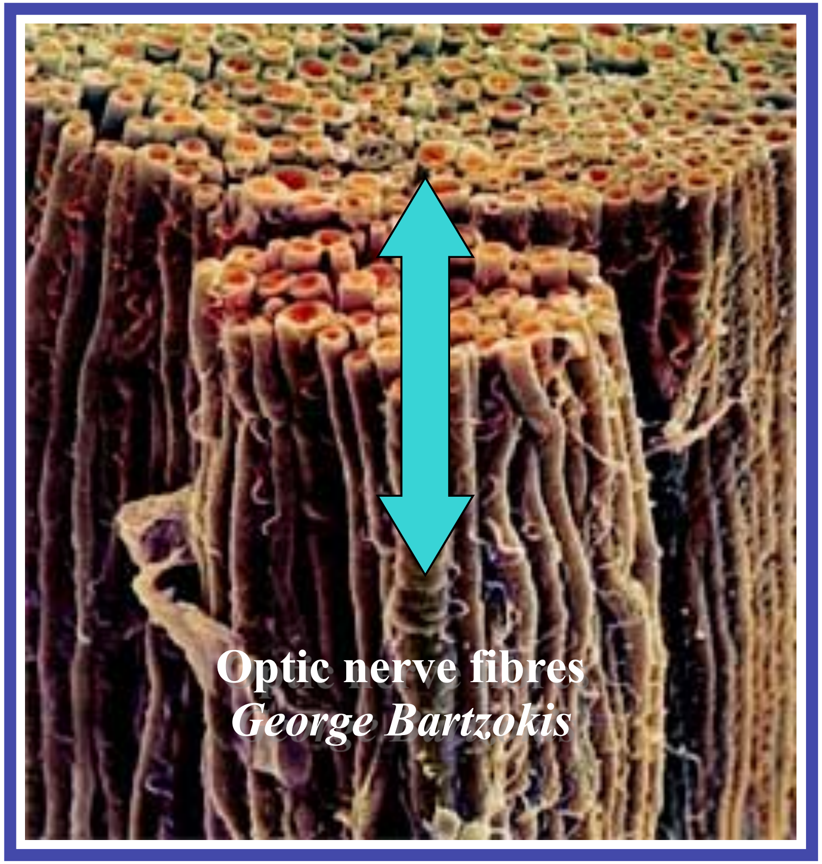
Diffusion probes brain microscopic structure

Parallel diffusivity (μm^2/ms)



Given a b-value and gradient direction, we measure **Apparent Diffusion Coefficient (ADC)**

Along the principal direction of axons, within the cytoskeleton, water displacement is large and signal is low



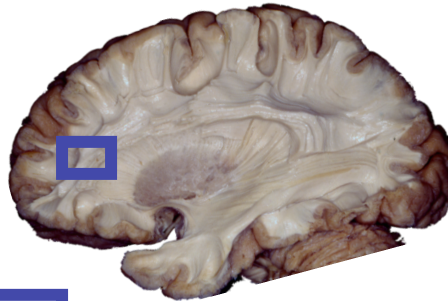
5 um

Equivalent names

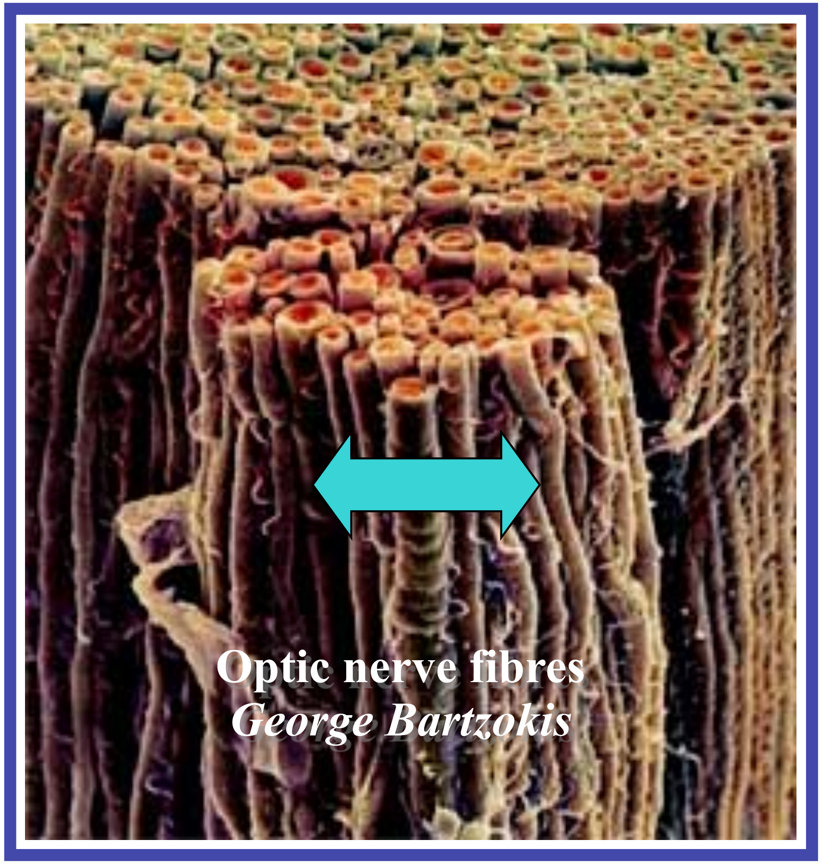
- Parallel, axial, longitudinal, principal diffusion direction (PDD)

Diffusion probes brain microscopic structure

Perpendicular diffusivity ($\mu m^2/ms$)



Perpendicular to the principal direction of axons, bi-lipid membranes limit water displacement so the signal is higher

