260-2015-08-28-methods

Rick Gilmore

2015-08-31 10:21:44

Announcements

- **NO CLASS** this Monday, 9/7
- **Quiz 1** on Monday 9/14
- **Exam 1** moved to Friday 9/25.

Today's Topics

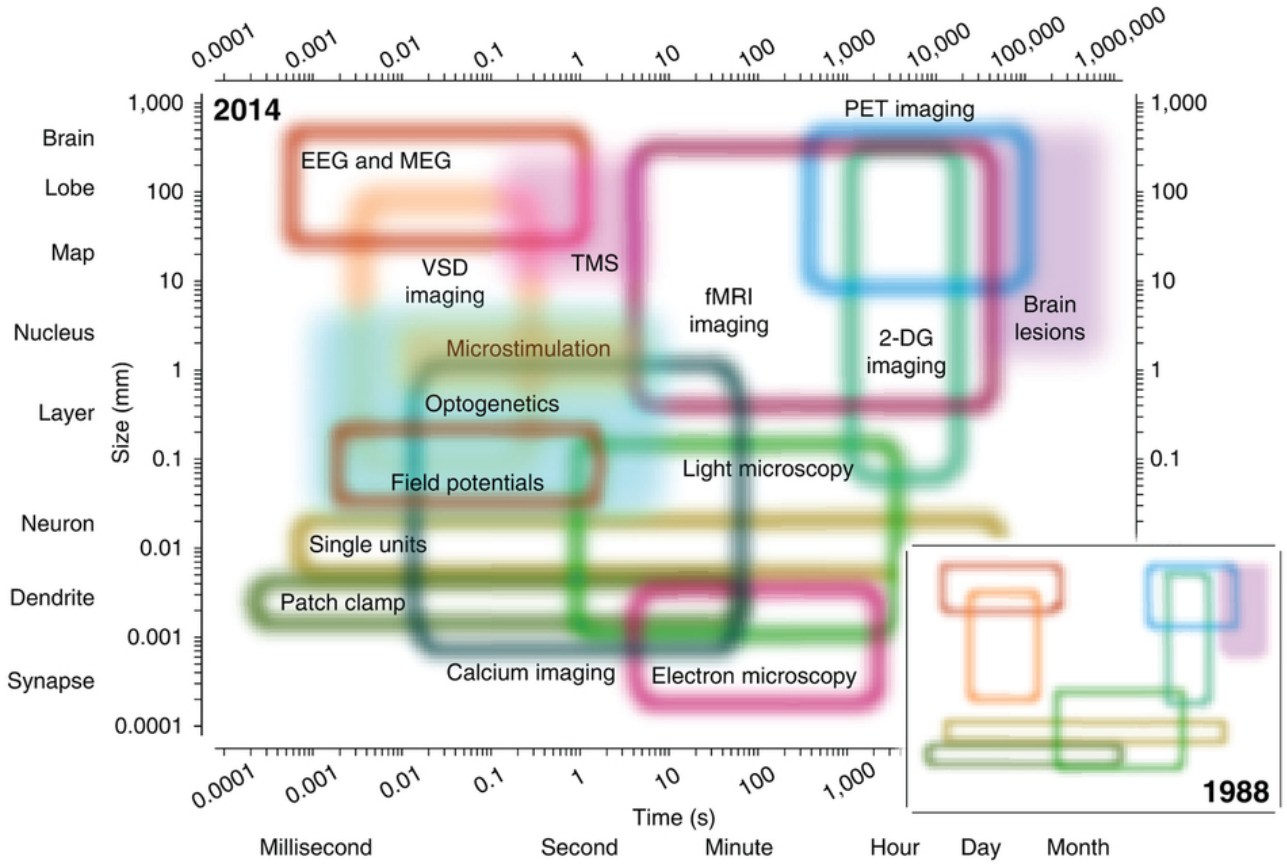
- Methods to the madness
- Tools in the neuroscientist’s toolkit
- What they tell us, and what they don’t

Evaluating methods

- What is the question?
- What are we measuring?
    - Structure
    - Activity
- Strengths & Weaknesses
    - Cost
    - Invasiveness
    - Spatial/temporal resolution

Spatial and Temporal Resolution

[@sejnowski2014putting]



Types of methods

- Structural
    - Mapping the circuitry
    - Anatomy
- Functional
    - What does it do?
    - Physiology/Activity

Mapping structures

- Cell/axon stains
  - Golgi stain – whole cells
  - Cellular distribution, concentration, microanatomy

