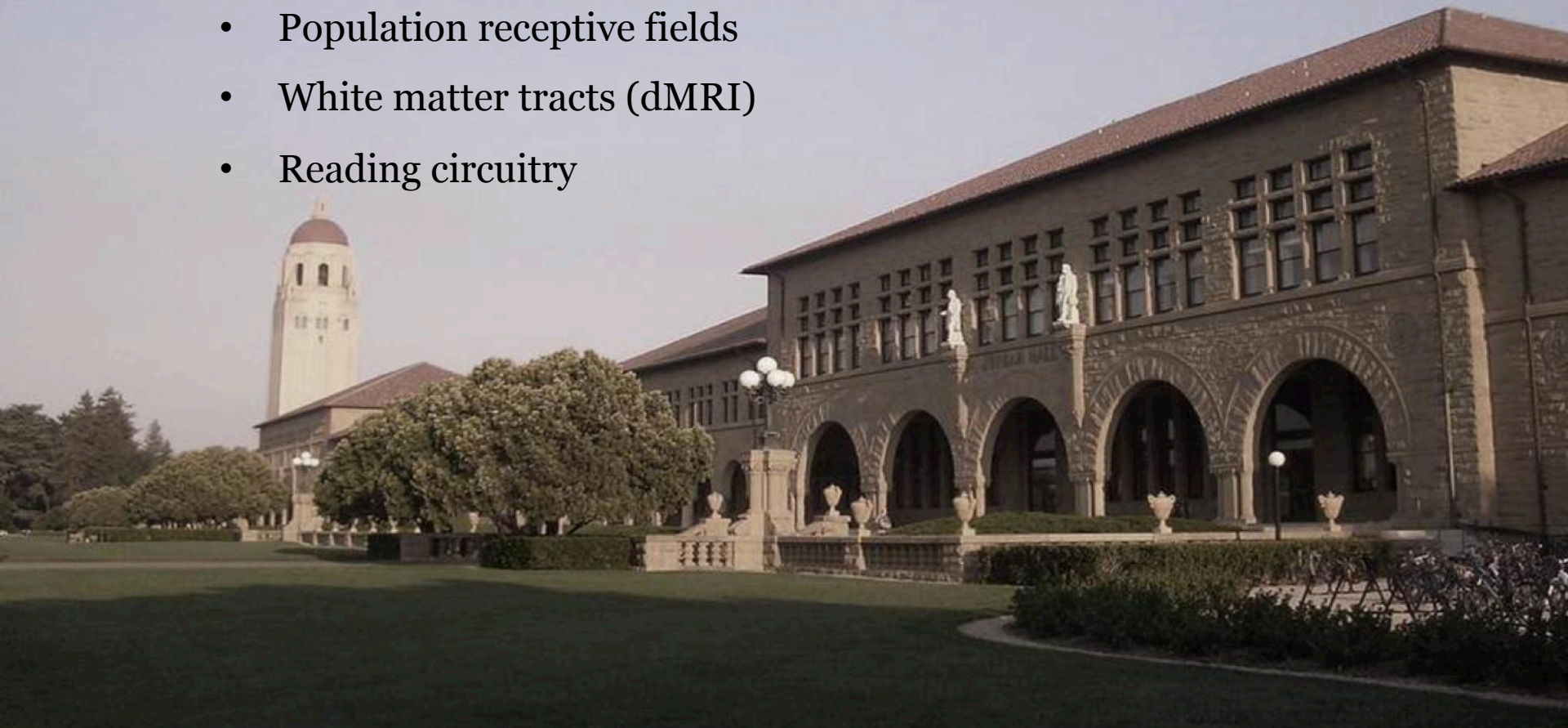


Progress in computational neuroimaging: the reading circuitry

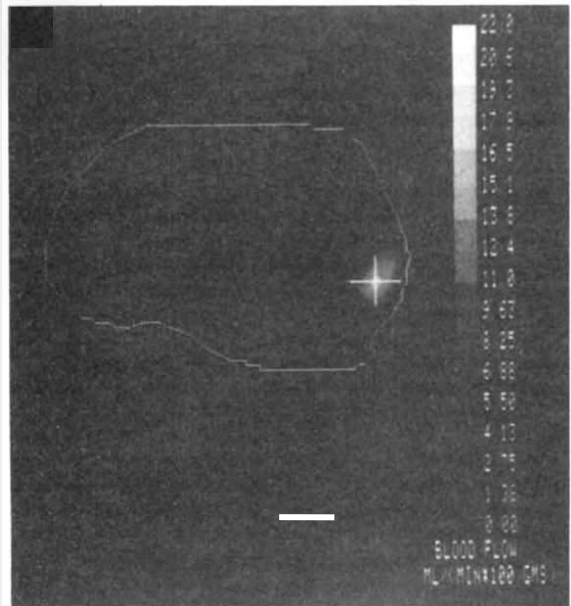
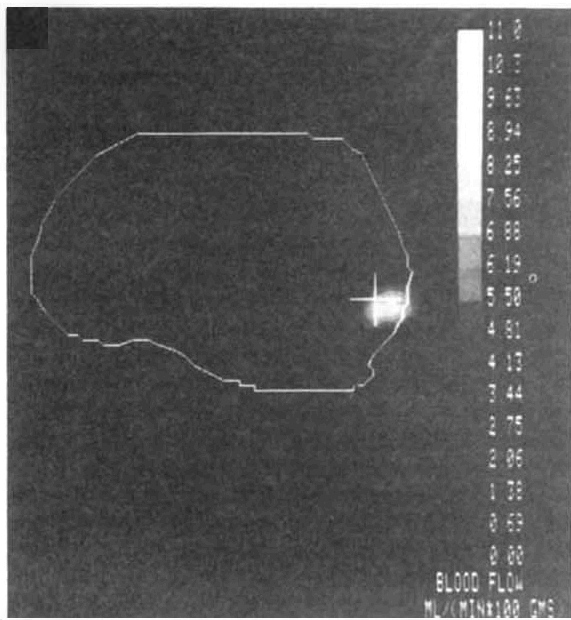
Professor Brian Wandell
Stanford Neurosciences Institute
Department of Psychology
Stanford University

- Retinotopic maps
- Population receptive fields
- White matter tracts (dMRI)
- Reading circuitry

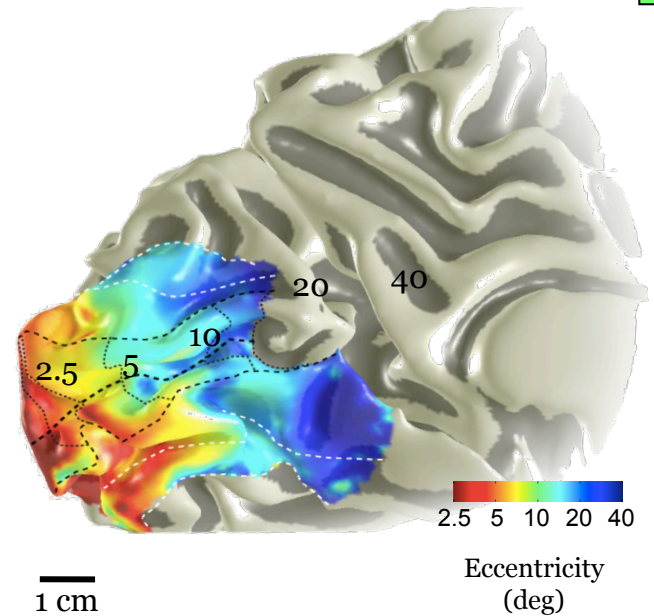
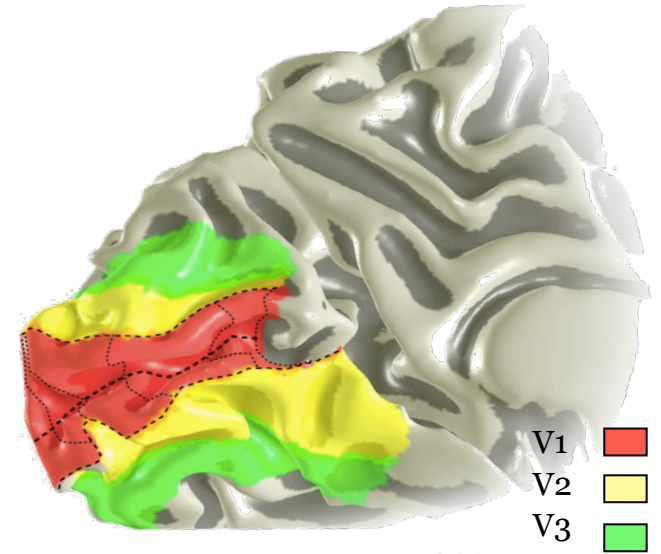
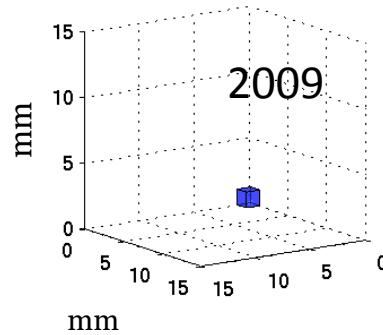
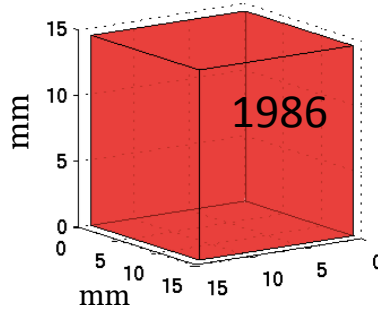


Remarkable progress in 25 years

(Wandell and Winawer, 2011)



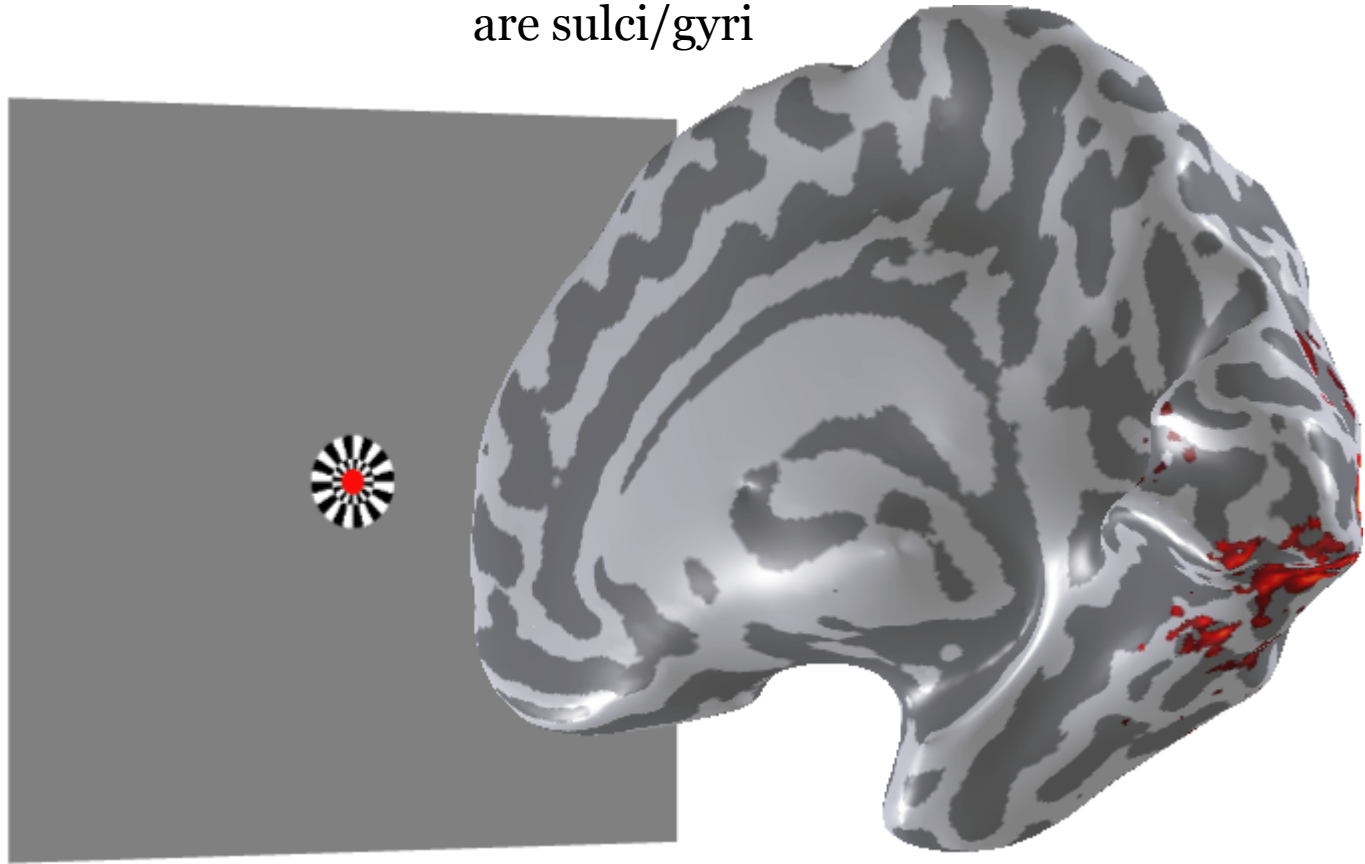
Voxel size



Human eccentricity mapping with fMRI

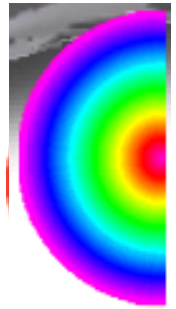
(Engel et al., 1994,1997; Sereno; Tootell, DeYoe; Others)

- Inflated brain
- Gray/white are sulci/gyri

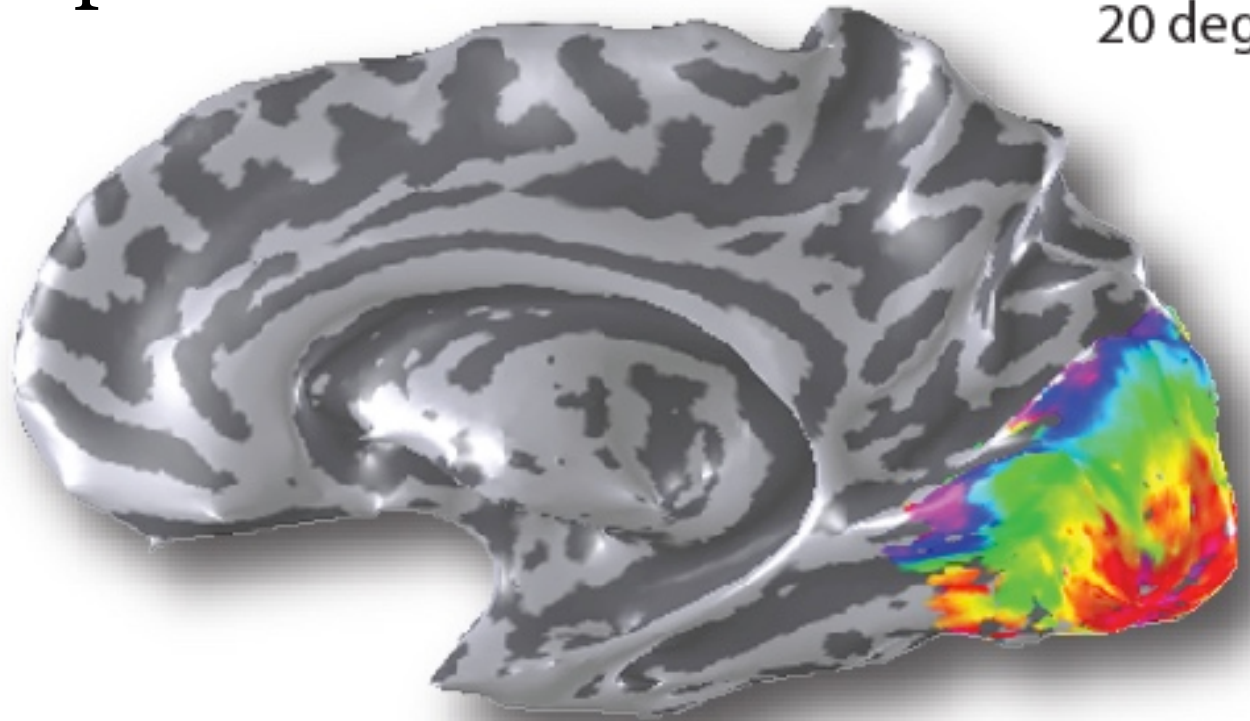


Pseudo-color representation of visual field map

- Inflated brain
- Gray/white are sulci/gyri



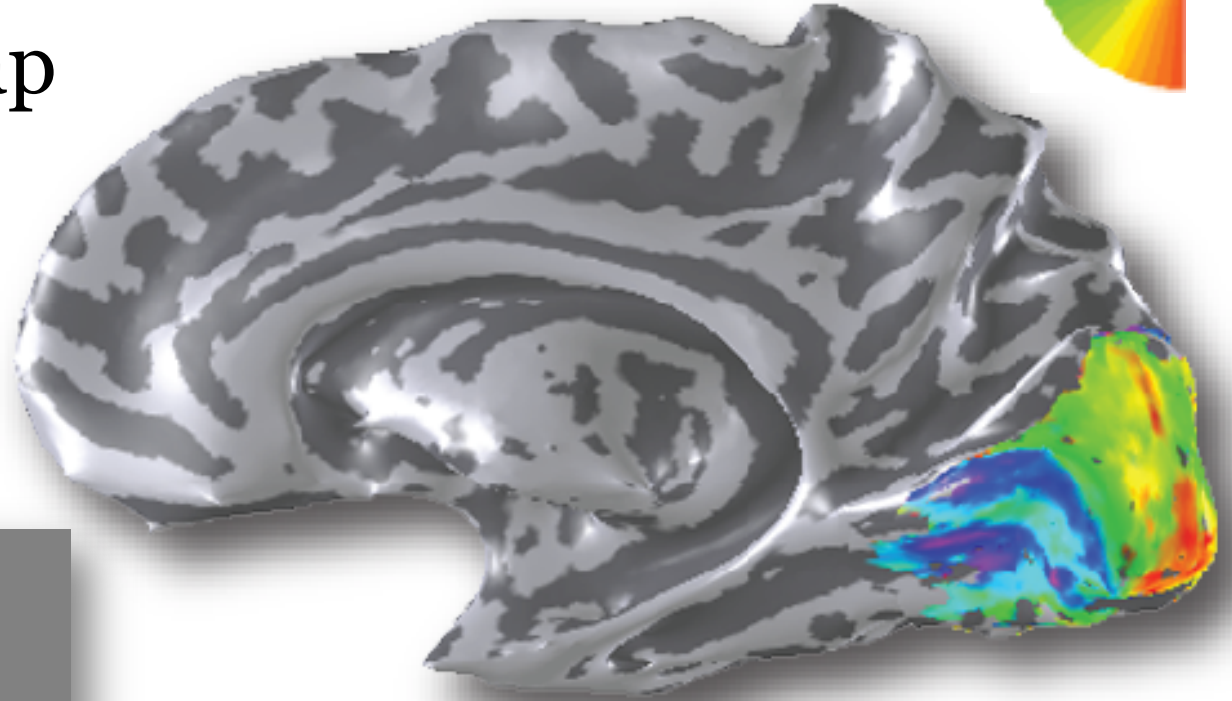
20 deg



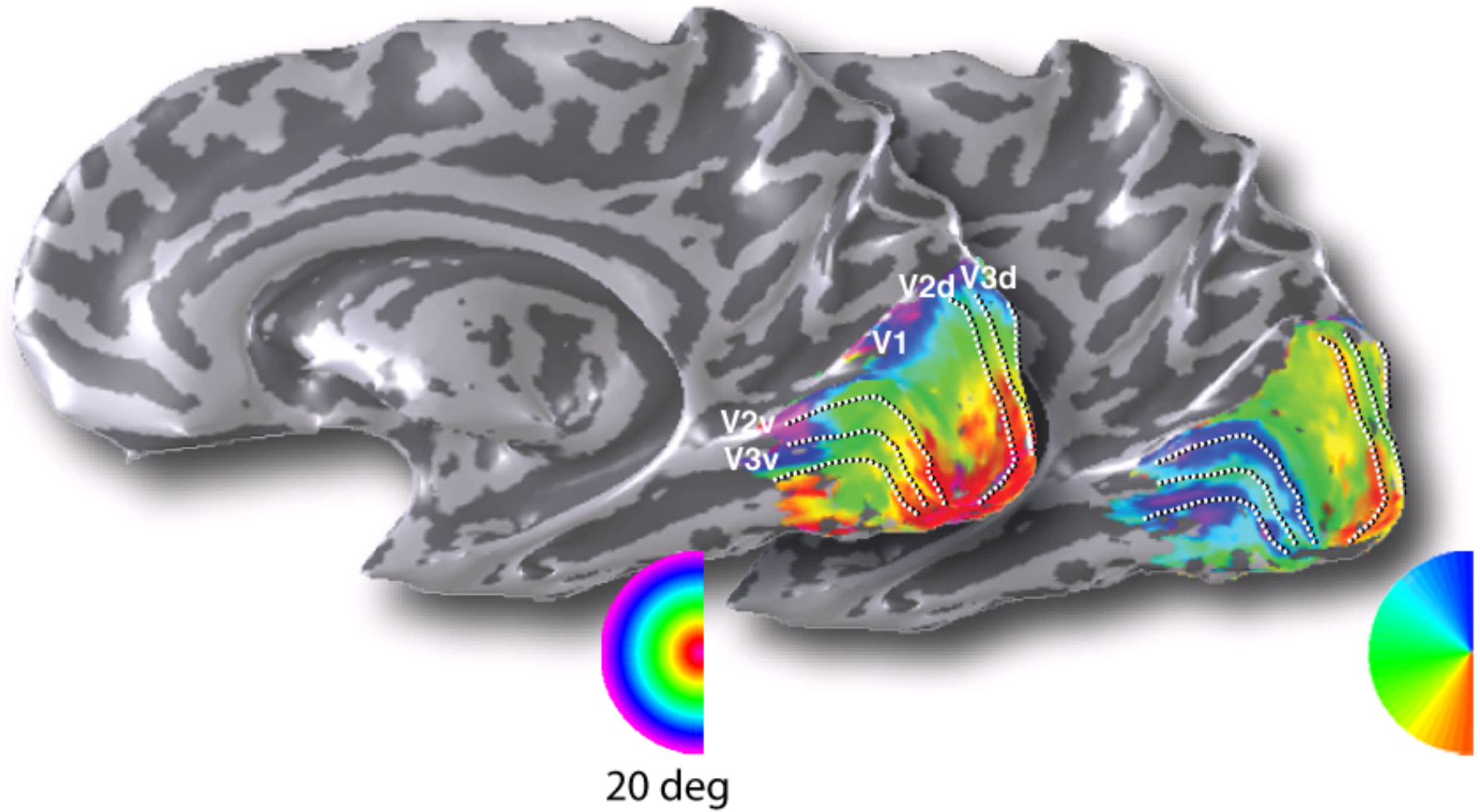
Angular

measurements
sharply delineate
visual field map
boundaries

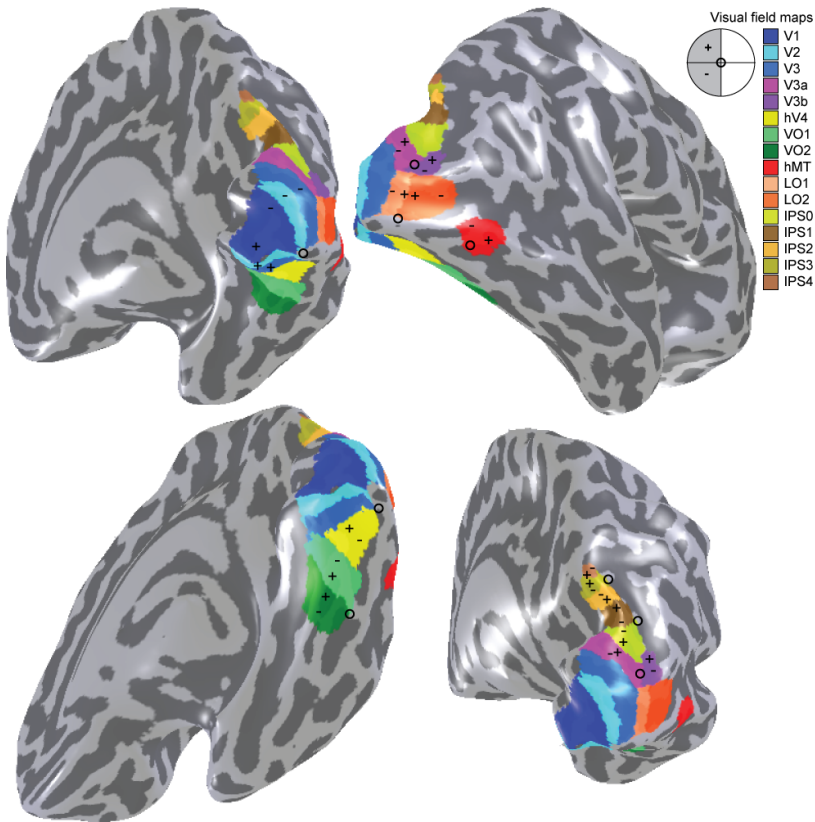
- Inflated brain
- Gray/white
are sulci/gyri



Combining eccentricity and angle data yields maps



Review articles



- Maps tile the occipital lobe
- Extend into IPS and VOT
- Response properties differ

366 Neuron 56, October 25, 2007

Cell
PRESS

Neuron
Review

Visual Field Maps in Human Cortex

Brian A. Wandell,^{1,*} Serge O. Dumoulin,¹ and Alyssa A. Brewer²

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²Department of Cognitive Sciences, University of California, Irvine, Irvine, CA 92697, USA

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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

