Unit 4: Life and Function

1. Homeostasis and Cybernetics

Recall Claude Bernard

- "The fixity of the milieu supposes a perfection of the organism such that the external variations are at each instant compensated for and equilibrated ... All of the vital mechanisms, however varied they may be, have always one goal, t**o maintain the uniformity of the conditions of life in the internal environment** .... The stability of the internal environment is the condition for the free and independent life."
  - Claude Bernard, from *Lectures on the Phenomena Common to Animals and Plants*, 1978. Quoted in C Gross, "Claude Bernard and the constancy of the internal environment," *The Neuroscientist*, 4:380-5 1998
- Note: the emphasis is not on the constancy of the internal environment itself but on the mechanisms of the body working to maintain *the conditions of life*

Compensatory Activities

- Fredericq (1885):
  - "The living being is an agency of such sort that each disturbing influence induces by itself the calling forth of **compensatory activity to neutralize or repair the disturbance**. The higher in the scale of living beings, the more numerous, the more perfect and the more complicated do these regulatory agencies become. They tend to **free the organism completely from the unfavorable influences and changes occurring in the environment.**"

Charles Richet

- Not Bernard's student!
- "The living system is stable . . . it must be in order not to be destroyed, dissolved or disintegrated by colossal forces, often adverse, which surround it. By an apparent contradiction, **it maintains its stability only if it is excitable and capable of modifying itself according to external stimuli and adjusting its response to the stimulation**. In a sense, **it is stable because it is modifiable** – the slight instability is the necessary condition for the true stability of the organism."
  - Richet, C. 1900. *Dictionnaire de Physiologie*, Paris, iv, 721

Walter Cannon (1871-1945)

- While monitoring the gastro-intestinal movements in a cat
  - A dog was brought into the laboratory
  - The strong peristaltic movements in the gut ceased abruptly
    - This effect was traced to adrenaline
    - Adrenaline also promoted glycogenesis in the liver for use by skeletal muscle
- Cannon viewed this as an adaptive stress response and made it the focus of much of his experimental investigation

Cannon: Homeostasis

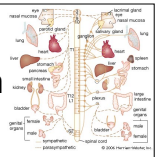
- Identifies Bernard's milieu intérieur as the fluid matrix
  - **made and controlled by the organism itself**
- Coined the term homeostasis
  - from words ὅμοιος (hómoios) "**similar**" and στάσις (stásis) "**state**"
- Distinguishes homeostasis from the physical processes of achieving equilibrium
  - "integrated cooperation of a wide range of organs—brain and nerves, heart, lungs, kidneys, spleen-which are promptly brought into action when conditions arise which might alter the blood in its respiratory services. . . . The coordinated physiological reactions which maintain most of the steady states in the body are so complex, and are so peculiar to the living organism, that it has been suggested (Cannon, 1926) that a specific designation for these states be employed—homeostasis."

Clicker Question

What is it that makes homeostasis of special import?

A. It is uniquely human
B. It maintains an animal at certain fixed points
C. It enables an organism to ignore any changes in its environment
D. It enables an organism to cope with a changing environment

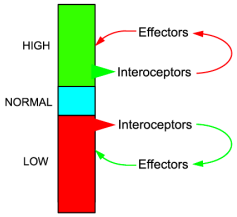
Cannon: function of the sympathetic nervous system



- Cannon removed the complete sympathetic chain of autonomic ganglia.
  - Found he could keep animals alive for prolonged periods and found few abnormalities after death
- But when put under stress:
  - Blood pressure falls slightly during moderate muscular activity
  - Lower tolerance for O_2 lack; they fainted at 8% O_2 (equivalent to 24,000 feet) after 15-20 min.
  - Blood sugar homeostasis is much reduced.
  - Temperature homeostasis is much reduced.
  - Homeostatic response to hemorrhage is much weaker.
- Concluded that the sympathetic nervous is system crucial for homeostasis

Regulation Beyond the Nervous System

- There are many systems for regulating bodily state that don't involve neurons
- Endocrines
- Insulin
- From Goldstein 2017: "Increases in blood glucose stimulate pancreatic islet cells to release **insulin**, which facilitates glucose uptake by organs such as the liver. Decreases in blood glucose reflexively stimulate adrenomedullary cells to release **adrenaline**, which augments glucose formation from liver glycogen and evokes glucose release into the bloodstream"