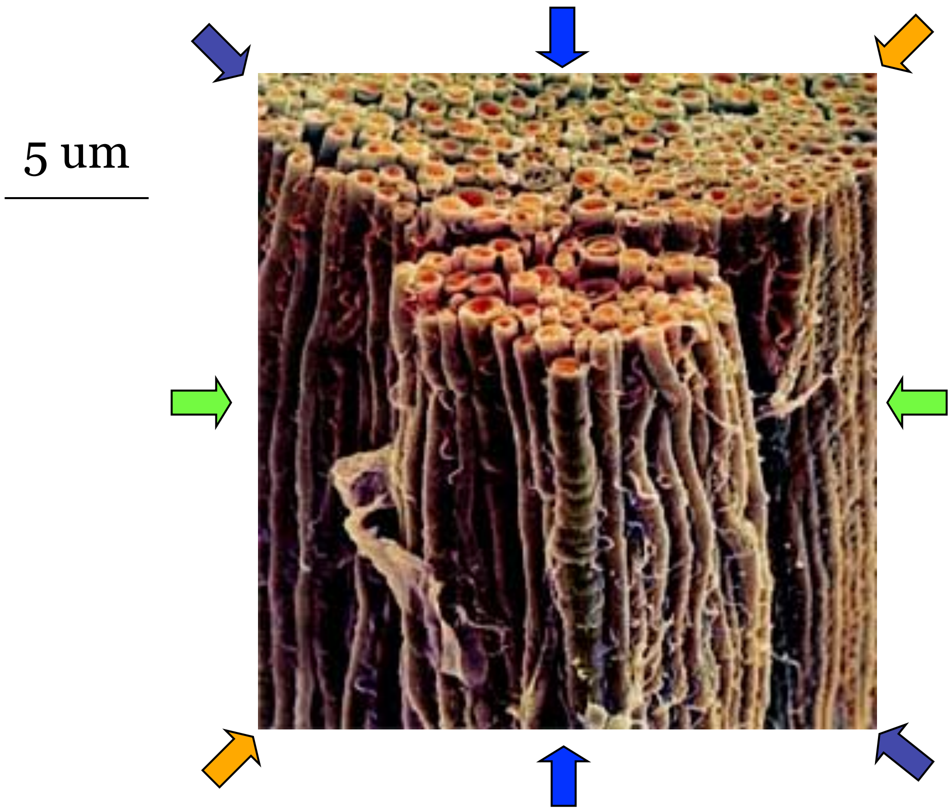


5 um

Other names

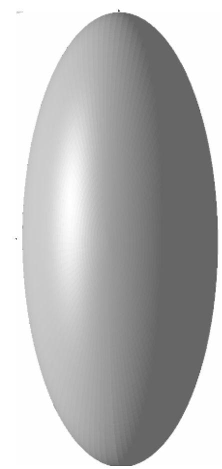
- Perpendicular, radial, transverse

Diffusion Tensor Imaging (DTI)
A summary of the ADC at low b-values



$$1 = v' Q^{-1} v,$$

v is a 3d-vector

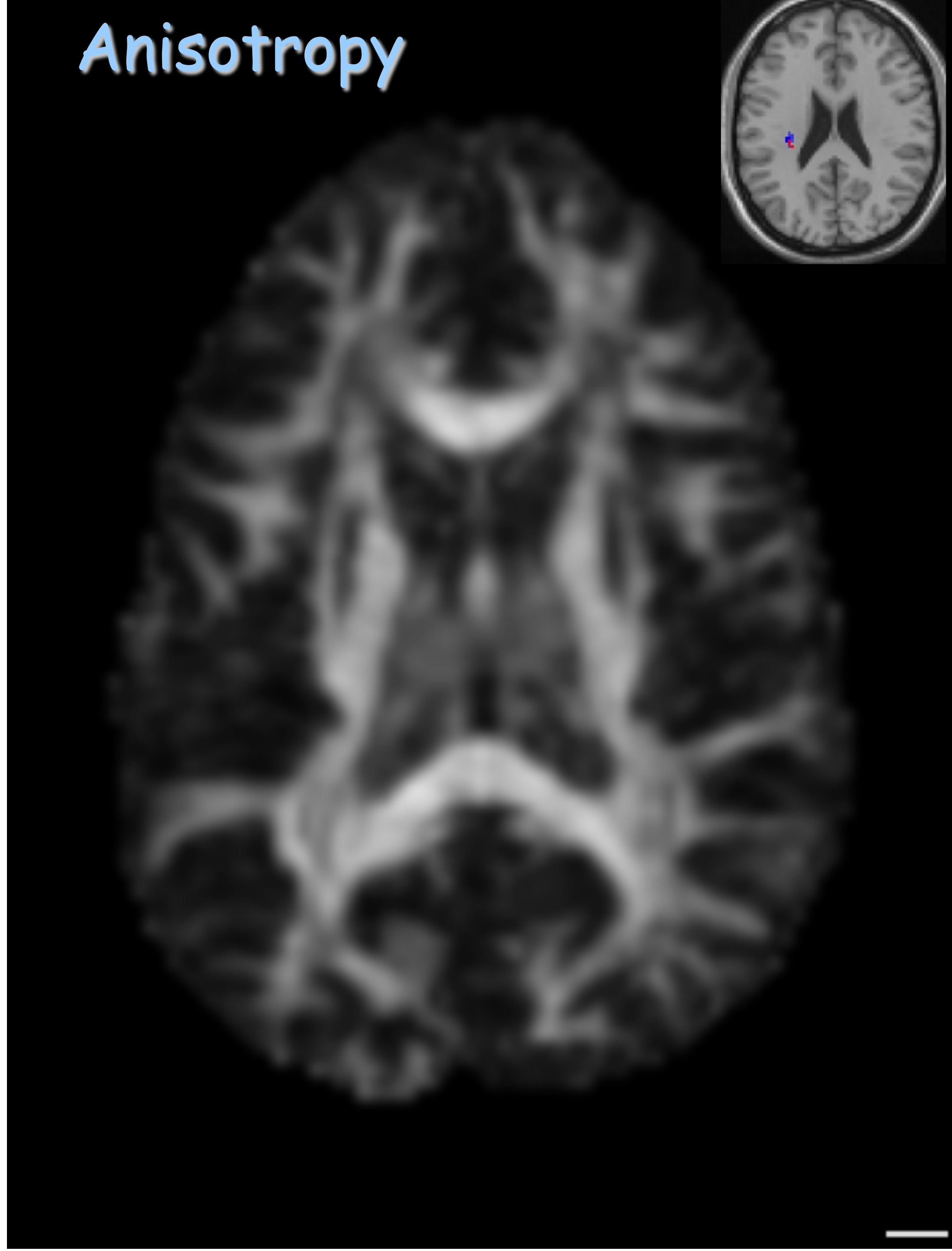


The **mean** distance a typical water molecule will diffuse in a unit of time

$$A = u' Q u$$

DTI summary measures of white matter microstructure

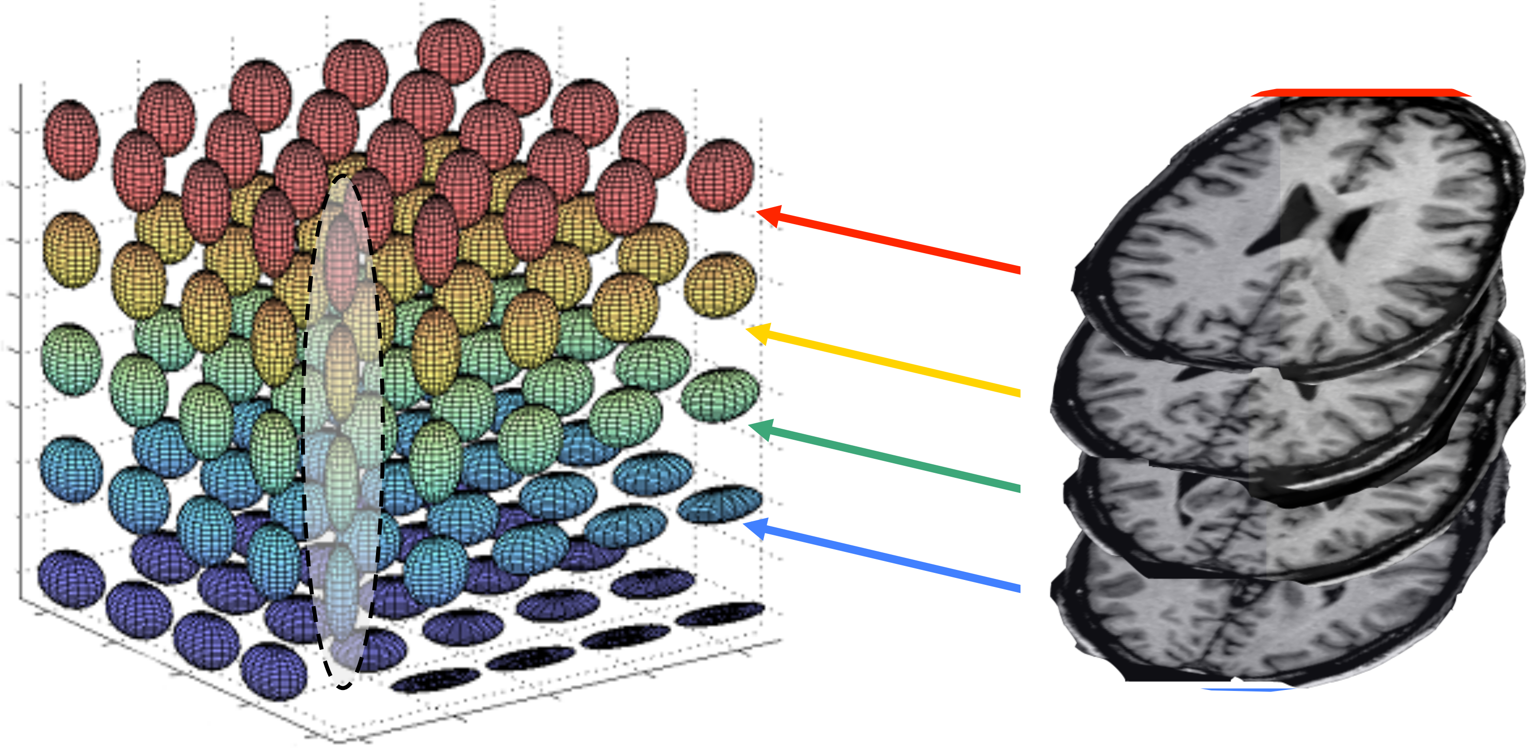
Fractional anisotropy



Tractography

Use the local (voxel) diffusion measurements to estimate white matter tracts

Diffusion data are surfaces



Diffusion and Tractography References

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Jason D. Yeatman, Robert F. Dougherty, Nathaniel J. Myall, Brian A. Wandell, Heidi M. Feldman (2012). **PLoS ONE** 7(11): e49790.

