New Biological Methods in the 19th Century

The rise of laboratory biology; the cell theory; experimental physiology

Waseda University, SILS,
History of Modern Earth and Life Sciences

Physical and chemical methods in the life sciences

The traditions of natural history that classified biological organisms and minerals and developed theories about the large scale course of historical change in the earth and in species, were principally based on observations that did not intervene in the course of natural processes. We can regard this sort of field observation or collecting, as one of the fundamental methodologies of *natural history*.

In the 19th century, however, we also see a trend in the biological sciences of adopting the interventionist and experimental methods of the physical sciences of chemistry and physics. These methods involve the detailed production of reproducible phenomena, which then serves as the evidential basis for further theorizing. The production of reproducible phenomena is itself a *technical skill* that often involves its own kind of problem-solving ingenuity.

Vitalism and mechanism

An important debate in the 19th century was that between vitalists and mechanists.

Mechanism

Mechanism holds that all natural phenomena – including living organisms – must be explained only by reference to the fundamental laws of matter and motion.

Vitalism

Vitalism is the position that living organisms are fundamentally different from non-living entities because they either (a) contain some physical or non-physical element, force or spirit, or (b) are governed by principles or laws that are different from those of their constituent physical materials.

We will see that these positions have various facets, and they were held to varying degrees by different practitioners.

Reductionism and holism

Another important debate that we will encounter is that between reductionism and holism.

Reductionism

Reductionism is a view that asserts (a, ontological) that entities of a given kind *are* only collections or combinations of entities of a simpler or more basic kind or (b, epistemological) that expressions denoting such entities are *knowable* in terms of expressions denoting the more basic entities, or (c, methodological) that we *should seek to understand* such entities by first understanding their constituent parts.

Holism

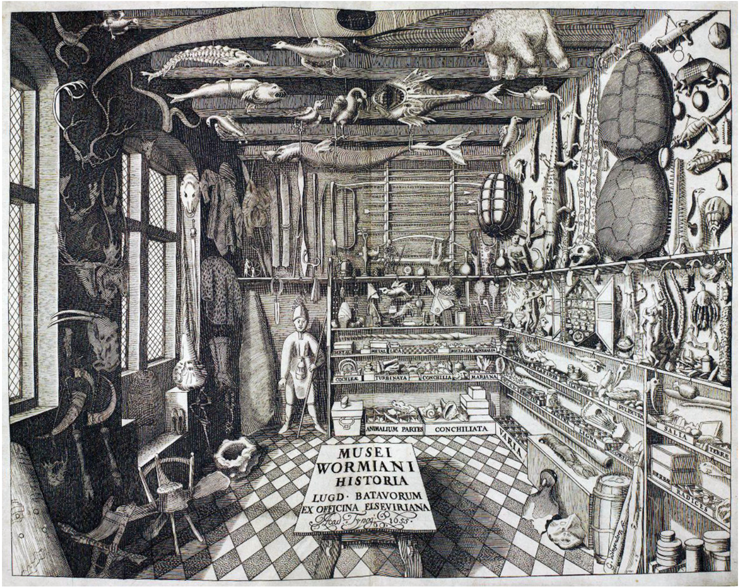
Holism claims that parts of a whole are in intimate interconnection and cannot exist independently of the whole, or cannot be understood without reference to the whole, which is thus regarded as *greater than the sum of its parts*.

The laboratory as a specialized space

Over the course of the 19th century, the concept of the "laboratory" went from meaning a general workspace or workshop, to meaning a specialized institution for scientific, and especially experimental, practice.

In the 17th and 18th centuries, the only scientific laboratories were those of the alchemist, and later chemists. The spaces or institutions associated with the life sciences were the cabinets of curiosities and the natural history collections.

Over the course of the 19th centuries, laboratories were established throughout Europe, the US, Japan, and many other countries. This process began with university laboratories in chemistry and then physics and finally physiology, and then spread to industrial labs and national and state labs.



