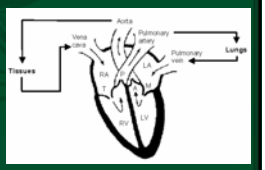
Living Mechanisms

Mechanisms as Coordinated Causal Systems

- A mechanism is a structure performing a function in virtue of its component parts, component operations, and their organization. The orchestrated functioning of the mechanism is responsible for one or more phenomena. (Bechtel and Abrahamsen 2005; see also Bechtel & Richardson, 1993, Glennan, 1996, 2002, Machamer, Darden, & Craver, 2000)
- Example: muscles in heart contract and relax while valves open and shut
  - Resulting in the phenomenon: circulation of the blood



But what Sort of Organization must a Mechanism have to Live?

- Bernard: a mechanism that maintains its internal environment
  - Account for both apparent indeterminism and resistance to death (Bichat)
- Cannon: mechanism that can maintain homeostasis
  - He provided numerous examples
- Cybernetics: mechanisms using negative feedback

- But is this enough?
  - Living things exhibit a kind of autonomy
    - They have an identity and maintain that identity in the face of an environment

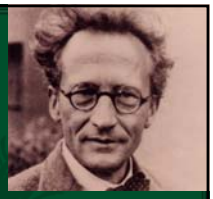
Living Systems as Enduring, Acting Individuals

- For the most part, living organisms stand out against their environments as enduring structured entities
  - Also true of individual cells, the fundamental living units
- Living organisms, including cells, are not just passive systems but active ones
  - Metabolic systems: changing chemical compounds into other chemical compounds
- Focal issue: how do living systems maintain themselves?

Hopkins' Vision

A living cell is "not a mass of matter composed of a congregation of like molecules, but a highly differentiated system: the cell, in the modern phraseology of physical chemistry, is a system of co-existing phases of different constitutions" (Hopkins 1913 [1949] p. 151)

"It is important to remember that changes in any one of these constituent phases ... must affect the equilibrium of the whole cell-system, and because of this necessary equilibrium-relation it is difficult to say that any one of the constituent phases ... is less essential than any other to the "life" of the cell ... Certain of the phases may be separated, mechanically or otherwise, as when we squeeze out the cell juices, and find that chemical processes still go on in them; but "life", as we instinctively define it, is a property of the cell as a whole, because it depends upon the organisation of processes, upon the equilibrium displayed by the totality of the co-existing phases."



Erwin Schrödinger: *What is Life?*

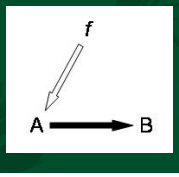
- The entropy problem
  - How could order be maintained in the face of the 2nd Law of Thermodynamics
  - Problem 1: how could genes retain their structure in the face of mutation?
  - Problem 2: how could metabolism enable organisms to maintain themselves in a non-equilibrium state
    - Negentropy: Organisms route energy through themselves in a manner that builds structure (reduces entropy) and increases entropy outside of the self

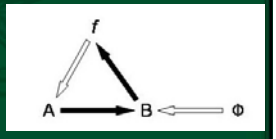
Organization in Living Systems

- Highly organized systems are not at equilibrium
  - Over time they will dissipate
  - Unless they are so organized as to maintain themselves
- Cannot rely on an external repair person
  - Nor on an external agent to build it in the first place
- Key element to solving this problem:
  - Cyclic organization—in biochemistry, reaction pathways which reconstitute earlier components

Rosen: Self-Repairing System

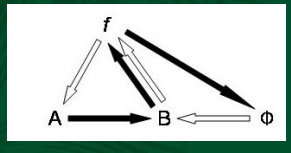
- Start with a simple metabolic operation:
  - Component *f* transforms substance A into B
  - *f* is an *uncaused* efficient cause
- Add B as a material cause of *f* and Φ as efficient cause of B →*f*
  - But now Φ is uncaused





Closing Efficient Causation

- Could add new material and efficient causes of Φ
  - But we are clearly into a regress
- Rosen's solution:
  - Let *f* be the material cause of Φ and B be the efficient cause of *f* → B

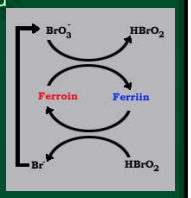


Beyond Mechanism?

- Rosen construes organisms, as systems "closed to efficient causation," as outside the scope of mechanistic science
  - He therefore calls for a new non-Newtonian, non-mechanistic paradigm in science
- Contrary to Rosen, such modes of organization are compatible with the mechanistic perspective ***as long as it focuses sufficiently on organization***

The Belousov-Zhabotinski (B-Z) Reaction

- Positive feedback between two reactions
  - Each supplying the input to the other can produce novel, complex patterns
- When Boris Belousov first proposed the oscillating set of reactions, his paper was rejected
  - The reactions were, after all, impossible

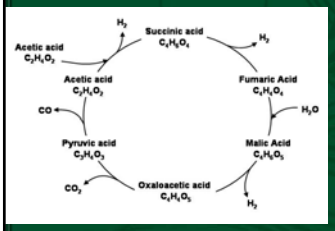


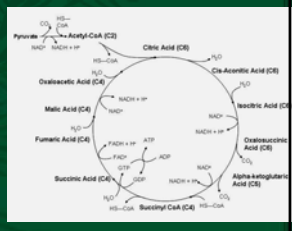
Biological Cycles

- To explain overall reactions, early biochemists tried to identify sequences of operations adding or removing biological groups
  - But sometimes this was not possible
- Thunberg (1920):
  - Succinic acid → fumaric acid → malic acid → oxaloacetic acid → pyruvic acid → acetic acid
  - What then happens to acetic acid?
  - Proposed two molecules of acetic acid combined to form succinic acid:
    - $2CH_3—COOH \rightarrow COOH—CH_2—CH_2—COOH + H_2$

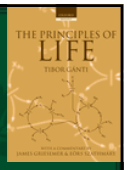
From Thunberg to Krebs' Cycle

- Closing the loop resulted in a cycle
- Krebs and Johnson (1937) modified the cycle, which was further modified with the discovery in the 1940s of coenzyme A





Why Cycles?



