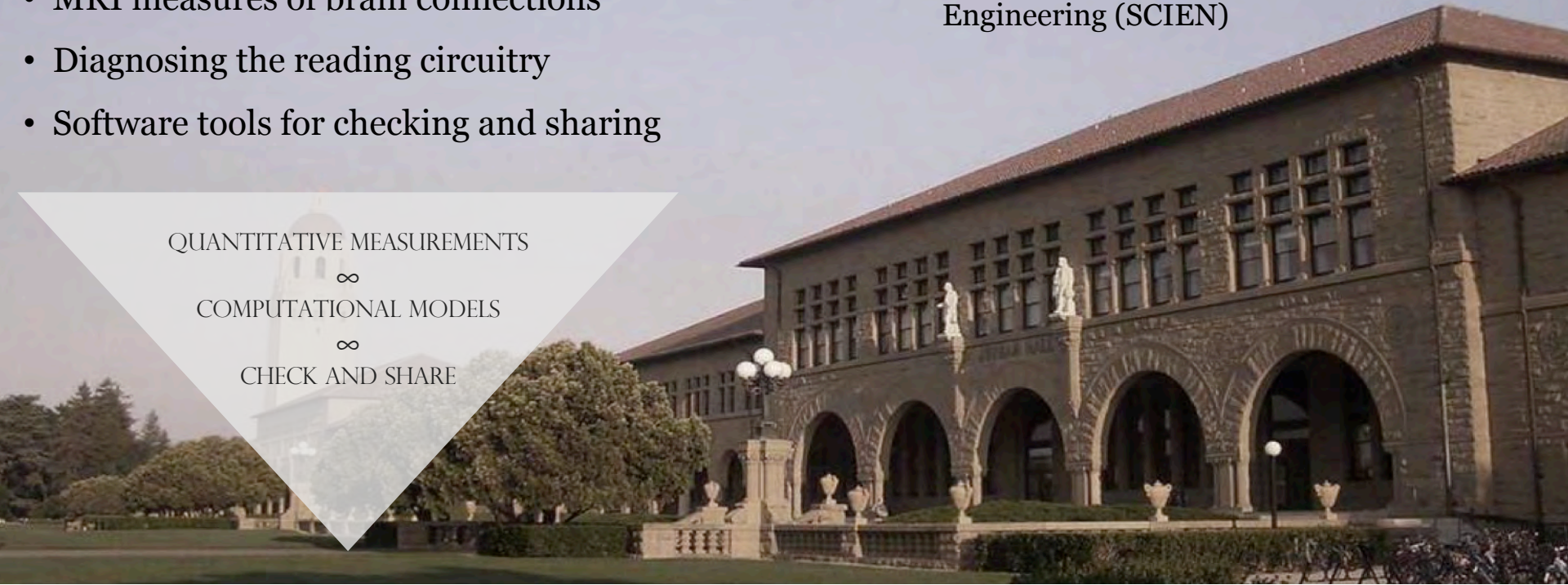
Diagnosing the reading circuitry

- About the human brain
- MRI measures of brain activity
- MRI measures of brain connections
- Diagnosing the reading circuitry
- Software tools for checking and sharing

Professor Brian Wandell

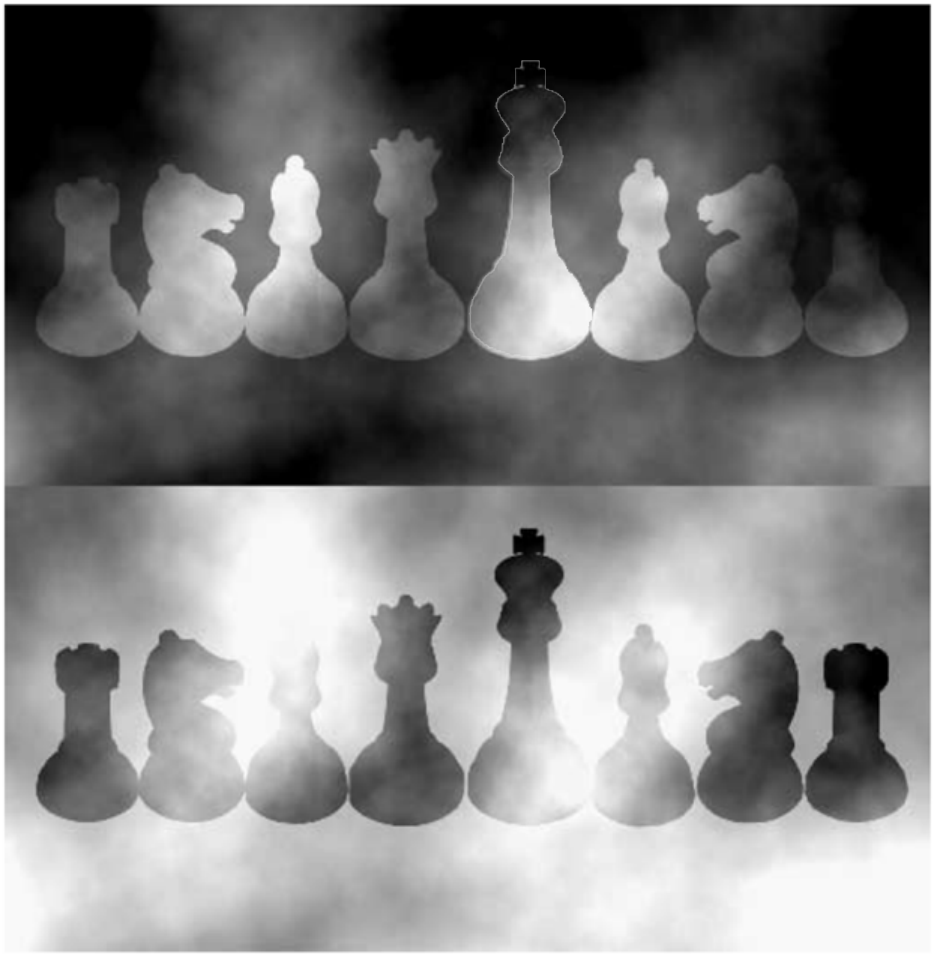
Director, Stanford Center for Cognitive and Neurobiological Imaging (CNI)
Deputy Director Stanford Neurosciences Institute (SNI)
Founding Director, Stanford Center for Image Systems Engineering (SCIEN)



The visual system actively interprets image data

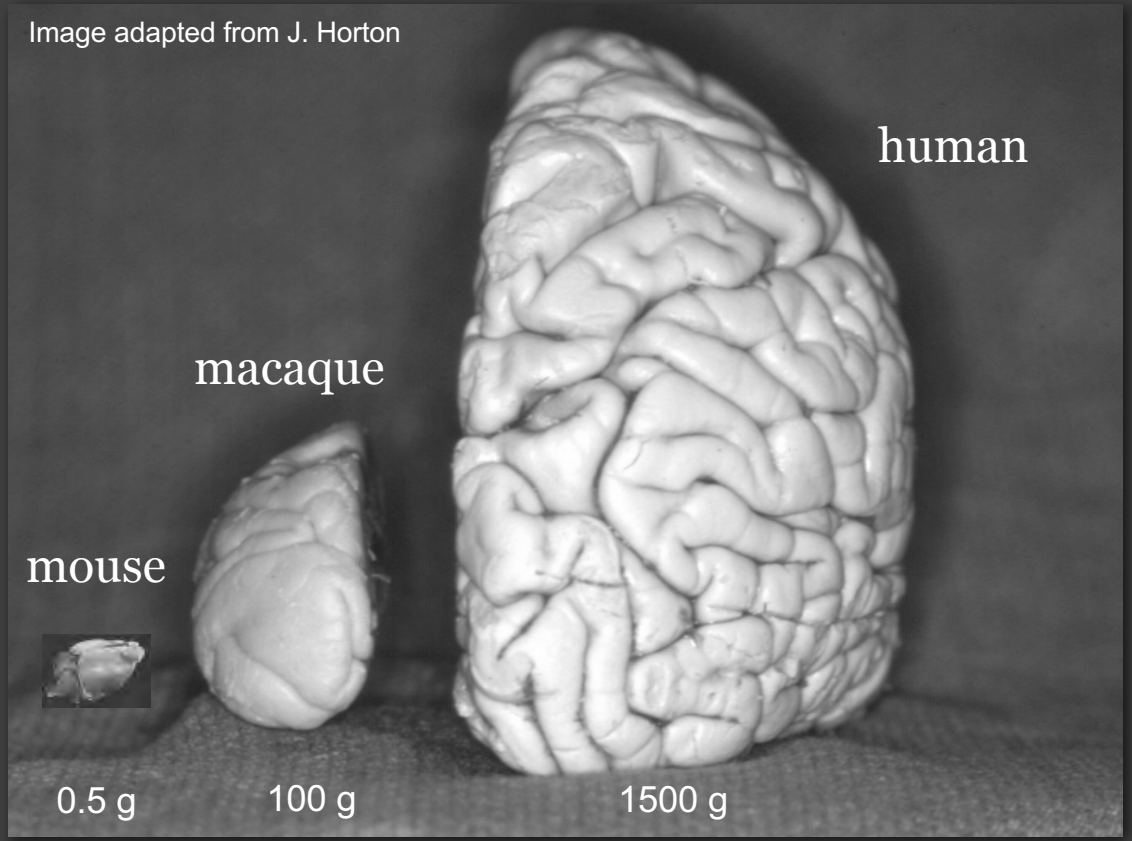
Even simple judgments – such as lightness - depend on substantial interpretation of the image data carried out by brain circuits

(Anderson and Winawer, Nature, 2005)



The human brain

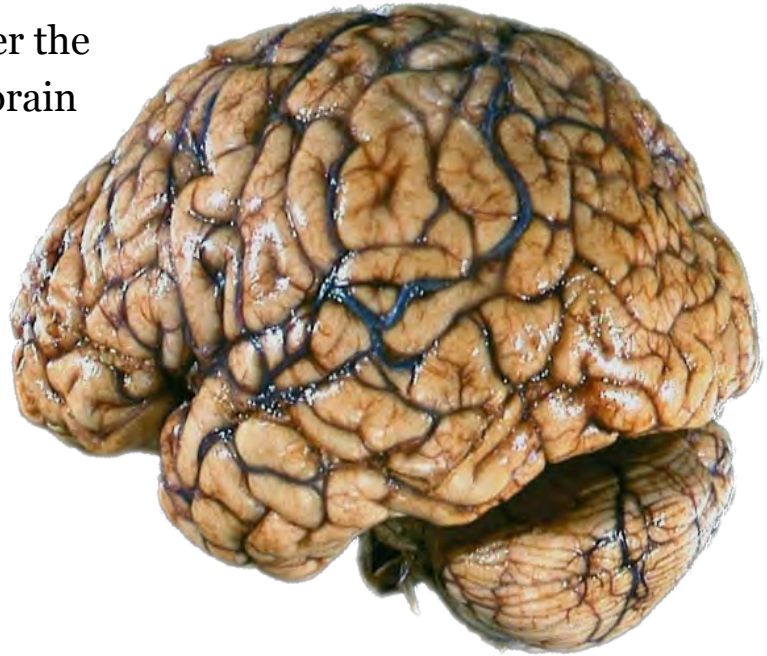
1: 15: 3000 (volume ratios)



- Brains differ
- Check which system was measured

Cortical computational elements

Brain computations takes place in the gray matter (also called cerebral cortex), a thin (2-4 mm) sheet of neural tissue that cover the surface of the brain



Neurons/mm^3: 10^4-10^6

Cortical Neurons: 10^{11}

Synapses/neuron: 10^3

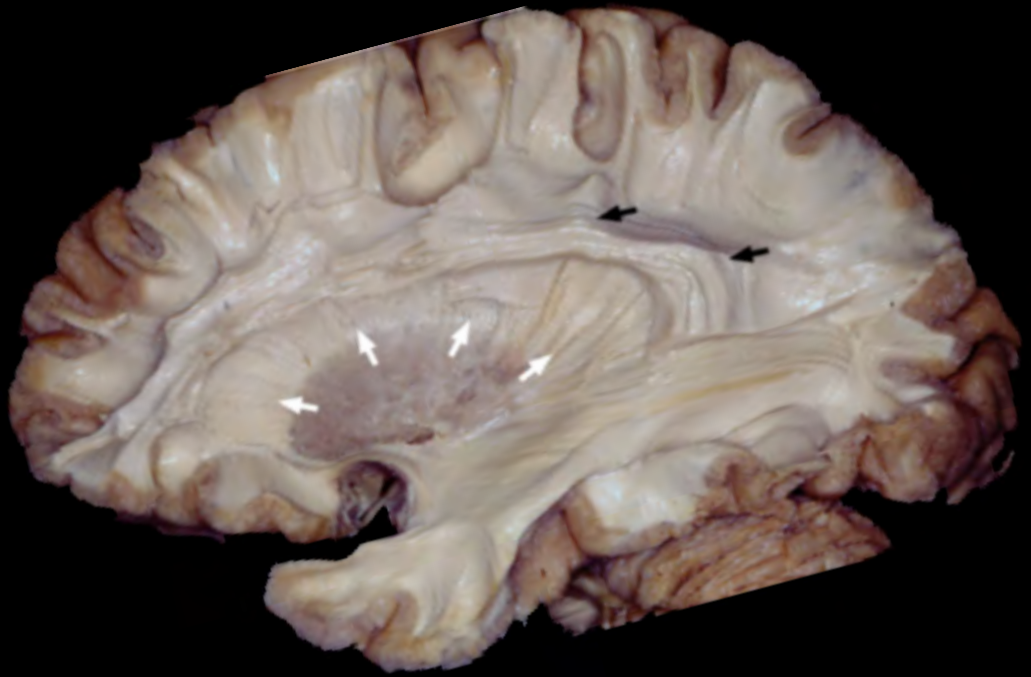
Cortical Synapses: 10^{14}

Surface area of each hemisphere: 25 x 30 cm^2

image from Graham Johnson

Long-range communication architecture (tracts)

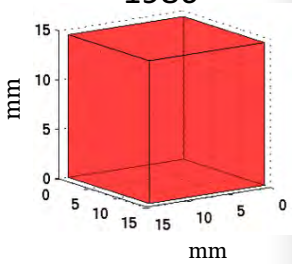
- There are many long-range connections
- These connections are not passive – they change their properties in response to use
- A system with active wires