Ole Worm's cabinet of curiosity, Copenhagen, *Musei Wormiani Historia*, 1655

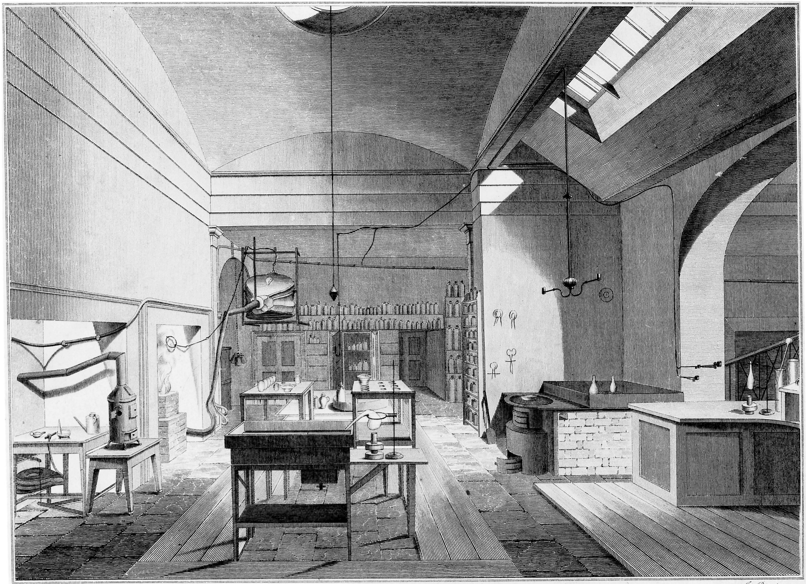
Gallery of comparative anatomy, École de Médecine, Paris

The laboratory revolution of the 19th century

Two of the most important early labs were that of the Royal Institution, London, around 1800, and Liebig's lab at Giessen in the 1820s. Liebig's laboratory lead a number of other German universities to establish chemical labs on this model, followed by the British, French, Americans, Japanese, and others.

Physical labs were established in the German universities from the 1830s. Starting with Göttingen, in 1833, a number of universities established physics labs, culminating in the establishment of the *Technisch Physikalische Reichsanstalt* in Berlin in 1887.

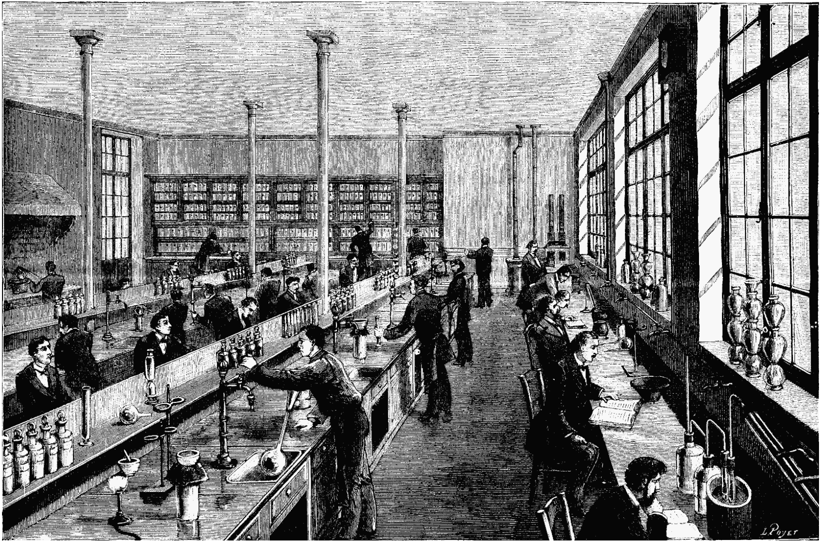
In physiology as well, the German universities lead the way and were followed by other counties. The first physiology lab was that of Jan Purkinje in Breslau, 1839, but this was not quickly copied. Modern physiology labs only began from around 1870: Leipzig in 1869, Utrecht in 1872, and so on.



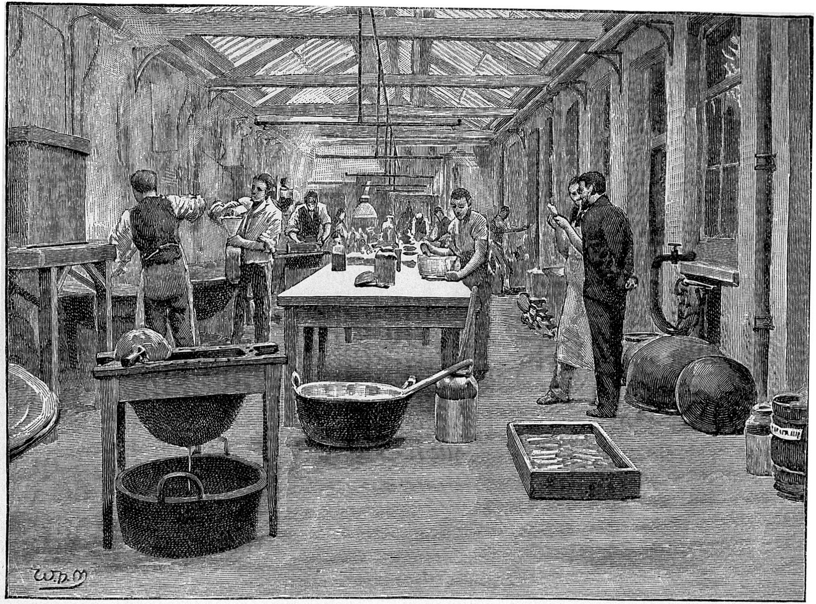
Interior View of the Laboratory in the Royal Institution.

