“Neuroimaging Methods and Theory: from image to inference”
What are neuroimaging methods?

Measures of Brain activity and function

neuron --> networks --> brain structures --> whole brain
Direct or Indirect?

Cognitive Psychology and the brain:

“The task of the psychologist trying to understand human cognition is analogous to a man attempting to find how a computer has been programmed...if a program seems to store and reuse information...he will not care much whether his particular computer stores information in magnetic cores or thin films; he wants to understand the program not the hardware...the utilization not the incarnation.”

--Ulrich Neisser, 1966--”Cognitive Psychology”

So as Psychologists: we are interested in $\Psi$

*The underlying phenomenology, i.e., perception, memory, cognition

*Learning, problem solving, insight, imagery, thinking...etc..*
Transformations, reductions, elaborations, encodings, retrievals and use

**PSI Phenomenology**

\[ \psi \sim B(P(S(N(\Delta)))) \leftarrow P(S(N(\Delta))) \leftarrow S(N(\Delta)) \leftarrow N(\Delta) \leftarrow \Delta \]

\[ \Psi \rightarrow N(N(\Delta)) \]

- **Ψ** psychological phenomenology
- **Δ** Distal Stimulus
- **N** Neural Response
- **S** Sensory Response
- **P** Perceptual encoding
- **B** Behavior
Why care about the brain?

“It would be convenient if we could understand the nature of cognition without understanding the nature of the brain itself. Unfortunately, it is difficult if not impossible to theorize effectively on these matters in the absence of neurobiological constraints.”

Patricia Churchland and Terry Sejnowski, SCIENCE 1988.

The “software separability” hypothesis was incorrect.

Brains don't run all algorithms efficiently or effectively.

Brains like parallism, associations, networks, distributed computing.

Unlikely we will find python, C++ or FORTRAN in the brain!
The Methods: Depend on Time/Space

Levels of Investigation

- 1 m: CNS
- 10 cm: Systems
- 1 cm: Maps
- 1 mm: Networks
- 100 μm: Neurons
- 1 μm: Synapses
- 1 Å: Molecules

Brain:
- ERP
- PET
- LESION

Gyrus:
- fMRI

Column:

Layer:
- SINGLE UNIT

Dendrite:

Synapse:
- ms
- sec
- min
- hr
- day
The Dilemma

What should we measure?

And how should we measure it?

Neurons? There are so many!
Behavior? Very Coarse-- how does it relate to PSI?

George Miller, 1980 coined the term “Cognitive Neuroscience”

And 10 years later CogNeuro became--> fMRI
The case for/against fMRI

Non-Invasive
Fast (sub-seconds)
High spatial precision (mm)
Captures Cognitive Dynamics
Gives up neuron doctrine
Has no cognitive epistomology
Subject to reverse inference
Requires constituent identification

http://www.youtube.com/watch?v=uhCF-zlk0jY&feature=related

http://www.youtube.com/watch?v=fd6GwIWiHho&feature=related
The time-space tradeoff: some techniques provide high temporal resolution of brain activity (such as EEG) while others provide higher spatial resolution (such as fMRI).
Brain recording: more and less direct measurements

How do brain recordings reflect human cognition? While they are indirect measures, each type of brain recording tells us part of the story of how the brain works.

Here is an image of the brain using diffusion tensor imaging: this technique allows us to view white (myelinated) fiber tracts.
A range of useful tools -- measuring electric and magnetic signals

Single-unit recording:

Recording from individual neurons can tell us about spiking patterns in the brain. Here you see that the activity in this single unit is most active (shown in red) during the delay period. Such neurons are thought to be involved in the working memory system.
A range of useful tools --
Homologies

Animal and human studies cast light on each other

Some macaque behaviors are similar to humans as well, such as close infant-mother bonding.
A range of useful tools --
Homologies

Animal and human studies cast light on each other

While humans and monkeys are very different, some monkeys, such as the macaque, are extensively studied because of the similarity between their brains and human brains.
A range of useful tools -- measuring electric and magnetic signals

Electroencephalography (EEG) recordings reveal brain rhythms such as Gamma (40Hz). Gamma activity is thought to signal exchange of information between cortical and subcortical regions.
A range of useful tools -- measuring electric and magnetic signals

Magnetoencephalography (MEG)

MEG recordings reflect magnetic -- not electric -- cortical activity. MEG has higher source localization capabilities than EEG.
A range of useful tools -- measuring electric and magnetic signals
Zapping the brain -- Transcranial Magnetic Stimulation (TMS)

TMS uses brief magnetic pulses over the scalp to inhibit or excite a small region of cortex. TMS is used to test causal hypotheses about the contribution of specific brain regions to complex cognitive processes.
fMRI provides a measure of hemodynamic (blood based) activity in the brain and is based on the premise that neuronal activation increases oxygen demand of neurons and related cells, leading to additional blood flow carrying oxygen molecules to the region. This can be measured using BOLD -- Blood Oxygen Level Dependent -- activity.

fMRI is the dominant neuroimaging technique today in research.
MRI studies brain anatomy.

