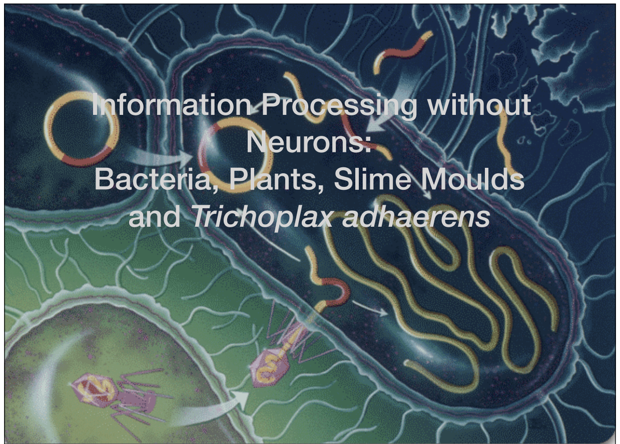


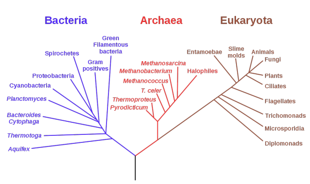
Information Processing without Neurons: Bacteria, Plants, Slime Moulds and *Trichoplax adhaerens*

Major Themes

- All organisms must continually carry out activities (procure materials and nutrients, build, repair, and replicate their bodies) to stay alive
  - Living systems are far from equilibrium, but all open systems tend towards equilibrium
- Organisms contain a vast array of production mechanisms—mechanisms that perform the work of maintaining and reproducing the organism
  - These include both physiological activities (processing nutrients) and performing activities in the environment
- Production mechanisms must be appropriately controlled to serve the end of maintaining the organism
  - A nervous system provides one way to accomplish this
  - But even organisms without neurons need to control their production mechanisms
    - They make use of many of the same components as figure in neural control systems
- The diversity of control is surprising for those who start thinking from the human model in which we think control is centralized in our conscious activity
  - But many of control mechanisms found in other species are conserved in humans

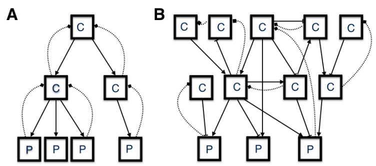
Evolutionary Conservation

- Once solutions to problems are developed in organisms, they tend to be maintained in their descendants
  - although with new accouterments
    - as genes are duplicated and differentiate
    - as new connections are formed between existing components



Major Themes

- Common conception: control systems are organized hierarchically, in a pyramid with a top-level controller (general, CEO, neocortex) in charge
- But biological systems often involve multiple independent controllers coordinating but not under a top-level controller



Why Non-neural Organisms?

- What can Bacteria, Plants, Slime Moulds, and *Trichoplax* teach us about behavior and cognition?
  - Like all other living organisms, these organisms must exercise control over their production mechanisms so as to maintain themselves as systems far from equilibrium with their environments
  - Control consists in procuring information relevant to the need for use of various production mechanisms and using this to alter the operation of production mechanisms
  - These are the same tasks as cognitive mechanisms in organisms with neurons perform
  - Considering how these tasks are performed without neurons can provide a comparative basis for understanding how organisms with neurons perform them

An Ecumenical Definition of Biological Cognition

- "Biological cognition is the complex of sensory and other information-processing mechanisms an organism has for becoming familiar with, valuing, and [interacting with] its environment in order to meet existential goals, the most basic of which are survival,[growth or thriving], and reproduction." (Lyon, 2014, p. 174)
  - Valence: information is assessed according to existential value—"attractiveness, acceptability, or tolerance of a stimulus"

Showing Respect for the Cognitive Capacities of Bacteria

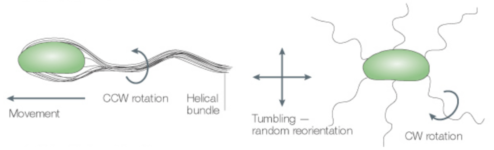
- In terms of cell morphology, bacteria seem extremely simple: a bag of chemicals. But
  - The bag itself is permeable and ingress and egress is partly controlled by the bacteria
  - The chemical reactions that bacteria can perform is enormous
- Bacteria have evolved over 4 billions years, developing new abilities to perform different reactions
  - To cooperate with each other to achieve shared ends
  - To complete with each other to take advantage of what the other can do for them
- Antibacterial drugs were mostly invented by bacteria to use on each other
  - And other bacteria developed defense strategies
- In defending against antibacterial drugs bacteria have an ability we don't
  - To borrow and, when appropriate, put to use genes from other bacteria
  - This requires processing information to do so effectively