Justus Liebigs chemisches Laboratorium auf dem Seltersberg zu Gießen um das Jahr 1840.

(Erbaut vom Universitäts-Baumeister Hofmann im Herbst 1839.)



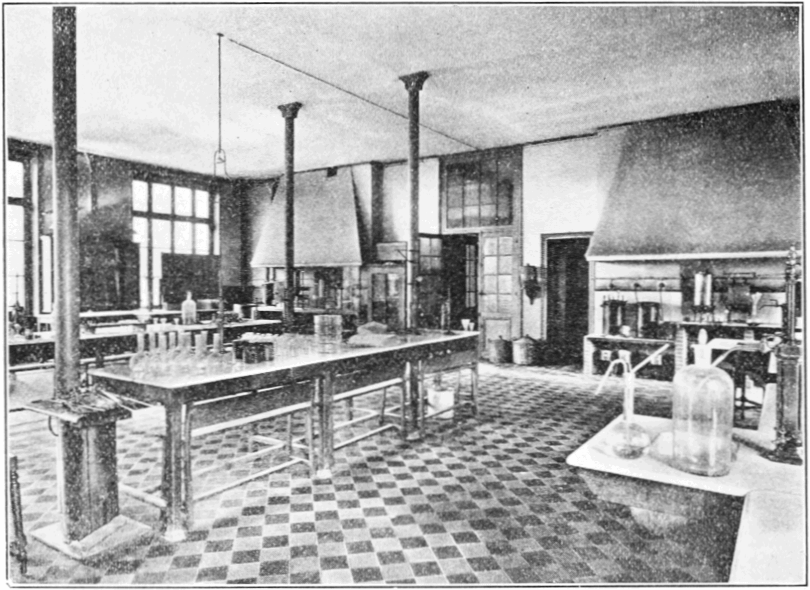
A physics and chemistry laboratory, Paris, 1884



GENERAL PHARMACEUTICAL LABORATORY.

The research laboratory of Allen & Hanbury

Aspatria Agricultural College, Cumberland, 1890s

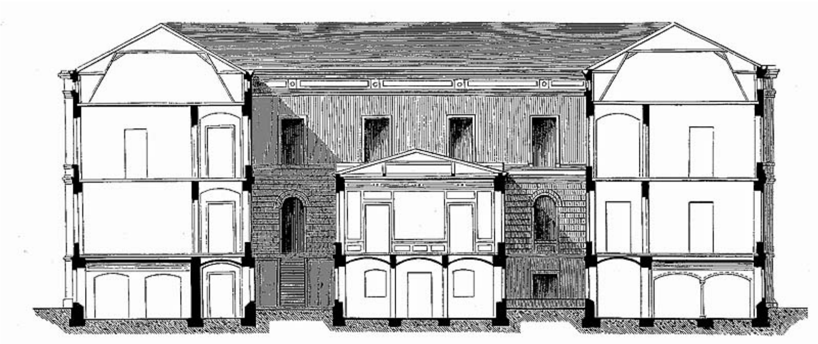


Émile Roux’s laboratory at the Institut Pasteur, 1908

The Wurtz Report

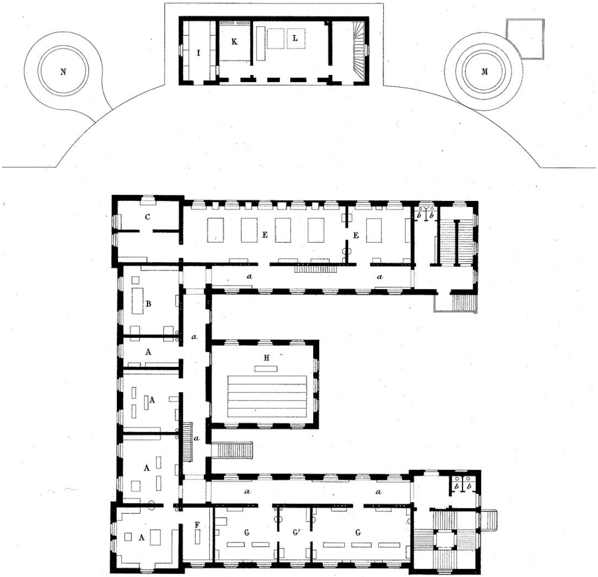
The transfer of institutions and institutional knowledge from centers in the German lands to other countries was generally local and particular, and often carried out by individuals who studied in German institutions. In the final quarter of the 19th century, however, there were organized efforts to replicate the German successes.

Adolphe Wurtz (1817–1884) was sent to study the major German labs and published a report titled *Les hautes études pratiques dans les universités allemandes*, 1870. The first part contained descriptions of chemical laboratories; the second part dealt with laboratories of physiology; while the third and last part was dedicated to the institutes for anatomy and pathological anatomy. The text gave detailed descriptions and was accompanied by 17 illustrations. This report was used by the French, such as Claude Bernard, to advocate for the construction of their own labs.