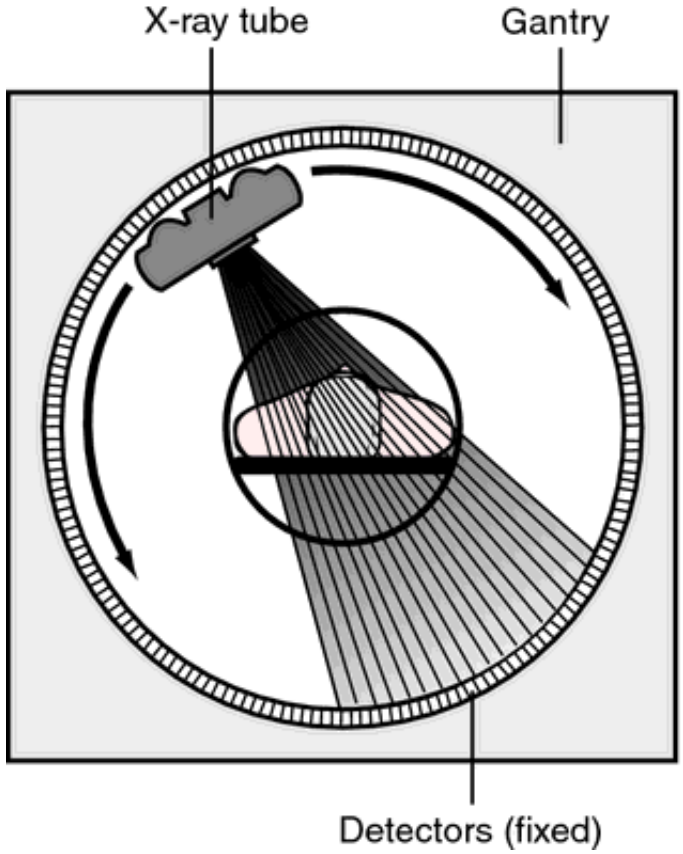
Retrograde vs. anterograde tracers

- What connects where

Mapping structures

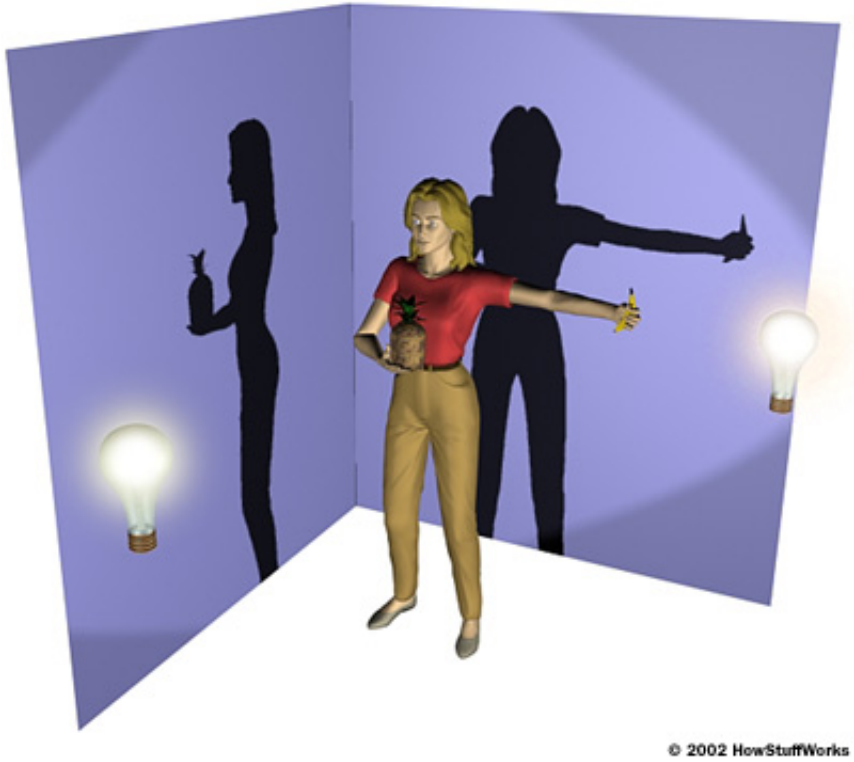
- Computed axial tomography (CAT), CT
- X-ray based

