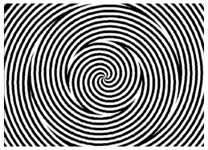
Discovering and Modeling Mechanisms



Clicker Question

When a scientist is interested in the mechanism responsible for the causal effect of aspirin on pain, she is

- Expressing skepticism that aspirin really affects pain
- Trying to understand how aspirin affects pain
- Trying to eliminate any confounds in experiments studying the affects of aspirin on pain
- Trying to determine whether aspirin does affect pain

Clicker Question

A reductionist, in contrast to a holist,

- Focuses on how the components of the system fit into an integrated whole
- Denies any importance to discovering the parts of the mechanism
- Denies that organization plays any role in the operation of a mechanism
- Emphasizes the discovery of components as the key to understanding how a mechanism behaves

Tasks in Developing a Mechanistic Explanation

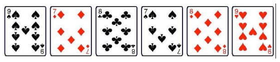
1. Describe the phenomenon
2. Identify the working parts
3. Identify the operations the parts perform
4. Discover how the parts are organized

Task 1: Describing the Phenomenon

- Before setting out to explain a phenomenon, need to characterize it as accurately as possible
  - Otherwise one risks trying to explain something that might not be possible
- An important role for purely observational research
  - Before seeking a mechanism by which the universe continues to expand, make sure it is
  - Before seeking a mechanism to explain global warming, make sure it is really occurring
- But the description of the phenomena may be revised in the process of figuring out the mechanism

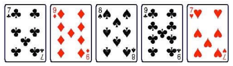
First step: Getting the Phenomenon Right

Pick a card and think real hard about it. Don't forget it.



Whoops. I thought you were cheating and tried to shoot you. But I got your card instead.

Check it out—did I take out your card



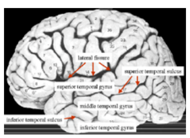
Task 2: Identify the working parts

- To understand a mechanism, one must decompose it—take it apart
  - Literally—actually remove the parts to study them in isolation
  - Figuratively—figure out what the parts are and what they do
- In identifying components, focus both on their
  - Structure—parts
  - Function—operations
- Different tools for identifying parts and operations

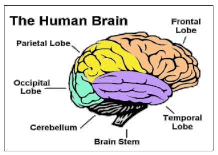
What are the parts of the brain?

- Open up the skull, and you see a hunk of grey matter highly convoluted
- What are the working parts of the brain?

Sulci and Gyri?

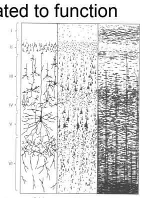


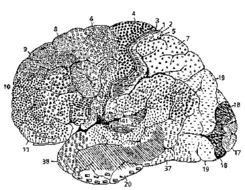
Lobes?



What are the working parts of the brain?

- Korbinian Brodmann (1909) assumed differences in neuron type, density, and layering were probably related to function

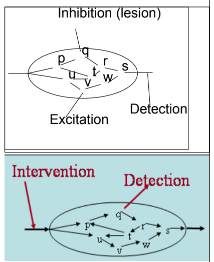




Delineated areas in the brains of humans and many other species

Task 3: What operations do the components perform?

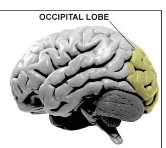
- Operations in a mechanism are causal processes
- Accordingly, they are typically investigated my manipulating components to determine their effects
  - Inhibit possible intermediate processes to see if that stops the reaction—lesion experiment
  - Insert possible intermediaries to see if they could produce the end product—excitation experiment
  - Record from possible intermediates as the mechanism is operating to determine what they respond to—recording experiment



Start with Lesions

- Until the 1940s, there was no way to record the activity of individual neurons in the brain
- Crude stimulation (with the electrodes of the 19th century) activated very wide areas, and so not sufficiently specific
- That left ablation or lesion as initially the tool of choice