Back view of the Leipzig physiology lab, Wurtz's report

Floor plan of the Leipzig physiology lab, Wurtz's report



The microscope

In the beginning of the 19th century there were a number of instrument makers producing high quality microscopes, such as Chevalier (France), Amici (Italy), Fraunhofer (Bavaria, German), and many firms in London. Because of chromatic aberration in compound microscopes, many still preferred single-lens configurations. Improved microscopes began to be used more frequently in anatomical studies, such as those of Müller and his students.

In the 1870s, Ernst Abbe worked on resolution and illumination, and eventually developed a physical theory of the vision in a microscope taking place through the diffraction of light. This was then used by the Zeiss optical company to produce an apochromatic lens system – bending the different colors differently so that they arrive at the focus. During the early period of apochromatic microscopes, the old compound microscopes were also improved through various improvements to lenses and so forth.

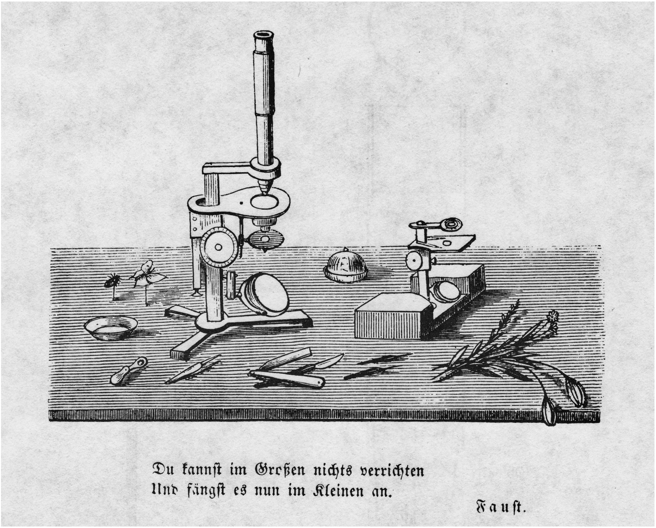


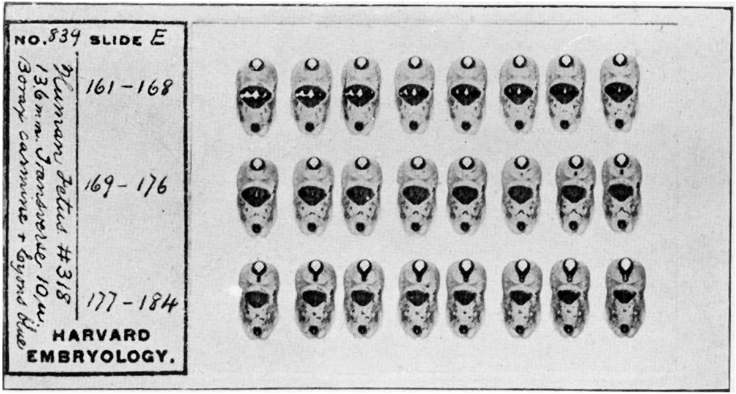
Plate from Schleiden's *Die Pflanze und ihr Leben* (1848)
Loosely: "You can't reslove anything on the large scale,
Start now from the small scale."

Histology

As well as relying on the microscope and its development, histology – the study of anatomical tissues – developed through the craft production of laboratory instruments, reagents, and hands-on methods – generally learned by practice and often transmitted through oral traditions of direct training.

To see detail in frail organic tissues that decay rapidly, it is necessary that specimens be cut into very thin slices and fixed with some agent such as an aldehyde, another oxide of alcohol or a metallic fixative. Soft tissue must be hardened and needs to be preserved in some medium such as wax or lacquer. In order to reveal structure, the specimen needs to be stained with various chemicals that will bring out different aspects of the composition.

Eventually, instrument-makers also started preparing histological specimens for reference and instruction.



Specially prepared slides of human embryos,
Harvard University, around 1900

The cell theory

Although "cells" had been recognized in cork, and other materials, by Hooke in his *Micrographia* (1665), he did not propose a general theory of these structures, and they were not related to all biological organisms. A number of other researchers in the 18th century discussed the role of cells in plant anatomy.

In 1839, however, Matthias Schleiden (1804–1881), a botanist, and Theodor Schwann (1810–1882), a physiologist, articulated a *cell theory of life*, based on previous research they had independently carried out on the microscopic anatomy of plants and animals. They argued that all organic beings are composed of cells, which are made up of a "nucleolus" (our nucleus), an inner medium (what we call cytoplasm), and a boundary (cell wall, or membrane). Extracellular structures were created by cells and extracellular fluids carried the materials that cells used.

