

## Vitalism and Organized Mechanisms

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### Albrecht von Haller (1708-1777): A prototypical mechanist

- Solid parts of bodies are fibrous, composed of particles held together in linear strands by gluten or jelly
  - Particles contain air, chalk, and iron
    - lost by mechanical abrasions or friction
  - Gluten contains air, oil, water, and volatile salts
    - lost by breathing, sweat, urine, tears and secretions
- Nutrition restored both the particles and the gluten
- Living things exhibit sensibility and irritability
  - Only nerve exhibits sensibility
  - Only muscle exhibit irritability
  - Von Haller attributed these properties to the gluten

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### John Hunter (1728-1793): A vitalist retort

- Ordinary matter is transformed into vegetable or animal matter, but
- “No chemist on earth can make out of the earth a piece of sugar, but a vegetable can do it.”
- So, there is something special about living things that sets them apart
  - For Hunter this is the *fact* that they can only be made by living things
- Hunter’s claim gives context to Wöhler’s excitement after synthesizing urea—chemists could, it seemed, make organic compounds

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## Marie François Xavier Bichat (1771-1802)

- “Life consists in the sum of the functions, by which death is resisted”
- “The measure, then, of life in general, is the difference which exists between the effort of exterior power, and that of interior resistance.”
  - What is meant by saying life is resisting death?
- “As Newton ascribed basic 'properties' (for example gravitation) to the physical matter of the cosmos, physicians should ascribe 'properties' to the physiological matter of life. But vital properties should be clearly distinguished from physical ones. Let us leave to chemistry its affinity, to physics its elasticity and gravity, and let us employ in physiology only *sensibility and contractility*.”

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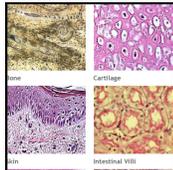
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## Bichat Allows Mechanistic Decomposition Down to Tissues

“Chemistry has its simple bodies, which form, by the combinations of which they are susceptible, the compound bodies; such are coloric, light, hydrogen, oxygen, carbon, azote [nitrogen], phosphorus, &c. In the same way anatomy has its simple textures, which, by their combinations four with four, six with six, eight with eight, &c., make the organs. These textures are, 1<sup>st</sup>. the cellular; 2<sup>d</sup>. the nervous of animal life; 3<sup>d</sup>. the nervous of organic life; 4<sup>th</sup>. the arterial . . . These are the true organized elements of our bodies. Their nature is constantly the same, everywhere they are met with.” *Anatomie générale*

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## Bichat: Tissues as Source of Vital Properties

“Shall I speak of the vital properties? See the animal sensibility predominant in the nerves, contractility of the same kind particularly marked in the voluntary muscles, sensible organic contractility, forming the peculiar property of the involuntary, insensible contractility and sensibility of the same nature, which is not separated from it more than from the preceding, charactering especially the glands, the skin, the serous surfaces, &c. &c. . . . [E]ach texture has a particular kind of force, of sensibility, &c. Upon this principle rests the whole theory of secretion, of exhalation, of absorption, and of nutrition. The blood is a common reservoir, from which each texture chooses, that which is adapted to its sensibility, to appropriate and keep it, or afterwards to reject it.”

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## Bichat's Vitalism

Lack of regularity in living bodies:

“One calculates the return of a comet, the speed of a projectile, but to calculate with Borelli the strength of a muscle, with Keill the speed of blood, with Lavoisier the quantity of air entering the lungs, is to build on shifting sand an edifice solid itself, but which soon falls for lack of an assured base. The instability of vital forces marks all vital phenomena with an irregularity which distinguishes them from physical phenomena [which are] remarkable for their uniformity” (1805, p. 81)

And opposition to physical forces: life is “the sum of all those forces which resist death.”



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## More of the Variability of Vital Powers

- “This instability of the vital powers, this facility which they have of varying more or less at every instant, impress upon all the vital phenomena a character of irregularity which distinguishes them from physical phenomena, remarkable for their uniformity”
- “The urine is not the same after a meal as after sleep; it contains in winter, principles which are foreign to it in summer, when the principal excretions are made by the skin; the simple accession of cold or heat may by suppressing the sweat and enfeebling the pulmonary exhalation, produce variations in its composition. It is the same with the other fluids: the state of the vital powers in the organs which are the sources of them, changes at every instant.