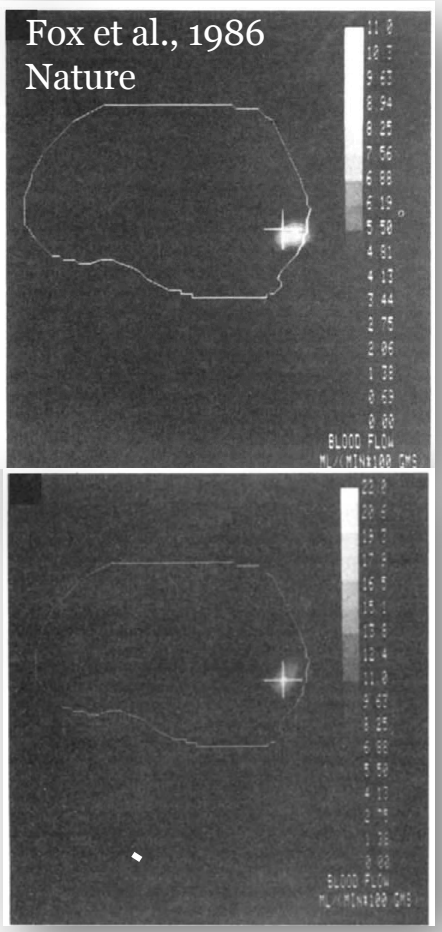


Courtesy Professor Ugur Ture

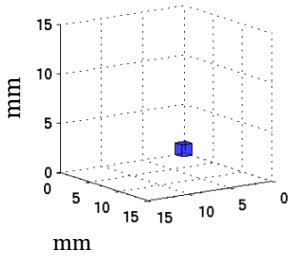
Remarkable progress in 25 years

Voxel size
1986

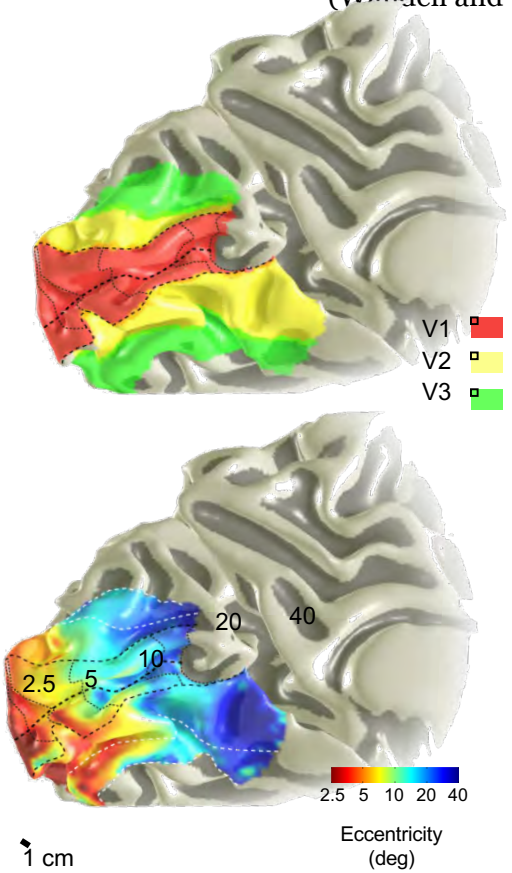




Voxel size
2009



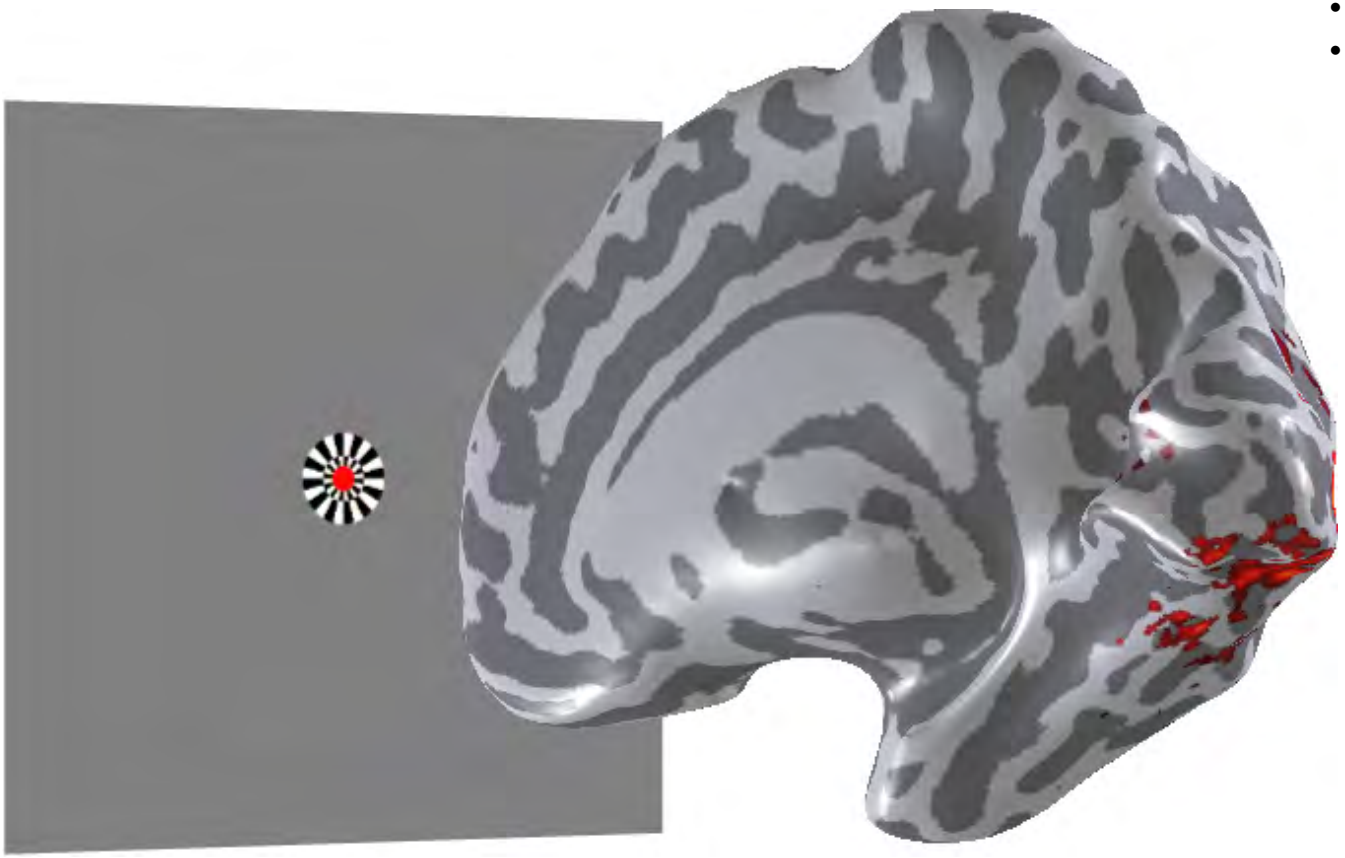
(Wandell and Winawer, 2011)



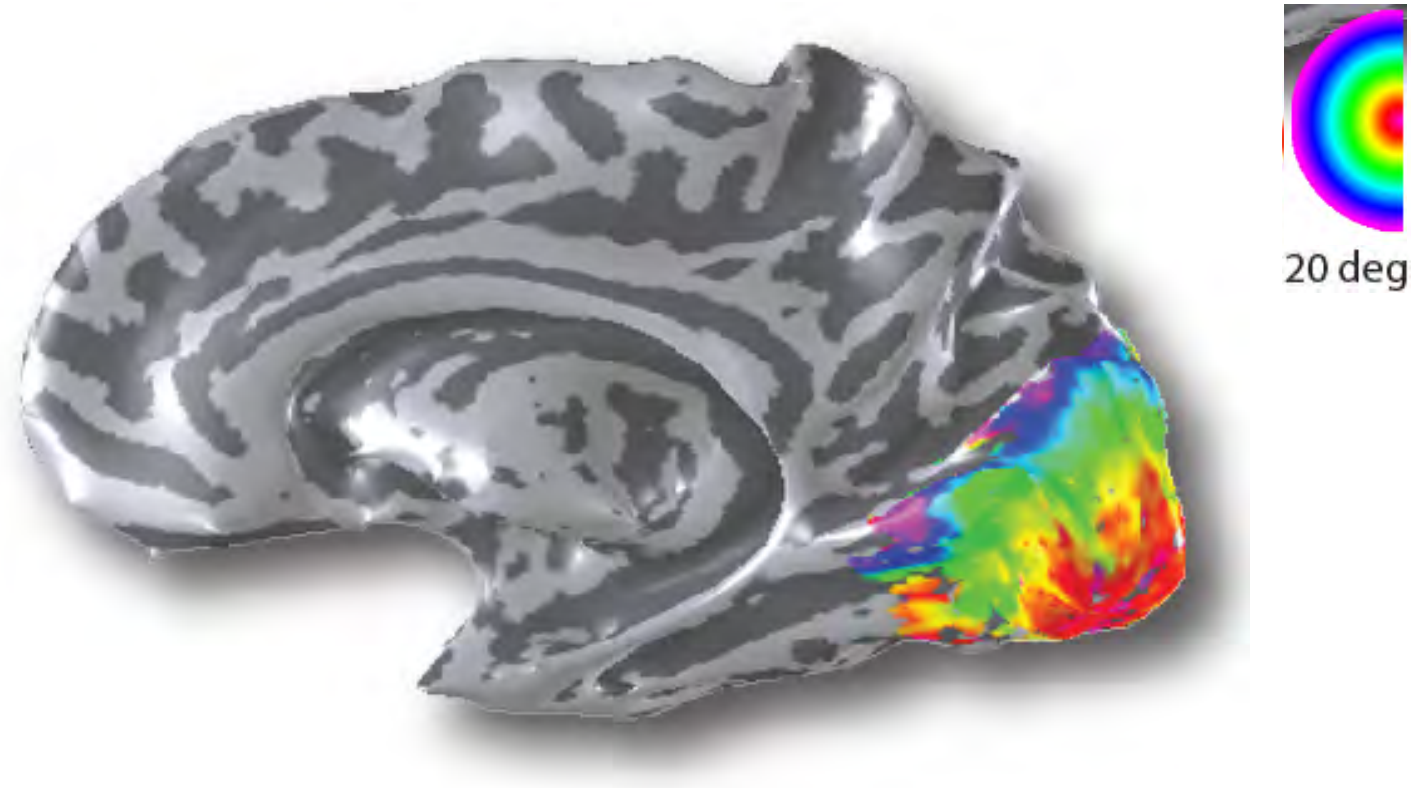
Human eccentricity mapping with fMRI

(Engel et al., 1994,1997; Sereno; Tootell, DeYoe; Others)

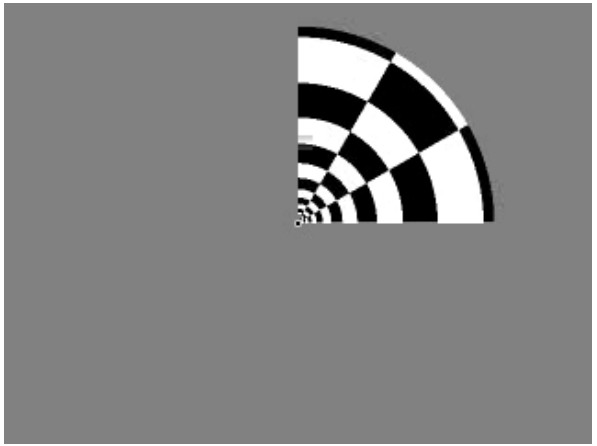
- Inflated brain
- Gray/white are sulci/gyri

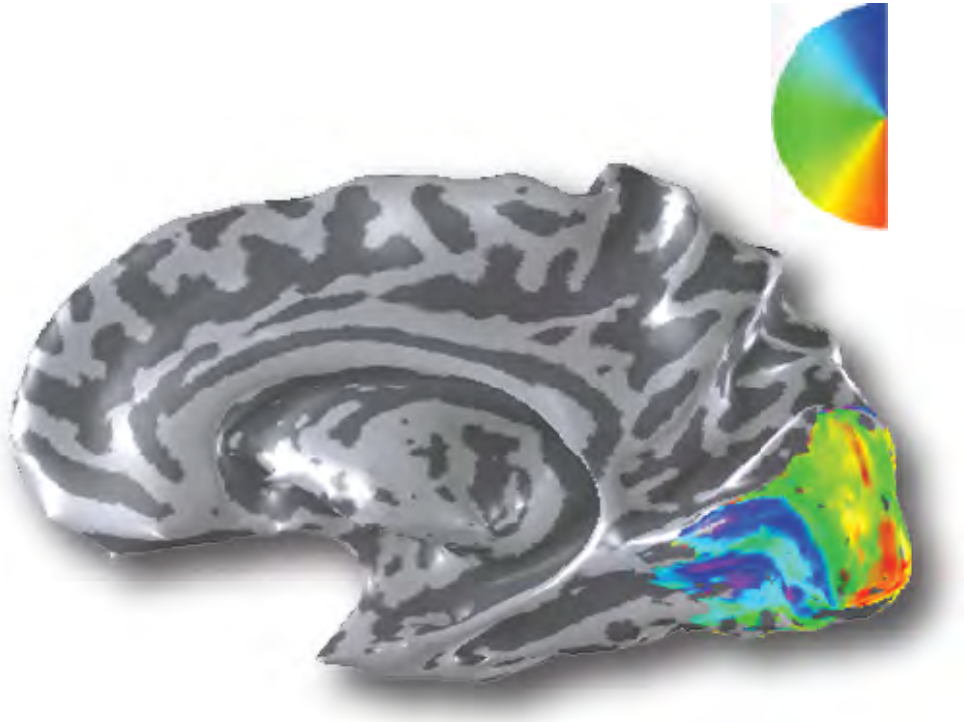


Pseudo-color representation of visual field map

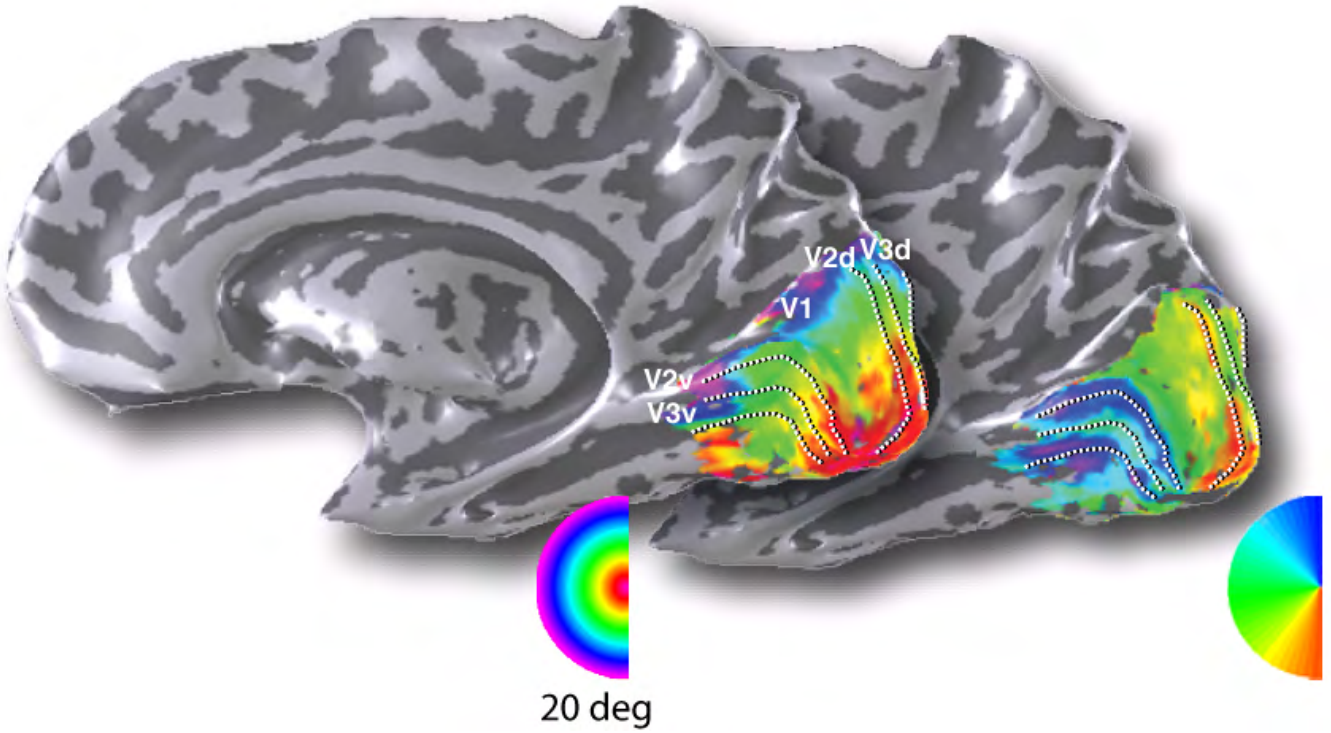


Angular measurements delineate visual field map boundaries

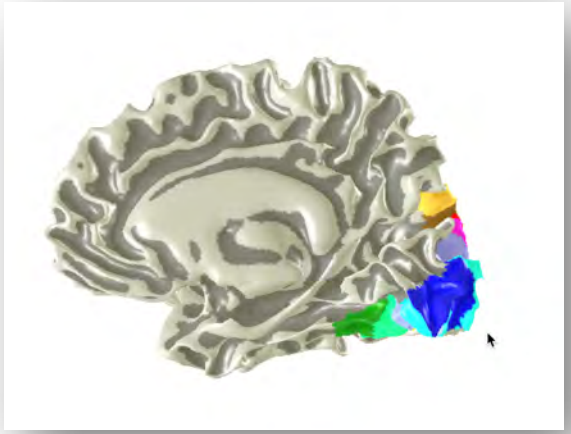




Combining eccentricity and angle data yields maps



Visual field map reviews



- Maps tile the occipital lobe
- Extend into IPS and VOT
- Response properties differ
- Identification from gross anatomy

366 Neuron 56, October 25, 2007

Neuron
Review

Visual Field Maps in Human Cortex

Brian A. Wandell,[1,*] Serge O. Dumoulin,[1] and Alyssa A. Brewer[2]
[1]Psychology Department, Stanford University, Stanford, CA 94305-2130, USA
[2]Department of Cognitive Sciences, University of California, Irvine, Irvine, CA 92697, USA
*Correspondence: wandell@stanford.edu
DOI 10.1016/j.neuron.2007.10.012

Much of the visual cortex is organized into visual field maps: nearby neurons have receptive fields at nearby locations in the image. Mammalian species generally have multiple visual field maps with each species having similar, but not identical, maps. The introduction of functional magnetic resonance imaging made it possible to identify visual field maps in human cortex, including several near (1) medial occipital (V1,V2,V3), (2) lateral occipital (LO-1,LO-2, hMT+), (3) ventral occipital (hV4, VO-1, VO-2), (4) dorsal occipital (V3A, V3B), and (5) posterior parietal cortex (IPS-0 to IPS-4). Evidence is accumulating for additional maps, including some in the frontal lobe. Cortical maps are arranged into clusters in which several maps have parallel eccentricity representations, while the angular representations within a cluster alternate in visual field sign. Visual field maps have been linked to functional and perceptual properties of the visual system at various spatial scales, ranging from the level of individual maps to map clusters to dorsal-ventral streams. We survey recent measurements of human visual field maps, describe hypotheses about the function and relationships between maps, and consider methods to improve map measurements and characterize the response properties of neurons comprising these maps.

Vision Research 51 (2011) 718-737

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Review

Imaging retinotopic maps in the human brain

Brian A. Wandell *, Jonathan Winawer

Psychology Department, Stanford University, Stanford, CA 94305, United States

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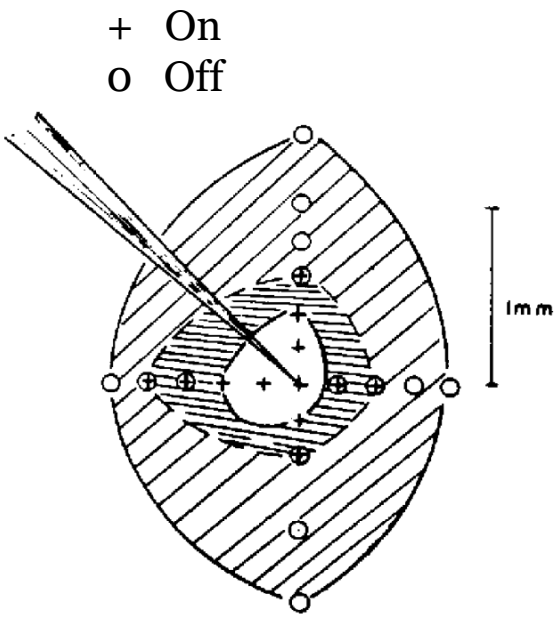
ABSTRACT

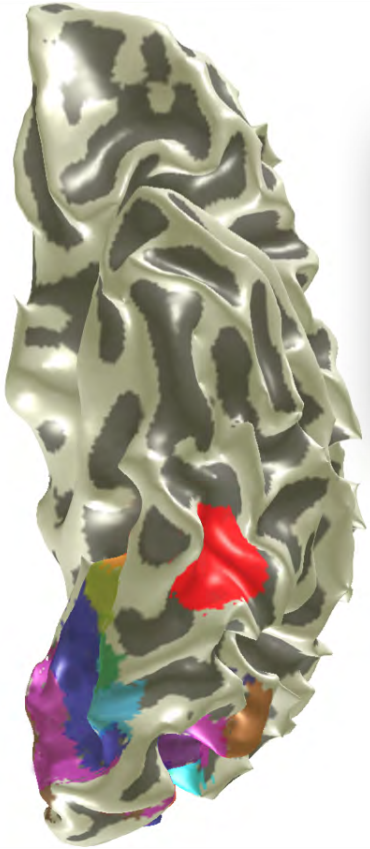
A quarter-century ago visual neuroscientists had little information about the number and organization of retinotopic maps in human visual cortex. The advent of functional magnetic resonance imaging (MRI), a non-invasive, spatially-resolved technique for measuring brain activity, provided a wealth of data about human retinotopic maps. Just as there are differences amongst non-human primate maps, the human maps have their own unique properties. Many human maps can be measured reliably in individual sub-

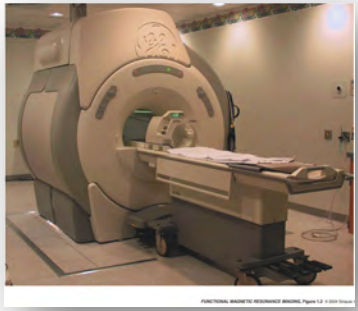
The population receptive field (pRF)

‘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)’.