Viewing Bacteria as Cognitive

- "Bacteria have an exquisite ability to sense and adapt to a constantly fluctuating environment. They have evolved the capacity to detect a variety of temporal and spatial cues, and in response to such stimuli, bacteria initiate signal transduction cascades that culminate in changes in gene expression. The ability to rapidly alter gene expression, and consequently behavior, in response to a dynamic environment presumably gives bacteria the plasticity to survive in rich, neutral, and hostile situations" (Lyon)

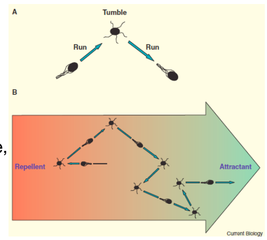
Moving About with a Flagellum

- Bacteria such as *E. coli* have a flagellum—a complex of a motor and a filament—that enables them to move about their environment
  - Running behavior when each filament rotates counter clockwise, causing the individual filaments to form a bundle
  - Tumbling episodes occur when one or more filaments rotates clockwise
    - Tumbling episodes last about 0.1 seconds and reorient the bacterium on average about 60º
- Bacteria move so as to procure food and avoid toxins
  - Challenge: how to use such a mechanism to achieve these goals?



Controlling Flagellar Navigation: Chemotaxis

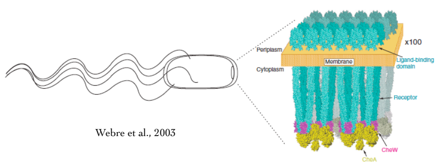
- Strategy: prolong runs when moving toward food or away from toxin
- Needs a sensory system
  - Example: sense glucose gradient
- Used not just for glucose gradients: find nutrients more generally, avoid toxic chemicals, respond to pH, light, temperature, electricity, or magnetism
- Also used to regulate symbiotic or pathogenetic interactions with other organisms



Webre et al., 2003

Sensing the Environment

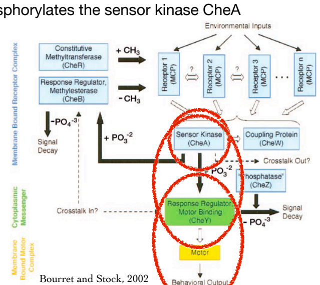
- What a bacterium needs is information about whether the concentration of a substance is increasing or decreasing
  - Since bacteria are too short to directly detect gradients, they must compare concentrations over time
    - If the gradient is changing in the desired direction, increase probability of flagellum action
- *E. coli* has five types of receptors (transmembrane proteins), although other species have as many as 40
  - Once chemical binds to the receptors, phosphosignaling ensues



Webre et al., 2003

Processing Sensory Information

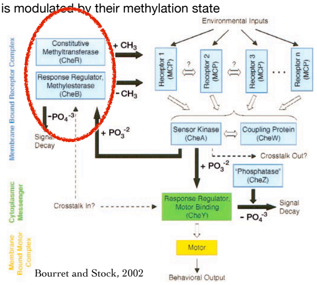
- The receptors (methylated chemotaxis proteins) share a signaling domain that phosphorylates or dephosphorylates the sensor kinase CheA
- CheA is a kinase that phosphorylates response regulator CheY
- CheY diffuses through the cytoplasm and when phosphorylated is able to bind to FliM, a flagellum protein that causes the motor to rotate clockwise (tumble)
  - Otherwise the motor rotates counterclockwise



Bourret and Stock, 2002

Detecting a Gradient

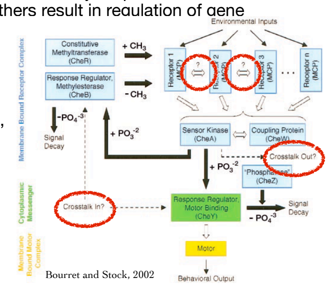
- To detect a gradient, the bacterium must alter the response of its sensors depending on its recent experience
- Ability of receptors to respond to stimuli is modulated by their methylation state
  - Constitutively methylated by CheR
  - Demethylated by CheB when it is phosphorylated by the sensory kinase CheA
    - The methylation process is slow relative to response regulator response, thereby rendering the receptors' sensitivity dependent on previous stimuli (memory)
- Concentrations of stimuli may vary over five orders of magnitude
  - As a result of a non-linear response function (due to a Hill coefficient of 10 or more), the response behaves in accord with Weber's Law