Tomography



http://img.tfd.com/mk/T/X2604-T-22.png

Tomography



http://static.howstuffworks.com/gif/cat-scan-pineapple.jpg

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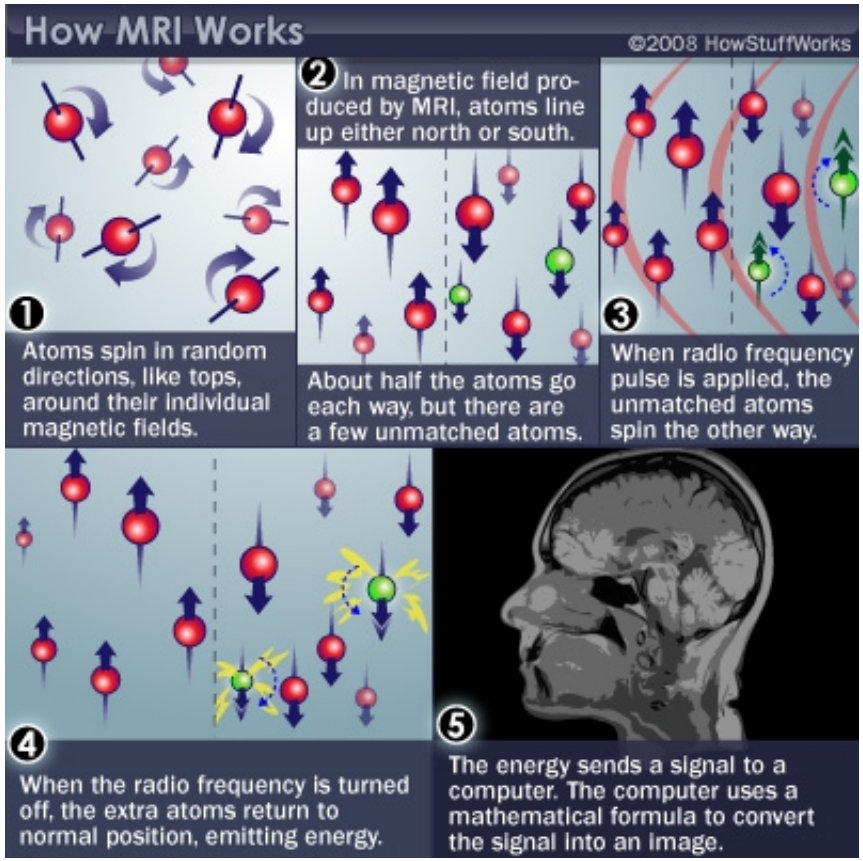
Magnetic Resonance Imaging (MRI)

- Magnetic resonance
- Protons have spin (magnetic dipole)
- Align with strong magnetic field
- When perturbed, speed of realignment varies by tissue
- Realignment gives off radio frequency signals

MRI



http://s.hswstatic.com/gif/mri-steps.jpg

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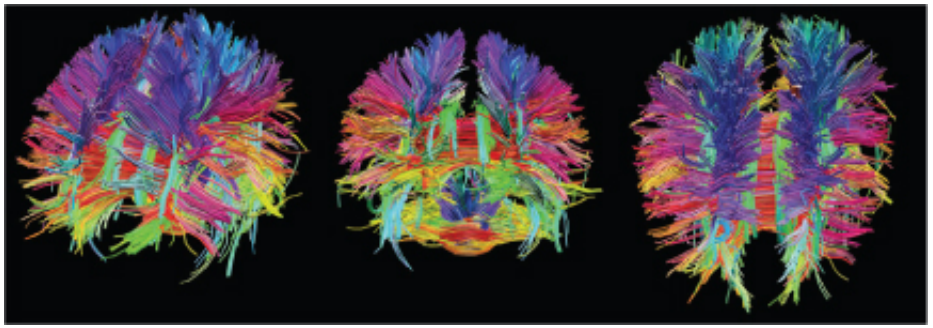
Structural MRI

- Tissue density/type differences
- Gray vs. white - Axon fibers
- Spectroscopy
- Region sizes/volumes

Diffusion tensor imaging (DTI)



https://www.simonsfoundation.org/wp-content/uploads/2012/02/hitting-nerve3.jpeg

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Voxel-based morphometry (VBM)

http://www.frontiersin.org/files/Articles/18691/fnhum-06-00184-HTML/image_m/fnhum-06-00184-g003.jpg