Sherrington, 1910
Kuffler, 1953



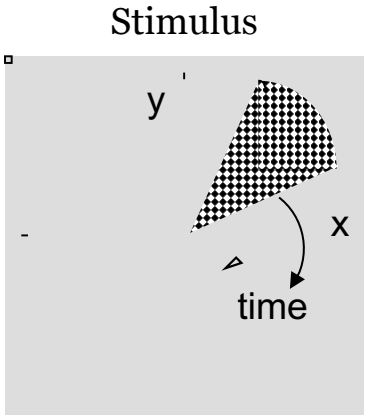


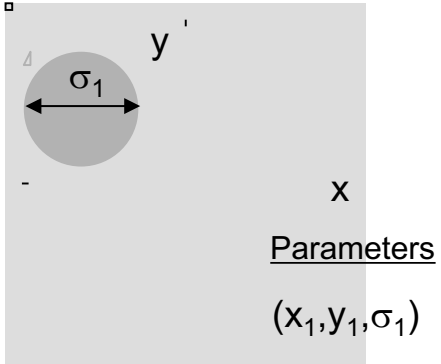


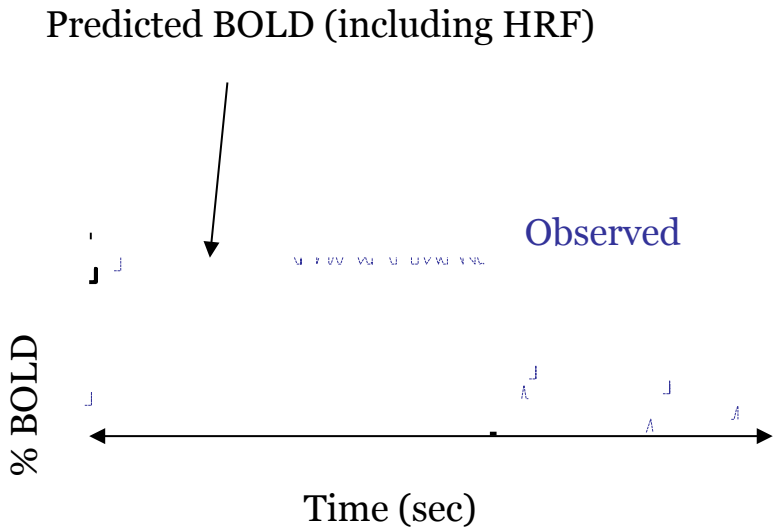
- Functional description
- Stimulus-referred

Population receptive field idea

- For each voxel, find a spatial receptive field that explains the fMRI measurement.
- The spatial RF model is the object of interest.
- Minimally, the model is linear in contrast and has an (x,y) location in the visual field and a spread
- More complex models are also being studied (e.g., CSS)







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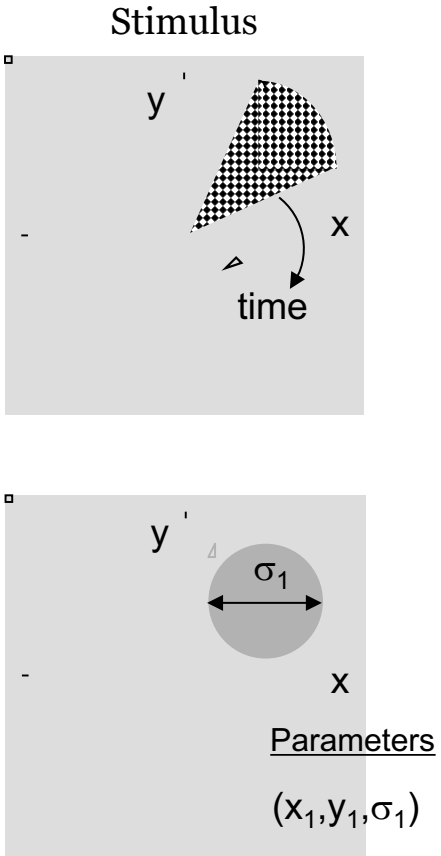

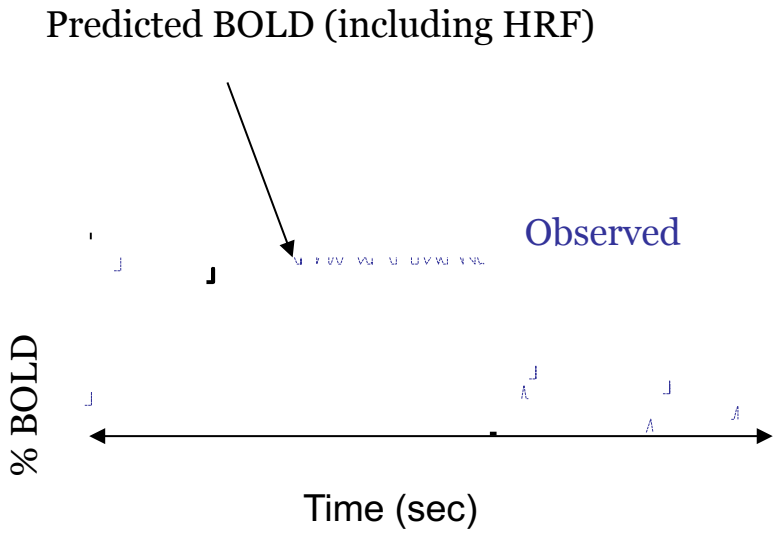

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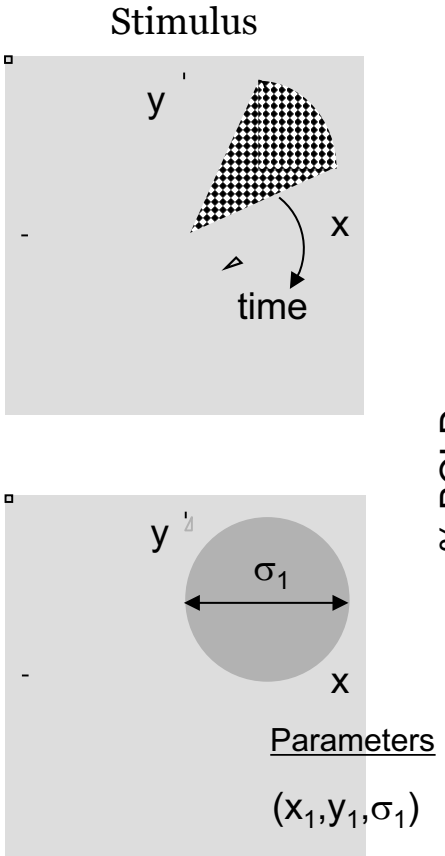
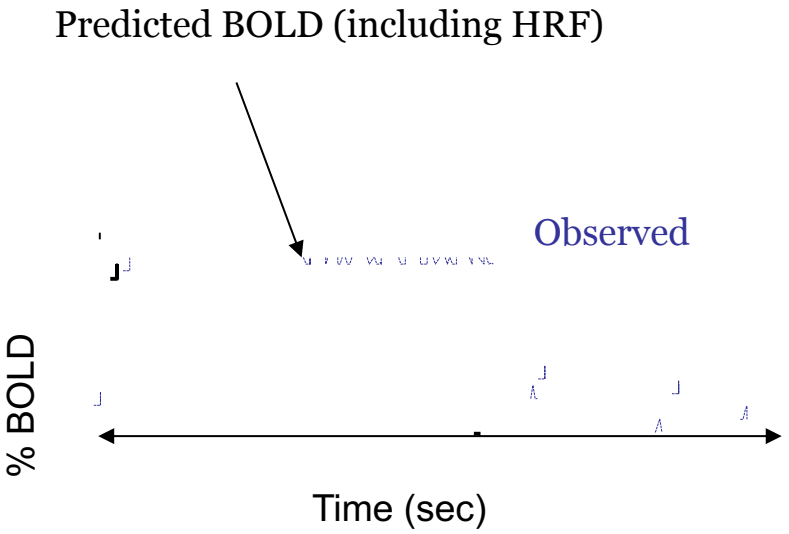
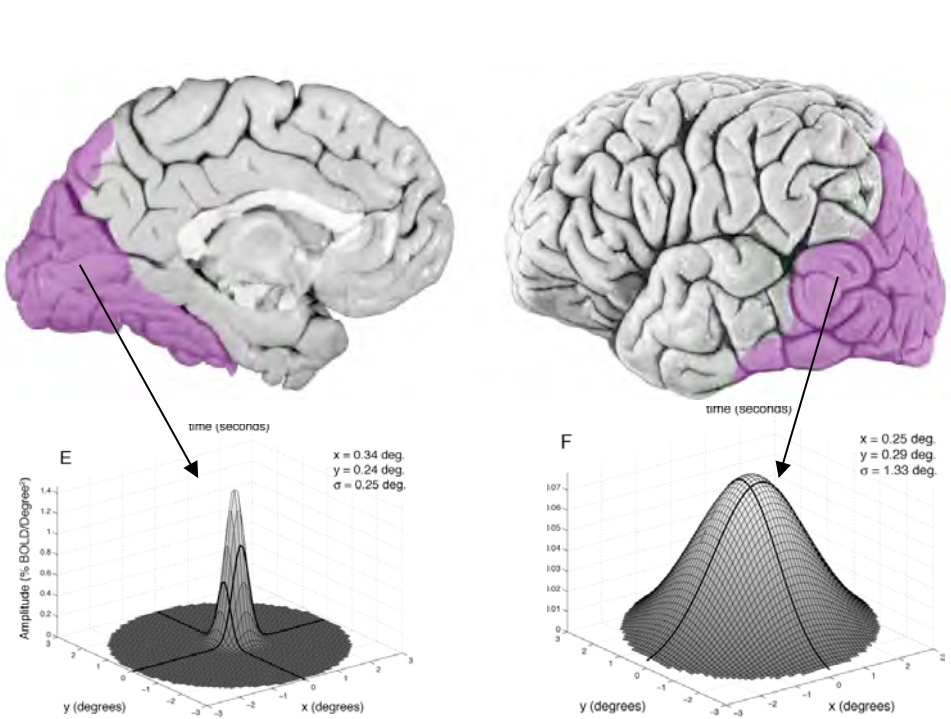
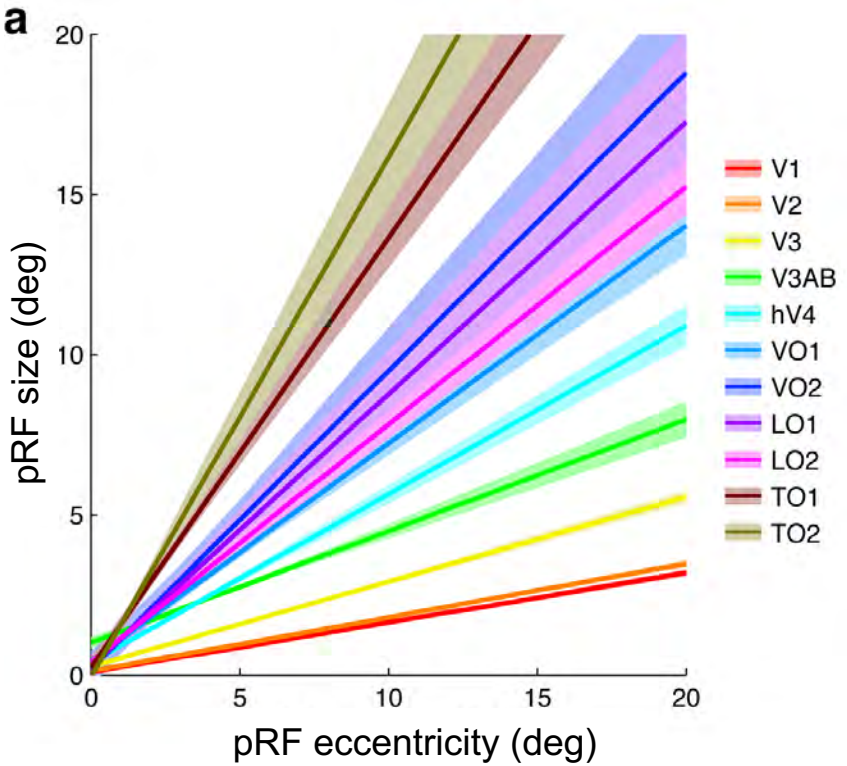




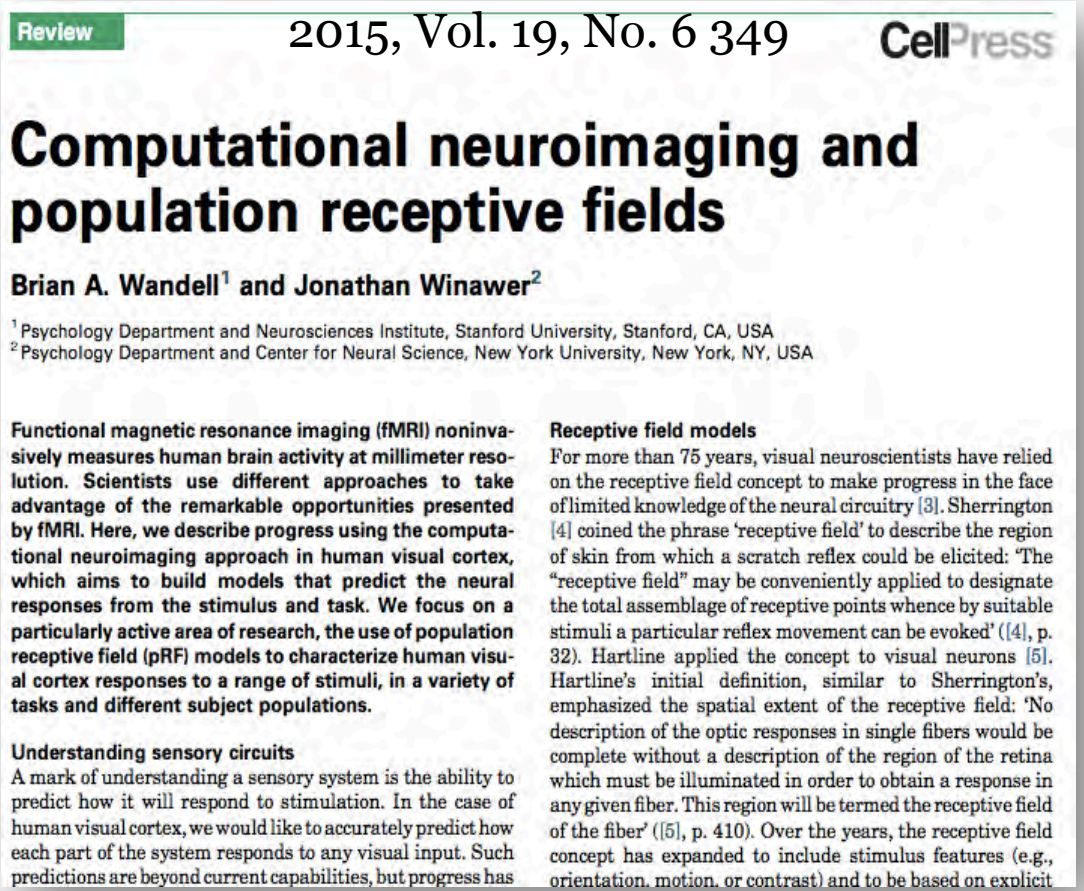
PRF size varies substantially and regularly across visual cortex

- At common eccentricities, different maps have different pRF sizes
- PRF size increases with eccentricity for all maps
- Bands are bootstrap estimates of the standard error





- Attention
- Stability and Plasticity
- Prosopagnosia
- Development and aging
- Autism
- Alzheimer's disease



Trends in Cognitive Sciences, June 2015, Vol. 19, No. 6 349

Review

CellPress

Computational neuroimaging and population receptive fields

Brian A. Wandell[1] and Jonathan Winawer[2]

[1] Psychology Department and Neurosciences Institute, Stanford University, Stanford, CA, USA
[2] Psychology Department and Center for Neural Science, New York University, New York, NY, USA

Functional magnetic resonance imaging (fMRI) noninvasively measures human brain activity at millimeter resolution. Scientists use different approaches to take advantage of the remarkable opportunities presented by fMRI. Here, we describe progress using the computational neuroimaging approach in human visual cortex, which aims to build models that predict the neural responses from the stimulus and task. We focus on a particularly active area of research, the use of population receptive field (pRF) models to characterize human visual cortex responses to a range of stimuli, in a variety of tasks and different subject populations.

