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

Professor Brian Wandell
Stanford Center for Cognitive and Neurobiological Imaging (CNI)
Department of Psychology
Stanford University
New methods for measuring activity, connections and tissue properties in the living human brain

• Human visual field maps (Kay, Winawer, Dumoulin)
• White matter tracts for reading development (Yeatman)
• Quantitative MRI of brain tissue (Mezer)
• Project on Scientific Transparency
Primary visual cortex (V1) contains a visual field map.

Horton and Hoyt (1991)
Human eccentricity mapping
(Engel et al., 1994, 1997; Sereno; DeYoe; Others)
Pseudo-color representation of visual field map
Angular measurements sharply delineate visual field map boundaries.
More than sixteen visual field maps


Wandell and Winawer (2011) Vision Research

- Tile the entire occipital lobe
- Extend into IPS and VOT
- Response properties differ
Modeling human visual field map responses

- Linear models of population receptive fields
The receptive field
A stimulus referred measurement

‘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
(Dumoulin and Wandell, 2008)

Stimulus

Population RF model

Parameters
\( (x_1, y_1, s_1) \)

Predicted BOLD (including HRF)

Observed

% BOLD

1 cycle

Time (sec)
Population RF estimation

Parameter estimation

Stimulus

\[ \text{Population RF model} \]

\[ (x_2, y_2, s_1) \]

Predicted BOLD (including HRF)

Observed

% BOLD

1 cycle

Time (sec)

(Dumoulin and Wandell, 2008)
Population RF estimation

Stimulus

Population RF model

Predicted BOLD (including HRF)

Observed

Parameters

$$(x_2, y_2, s_2)$$

(Dumoulin and Wandell, 2008)

- Prediction: Weighted linear summation of over a portion of the visual field
- Spatial weights are Gaussian
- Model estimates Gaussian center \((x,y)\) and size (\(\sigma\))
Population receptive field vary significantly across human visual cortex
Population RF size increases with eccentricity within each map.
Neurological surprises

The case of the missing chiasm
Plasticity and stability of the visual system in human achiasma.
Conventional optic chiasm

Control
Missing optic chiasm

Achiasma
Normal

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

Right visual field

Left visual field

Apkarian et al., E.J.N. 1994
Apkarian et al., Brain, 1995
Victor et al., Cer. Cortex, 2000
Jansonius et al., JNO, 2001
Prakash et al., JNO, 2009
Subject AC2 characteristics

- Slight decrease in visual acuity
- Slightly reduced peripheral visual fields
- No stereopsis
- Prominent infantile and see-saw nystagmus (resolved)
Right and left hemifield maps are overlaid in both hemispheres.
Right and left hemifield maps are overlaid in both hemispheres.
Modeling the time course (1 Gaussian)
Modeling the time course (2 Gaussians)
Achiasmic - Folded representation

Right retina

Temporal

Control

V1
Achiasmic - Folded representation

Right retina

Temporal

Control
Achiasmic - Folded representation

Right retina

Temporal

Achiasma

(No evidence of an inserted map, re: Muckli et al.)
Summary – the system view

1. A genetic defect that disrupts crossing at the chiasm signaling causes a developmental reorganization in visual cortex.

2. Despite the profoundly disrupted V1 maps, the rest of the brain figures out what to do.
FMRI References


Cortical maps and white matter tracts following long period of visual deprivation and retinal image restoration N. Levin, S. Dumoulin, J. Winawer, R. Dougherty and B. Wandell (2010). Neuron V. 65, pp. 21-31

Seeing words

- Identify the reading circuitry in the developing child’s brain
- Use this knowledge to predict reading outcomes and guide education
Suppose we could identify the different neural reasons why a young child is having difficulty learning to read. What would we do to help the child?

Step 1.0 Learn how to identify and classify such children

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

These comments are about Step 1.0. I believe understanding 1.0 will help with 2.0.
Locating reading circuits and maps

VWFA - essential for reading, but not unique to reading
The cortical reading network

Learning to See Words
B.A. Wandell, A. Rauschecker and
J. Yeatman (2012).
Diffusion weighted terminology

- Apparent diffusion coefficients
- Parallel and perpendicular diffusivity
- Diffusion images
Human fascicles (tracts)

- There are many long-range connections

- These connections are not passive – they change their properties in response to use

- A system with active wires

*Courtesy Professor Ugur Ture*
Diffusion probes brain microscopic structure

Parallel diffusivity ($\mu m^2/\text{ms}$)

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

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

Equivalent names
- Parallel, axial, longitudinal, principal diffusion direction (PDD)
Diffusion probes brain microscopic structure

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

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

Other names
- Perpendicular, radial, transverse

Optic nerve fibres
George Bartzokis

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

\[ 1 = v'Q^{-1}v, \]

\( v \) is a 3d-vector

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

\[ A = u'Qu \]
DTI summary measures of white matter microstructure

Fractional anisotropy
Tractography

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

Diffusion data are surfaces
Diffusion and Tractography References

Tract profiles of white matter properties: automating fiber-tract quantification.

