260-2017-01-13-levels-methods

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Prelude

Classic "Powers of Ten" movie by Charles and Ray Eames (10 min).

Today's Topics

- Levels of analysis in the study of brain and behavior
  - Spatial
  - Temporal
- Methods to the madness

Review of key concepts

What does the practice of trephining suggest about our human ancestors?

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Which of the following statements about the Egyptians is false?

- A. They employed a word meaning "brain".
- B. They removed the brain in the process of mummification.
- **C. They created detailed drawings of human brain anatomy.**

Levels of analysis

Spatial resolution

Spatial and Temporal Resolution

(Sejnowski, Churchland, and Movshon 2014)

Spatial Resolution in Detail

- Within an individual
  - molecular
    - genetic
    - receptor
  - chemical
    - neurotransmitter
  - cellular
    - neuronal firing

Spatial Resolution in Detail

- Internal to individuals
  - network
    - lateral inhibition
  - area
  - region
  - system

Spatial Resolution in Detail

- External to individuals
  - Social
    - Friends, family, teachers, others
  - Non-social
    - neighborhood, school, state/region, country
    - Physical environment

Temporal Resolution in Detail

- Within one lifetime
  - Microseconds
    - detection position from acoustic stimulation
  - Milliseconds
    - action potential

  - Seconds
    * changes in EEG power
    * short-term memory

Temporal Resolution in Detail

- Within one lifetime
  - Minutes
    * synaptic plasticity
  - Hours
    * memory consolidation
  - Days
  - Weeks
  - Months

Temporal Resolution in Detail

- Within one lifetime
  - Years
    * education & training
    * disease processes
    * cultural change

Temporal Resolution in Detail

- Across lifetimes
  - Centuries
    * cultural changes
  - Millenia

Why does this matter?

- Different methods, different levels of analysis.
- Challenge of interpretation.
- Challenge of linking phenomena across levels.
  - How does the micro affect macro or vice versa?

Neuroscience methods

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

(Sejnowski, Churchland, and Movshon 2014)

Types of methods

- Structural
    - Mapping the circuitry
    - Anatomy
- Functional (next time)
    - What does it do?
    - Physiology/Activity

Mapping structures

- Cell/axon stains
    - Golgi stain – whole cells
        * Camillo Golgi
    - Nissl stain – cell bodies only
        * Franz Nissl
    - Cellular distribution, concentration, microanatomy

Golgi stain

Nissl stain

Retrograde vs. anterograde histochemical tracers

- *Retrograde* (from axon terminal to cell body); *anterograde* (from cell body to axon terminal)
- What connects where

Retrograde vs. anterograde tracers

Brainbow

(Lichtman, Livet, and Sanes 2008)

Brainbow

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Eyewire.org

Clarity

Mapping structures

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

Tomography

Tomography

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

CT scan of stroke

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

How MRI works

Structural MRI

- Tissue density/type differences
- Gray matter (neurons & dendrites & axons & glia) vs. white matter (mostly axons)
- MR Spectroscopy
- Region sizes/volumes

Structural MRI of the brain

Diffusion tensor imaging (DTI)

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

Diffusion tensor imaging (DTI)

- Type of structural MRI
- Reveals integrity/density of axon fibers
- Measure of connectivity

Voxel-based morphometry (VBM)

- Voxels (volume-based elements)
- Morphometry, measure ("metry") form/morphology.
- How does brain size or thickness vary by age, disease status, etc.?

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

Next time

- Functional methods, including functional MRI (fMRI)

References

Lichtman, Jeff W., Jean Livet, and Joshua R. Sanes. 2008. "A Technicolour Approach to the Connectome." *Nature Reviews Neuroscience* 9 (6): 417–22. doi:10.1038/nrn2391.

Sejnowski, Terrence J, Patricia S Churchland, and J Anthony Movshon. 2014. "Putting Big Data to Good Use in Neuroscience." *Nature Neuroscience* 17 (11). Nature Publishing Group: 1440–1. doi:10.1038/nn.3839.