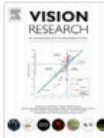


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Review

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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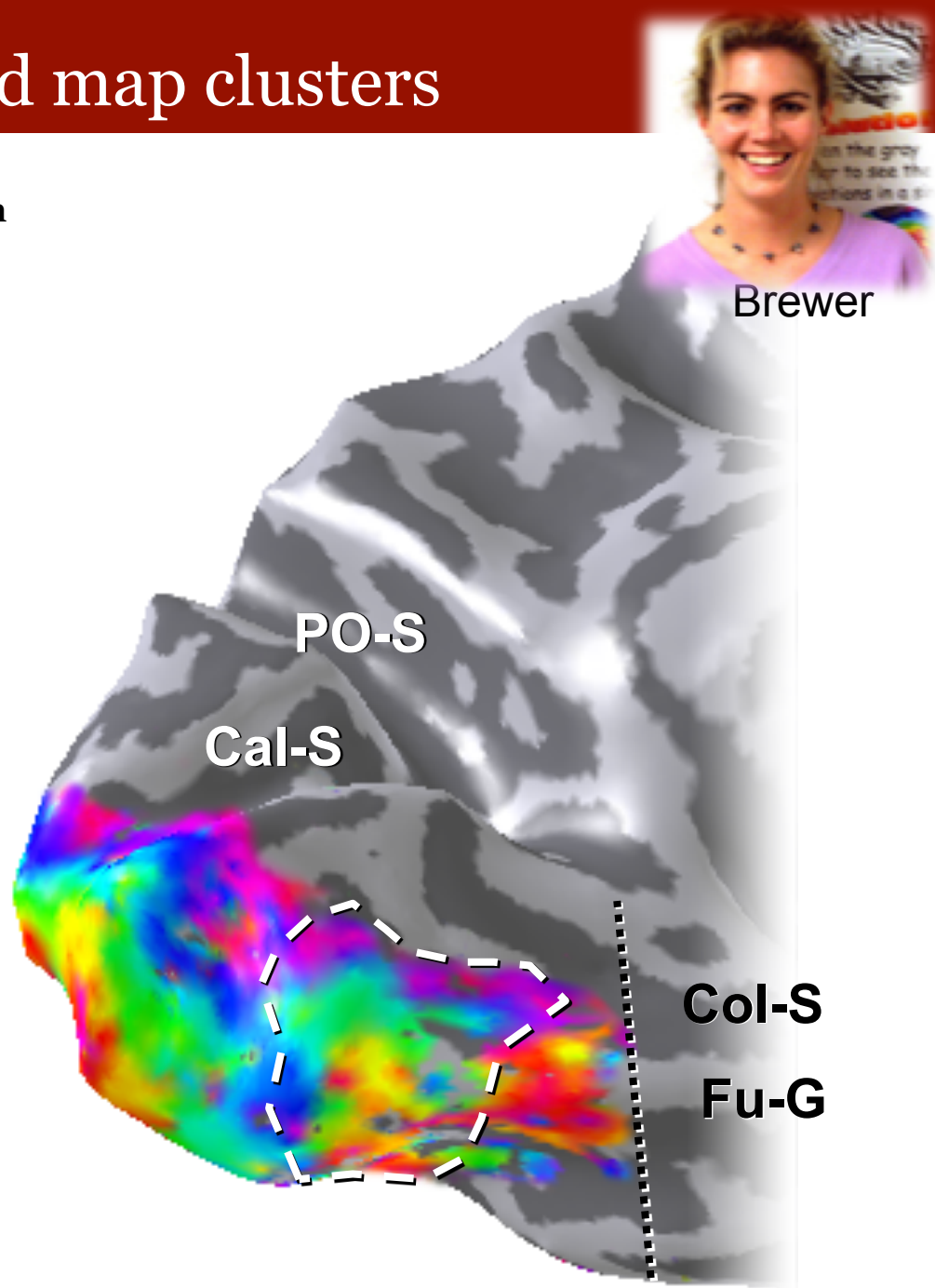
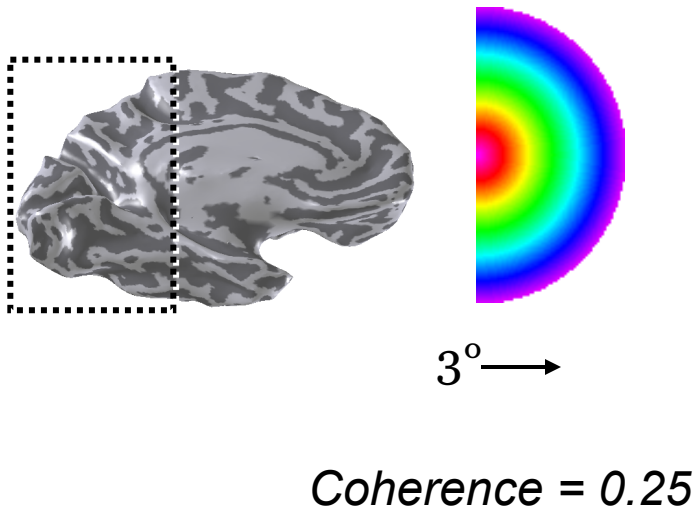
ABSTRACT

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 (fMRI), 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-

Visual field map clusters

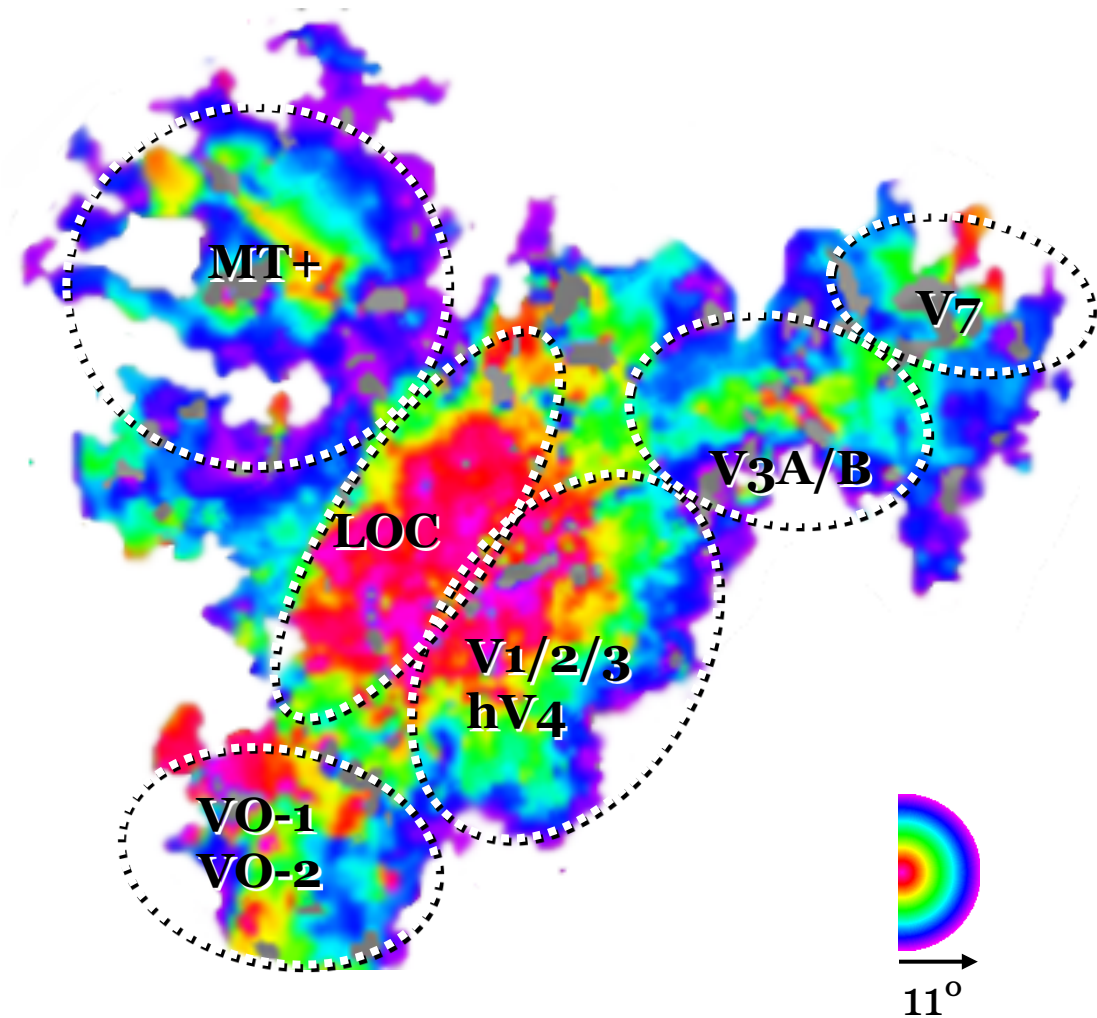
Visual field maps and stimulus selectivity in human ventral occipital cortex.

A.A. Brewer, J. Liu, A.R. Wade, B.A. Wandell
Nat Neurosci., vol. 8 no. 8, pp. 1102-9



Clusters

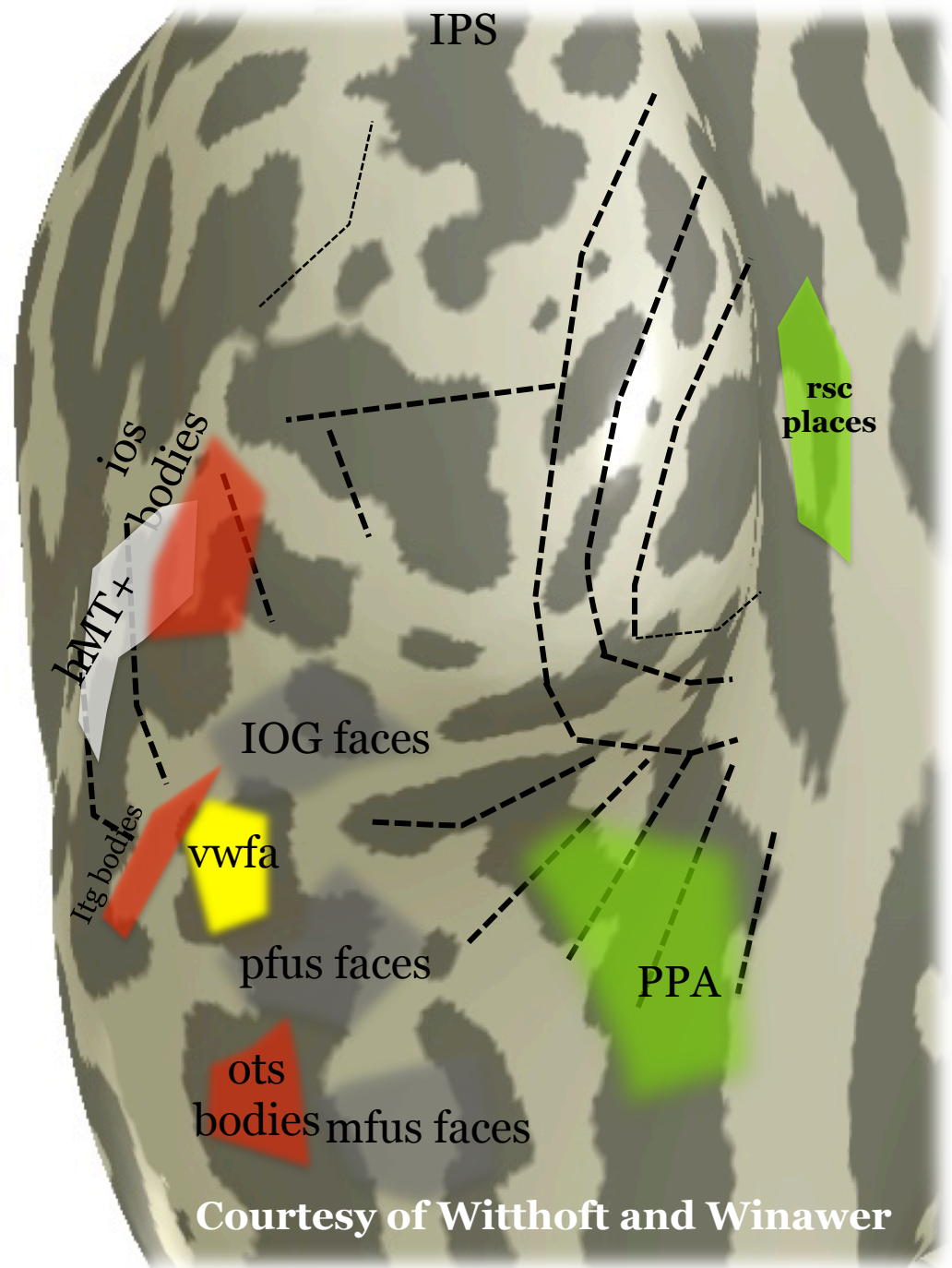
- Share a common circular or semi-circular eccentricity map.
- Contain multiple angle maps within the eccentricity representation.
- May share similar computational resources.



Occipital cortex is tiled by retinotopic maps and object-prefering regions

- 3 face-selective patches
- VWFA – Visual word form area
- PPA – Places
- Body parts

- Some object-prefering regions have retinotopic information as well



Courtesy of Witthoft and Winawer

Computational neuroimaging

- Population receptive field models

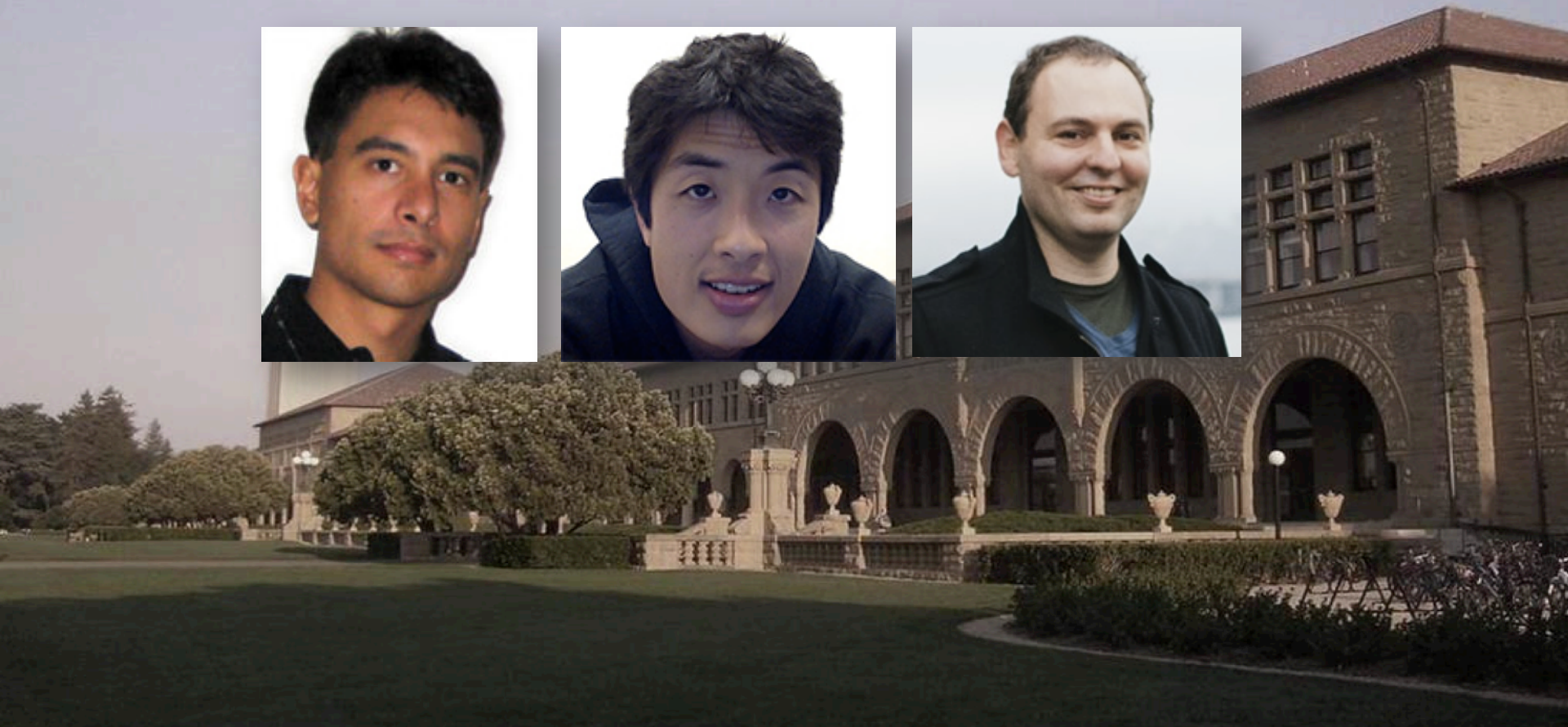
Serge Dumoulin



Kendrick Kay



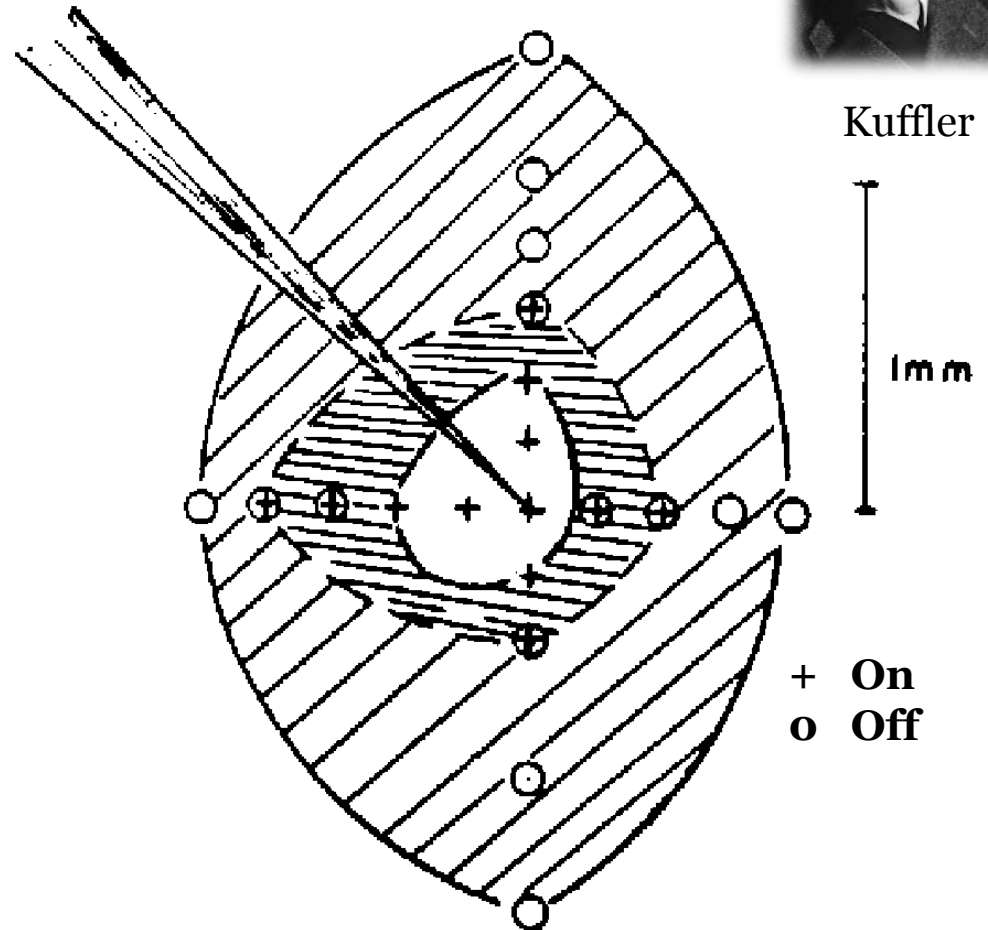
Jon Winawer



The receptive field - a stimulus referred measurement

‘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)’.

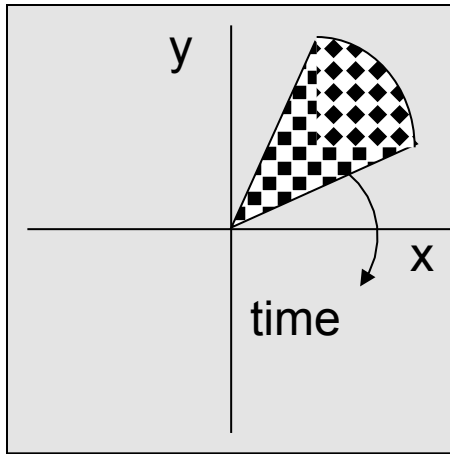
- Functional description
- Stimulus-referred



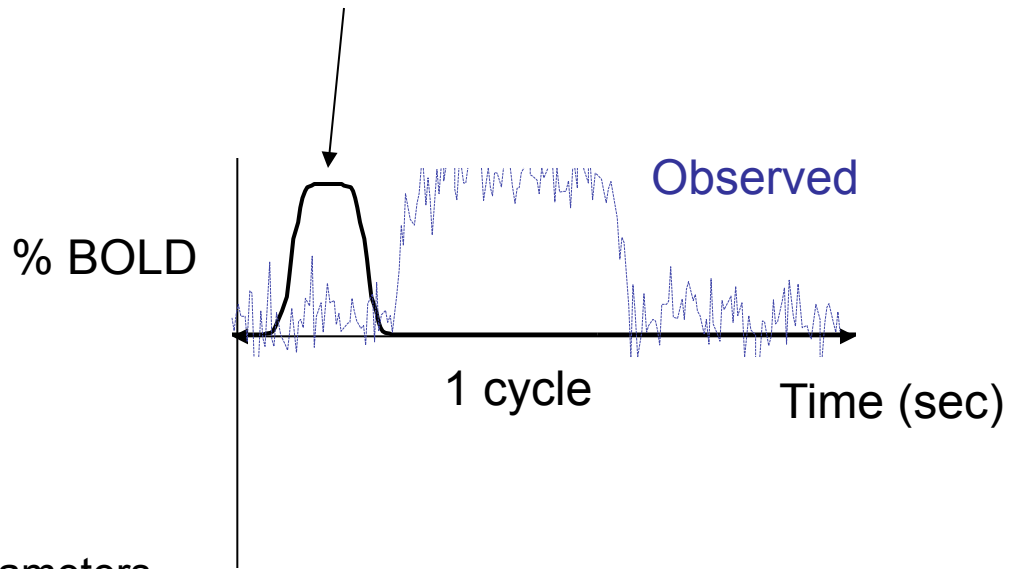
Kuffler

Population RF estimation

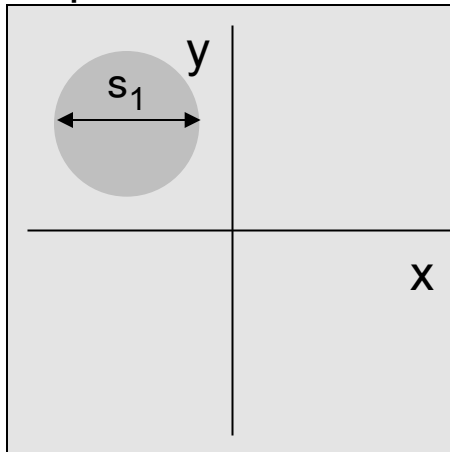
Stimulus



Predicted BOLD (including HRF)



Population RF model



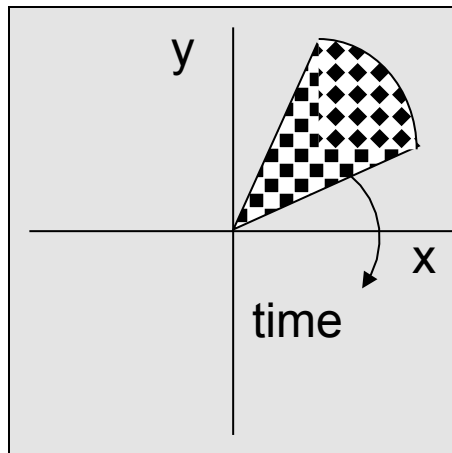
Parameters

$$(x_1, y_1, s_1)$$

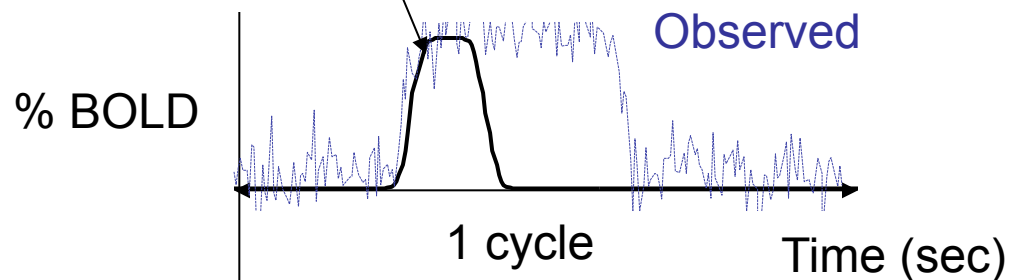
Population RF estimation

Dumoulin and Wandell, 2008
Neuroimage

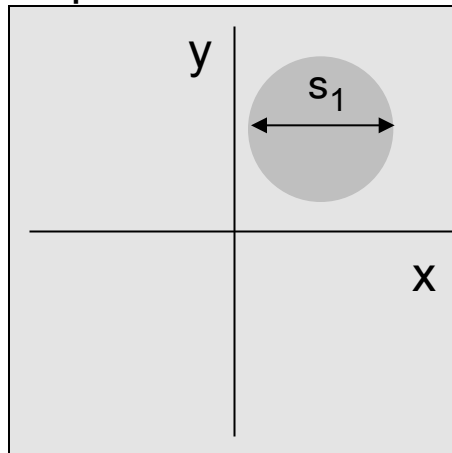
Stimulus



Predicted BOLD (including HRF)



Population RF model



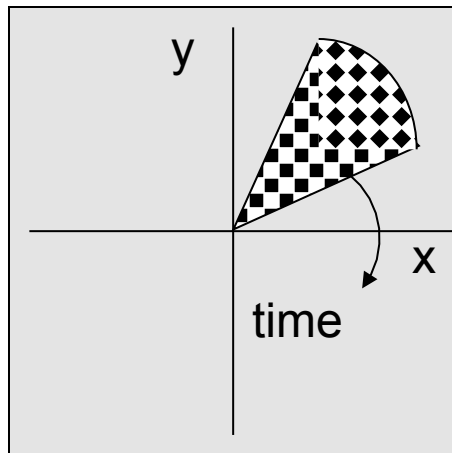
Parameters

(x_2, y_2, s_1)