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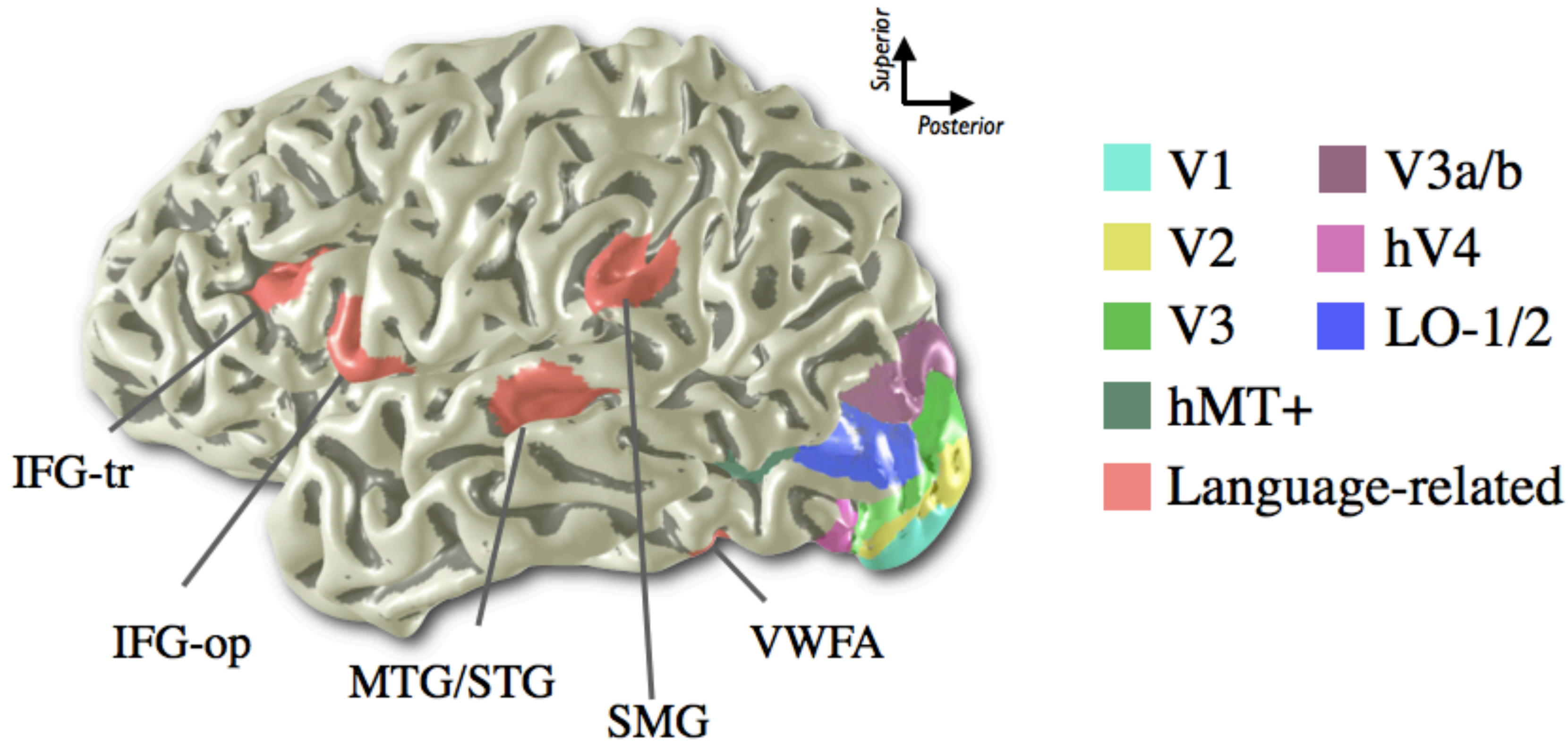
B. A. Wandell, A. Sherbondy and R.F. Dougherty (2006). **Neural Information Processing Society** (NIPS)

Predicting how well a child will read from white matter measurements

- Cortical reading circuitry
- Predicting reading skill from long-range (white matter) properties

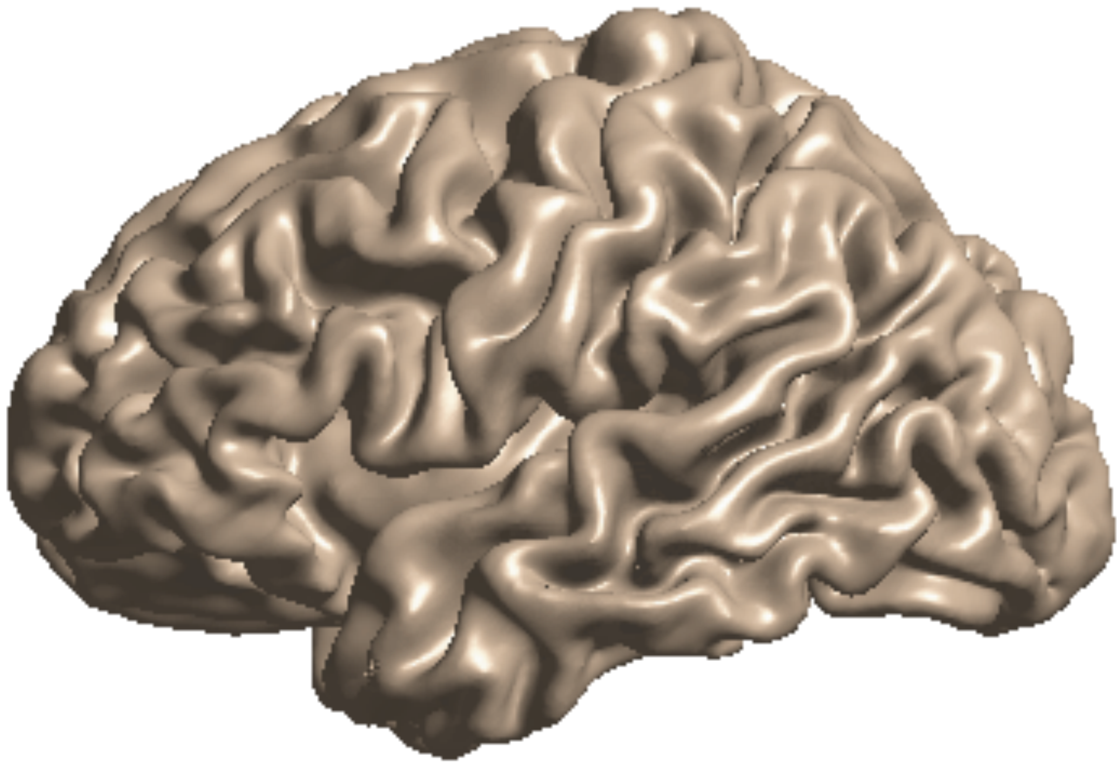
The cortical reading network

Learning to See Words
B.A. Wandell, A. Rauschecker and
J. Yeatman (2012).
Annual Review of
Psychology Vol. 63, pp.31-53.



Seeing the white matter reading tracts

(Yeatman et al., 2011)

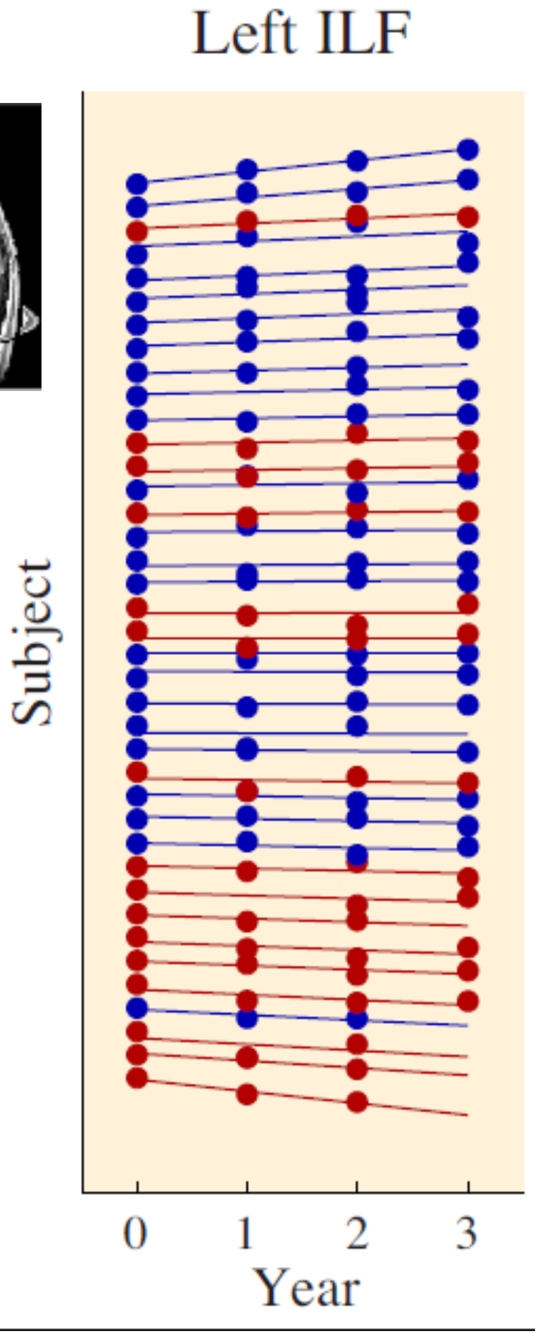


Longitudinal measures of diffusion and reading

(Yeatman et al., 2012)

- Measured brain and behavior at 4 time points
- Found that first measurements predict reading development