Goldstein 2017

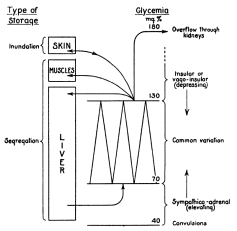
Conditions Cannon Claimed Exhibited Homeostasis

A. Material supplies for cellular needs.
   1. Material serving for the exhibition of energy, and for growth —glucose, protein, fat.
   2. Water.
   3. Sodium chloride and other inorganic constituents except calcium.
   4. Calcium.
   5. Oxygen.
   6. Internal secretions having general and continuous effects.

B. Environmental factors affecting cellular activity.
   1. Osmotic pressure.
   2. Temperature.
   3. Hydrogen-ion concentration.

Mechanisms for Regulating Homeostasis

- Regulating supplies
  - Storage by inundation
    - water
    - sodium chloride
  - Storage by segregation
    - Carbohydrate as glycogen
    - Plasma protein
- Regulating processes
  - pH
  - Temperature—regulating blood flow, sweating and shivering, regulating metabolism

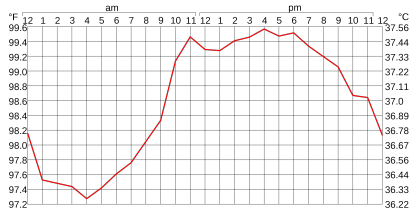


Six Postulates of Homeostatic Regulation

1. "In an open system such as our bodies represent, compounded of unstable material and subjected continually to disturbing conditions, **constancy is in itself evidence that agencies are acting, or ready to act**, to maintain this constancy."
2. "If a state remains steady it does so because any tendency towards change is **automatically met by increased effectiveness** of the factor or factors which resist the change."
3. "Any factor which operates to maintain a steady state by action in one direction does not also act at the same point in the opposite direction."
4. "Homeostatic agents, antagonistic in one region of the body, may be cooperative in another region."
5. "The regulating system which determines a homeostatic state may comprise **a number of cooperating factors brought into action at the same time or successively**."
6. When a factor is known which can shift a homeostatic state in one direction it is **reasonable to look for automatic control of that factor or for a factor or factors having an opposing effect**."

Mistaken Assumptions of Constancy Constancy

- Assumption that this is a *normal* body temperature
- Regular variation



Discussion Question

What reason might there be to have body temperature vary over 1° C. per day?

A. None. It just reflects a sluggish response to changes in the environment
B. None. It is a side effect of other changes organisms implement during daytime
C. Higher body temperature during daytime enables organisms to work harder
D. Higher body temperature during daytime requires less compensation to daytime heat
E. Other

Physiological Adaptation to Temperature Change

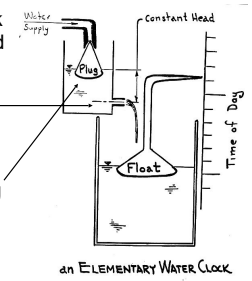
- Responses to cold
  - Vasoconstriction
  - Counter current exchange: warm venous blood returning to the heart with arterial blood
    - reducing heat loss from the extremities
  - Increased metabolism
  - Shivering—heat from muscle contraction
- Response to Heat
  - Vasodilation
  - Sweating

Behavioral Adaptation to Temperature Change

- Among the changes an animal can make to cope with changing conditions in its environment are behavioral
  - An animal can seek an environment that protects from either excess heat or cold
    - burrowing in the ground
  - An animal can alter its environment in ways that maintain environment facts in a more constant state
    - building a dam to maintain water

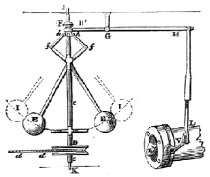
The Origins of Negative Feedback

- First known example of negative feedback: Water clock designed by Ktsebios in the 3rd century BCE
  - Need to maintain constant water pressure
  - Employed a float that would start or halt the inflow from the water supply, maintaining a constant level
- The function of the plug is to maintain a constant flow of water



Industrialization and Negative Feedback

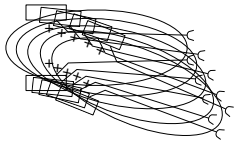
- James Watt faced a serious practical challenge
  - How to control the speed of the steam engine so that all appliances would run at the same rate despite different number being on line at a time
  - Devised an elegant mechanism for feedback control