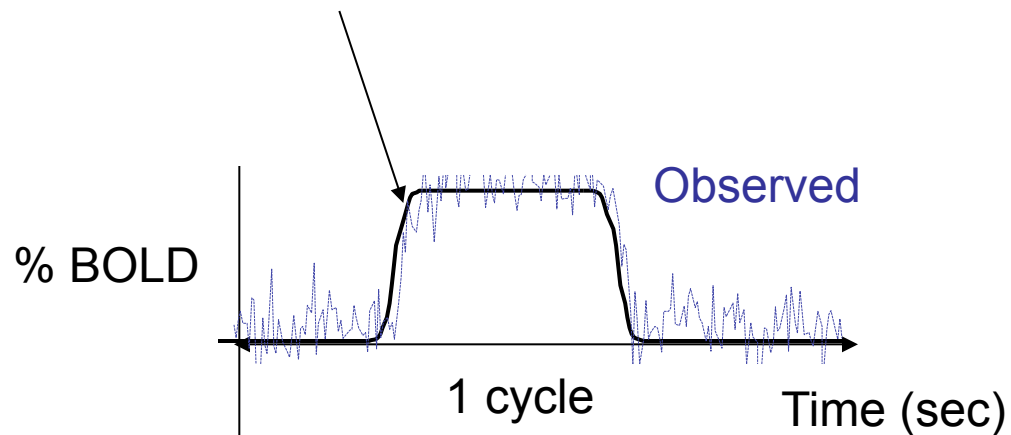
Population RF estimation

Dumoulin and Wandell, 2008
Neuroimage

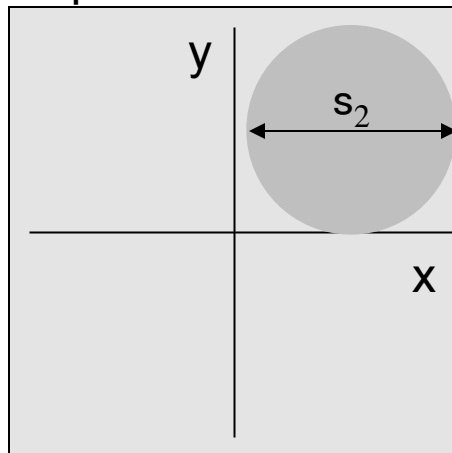
Stimulus



Predicted BOLD (including HRF)



Population RF model

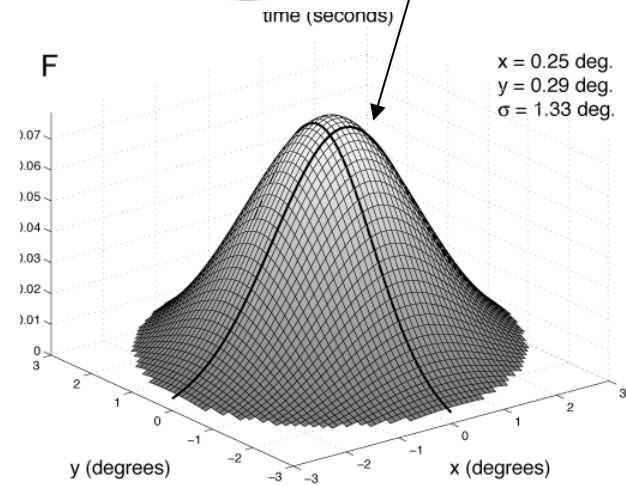
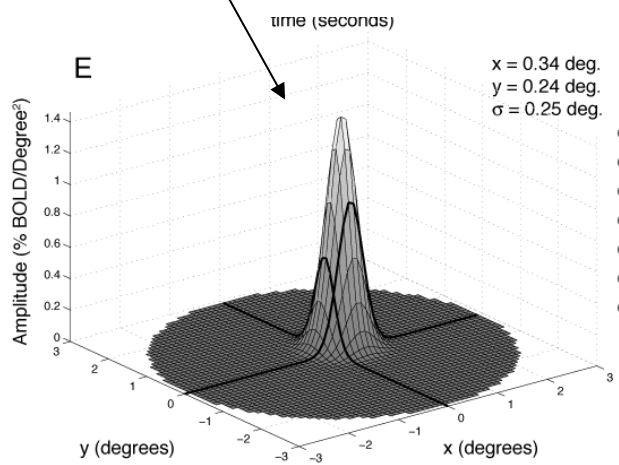
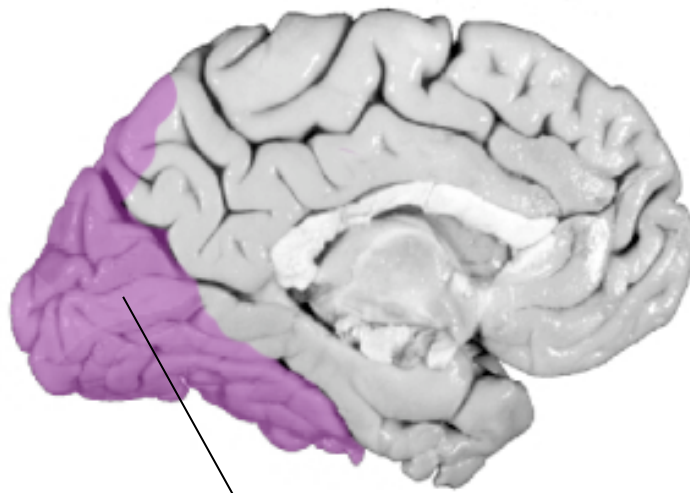


Parameters

$$(x_2, y_2, s_2)$$

Population receptive fields vary significantly across human visual cortex

Dumoulin and Wandell, 2008
Neuroimage



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

Review

CellPress

Computational neuroimaging and population receptive fields

Brian A. Wandell¹ and Jonathan Winawer²

¹Psychology Department and Neurosciences Institute, Stanford University, Stanford, CA, USA

²Psychology 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

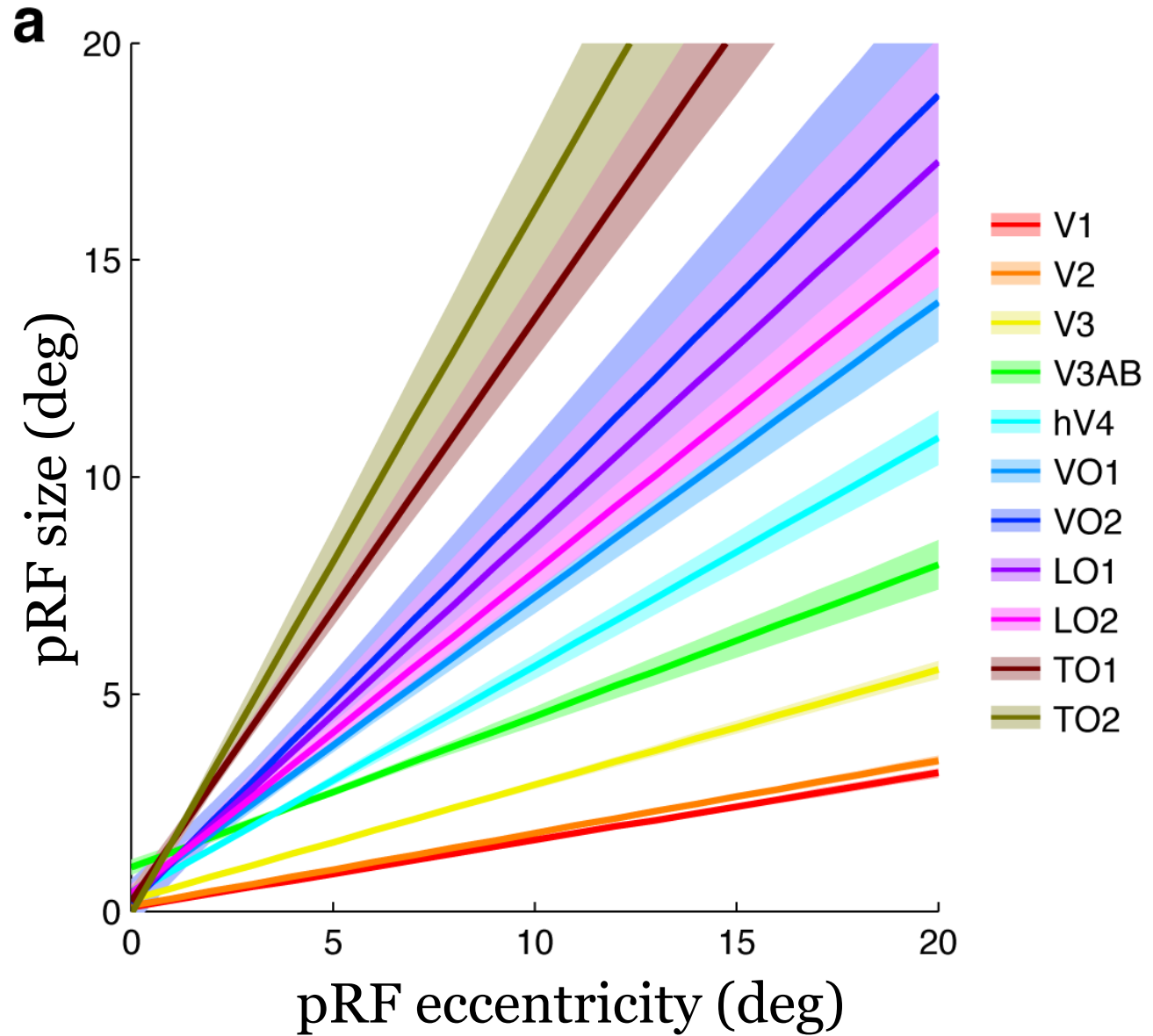
Receptive field models

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

Population RF (pRF) size

Kay et al., 2012
J. Neurophys

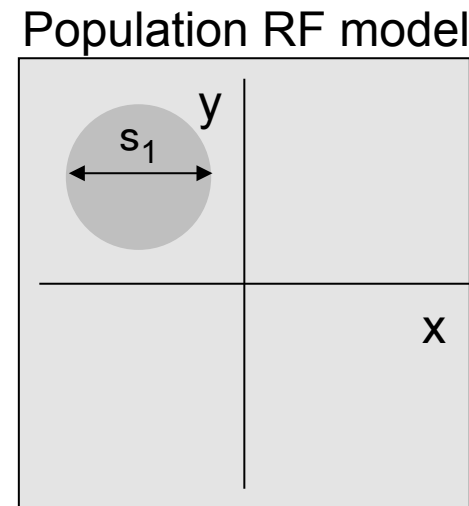
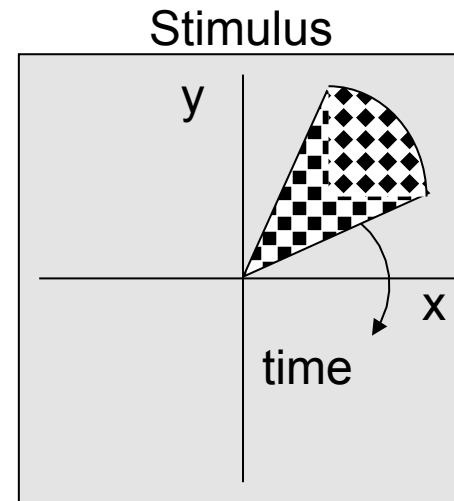
- At common eccentricities, different maps have different pRF sizes
- pRF size increases with eccentricity for all maps
- Bands are bootstrap estimates of the standard error



Linear pRF models account well for a narrow range of stimuli

“... all models are wrong, but some are useful “

Box, G. E. P., and Draper, N. R., (1987), *Empirical Model Building and Response Surfaces*, John Wiley & Sons, New York, NY.

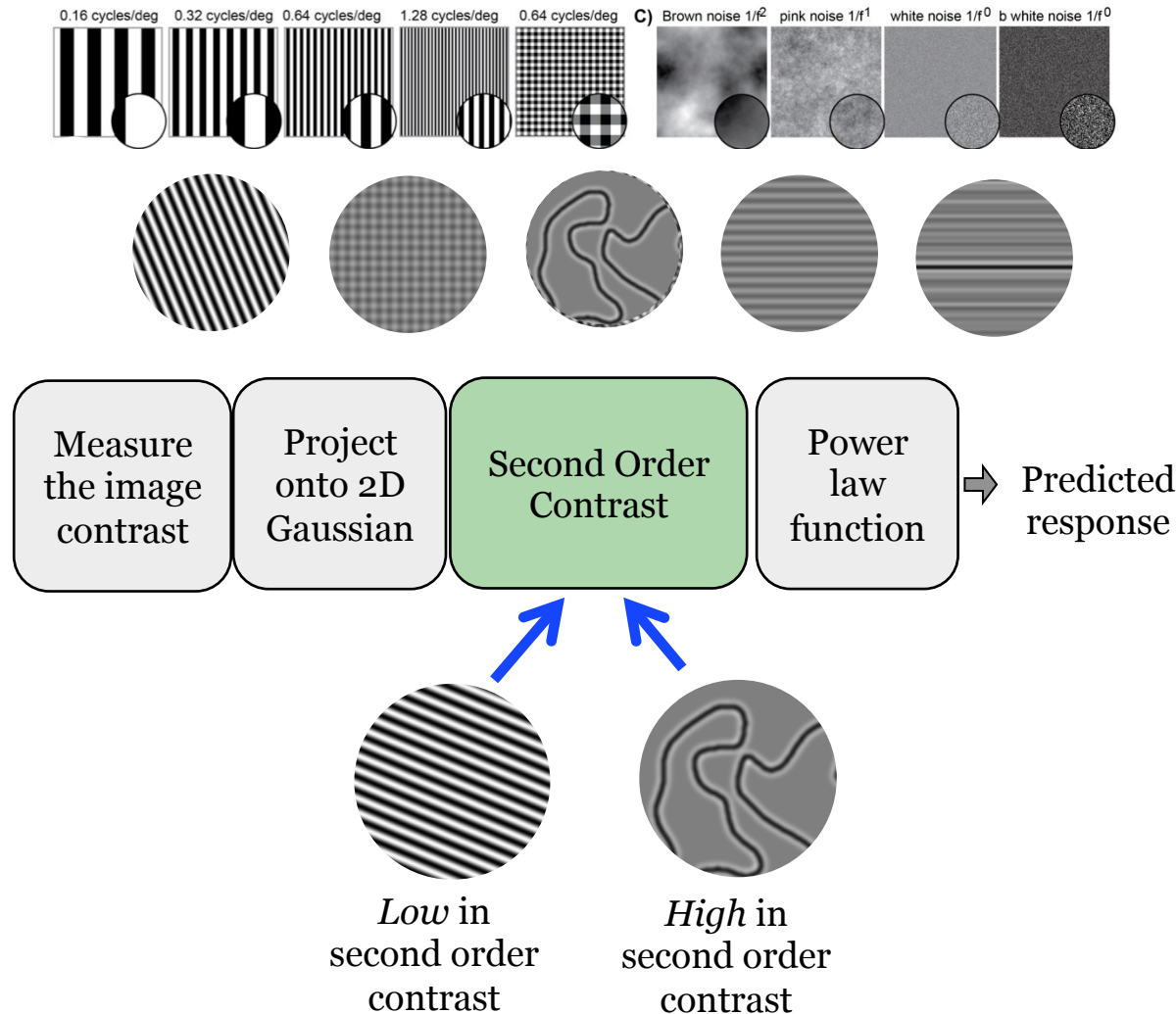


Parameters
 (x_1, y_1, s_1)

New models account for larger range of stimuli with high accuracy

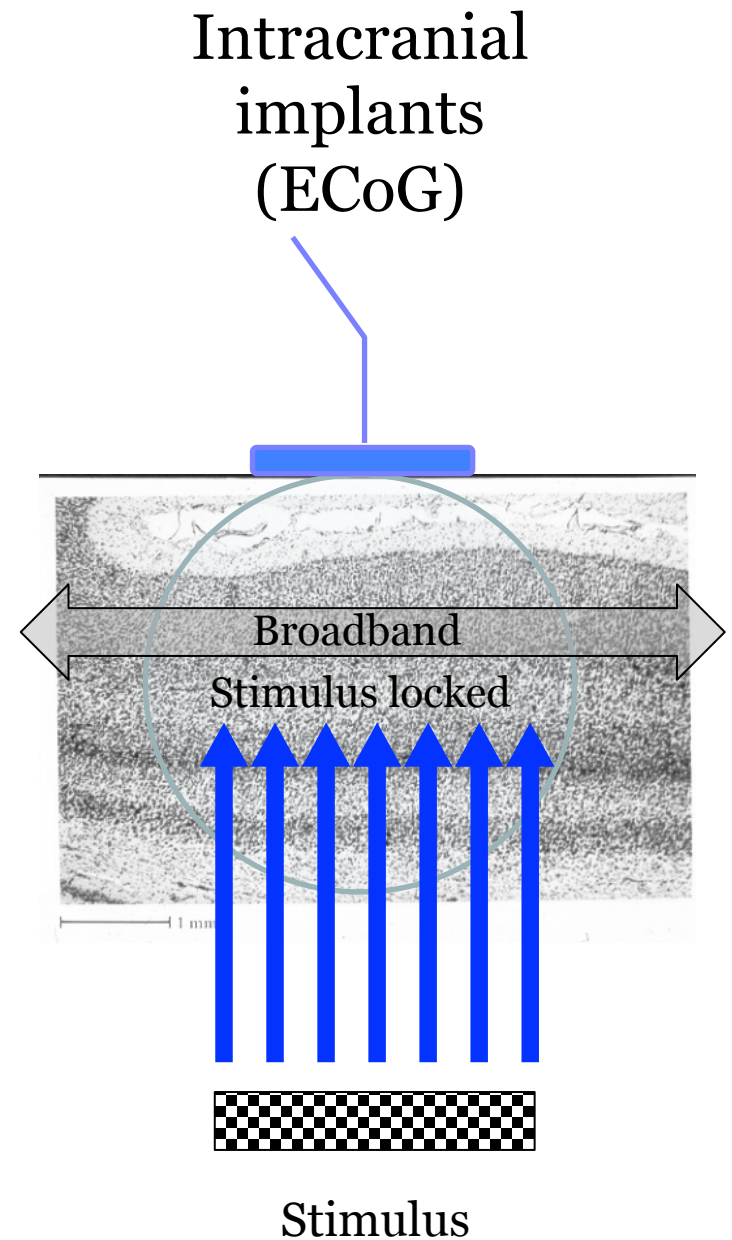
- **Prediction:** Start with image and produce BOLD time series
- For achromatic, bandpass stimuli, **the model accounts for about 80-90% of the explainable variance** (cross-validation) in V1, V2, V3, hV4

Greatly extended range of stimuli



Open-source models integrate data from multiple modalities

- PRF methods applied to BOLD and intracranial electrical recordings (ECoG)
- Showed relationship between BOLD and specific ECoG response components (and not others)



White matter in the human brain

- Diffusion and tractography

Ariel Rokem



Franco Pestilli



Hiromasa
Takemura



Jason Yeatman



Human fascicles (tracts)

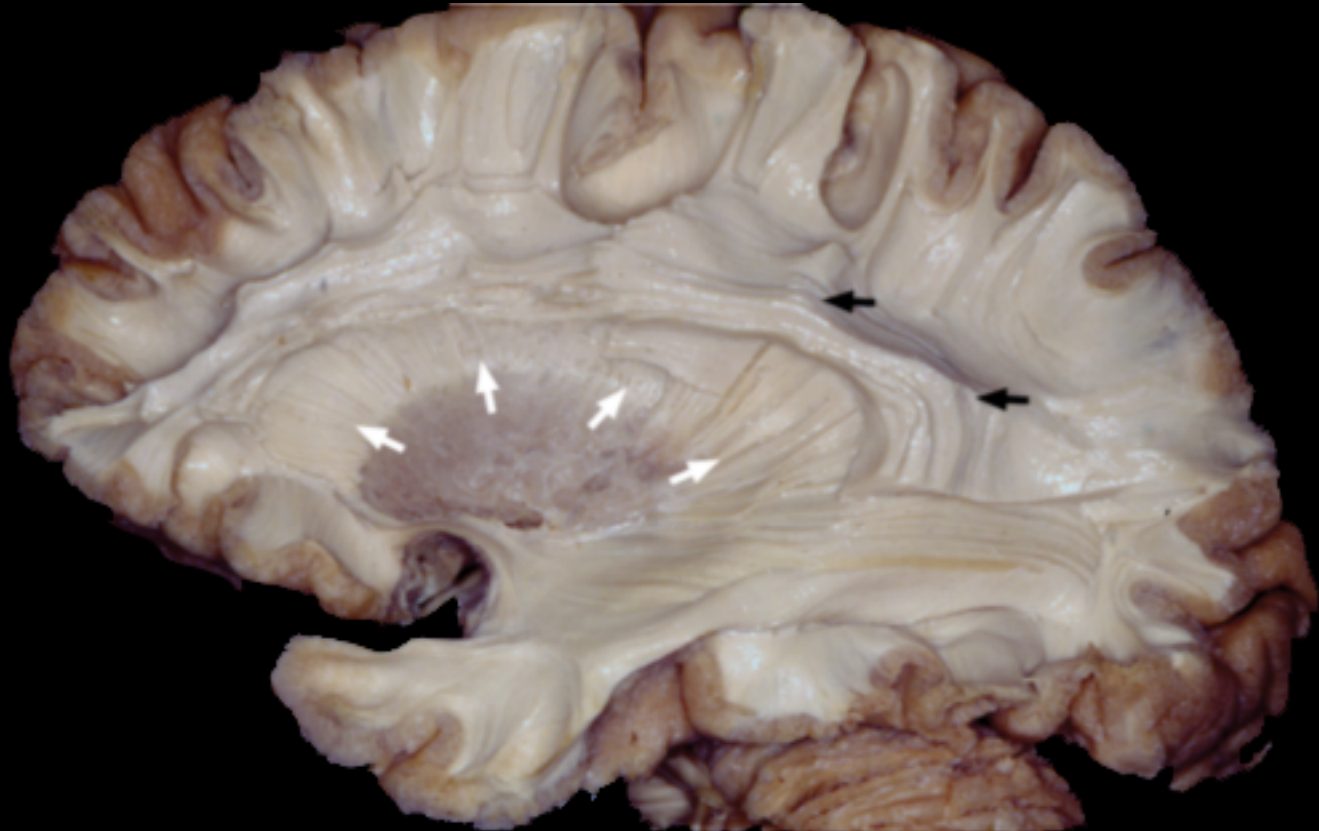
- There are many long-range connections
- These connections are not passive – they change their properties in response to use
- A system with active wires