Blue: Good readers
Red: Poor readers



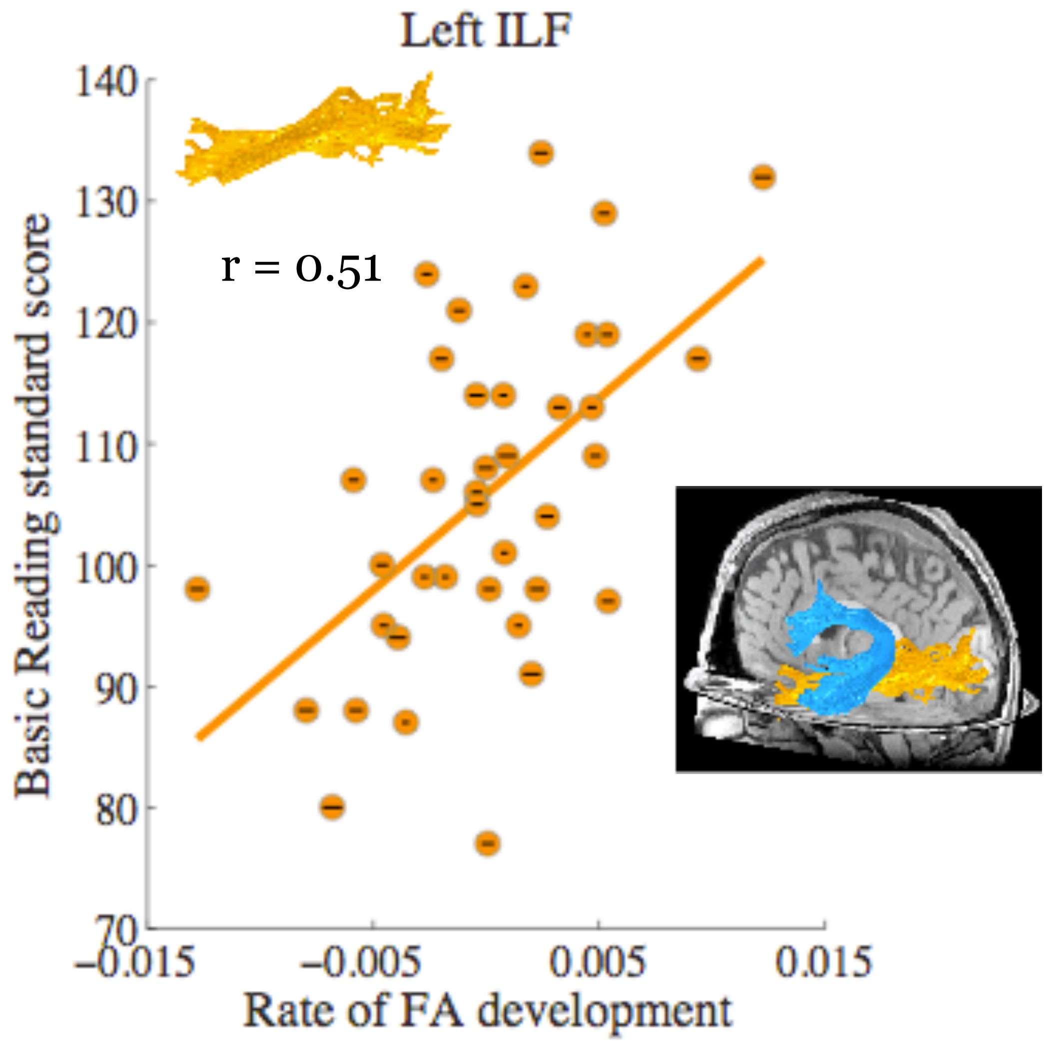
More extended

(FA)

More circular

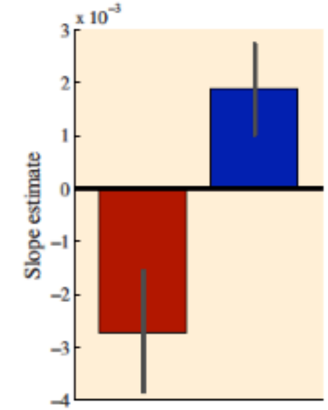
Strong associations between tract diffusion change and seeing words
(Yeatman et al., 2012)

- Diffusion development rate within certain tracts, but not others, correlates with the ability to see words
- This is one reason we think that the wires are active, changing in response to learning and memory

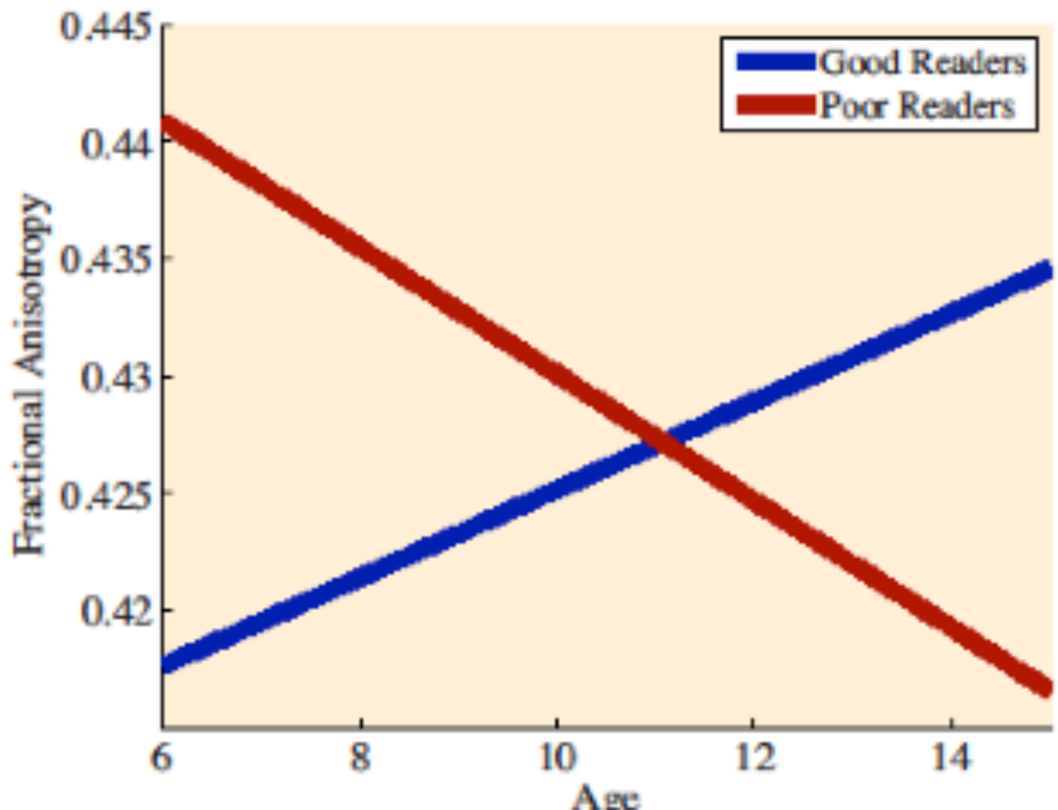


Diffusion changes during development differs between good and poor readers

FA slopes of good and poor readers



Left Inferior Longitudinal Fasciculus



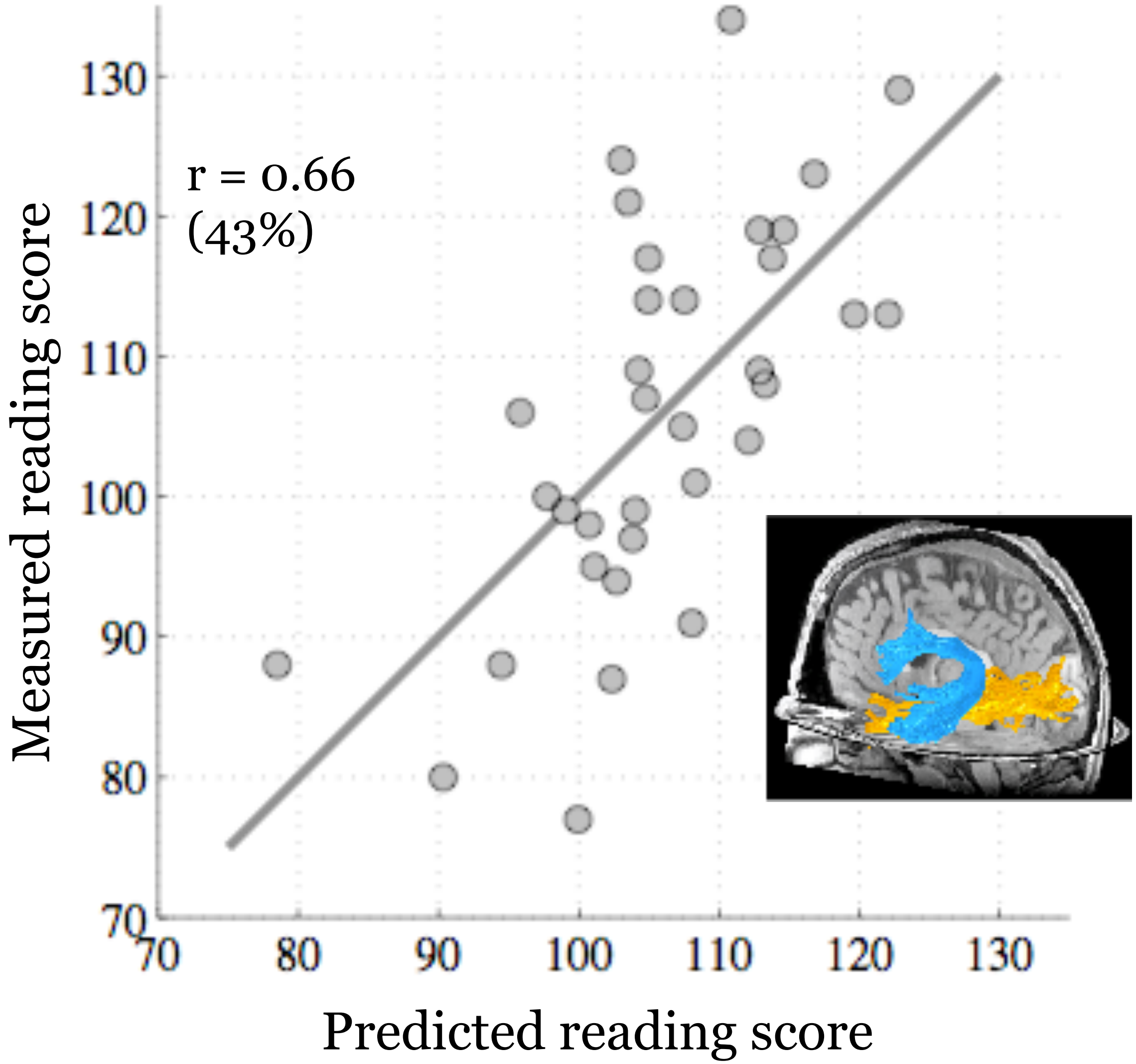
- FA in the ILF increases for good readers and declines for poor readers (6 – 14 years)
- The FA developmental trajectory, not the FA level, matters