Understanding sensory circuits

A mark of understanding a sensory system is the ability to predict how it will respond to stimulation. In the case of human visual cortex, we would like to accurately predict how each part of the system responds to any visual input. Such predictions are beyond current capabilities, but progress has

Receptive field models

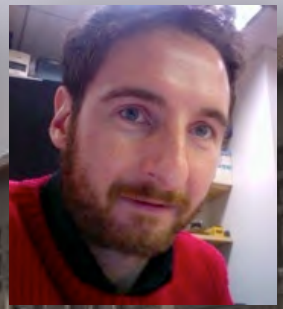
For more than 75 years, visual neuroscientists have relied on the receptive field concept to make progress in the face of limited knowledge of the neural circuitry [3]. Sherrington [4] coined the phrase 'receptive field' to describe the region of skin from which a scratch reflex could be elicited: 'The "receptive field" may be conveniently applied to designate the total assemblage of receptive points whence by suitable stimuli a particular reflex movement can be evoked' ([4], p. 32). Hartline applied the concept to visual neurons [5]. Hartline's initial definition, similar to Sherrington's, emphasized the spatial extent of the receptive field: 'No description of the optic responses in single fibers would be complete without a description of the region of the retina which must be illuminated in order to obtain a response in any given fiber. This region will be termed the receptive field of the fiber' ([5], p. 410). Over the years, the receptive field concept has expanded to include stimulus features (e.g., orientation, motion, or contrast) and to be based on explicit

Modeling the diffusion signal in a voxel

Ariel Rokem

Aviv Mezer

Franco Pestilli



Hiromasa Takemura

QUANTITATIVE MEASUREMENTS

∞

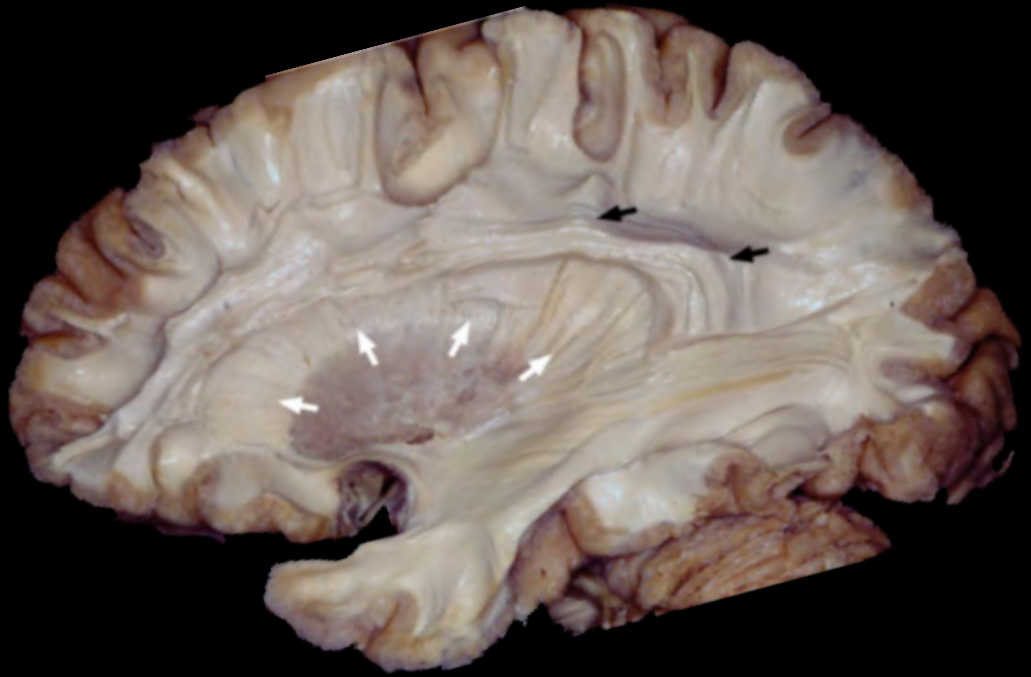
COMPUTATIONAL MODELS

∞

CHECK AND SHARE

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

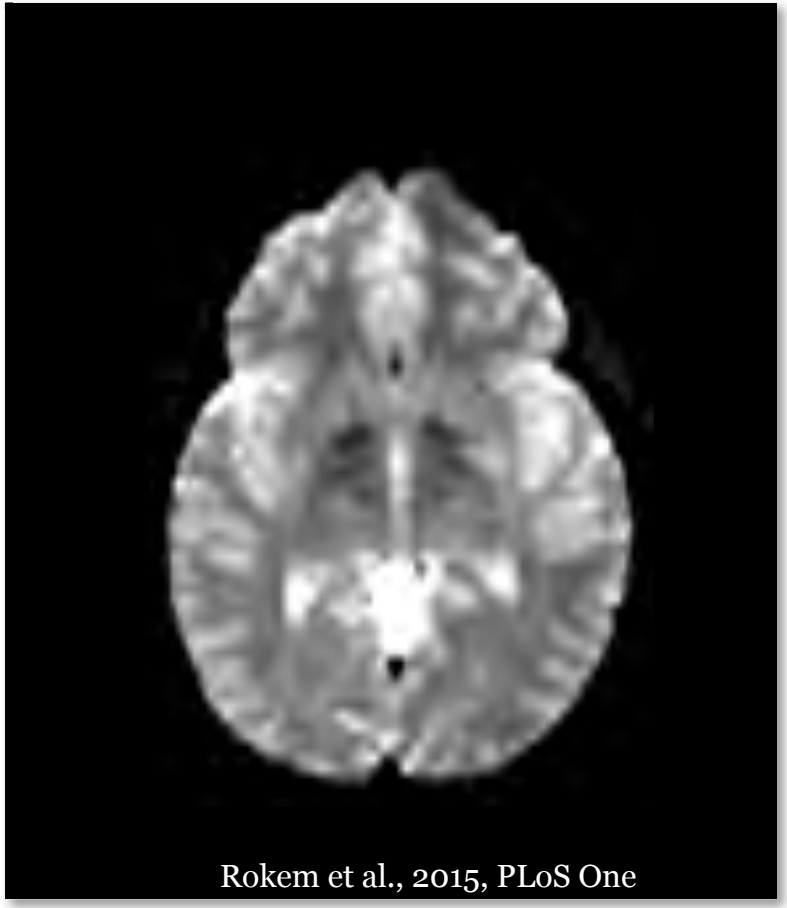


Courtesy Professor Ugur Ture

Non-diffusion MR image

Dark means large signal attenuation
High ADC

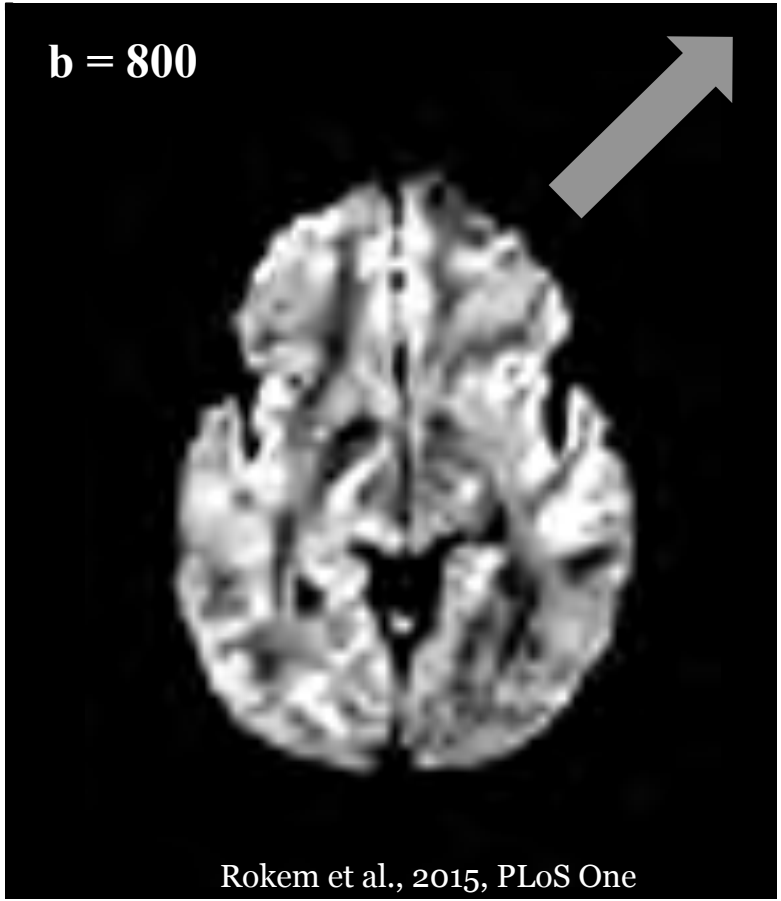
b = 0



Rokem et al., 2015, PLoS One

Diffusion weighting: Directions

Dark means large signal attenuation
High ADC



Diffusion weighting: Directions

Dark means large signal attenuation
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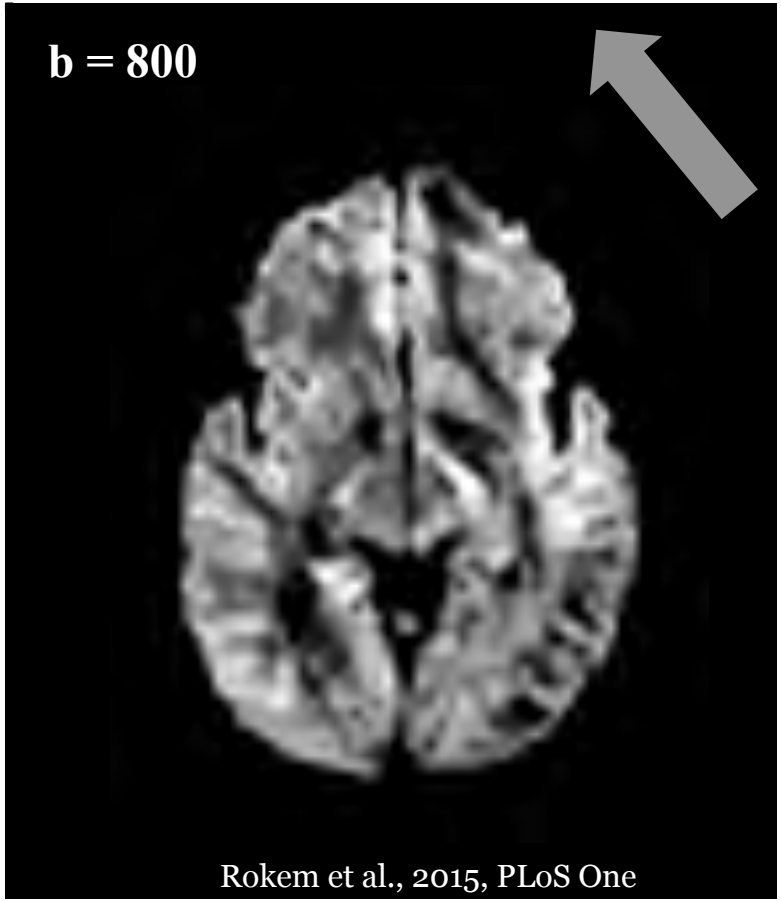
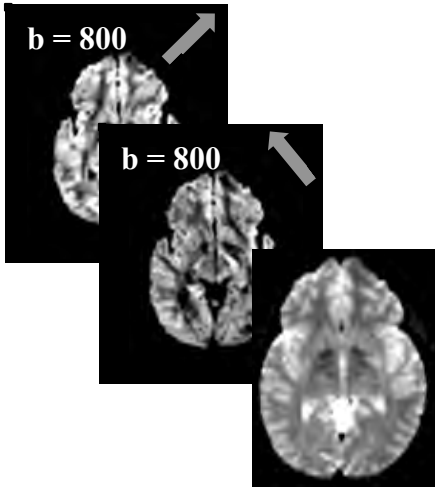
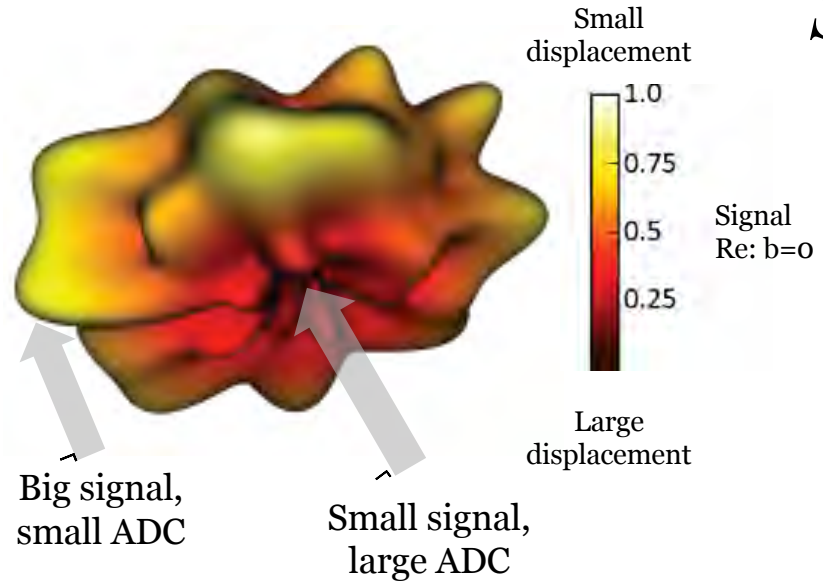


Diffusion signals in different directions

Apparent diffusion coefficient (ADC)
Diffusion data are surfaces at every voxel



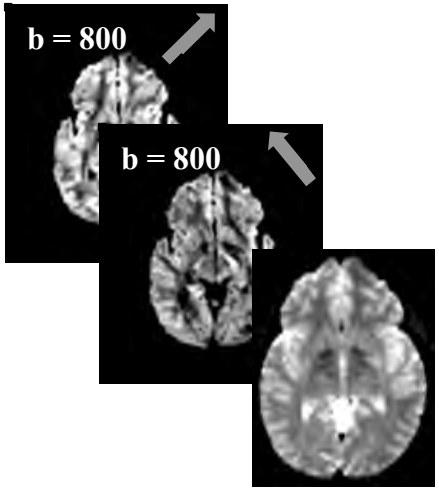


E. O. Stejskal and J. E. Tanner (1965)

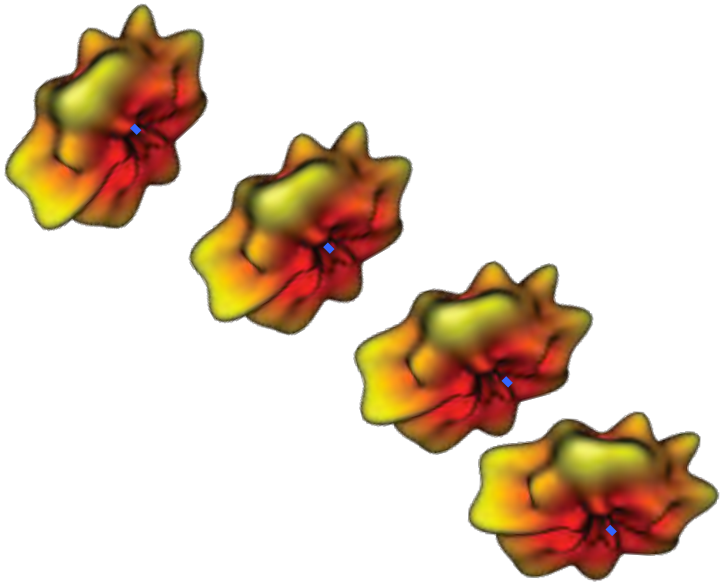
$$S(\theta) = S_0 \, e^{-bD(\theta)}$$

The measured diffusion signal in a direction, θ, is related to the apparent diffusion coefficient in that direction, D(θ)

Diffusion signals in different directions



Tractography algorithms combine the local (voxel) diffusion measurements to estimate white matter tracts (streamlines)



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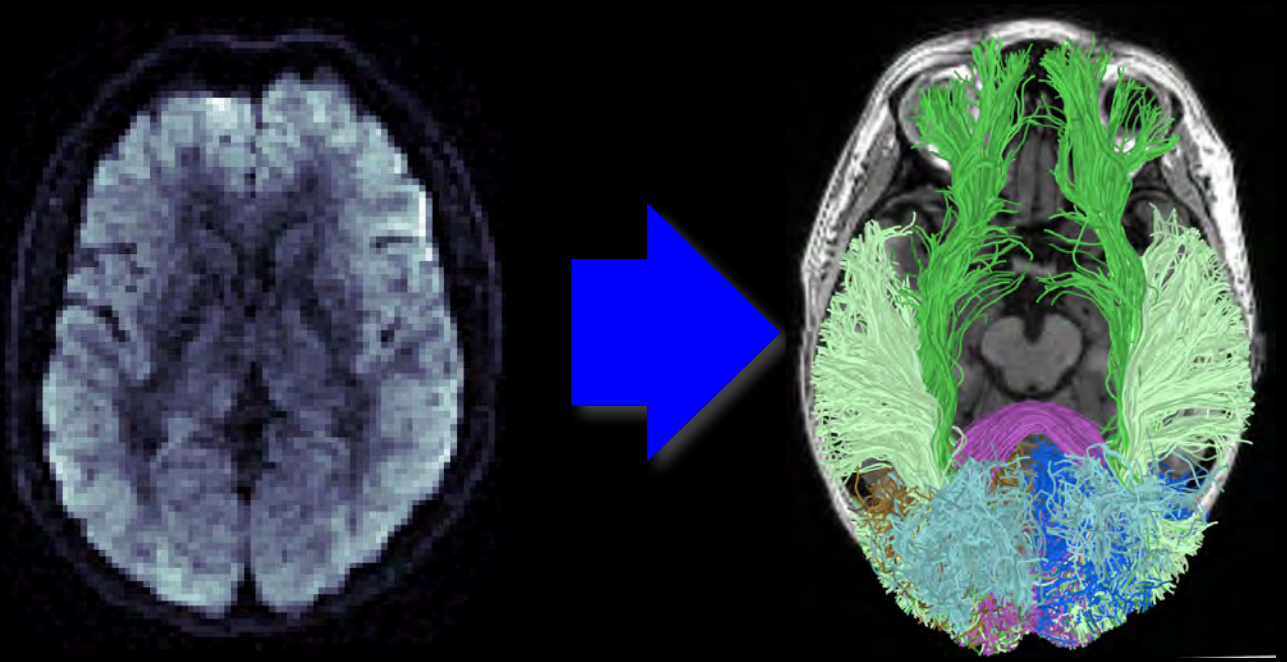
The measured diffusion signal in a direction, θ, is related to the apparent diffusion coefficient in that direction, D(θ)