Courtesy Professor Peggy Mason

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



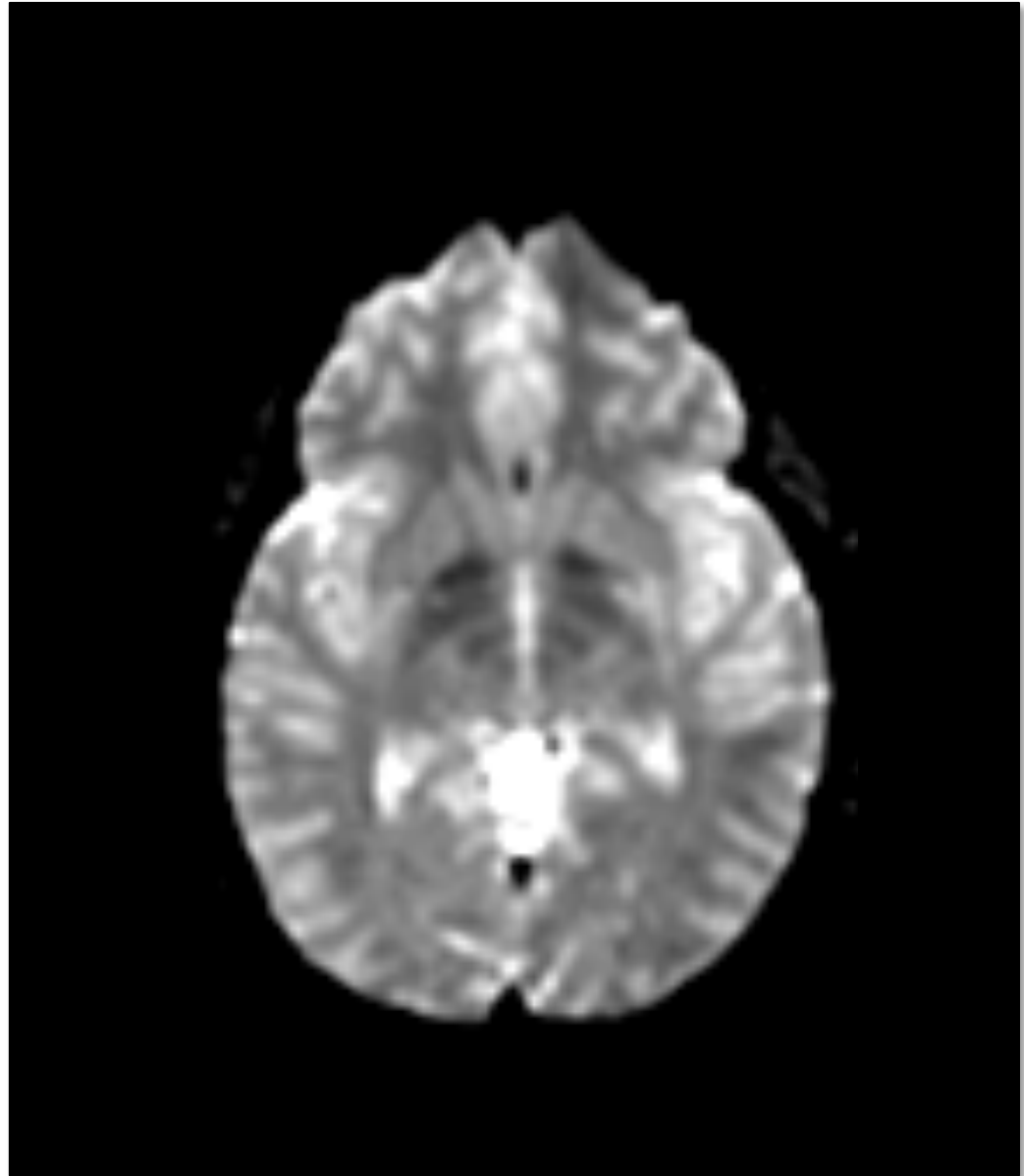
Courtesy Professor Ugur Ture

Non-diffusion MR image

Dark means large
signal attenuation
High ADC

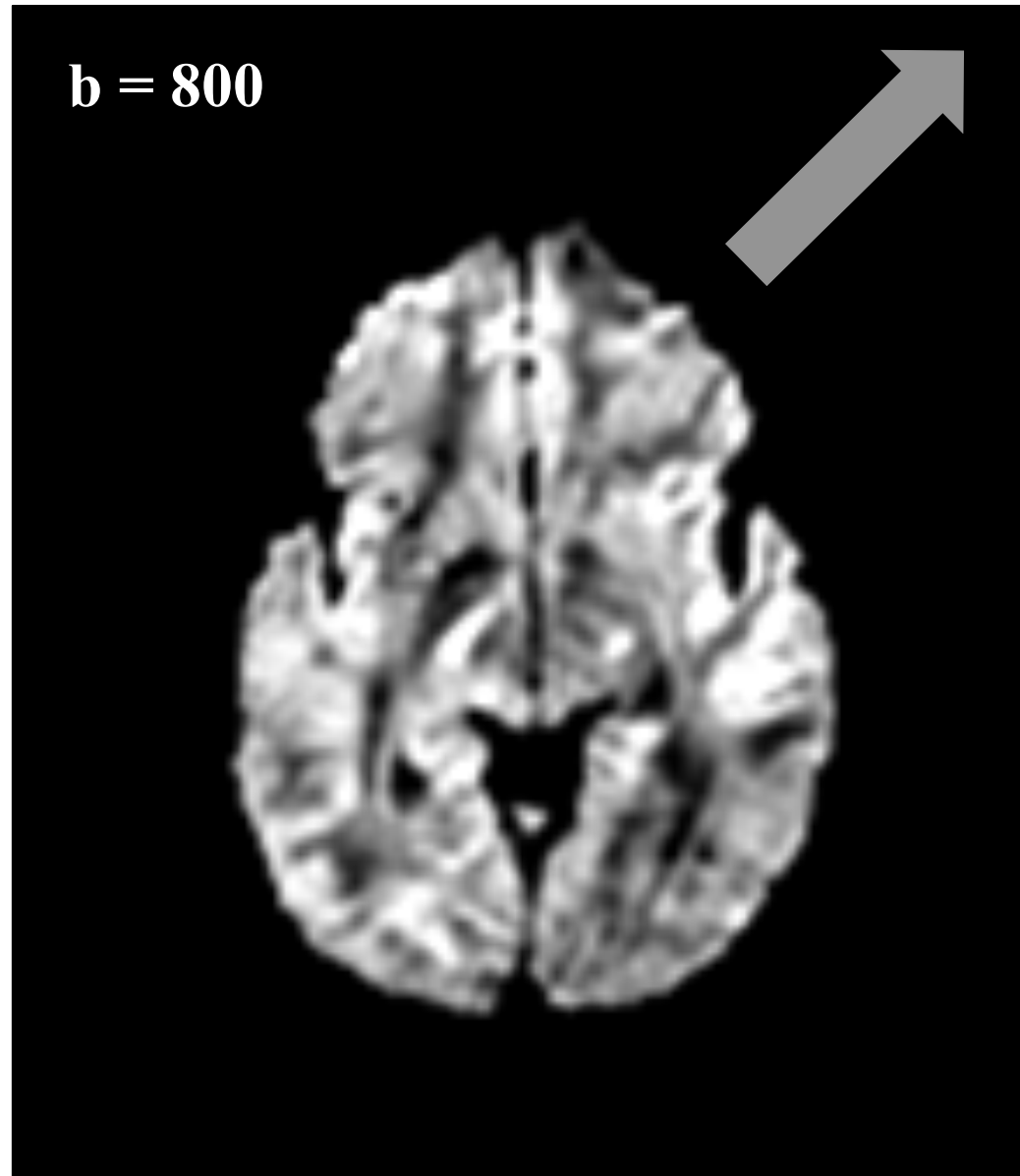


b = 0



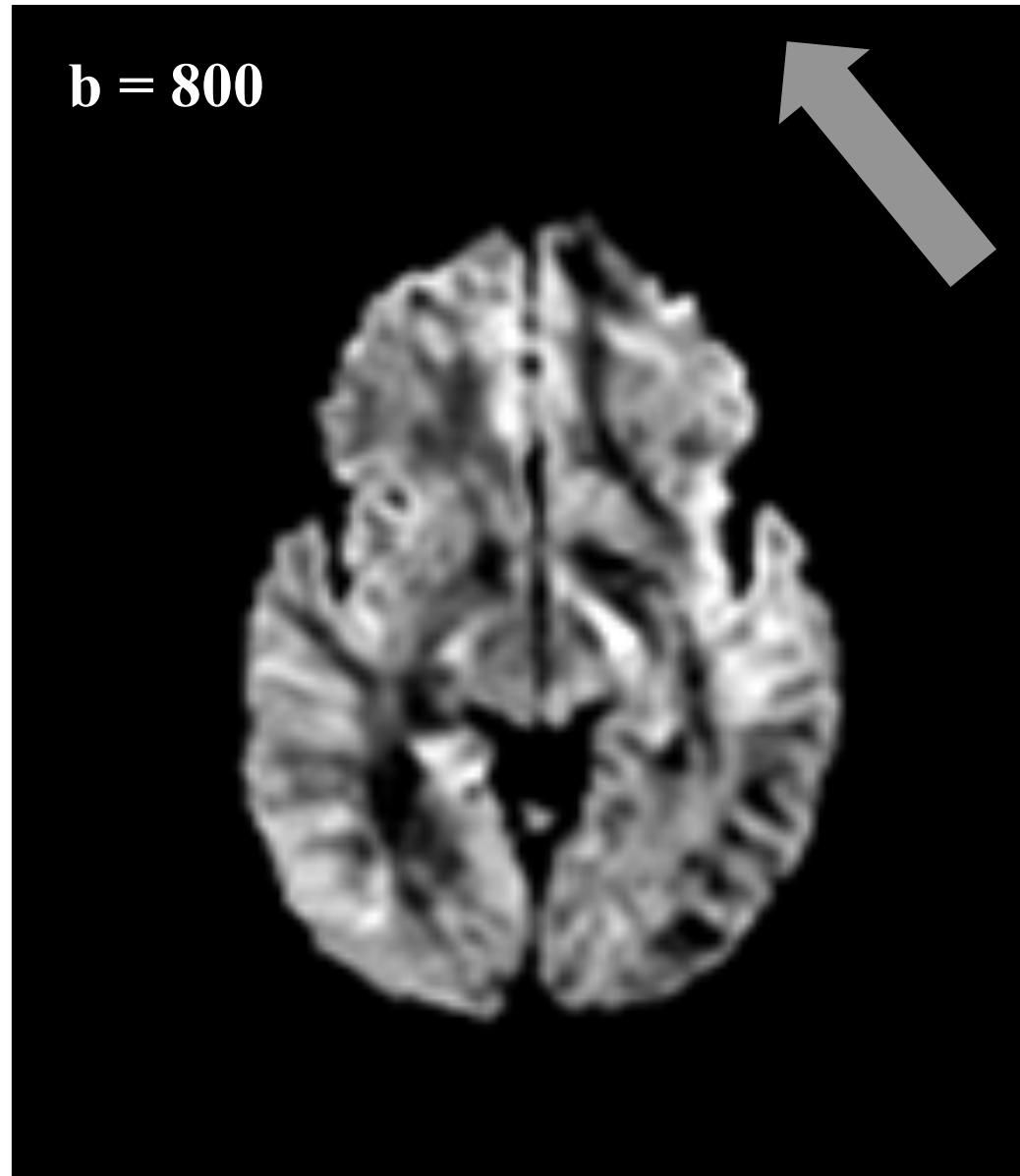
Diffusion weighting: Directions

Dark means large
signal attenuation
High ADC



Diffusion weighting: Directions

Dark means large
signal attenuation
High ADC

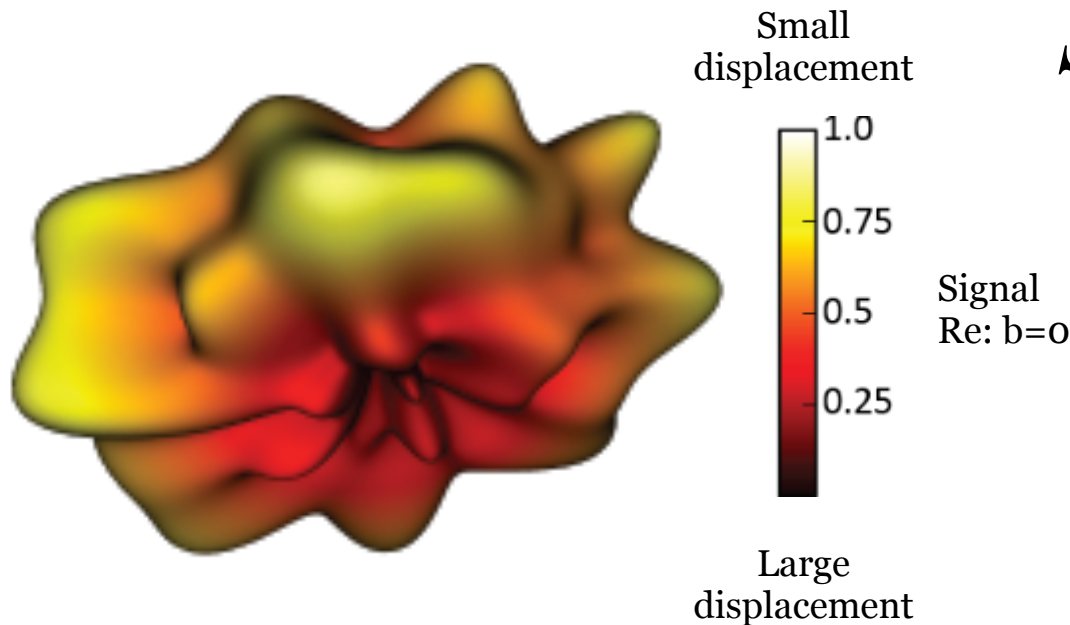


Diffusion signals in different directions

ADC – apparent diffusion coefficient

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, $D(\theta)$

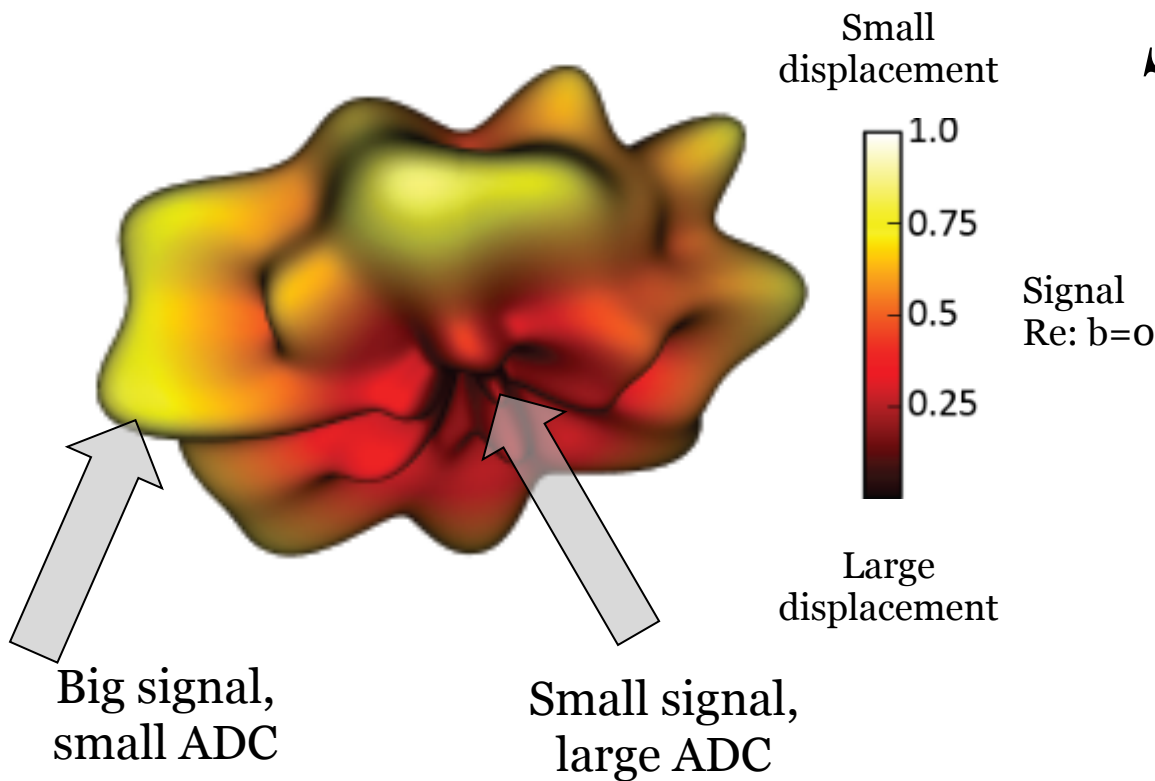
Diffusion signals in different directions

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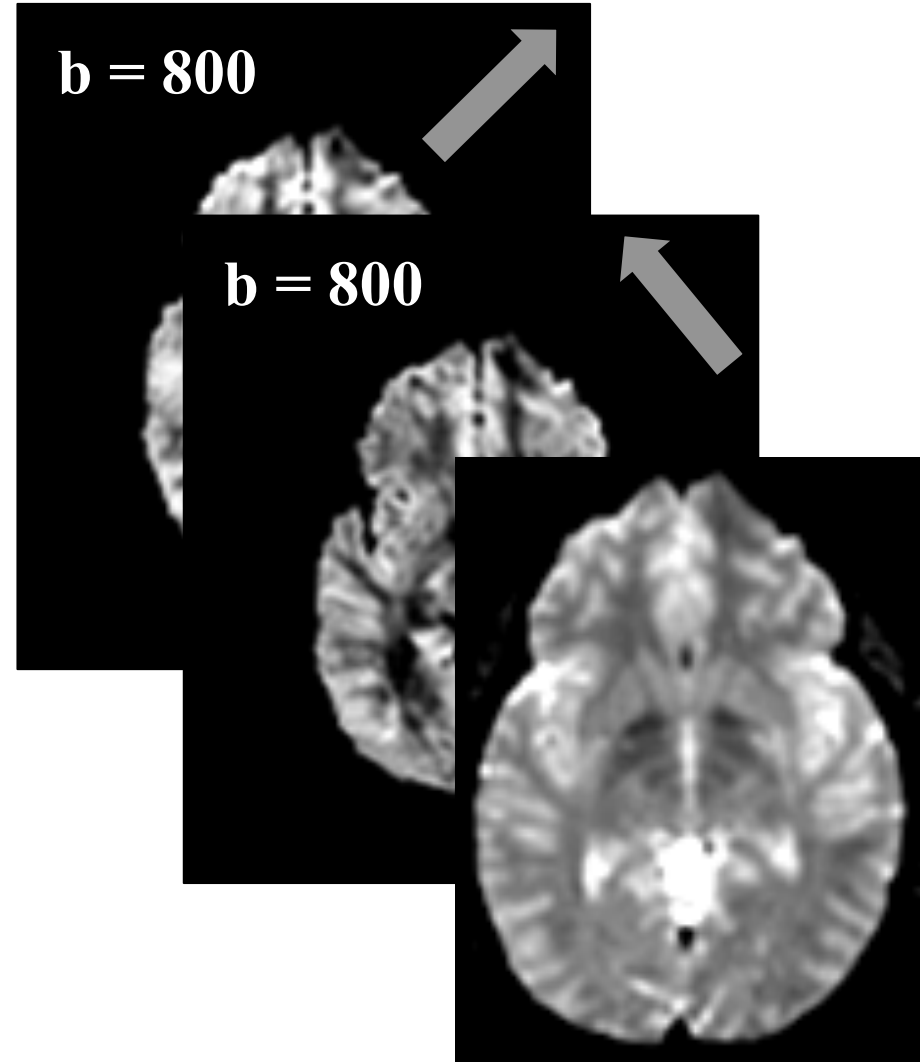
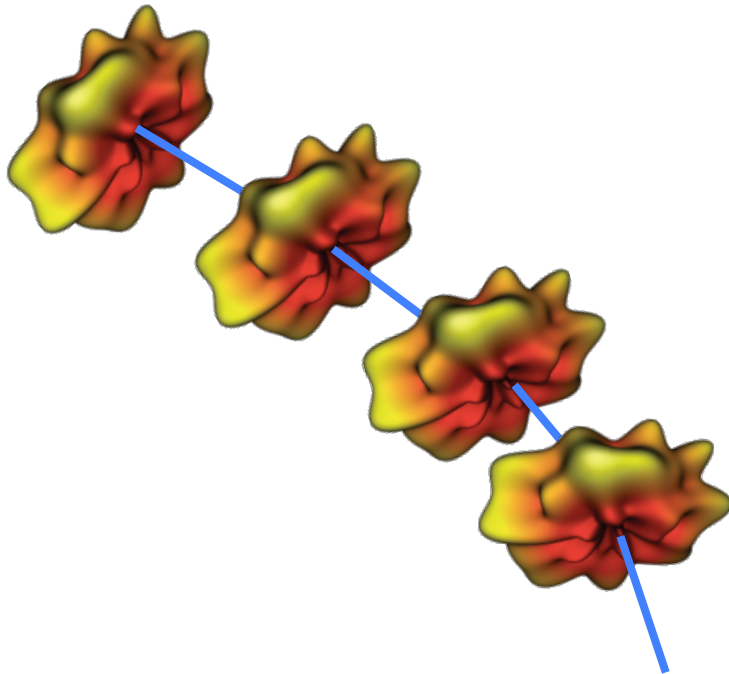
The measured diffusion signal in a direction, θ , is related to the apparent diffusion coefficient in that direction, $D(\theta)$



Tractography

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

Diffusion data are surfaces



Annual Review of Neuroscience (advance)

Published online, 2016

Clarifying Human White Matter

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Annu. Rev. Neurosci. 2016. 39:103–28

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[10.1146/annurev-neuro-070815-013815](https://doi.org/10.1146/annurev-neuro-070815-013815)

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Keywords

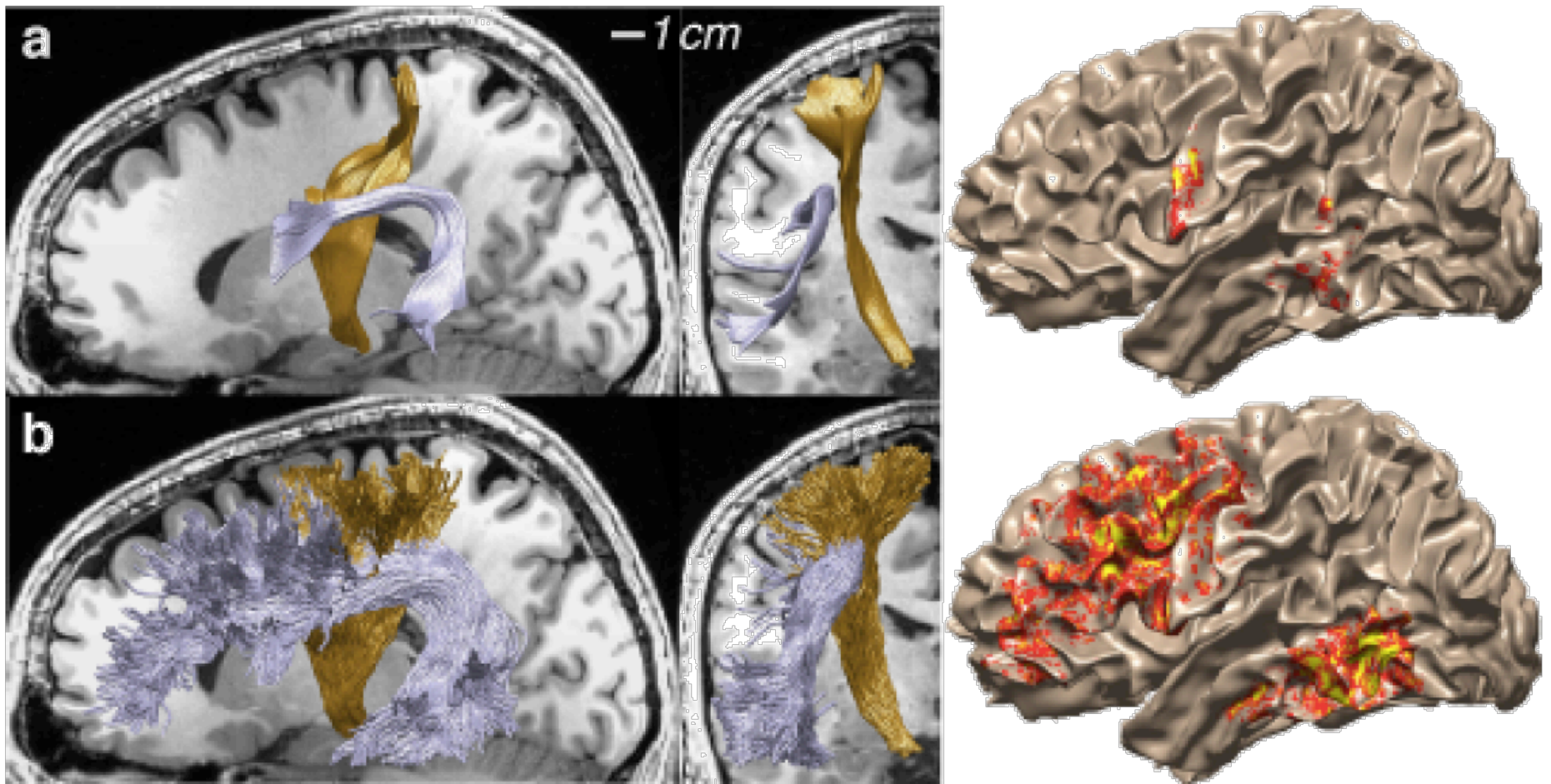
tractography, connectome, diffusion weighted imaging, dMRI, diffusion spectrum imaging, diffusion tensor imaging, white matter, oligodendrocytes, quantitative MRI

Abstract

Progress in magnetic resonance imaging (MRI) now makes it possible to identify the major white matter tracts in the living human brain. These tracts are important because they carry many of the signals communicated between different brain regions. MRI methods coupled with biophysical modeling can measure the tissue properties and structural features of the tracts that impact our ability to think, feel, and perceive. This review describes the fundamental ideas of the MRI methods used to identify the major white matter tracts in the living human brain.