Neuroprognosis

Predicting reading scores from rate of white matter development
(Yeatman et al., 2012)

- Simple models that combine data from two tracts (ILF and AF) predict reading skill from diffusion development

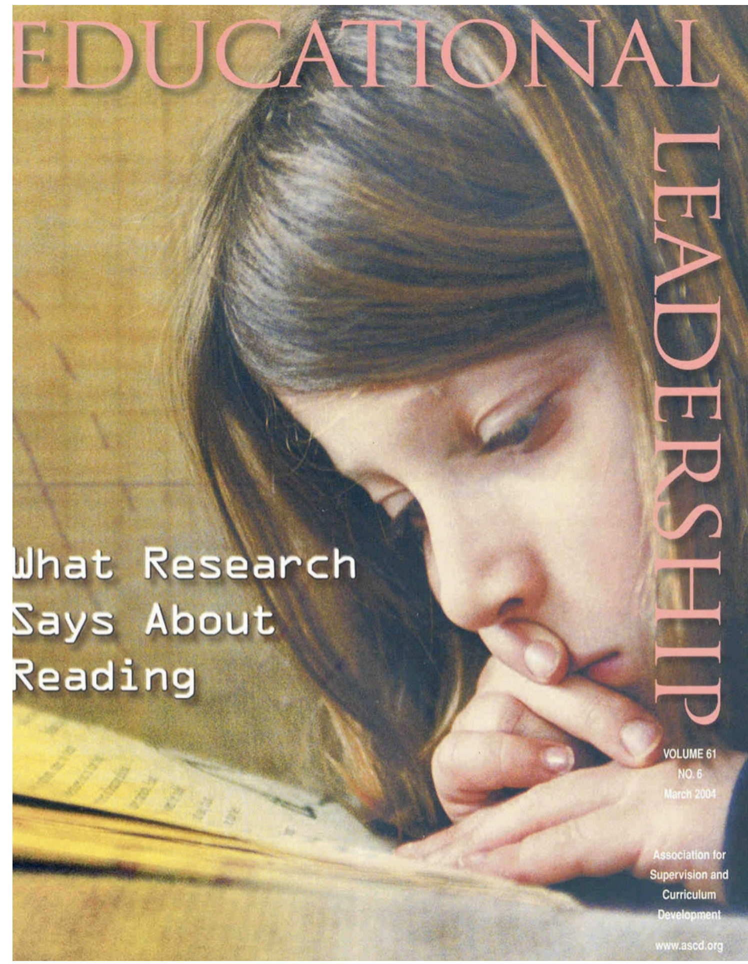
- The predictions are not yet useful; they are statistically reliable



Neuroscience for Society

Wandell and Yeatman, CONB, 2013

- Some behaviors, such as psychological tests of performance during brief trials, may be best understood by measuring synaptic activity or spikes.
- Other important behaviors - learning to read or to regulate emotions - take place over longer time periods. These skills may depend on biological processes such as cell development, growth and pruning of dendritic arbors, the proliferation and activity of glia.
- Scientists need to account for the entire range of processes to understand circuit function in health and disease.



Reading references

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The *Annual Review of Psychology* is online at psych.annualreviews.org

This article's doi:
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0066-4308/12/0110-0001$20.00

Learning to See Words

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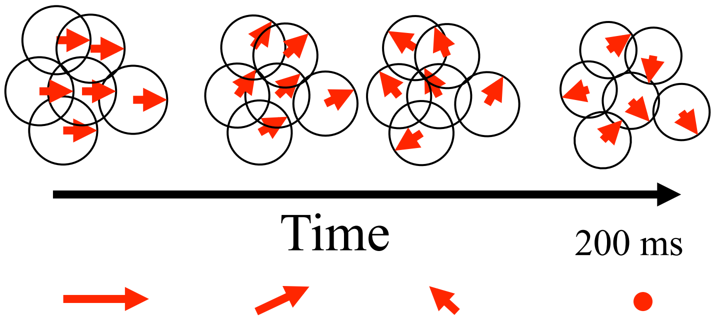
Quantitative MRI of the fascicle tissue

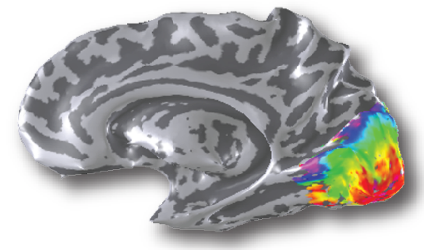
(Mezer et al., Nature Medicine, 2013)

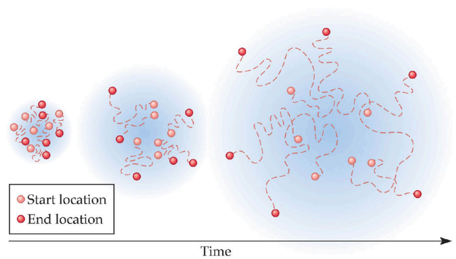
- What tissue properties change?
- T1, Macromolecular tissue volume (MTV), and Surface interaction rate (SIR)
- Single patient diagnosis

There are multiple types of MR mechanisms

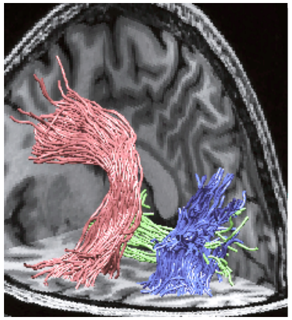


The spins dephase
(T2*)

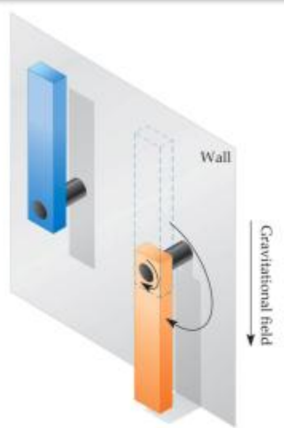




The spins move
(diffusion)



