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RELIZANE UNIVERSITY
FACULTY OF SCIENCES AND TECHNOLOGY
BIOLOGICAL SCIENCES DEPARTMENT

COURSE HANDOUT

1ST YEAR L.M.D

Life and Natural Sciences

Intitled:

UNIVERSAL HISTORY OF BIOLOGICAL SCIENCES

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FOREWORD

The course of "Universal History of Biological Sciences" is intended for students of the first year L.M.D, field of nature and life sciences.

The knowledge required to follow this course is some basic notions of prehistoric archaeology: analysis of artifacts, cave paintings, petrography, ...etc, some notions of metallurgy and knowledge on the different fields of biology: Anatomy; Embryology; Genetics; Physiology, Botany, Zoology.

This course traces the human understanding of the living world from the earliest recorded history to the present day. Although the concept of biology as a coherent field of knowledge emerged only in the 19th century, the biological sciences are derived from the traditions of medicine and natural history, dating back to the ancient Greeks (in particular Galen and Aristotle, respectively).

At the end of this course, the student will be able to:

- Know the history of biology and the question of life through eras and civilizations.
- Discover the place of technical progress in the evolution of experimental sciences and natural sciences, from prehistory to antiquity to the Middle Ages then the 16th, 17th, 18th, 19th, 20th and 21th centuries.
- Know the different scientists who contributed to the development of biological sciences.

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INTRODUCTION

I. INTRODUCTION

What is science in modern times?

Sciences are omnipresent, major contributors to the «shaping» of the world. But they were not born of contemporary times: they are the result of an accumulation of knowledge since prehistory: it can be said without exaggeration that the origin of science goes back to the origins of the civilization and that their development is linked to that of human societies. But all this requires first of all to define the notion of «science», often approached in a too general way, and so a little skewed (**Belhoste, 2016**).

Etymologically, the word «science» is borrowed from the classical Latin scientia, which means literally knowledge. In classical times, the Latin term was enriched by the epistemic Greek term, for meaning «theoretical knowledge».

From the 12th century, the French takes up these two visions of the word in the sense. Science refers first to the know-how that knowledge gives. Then, science refers to the extensive knowledge acquired on a specific object of study (the "knowledge").

Since the 13th century, with a value close to the modern sense, science means a body of knowledge having a specific object and its own method. The sciences, in the plural, refer to all disciplines that form theoretical knowledge (**Nevejans, 2016**).

This distinctive value between singular and plural is clarified with the emergence of the word "scientific" in the 14th century.

With the Renaissance, the term took on a new meaning. The "science" of the Renaissance contrasts two types of knowledge. First, law, emanation of the divine thought and regulator of human life. Second, mathematics, which manifests the order of the world.

Thinkers like Leonardo Da Vinci then argue that science must be based on formal reasoning and observation of controlled experience. Gradually the word «science» is closer to the notion of rationality: what is scientific can be proven.

In the seventeenth century, under the impulse of Baconian and Cartesian thoughts, science takes even more this meaning, leaving aside philosophy and theology, too abstract (**Nevejans, 2016**).

Summarize, in modern times, "science" is said to be of all knowledge quite precise. Over the eighteenth century especially, this knowledge is more and more «exact»: one enters the reign of sciences hard.

<u>STATE OF BIOLOGICAL SCIENCES DURING PREHISTORIC PERIOD</u>

II. STATE OF BIOLOGICAL SCIENCES DURING PREHISTORIC PERIOD

1. Prehistory (to 35000 BC - to 3000 BC)

It is conventional to start history at the time of the invention of writing. Our knowledge of prehistory is therefore based exclusively on the analysis of artifacts discovered during archaeological excavations. Prehistory is divided into different periods characterized by particular techniques:

1.1. The Palaeolithic

The Palaeolithic is the oldest period, characterized by the technique of **carved stone and a nomadic way of life** ignoring breeding or agriculture. **Humans lived by hunting and gathering**. This epoch begins three million years ago, long before the human species reached its present appearance. **Techniques developed during the Palaeolithic** included the domestication of fire, the manufacture of clothing and containers from animal skins, the manufacture of hunting tools and canoes. The domestication of the dog probably dates from the Paleolithic (**Sénéchal, 2009).**

1.2. The Neolithic

The Neolithic is defined originally by the use of **polished stone**, but is mainly characterized by the **appearance of breeding** (goat, pig and cattle) and **agriculture, thus by a sedentarization** (at least seasonal) of populations. **The earliest evidence of a Neolithic population** can be found in the Middle East, dating from between 9,000 and 6,000 BCE. At that time, the **art of pottery, weaving and stone construction** was also developed. The **wheel** was invented at that time (**Sénéchal, 2009)**.

