

# Unit 1: Mechanistic Cell Biology

## 2. Vitalism and Organized Mechanisms

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### Descartes: The Father of Mechanism

- Recall that Descartes maintained that, except for two phenomena he thought only occurred in humans (reasoning and language use), all of nature operated in a mechanistic fashion
- For him, that meant that all phenomena, including those exhibited by living organisms, were due to the shape and movement of component particles: atoms or corpuscles
- While his proposed explanations were speculative, many others began to investigate the composition of organisms and to offer mechanistic accounts
  - While yet others rejected them, treating life as outside the scope of mechanical science

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

- von Haller treated the solid parts of bodies as 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
- He construed nutrition as restoring both the particles and the gluten
- von Haller introduced the vocabulary of sensibility and irritability to describe animal tissues
  - Nerves exhibit sensibility
  - Muscles exhibit irritability
  - Von Haller attributed these properties to the gluten in their constitution

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

- Hunter allowed that ordinary matter is transformed into vegetable or animal matter, but claimed that only living organisms can carry out the transformation
  - “No chemist on earth can make out of the earth a piece of sugar, but a vegetable can do it.”
- Like other opponents of mechanism, he maintained that something special sets living things apart from other material objects
  - For Hunter this is the fact that they can only be made by living things
- Hunter’s claim gives context to Wöhler’s excitement when, in the 1830s, he succeeded in synthesizing urea—chemists could, it seemed, make organic compounds

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## Clicker Question

What is the definition of life with which Bichat begins?

- A. Life consists of metabolic processes in cells
- B. Life consists in the sum of functions by which death is resisted
- C. Life consists in the operation of vital forces which oversee chemical reactions in organisms
- D. Life is so multifaceted that it cannot be defined

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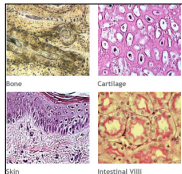
## Marie François Xavier Bichat (1771-1802)

- “Life consists in the sum of the functions, by which death is resisted”
- “In living bodies, such in fact is the mode of existence, that whatever surrounds them, tends to their destruction. They are influenced incessantly by inorganic bodies; they exercise themselves, the one upon the other, as constant an action; under such circumstances they could not long subsist, were they not possessed in themselves of a permanent principle of reaction.”
- Bichat is working well before the development of thermodynamics, but he has already recognized the basic idea that the natural world tends towards disorder
  - Organized systems are subject to breakdown
- But living organisms resist this

## Resisting Death

- “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 the basis of this ability to resist death?
  - Something different from physical properties
  - “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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## 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*

## But Treats Tissues as Loci 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.”

## 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)



## 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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## Dual Roots of Bichat's Vitalism

- Bichat's rejection of mechanism was based on both
  - living organisms are not sufficiently regular in their responses
  - living organisms resist physical forces: life is "the sum of all those forces which resist death."
- Like other vitalists, he argued against mechanism, not for vitalism

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## The Contributions and Limitations of Vitalism

- Bichat and other vitalists 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 to explain the phenomena
  - They were left with describing the phenomena and hypothesizing vital properties, forces, etc.

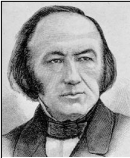
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## Discussion Question

What do you find to be the strongest (or least weak) argument for vitalism?

- A. Living organisms lack sufficient regularity in their behavior to be explained in the manner of the physical sciences
- B. Living organisms operate in opposition to the processes of the inorganic world
- C. Living organisms determine their own actions and are not governed solely by the physical processes of nature
- D. The process of development, whereby from a single cell many different cell types all arise in proper order, cannot be explained mechanistically
- E. Other

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### Claude Bernard (1813-1878)

- Pioneer in detailed experimentation on living organisms with the objective of figuring out how they work
- 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: identify the role of pancreatic juice in emulsifying 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.

## 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

Bernard sets out the view of those he is opposing (e.g., Bichat):

"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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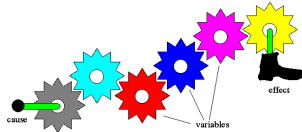
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## Bernard's Commitment to Determinism

"I propose therefore to establish that the science of the phenomena of life must have the same basis as that of the science of inorganic bodies, and that there is no difference in this respect between the principles of the biological sciences and those of the physico-chemical sciences. . . 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 acid urine could result from 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, but could not find a point where the concentration of glucose dropped, as it should if it was consumed

- Instead, 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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## Clicker Question

What two environments does Bernard think it important to distinguish in order to understand the behavior of living systems?

- A. The internal environment and the external environment
- B. The environment in which the organism first develops and the environment in which it lives its adult life
- C. The physical environment from the organic environment
- D. The environment of plants from the environment of animals

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## Clicker Question

What does Bernard have in mind when he talks of the internal environment (milieu intérieur)?

- A. The environment inside a shelter (e.g., the den of a lion)
- B. The conditions inside the nucleus of a cell
- C. The environment in which the chemical and physiological processes of life occur
- D. The environment created in the laboratory in which research is done

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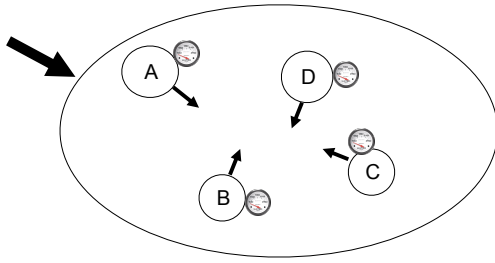


## Explaining Resistance to Death: Bernard's *milieu intérieur*

- 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.**"

## Maintaining Constancy of the Internal Environment

The fixity of the milieu supposes a perfection of the organism such that the external variations are at each instant compensated for and equilibrate



## Independence of Organisms from their Environment

- A living machine keeps up its movement because the inner mechanism of the organism, by acts and forces ceaselessly renewed, repairs the losses involved in the exercise of its functions. Machines created by the intelligence of man, though infinitely coarser, are built in just such a fashion. A steam engine's activity is independent of outer physico-chemical conditions, since the machine goes on working through cold, heat, dryness and moisture.  
» Experimental Medicine, p. 79
- The ancient emblem representing life as a closed circle, formed by a serpent biting its own tail, gives a fairly accurate picture of things. In complex organisms the organization of life actually forms a closed circle, but a circle [that] has a head and a tail in this sense, that vital phenomena are not all of equal importance, though each in succession completes the vital circle  
» p. 88

## Rescuing Mechanism: Organization

- "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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## The Ongoing Legacy of Vitalism

- Bernard did not kill vitalism. Far from it
  - There have continued to be theorists, many of them biologists, who have construed mechanism as insufficient to explain living phenomena
- Those who oppose mechanism have varied greatly in what they thought was required to overcome its deficiencies
  - Vital forces or vital powers (only manifest in living organisms)
  - Integration of the whole—the whole is not the "sum of its parts"
    - physical processes occur different when in the whole

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