High energy



Low energy

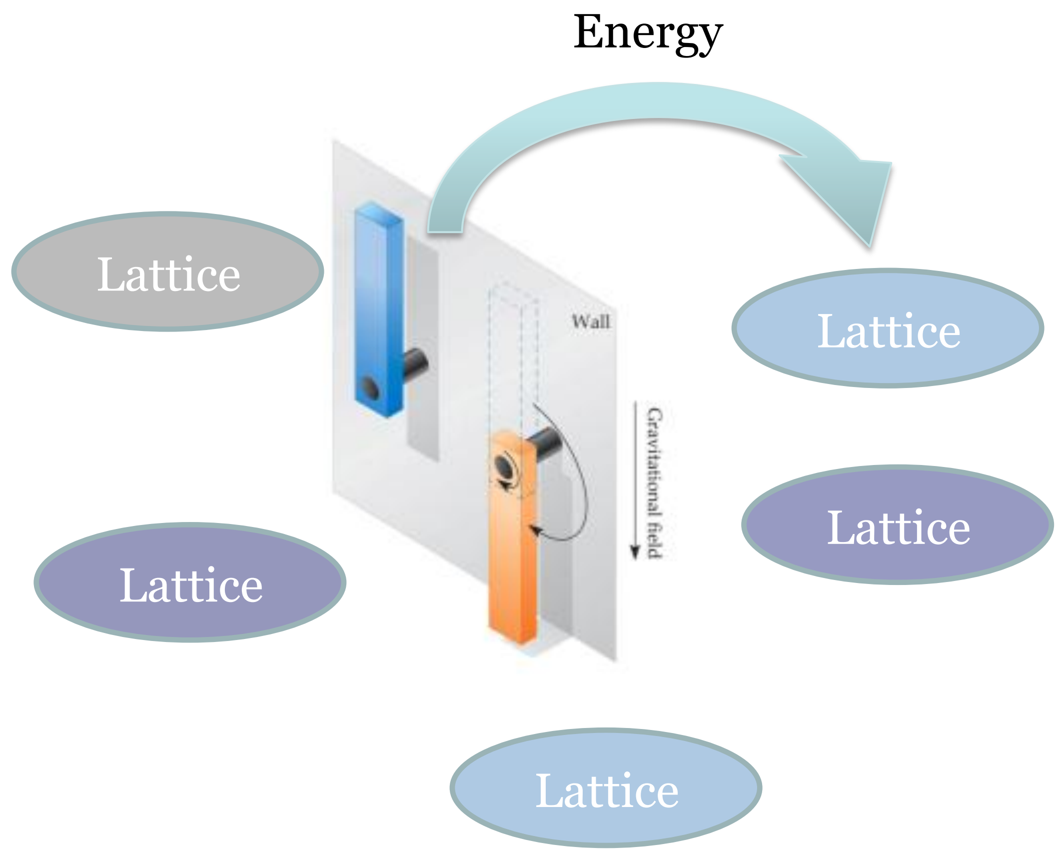
Anti-parallel spins give up
energy to lattice and return
to lower parallel state
(T1)

Analyzing spin-lattice exchange (T1)

Energy from anti-parallel spins is absorbed by the macromolecules in the environment (lattice)

How efficient is this energy exchange?

I am glad you asked.

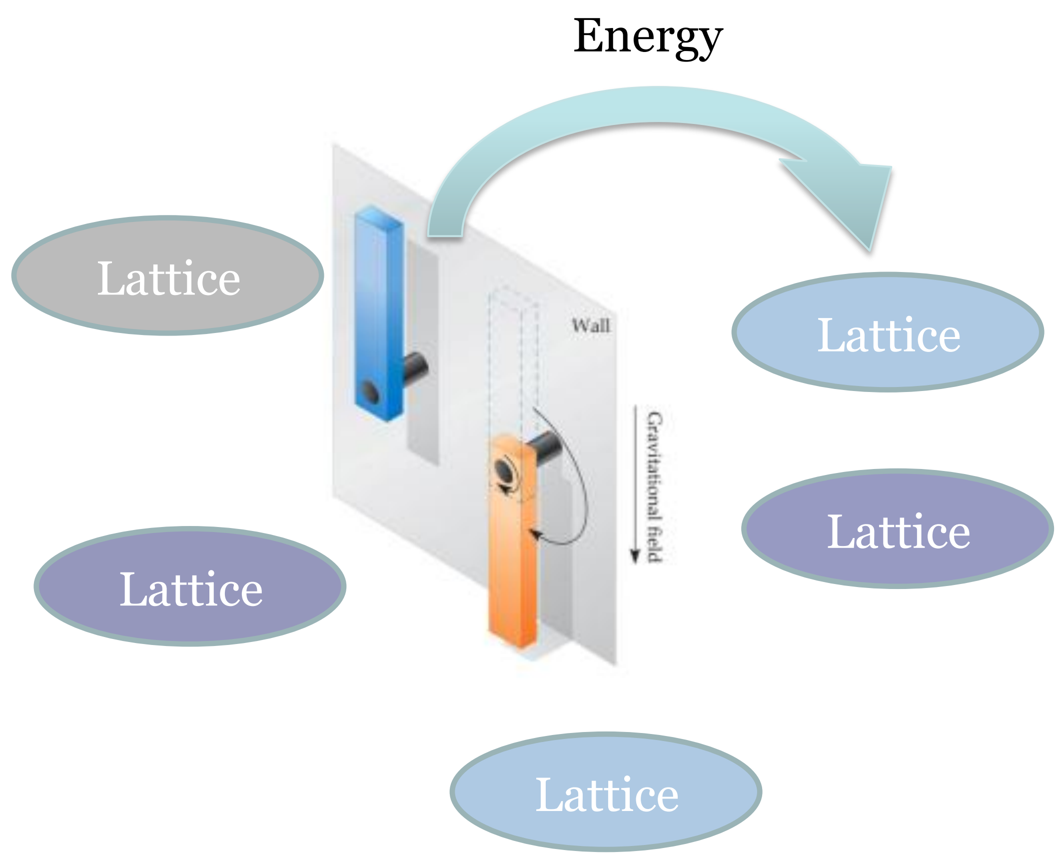


Analyzing spin-lattice exchange (T1)

Spin-lattice energy exchange rate (T1) depends on

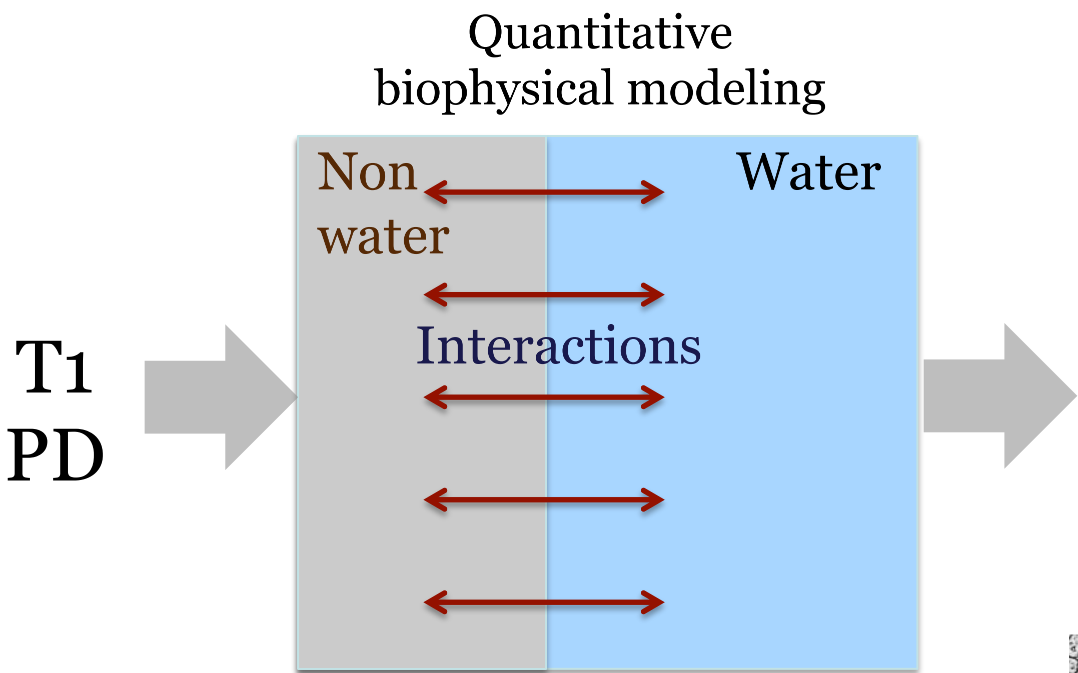
- How many macromolecules are in the lattice
- The type of macromolecules

If you could measure this in the brain, these are pretty good things to know (noninvasively)



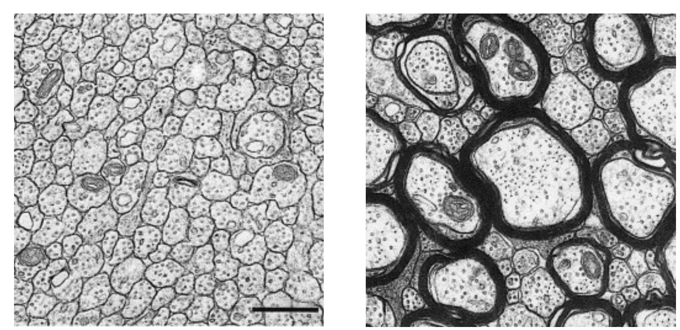
Modeling and calibration of the MRI signal yields quantitative measures of tissue

Mezer et al., Nature Medicine (2013)