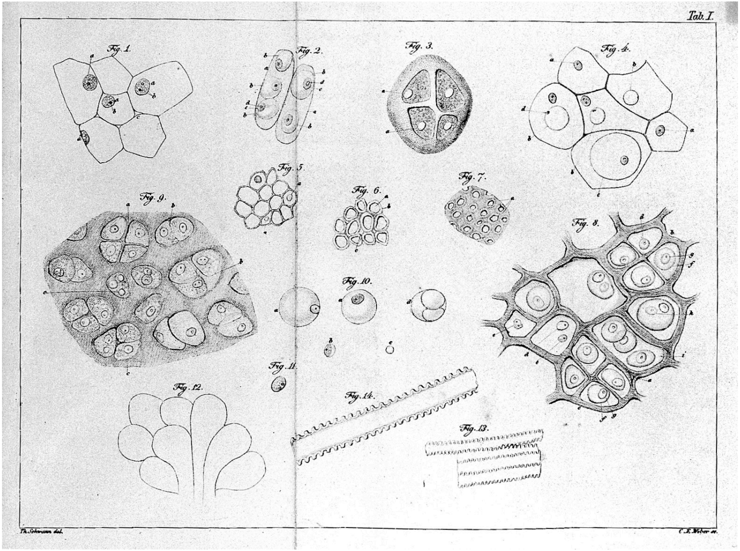
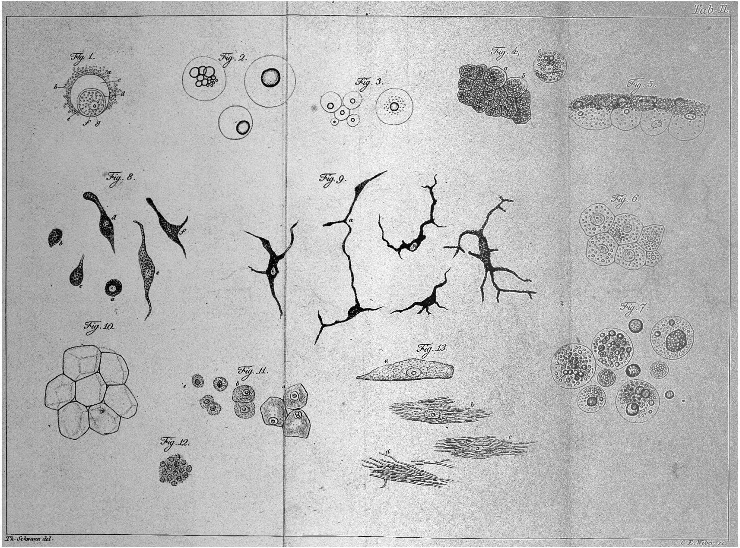


Plate from Schwann's *Mikroskopische Untersuchungen …* (1839)



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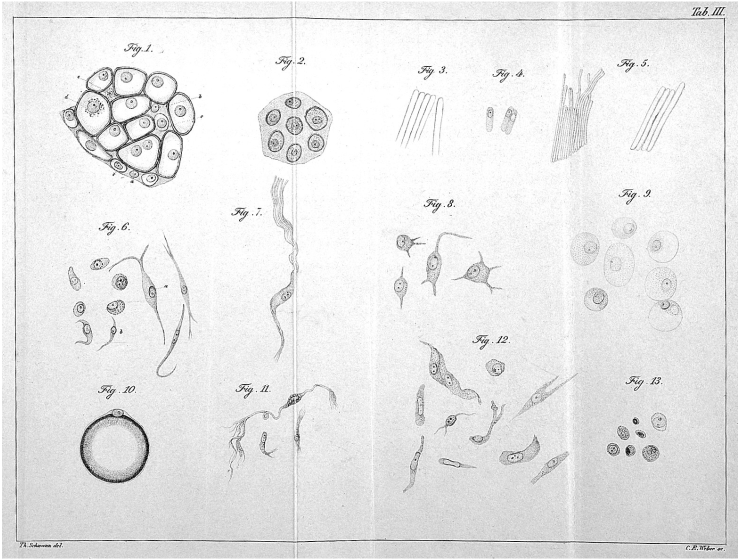