Functional MRI (fMRI) studies brain function.
fMRI Setup

[Diagram of fMRI setup with labels for magnet, gradient coil, video screen, video projector, stimulus control computer, spectrometer control computer, radio-frequency coil, prism glasses, headphones, button response box, and amplifier controls.]
fMRI depends on 3 lucky aspects of the human body

1. We're mostly made out of Water allowing for magnetic susceptibility in tissue (Protons)

3. Changes in neural activity produce changes in local blood flow

4. Local blood flow disrupts local tissue magnetic susceptibility – allowing for localization
Protons Align in Magnetic Field

Outside the Magnet

Brain is 70% water—High abundance of H protons
When placed in a Magnetic Field (50k times > Earth's)
Protons in the brain begin to align in the direction of M

A radio frequency Pulse at the frequency of the HYDROGEN PROTON (170.3 MHz) aligns them in the tissue which thereafter decays back to normal at Different rates in Different Tissues.. producing A contrast between Grey Matter White Matter, Blood, CSF etc..

Inside the Magnet
Getting fMRI Data
Like a human Radio

1) Put subject in big magnetic field (leave him there)
2) Transmit radio waves into subject [about 3 ms at a specific frequency]
3) Turn off radio wave transmitter
   Receive radio waves
   - Manipulate re-transmission with magnetic fields during this readout interval [10-100 ms: MRI is not a snapshot]
4) 
5) Store measured radio wave data vs. time
   - Now go back to 2) to get some more data
   Process raw data to reconstruct images (Fourier analysis)
6) 
7) Allow subject to leave scanner (this is optional)
Ideal HDR

% signal change
= (point – baseline)/baseline
usually 0.5-3% could be as high as 10%

initial dip
- more focal and potentially a better measure
- somewhat elusive so far, not everyone can find it

time to rise
signal begins to rise soon after stimulus begins

time to peak
signal peaks 4-6 sec after stimulus begins

post stimulus undershoot
signal suppressed after stimulation ends
HRF time evolution appears useful for maximizing signal.

**Experimental Stimulus Function**

**Hemodynamic Response Function**

**Predicted Response**

**Block Design**

**Event-Related**
OVERVIEW OF BRAIN IMAGING ANALYSIS

fMRI time-series → Motion Correction → Smoothing → General Linear Model → Design matrix → Statistical Parametric Map

Spatial Normalisation → Anatomical Reference → Parameter Estimates
Finger tapping
MRI vs. fMRI

**fMRI**

Blood Oxygenation Level Dependent (BOLD) signal
indirect measure of neural activity

neural activity ➔ ↑ blood oxygen ➔ ↑ fMRI signal
fMRI Activation: AVERAGING

Stimulation - Control = Difference

Individual difference images

+ + + + +

Mean difference image
Activation Statistics

Functional images

Condition 1

Condition 2

Region of interest (ROI)

~ 5 min

Statistical Map superimposed on anatomical MRI image

Signal (% change)

ROI Time Course

Region of interest (ROI)
Statistical Maps & Time Courses

Use stat maps to pick regions. Then extract the time course.
What are the temporal limits?

Blamire et al. (1992) – 2 sec
Bandettini (1993): 0.5 sec
Savoy et al. (1995): 34 msec

With enough averaging, anything seems possible.
The shape of the HRF is predictable.
Event-related potentials (ERPs) are based on averaging small responses over many trials.
Can we do the same thing with fMRI? Apparently but WHY?
Subject Safety

Subjects must have no metal in their bodies:
• pacemaker
• aneurysm clips
• metal implants (e.g., cochlear implants)
• interuterine devices (IUDs)
• some dental work (fillings okay)

Subjects must remove metal from their bodies
• jewellery, watch, piercings
• coins, etc.
• wallet
• any metal that may distort the field (e.g., underwire bra)

Subjects must be given ear plugs (acoustic noise can reach 120 dB)
Regions of interest:

The brain is a dynamic, complex entity. How do you know which brain activity corresponds to your research experiment? One technique is to define regions of interest (ROIs) before scanning to identify which areas you expect to see changes in activation.
Conscious and unconscious brain events

A recent wave of brain studies are investigating conscious and unconscious phenomena in the brain.

For example, a fMRI study compared brain activation for conscious and unconscious events: unconscious viewing of words activated visual areas only, while conscious viewing activated expanded regions in the cortex.