Tractography modeling, like pRF modeling, is critical for progress

We estimate fascicles from diffusion data, but most investigators do not check the model

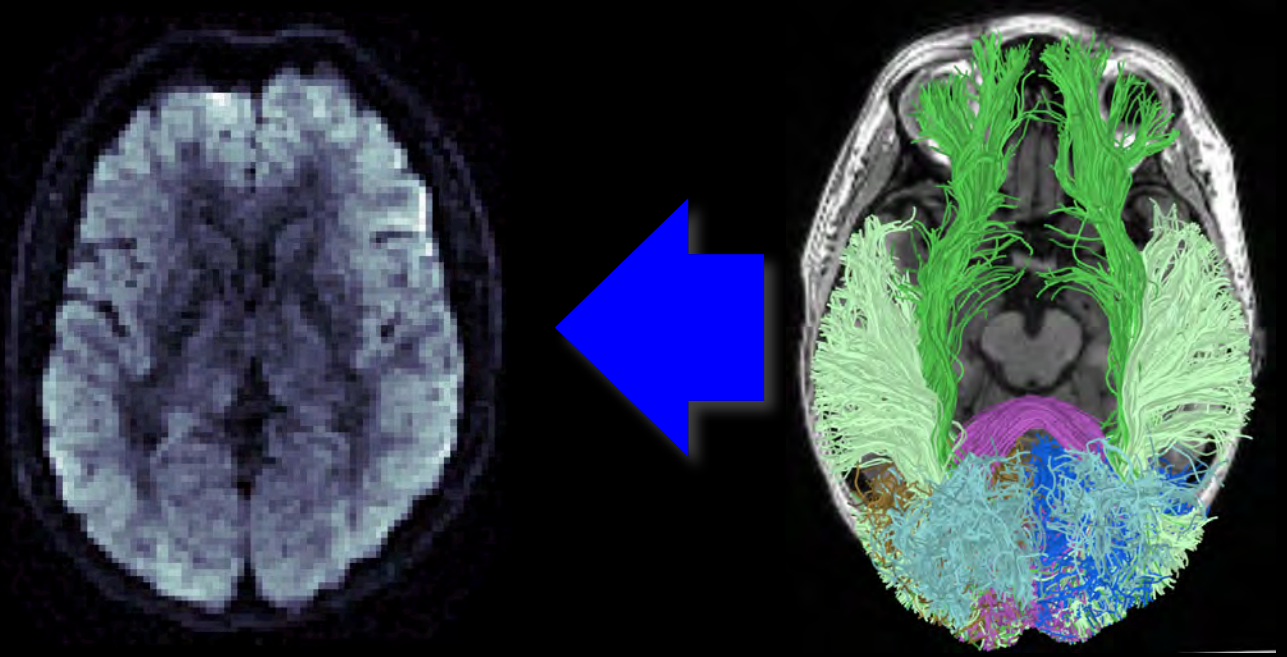


Linear Fascicle Evaluation (LiFE)

Pestilli et al., 2014, *Nature Methods*

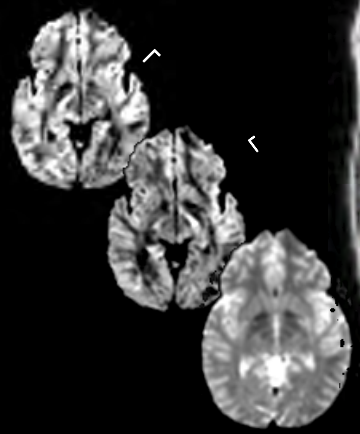
Treat the estimates as a model

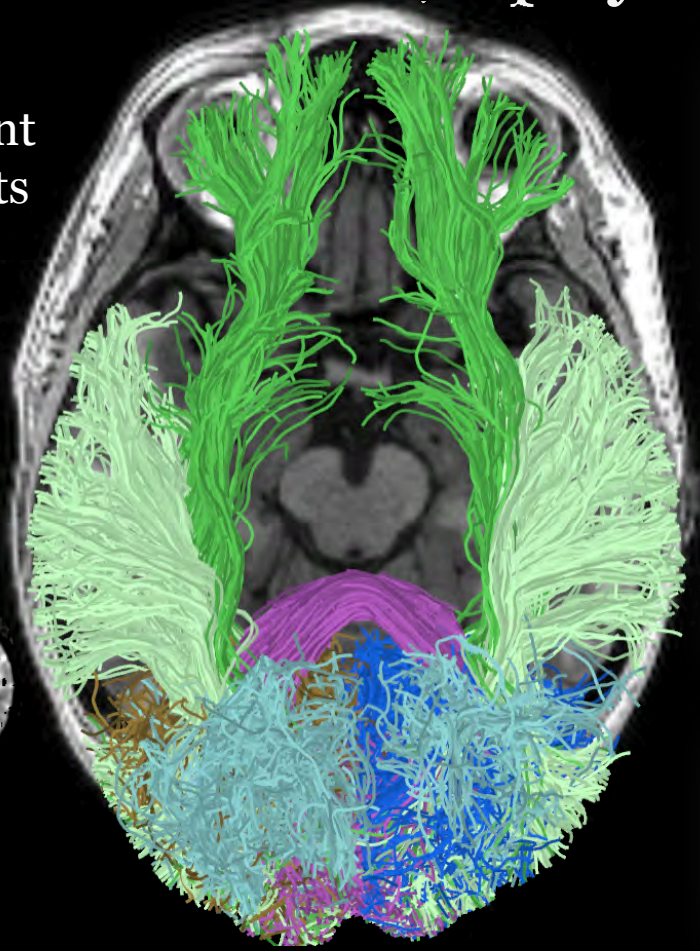
Calculate statistical evaluations of model validity



Tractography modeling

Tracts with at least one endpoint in the visual parts of the brain





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NATURE METHODS | ARTICLE
Evaluation and statistical inference for human connectomes
Franco Pestilli, Jason D Yeatman, Ariel Rokem, Kendrick N Kay & Brian A Wandell

Introduction to LiFE

PLOS | COMPUTATIONAL BIOLOGY
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RESEARCH ARTICLE
Ensemble Tractography
Hiromasa Takemura, Cesar F. Caiafa, Brian A. Wandell, Franco Pestilli
Published: February 4, 2016 • http://dx.doi.org/10.1371/journal.pcbi.1004692

Extension to ensemble method

Annual Review of Neuroscience
Vol. 39: 103-128 (Volume publication date July 2016)
Clarifying Human White Matter
Brian A. Wandell
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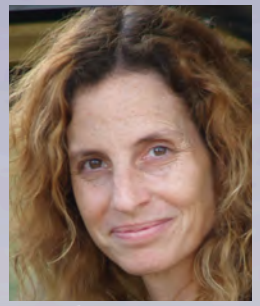
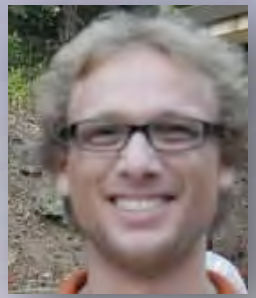
Review of diffusion imaging

Building a model of the circuit for seeing words

Michal Ben-Shachar



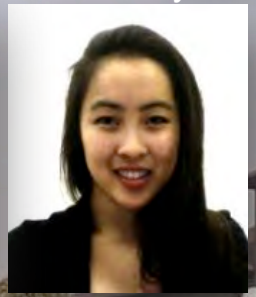
Jason Yeatman



Andreas Rauschecker

Bob Dougherty

Rosemary Le



Nathan Witthoft

Kaoru Amano

QUANTITATIVE MEASUREMENTS

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COMPUTATIONAL MODELS

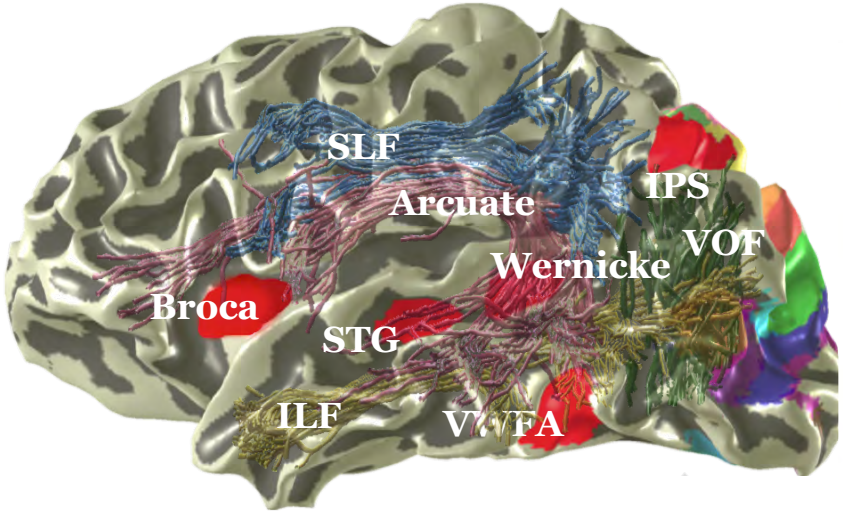
∞

CHECK AND SHARE

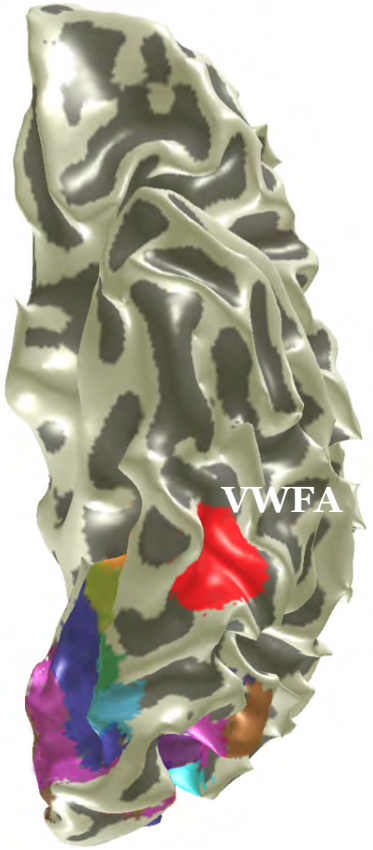
Major components of the reading pathway

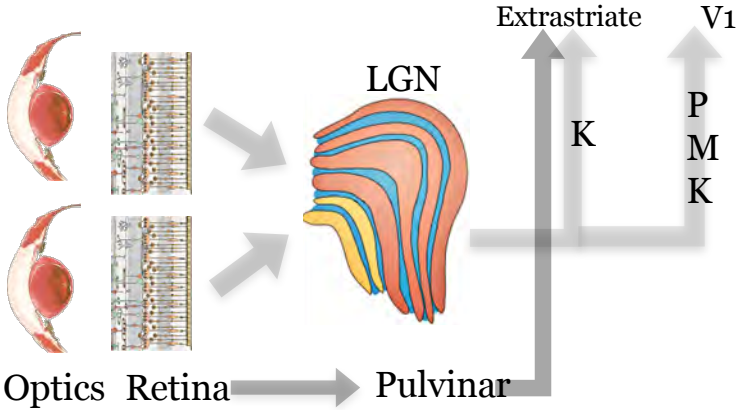
The goal: Diagnosis

Identifying the locations and responses in a poor reader that differ significantly from measurements in good readers



Wandell and Le (2017)



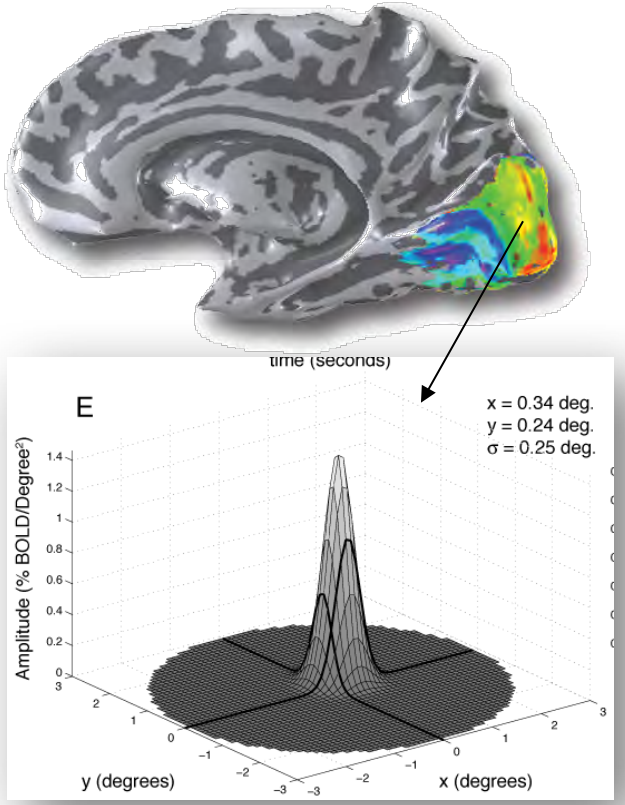


Learning to See Words
B.A. Wandell, A. Rauschecker and J. Yeatman (2012).
Annual Review of Psychology Vol. 63, pp.31-53.

Tracing the signal through the system

Amano et al. 2009

- A single voxel within, say, V1 has a pRF position and size
- Combining the pRFs from the voxels in a region tells us about its field of view
- In early visual field maps, the population receptive fields tile large portions of the visual field



Measuring the field of view of cortical regions

Amano et al. 2009

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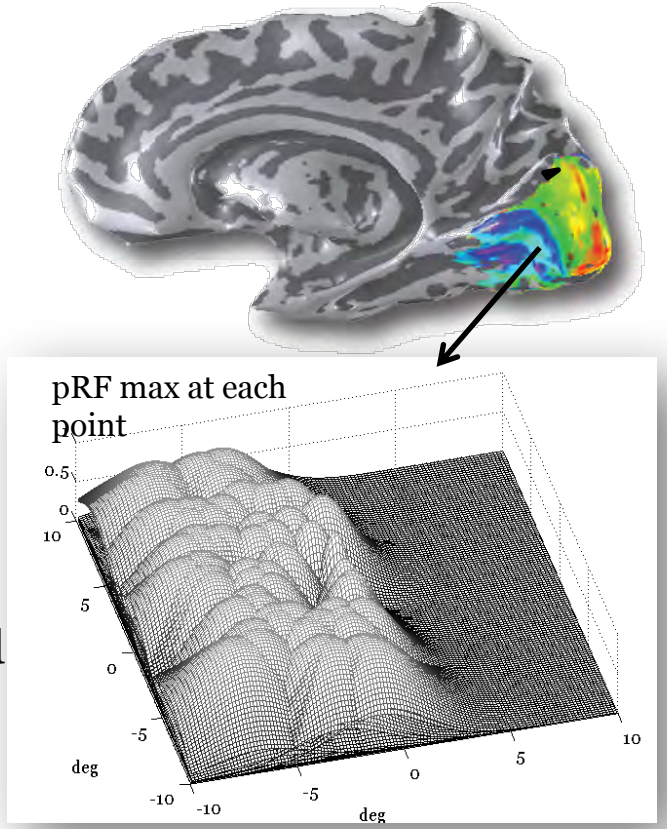

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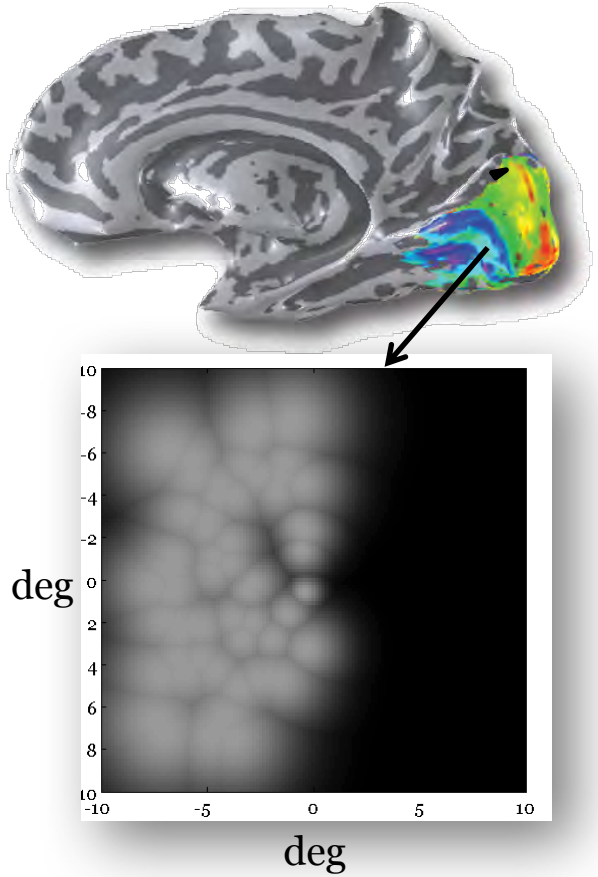
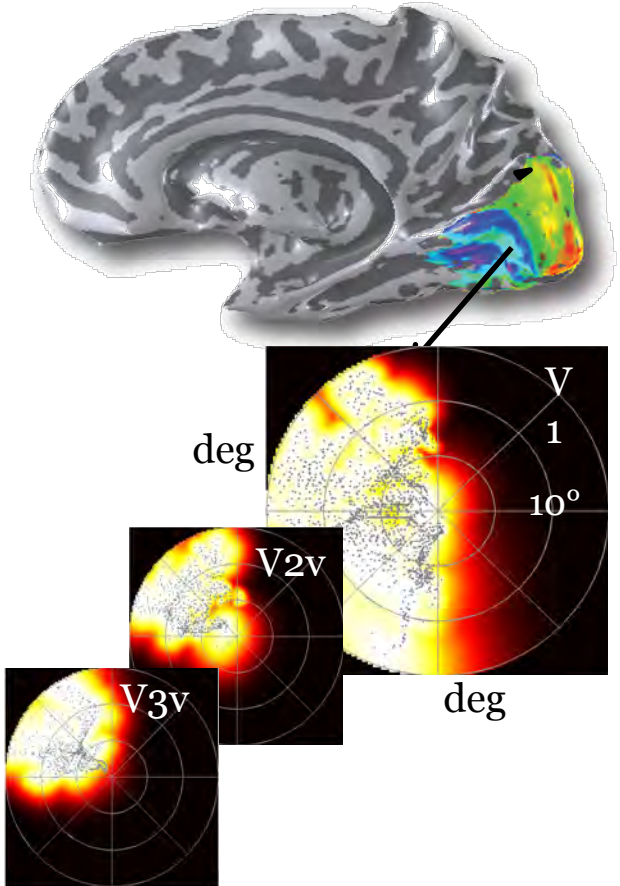