Lesion Experiments Revealed the Occipital Lobe as Locus of Vision



- Bartolomeo Panizza,1855
  - Proposed occipital lobe as locus of vision based on patients who experienced blindness after strokes (experiments of nature)
- Hermann Munk, 1870s
  - Unilateral removal of the occipital lobe in dogs resulted in partial blindness
  - Bilateral removal resulted in total blindness

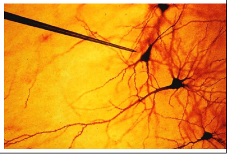
Clicker Question

If you removed a part from your MP3 player and it no longer produces sound, you can infer

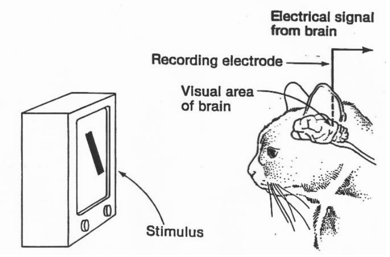
A. The part you removed was itself causally responsible for generating sound
B. The part you removed probably had no direct role in generating sound
C. The part you removed probably figured in the process of generating sound
D. The part you removed probably performed a lot of other operations as well

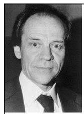
So Visual Cortex is Needed—but What does it actually do?

- Lesions can show that a part of the mechanism seems to be necessary for it to perform a specific phenomenon
  - But are not able to show more specifically what the damaged part does in normal situations
- A powerful *complement* is to record from the component while it is in operation to see what elicits its activity
- Made possible by the development of electrodes wired to amplifiers and speakers



Single-cell recording

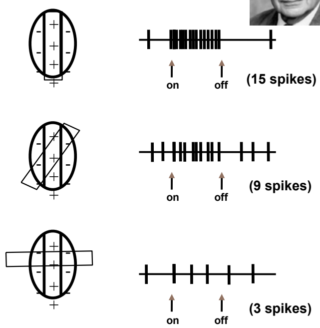




Hubel and Wiesel's Simple Cortical Cells

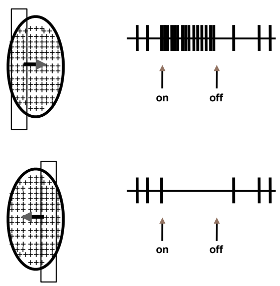
Many of the cells Hubel and Wiesel tested in occipital lobe responded to bars of light

If they were properly oriented



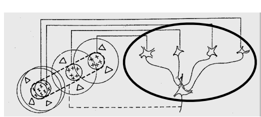
Hubel and Wiesel's complex cells

Some cells Hubel and Wiesel tested responded to bars of light anywhere in the receptive field of the cell
or
If they were moving in a preferred direction across the field

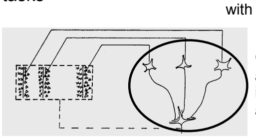


How do Simple and Complex Cells do it?

Hubel and Wiesel proposed simple model wiring diagrams to show how simple and complex cells could perform their different tasks



Simple cells: Fire if enough LGN cells with centers on the bar are active



Complex cells: Fire if one or another simple cell detecting a bar is active (or if several become active in sequence)

Clicker Question

What can lesion studies show that recording studies cannot?

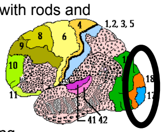
A. That the part in question is needed to perform the activity
B. That the part in question might be sufficient for performing the activity
C. That if the part in question were stimulated, it would enhance the activity
D. That the part in question actually performs a wide range of operations

Beyond edge detection

The cells Hubel and Wiesel found are all located in one part of the occipital lobe known as the striate cortex, Brodmann's area 17, or V1 (visual area 1).

Detecting edges is important to seeing, but it isn't the whole story, as Hubel and Wiesel recognized:

> "Specialized as the cells of 17 are, compared with rods and cones, they must, nevertheless, still represent a very elementary stage in the handling of complex forms, occupied as they are with a relatively simple region-by-region analysis of retinal contours. How this information is used at later stages in the visual path is far from clear, and represents one of the most tantalizing problems for the future" (Hubel and Wiesel, 1968, p. 242).