Bourret and Stock, 2002

Coordinating Responses

- Remember, motor activity is not the only output of the chemotaxis system (many others result in regulation of gene expression)
  - Note the question marks in the diagram
  - There is suggestive evidence of crosstalk, i.e., integration of information between different sensor kinases that may affect the response regulators as well as the methylation of the receptors



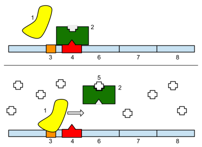
Bourret and Stock, 2002

Lesson From Chemotaxis

- Using only a small set of chemical reactions, *E. coli* are able to navigate their environment to procure food and avoid toxins
- The constitution of the receptors determines how the bacterium will assess different chemicals—pursue them or move away
- Through the way multiple sensors interact, it exhibits preferences
- Using a feedback system it can alter the responsiveness of its sensors so as to detect changes over time

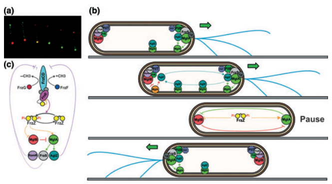
Determining One's Own Constitution

- The chemotaxis system results in overt behavior, but much of what any organism does is alters its own constitution
  - Often this involves determining which genes to express at a given time
- One way gene expression is controlled is through an *operon*—a system that detects a signal and responds by relieving inhibition or actively initiating gene transcription and creation of proteins
  - The molecules that turn gene expression on or off are known as transcription factors
- This machinery of gene expression is often the target of information processing



Controlling Constantly Changing Bodies

- Flagella themselves are complex structures that are regularly being synthesized and degraded
- But they are not the only type of mechanism bacteria use to navigate.
  - Many rely on pili—extendable and retractile appendages involving thin filaments (5 to 8 nm) that extend out to attach to another cell or other structure and retract to pull the cell body forward, generating twitching movements.
- Every few minutes the pili at one pole of the cell are broken down, and new ones synthesized at the other pole

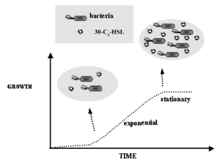


Colony Formation and Behavior

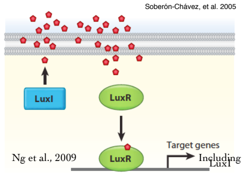
- Bacteria have largely been construed as solitary organisms--even in colonies, each bacterium was assumed to behave solely as an individual, not altered by being part of a collective
  - But this was an artifact of the techniques employed for studying their behavior
- Many species of bacteria self-organize into structured colonies containing from a million to a billion bacteria
  - Working together, bacteria can accomplish ends that cannot be accomplished alone
  - Bacteria can specialize to perform different tasks, relying on others to perform other tasks they require
- But before an organism can engage and coordinate behavior with other organisms, it must be able to detect their presence
  - This is often accomplished through quorum sensing.

Quorum Sensing in *Vibrio Fischeri*

- *Vibrio Fischeri* colonize the light organ of the squid *Euprymna scolopes*
  - *V. Fischeri* generates light which enables the squid mask its shadow
  - The squid provides *V. Fischeri* an environment rich in nutrients
- It only makes sense for one bacterium to generate ligh there are enough others to create sufficient light
  - Individual *V. fischeri* synthesizes Acyl homoserine lactone (AHL), which disperses into the environment where it is picked up by other *V. fischeri*
  - In the recipient bacteria it binds to LuxR and bound LuxR binds to DNA at *lux*-boxes, activating transcription of genes involved in bioluminescence as well as *luxI*, which then generates more AHL



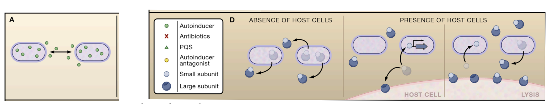
Soberón-Chávez, et al. 2005



Ng et al., 2009

Quorum Sensing

- Quorum sensing is widespread both within and between bacterial species and between bacteria and eukaryotic hosts
  - Allowing organisms to detect who is in their environment and adjust their behavior accordingly
  - Figures in biofilm formation, swimming, bioluminescence, virulence factor secretion, antibiotic synthesis, and stress responses including sporulation
- Different species produce and detect different molecules, thus keeping their conversations private



Bassler and Losick, 2006

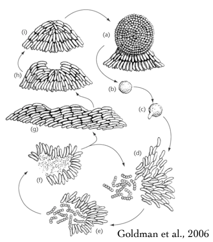
Clicker Question

What activities do Myxococcus xanthus bacteria perform socially?