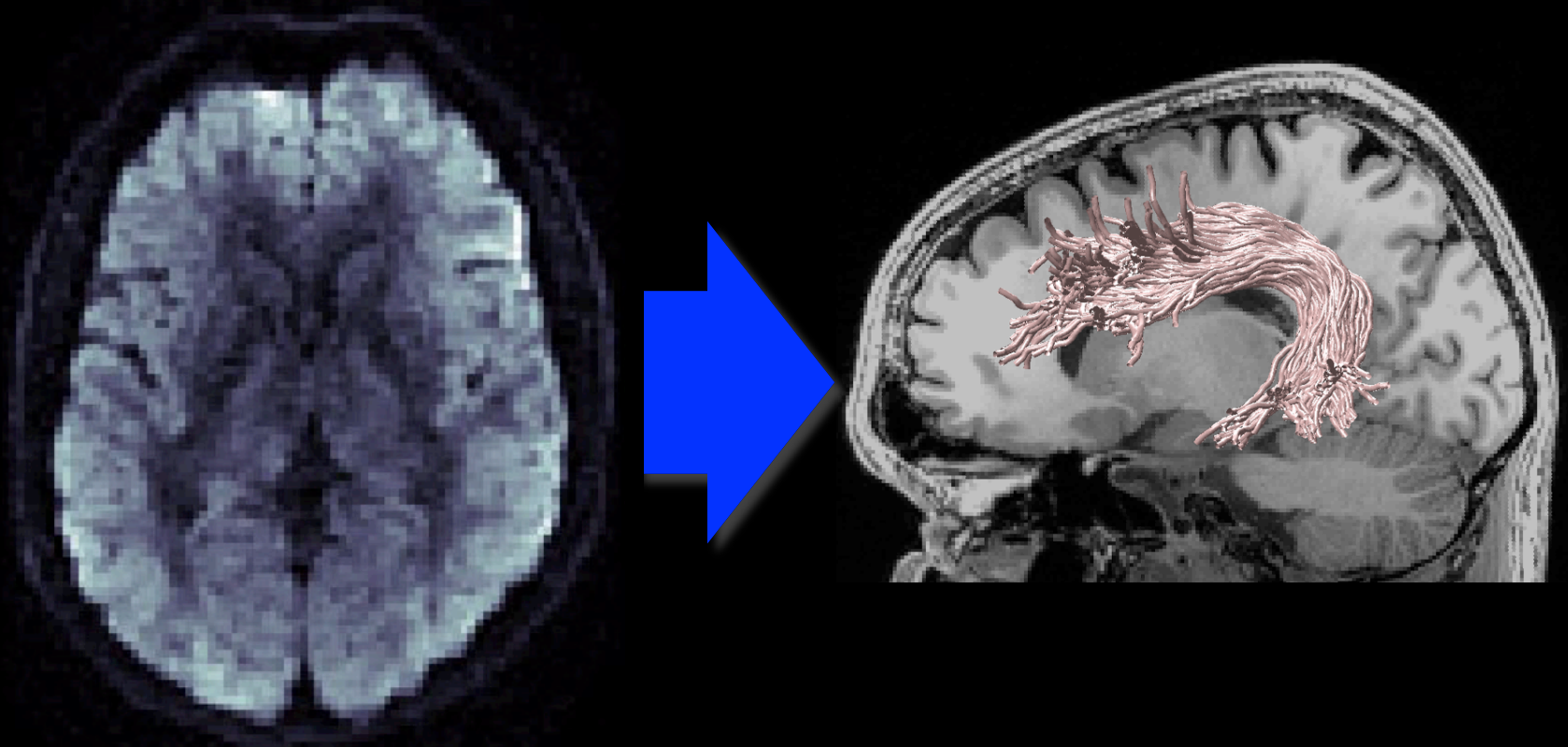
Different methods and parameters make different predictions

A key tractography problem we must solve
– parameter and instrument dependency



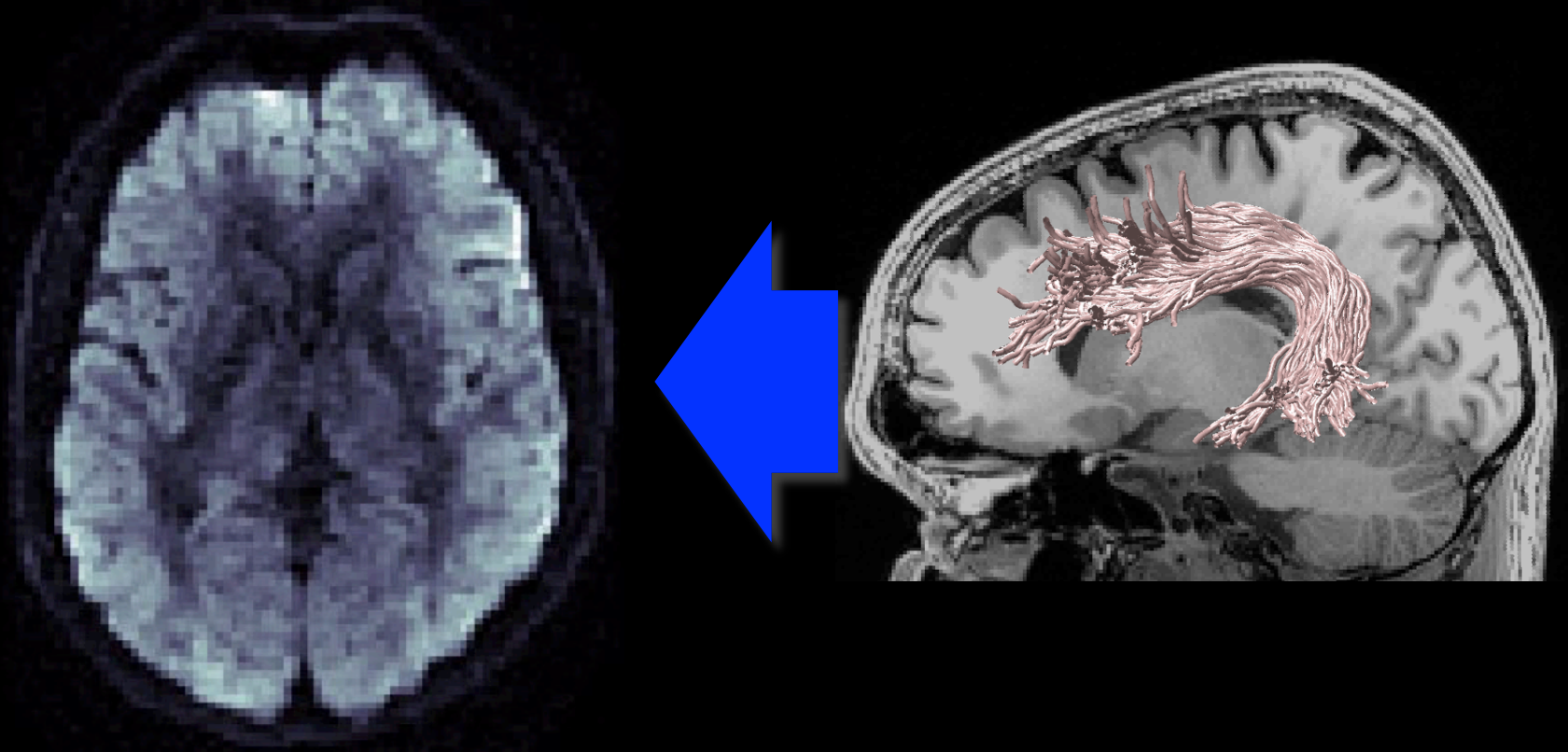
Tractography limitations

We estimate fascicles from diffusion data, but never check the model



Tractography solution

Treat the estimates as a model and calculate statistical evaluations of model validity

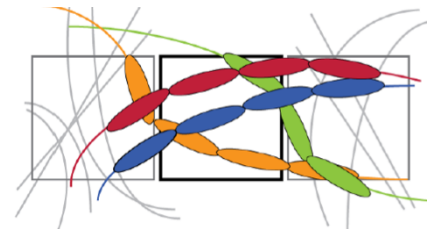
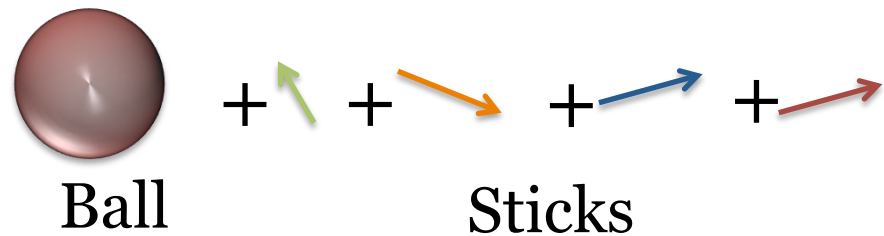


Stages of LiFE: Set up diffusion predictions for each voxel

- In each voxel use the conventional fascicle diffusion model to predict the diffusion signal from the candidate connectome
- Each fascicle is assigned a weight to indicate the strength of its contribution to the data

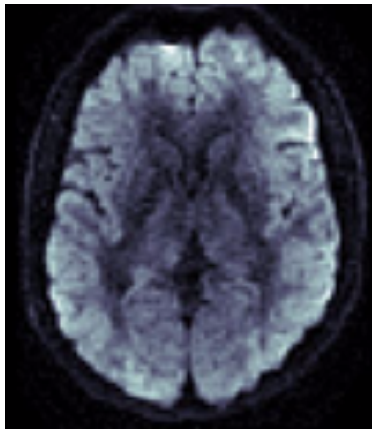
$$S(\theta) = w_0 D_0 + \sum_f w_f e^{-bD_f(\theta)}$$

isotropic weights fascicles



Stages of Life: Solve for the fascicle weights

Diffusion
signal, $S(\theta)$



$$\begin{matrix} S(\theta) \\ \left[\begin{array}{c} v1 \\ \text{---} \\ v2 \\ \text{---} \\ \vdots \\ \text{---} \\ vN \end{array} \right] \end{matrix}$$

=

Each column is
the prediction
of a fascicle

Each entry is
the fascicle
contribution
for a voxel in a
direction

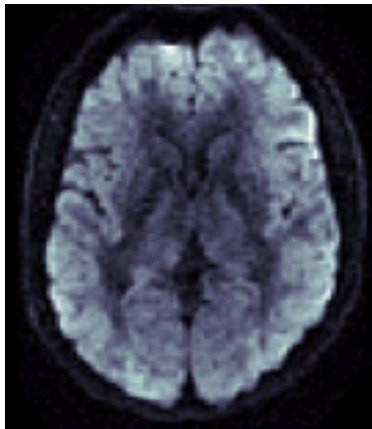
w_f

Solve for a
non-negative
weight for each
fascicle (least-
squares)

$10^7 \times 10^6$

Stages of Life: Solve for the fascicle weights

Diffusion
signal, $S(\theta)$



$S(\theta)$
v1
v2
vN

=

Each column is
the prediction
of a fascicle

Each entry is
the fascicle
contribution
for a voxel in a
direction

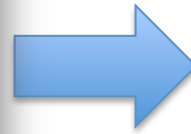
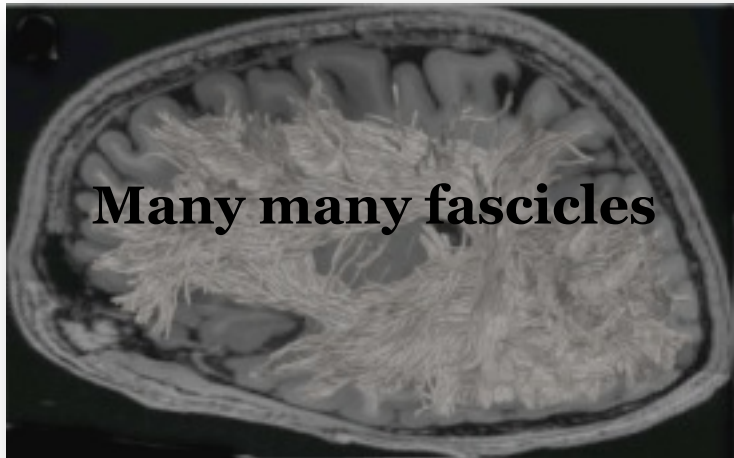
w_f

Depending on
voxel size,
number of
directions, and
so forth, about
80% of typical
tractography
weights are zero.

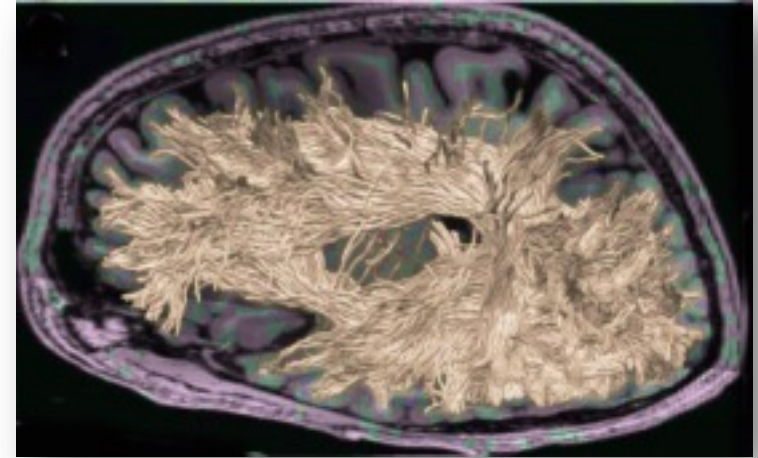
$10^7 \times 10^6$

Stages of LiFE: Eliminate zero weight fibers (false alarms)

Candidate
connectome



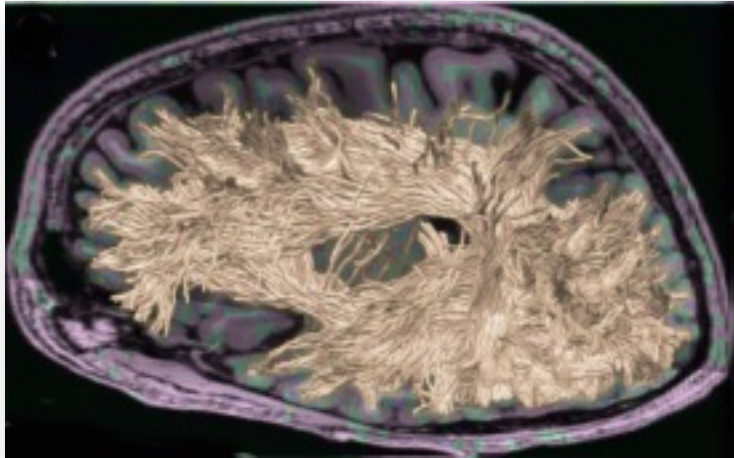
Optimized
connectome



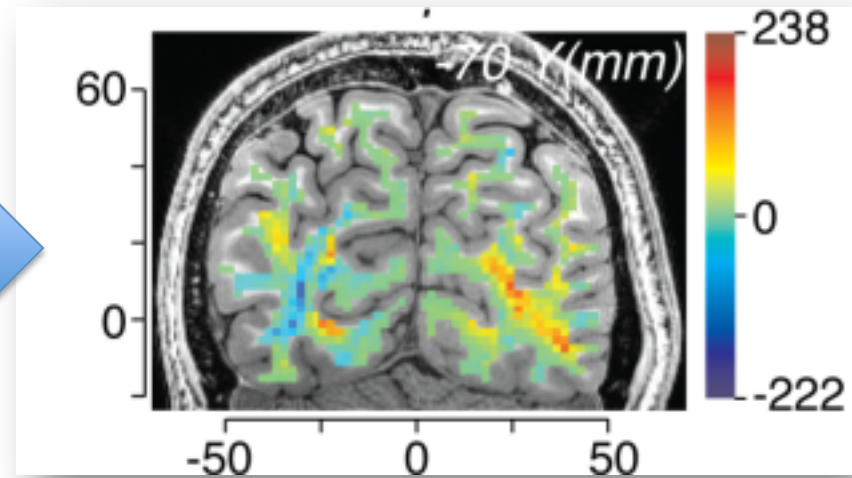
Solving a system of linear equations
(non-negative least-squares)

Stages of LiFE: Predict diffusion signal

Optimized connectome
and weights



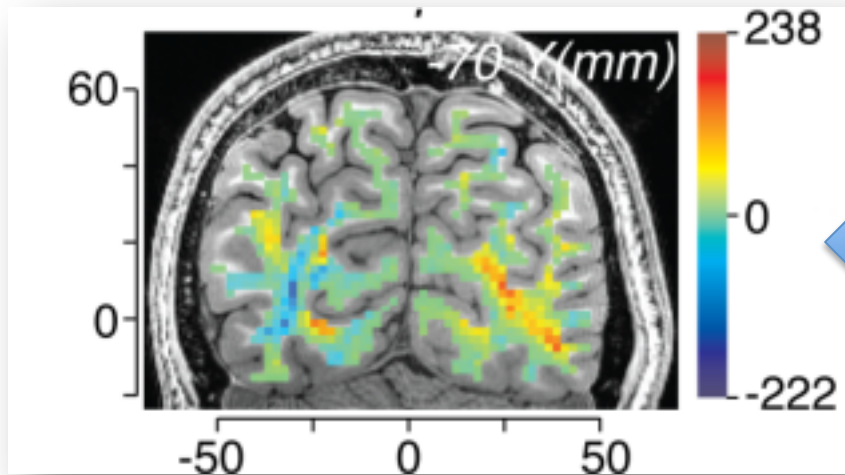
Prediction



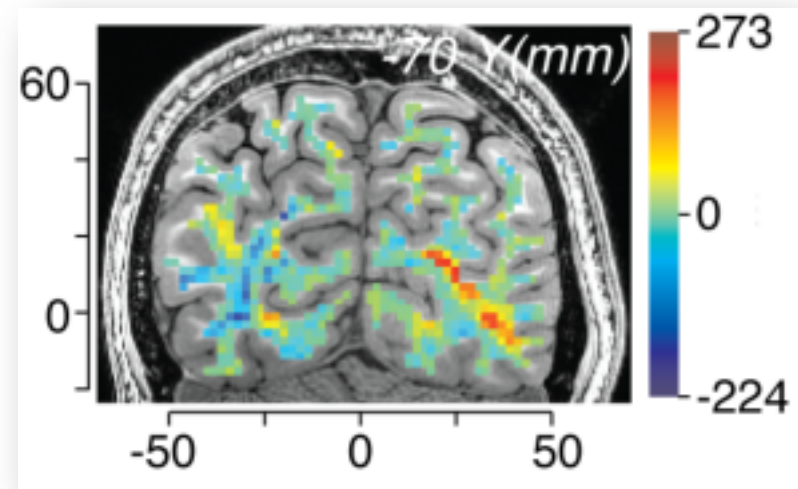
Big matrix multiplication

Stages of LiFE: Cross-validation error

Prediction

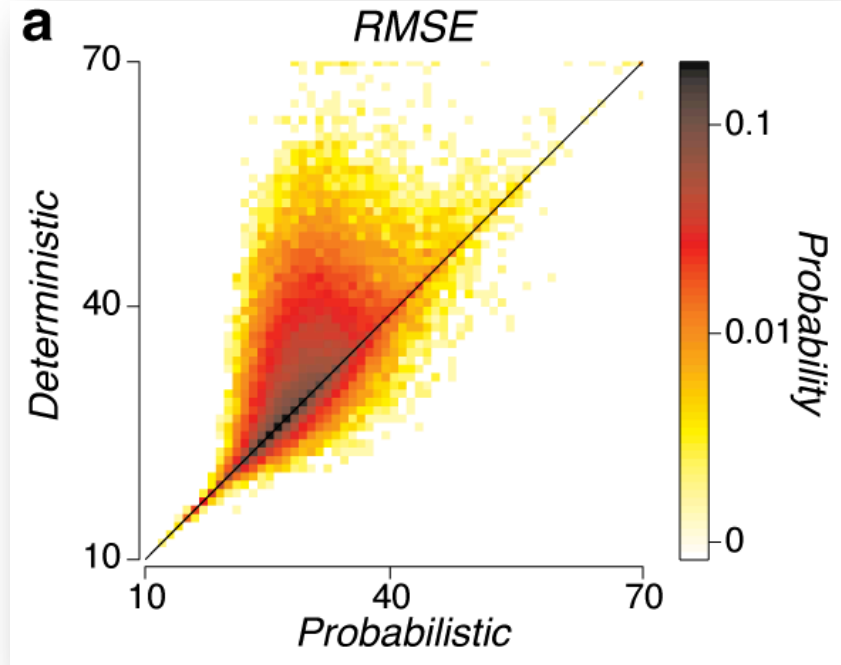
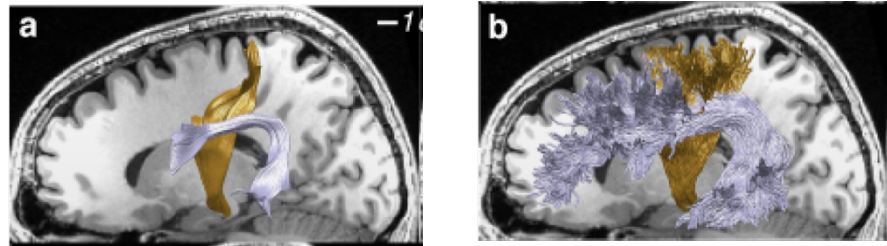


Second data set

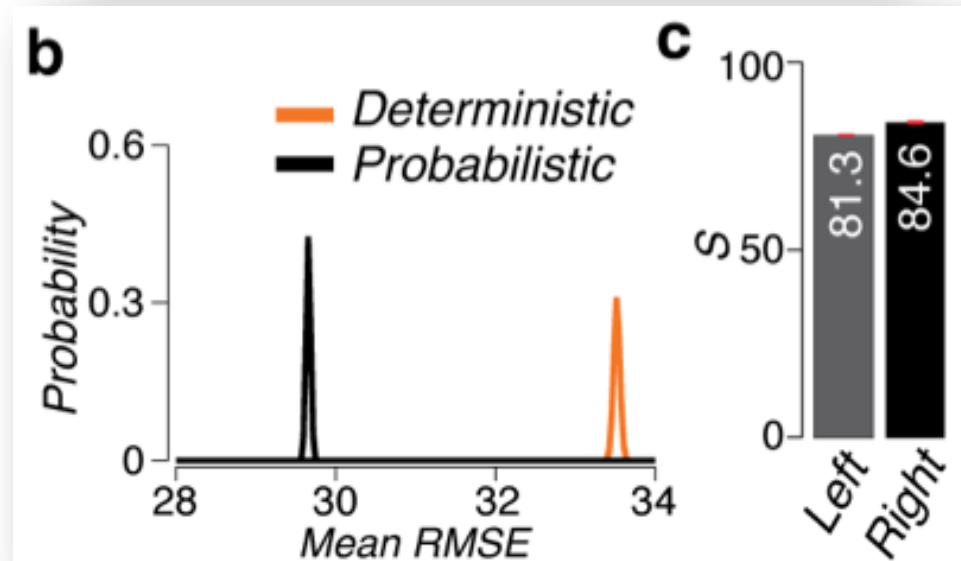


Subtraction and root mean square error

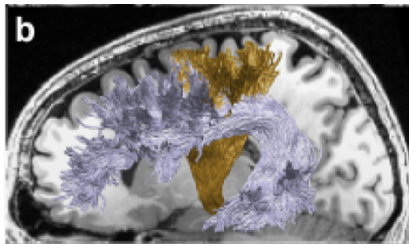
Statistical comparisons of cross-validated model accuracy



- Different models, or even specific parts of the tractography model, can be compared
- These comparisons provide a means to judge the strength of evidence in support of a particular idea
- These graphs show that the probabilistic model is a much better explanation of the dMRI data

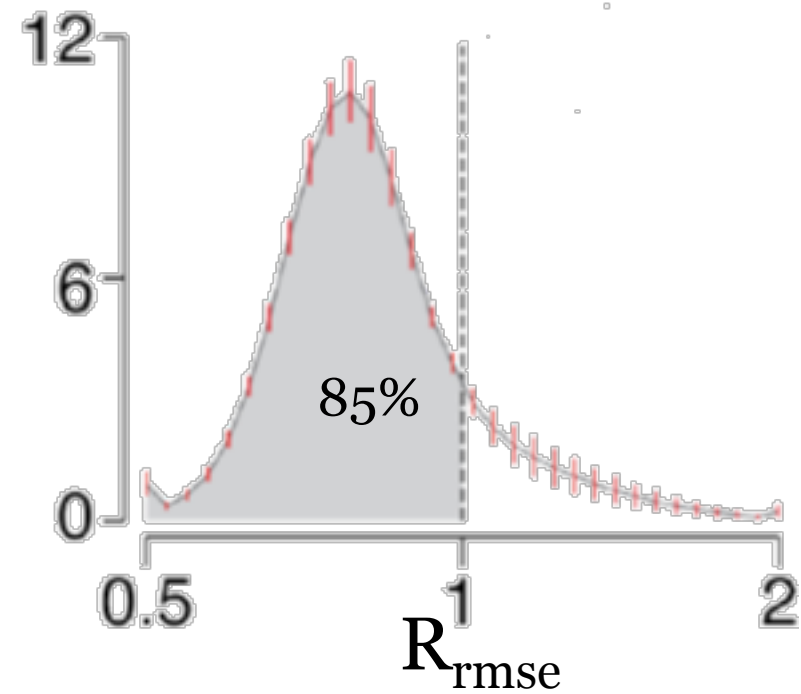
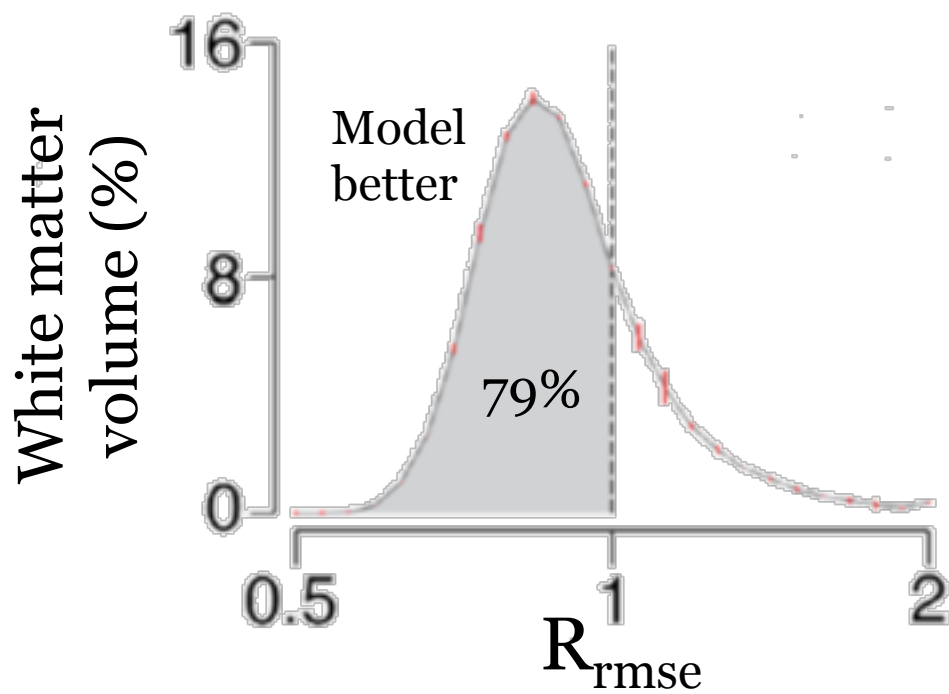


The optimized connectome predicts diffusion data better than test-retest reliability



150 directions (N=3)

96 directions (N=6)



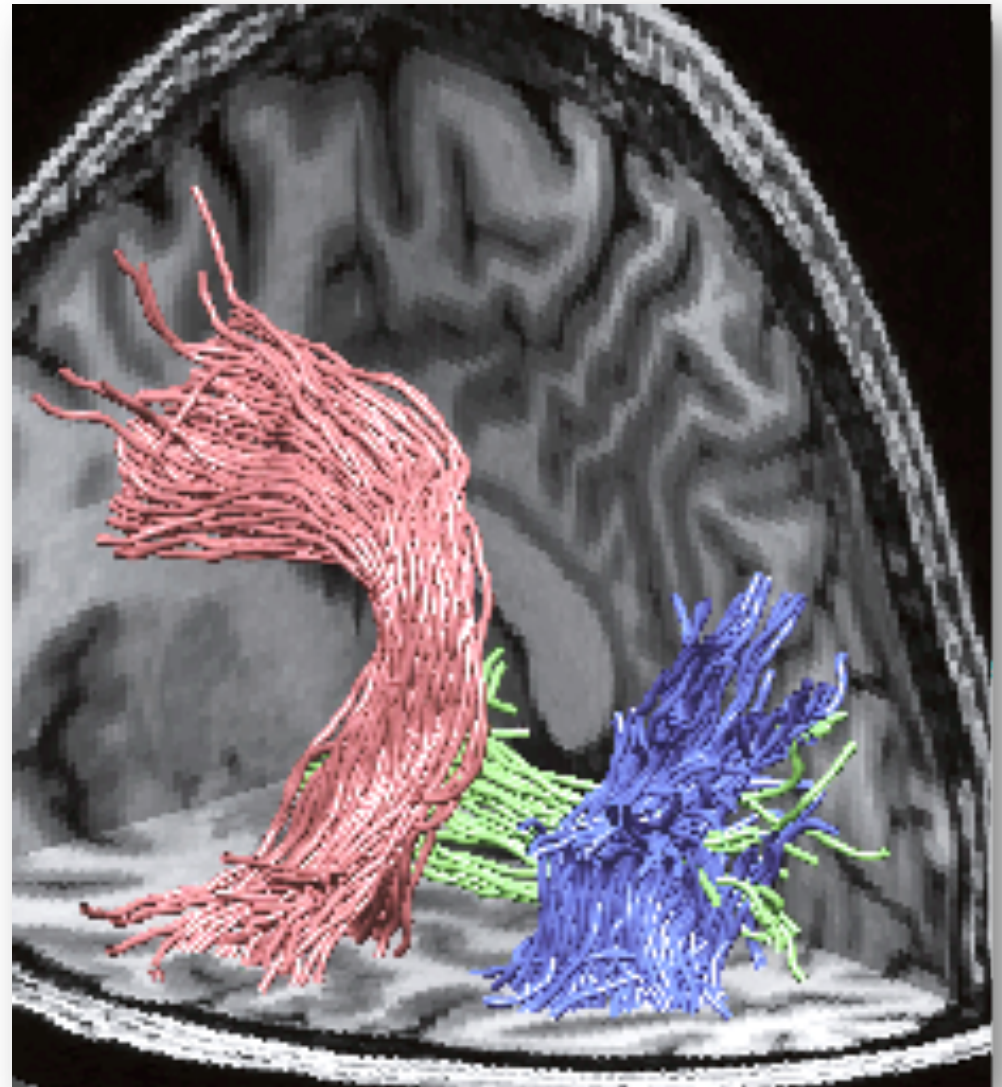
R_{rmse} = Ratio of model error to reliability error

Tractography

(Sherbondy et al., 2008;
Yeatman et al., 2012)

- We created Automated Fiber Quantification (AFQ) software to reproducibly identify the major tracts in individual subjects
- AFQ is open-source tractography method available on github and supported by Yeatman and his colleagues (like me)

Arcuate
Inferior longitudinal fasciculus
Vertical occipital fasciculus



Building a model of the circuit for seeing words

Michal Ben-Shachar



Jason Yeatman



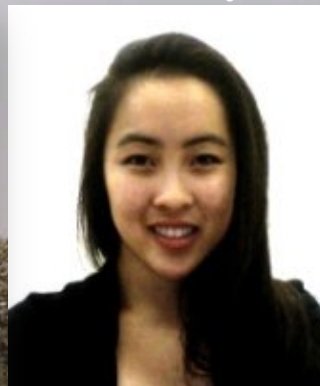
Andreas Rauschecker



Bob Dougherty



Rosemary Le



Nathan Witthoft



Kaoru Amano



The cortical reading network









- Reading and learning disabilities are an important problem in society
- Can we understand the brain networks that are essential for reading and diagnose these disabilities?