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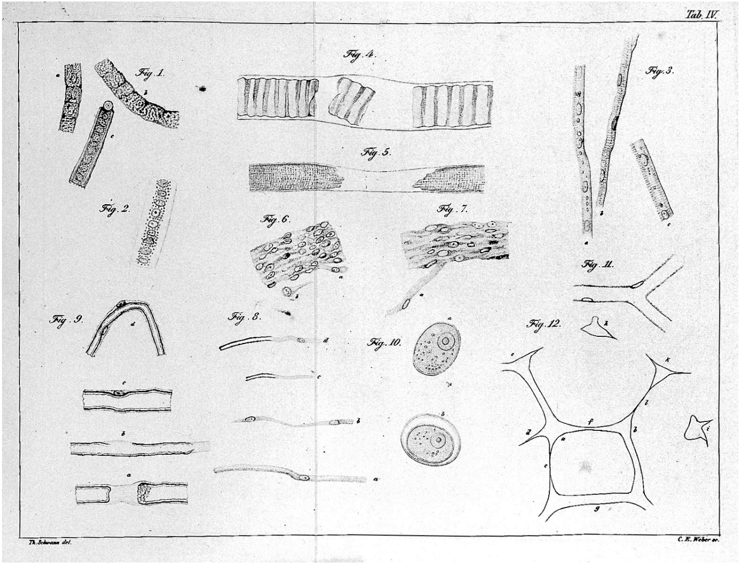


Plate from Schwann's *Mikroskopische Untersuchungen …* (1839)

Cell formation

Schleiden and Schwann were *mechanists* and wanted to show that organic growth was determined by purely mechanistic, or mineral, processes that had no vital element. They both maintained that cell formation follows a strictly materialistic pattern – similar to the process of crystallization. Once formed, cells served as the structural and functional unit of all life.

Schleiden argued that plant cells are formed *inside* another cell by pulling in the surrounding material, forming a nucleus, and then constructing a surrounding membrane that then differentiates from the parent cell. Schwann claimed that animal cells were formed *outside* the other cells, from a structureless substance in which a nucleus is first produced.

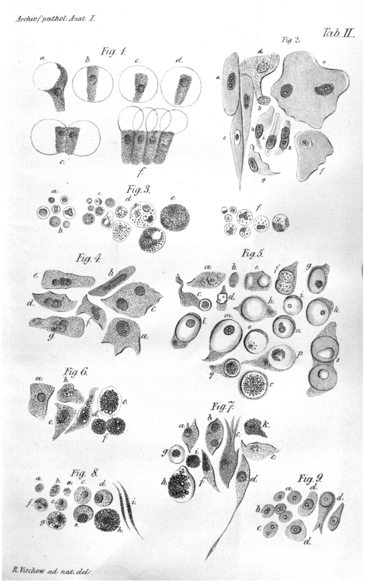
Because of the quality of their microscopes and preparations, they could not see these processes clearly.

Cell division

In 1855, Robert Remak (1815–1902) published his studies of fertilized frog eggs and chick embryos, arguing that cell formation took place inside existing cells, beginning from a fertilized egg and proceeding by a series of divisions directed by the nucleus.

In his *Cellularpathologie* (1858), Rudolf Virchow (1821–1902) described the process of cell division, beginning from a granular nucleus inside an existing cell and completing with the construction of a separating membrane. He asserted that each cell arises from another cell – leading to the expression *omnis cellula a cellula* (every cell from a cell). Life is continuous, as one cell gives rise to another, generation after generation. In this way, the cell becomes seen as the unit of *life itself*.

The structure of the cell and the role of the nucleus



Virchow's *Cellularpathologie* (1858)

In the 1860s and 70s, new techniques for fixing, staining, preserving and cutting cells made it possible to develop a better understanding of the structure of the cell, and the role of the nucleus in cell division.

Since cells could only be seen in preparation, they could not be seen going through any transformation. The stages of cell division had be deduced from many different *still images*.

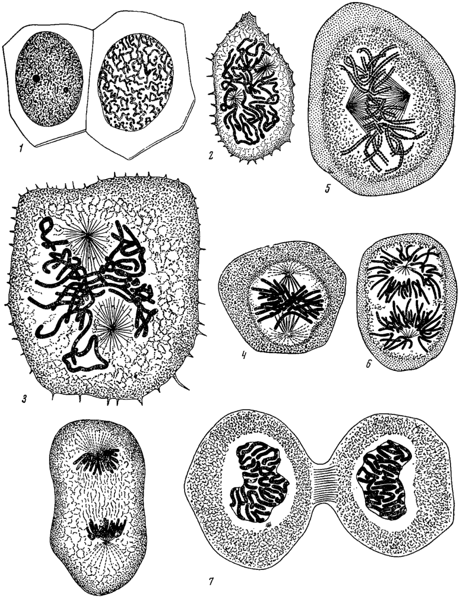
The stages of cell division

In the 1870s and 80s, Walther Flemming (1843–1905) and Heinrich Waldeyer (1836–1921) described the stages of cell division of a normal somatic cell – a body cell.

The stained rods, or threads – which Waldeyer called "chromosomes" due to the fact that the were colored from the dying process – seemed to come together, then line up, or clump together, and finally separate into two new clumps.

In somatic cells, this process was called mitosis and lead to the development of two new cells from each division.

