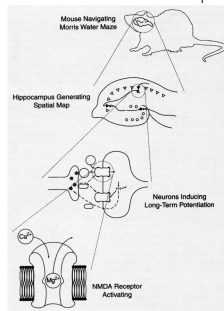


NEUROPHILOSOPHICAL FOUNDATIONS 2

Hierarchy of Mechanisms

- ※ The entities (parts) of a mechanism may themselves be mechanisms
- ※ One explains how they perform the activity (operation) in virtue of the parts and operations within them
- ※ Important to note that there is now a new explanatory goal—explain the operation within the previous mechanism
- ※ Explanatory hierarchies bottom out in activities left unexplained
- ※ The question that motivated the inquiry can be answered without explaining these activities
- ※ Someone else, however, may find it worthwhile to explain them
- ※ Or some puzzles arise that require investigating them

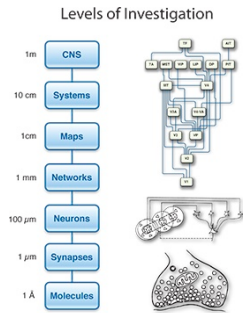


Contrasting Meanings of Reduction

- ※ *Reduction* generically refers to explaining a given phenomenon in terms of something more basic
- ※ But the alternative senses of explanation offer a different view of reduction
- ※ On the received view, laws are central to explanation
 - ※ Laws are in turn explained by deriving them from more basic laws
 - Laws of reducing science (Neuroscience)
 - Boundary Conditions
 - ∴ Laws of the reduced science (Psychology)
- ※ On the mechanistic picture, the operations of parts of a mechanism are explained by decomposing them into their own parts and operations
 - ※ But at each level one must recombine the parts—understand how they are organized so as to work together
 - ※ The lower-level parts are not privileged since we also need to understand the organization and context in which the mechanism functions, which is not found at the lower-level

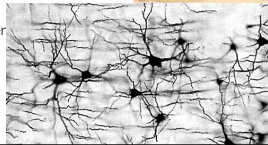
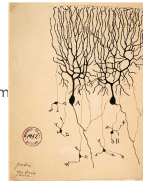
LEVELS OF ORGANIZATION

- Multiple levels in a part-whole hierarchy
- Different phenomena found at different levels
 - Molecules bind
 - Neurons spike (amongst other things)
 - Brain areas have maps
 - Systems engage in mental activities
- Different tools are needed to study entities at different levels
 - Biochemical techniques for molecules and synapses
 - Electrophysiological techniques for individual neurons
 - Single-cell recording to identify maps



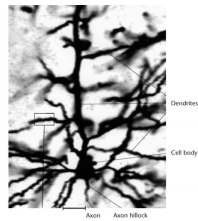
CELL THEORY AND NEURON DOCTRINE

- Cells were only recognized as distinct entities with improved microscopes in the middle decades of the 19th century
- Theodor Schwann (1838) claimed cells were the basic living unit in the organs and tissues of animals
 - He claimed that all are the same because they originate through a process analogous to crystal formation
 - New material is gradually absorbed around the nucleolus to create first a nucleus and then the cytoplasm of cells
- Among the early cells to be identified were various types of neurons--Purkinje cells discovered by Purkinje in the cerebellum
- But not everyone thought they were cells
 - Camillo Golgi developed a stain using silver nitrate that sharply stained some neurons
 - Which he took to constitute a large reticulated network--not separate cells



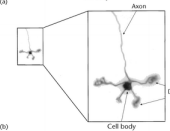
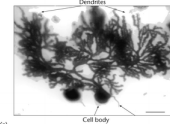
VISUALIZING NEURONS

Large cortical neuron stained with silver nitrate



Cells from two adjacent layers of the cerebellum:

- (a) 2 Purkinje cells
- (b) granule cell



Figures from Matus, A. (2001). Neurons. eLS: John Wiley & Sons, Ltd.