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## The Contributions and Limitations of Vitalism

- Bichat and other vitalists such as Pasteur made important contributions in drawing attention to the complexity of biological phenomena
  - Especially ways in which living systems seemed to vary in their behavior at different times (unlike ordinary physical substances)
- But they typically lacked a research program
  - They were left with describing the phenomena and hypothesizing vital properties, forces, etc.
    - As they rejected the mechanists' strategy of taking systems apart so as to show how the phenomena resulted from the parts and operations within the living organism, they could not explain why these properties/forces operated as they did

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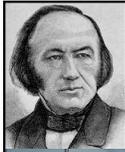
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## Claude Bernard (1813-1878)

- 1843: fundamental research on the 7th cranial nerve (facial muscles and taste) and role of the gastric juice in breakdown of disaccharides. Determined the action of the stomach proteolytic enzyme which Schwann had named 'pepsin' in 1836.
- 1848-49: one role of the pancreatic juice is to emulsify fat.
- 1848-50: proved that the liver played a major role in regulating blood sugar—In particular provided the proof that the liver could synthesize sugar from other substrates (prevailing theory was that all sugars came directly from the diet).
- 1849-52: Demonstrated that curare paralyzes striated muscle by acting somewhere in the neuromuscular junction (not on the nerve nor the muscle). Introduces it as a therapeutic muscle relaxant during surgery.
- 1856-59: first to demonstrate mechanism by which CO causes asphyxiation.

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## Bernard's Quest for Determinism

- "The doubter is the true scientist; he only doubts himself and his interpretations, but he believes in science; he even admits a criterion or an absolute scientific principle in the experimental sciences. This principle is the **determinism of phenomena**, which is as absolute in the phenomena of living bodies as in inorganic bodies."



*"God does not play dice with the universe."*

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## The vitalist's challenge for Bernard

"The spontaneity enjoyed by beings endowed with life has been one of the principal objections that has been raised against the use of experimentation in biological studies. Each living being, in effect, appears to us as if provided with a kind of **interior force** which presides over vital manifestations, which become more and more independent of the general influence of the cosmos, the more the being in question rises in the scale of organization. In the higher animals and in man, for example, this vital force appears to result in the withdrawal of the living body from general physico-chemical influences, and thus renders experimental access to it very difficult."




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## Bernard: Vitalism an Obstacle to Progress



"Many doctors and speculative physiologists, along with some anatomists and naturalists . . . have supposed that the vital force was in opposition to the physico-chemical forces, and that this vital force dominated all the phenomena of life, subjecting them to altogether special laws, and making the organism an organized whole which the experimenter could not touch without destroying the very character of life itself. . . . These ideas, which were current in other time periods, are undoubtedly fading away now more and more; however, it is important to **wipe out the final traces** of them, because whatever remains of these so-called vitalist ideas in certain minds represents a **real obstacle to the progress of experimental medicine.**"

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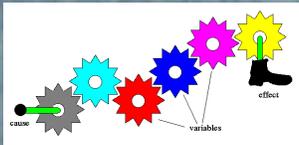
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## Bernard's commitment to determinism

"there is an absolute determinism in all of the sciences because, each phenomenon being linked necessarily to physico-chemical conditions, **the scientist can modify these conditions to master the phenomenon**, that is to say, to hinder or favor its manifestation. In the case of inorganic bodies, there is no debate on this subject. I would like to prove that it is the same for living bodies, and that, for them also, determinism exists."



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## Bernard on the need for experiment

"The inductive reasoning which I implicitly made consisted of the following syllogism: the urine of carnivores is acid; now, the rabbits which I observed had acid urine; therefore they are carnivores, that is to say, in a state of fasting. This is what remained to be established by experiment."

Argument structure:

If an animal is a carnivore, then its urine is acid

Starving rabbits have acid urine

∴ Starving rabbits are carnivores (digesting their own bodily substance)

Note: this is not a valid argument  
thus the need to establish the conclusion by experiment

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## What does experiment accomplish?

By alternating starvation and feeding, Bernard shows that he can *control* whether the animals generate acid urine or not  
– Why is this important?