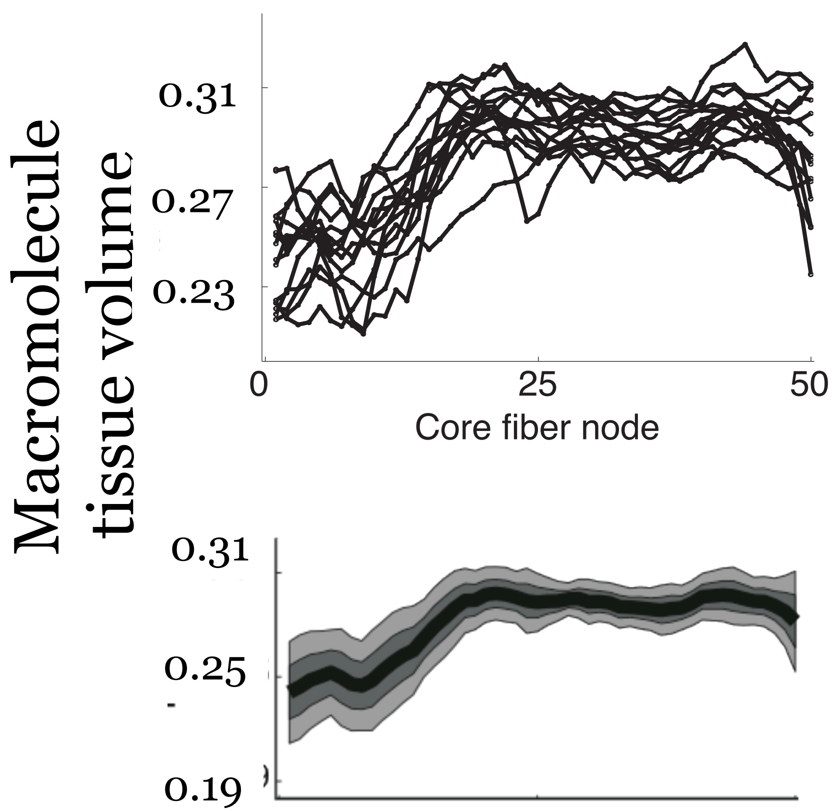
Macromolecule tissue volume (MTV)

Surface interaction ratio (SIR)