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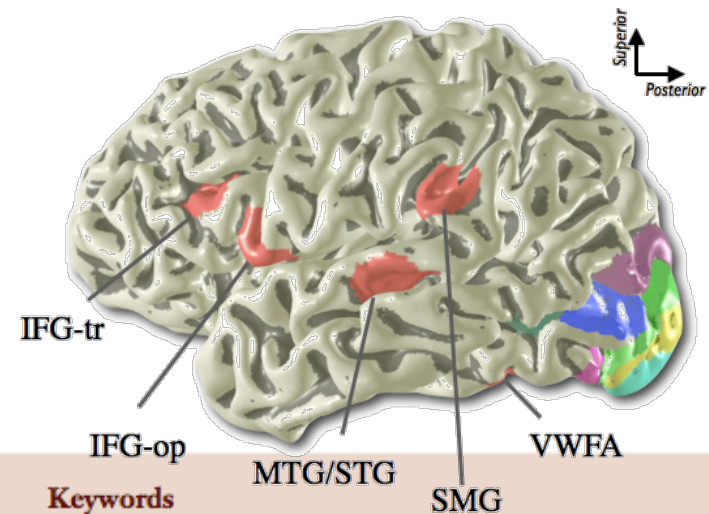
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 V2	 hV4
 V3	 LO-1/2
 hMT+	
 Language-related	

Learning to See Words

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¹Psychology Department, ²Medical Scientist Training Program and Neurosciences Program, Stanford University, Stanford, California 94305; email: wandell@stanford.edu, andreasr@stanford.edu, jyeatman@stanford.edu



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Keywords

reading, visual word form area, dyslexia, visual field maps, diffusion tensor imaging (DTI), fMRI

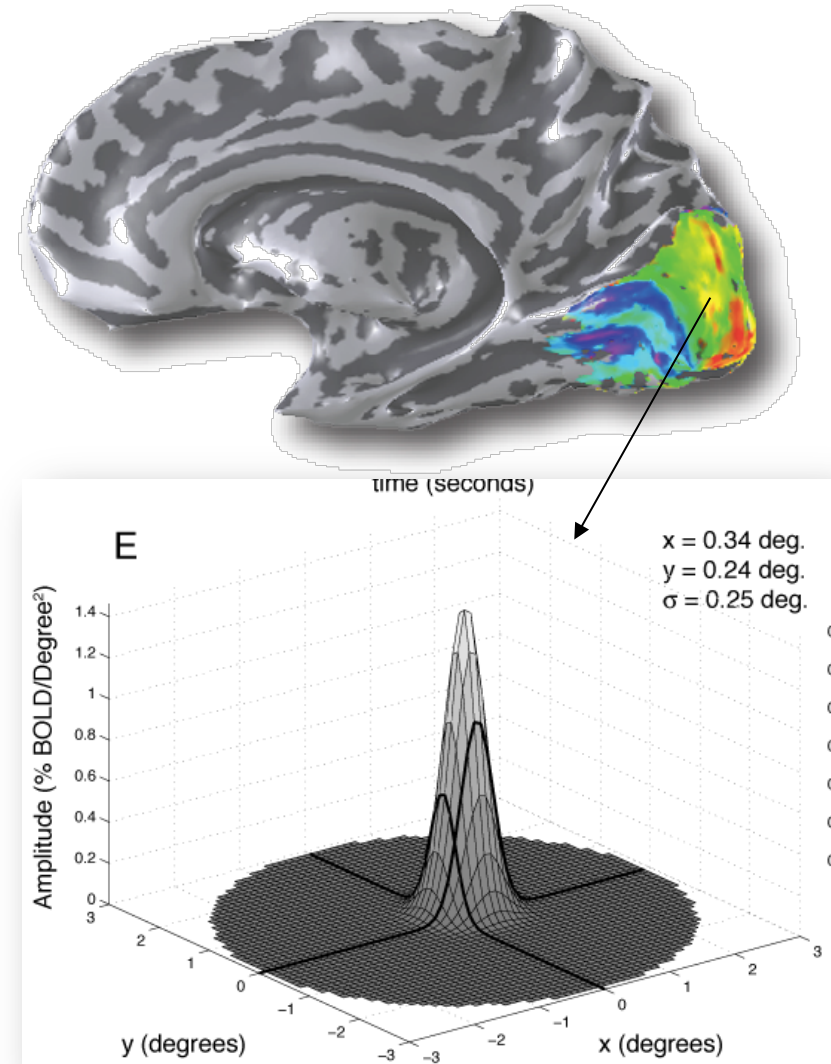
Abstract

Skilled reading requires recognizing written words rapidly; functional neuroimaging research has clarified how the written word initiates a series of responses in visual cortex. These responses are communicated to circuits in ventral occipitotemporal (VOT) cortex that learn to identify words rapidly. Structural neuroimaging has further clarified aspects of

Tracing the signal through the system

Amano et al. 2009

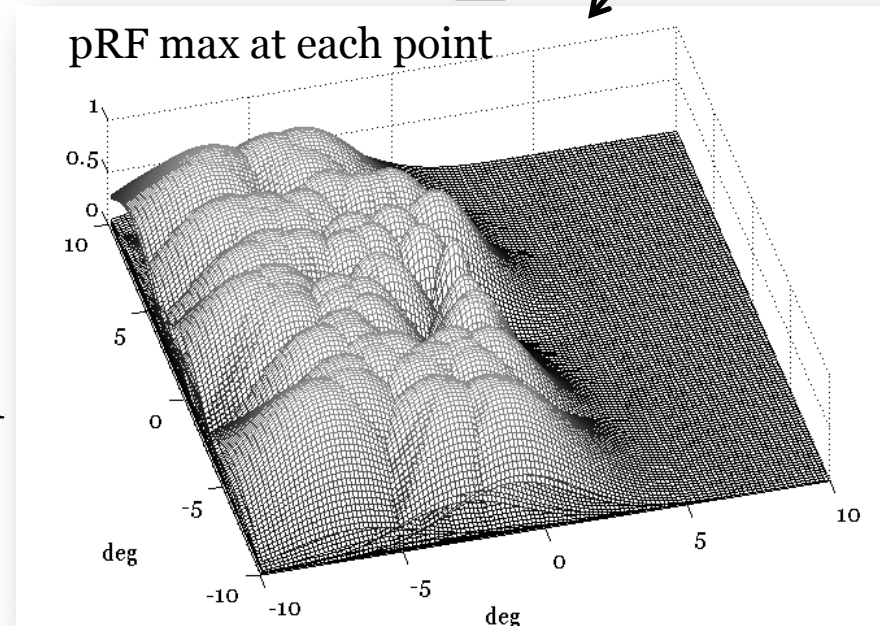
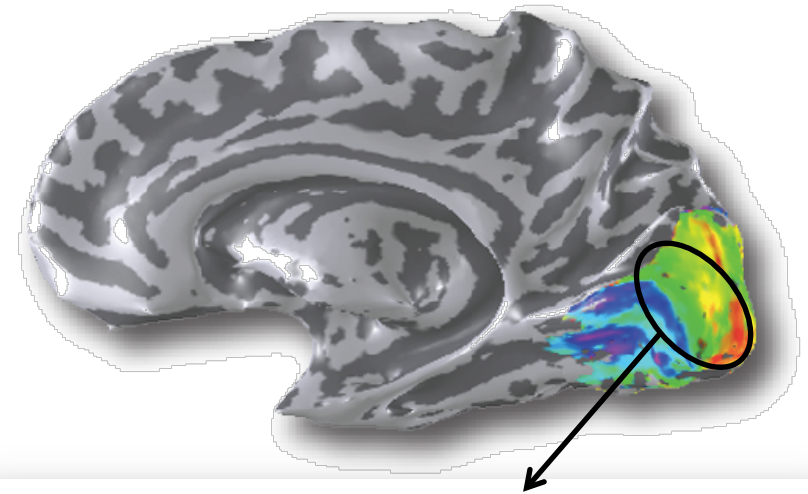
- A single voxel within, say, V1 has a pRF position and size
- Combining the pRFs from the voxels in a region tells us about its field of view
- In early visual field maps, the population receptive fields tile large portions of the visual field



Measuring the field of view of cortical regions

Amano et al. 2009

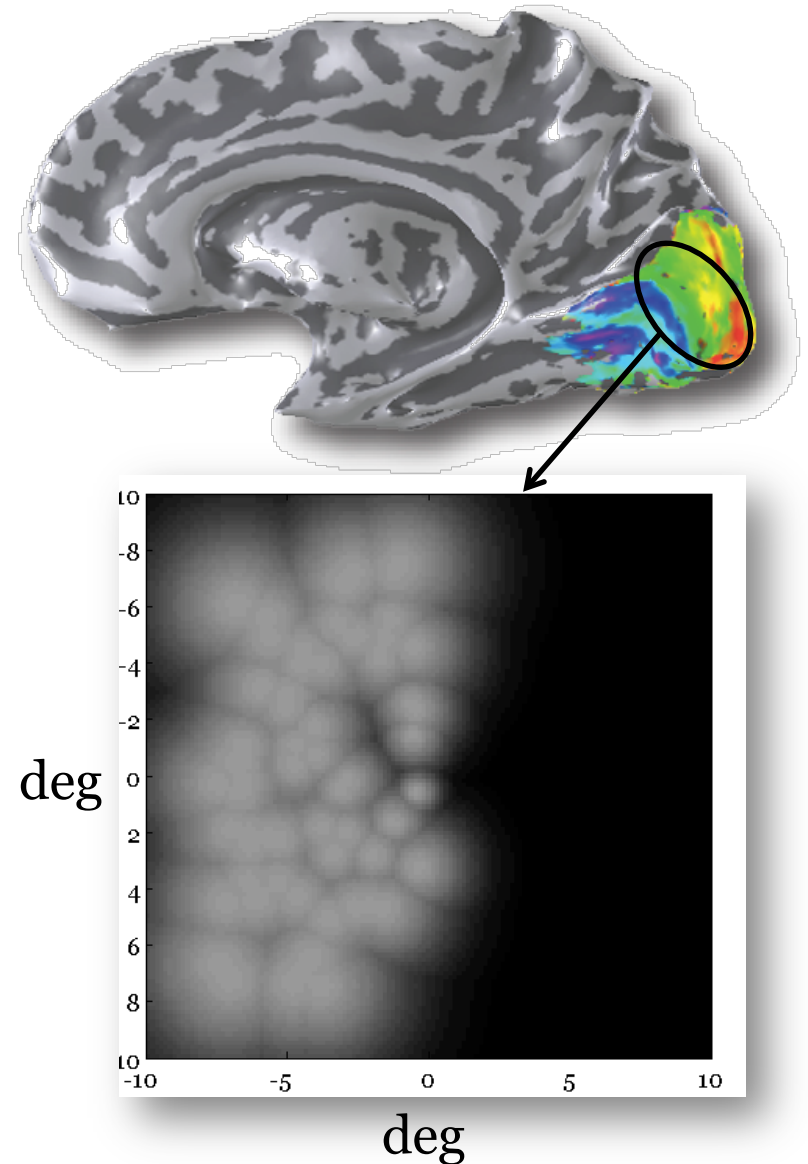
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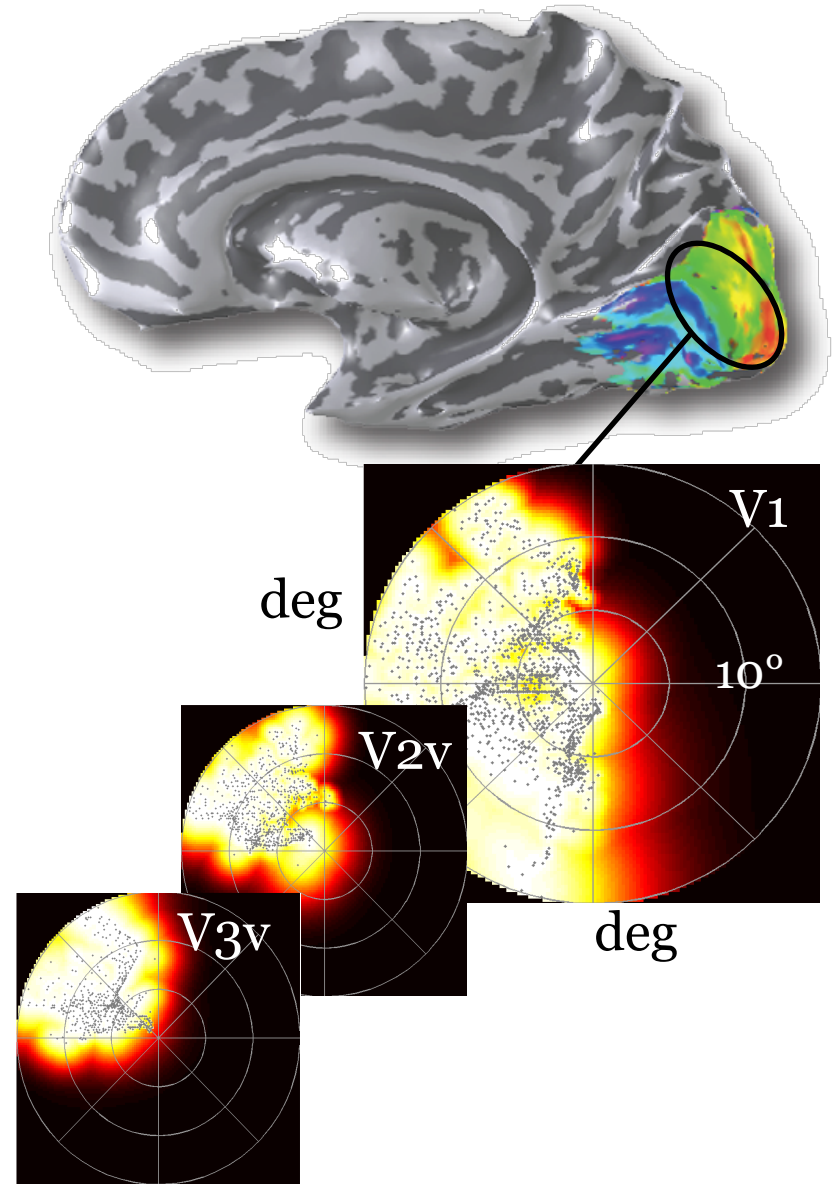
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Measuring the field of view of cortical regions

Amano et al. 2009

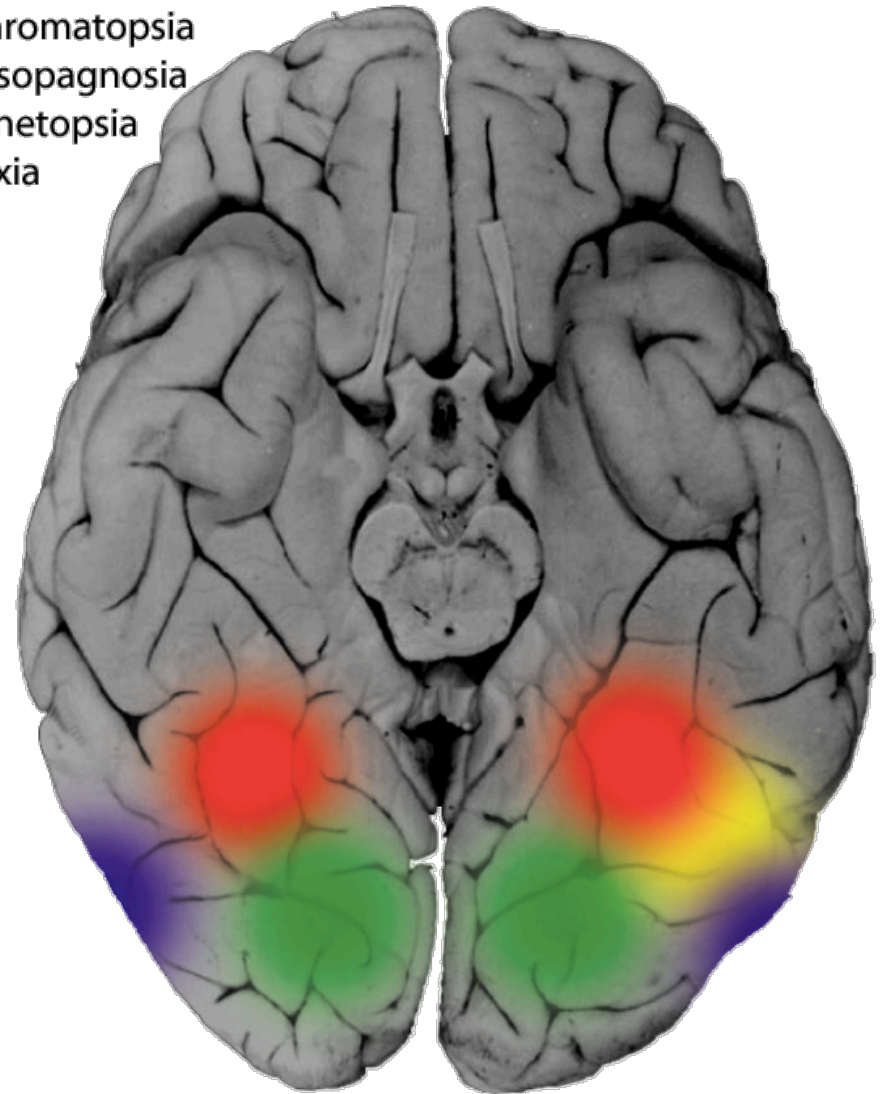
- A single voxel within, say, V1 has a pRF position and size
- Combining the pRFs from the voxels in a region tells us about its field of view
- The early visual field maps, the pRF field of view covers large portions of the visual field



Visual field coverage in face-responsive regions

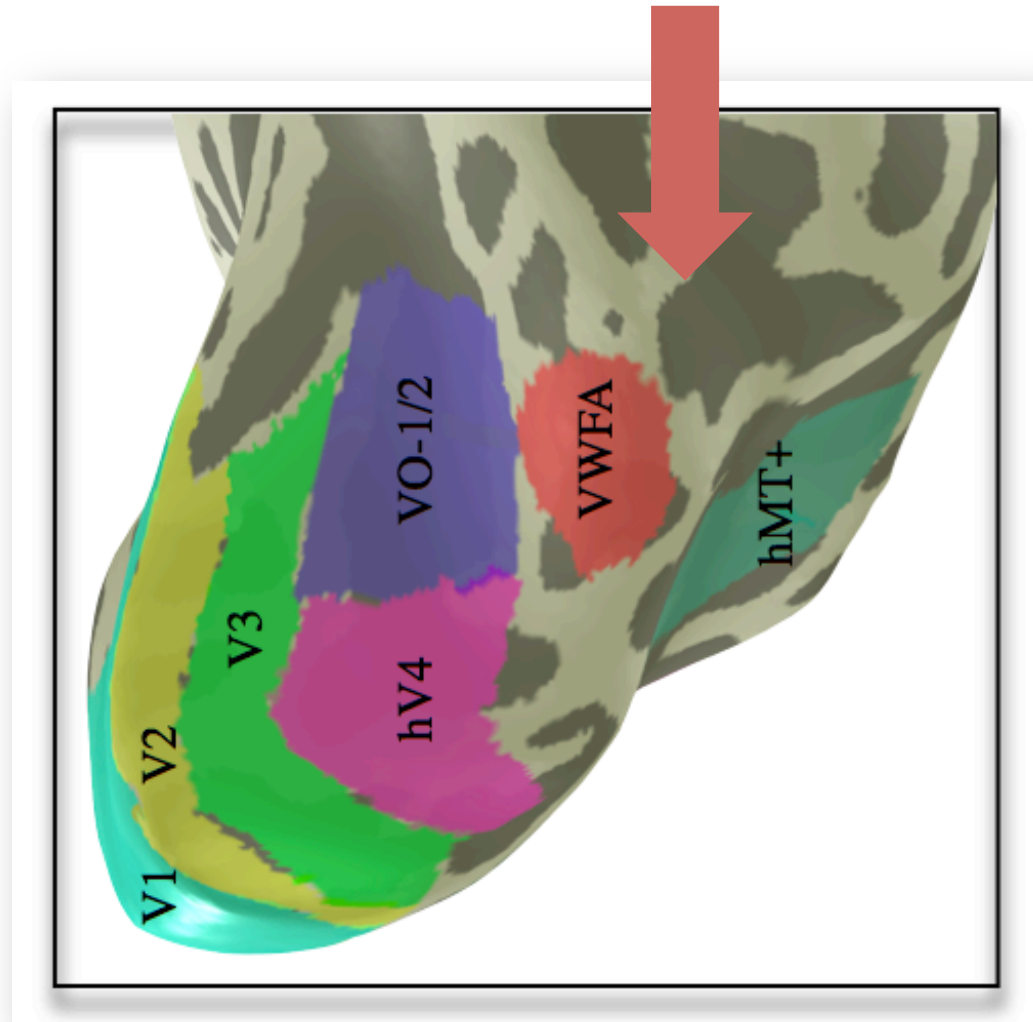
- Ventral occipitotemporal cortex (VOT) includes many regions that appear to play a special role in visual function
- Neurological studies from the 70s on show that these regions play an essential role in perceiving color, faces, motion, word recognition (Meadows, Zeki, Geschwind, Greenblatt, Nobre, McCarthy, Cohen, Dehaene)

- Achromatopsia
- Prosopagnosia
- Akinetopsia
- Alexia



Visual field coverage in VOT

- Ventral occipitotemporal cortex (VOT) includes many regions that appear to play a special role in visual function
- Neurological studies from the 70s on show that these regions play an essential role in perceiving color, faces, motion, word recognition (Meadows, Zeki, Geschwind, Greenblatt, Nobre, McCarthy, Cohen, Dehaene)
- Can we trace the signals and field of view from cortex into VOT, and particularly the reading circuitry?



VWFA Localizer

VWFA: voxels within an anatomical region whose amplitude when shown words, exceeded that of phase-scrambled objects and faces.