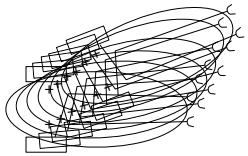
The Military Kick-Starts Negative Feedback

- Enduring challenge: How to target gunfire
  - With guns, look down the site
    - If the target is moving, anticipate where it will be when the bullet arrives
  - With artillery, fire two shots, deliberately undershooting and deliberately overshooting
    - Calculate how to change the elevation to hit the target
  - Airplanes create more of a challenge as they evade
    - Heat seeking missiles

Designing a Target-Seeking Machine

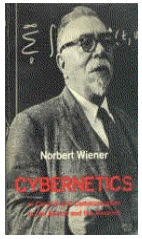


Designing a Target-Seeking Machine



Cybernetics (1940s-1950s)

- An interdisciplinary group of researchers who viewed negative feedback as a general organizing principle not just for the military but for biology, society, and engineering
  - Cybernetics—from the Greek for helmsperson



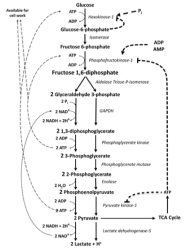
Discussion Question

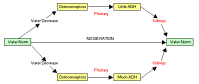
Why don't rowers look in the direction they are going?

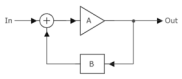
A. They are going so slow it doesn't matter what direction they are going
B. They never figured out how to navigate to a destination
C. They are looking in the direction that is most useful
D. They don't have the strength to push the oars so they have to rely on pulling

Negative Feedback in Biology

- Negative feedback is widespread in biology
  - Biochemical systems: products of reactions feed back to slow reactions earlier in the pathway
  - Physiological systems: when variable deviates from norm, processes initiated to restore it to normal
  - Motor systems: when action misses the mark, change to guide it to the target







Oscillation: A Sometimes Negative Consequence of Negative Feedback

- Ironically, it was oscillation in the guidance systems for anti-aircraft guns that triggered the comparison to biological systems
  - Tremors are often a side effect of negative feedback regulation
- For designers, a challenge is often to dampen oscillations from negative feedback
- But sometimes oscillations are useful
  - E.g., if one is trying to track a system that is itself oscillating, it is useful to oscillate in synchrony with it

25

Behavior, Purpose, and Teleology

- Rosenblueth, Wiener, and Bigelow propose that negative feedback can explain how purposive behavior/teleology can exist in a purely physical world
- They distinguish
  - behavioristic approach
  - functional analysis
- Is the output determined by the input or by the system itself?
  - Follow the energy
    - does the energy (or control of it) come from the system? Active
    - or from the immediate input? Passive
- Is there a purpose to the active behavior?
  - or is it random?

26

Clicker Question

Which of the following do Rosenbleuth et al. use as an example of a purposive machine?

A. Roulette wheel
B. Clock
C. Gun
D. Target seeking torpedo

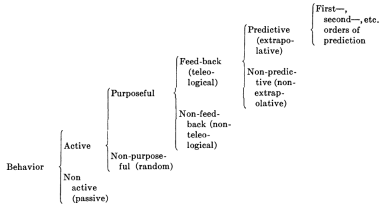
27

Purpose

- Many machines lack a purpose of their own
  - E.g., a clock or a gun
- But some exhibit a purpose
  - E.g., “a torpedo with a target-seeking mechanism”
  - Why would one think that such a torpedo has a purpose of its own
- Distinction between feedback (teleological) and non-feedback
  - Negative feedback: corrects an output
    - Purpose requires negative feedback

Beyond Negative Feedback

- Negative feedback is totally reactive
- An alternative is to anticipate changes and do something in advance
  - One thing an anticipatory system can do is alter the goal of negative feedback
    - Change target blood pressure during exercise



The Homeostat

- W. Ross Ashby designed an electromagnetic machine to maintain a stable state despite perturbations
- “Law of Requisite Variety” for a system to be stable, the states of its control mechanism must be at least as numerous as the number of states of the system to be controlled
  - “variety is necessary to destroy variety”
    - Ashby (1956) *Design for a Brain:* a good brain is a good controller