Flemming's images of mitosis



The cell in reproduction and development

In the late 1880s, Édouard Van Beneden (1846–1910), Theodor Boveri (1862–1915), and Oscar Hertwig (1849–1922) observed that the process of division was different for germ or sex cells – that is, eggs and sperm. In this case, although the process of division looks somewhat the same, four cells are produced from each division – two divisions of the cell following one division of the chromosomes – and the amount of chromatin seems to be less. This type of division is known as meiosis.

The cellular process of development from the embryo was studied by Wilhelm Roux (1850–1924), who performed a number of interventions – such as using a heated needle to destroy half of the first embryonic division – in the developmental process to see what effects this would have. August Weismann (1834–1914) produced a theoretical account of reproduction in his *Das Keimplasm* (1892), in which he argued that the nucleus carries some sort of genetic material.

Müller's school

Johannes Müller (1801–1858), was a *vitalist* and one of the foremost physiologists of the early 19th century. From his chair at the University of Berlin, he mentored a number of important physiologists such as Hermann von Helmholtz (1821–1894), Emil du Bois-Reymond (1818–1896), Schwann, and Virchow.

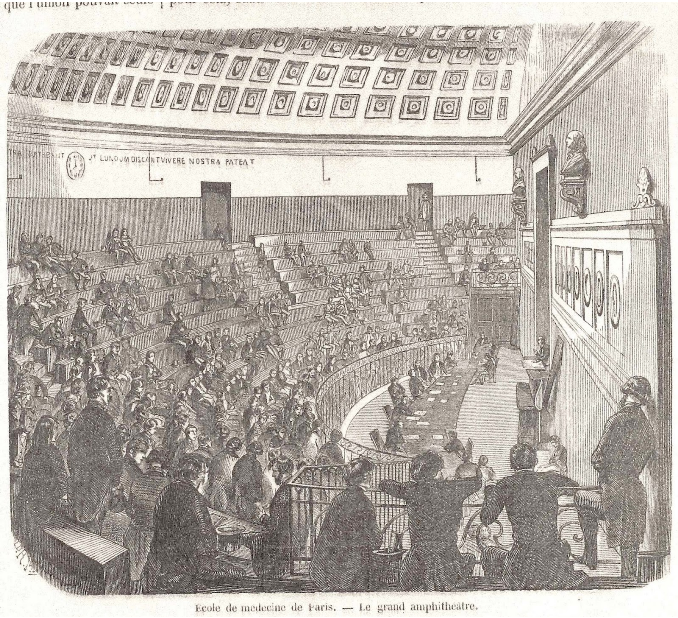
Almost all of his students reacted to his vitalism by taking a *mechanistic*, *reductionist* approach to physiology. Helmholtz, who was self taught in mathematics, advanced the 1st law of thermodynamics in its general form, and used electrical apparatus to study nerve and optical physiology, among many other things. Du Bois-Reymond developed a theory that living tissues contained "electric molecules" and developed experimental methods to test the effect of electrical impulses on nerves and muscles. The idea was to *reduce* the phenomena of living things to the phenomena of physics.

François Magendie (1783–1855)

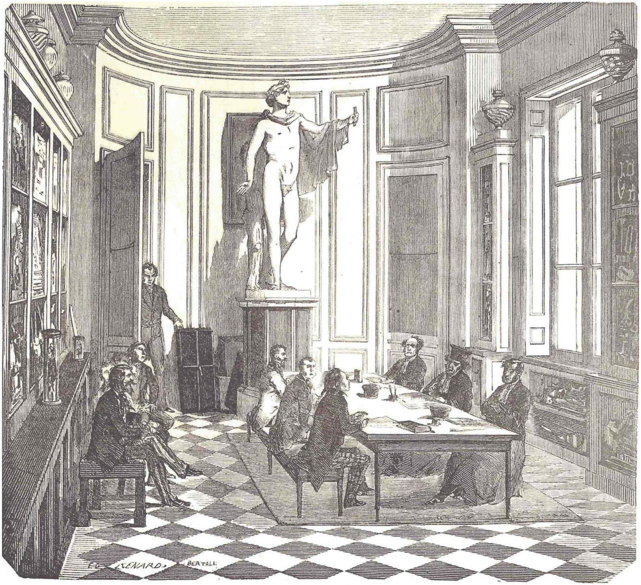
Magendie was a pioneer of experimental physiology and Chair of Medicine at the Collège de France. We was known for being highly skeptical of anatomical claims, deeply critical of his students, and for always insisting that every claim be subjected to experimental testing.

His research focused on the nervous system, and his findings were only made possible through vivisection. One of his well known demonstrations concerned the difference between sensory and motor nerves, which was confirmed by vivisection. He carried out numerous public vivisections of experimental animals, some of which went on for days – which led to public outcries against the practice, and eventually laws prohibiting it in some jurisdictions.

He was succeeded in his Chair by Claude Bernard, who had been his student assistant whose research had shown the most promise.