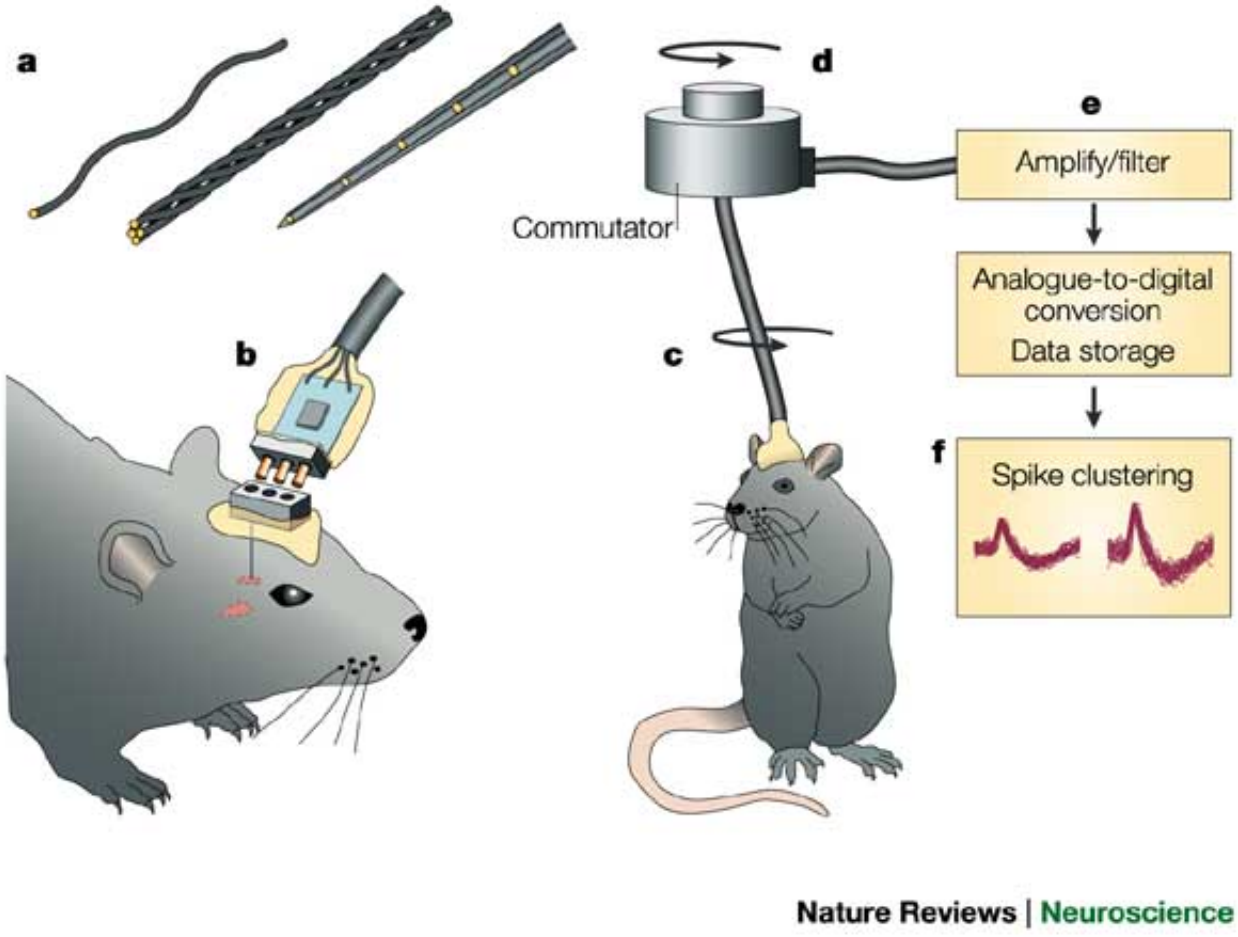
Functional methods

- Recording from the brain
- Interfering with the brain
- Stimulating the brain

Recording from the brain

- Single/multi unit recording
- Microelectrodes
- Small numbers of nerve cells

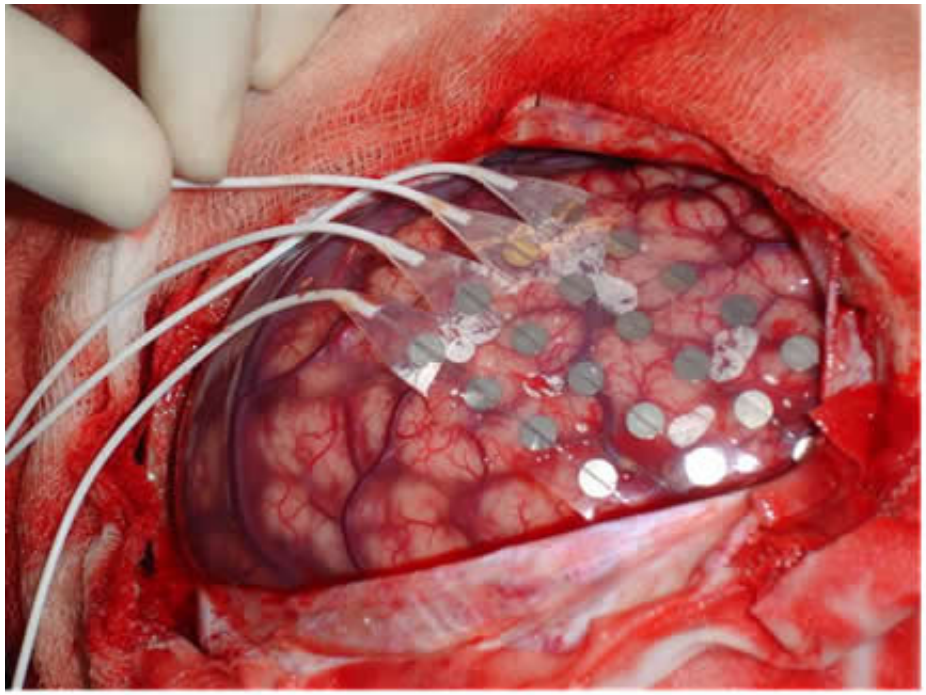
Single/multi-unit Recording



Single/multi-unit recording

- What does neuron X respond to?
- Great temporal (ms), spatial resolution (um)
- Invasive
- Rarely suitable for humans, but…