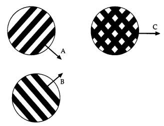
The Woman Who Couldn't See Motion

- When Gisela Leibold tried to pour coffee, she could see the cup's color, shape, and position, and could tip the pot
  - But what she saw was like a frozen waterfall
  - She couldn't see anything moving
  - Just a sequence of still life paintings
- Result of a stroke she had suffered that affected area known as MT

Recording Cells That Respond to Motion

The phenomenon of perceived motion:

- Two stimuli, moving in different directions, will sometimes be seen as one stimulus moving in a combined direction

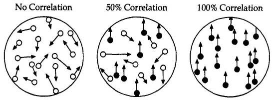


V1 cells respond only to actual motion, not perceived motion

- So they do not compute perceived motion

But cells in area V5 (MT) do respond to perceived motion

Adding microstimulation



William Newsome trained monkeys to indicate the direction of motion they perceived correlated motion in ambiguous displays

- Recording from MT cells showed that the responses of those cells predicted the animal's behavior
- Microstimulation of those cells biases the behavioral response

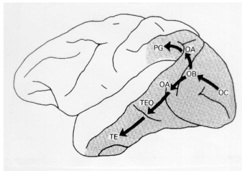
This combination of recording and stimulation studies (when combined with the lesion results) offers powerful evidence about what these components are doing

Clicker Question

Making a mechanism produce the phenomenon of interest by stimulating a part of it serves to establish

A. That the part is sufficient for the mechanism to perform the phenomenon of interest
B. That the part is necessary for the mechanism to perform the phenomenon of interest
C. That the part can initiate a causal process resulting in the phenomenon of interest
D. That if one lesioned the part, the phenomenon would be destroyed

Task 4: Discover How the Parts are Organized



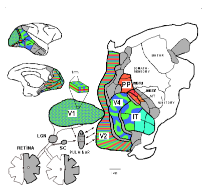
Ungerleider and Mishkin (1982): two pathways of visual processing

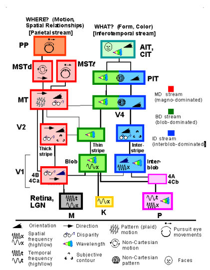
- Pathway into temporal cortex: what
- Pathway into parietal cortex: where

Mechanism for Visual Processing

Van Essen: Schema of overall organization of visual processing

Represents the combined efforts of recording, lesion, stimulation





Each technique is limited

Each approach—recording, lesioning, and stimulating—requires inference *and inference is fallible*

- Just showing that a component is active given a specific stimulus does not tell you
  - Specifically what about the stimulus it is responding to
  - What it is doing in response to that feature
- Just showing that lesioning a component interrupts an activity does not tell you
  - That it alone was responsible for the activity
  - What it contributed to the activity
- Just showing that stimulating a component increases the performance of the activity
  - Does not tell you how it figured in generating the activity

Need to orchestrate multiple techniques

- There is no foolproof strategy for figuring out how a mechanism works
- The best results stem from combining different strategies to determine what the components of a system are and what they do

Where we have been in this class

- Logic: structure of arguments for confirmation and falsification
- Observation: variables and their measurement
- Correlation: predictions based on correlations and statistically significant differences within samples
- Causation: experimental and non-experimental evidence, and strategies for controlling confounds
- Mechanisms: discovering how component parts, operations, and their organization yield a system that exhibits the phenomenon of interest

Final Thought—Or a First Thought Repeated

Reasoning and making decisions, whether about

Perception
Correlation
Causation
Mechanism

is fallible

We can (and should) strive to come closer to the truth and rely on the best information available now

But we must also recognize that tomorrow something might be discovered that makes us revise our best conclusions of today