Fig.1: Prehistoric stone tools (sciencephoto.com)

2. Age of metals / Bronze age

The appearance of the first furnace coincides with the beginning of the **age of metals.** The first metals were native (gold, silver and copper) and used mainly for decorative purposes. Copper was then extracted from its ores, and combined in alloy with tin to form **bronze** (or brass), a metal both harder and having a lower melting point than copper. This metal age coincides approximately with the appearance of the first civilizations, but is not a necessary technical prerequisite, because stone tools are still predominant at this time. Moreover, the pre-Columbian civilizations (Mayas, Aztecs, Incas) used metals only as ornaments (**Sénéchal, 2009)**.

Metallurgy, even primitive, is a relatively sophisticated activity requiring a keen sense of observation and an evolved form of knowledge transmission. However, it does not require extensive, rational and systematic knowledge of nature: it is a technique and not a science.

The historical period as such begins with the invention of writing, around 3000 BC, in **Mesopotamia and Egypt.** With writing appears the class of scribes, those who master this complicated art and who can now transmit knowledge more precisely and permanently than by oral tradition. **The writing** seems to have arisen directly from the need to **<u>maintain an inventory of agricultural products</u>**, and thus was used first in conjunction with the early numeration systems. Egypt and Mesopotamia were **Bronze Age** civilizations (**Sénéchal, 2009)**.

Fig. 2 : Jewelry of bronze age (cambridge.org, photographs by A. Piasecka)

Fig. 3 : The warrior's kit of bronze age discovered in the remains of an epic prehistoric battle (gizmodo.com, image: Volker Minkus)

3. The Iron Age

These civilizations were shaken in the middle of the second millennium BC by the arrival of the **Iron Age,** whose historic meaning was immense. Iron is more difficult to work than bronze, because of its greater melting temperature, requiring more sophisticated furnaces. Note that the bronze was cast in molds, while the iron was only softened and forged. The melting of the iron requires furnaces more effective still, and was not realized until later, **first in China (2nd century BC) and in India before reaching the Middle East and Europe**.

On the other hand, **iron ore is much more abundant than copper ore.** During the Bronze Age, the rarity of metal made it a luxury object, the prerogative of nobles and warriors.

The peasants had only stone tools making any agriculture outside narrow areas near rivers, where the land is easy to work, **such as Egypt and Mesopotamia** (**Sénéchal, 2009).**

In these countries, **agriculture** was a state enterprise because of the important community work it involved (irrigation, distribution, etc.).

The limited technology of bronze therefore imposed a rigid and stable social system, based on powerful states and also including important cities.

The arrival of **iron** democratized metal tools. Iron has **made it possible to extend agriculture to areas otherwise** covered by forests, such as Europe, where the climate does not require major irrigation work. It thus reduced the minimum social unity, because agriculture no longer required heavy social organization.

As it also spread the use of very effective weapons, the arrival of iron led to a period of rather severe chaos, punctuated by incessant wars. It is likely that the inhabitants of the **Iron Age nostalgically considered the more stable and seemingly richer civilizations of the Bronze Age.**

However, iron has allowed many technical and economic innovations, especially in **navigation,** which have gradually favored the emergence of **new civilizations: Hittites, Phoenicians and especially Greeks** (**Sénéchal, 2009).**

ANTIQUITY AND BIOLOGICAL PRACTICES

III. ANTIQUITY AND BIOLOGICAL PRACTICES

1. EASTERN ANTIQUITY

1.1. Pharaonic Egypt

The **writing of hieroglyphs (-3100 BC)** allows the more precise representation of concepts; we speak of an ideographic writing.

The number is base 10, but the Egyptians do not know zero. Unlike the Sumerian numeration, the **Egyptian numeration** evolves towards a system of writing large numbers (between - 2000 and - 1600 BC) by "**juxtaposition numeration**".

Geometry mainly made a leap forward. The Egyptians **built grandiose monuments** using only the system of fractions symbolized by the **eye of Horus**, each element representing a fraction.

As early as - 2600 BC, the Egyptians correctly calculated the area of a rectangle and a triangle. There are few documents proving the extent of Egyptian mathematics, only the **papyrus of Rhind** (dating from - 1650 BC) illuminates the innovations of this civilization which are primarily those of algebraic problems (division, arithmetic progression, geometric).

The Egyptians also approach the number Pi, rising to square the 8/9 of the diameter, discovering a number equivalent to 3.1605 (instead of 3.1416). The problems of volume (pyramid, grain cylinder) are solved easily.