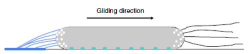
A. Sexual reproduction and creation of spore-filled fruiting bodies
B. Pack hunting and creation of spore-filled fruiting bodies
C. Synthesizing new body parts
D. Defending against predators and pack hunting

The Social Lives of *M. xanthus*

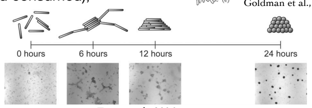
- (a-d) Bacteria emerge from spores when nutrients are available and form a swarm
- (e-f) While food is available, swarms move as predatory collectives gliding over solid surfaces, communally generating extracellular enzymes to lyse and consume prey
  - The bacteria move by pulling themselves with pili and pushing themselves with slime nozzles
  - Every 8-9 minutes they disassemble the pili and reassemble them on the other end
- (g-i) When food is scarce, bacteria begin stress response that involves streaming into aggregates (where many cells are lysed and consumed), building a mound, and creating spores



Goldman et al., 2006



Wu et al., 2011



Tzeng et al., 2006

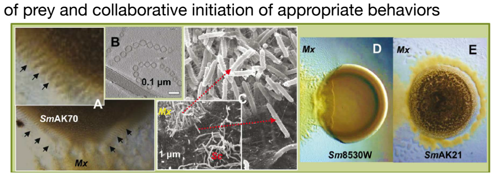
Clicker Question

What is cheating a concern in bacterial social hunting

A. Cheaters eat more than their share of the prey that are captured.
B. Cheaters to produce the needed toxins and so reduce the ability of the collective to catch prey effectively.
C. Cheaters often turn on the swarm itself, killing those who are working together.
D. Other individuals start to imitate the cheaters and soon no one is working.

Killing Prey Together

- When a biofilm of *M. xanthus* encounters prey, each organism releases a cocktail of hydrolytic enzymes, antibiotics, and other metabolites that lyse the prey cells
- Once the contents of the prey are released, individual bacteria feed off of them
- *M. xanthus* use quorum sensing to determine whether there are enough other bacteria to generate enough of the cocktail
- Different attack strategies for different prey—requiring identification of prey and collaborative initiation of appropriate behaviors



Sporulation: The Desperation Alternative

- Spores have no control over their fate
  - They are blown about by the wind and may happen to land in a location where conditions are favorable
  - If they do, they begin life again
  - But most spores won't find opportune conditions
- Determining whether to procedure with formation of fruiting bodies and then spores depends on integration information about
  - internal state—am I starving?
  - external environment—is there no food nearby?
  - colony condition—are there enough of us to carry out the process
- Timing is crucial: if delayed too long, bacteria don't have the energy to generate spores

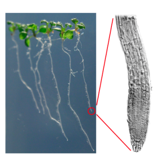
Discussion Question

What information is it important for a plant to possess if it is to grow successfully?

A. Who are its predators so it can resist them
B. What time it is so it can orient towards the sun
C. Where are nutrients in the soil so it can direct its roots appropriately
D. Where are the roots of competing species so it can avoid them or combat them

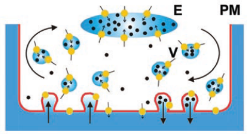
Plant Brains

- Charles Darwin, *The Power of Movement of Plants*:
  - "It is hardly an exaggeration to say that the tip of the radicle thus endowed [with sensitivity] and having the power of directing the movements of the adjoining parts, acts like the brain of one of the lower animals; the brain being seated within the anterior end of the body, receiving impressions from the sense-organs, and directing the several movements."
- For plants to survive, their roots must grow strategically
  - This is determined by the root cap
- Removal of the root cap results in uncontrolled rapid growth
  - Perhaps itself useful if damage to the cap is caused by local factors and growth can escape them



Plant Neuroscience?!

- Signal transduction along the elongation region (green) of root through a cell to cell network of secreting and absorbing cells
- Endocytosis and reabsorption of auxin, facilitated by PIN1
- Auxin transport system is gravity sensitive
  - causes endocytic vesicles to align with the bottom edge of the root
- Factor in roots growing down, not up (light is toxic to roots)



Black dots: auxins
Yellow: PIN1
E: endosome
V: endocytic recycling vesicles
Baluska et al., 2009

Directing Root Growth

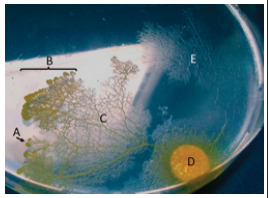
- Two regions capable of bending and thus steering the root:
  - in transition zone (yellow)
  - midway down the elongation zone (green)
  - ethylene is essential to coordinate them
- Result is a crawling movement