Electrocorticography



http://www.neurofisiologia.net/wp-content/uploads/2009/07/corticografia.jpg

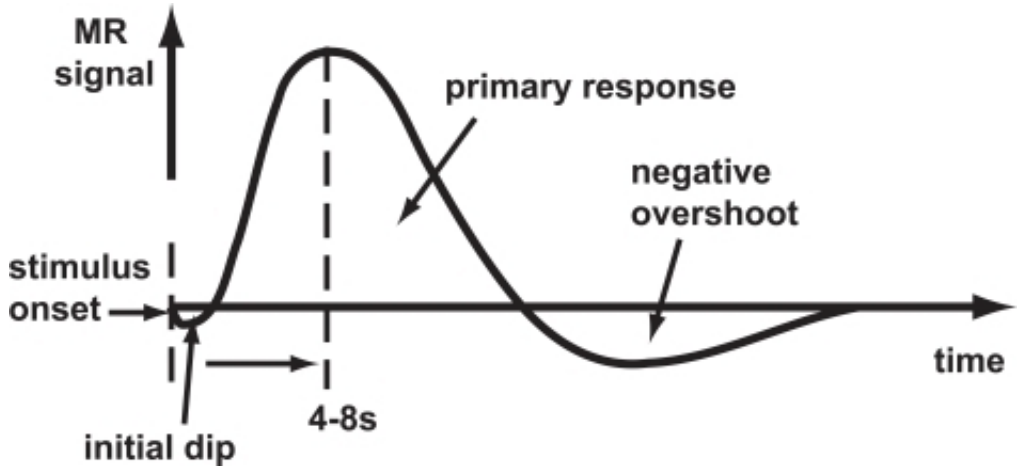
Positron Emission Tomography (PET)

- Radioactive tracers (glucose, oxygen)
- Positron decay
- Experimental condition - control
- Average across individuals
- Evaluating PET
  - Temporal (~ s) and spatial (mm-cm) resolution worse than fMRI
  - Radioactive exposures + mildly invasive
  - Dose < airline crew exposure in 1 yr

Functional Magnetic Resonance Imaging (fMRI)

- Neural activity -> local O^^2 consumption increase
- Blood Oxygen Level Dependent (BOLD) response
  - Oxygenated vs. deoxygenated hemoglobin
  - Do regional blood O^^2 levels (and flow) vary with behavior X?
- Evaluating
  - Non-invasive, but expensive
  - Moderate but improving (mm) spatial, temporal (~sec) resolution
- Hemodynamic Response Function

Hemodynamic Response Function (HRF)



http://openi.nlm.nih.gov/imgs/512/236/3109590/3109590_TONIJ-5-24_F1.png

Electroencephalography (EEG)

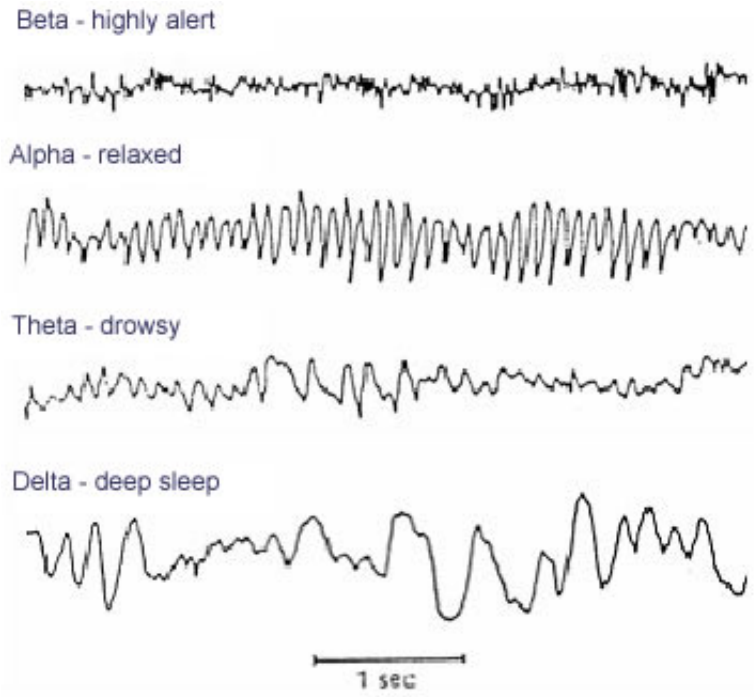
- How does it work?
- Electrodes on scalp or brain surface
- What do we measure?
- Combined activity of huge # of neurons