Astronomy is also progressing: the **Egyptian calendar has 365 days**, time is measured from a **"star clock"** and visible stars are counted (**Chatelain, 2004; Sénéchal, 2009).**

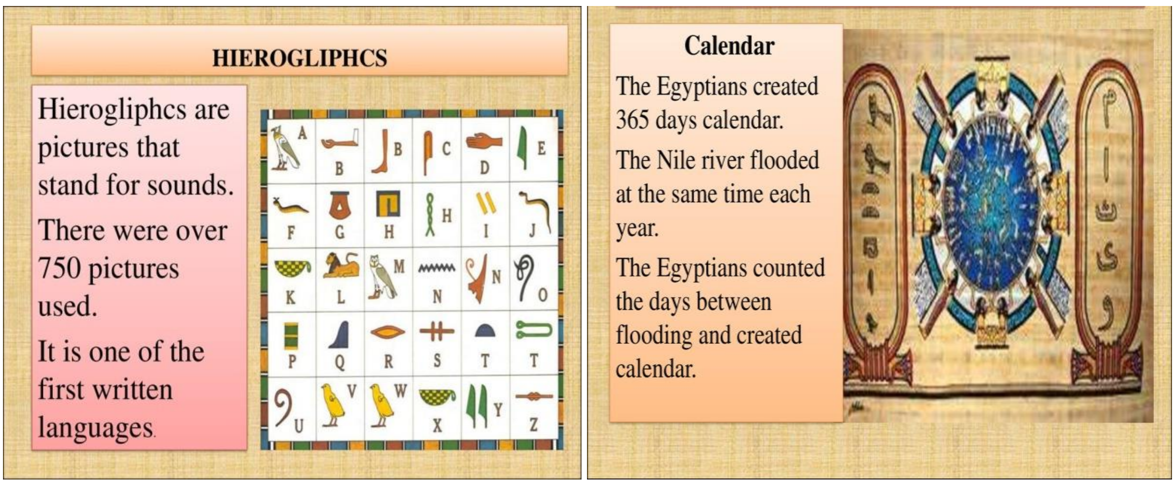


Fig. 4: Hieroglyphs writing and Egyptian calendar **(Pushina, 2023)**

The Egyptians apparently had knowledge of **human anatomy**, but were hardly inclined to study animals (there are some papyrus on the metamorphosis of frogs) and even less plants.

Egypt medicine included a large part of mysticism and surgery appeared. A medical theory is set up, with the analysis of **symptoms and treatments** and this from - 2300 BC (the Ebers papyrus is a real medical treatment) (**Chatelain, 2004; Sénéchal, 2009; Pushina, 2023).**

Fig. 5 : Medical papyri and herbal medicine **(Pushina, 2023)**

1.2. Mesopotamia

Science was born in Mesopotamia, around - 3500, mainly in the cities of Sumer and Elam.

The most important innovation comes from the invention by Sumerians (3500 BC) of **cuneiform writing** (in the form of nails), which, through pictograms, allows the reproduction of texts.

Fig. 6 : Cuneiform writing (Britannica.com)

Numeration is thus the first scientific method to emerge, making increasingly complex calculations, even if it was based on rudimentary material means.

The writing being perfected (so-called Akadian period), the Sumerians discover the fractions as well as the so-called **"position" numeration**, allowing the calculation of large numbers.

The **decimal system** also appears, via the pictogram of the initial zero, having the comma value, to note fractions.

Mesopotamian civilization thus leads to the constitution of **the first sciences** such as:

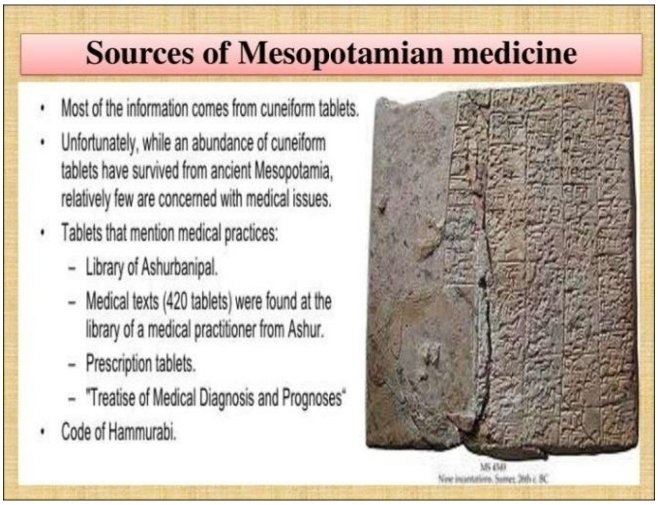
- Metrology, very adapted to practice, (measurement science)
- Algebra (discoveries of "calculation boards" allowing multiplication and division operations - or inverse tables for the latter; but also powers, square roots, cubic as well as equations of the first degree, with one and two unknown)
- Geometry (surface calculations, theorems),
- Astronomy (calculations of celestial mechanics, forecasts of equinoxes, constellations, naming of stars (**Chatelain, 2004; Sénéchal, 2009**).