Clicker Question

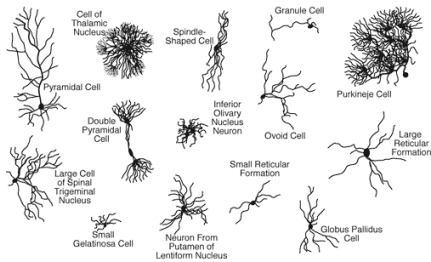
What is meant by the neuron doctrine?

- Neurons are individual cells
- Neurons are simply parts of a connected reticulum
- Neurons are far more important than other cells
- All brain cells are essentially alike

7

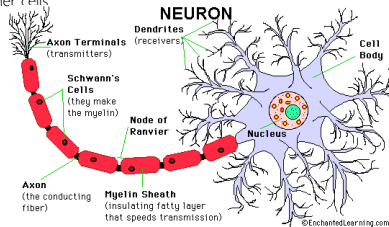
DIVERSITY OF NEURONS

- While the pyramidal cells has been the prototype of a neuron, there is actually a huge variety of types of neurons
- Some are excitatory, but others are inhibitory



PROTOTYPICAL NEURON

- Pyramidal cells are large, with a thousand or more dendritic spines that receive input from other cells, a cell body onto which they project, and a long axon that can span large distances in the brain before synapsing onto other cells



Clicker Question

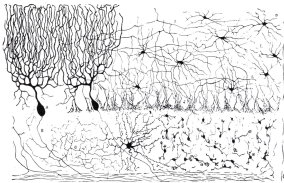
What features made it difficult to determine whether neurons really are cells?

- They don't have an obvious nucleus
- The nerve fibers appear to run between neurons linking them into a network
- They are much smaller than normal cells and so hard to see with a microscope
- They are so much larger than typical cells such as blood cells or liver cells

10

CELL THEORY AND THE NEURON DOCTRINE

- Golgi's staining technique was adopted and modified by Santiago Ramón y Cajal
- Cajal soon took issue with Golgi's interpretation of what was to be seen
 - Cajal maintained that neurons were separate cells--he saw them as separate
- How could Golgi and Cajal look at the same thing but see something different?
 - For Golgi, what mattered was communication through nerves--for which purposes a continuous network was needed
 - For Cajal, neurons were basic units that functioned independently and out of which a system could be built
- Charles Scott Sherrington introduced the concept of a synapse for the gap between neurons



Discussion Question

What do you see looking at the picture to the right?

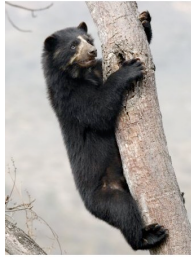
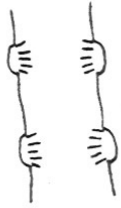
- Just a mess of lines on a page
- A couple sitting at a table with wine
- A skull
- I see both B and C



Duchamp's Ill-Fated Lovers

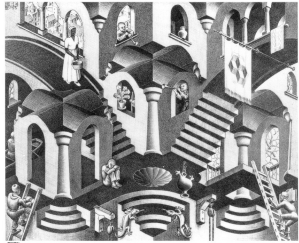
12

WHAT DO YOU SEE IN THIS IMAGE?



THEORY-LADEN PERCEPTION

- Observations are generally taken as the foundations on which science is built
 - Hypotheses (of laws or mechanisms) advanced to explain them
- But observation (perception) is influenced top-down by our previous experience as well as bottom-up by what is in front of our eyes



SCIENTIFIC "SEEING"

- Scientific observations are even more affected by theories
- Scientists do not just open their eyes and look at the world
- Often they create the preparations that they then observe
 - Golgi comments of the challenges in using his stain:
 - "For microscopic examination the sections are placed in damar varnish ... or in Canada balsam after they have been dehydrated through the use of absolute alcohol and have been rendered transparent with creosote. Time and light continually spoil the microscopic preparations obtained with my method ..."
 - "I must equally declare that I have not yet succeeded in determining with certainty why under the same conditions ... I have obtained very different results"
 - "Permit me to advise, however, that I do not find myself as yet in a position to explain with precision all the necessary procedures for the best results. They are still partly fortuitous"