EEG

EEG

- High temporal, poor spatial resolution
- Analyze frequency bands
  - LOW: deep sleep
  - MIDDLE: Quiet, alert state
  - HIGH:“Binding” information across senses

EEG Frequency



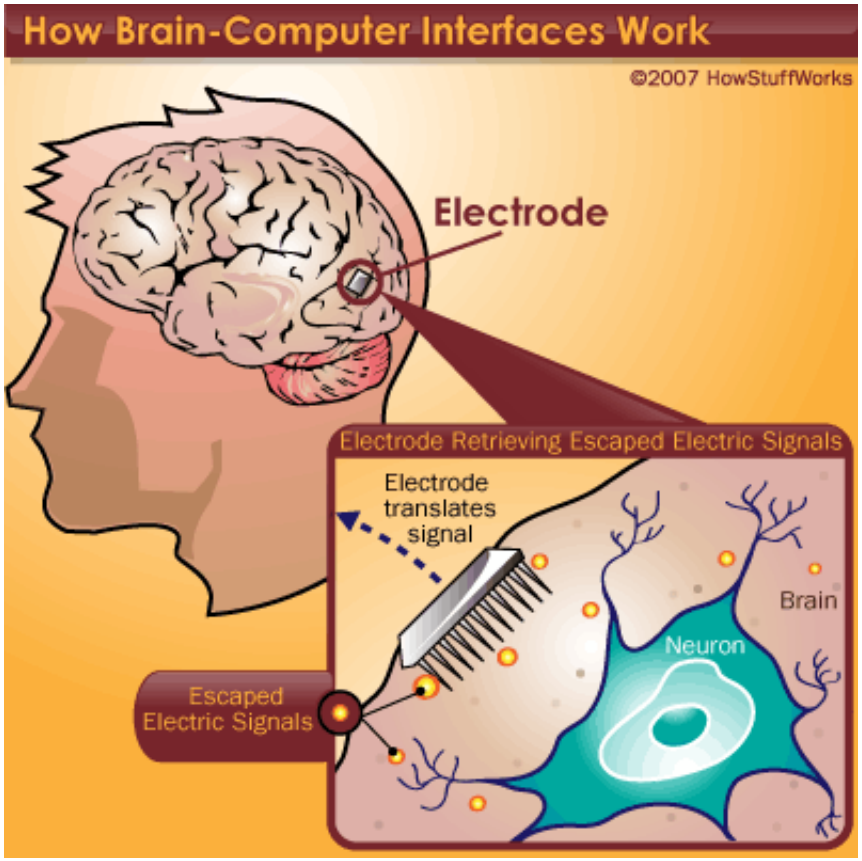
http://www.peakmind.co.uk/images/frequency.jpg

Event-related potentials (ERPs)

- EEGs time-locked to some event - Averaged over many trials

ERPs

Brain Computer Interface (BCI)



http://s.hswstatic.com/gif/brain-computer-interface-3.gif 31/43

Magneto-encephalography (MEG)

- Like EEG, but measuring magnetic fields
- High temporal resolution
- Magnetic field propagates w/o distortion