The same effect is achieved by feeding them meat, showing that the source of the acid urine is digesting animal material



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## Discovery of glycogenesis

“The dominant theory at that time, which naturally was my starting point, claimed that the sugar which existed in animals originated exclusively in food and that it was destroyed in the animal organism by the phenomenon of combustion, that is to say, respiration. This is why sugar was given the name respiratory nutriment.”  
—Theory due to Justus Liebig

Bernard sought, could not find a point where glucose content dropped, as it should if it was consumed  
– Rather, he found a location where it increased—in the blood vessels near the liver  
– Conclusion: Animals do synthesize substances such as glucose as they need them

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## Explaining Resistance to Death: Bernard’s *milieu intérieur*

- The organs of an animal are “enveloped in an internal environment which acts for it as an atmosphere of its own in the midst of an ever changing outer cosmic environment. The higher organism has, in effect, been placed in a hot house. Here it is **beyond the reach of the perpetual changes of the cosmic environment. It is not bound up in them; it is free and independent**” (1879, p. 414).
- “In all living beings, the *milieu intérieur*, which is a true *product of the organism*, preserves the necessary relations of exchange and equilibrium with the external cosmic environment; but, as the organism becomes more perfect, the organic environment becomes more specialized **and in some manner isolates itself more and more from the ambient environment.**”

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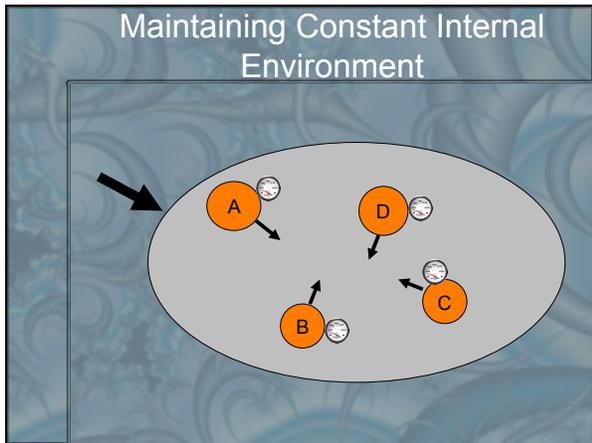
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### Rescuing Mechanism

"the real explanation of the phenomena of life rests on the study and knowledge of the most tenuous and subtle particles which form the organic elements of the body. This idea, set down in biology long ago by the great physiologists, appears more and more valid as the study of the organization of living beings makes greater progress. We must learn in addition that these *intimate particles* of the organization only manifest their vital activity by a necessary physicochemical relation with *intimate environments* which we should equally study and know. Otherwise, if we limit ourselves to the examination of the total phenomena visible from the outside, we might falsely believe that there is a unique force in living beings which violates the physicochemical laws of the general cosmic environment, in the same way an ignorant person could believe that there is a special force which violates the laws of gravity in a machine which mounts into the air or runs along the ground. **Now a living organism is nothing but an amazing machine endowed with the most marvelous properties and activated by the aid of the most complex and delicate mechanisms.**

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### 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
  - Traced effect to adrenaline
  - Adrenaline also promoted glycogenesis in the liver for use by skeletal muscle
  - An adaptive stress response
- Homeostasis: reestablishing target state in response to perturbations
  - Maintaining constant conditions in the face of dynamically changing environment
  - Negative feedback (ex. thermostat)

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## Cannon: function of the sympathetic nervous system

- Removed the complete sympathetic chain of autonomic ganglia.
- Found he could keep animals alive for prolonged periods and on autopsy after death, few abnormalities
- But when put under stress:
  - Blood pressure falls slightly during moderate muscular activity
  - Lower tolerance for O<sub>2</sub> lack; they fainted at 8% O<sub>2</sub> (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.
- Sympathetic nervous system crucial for homeostasis




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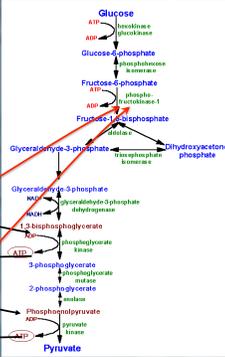
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## Negative Feedback Regulation in Basic Biochemical Pathways

Glucose consumption regulated by the needs of for energy via regulation of phosphofructokinase

- Not just the availability of glucose




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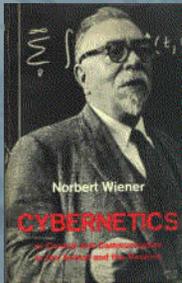
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## Cybernetics (1940s-1950s)

- Negative feedback as a general organizing principle for biology, society, and engineering




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