Happy Birthday to Dave!

• About the human brain
• MRI measures of brain activity
• MRI measures of brain connections
• **Diagnosing reading impairments**
• Software tools for checking and sharing
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
Brain parts

Brain computations take 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.

**Neuron**: impulse-conducting cell; bodies are in the cerebral cortex

**Axon**: a thin fiber that carries the output impulses from a neuron

**Dendrite**: a branching process of a neuron that receives impulses from other neurons

**Synapse**: The point of connection between neurons

Image from Graham Johnson
Brain computations take 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$^3$: $10^4$-$10^6$
- Total Cortical Neurons: $10^{11}$
- Synapses/neuron: $10^3$
- Total Cortical Synapses: $10^{14}$
- Surface area of each hemisphere: $25 \times 30$ cm$^2$

Image from Graham Johnson
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)

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Courtesy Professor Ugur Ture
The functional MRI signal (BOLD, fMRI)
“On turning down a left occipital bone flap, a large angry-looking angioma arteriale racemosum of the left occ. Lobe was disclosed which extensively involved the visual cortex. The haemorrhage occasioned by the bone flap was so excessive that the operation had to be abandoned without touching the tumour. A decompression, however, was made. The patient was discharged ... with greatly improved vision.”
• Subject noted that ‘the noise in the back of his head increased in intensity when he was using his eyes.’

• No increase for hearing, touch or smell

• Increased more when he tried harder
MRI scanners measure the blood oxygen level

• Around 1990, Ogawa, Tank, Ugurbil showed how to use MRI to measure changes in blood oxygenation in the living human brain

• Functional MRI (fMRI) measures a Blood Oxygen Level Dependent (BOLD) signal that is driven by neural activity

• High spatial resolution (mm), low temporal resolution (sec)
Remarkable progress in 25 years

Fox et al., 1986
Nature

Voxel size

(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 sharply delineate visual field map boundaries
Combining eccentricity and angle data yields maps.
More than sixteen visual field maps

Wandell, Dumoulin, Brewer (2007)
Neuron

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

Wandell and Winawer (2011)
Vision Research
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

Rokem et al., 2015, PLoS One
Diffusion weighting: Directions

Dark means large signal attenuation
High ADC

$b = 800$

Rokem et al., 2015, PLoS One
Diffusion weighting: Directions

Dark means large signal attenuation
High ADC

Rokem et al., 2015, PLoS One
Diffusion signals in different directions

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

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

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

E. O. Stejskal and J. E. Tanner (1965)
Diffusion signals in different directions

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

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

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

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

Tracts with at least one endpoint in the visual parts of the brain
The circuit for seeing words
Major components of the reading pathway

The goal: Diagnosis
- Quantitative measures
- Computational modeling
- Check and share

Learning to See Words
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.
Small field of view for the reading circuitry

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.
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
Diffusion (FA) changes differ 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 differ between good and poor readers in both the Arcuate and the ILF

![Diagram showing Fractional anisotropy (displaced) for left ILF with blue dots for good readers and red dots for poor readers. The graph indicates more linear (FA) for good readers and more circular (FA) for poor readers.](image)
Diffusion (FA) changes differ between good and poor readers.

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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)
Project on Scientific Transparency

POST aims to revolutionize the way neuroscience imaging research is done. Click to learn more about the Project on Scientific Transparency.
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.
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

Control ± 2SD

The expectation based on data acquired and stored
Compare your subject with the distribution and think

Control \( \pm 2SD \)

Control

LHON

Leber’s hereditary optical neuropathy

Fractional anisotropy

LGN Location V1

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.
Commercial disclosure: I am a co-founder of Flywheel Exchange
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B. MRI measures of brain activity

C. MRI measures of brain connections

D. Diagnosing reading impairments

E. Software tools: checking and sharing
Happy Birthday to Dave (with love to Miki and Dan, too)

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