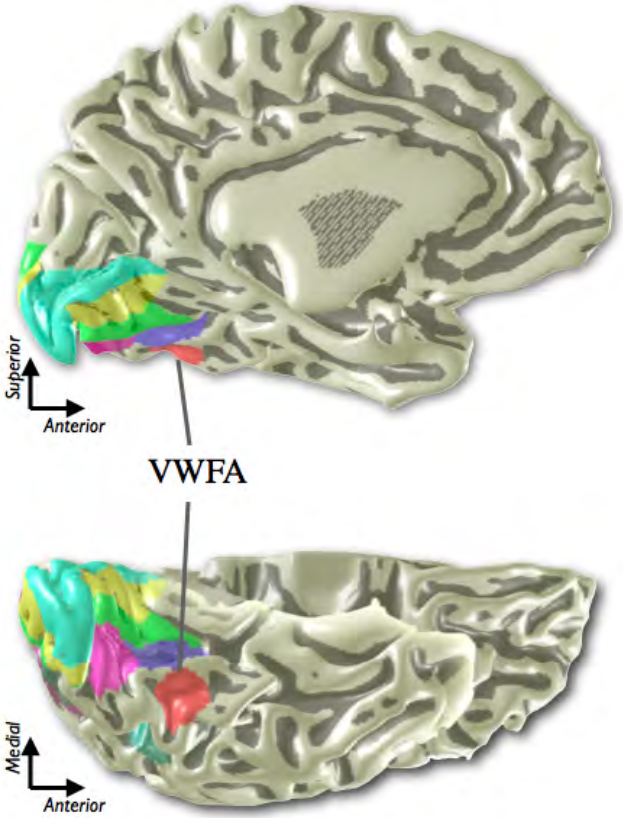
Measuring the field of view of cortical regions

Amano et al. 2009

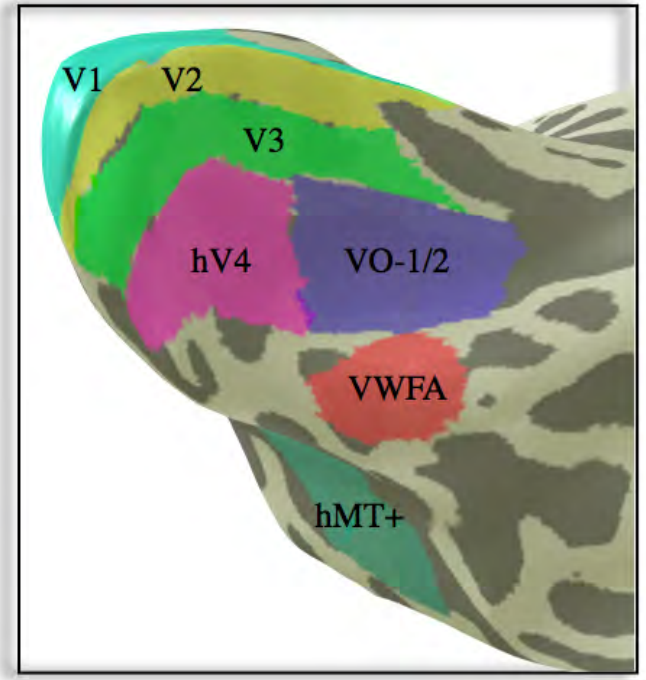
- A single voxel within, say, V1 has a pRF position and size
- Combining the pRFs from the voxels in a region tells us about its field of view
- The early visual field maps, the pRF field of view covers large portions of the visual field



Locating reading circuits and maps



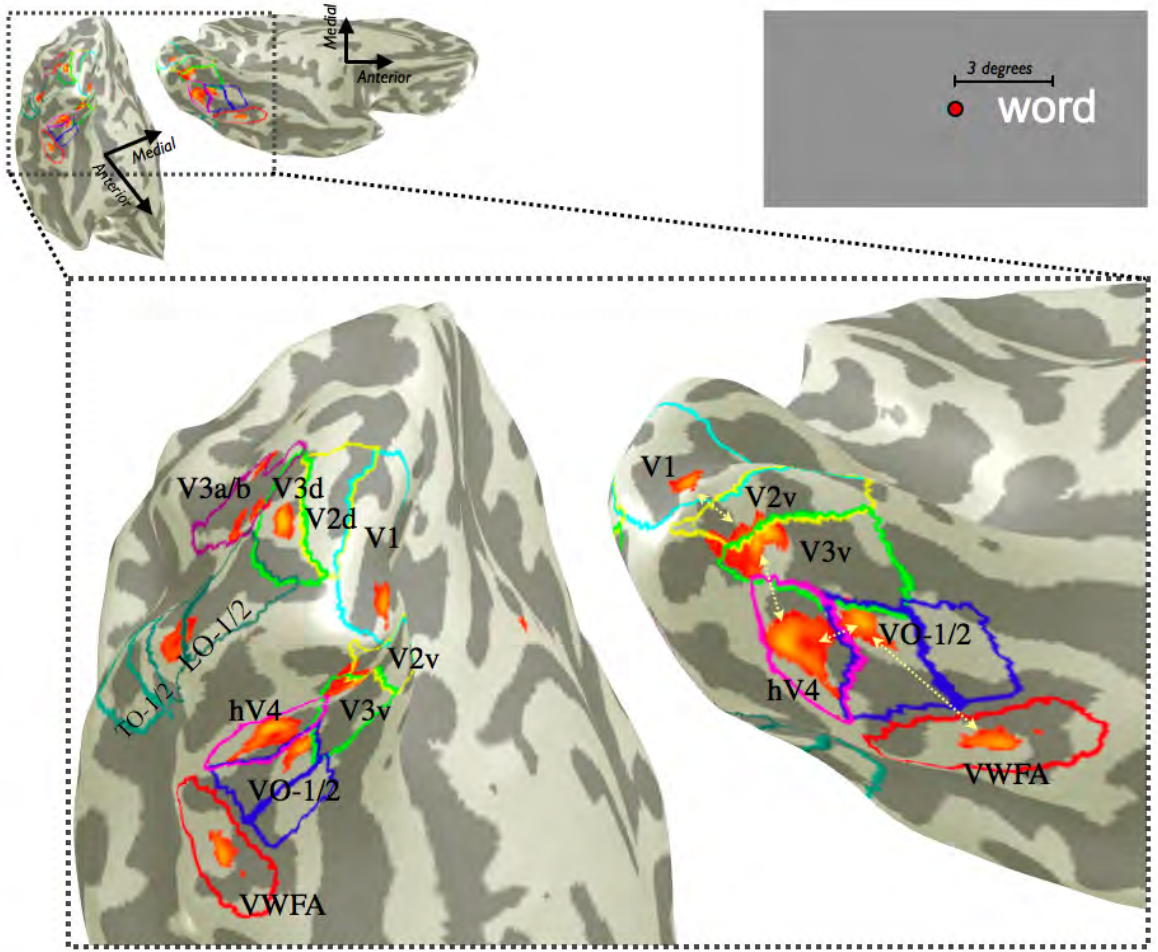
VWFA - essential for reading, but not unique to reading



Measuring the activity while reading (fMRI)

We can see the locations of the cortical activations during reading

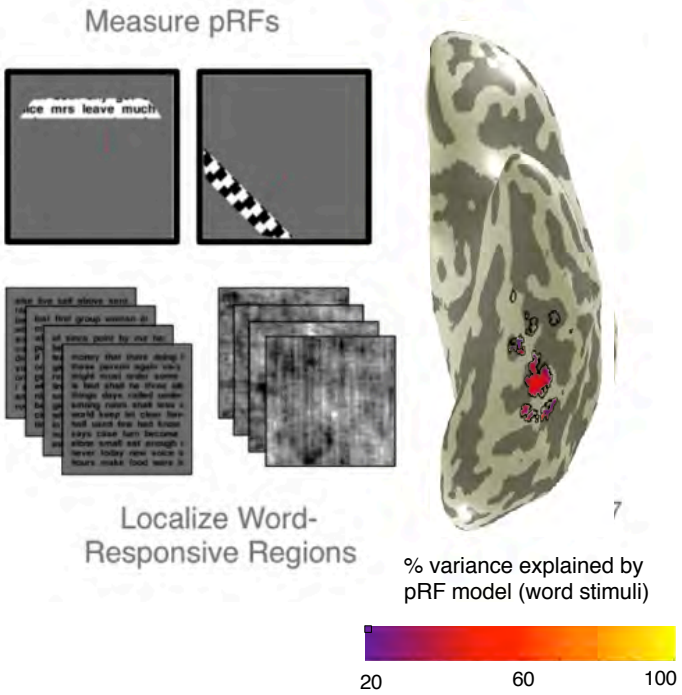
Through the maps and on to the VWFA

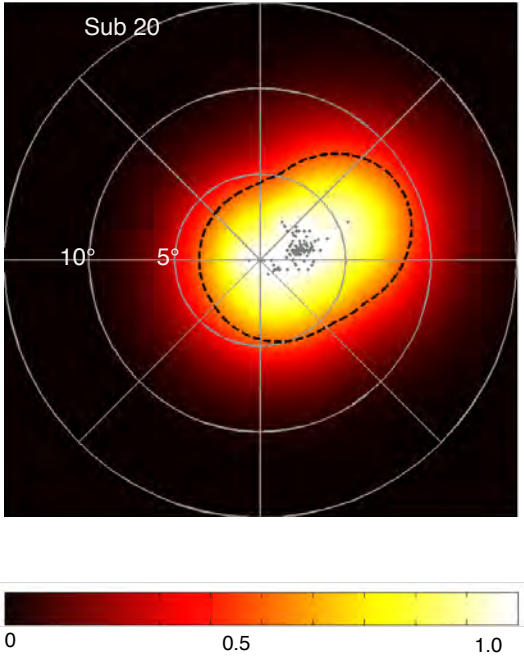


Field of view in reading circuitry of a single subject

The portion of cortex engaged in reading only sees a small part of the visual field

This may be why it is very hard to read in the peripheral field





Small field of view for the reading circuitry

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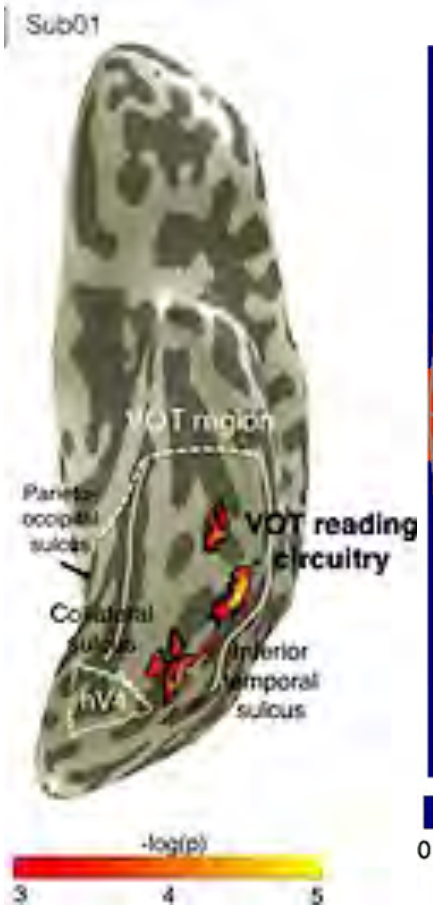
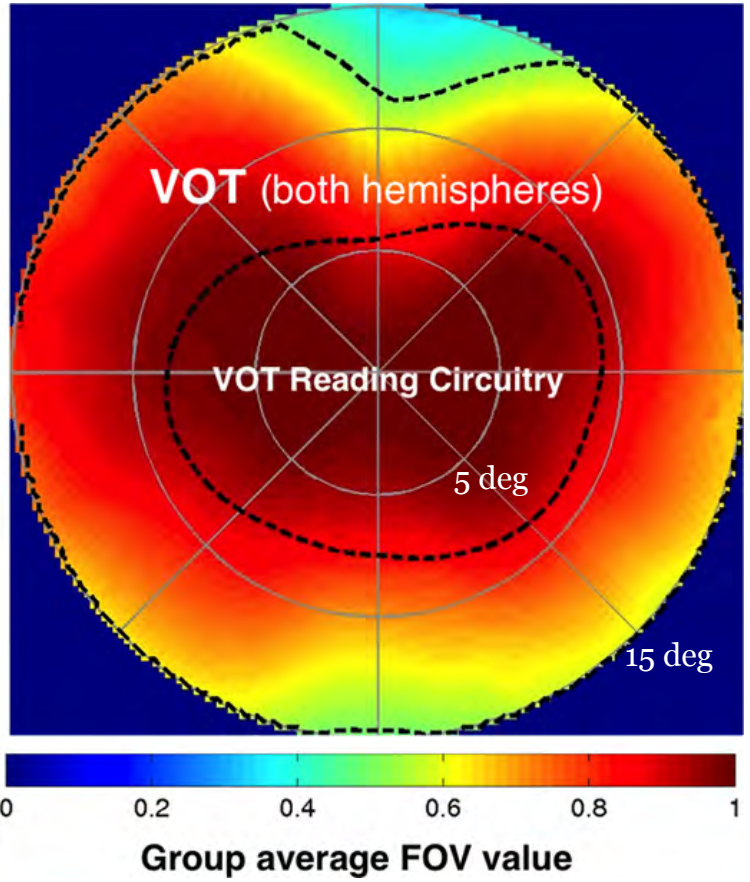


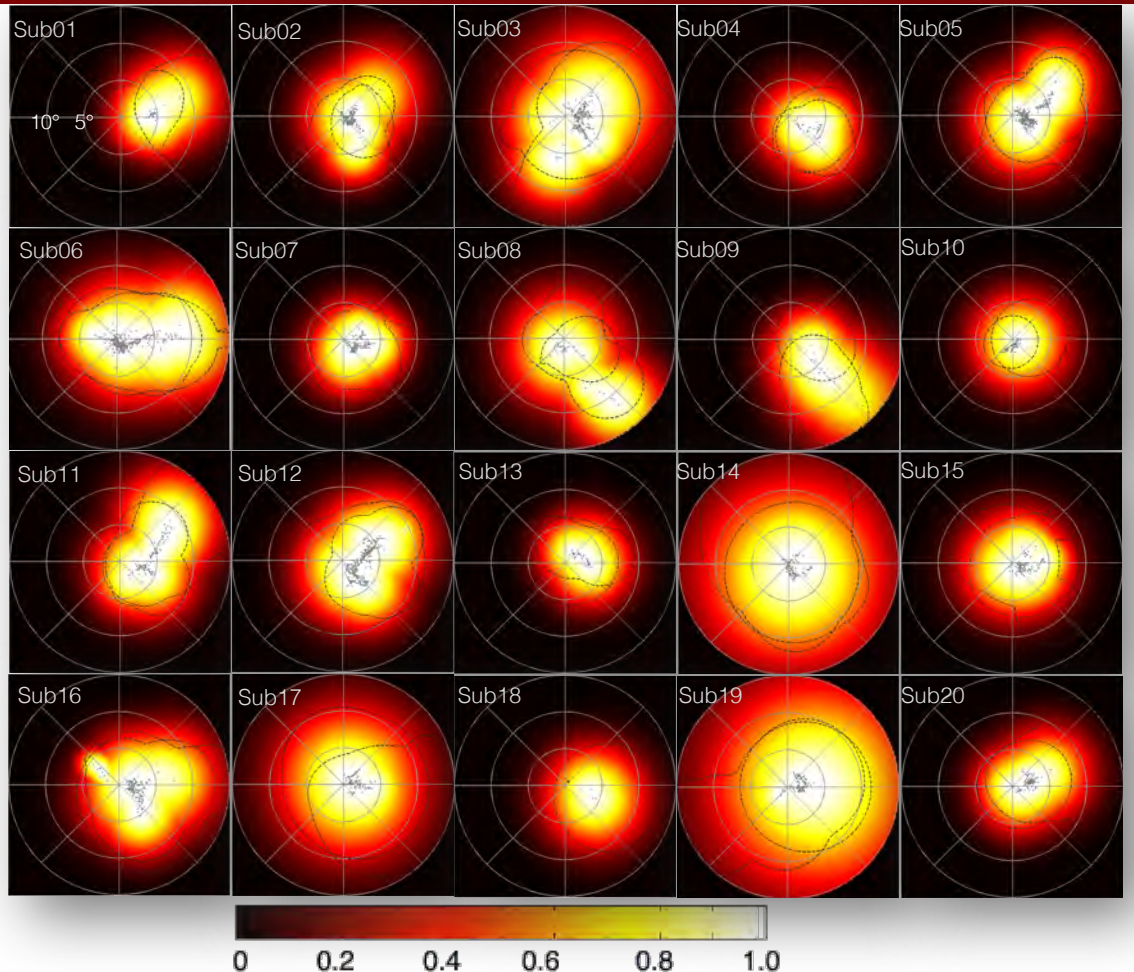
Left and right hemispheres



Le et al. 2017
Journal of Vision

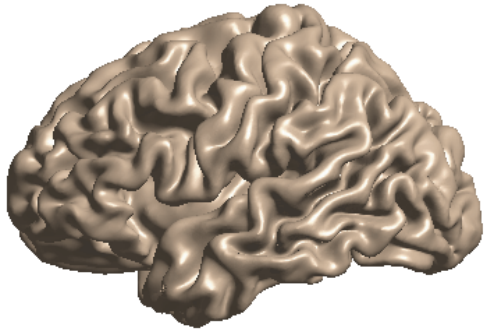
Field of view of the VOT reading reading circuitry