- Cycles reconstitute themselves, leaving the overall organization unchanged:
  - "Continuous work performance can only be achieved by means of suitable work-performing systems characterized by changes occurring through a series of constrained motions, such that the inner organizational characteristics of the system remain unchanged" (Gánti, p. 68).
  - "In an internal combustion engine the explosion moves the piston from its original location, but the engine is so constructed that the displacement occurs on a constrained path and after performing work the piston returns to its starting position. . . . The ability of non-mechanical systems to perform continuous work also depends on cyclic processes or, as they are often call for simplicity, cycles" (Gánti, p. 72).

From Cycles to the Chemoton

- Tibor Gánti conceptualized the Krebs cycle thus:

Krebs

Oxaloacetic acid —(1)→ Oxaloacetic acid

- To show that nutrient (energy) is entering and waste leaving, Gánti expands the representation:

Krebs

Oxaloacetic acid + CH_3—CO + $3H_2O$ —(1)→ Oxaloacetic acid + $2CO_2$ + 9H

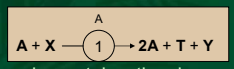
- To capture growth, Gánti moves from the Krebs cycle to the malic cycle, in which 2 substrates are formed for each one consumed:

Krebs: **A + X** —(1)→ **A + Y**

Malate: **A + X** —(1)→ **2A + Y**

Adding a Membrane System

- In a fluid system, reactants must be in high enough concentration that diffusion will bring them together
- Membranes provide a means of segregating reactants in higher concentrations
- But for the chemoton to be a biological system, it must build its own membrane. Gánti proposes the following reaction combining metabolism with membrane synthesis:



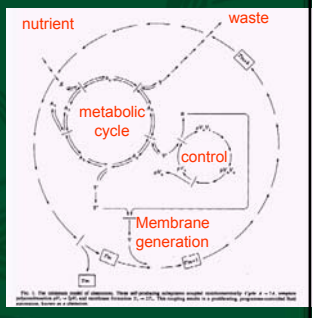
- Assuming the membrane takes the shape of a sphere, this results in the membrane growing faster than the contents. Gánti proposes that it will eventually bud into separate spheres

Metabolism + Membrane = Super-system

"We have combined two systems of a strictly chemical character into a 'super-system' (or, to put it another way, we have combined two chemical subsystems), and we have obtained a system with a surprising new property of expressly biological character. What can this system do? It is separable from the external world and its internal composition differs from that of the environment. It continuously consumes substances that it needs from the environment which are transformed in a regulated chemical manner into its own body constituents. This process leads to the growth of spherule; as a result of this growth, at a critical size the spherule divides into two equal spherules, both of which continue the process" (Gánti , p. 105)

The Chemoton

- For Gánti the super-system was not yet alive, as it lacked an information storage or control system
- Gánti proposed to add this by adding a subsystem that generates a polymer
- Griesemer proposes that the polymer generation system can introduce a property free from stoichiometric constraint and hence available to be selected independently



Varela: Autopoietic Mechanisms

- "An autopoietic system is organized (defined as a unity) as a network of processe production (transformation and destruction) of components that produces the components that: (1) through their interactions and transformations continuously regenerate and realize the network of processes (relations) that produce them; and (2) constitute it (the machine) as a concrete unity in the space in which they exist by specifying the topological domain of its realization as such a network." (1979, p. 13).

From Autopoiesis to Autonomy

- "Autopoietic machines are autonomous: that is, they subordinate all changes to the maintenance of their own organization, independently of how profoundly they may be otherwise transformed in the process. Other machines, henceforth called *allopoietic* machines, have as the product of their functioning something different from themselves" (Varela, 1979, p. 15)

Thermodynamic Autonomy

- Moreno provides a thermodynamic characterization of an autonomous system:
  "a far-from-equilibrium system that constitutes and maintains itself establishing an organizational identity of its own, a functionally integrated (homeostatic and active) unit based on a set of endergonic-exergonic couplings between internal self-constructing processes, as well as with other processes of interaction with its environment"

Kepa Ruiz-Mirazo, Juli Peretó and Alvaro Moreno, A Universal Definition Of Life: Autonomy And Open-ended Evolution

Beyond the Chemoton

- While a chemoton exhibits many of the features we associate with living organisms, it is much simpler than any living organism we know
- What more is needed?
  - More parts performed more differentiated operations
  - Organized in the service of the autonomy of the organism
- Segregation of parts, so that there operations do not impede each other
- Yet linked so that their operation subserves the needs of the system

Living Mechanisms

- Mechanisms organized so as to maintain themselves far from equilibrium
  - Or parts of such mechanisms that are subserving the ability of the whole to maintain itself far from equilibrium
- Such mechanisms must recruit matter and capture free energy and utilize it in their own self-construction and repair

Vitamins: Vital Amines

The challenge of beriberi: what was the responsible germ (bacterium)?

- Christiaan Eijkman discovered a similar disease in chickens and that it was related to a change from raw rice to boiled polished rice
  - Adding rice bran (the outer coating) countered the disease
  - Proposed that the bran operated to counter a poison in the rice
- Frederic Gowland Hopkins
  - Animals don't grow on artificial diets
  - But very tiny amounts of milk make the diet sufficient