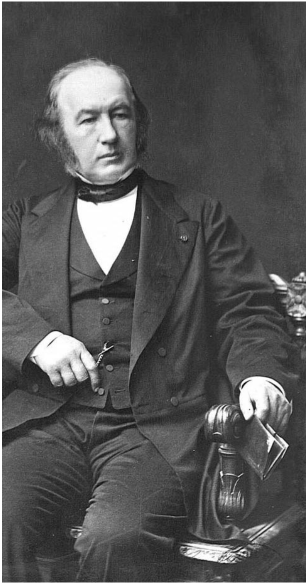
The great hall, École de Médecine, Paris



École de médecine de Paris. — Un examen dans la salle des instruments.

An examination in the instrument room, École de Médecine, Paris

Claude Bernard (1813–1878)



- Born in the village of Saint-Julien, to a family of grape growers.
- Educated at a Jesuit College, and became a pharmacist's assistant.
- He moved to Paris when he was 21 to pursue a career as a playwright.
- Studied medicine under Magendie, and eventually succeeded him as Chair of Medicine.
- Later, Napoleon III built him a lab at the Muséum d'Histoire Naturelle.
- He became a professor at the Sorbonne, then the Collège de France, and a member of the Académie Française.

Léon l’Hermitte, “La Leçon de Claude Bernard” (1889)

The functions of the pancreas and the liver

Bernard made a number of important discoveries in physiology during his time at the Collège de France.

For example, by changing the diet of rabbits and checking their urine and autopsying them, he was able to infer, and then to demonstrate, that the pancreas secrete a fluid that emulsifies fat, producing a white chyle – which he showed was fatty acids and glycerine – which is then absorbed into the lymphatic system. He also showed that pancreatic juice plays a role in transforming starch into sugar.

Another major series of experiments – involving varying the diets of animals and then vivisecting them to test the glucose content of their blood – led him to the conclusion that blood sugar is produced by the liver. He then went on to investigate which nerves control this function.

Bernard's scientific methodology

Bernard took Laplacian *determinism* as a general principle that could be applied to living as well as nonliving things. He claimed that the goal of the experimental scientist should be the production of stable, *reproducible phenomena*. This was a methodological assumption that allowed him to *reduce* living organisms to physical systems.

Bernard, *Introduction to the Study of Experimental Medicine* (1865)

"We must acknowledge as an experimental axiom that in living beings as well as in inorganic bodies the necessary conditions of every phenomena are absolutely determined. That is to say, in other terms, that once the conditions of a phenomenon are known and fulfilled, the phenomenon must always and necessarily be reproduced at the will of the experimenter."

Here he describes we call the *necessary and sufficient* conditions.

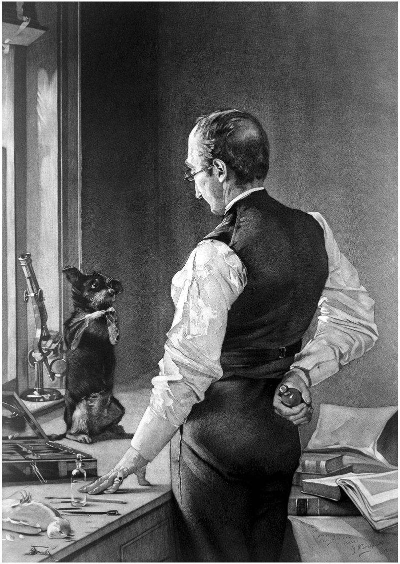
The *milieu intérieur*

Although Bernard rejected *vitalism* in its original articulation, and argued that all physiological phenomena must be described in terms of the underlying physical and chemical laws, he still held that living beings have a special organization that gives them a status that is different from non-living beings, and which is not, itself, reducible to the physical sciences.

Bernard, *Lectures on the Phenomena of Life …* (1878)

"The constancy of the [internal] environment presupposes a perfection of the organism such that external variations are at every instant compensated and brought into balance. In consequence, far from being indifferent to the external world, the higher animal is on the contrary in a close and wise relation with it, so that its equilibrium results from a continuous and delicate compensation established as if the most sensitive of balances."

Public reactions to vivisection



Hamilton , “Vivisection,” 1883

Many nonscientists considered the vivisections of the physiologists to be excessively cruel and unnecessary. For example, they pointed out that Magendie and Bernard often worked on the same animal for days or weeks at a time.

Throughout the 19th, the antivivisection movement became a nexus for popular objections to science. In the second half of the century, there were active campaigns to end vivisection. Bernard’s wife and the physician George Hoggan, who studied in Bernard’s lab, joined these efforts.

Overview

- We have looked at a number of key areas were the methodologies of the physical sciences were fruitfully used in the life sciences of the 19th century.
- We have discussed the rise of the laboratory as a specialized modern space.
- We looked at the rise of histology and the development of the cell theory.
- We have considered some of the results and implications of experimental physiology.