MEG

Manipulating the brain

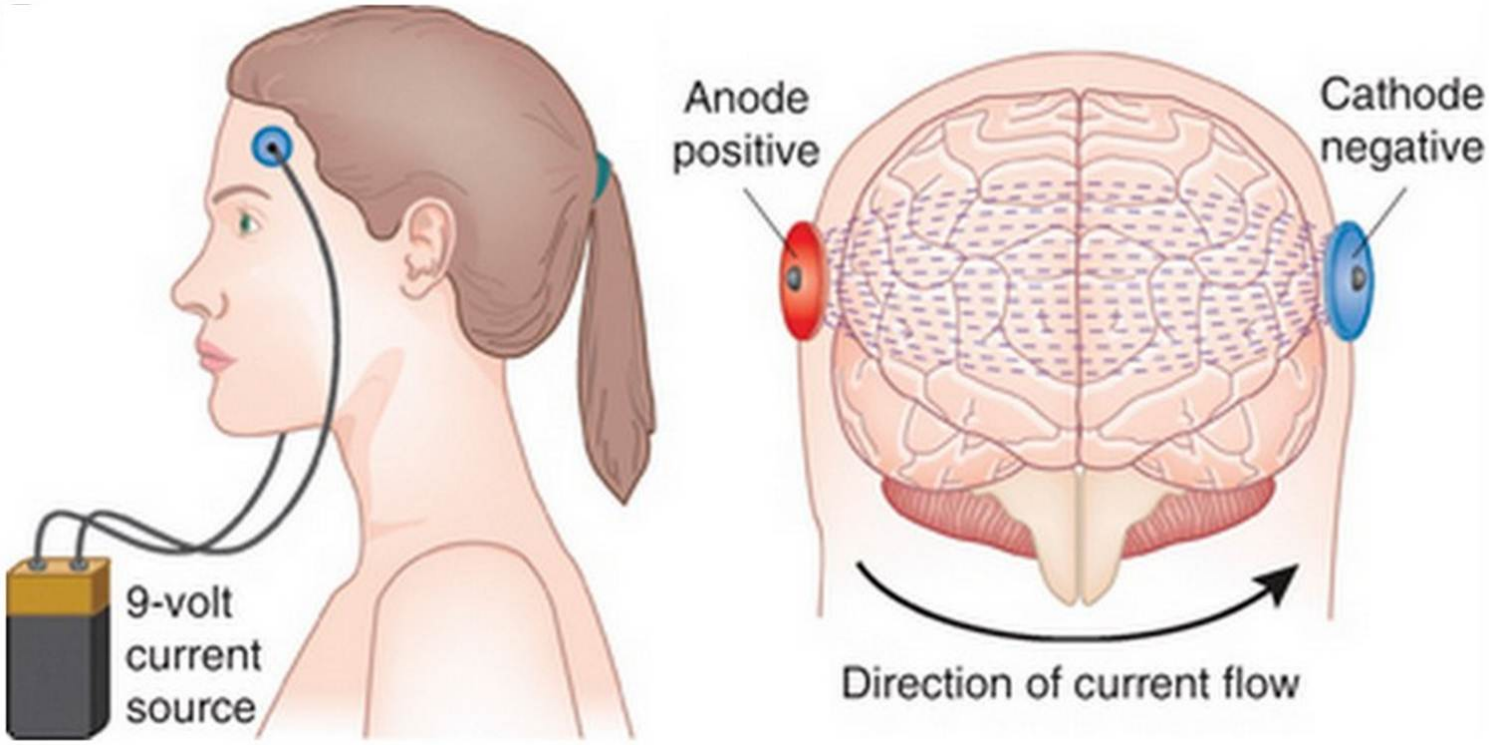
- Nature's "experiments"
  - Stroke, head injury, tumor
  - Neuropsychology
- Logic: damage impairs performance = region critical for behavior
- Poor spatial/temporal resolution, limited experimental control

Phineas Gage

Stimulating the brain

- Pharmacological
- Electrical (transcranial Direct Current Stimulation - tDCS)
- Magnetic (Transcranial magnetic stimulation - TMS)

tDCS



http://sci2.haifa.ac.il/faculty/kaphzan/images/stories/tdcs%20stimulation2

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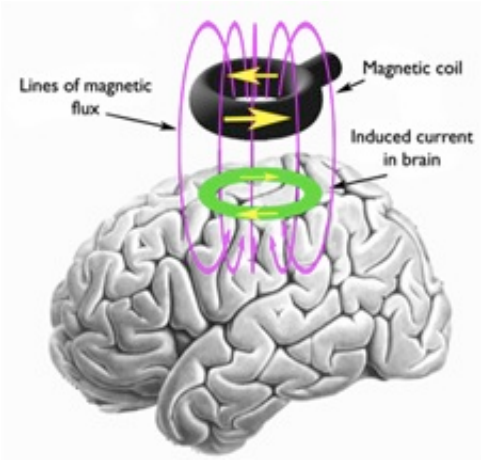
TMS