Root Sensory System

- Constantly dividing cells push previous cells upwards in the root cap until they are sloughed off. These cells sense
  - Gravity (statolith-sensing mechanism)—>faster bending
  - Touch—>inhibits gravity sensing and turns root sidewise
  - Phosphate deficiency—>signal to leaf shoots which synthesizes sRNAs sent back to the root to synthesize enzymes to break down complexes of phosphates with calcium, aluminum, or iron
  - Nitrate concentration—>increased growth, especially along gradient, but stops when source is reached
  - Ammonium ion deficiency—>signal to leaf shoots which returns a signal that alters branching and increases growth
  - When water is short, follow humidity gradient and dismember statoliths
- Root cap integrates these signals and selects a course of action

Slime Moulds

- *Physarum polycephalum*—an acellular slime mould
- In the Plasmodium stage (it also develops fruiting bodies, turns into spores, etc.) it exists as a large single cell (covering as much as 900 cm.[2]) with multiple nuclei—nuclei divide without the cell dividing
  - consumes microscopic particles, bacteria, and oat flakes (D) by covering them and absorbing material
  - Pseudopodia (A) extend out through chemotaxis, creating a search front (B) while maintaining protoplasmic tubes (C)
  - Cytoplasm consists of oscillators which synchronize to create waves that move food through the tubules
  - Minimizes distances food must be transported



Reid et al. 2013

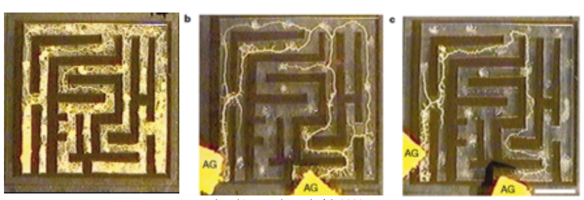
Clicker Question

Why were the slime moulds described in the reading solving maze problems

A. Their natural environments are full of complex pathways and they must find efficient routes
B. Food locations are scare and slime moulds must figure out how to get to them
C. Researchers made them solve mazes in order to get their food
D. Researchers just let them live in the mazes and they self-organized to fit the maze

Slime Mould Maze Solving

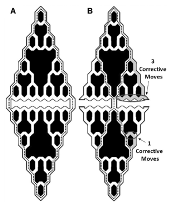
- Nakagaki, Yamada, and Tóth (2000) placed small pieces of a large slime mould at various places in the maze and allowed them to grow and join together in one cell
- Inserted agar blocks containing ground oat flakes at the beginning and end of the maze.
- After 4 hours the protoplasmic tubes on many of the dead-end paths shrank, leaving only paths between beginning and end
- After eight hours, only one of the solutions remains.
  - In one part of the maze where the alternative solutions differed significantly in length, the slime mould shrank to leave only the shortest path
  - In another part where the two paths were nearly equivalent, either one was selected.



Nakagaki, Yamada, and Tóth 2000

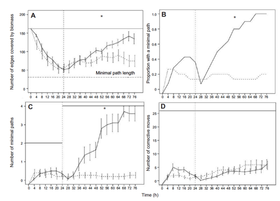
Slime Moulds Solve Tower of Hanoi

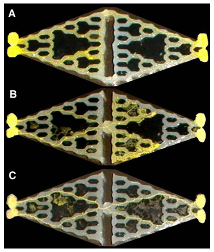
- Standard problem-solving task in human psychology
  - Moving one disk at a time and never putting a larger disk on top of a smaller one, move the stack to the rightmost pole
- Transform the task into a maze solving task
  - Slime moulds retreated to a solution
  - Rendered dynamic by changing the maze after 24 hours requiring a new solution



Static vs. Dynamic Mazes

- In the static condition, few slime moulds found the most efficient path
- In the dynamic condition (most efficient path blocked), all found what was then the most efficient





Animals with no Neurons: *Trichoplax adhaerens*

- A flat, millimeter-sized marine animal that adheres to surfaces and grazes on algae
- Very simple animal with only six cell types arranged into two layers, with a liquid-filled cavity between them
  - coordination between cell types
- Feeding behavior:
  - Endomorphin-like peptides released by sensory cilia arrest beating of motor cilia
  - Secretion of granules that lyse algae.
  - Groups of cells engage in churning movements that may aid in mixing and uptake of material released from the lysed algae
- The endomorphin-like peptides also facilitate communication between organisms