A campus-wide interdisciplinary research initiative
**Neuro-Discovery**
Our scientists develop cutting-edge techniques to make fundamental discoveries in brain science — discoveries that could unlock new medical treatments, transform education, inform public policy.

**Neuro-Engineering**
Our engineers are developing ways to manipulate neural circuits with electricity, light, ultrasound and magnetic fields.

**Neuro-Health**
Our clinicians collaborate with scientists and engineers to pioneer novel treatments for psychiatric and neurological disease, easing the devastating consequences of diseases such as stroke, epilepsy, and depression.
Stanford Neurosciences Institute – the new building

- 25 research labs (10 new hires)
- Theory center (6 PIs)
- Campus hub for 200 neuroscience labs
Stanford Neurosciences Institute – the new building

SNI Executive Committee

Bill Newsome,
Brian Wandell,
Rob Malenka, Scott Delp,
Marion Buckwalter
AN MRI SERVICE CENTER

The CNI’s Mission

• Support neuroscience discovery for enhancing society
• Develop and disseminate imaging methods
• Create a structured, safe, and innovative teaching environment for human neuroscience research
The CNI is now the most active MRI research scanner on Stanford campus

**CNI Investigators**

- More than 40 research groups and 200 grants
- More than 1050 students and postdocs trained
- Users from Med School, Basic Sciences, Engineering, Ed School and Business School

**CNI Data**

- 27,000 anatomicals
- 73,000 functional acquisitions
- 7400 diffusion scans
- 100T of MRI data just at this one center

Scanner uptime estimated at 99%
Quantitative Measurements

Computational Models

Check and Share

Presenting the work of many people from my lab at Stanford
• Even simple judgments – such as lightness – depend on substantial interpretation of the image data carried out by brain circuits

• The vision science has been influential in developing principles for other neuroscience fields and artificial intelligence

• Vision science fundamentals are important for the entire imaging industry

(Anderson and Winawer, Nature, 2005)
Vision and computation

http://illusionoftheyear.com/
Main points

• The human brain – its special properties
• Progress in measuring the human brain with magnetic resonance imaging
• Mis-wiring at birth: Amazing recovery
• Damage a few years later: Not much recovery
• Diagnosing the human brain: Reading circuitry
MRI instrumentation can be used in many ways to learn about brain tissue, structure, and activity.
Brain computations depend on a variety of cells; one important cell type, the neurons, have their cell bodies located in the cerebral cortex (gray matter).

The cortex is a sheet (2-4 mm thick) of tissue that covers the surface of the brain; other subcortical regions and types of cells matter too!

- **Neurons/mm³**: $10^4$-$10^6$
- **Cortical Neurons**: $10^{11}$
- **Synapses/neuron**: $10^3$
- **Cortical Synapses**: $10^{14}$
- **Surface area of each hemisphere**: $20 \times 30 \text{ cm}^2$

**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
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
The human brain

1: 15: 3000 (volume ratios)

- Brains differ
- Check which system was measured
• Human visual cortex – some things we know that we didn’t know when I started
Early days of MRI

1992

- MRI acquisition methods have become more complex

- MRI computations (reconstruction, data analysis) have become more complex

- Networking and computer technology have advanced
Remarkable progress from PET to advanced MRI in 25 years

Fox et al., 1986
Nature

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
• Maps tile a lot of the back part of the brain

• The maps appear to be specialized for important stimuli – motion, depth, faces, navigation

• We have learned how to find the positions to within a couple of millimeters just from the anatomy
Mis-wiring at birth

The case of a missing optic chiasm
(Hoffman et al., 2012)
The axonal pathways from the eye to brain

- The optic nerve from each eye meets in the optic chiasm
- Half the fibers cross to the other side of the brain
The axonal pathways from the eye to brain

- The optic nerve from each eye meets in the optic chiasm
- Half the fibers cross to the other side of the brain
- In the typical brain to the right of fixation drives activity left hemisphere activity; and conversely
The optic chiasm

- The chiasm is visible in a standard anatomical image
• We can measure the axonal pathways using another MRI modality, diffusion MRI (dMRI) coupled with computational algorithms (tractography)
• Eye movement (nystagmus)

• Discovered during routine testing for nystagmus

• Resolved after a few weeks
• For this subject, the optic nerves do not cross!

• The right eye sends signals only to the right brain, and the left eye only to the left brain
FMRI confirms that in this person’s brain the right and left visual fields are overlaid in cortex.

[Diagram of brain with overlaid visual fields and hemispheres labeled]
FMRI confirms that in this person’s brain the right and left visual fields are overlaid in cortex.
1. A genetic defect that disrupts crossing at the chiasm signaling causes a developmental reorganization in visual cortex.

2. Despite the profoundly disrupted maps, the rest of the brain figures out what to do.
Brain plasticity and stability
Gregory’s patient SB

• Born in 1900, lost site in both eyes because of corneal infections
• Prior to 2 years of age; kept bandaged to reduce puss
• Went to a school for the blind to learn a trade; married
• Received a corneal graft in London at the age of 52
Quite recently he had been struck by how objects changed their shape when he walked round them. He would look at a lamp post, walk round it, stand studying it from a different aspect, and wonder why it looked different and yet the same. (Gregory, 1974, p. 111)
Brain plasticity
• Chemical explosion (3 yrs old)
• One eye lost; other cornea (and limbic stem cells) destroyed
• Blind (no contrast or form) from age 3 through 46

Images courtesy of Michael May, Sendero Group
Recovered sight?
(images courtesy Michael May)

Limbic stem cells and corneal replacement
Perceptual contrast sensitivity functions

- Similar to controls at low spatial frequency
- Substantially worse above 0.25 cpd
- Constant for the 7 years following surgery
MM has an unusual cortical map
In development, timing Matters: The search for miracle cures

Recovery from early blindness
(Gregory and Wallace, 1963)

Recovery from Early Blindness
A Case Study
Damage to small regions of gray matter can produce very specific cognitive problems, such as face-blindness, loss of color vision, loss of motion perception, or **loss of reading ability**.
Motion selective cortex

- Responds powerfully
- Is organized as a map
- Has the same size as in controls
Object and face-related responses

[Image of brain imaging with labels: Medial, Posterior, LiG, FuG]
Diagnosing the reading circuitry

Long-range neural connections for reading
White matter fascicles are generated by step-wise sampling of local diffusion information.
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

Learning to See Words
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
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.
• 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)
Connectionism: Mismatch hypothesis

- Specialized processing for faces, words, other things
- General visual inputs
- VOT: Specialized processing for faces, words, other things
Connectionism: Mismatch hypothesis

General visual inputs
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.
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