Discovering the Basic Units of the Brain: From Neurons to Brains

Division of Labor in Multicellular Organisms

- In a single-cell organism, each cell has to perform all of the activities needed for life
  - Take in nutrients
  - Digest and distribute them
  - Synthesize new tissue out of them
  - Get rid of waste products
  - Replicate itself
  - Coordinate all of these processes
- Multi-cellular organisms allow for different cell types to specialize in doing different tasks
  - Example: contractility in muscle cells
    - taking advantage of the more ancient actin-myosin molecular mechanism but packaging it in a specialized cell
  - But this requires a way to coordinate individual muscle cells

Evolving Neurons

- Electrical transmission along cell bodies and the establishment of modes of transmission between cells is found in both bacteria and plants
- What is special about neurons are the extended processes—axons and dendrites—which allow for long distance transmission of electrical potentials within a single cell
- Among other things, neurons can distribute signals so as to enable muscle cells to contract in a coordinated fashion (together, in a wave, in sequence, etc.)

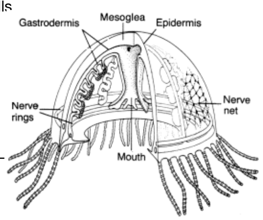
Discussion Question

Why is it important to get muscles to contract in a coordinated manner?

A. Individual muscles aren't capable of doing very much—they need to work together to accomplish anything
B. If muscles are not coordinated, they might oppose each other, preventing the animal from performing actions
C. Muscles on their own would just relax unless instructed to contract
D. If muscles have a tendency to contract and are coordinated, they may generate behavior without an external stimulus

The Jellyfish Nerve Network

- The bell of jellyfish is characterized by two layers of myoepithelia cells (epidermis and gastrodermis) that act like muscles
  - By contracting, they squeeze the bell and force water out, creating propulsion.
  - In many species, the myoepithelia cells are connected by gap junctions, which enable direct cell-to-cell communication
    - This is relatively slow
  - An additional form of communication is provided by a network of neurons existing between the layers
    - they communicate bidirectionally—whenever processes cross, one releases peptides that gate ion channels in the other



Clicker Question

What do Keizer et al. mean by a skin-brain?

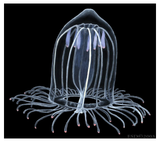
A. Skin cells carry out the tasks of processing information
B. Neurons probably evolved from skin cells
C. Skin cells probably evolved from neurons
D. The earliest function of neurons was to coordinate contractions of proto-muscle skin cells

The Skin-Brain of Jellyfish

- Within the nerve net, some neurons act as sensors of muscle cells, others as effectors on other muscle cells, coordinating behavior
  - In some species (e.g., among cubomedusae or box jellfish), these form two distinguishable nerve nets
    - These neurons are identified by stains that react to different peptidergic transmitters (RFamide or tubulin)

- Rhopalia (proto-ganglia)—sites where sensory information is integrated to modulate motor nerve network
  - also integrate signals from their own sensory ocelli
  - serve as pacemakers to generate rhythmic contractions of the bell

Aglantha digitale



- In addition to the nerve net, giant neurons form two rings around the base of the bell as well as runningup the bell
- Inner ring of neurons functions as a pacemaker, generating spikes every 2 seconds
  - via the nerve net, it causes muscular contractions to occur on the same interval
- Outer ring of neurons responds to stimulation of the tentacles, resulting in a much higher frequency activity in the inner nerve ring that leads to fast swimming (an escape response)
- Many other signals (14 conducting systems have been detected) impinge on the ring neurons, resulting in diversity of behaviors
  - Four inhibit swimming, including inhibiting swimming briefly while eating (preventing dislodging of food)

Reactive vs. Endogenously Active

- A reactive system is one that only responds when stimulated
- An endogenously active system is one that generates behavior independent of stimulation
  - Stimuli don't initiate its activity, but they can modify it

- We have tended to adopt a reactive view of organisms—our behaviors are determined by the stimuli we receive
- But if the nervous system generates activity on its own (as the skin-brain thesis proposes for early organisms), organisms may act without stimulation

Discussion Question

Where in mammals (including us) is one likely to find nerve nets providing rhythmic contraction such as found in the bell of the jellyfish?

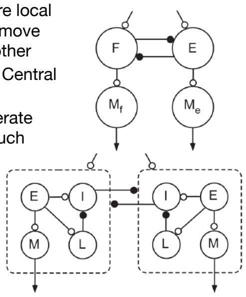
A. In the cerebral cortex
B. In the heart
C. In limbs such as arms
D. No where

Lessons from the Jellyfish

- A basic function of neurons is to coordinate the activity of muscles
  - By generating rhythms
  - This function is also manifest in central pattern generators in later evolved species
- A variety of other signals, derived from sensors, impinge of the nerve net, halting or altering its operation
  - These various inputs enable regulation appropriate for various conditions
    - without there being a central executive directing overall activity