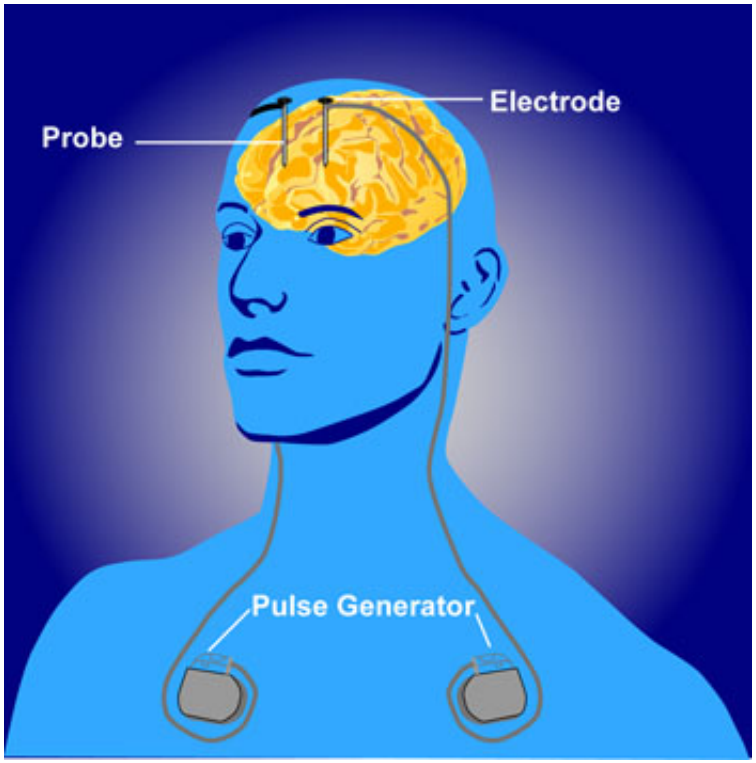


http://www.med.upenn.edu/lcns/images/TMS.jpg

Evaluating stimulation methods

- Spatial/temporal resolution?
  - Assume stimulation mimics natural activity?
- Deep brain stimulation as therapy
  - Parkinson's Disease
  - Depression
  - Epilepsy

Deep brain stimulation



http://www.nimh.nih.gov/images/health-and-outreach/mental-health-topic-brain-stimulation-therapies/dbs_60715_3.jpg

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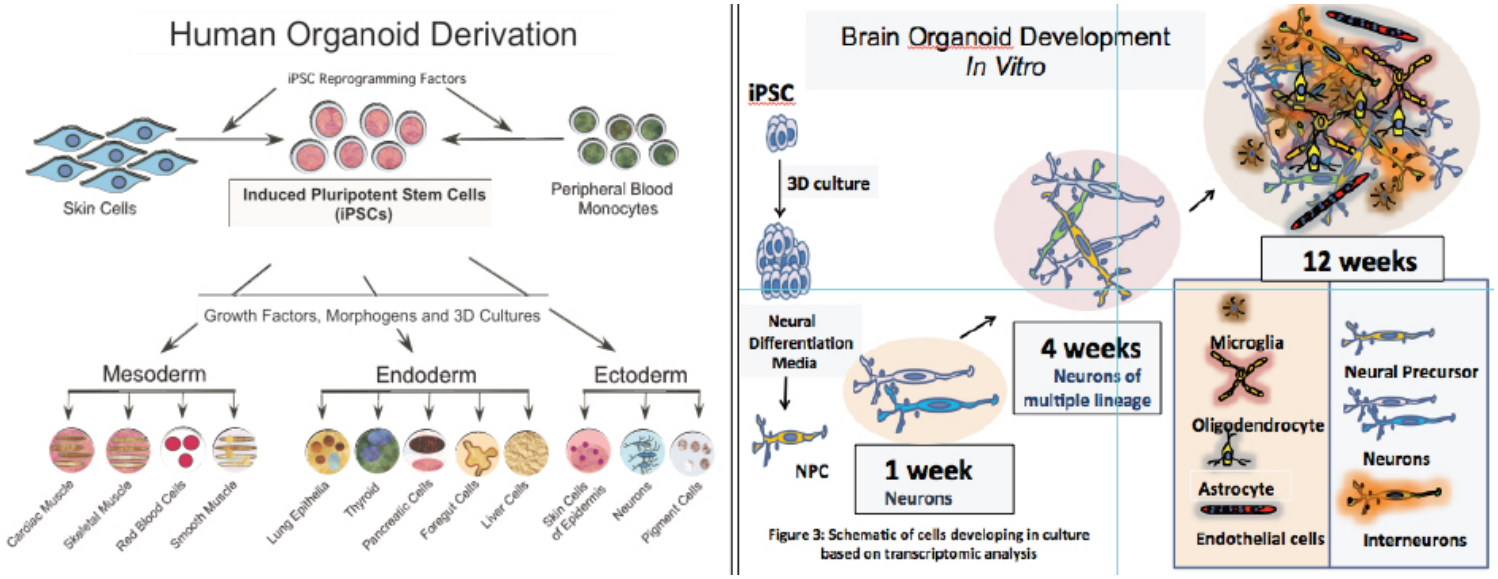
Simulating the brain

- Computer/mathematical models of brain function
- Example: neural networks
- Cheap, noninvasive, can be stimulated or “lesioned”

Growing a brain

http://www.kurzweilai.net/most-complete-functioning-human-brain-model-to-date-according-to-researchers



http://www.kurzweilai.net/images/organoid-derivation-development.jpg

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Main points

- Multiple structural, functional methods
- Different levels of spatial and temporal resolution
- Goal is converging evidence