- There are significant differences between subjects
- Yes, we are correlating these differences with measures of word recognition
- FOV value: relative effectiveness in evoking a response in ROI

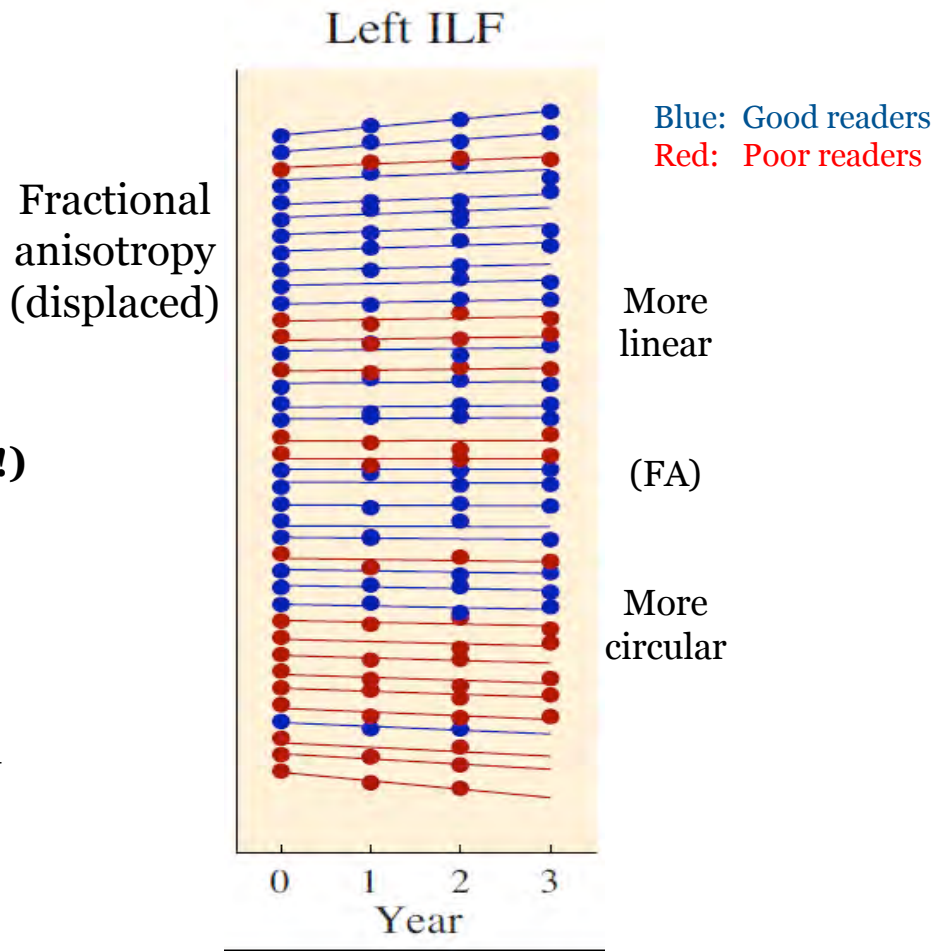


Left hemisphere only

Diffusion (FA) changes differs between good and poor readers



- Measured brain and behavior at 4 time points **(data management!)**
- The first measurements predict reading over the next few years
- The rate and direction of FA development differs between good and poor readers in both the Arcuate and the ILF



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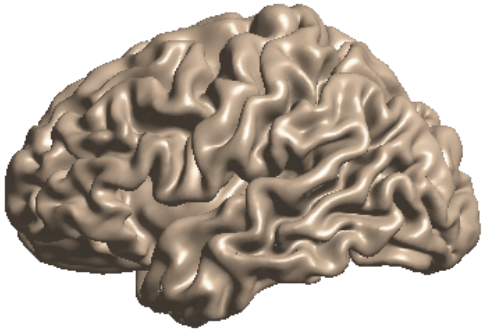

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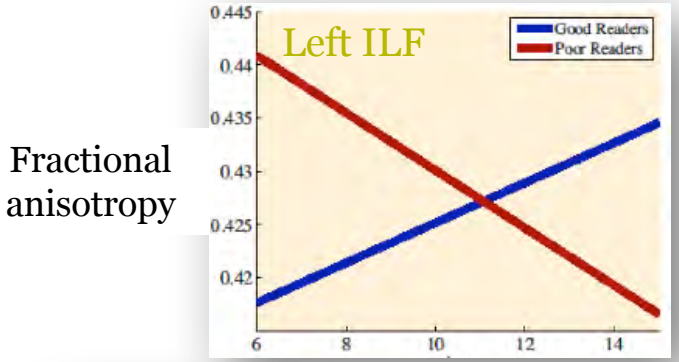
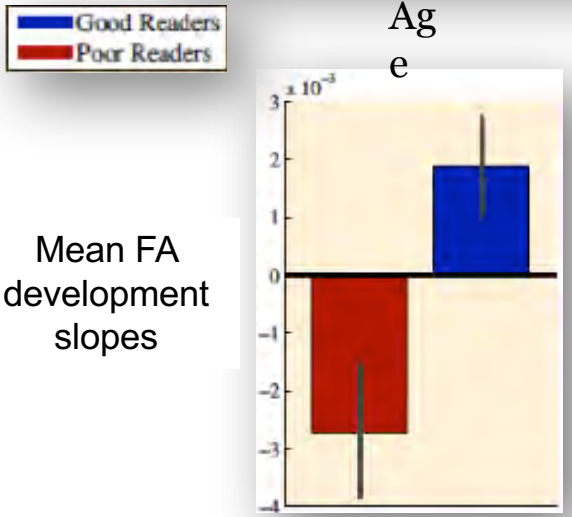


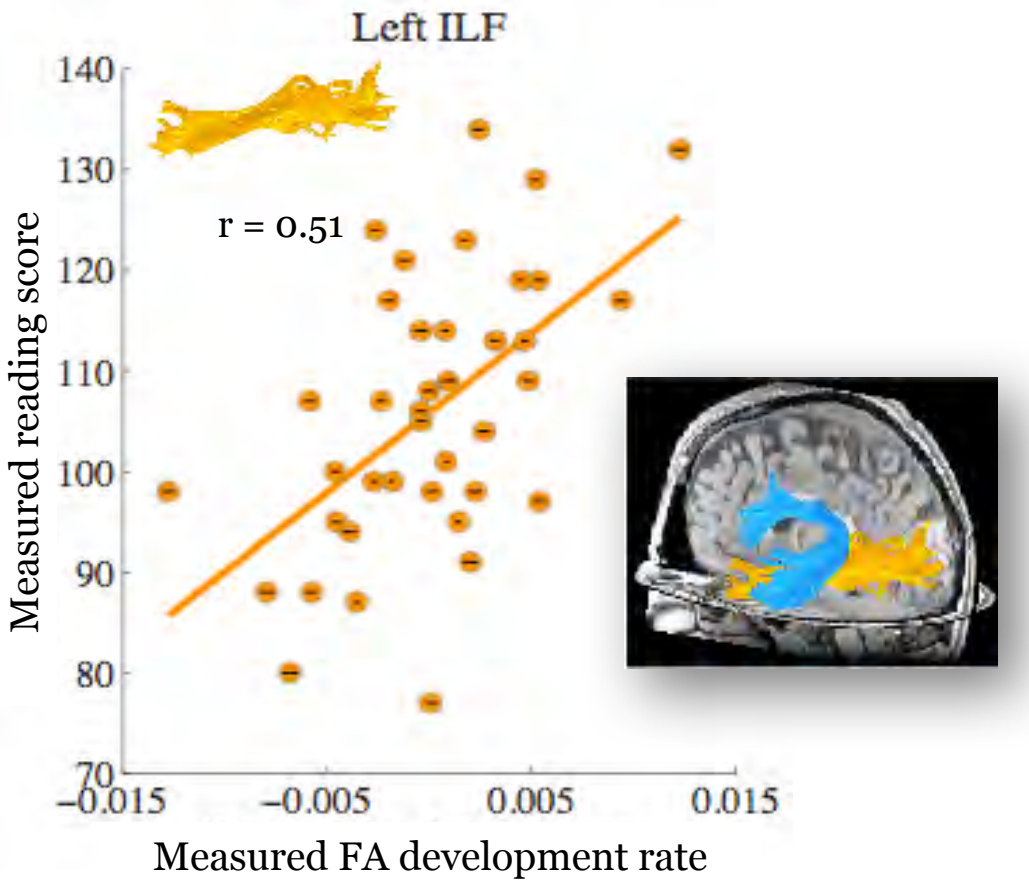


Correlations between tract diffusion change and seeing words

(Yeatman et al., 2012, *PNAS*)

- Development measured by dMRI in the ILF and Arcuate, but not others tracts, correlates with the ability to rapidly see words

- This is one reason we think that the wires are active, changing in response to learning and memory

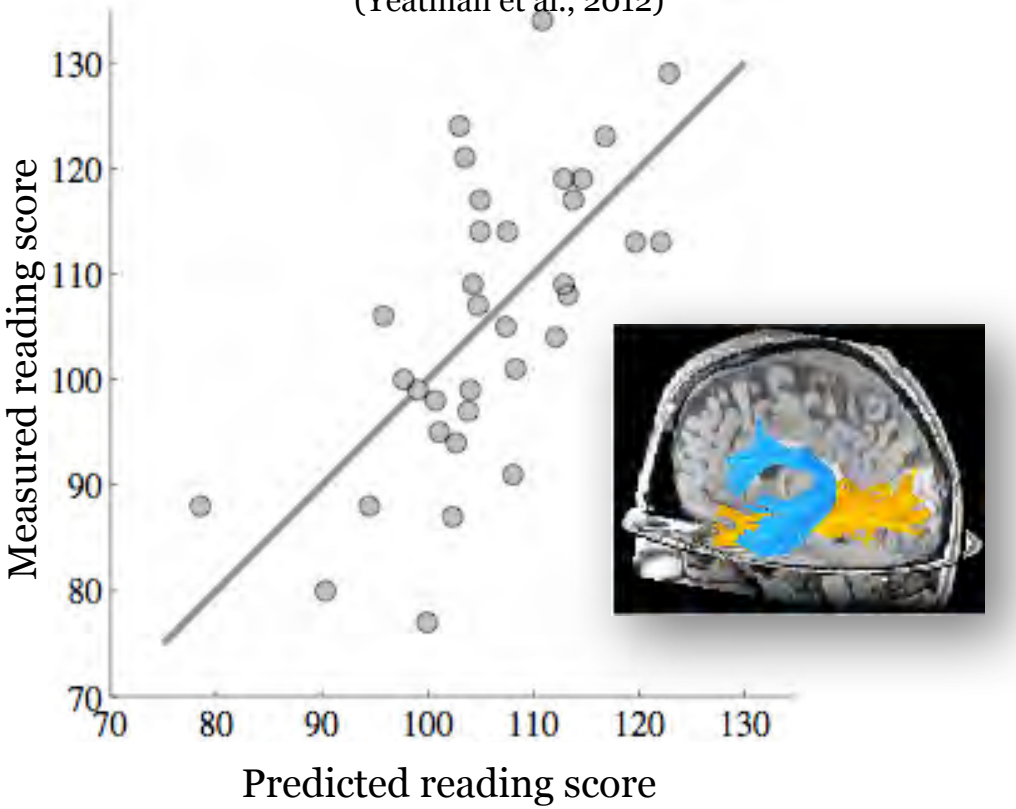


Neuroprognosis

- Simple models that combine tissue properties from two tracts (ILF and AF) predict measured reading skill

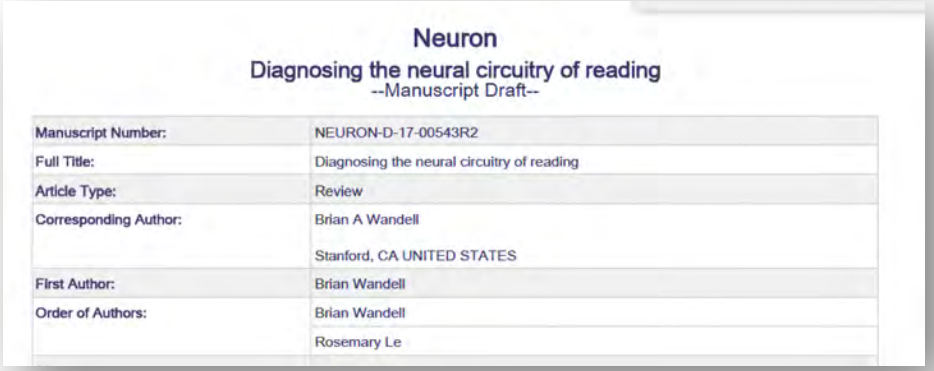
- The predictions are not yet useful; they are statistically reliable

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



Diagnosing the reading circuitry

To appear in Neuron, Oct. 2017



Neuron

Diagnosing the neural circuitry of reading

--Manuscript Draft--

Manuscript Number:	NEURON-D-17-00543R2
Full Title:	Diagnosing the neural circuitry of reading
Article Type:	Review
Corresponding Author:	Brian A Wandell Stanford, CA UNITED STATES
First Author:	Brian Wandell
Order of Authors:	Brian Wandell Rosemary Le

Diagnostics

Identifying the locations and responses in a poor reader that differ significantly from measurements in good readers

We summarize the current state of knowledge of the brain's reading circuits, and then we describe opportunities to use quantitative and reproducible methods for diagnosing these circuits. Neural circuit diagnostics -- by which we mean identifying the locations and responses in an individual that differ significantly from measurements in good readers -- can help parents and educators in selecting the best remediation strategy. A sustained effort to develop and share diagnostic methods can support the societal goal of improving literacy.

Project on Scientific Transparency

Reproducible research and diagnosis

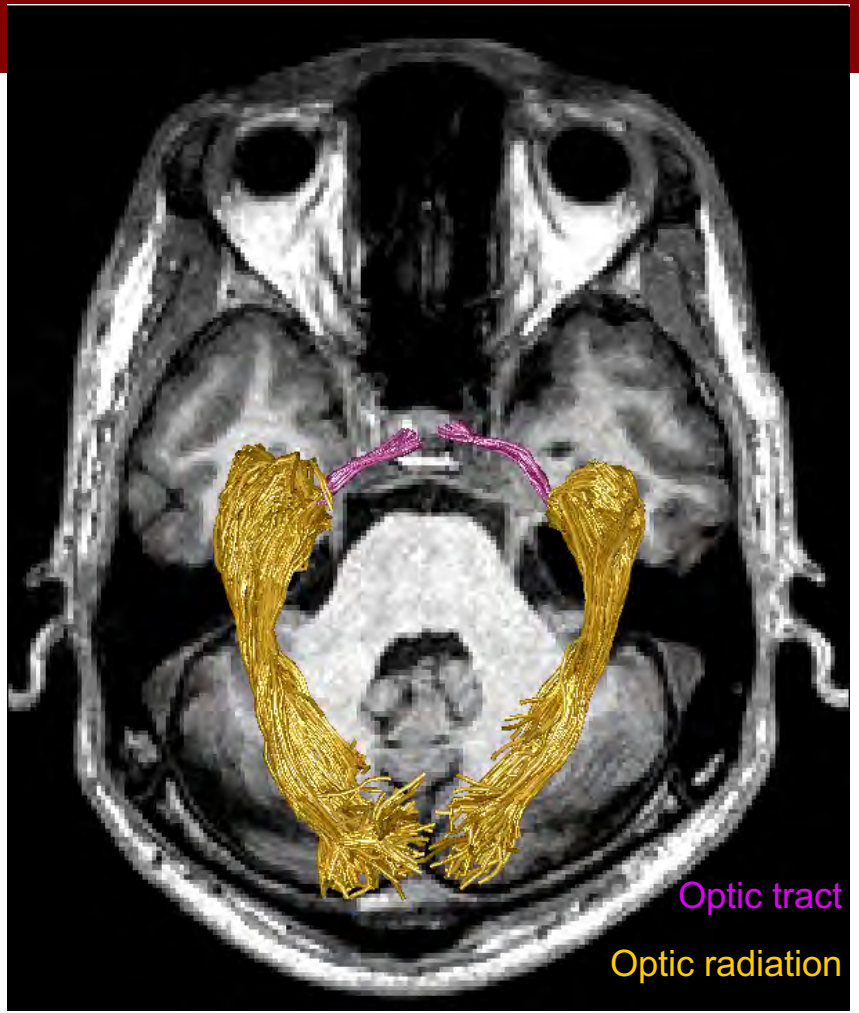
Computational reproducibility is not an afterthought—it is something that must be designed into a project from the beginning. **One does need to develop a whole set of programming and research disciplines** with the end result in mind and stick with them.