Anatomical region: Anterior of hV4, posterior of mid-fusiform sulcus, lateral of collateral sulcus, medial of middle temporal sulcus

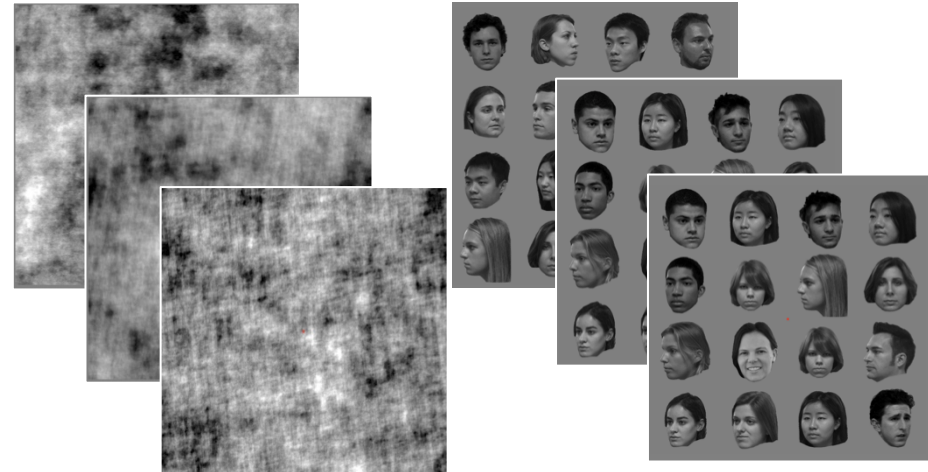
Words

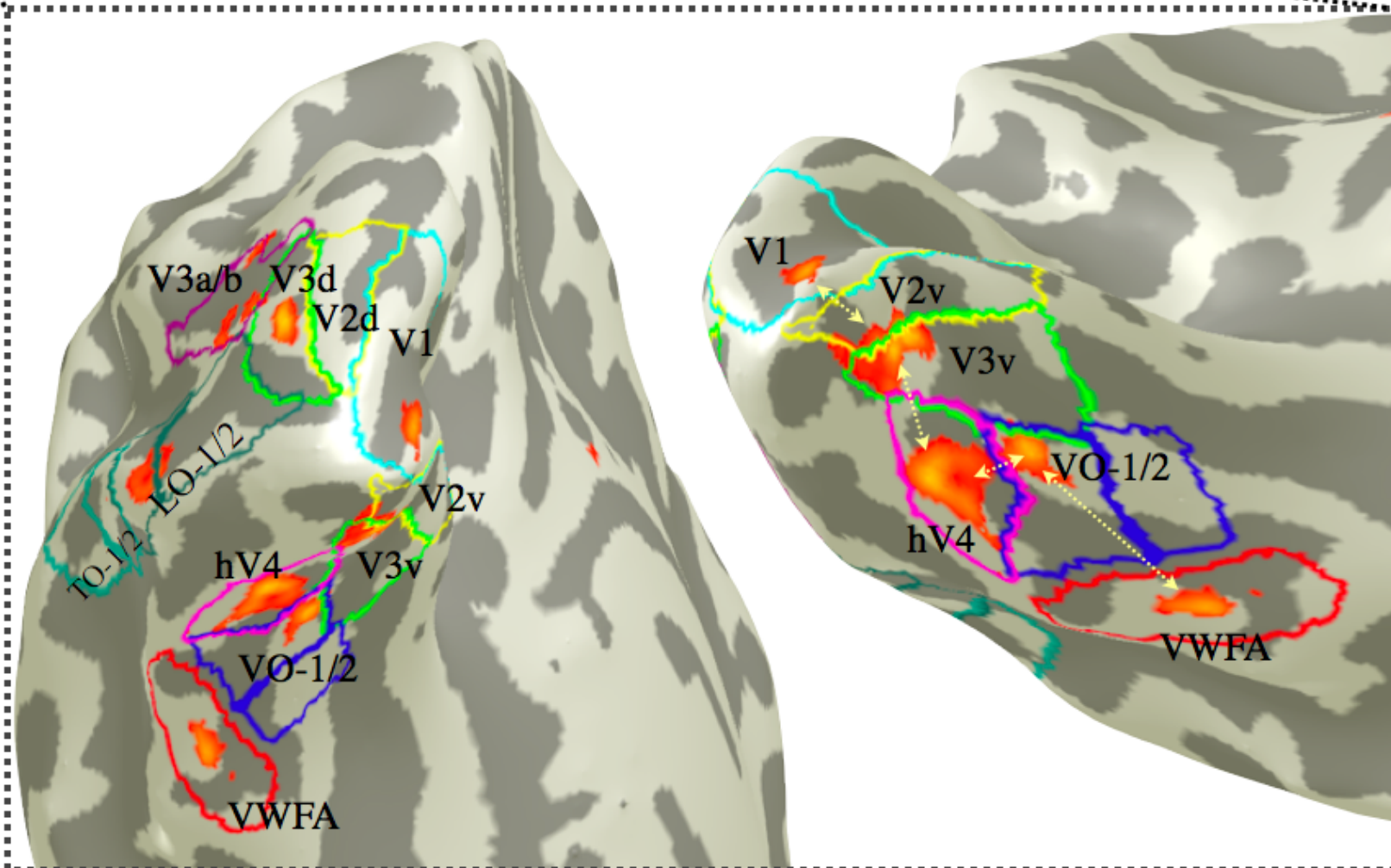
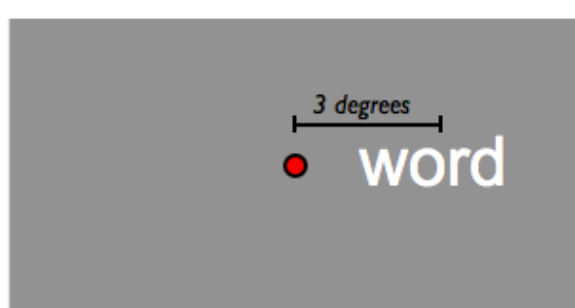
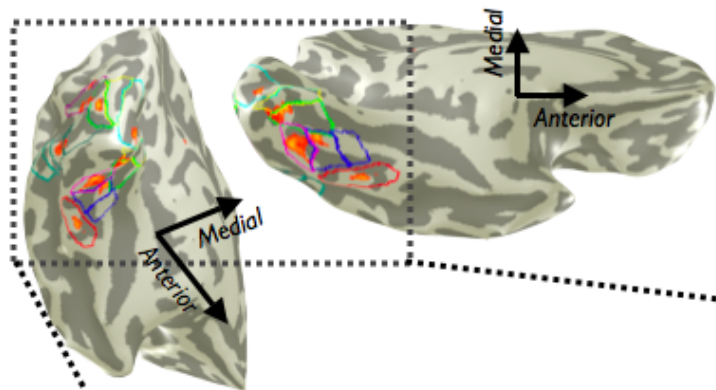
Textures and Faces

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2hz

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voice mrs leave much s
again months alone things help
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door are ago right only book
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view shall land itself then hand the
sat in boy c
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asked state real see pla
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well eyes if been person
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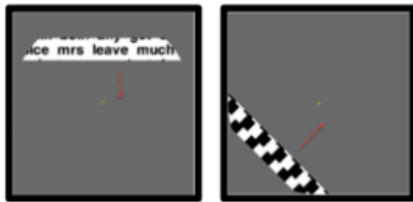
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f



Field of view in reading circuitry of a single subject

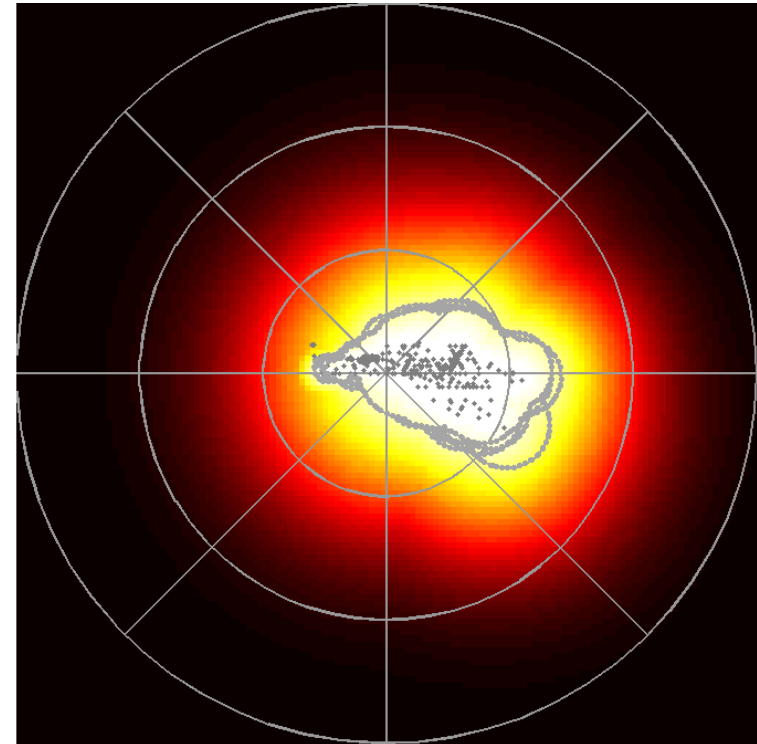
Measure pRFs



Localize Word-Responsive Regions

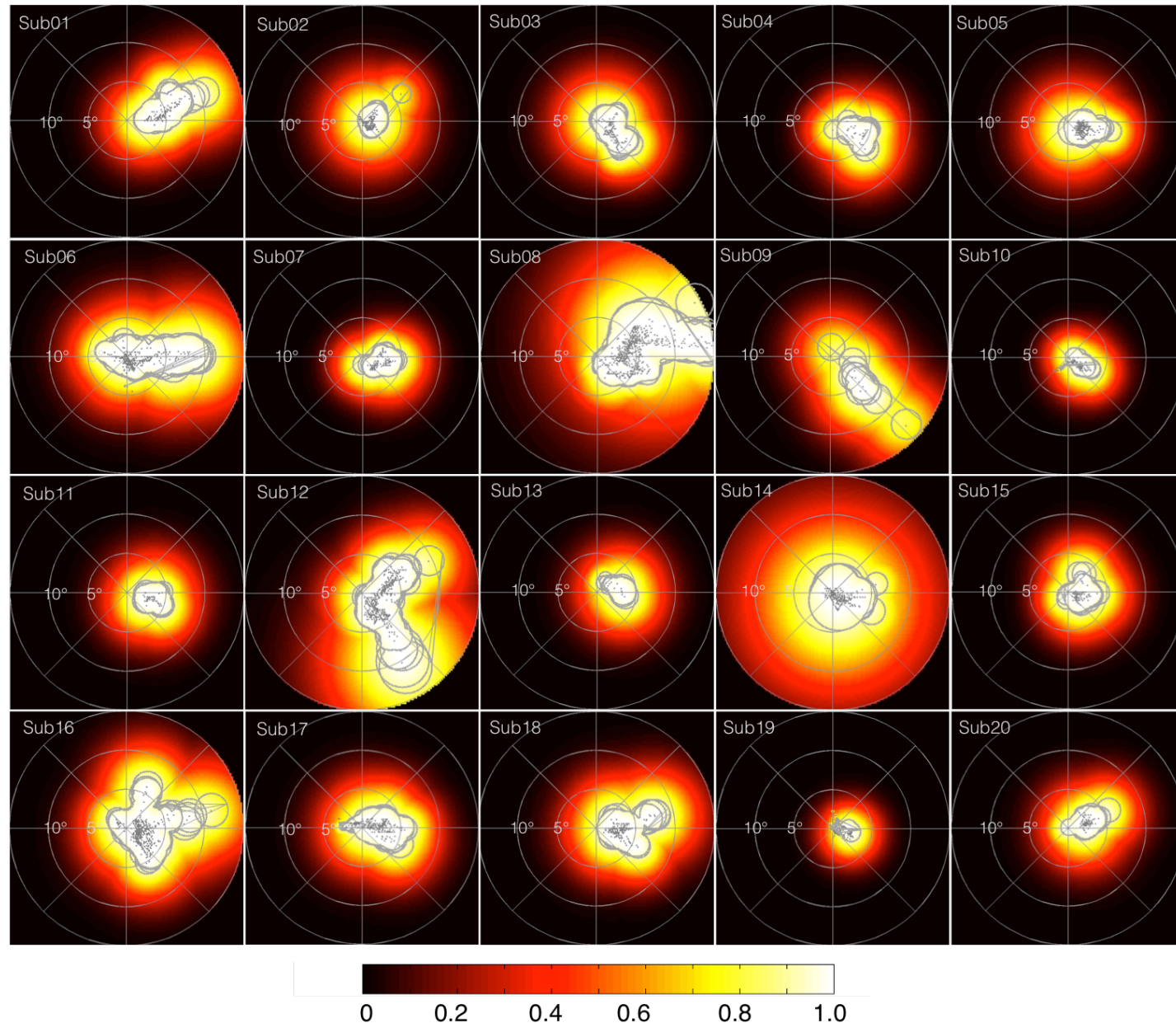


Sub17



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

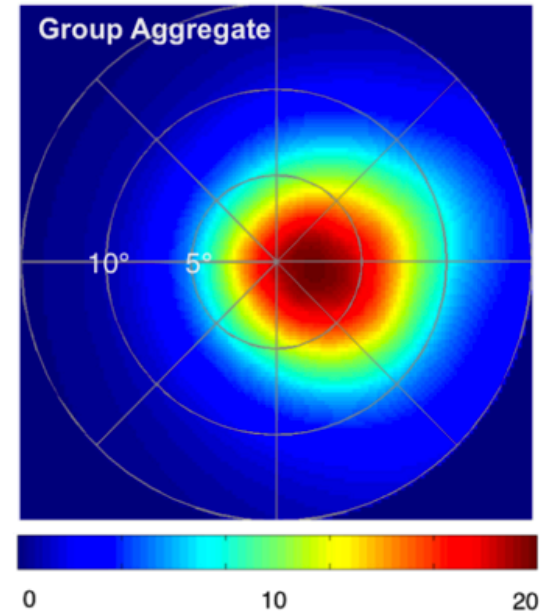


Reading circuitry FOV is more foveal than VOT

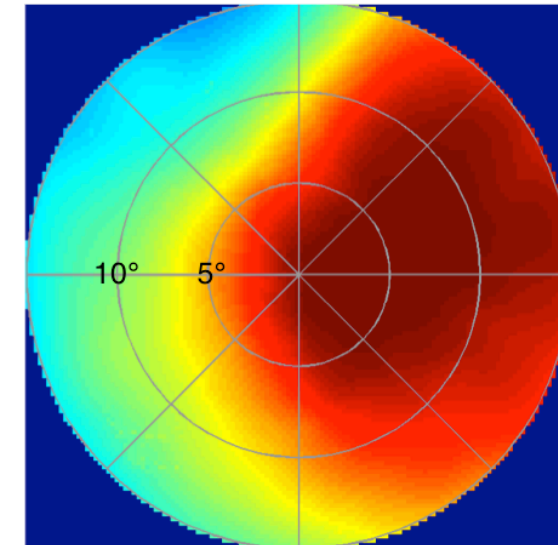
- The VOT field of view covers a larger portion of the field than the portion specialized for seeing words (cf. Levy, Hasson, Malach)



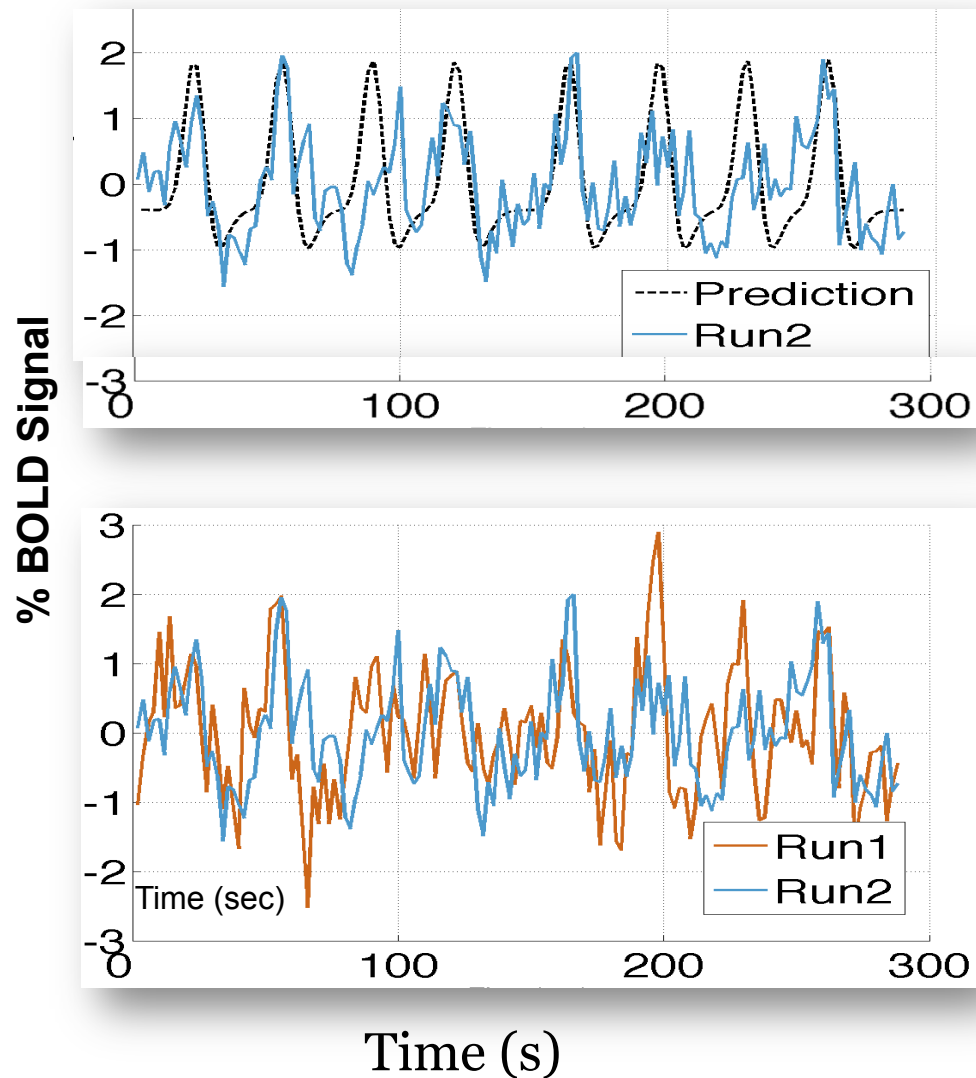
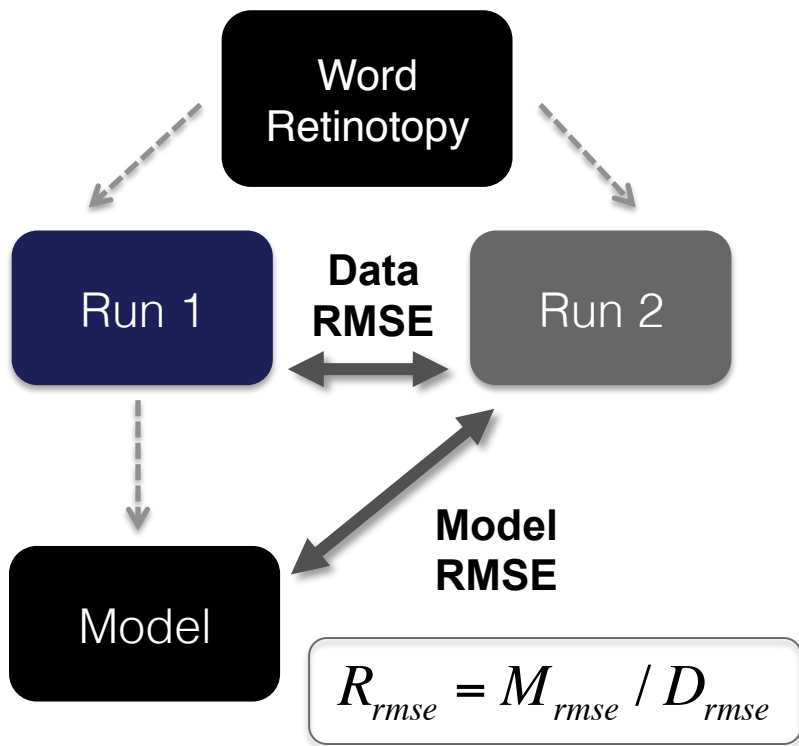
VWFA



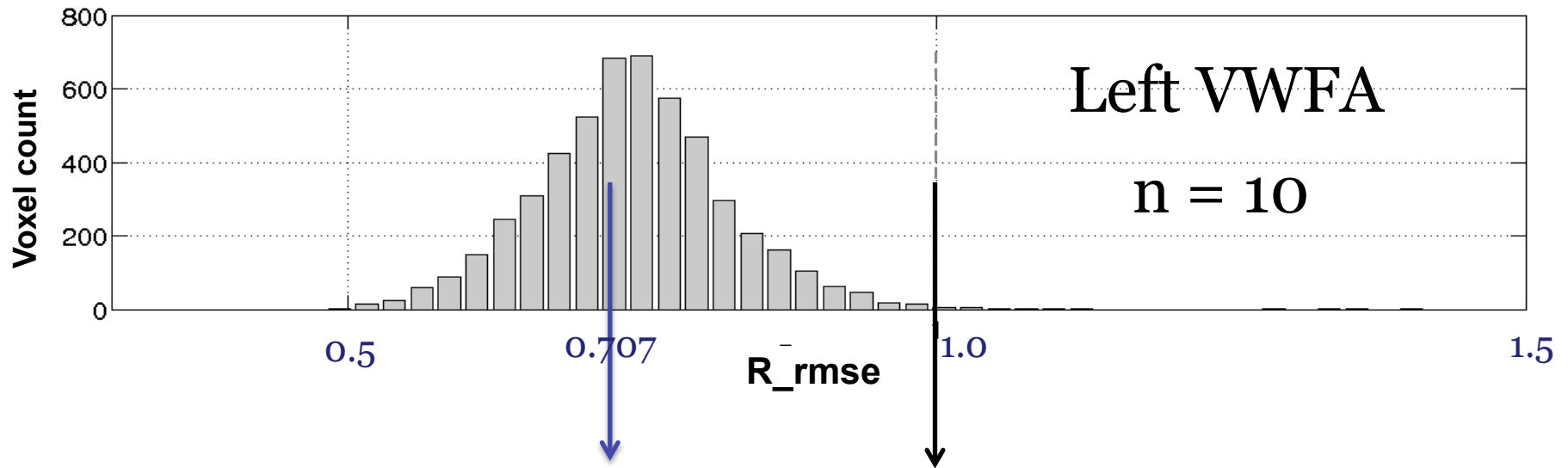
VOT



pRF model cross-validates better than test-retest



Ratio of RMSE (R_rmse) between model and test-retest

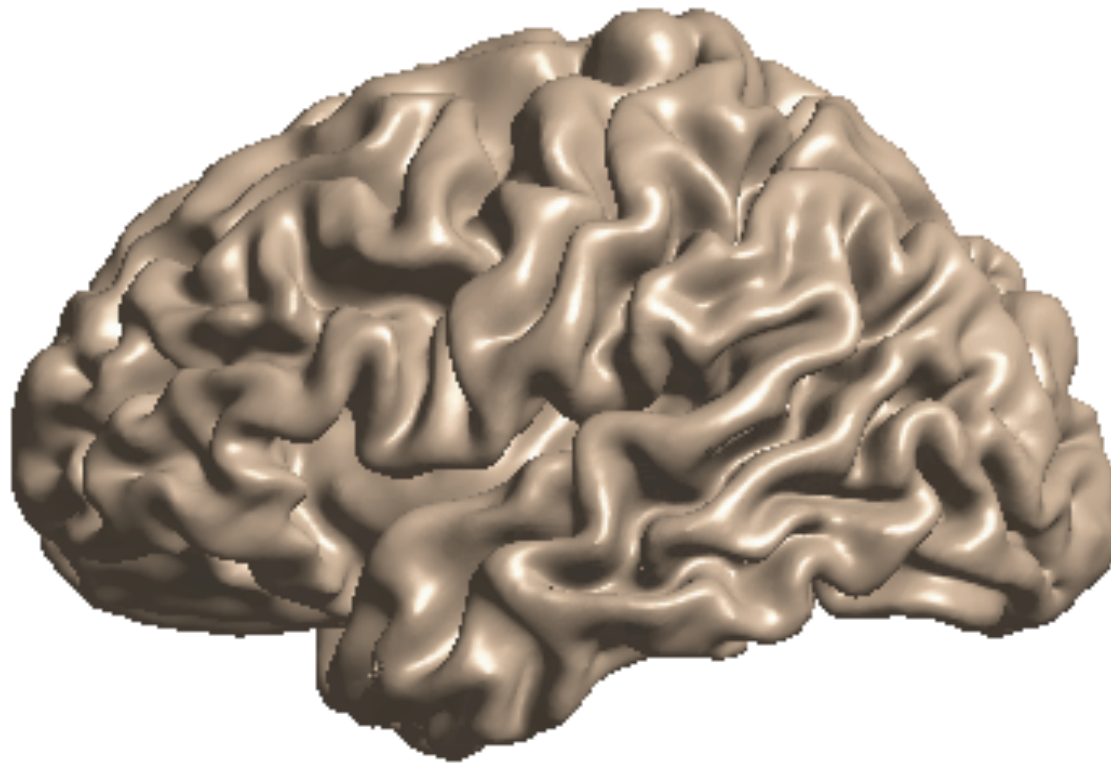


With iid voxels $\sim N(0, \sigma)$, a perfect model has an expected value of 0.707 (Rokem et al. 2015)

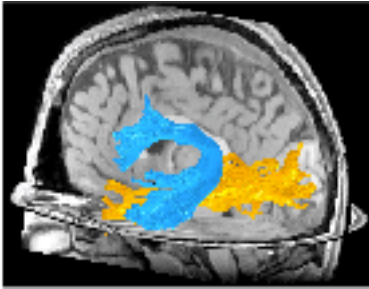
When $R_rmse < 1$, the model predict the data better than test-retest reliability.