Think global, act local: Projectome estimation with BlueMatter
G.Z. Yang et al. (Eds): MICCAI 2009 pp. 861-868

ConTrack: Finding the most likely pathways between brain regions using diffusion tractography.

Identifying the human optic radiation using diffusion imaging and fiber tractography

NIPS Tutorial on Diffusion Tensor Imaging.
Predicting how well a child will read from white matter measurements

• Cortical reading circuitry

• Predicting reading skill from long-range (white matter) properties
The cortical reading network

Learning to See Words

Seeing the white matter reading tracts
(Yeatman et al., 2011)
Longitudinal measures of diffusion and reading (Yeatman et al., 2012)

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

Blue: Good readers
Red: Poor readers
Strong associations between tract diffusion change and seeing words (Yeatman et al., 2012)

• Diffusion development rate within certain tracts, but not others, correlates with the ability to see words

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

![Graph showing correlation between Basic Reading standard score and Rate of FA development with r = 0.51]
Diffusion changes during development differs between good and poor readers

- FA in the ILF increases for good readers and declines for poor readers (6 – 14 years)

- The FA developmental trajectory, not the FA level, matters

FA slopes of good and poor readers

Left Inferior Longitudinal Fasciculus
Neuroprognosis
Predicting reading scores from rate of white matter development (Yeatman et al., 2012)

- Simple models that combine data from two tracts (ILF and AF) predict reading skill from diffusion development
- The predictions are not yet useful; they are statistically reliable

\[ r = 0.66 \] (43%)

Measured reading score

Predicted reading score
Some behaviors, such as psychological tests of performance during brief trials, may be best understood by measuring synaptic activity or spikes.

Other important behaviors - learning to read or to regulate emotions - take place over longer time periods. These skills may depend on biological processes such as cell development, growth and pruning of dendritic arbors, the proliferation and activity of glia.

Scientists need to account for the entire range of processes to understand circuit function in health and disease.
Reading references

Quantitative MRI of the fascicle tissue
(Mezer et al., Nature Medicine, 2013)

• What tissue properties change?
• T1, Macromolecular tissue volume (MTV), and Surface interaction rate (SIR)
• Single patient diagnosis
There are multiple types of MR mechanisms

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

- **High energy**
  - The spins dephase (T2*)

  - The spins move (diffusion)
Analyzing spin-lattice exchange (T1)

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

How efficient is this energy exchange?

I am glad you asked.
Spin-lattice energy exchange rate ($T_1$) depends on

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

If you could measure this in the brain, these are pretty good things to know (noninvasively)
Modeling and calibration of the MRI signal yields quantitative measures of tissue
Mezer et al., Nature Medicine (2013)

Quantitative biophysical modeling

Non-water
Interactions
Water

Macromolecule tissue volume (MTV)
Surface interaction ratio (SIR)

T1
PD
Single subject measures and multiple sclerosis

Control distribution

Cortical spinal track

Macromolecule tissue volume

Core fiber node

MTV
Single subject measures (MS)

Cortical spinal track

Macromolecule tissue volume

Individual A

Individual B

Core fiber node

0

50
The promise: quantitative MRI measurements enable coordinating across sites and instruments.
Clinical applications of quantitative methods

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

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

EXAMPLELAB's data:

- **exampledata**
  - Process started December 8, 2013.
  - Processing finished December 9, 2013.
  - Success!

- **exampledata2**
  - Process started December 8, 2013.
  - Processing finished December 9, 2013.
  - Success!

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- **exampledata2**
  
  Process started December 8, 2013.  
  Processing finished December 9, 2013.  
  Success!

Specific advanced analyses such as MTV, SIR, Tract Profiles and others can be executed on this site. The results are stored and returned to you on a web-page.
This is an example page of a tract profile analysis (AFQ) for diffusion.
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Modeling visual field maps
Serge Dumoulin
Kendrick Kay
Jon Winawer
Alyssa Brewer
Joyce Liao
Netta Levin

Quantitative MRI
Aviv Mezer
Jason Yeatman
Nikola Stikov
Robert Dougherty

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