ESTABLISHMENT OF THE NEURON DOCTRINE

- In subsequent decades, researchers succeeded in making the idea of neurons as separate cells fit their observations
- New and improved staining techniques presented images that supported the individual cell account
- The introduction of the electron microscope in the 1950s provided the final visual evidence, but by then there were few who needed convincing
- But it also brought evidence that there are some points of contact that are so close that electric currents are directly transmitted from one cell to another—
gap junctions
- Reintroducing an important claim of the reticular account



Clicker Question

How does the neuron doctrine relate to localization?

They are two names for the same thing—neurons are local units

They are direct competitors—a localizationist denies that neurons are distinct units

They are mutually supporting views—distinct neurons would support localization of function

There is great tension between the views—distinct neurons does not fit well with localization of function

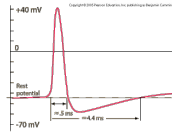
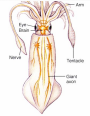
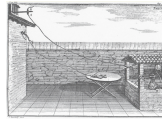
17

NEURONS AND THE HOLIST-LOCALIZATIONIST CONTROVERSY

- Cajal's neuron doctrine, according to which each neuron is a distinct entity, fits comfortably with the view that individual operations can be assigned to distinct units in the brain
 - The mechanism works by each part performing its operation
 - Even if the units for a given activity are not individual neurons but larger units (brain areas), because they are built from components they are themselves distinct units
- Golgi's reticularist view, according to which nerves form a continuous network, fits with a holist perspective in which the relevant unit is the whole system
 - The system operates through the coordinated activity of the whole, not through individual parts performing distinct operations
 - Even if some parts of the network are more active on some occasions than on others, one cannot assign distinct operations to separate parts

ELECTRICAL CONDUCTION

- A separate line of research led to the recognition that nerves transmit electrical charges
 - Galvani's experiments with frog muscles
 - Development of galvanometers to measure electrical transmission through nerves
 - Bernstein determined that electrical charge is due to differential concentration of ions inside and outside the cell
- In the early 20th century placement of electrodes next to cell could detect individual action potentials
- By inserting electrodes into the giant axon of the squid, Hodgkin and Huxley were able to measure the currents of sodium and potassium ions across the axonal membrane at different set voltages and advanced a hypothesis as to how they generated action potentials
- Subsequently, individual channels (many voltage gated) for different ions were found
 - And ongoing dynamical activity identified



FROM SIMPLE TO MORE AND MORE COMPLEX VIEWS OF NEURONS

- The *classical* conception of a neuron viewed it as a fairly simple processing unit in which inputs arrived at the dendrite, were summed in the soma (cell body) and if they exceeded a threshold, generated an action potential
- Discovery of processes that alter neuron behavior: long term potentiation (LTP) and long-term depression (LDP)
 - When a neuron generates a spike it adds receptors to the synapses on which it was receiving inputs, resulting in an increased likelihood that it will generate a spike in response to such inputs in the future
 - A variety of mechanisms work to reduce the likelihood of a spike (e.g. to inputs that were below the threshold for producing a spike)
- Discovery of a wide variety of voltage-dependent ion channels that produce complex dynamical electrical behavior of neurons that sometimes pushes them above the threshold for spiking (spontaneous spiking)
 - This sub-threshold electrical activity of neurons oscillates, and collectives of neurons can synchronize these oscillations

MACRO-ORGANIZATION OF THE BRAIN

- Despite the success of researchers in recording from individual neurons in the performance of cognitive activities, the neuronal level is *generally* regarded as too low a level of organization to make sense of cognition
 - Populations of neurons seem to be involved in a cognitive task
- Challenge: can one distinguish brain structures at a higher level of organization, one that might be related to cognitive activities
 - 19th century: sulci and gyri were hypothesized to be the relevant units of the brain
 - With the identification of neurons, researchers began to focus on how different types of neurons are found in different tissue