Donoho

An invitation to reproducible computational research DAVID L. DONOHO

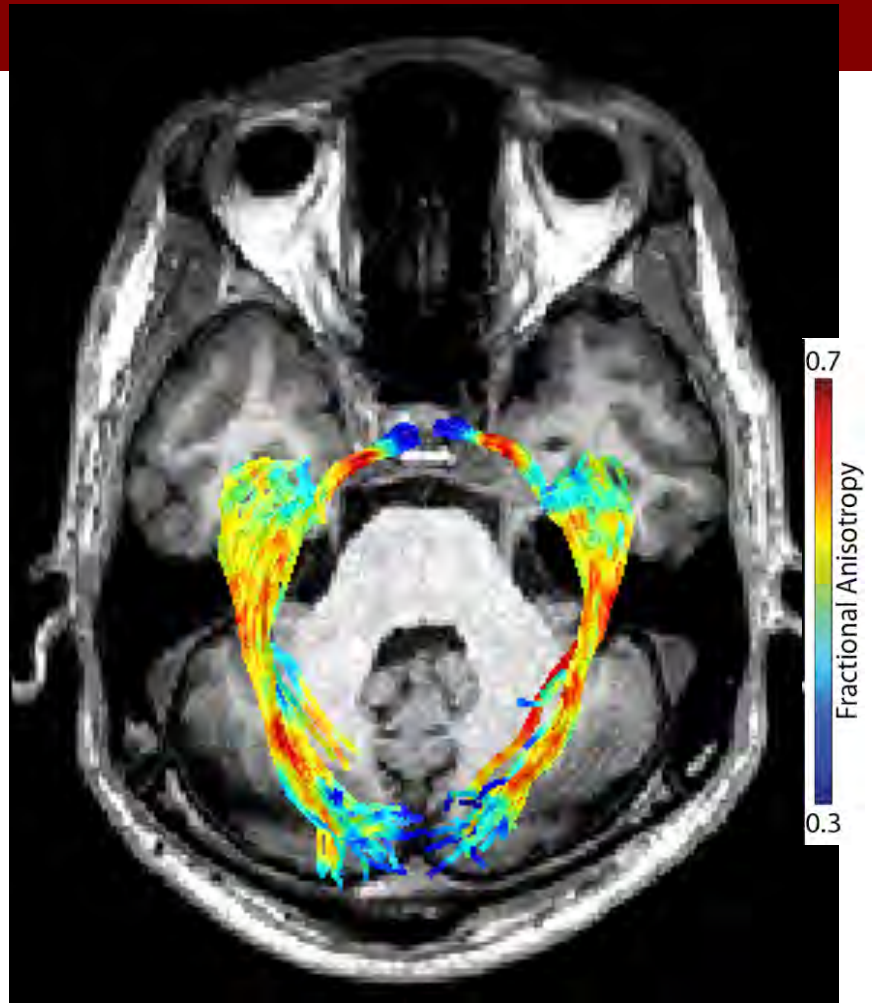
A motivating example

- A subject or patient with a retinal eye disease comes to the lab
- We want to know the consequences of retinal degeneration on cortical structures

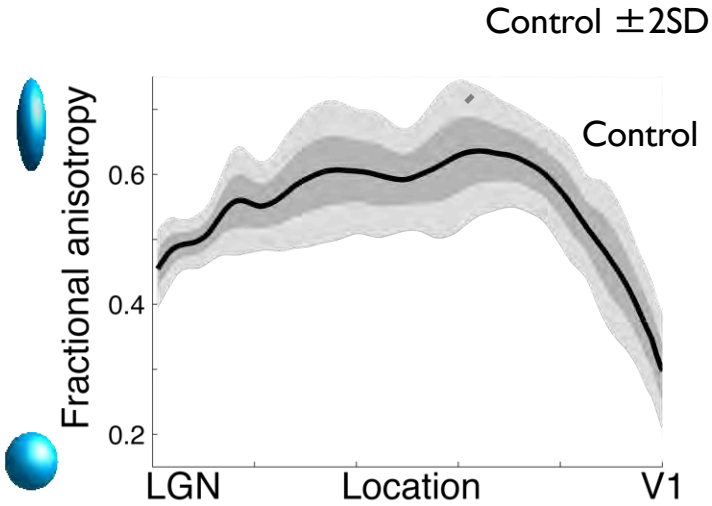


A motivating example

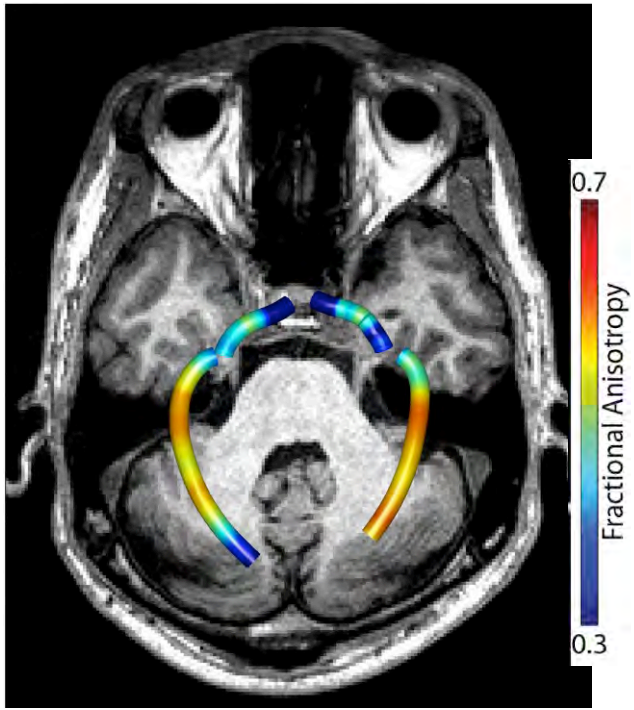
- Measure the subject's visual white matter and secure the data!
- Use validated computational tools for quality assurance
- Use open-source software for tract identification, tissue estimation and comparison with other populations



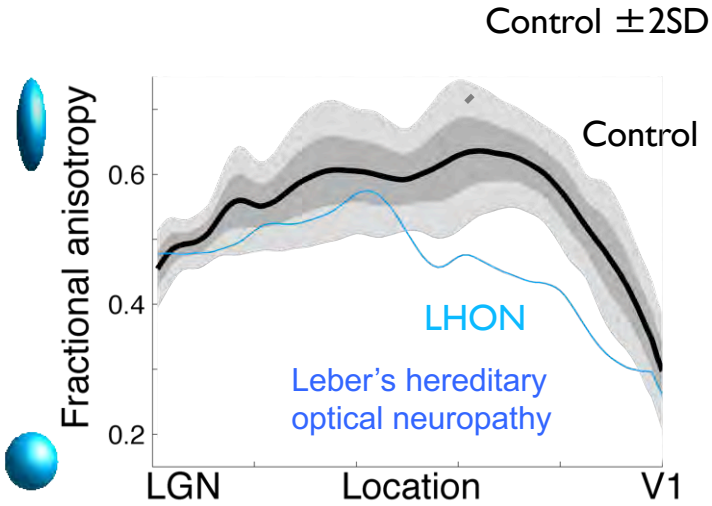
Use databases to find control data



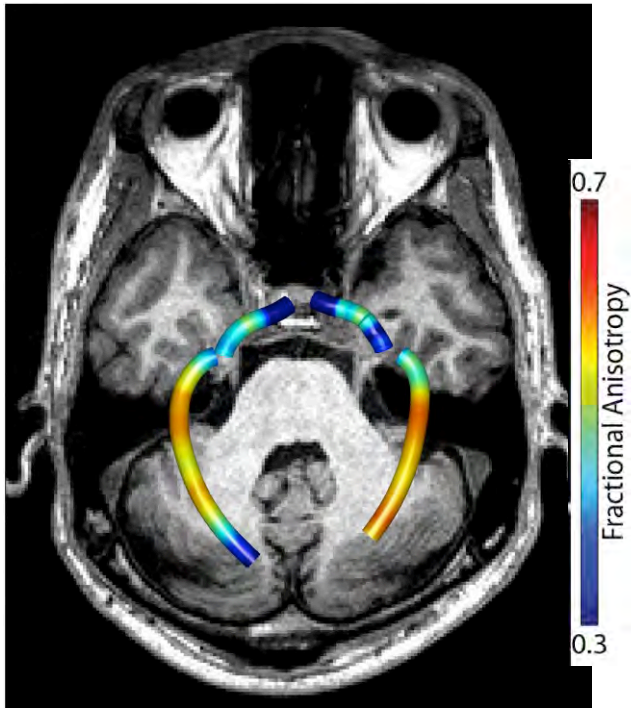
The expectation based on data acquired and stored



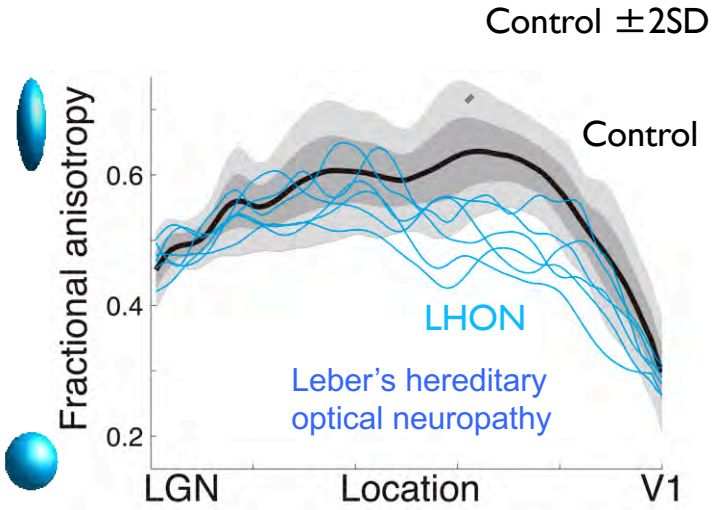
Compare your subject with the distribution and think

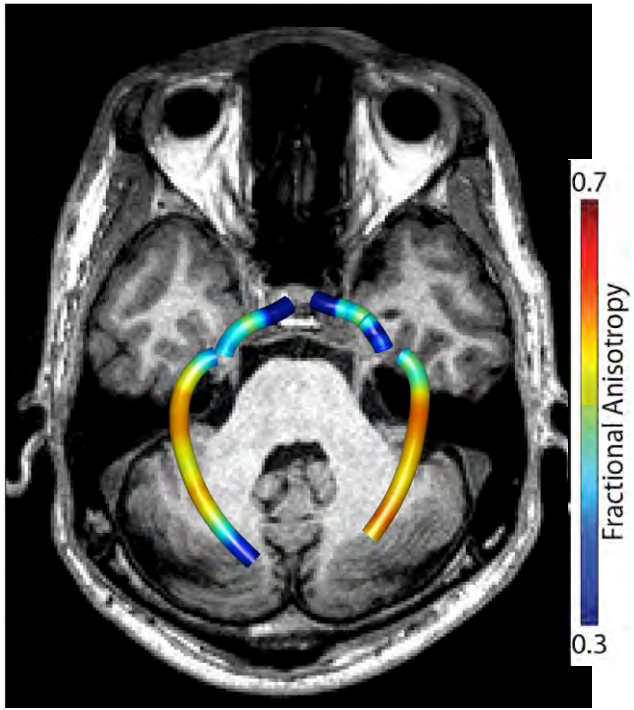


This subject compared to the expectation



Data science and statistics issues



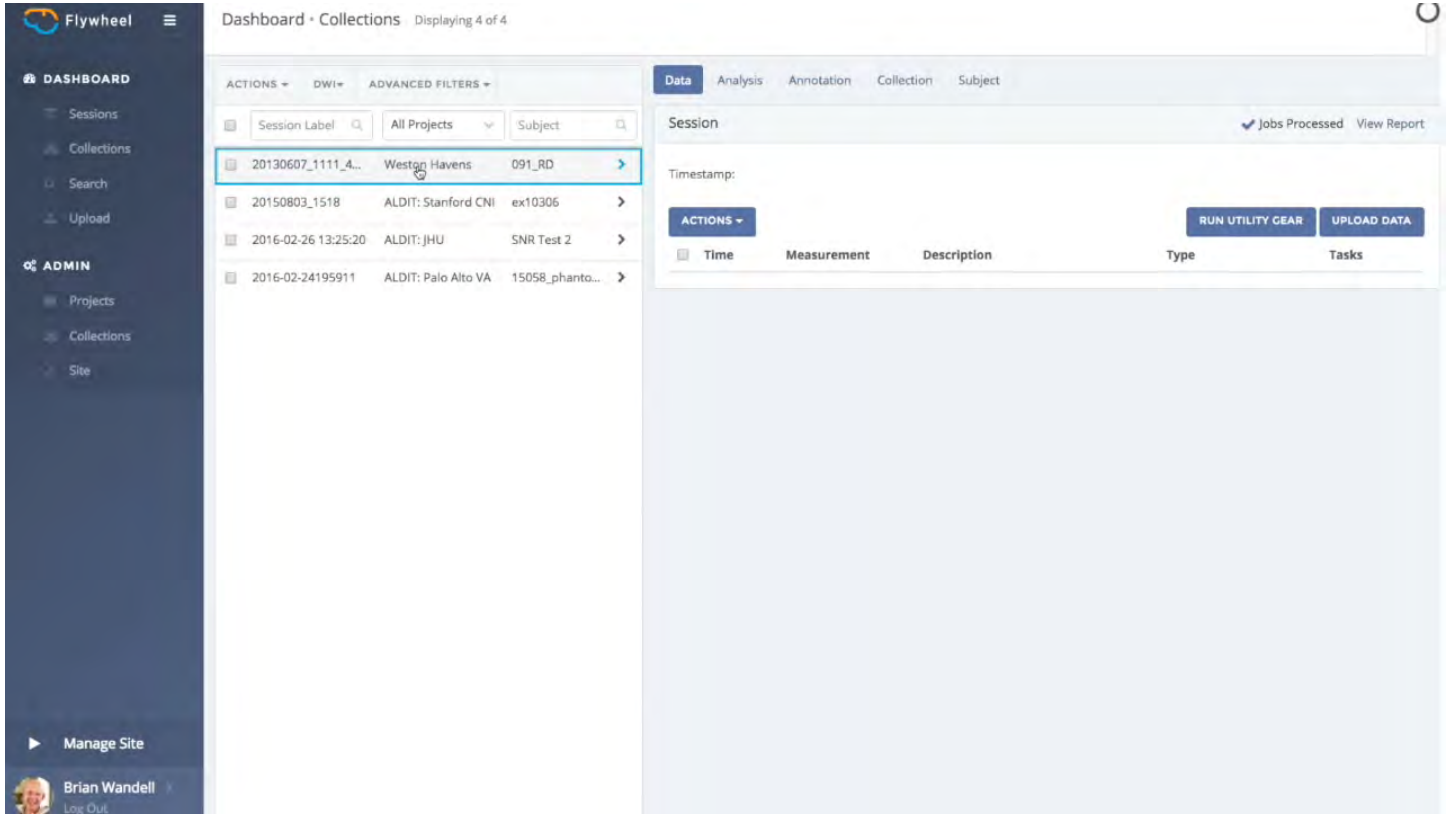


Each subject with the disease has some variation and we would like to know, and track each one over time

Advanced analysis in the Flywheel database (AFQ)

Commercial disclosure:
I am a co-founder of Flywheel, LLC

My lab and MRI center has developed a set of modern software tools to implement these analytical methods



Summary

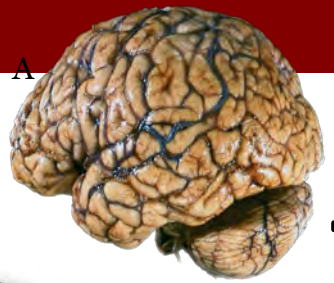
A. About the human brain

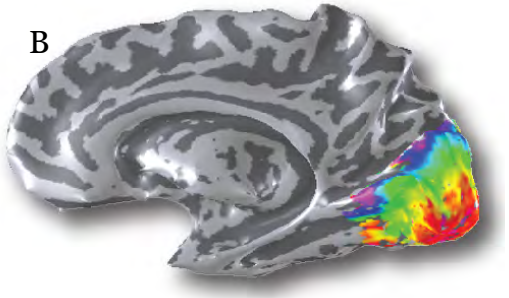
B. MRI measures of brain activity

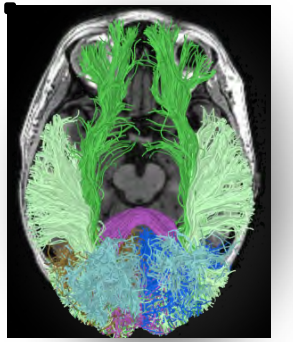
C. MRI measures of brain connections

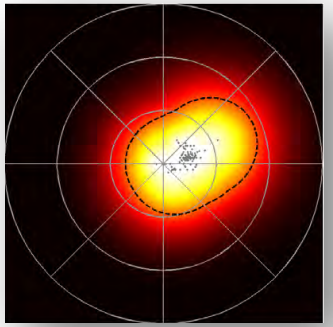
D. Diagnosing reading impairments

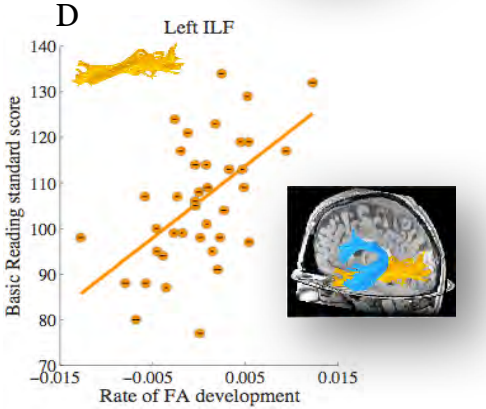
E. Software tools: checking and sharing











Diagnosing the reading circuitry

Thanks to NIH, NSF as well as the Simons, Weston-Havens, and Wallenberg Foundations

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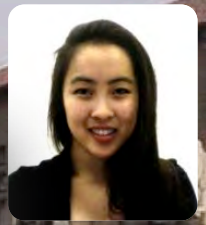
Nathan Witthoft


Alyssa Brewer

Michal Ben-Shachar

Serge Dumoulin

Rosemary Le

Franco Pestilli

Hiromasa Takemura

Jason Yeatman

Kendrick Kay

Jon Winawer

Ariel Rokem