Central Pattern Generators

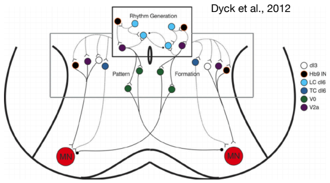
- Muscles acting on internal organs in vertebrates are controlled by nerve networks much like those in the jellyfish
- But skeletal muscles require much more local control so that individual muscles can move in variable ways with respect to each other
- The most basic level of control involve Central Pattern Generators
  - small networks of neurons that generate rhythmic behavior that coordinate such things as alternation of extensor and flexor muscles or of muscles on opposite sides of the body
  - Often based on paired inhibitory neurons that generate an oscillation



The Vertebrate Skin-Brain: Local Pattern Generators

- Circuits sending input to motor neurons acting on muscles (skeletal and smooth) operate as pattern generators generating rhythmic contractions
- These local circuits integrate input from
  - local sensors
  - higher-level controllers

Dyck et al., 2012



Ganglia and Nuclei

- In invertebrates and in sub-cortical regions of the vertebrate brain, neurons with
  - similar patterns of projection
  - reliance on the same transmitters

  often cluster into nuclei (referred to as ganglia in invertebrates and in the periphery in vertebrates)
- Neurons in different nuclei are often highly interconnected
  - receiving inputs from other nuclei
  - sending outputs to other nuclei

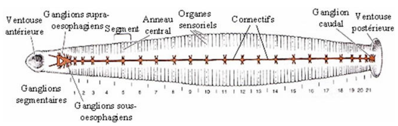
Clicker Question

What is a neural ganglion or nucleus?

A. The part of the cell in which genes are located
B. The core of the brain which determines all activities
C. Collections of neurons that use the same transmitters and project to the same targets
D. A network that insures that muscles contract in synchrony with each other

Decision Making in Leeches

- The medicinal leech provides a useful invertebrate model for decision making
  - Its decisions whether to swim or crawl are made in the 21 segmental ganglia in the nerve cord, which can be exposed so as to record from the approximately 400 neurons in each ganglion
  - Overall behavior results from interactions between these ganglia



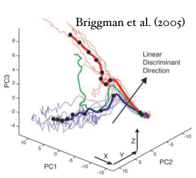
Discussion Question

If one ganglion decides to swim and the next to crawl, how could the whole organism arrive at a activity?

A. Do whatever the ganglion in the front does
B. Take a vote and do what a majority of the ganglia select
C. Engage in an iterated process in which each ganglion takes into account what its neighbors are doing
D. Employ a central executive which directs the activity of all the gang

Decision Making in Leeches

- Briggman, Abarbanel, and Kristan (2005) used a stimulus equally likely to elicit swimming and crawling
- If there were command neurons engaged in competition, they should be found among the 17 neurons exhibiting activity predictive of a behavior before motor neurons begin to respond
  - But hyperpolarizing these neurons did not affect behavior
- Principal components analysis and linear discriminant analysis revealed a different population of neurons that collectively behaved in a way that corresponded to subsequent behavior
  - Manipulating the activity of these 17 neurons, the researchers found one that, 208, did reliably bias subsequent behavior, but only as part of the collective
  - Briggman et al. interpreted this as reflecting attractor dynamics in a population, not competition between command neurons

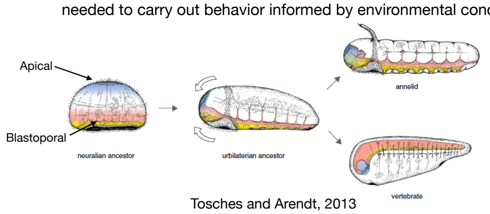


Dual Origins of the Brain

- Tosches and Arendt (2013) hypothesize that early in evolution, two separate sets of ganglia evolved that acted on nerve nets
  - neurons around the digestive opening acted to control feeding and exercised control over individual sets of muscles (blastoporal nervous system or BNS)
  - neurons at the other pole sensed conditions in the organism and its environment and promoted activities appropriate to these conditions such as feeding or locomotion (apical nervous system or ANS)

A Chimeric Brain

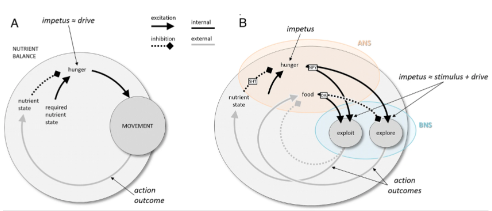
- As organisms became bilateral, both moved to the front but formed distinct parts of a chimeric brain
  - ANS: hypothalamus, which relies heavily on hormones and volume transmitters to measure conditions and set objectives for behavior
  - BNS: brainstem and midbrain motor control areas, thalamus, basal ganglia, and eventually the neocortex, which process information needed to carry out behavior informed by environmental conditions



Tosches and Arendt, 2013

Integrating the ANS and the BNS

- Cisek (2019) suggests how the two type of neural components can integrate to regulate behavior
  - ANS: Measurement of bodily state and environment conditions provides impetus for different action
  - BNS: Direct motor activity to different patterns of a action that continue until ANS no longer



The Vertebrate Brain Bauplan

- Sten Grillner and his collaborators compared the brain of species of contemporary vertebrates that are evolutionarily extremely distant from each other: the lamprey and primates
  - Nearly all the brain structures are the same, although some have expanded much more than others
  - The small, three-layer pallium in the lamprey has expanded into the huge primate cerebral cortex