Seeing the white matter reading tracts

(Yeatman et al., 2011)

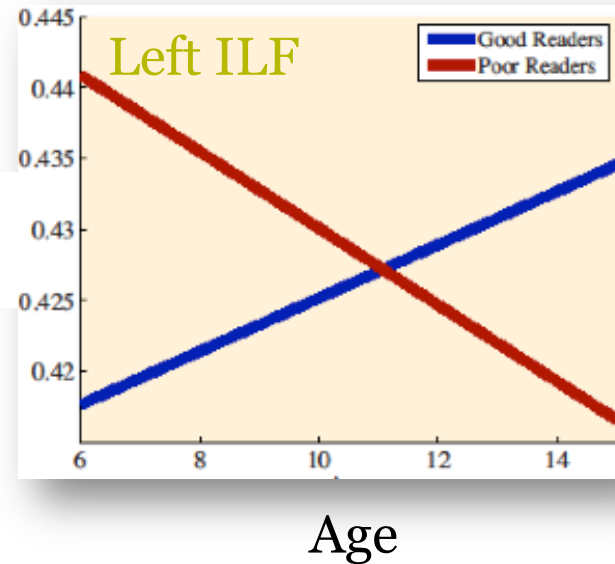


Diffusion (FA) changes differs between good and poor readers

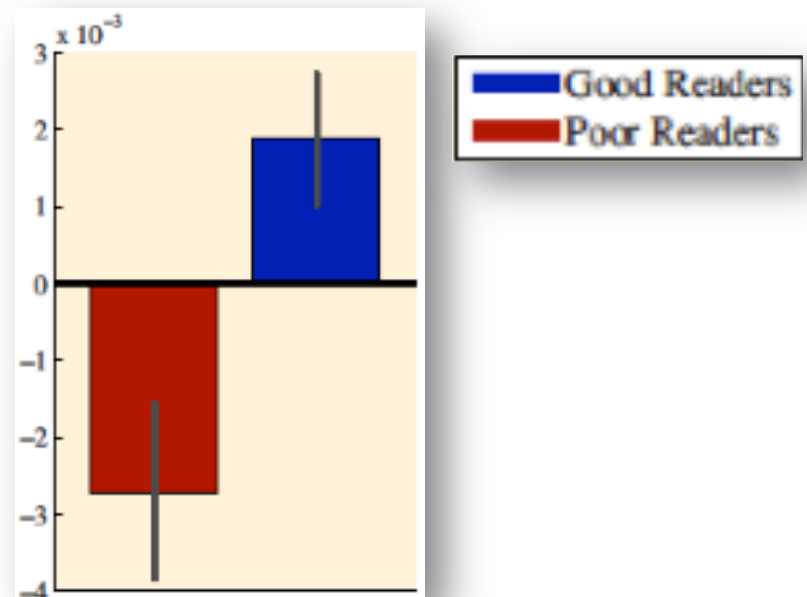


- Measured brain and behavior at 4 time points
- The first measurements predict reading over the next few years
- The rate and direction of FA development differs between good and poor readers in both the Arcuate and the ILF

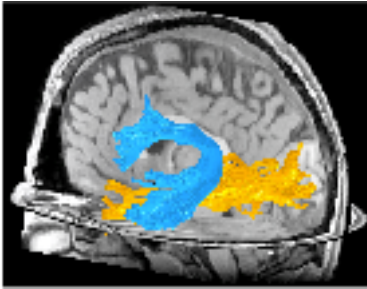
Fractional anisotropy



Mean FA development slopes

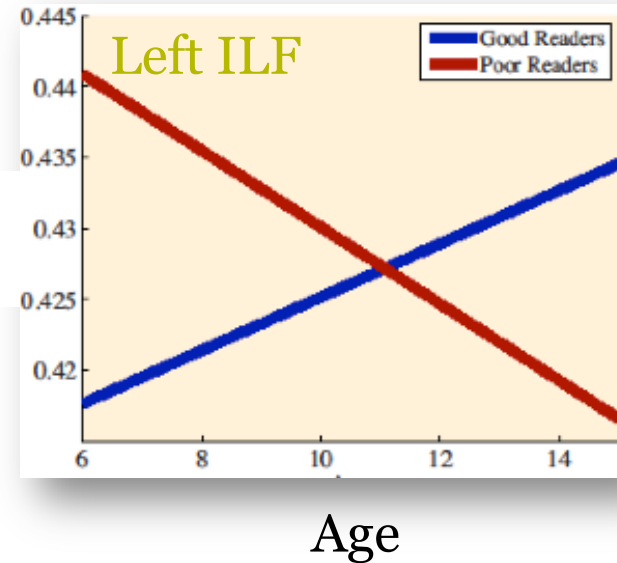


Diffusion (FA) changes differs between good and poor readers

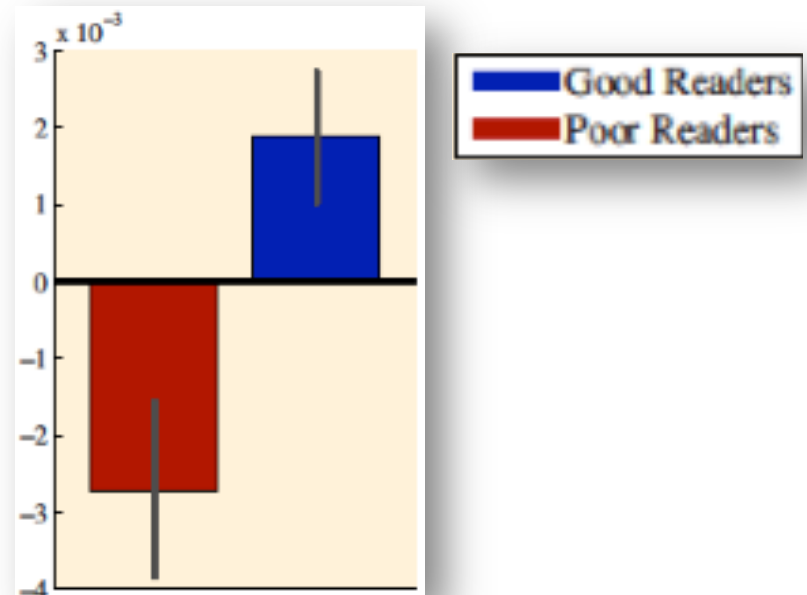


Fractional anisotropy

- FA in the ILF increases for good readers (6 – 14 years)
- Over the same ages, the FA declines for poor readers
- The FA development, not the FA level, matters



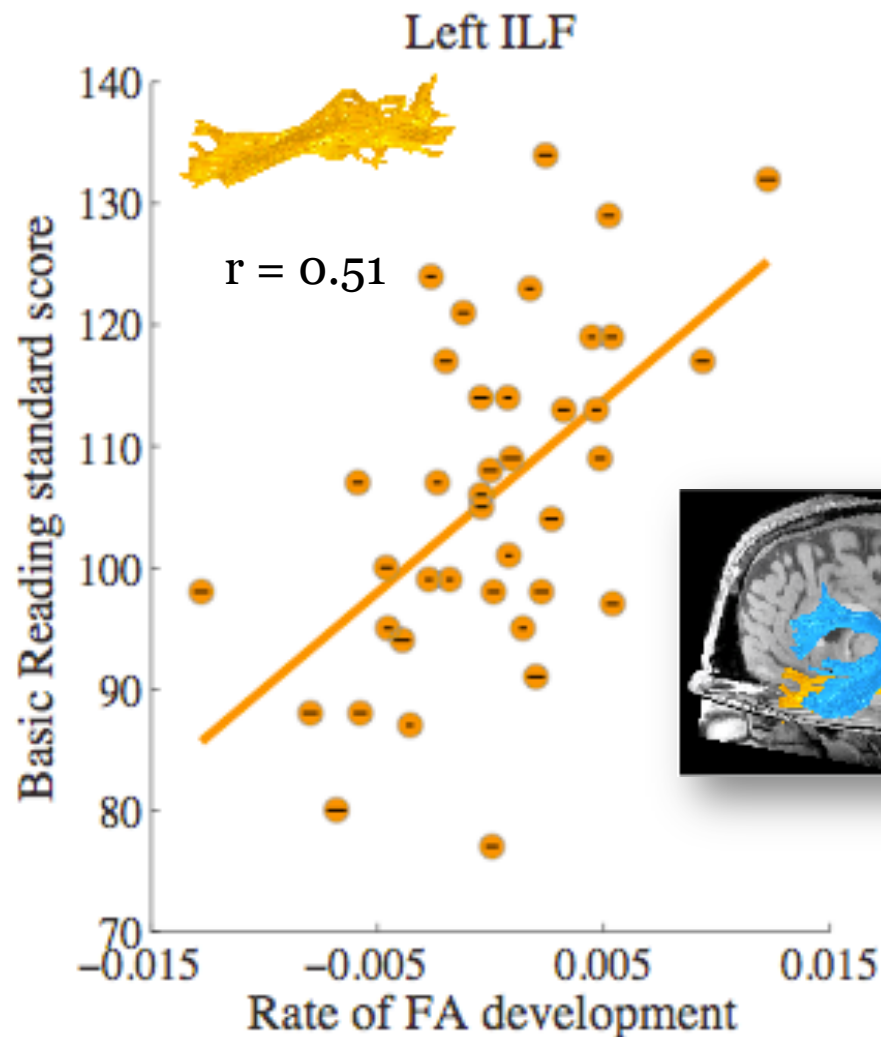
Mean FA development slopes



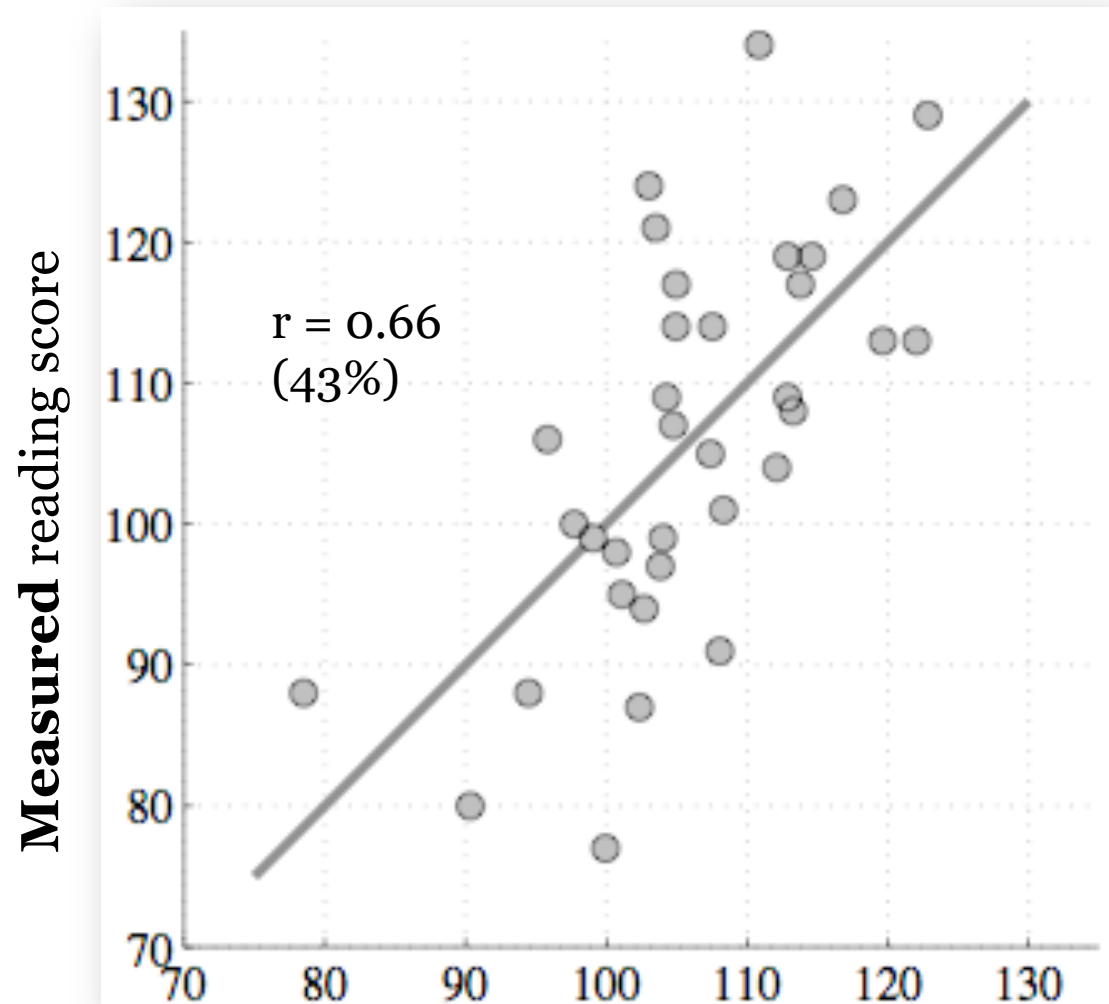
Correlations between tract diffusion change and seeing words

(Yeatman et al., 2012)

- 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



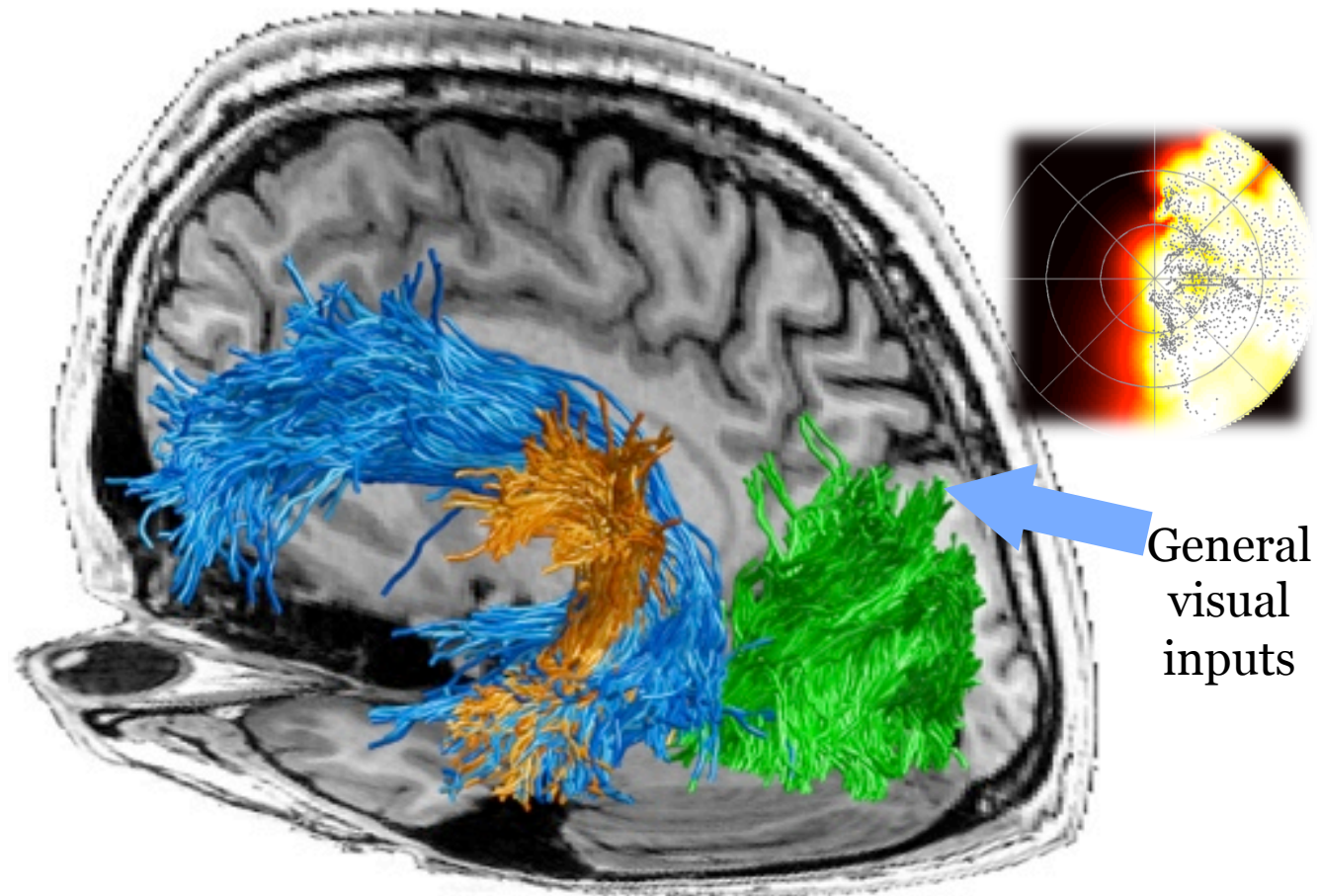
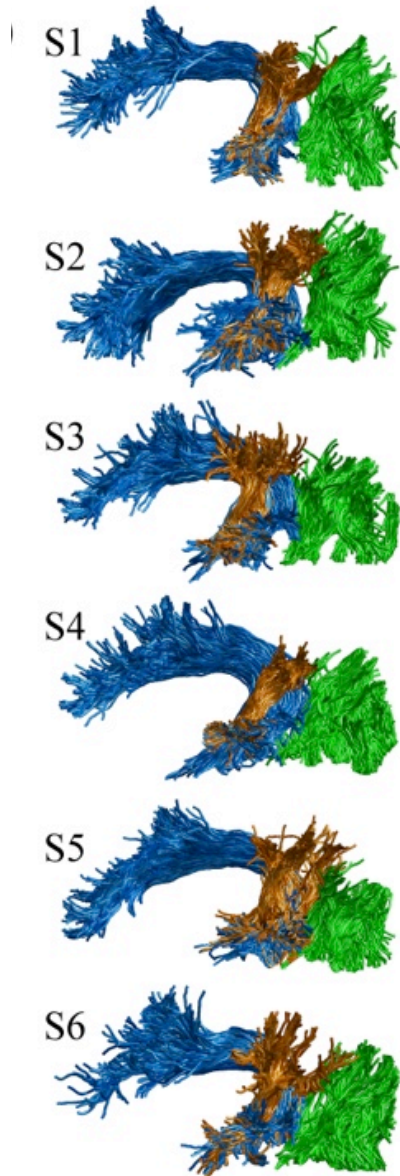
- Combining FA measurements of the two tracts (ILF and AF) predicts reading skill
- The predictions are not yet useful; they are statistically reliable



$$w_1 F_{ilf} + w_2 F_{arc}$$

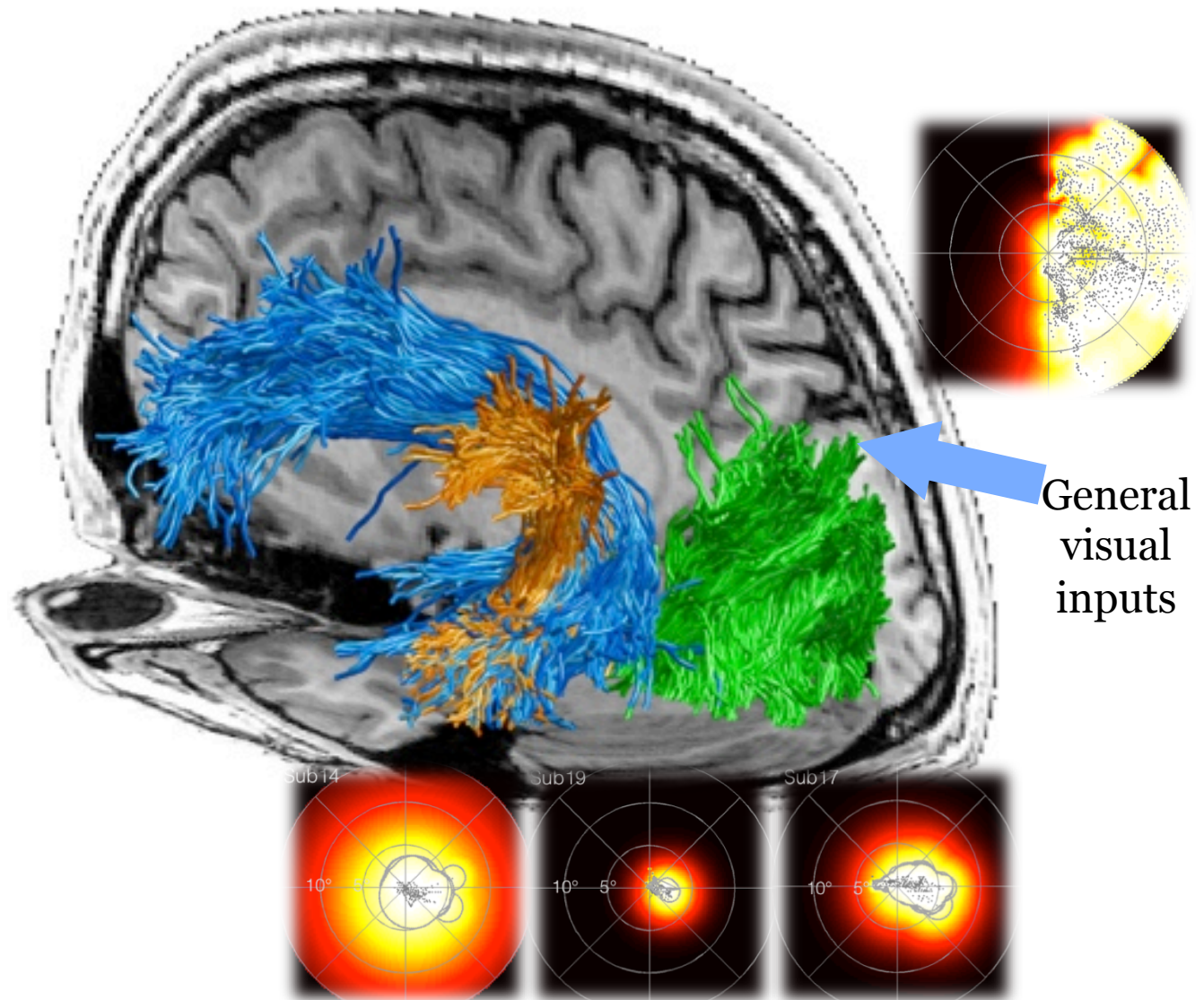
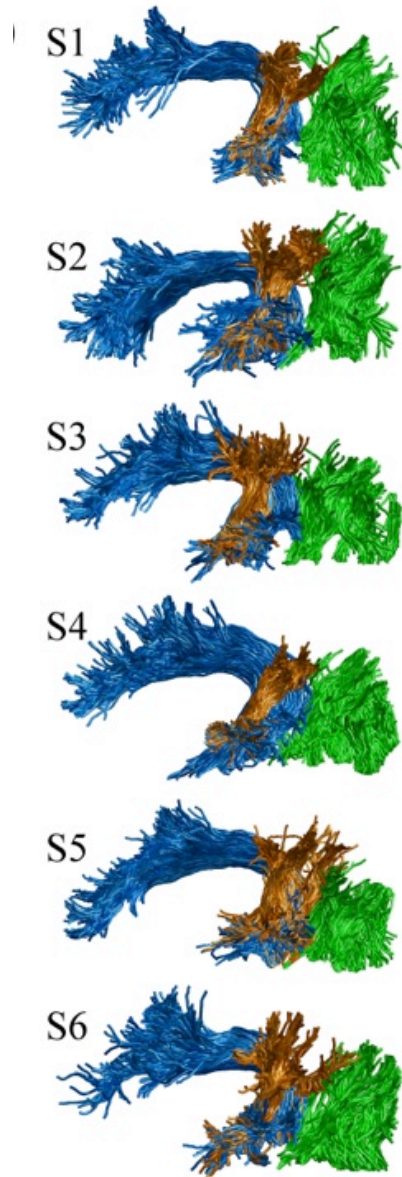
Predicted reading score
(weighted sum of ILF and AF FA)

Connectionism: Mismatch hypothesis



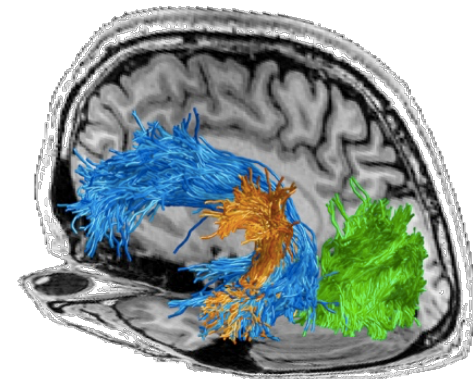
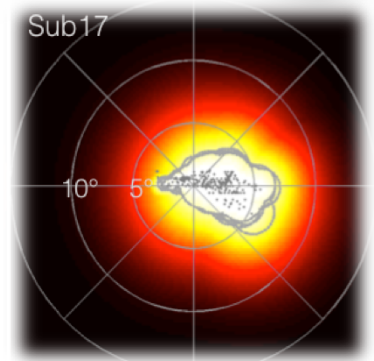
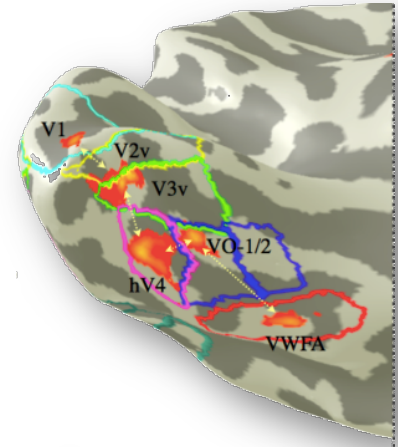
VOT
Specialized processing for
faces, words, other things

Connectionism: Mismatch hypothesis



Computational neuroimaging: Reading circuitry

- We have made progress in computational neuroimaging methods, so that we have the maps and some computational methods for key properties (pRF)
- We can follow responses to words up to VOT cortex in living human subjects at mm resolution; using dMRI we can identify the major tracts that carry these signals and that the cortex learns to recognize words using these circuits
- We hope to build computational models based on these MR measurements of the reading circuits, relating the neuroimaging measures to behavior, and to understand the biological reasons for success and failure of the reading circuitry in each child



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

Alyssa Brewer

Michal Ben-
Shachar

Serge
Dumoulin



Bob
Dougherty

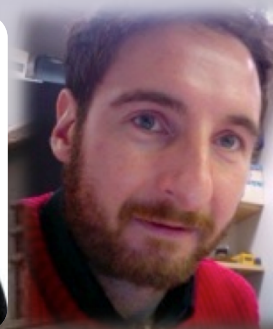


Rosemary
Le

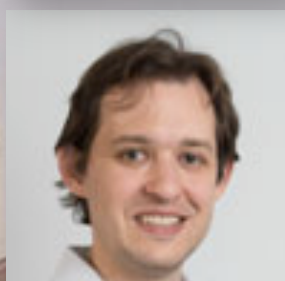
Franco Pestilli

Hiromasa
Takemura

Jason
Yeatman



Andreas
Rauschecker



Nathan
Witthoft

Kendrick Kay

Jon
Winawer

Ariel
Rokem



Kaoru
Amano