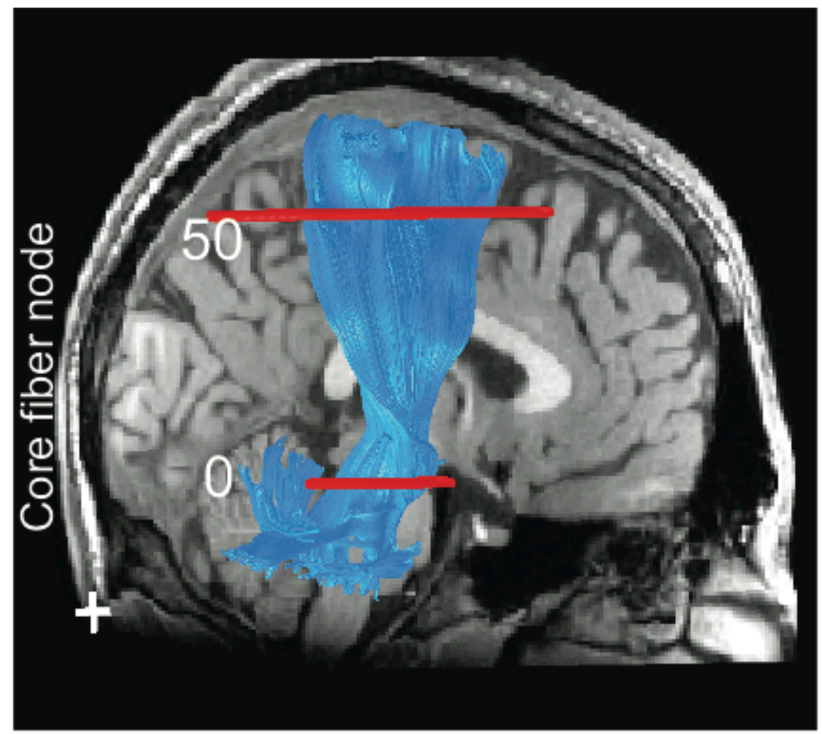


Single subject measures and multiple sclerosis

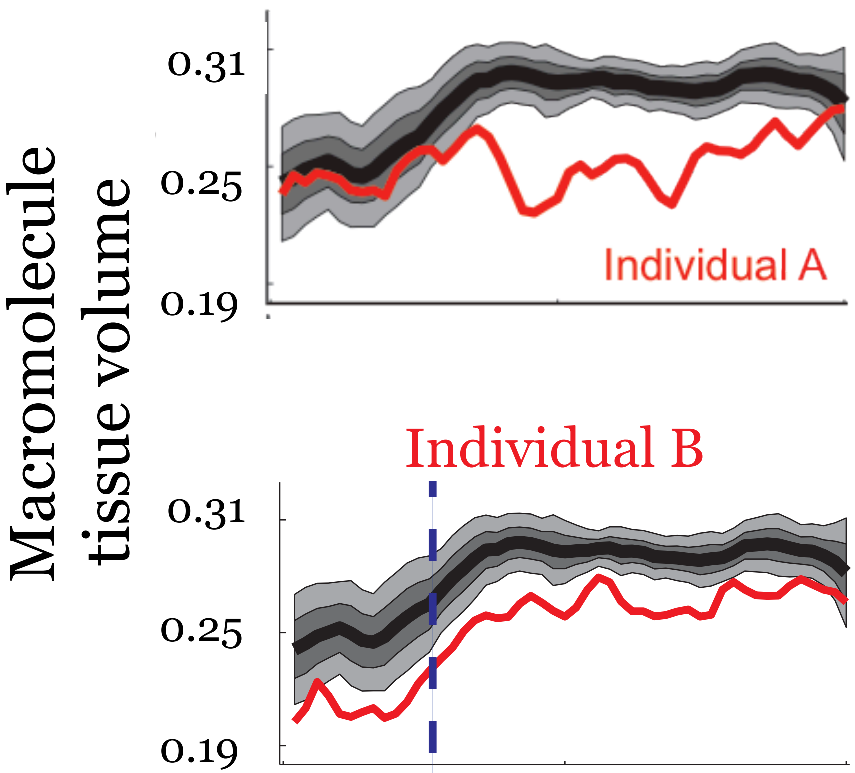
Control distribution



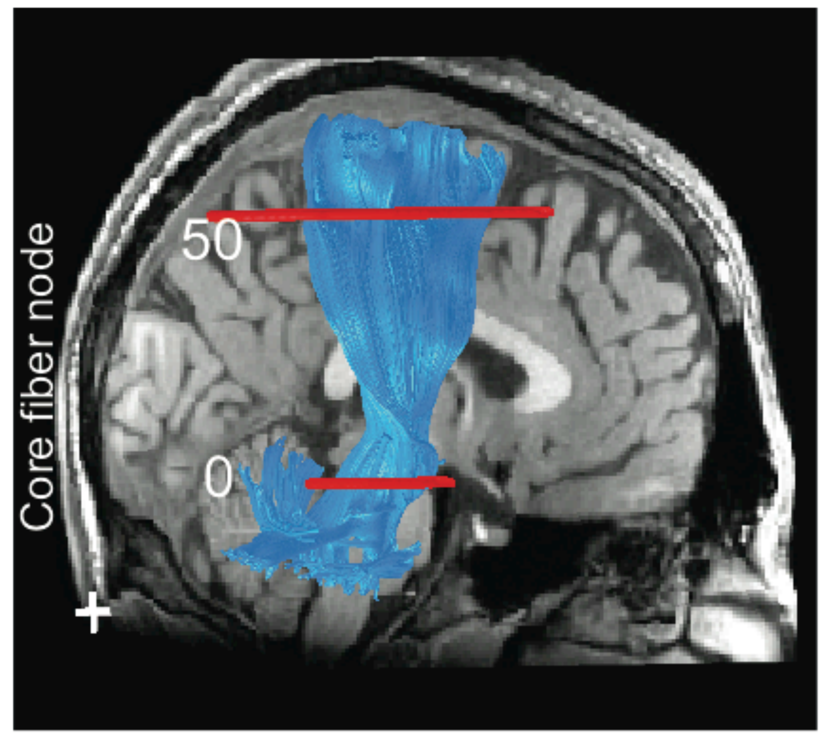
Cortical spinal track



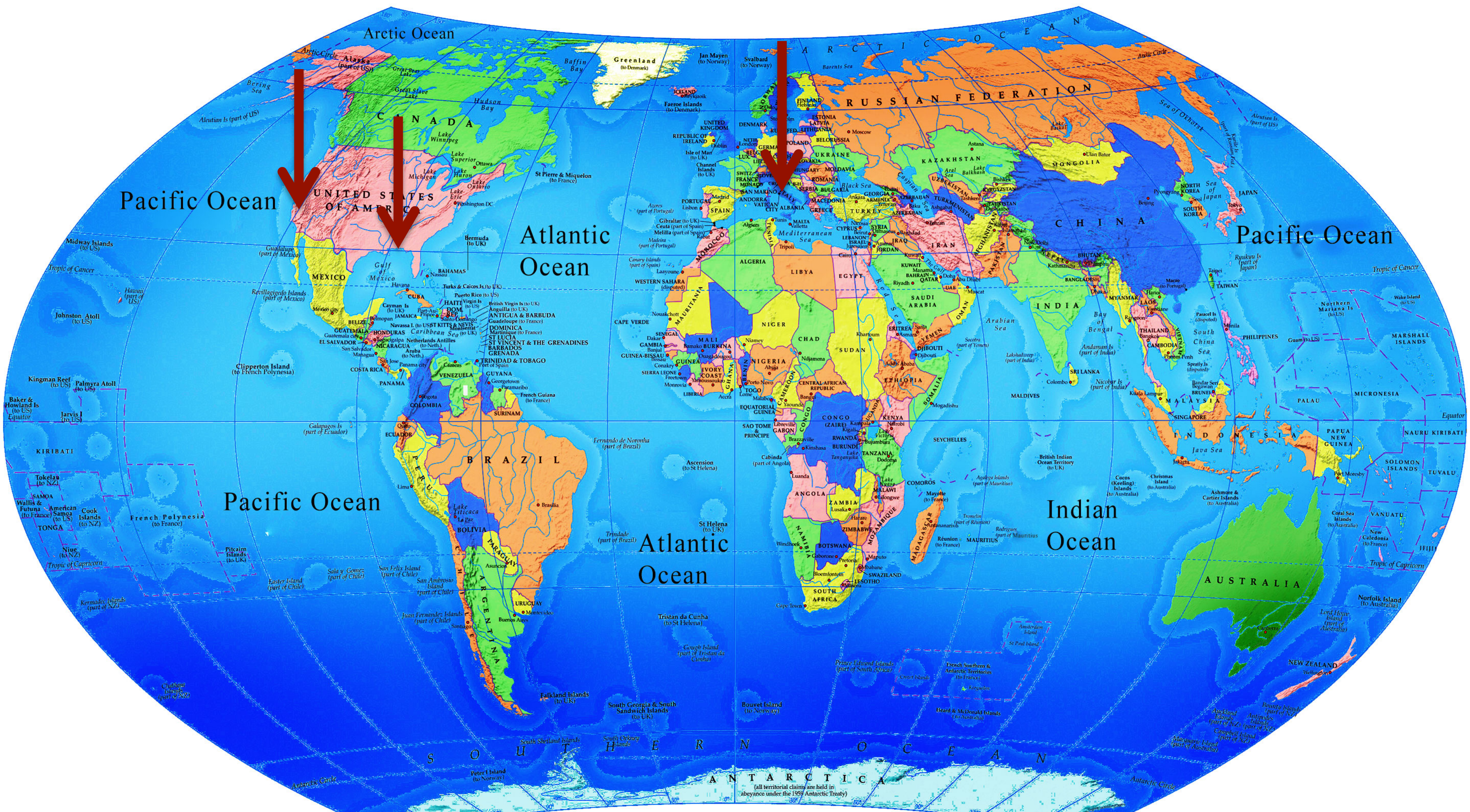
Single subject measures (MS)



Cortical spinal track



The promise: quantitative MRI measurements enable coordinating across sites and instruments



Clinical applications of quantitative methods

- Monitor changes in disease state
- Monitor the effects of drug therapy
- Diagnose neurological disorders (MS)
- **Aggregate data across sites and populations**

Project on Scientific Transparency

- Many MRI techniques are being invented
- There are limited tools for sharing data and methods
- This limits replication and thus trust in published data and analyses
- We are working on technology to improve sharing, transparency and trust

Welcome *EXAMPLELAB!*

LAB

examplelab

VIEW RESULTS

exampledata

exampledata2

PROCESSING INFO

AFQ Pipeline

Vista Lab NIMS

Stanford VISTA Lab

FUNDING

This research project is funded by the Weston Havens Foundation

EXAMPLELAB's data:

- exampledata

  Process started December 8, 2013.

  Processing finished December 9, 2013.

  Success!

- exampledata2

  Process started December 8, 2013.

  Processing finished December 9, 2013.

  Success!

You can drag and drop your data onto this page to upload it for processing.

You still maintain private ownership, or you can share.

We have a record of the data and its provenance

STANFORD UNIVERSITY | NEUROBIOLOGICAL IMAGE MANAGEMENT SYSTEM (NIMS)

WELCOME, BRIAN WANDELL
STATUS: 400/0/0

My Data | Search | Manage Experiments | Manage Groups | Logout

My Data

- Move Sessions to other Experiments via drag-and-drop.
- View and update an entry's metadata via double-click.
- Download Sessions or Datasets by dragging them to the Download area.
- Trash entries by dragging them to the Trash area.

Download
- Include raw
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Trash

- Hide Trash
- Show Trash
- Trash Only

Experiments

Group	Experiment
wandell	achiasma
wandell	anatomicals
wandell	anatomy
nordahl	app
wandell	aviv
wandell	dwi
wandell	ecog
wandell	fmri
wandell	frk
wandell	hld
wandell	hlf
wandell	hlf75
wandell	hlf175
wandell	jyeatman
wandell	kmain
wandell	knk
wandell	lb
wandell	main
wandell	mrarc

Sessions

Date & Time	Exam	Subj.
2013-11-22 22:15	1	110074-1
2013-10-18 21:11	1	110007-1
2013-10-11 20:51	1	109724-1
2013-10-04 20:38	1	110114-1

Epochs

Time	Description
22:15:58	PhoenixZIPReport
22:20:42	localizer
22:22:10	MPRAGE_1mm_TR2500_140Hzp78
22:33:38	DTI_siemens_TClessdistort_ColFA
22:33:38	DTI_siemens_TClessdistort_EXP
22:33:38	DTI_siemens_TClessdistort
22:33:38	DTI_siemens_TClessdistort_ADC
22:33:38	DTI_siemens_TClessdistort_FA
22:33:38	DTI_siemens_TClessdistort_TRACEW
22:39:58	phsemap_TC
22:39:59	phsemap_TC
22:42:51	restingstate_TC
23:51:40	true_sag_fl
23:52:58	MPRAGE_1mm_224sl_ND
23:52:58	MPRAGE_1mm_224sl

Datasets

Data Type

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Welcome *EXAMPLELAB!*

LAB

examplelab

VIEW RESULTS

exampledata

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NIMS
Neurobiological Image Management System

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- exampledata2

  Process started December 8, 2013.

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  Success!

Specific advanced analyses such as MTV, SIR, Tract Profiles and others can be executed on this site

The results are stored and returned to you on a web-page

Analysis Summary

DATA IDENTIFIER

exampledata

VIEW RESULTS

Analysis Summary

Axial Diffusivity

Fractional Anisotropy

Mean Diffusivity

Radial Diffusivity

DOWNLOAD

Figures

Analyzed Data

PROCESSING INFO

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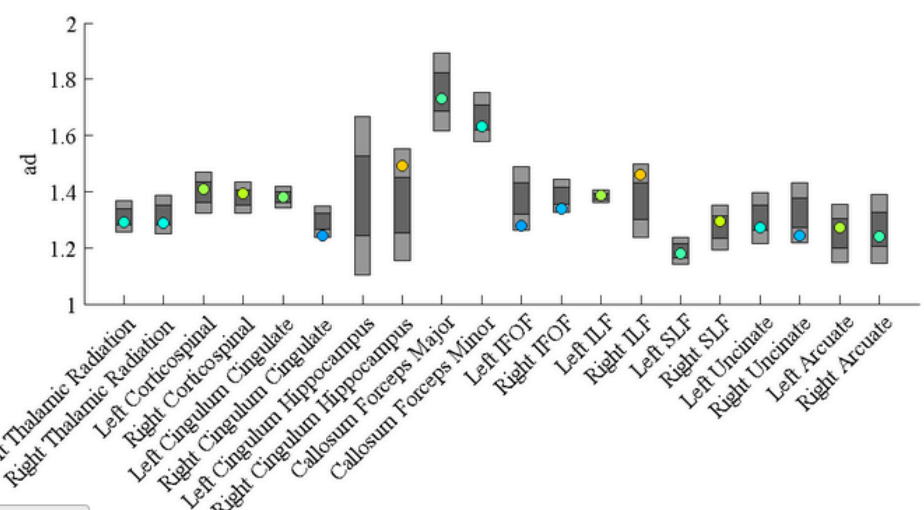
This is an example page of a tract profile analysis (AFQ) for diffusion



New methods for measuring activity, connections and tissue properties in the living human brain

- Human visual field maps
- White matter tracts for reading development
- Quantitative MRI of brain tissue
- Project on Scientific Transparency

New methods for measuring activity, connections and tissue properties in the living human brain

Modeling visual field maps

Serge Dumoulin
Kendrick Kay
Jon Winawer
Alyssa Brewer
Joyce Liao
Netta Levin

Reading development

Jason Yeatman
Andreas Rauschecker
Michal Ben-Shachar
Gayle Deutsch
Robert Dougherty

Quantitative MRI

Aviv Mezer
Jason Yeatman
Nikola Stikov
Robert Dougherty

Tractography (LIFE)

Franco Pestilli
Hiromasa Takemura
Ariel Rokem
Jason Yeatman
Anthony Sherbondy
Robert Dougherty
Michal Ben-Shachar

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