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)

Figure 3
The visual field eccentricity map in human primary visual cortex (V1)

Voxel size

1986

2009

V1
V2
V3

Eccentricity (deg)

1 cm
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
Angular measurements sharply delineate visual field map boundaries.

- Inflated brain
- Gray/white are sulci/gyri
Combining eccentricity and angle data yields maps
• Maps tile the occipital lobe
• Extend into IPS and VOT
• Response properties differ
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-preferring regions

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

- Some object-preferring regions have retinotopic information as well

Courtesy of Witthoft and Winawer
• Population receptive field models

Serge Dumoulin    Kendrick Kay    Jon Winawer
‘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
Population RF estimation

Stimulus

Population RF model

Predicted BOLD (including HRF)

Parameters $(x_1, y_1, s_1)$

Observed

% BOLD

1 cycle

Time (sec)
Population RF estimation

Stimulus

\[
y \rightarrow \text{time} \rightarrow x
\]

Predicted BOLD (including HRF)

\[
\%
\]

Observed

1 cycle

Time (sec)

Population RF model

\[
y \rightarrow s_1 \rightarrow x
\]

Parameters

\[
(x_2, y_2, s_1)
\]

Dumoulin and Wandell, 2008

Neuroimage
Population RF estimation

Stimulus

% BOLD

Predicted BOLD (including HRF)

Observed

1 cycle

Time (sec)

Parameters

$(x_2, y_2, s_2)$

Dumoulin and Wandell, 2008
Neuroimage
Population receptive fields vary significantly across human visual cortex

Dumoulin and Wandell, 2008
Neuroimage
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.

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...

- Attention
- Stability and Plasticity
- Prosopagnosia
- Development and aging
- Autism
- Alzheimer’s disease
• 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 “

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

Kay et al., 2013, PLoS Computational Bio
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)

Winawer et al., Current Biology, 2013
White matter in the human brain

• Diffusion and tractography

Ariel Rokem  Franco Pestilli  Hiromasa Takemura  Jason Yeatman
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.
• 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

$b = 800$
Diffusion weighting: Directions

Dark means large signal attenuation
High ADC

$b = 800$
The measured diffusion signal in a direction, $\theta$, is related to the apparent diffusion coefficient in that direction, $D(\theta)$.

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

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

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

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

E. O. Stejskal and J. E. Tanner (1965)
Algorithms to combine the local (voxel) diffusion measurements to estimate white matter tracts (streamlines)

*Diffusion data are surfaces*
Clarifying Human White Matter

Brian A. Wandell

Department of Psychology and Neurosciences Institute, Stanford University, Stanford, California 94305; email: Wandell@stanford.edu

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

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

- Each fascicle is assigned a weight to indicate the strength of its contribution to the data
Stages of Life: Solve for the fascicle weights

Diffusion signal, $S(\theta)$

\[
\begin{pmatrix}
  v_1 \\
v_2 \\
v_N \\
\end{pmatrix}
\]

Each column is the prediction of a fascicle

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

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, $S(\theta)$

$$
\begin{bmatrix}
v_1 \\
v_2 \\
v_N
\end{bmatrix}
= 
\begin{bmatrix}
S(\theta)
\end{bmatrix}
$$

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

Each column is the prediction of a fascicle

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

$10^7 \times 10^6$
Stages of LiFE: Eliminate zero weight fibers (false alarms)

Candidate connectome

Many many fascicles

Optimized connectome

Solving a system of linear equations (non-negative least-squares)
Stages of LiFE: Predict diffusion signal

Optimized connectome and weights

Big matrix multiplication

Prediction
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.

White matter volume (%)

150 directions (N=3)  96 directions (N=6)

Model better

$R_{\text{rmse}} = \text{Ratio of model error to reliability error}$
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)
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?
Tracing the signal through the system

• 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

Amano et al. 2009
Measuring the field of view of cortical regions

- 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

Amano et al. 2009
Measuring the field of view of cortical regions

- 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.

Amano et al. 2009
Measuring the field of view of cortical regions

- 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

Amano et al. 2009
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)
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**

```
new so young with moth within both any got off n
voice mrs leave much s again i put door death
our in view sat in mrs her above
months alone things help to few office where and are ago right only book
talk of let food small fac asked state real see pla
land itself then hand the take told me per whose life ask try past home y
eyes poor or its case a large do seen idea time
shall now days wife foun well eyes if been person
death an seems high put is part ago war ten simp them is out number mor
```

**Textures and Faces**

8 sec, 2hz
The word-bar stimulus gave it away. The man with the almanac took free.
Field of view in reading circuitry of a single subject
Field of view of the VOT reading circuitry

- There are significant differences between subjects.
- Yes, we are correlating these differences with measures of word recognition.
The VOT field of view covers a larger portion of the field than the portion specialized for seeing words (cf. Levy, Hasson, Malach)
pRF model cross-validates better than test-retest

\[ R_{rmse} = \frac{M_{rmse}}{D_{rmse}} \]
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.

Left VWFA

$n = 10$
Seeing the white matter reading tracts

(Yeatman et al., 2011)
Diffusion (FA) changes differ 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

Age

Mean FA development slopes
Diffusion (FA) changes differ between good and poor readers

- 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
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 with an $r = 0.66$ (43%).

The predicted reading score can be calculated as:

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

Predicted reading score (weighted sum of ILF and AF FA)
Connectionism: Mismatch hypothesis

VOT
Specialized processing for faces, words, other things

General visual inputs
Connectionism: Mismatch hypothesis

General visual inputs
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