Agriculture requires specific knowledge of plants and animals. The ancient eastern populations had very early knowledge about the **pollination** of date palms. In Mesopotamia, the population knew that pollen could be used in **the fertilization of plants**. A commercial contract dating from the Hammurabi period (18th century BC) mentions date flowers as a commercial item.

The first questions about matter, with **alchemy experiments**, are related to the discoveries of metallurgical techniques that characterize this period.

Medicine has a special status; it is the first "practical" science, inherited from a groping know-how. The Babylonians had knowledge in **anatomy and physiology** to some extent (**Mazliak, 2007)**.

In Mesopotamia, animals were sometimes kept in what could be compared to the first **zoological gardens**. In any case, superstition has often been mixed with real facts. In Babylon and Assyria, animal organs were used for predictions (**Chatelain, 2004; Sénéchal, 2009)**.



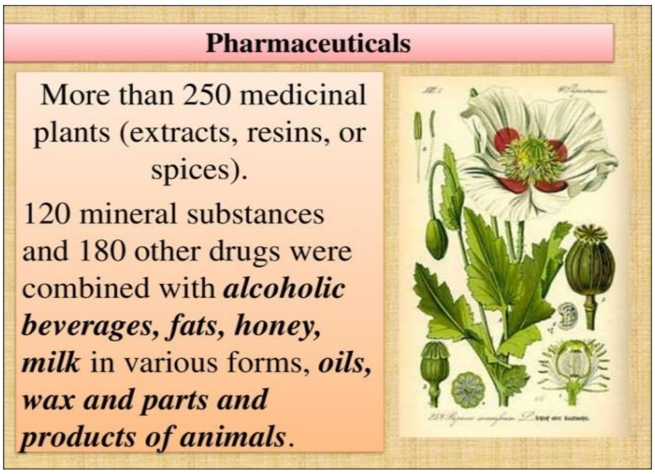


Fig. 7 : Source of Mesopotamian medicine and pharmaceuticals **(Pushina, 2023)**

1.3. Chinese Civilization

In mathematics, the Chinese invented, around the 2nd century BC, "**stick numeration**". It is a positional notation at base 10 with eighteen symbols, with a blank to represent the zero, i.e., ten, hundred, etc.

The Chinese discovered what is usually called the **Pythagoras theorem** (which the Babylonians knew fifteen centuries before the Christian era). In -104, is promulgated the **Taichu calendar**, first real Chinese calendar. They identify also Halley's Comet and understand the periodicity of **eclipses**.

They also invented **iron melting**, which Europe would not experience until the 18th century.

The Chinese of Antiquity mainly contributed to **technical innovation**, with the main inventions:

- **Paper** (dated from the 2nd century BC),
- **Gunpowder** from the 10th (the first documented written trace seems to be the Wujing Zongyao which would date from around 1044).
- They built **lenses** from the 10th century without making glasses or telescopes.
- And the **compass**, used as early as the 11th century, in geomancy.

Chinese scientist **Shen Kuo** (1031-1095) of the Song Dynasty described the magnetic compass as a navigational instrument. In 132, **Zhang Heng** invented the **first seismograph** for earthquake measurement and was the first person in China to build a rotating celestial globe (**Chatelain, 2004; Pushina, 2023)**.

Fig. 8: Zhang Heng and the first seismograph (safecommunitiesportugal.com)

The Chinese practiced alchemy in the quest for immortality (they obtained the preservation of bodies without putrefaction). **Chinese alchemy** nevertheless led to progress in the industrial fields (extraction of copper by precipitation) (**Chatelain, 2004)**.

The **practice of sericulture**, in the culture of Yangshao, (Middle Chinese Neolithic) shows that the Chinese already had important knowledge of biology at that time (**Wang, 2021**).

Fig. 9: Chinese sericulture practices (**Wang, 2021**)

Ancient China valued **hygiene**, and their practices, while different from ours, laid the foundation for many aspects of modern personal care. In China has been surgical in nature, used anesthesia and asepsis. The first vaccinations against **smallpox** were made in China over a thousand years BC.

Medicine progressed under the Eastern Han with **Zhang Zhongjing** that established medication principles and summed up the medicinal experience until that time, thus making a considerable contribution to the **development of Traditional Chinese Medicine**. And also **Hua Tuo**, that performed surgery under **general anesthesia** using a formula he had developed by mixing wine with a mixture of herbal extracts he called **mafeisan**. Some authors believe that Hua Tuo may have discovered surgical analgesia by acupuncture (**Taha *et al.*, 2022)**.

Chinese physics is based on two principles (yin and yang) and five elements. In traditional Chinese medicine five elements : **wood, fire, earth, metal and water**, relate to the organs and tissues of the human body. Many **chinese medical texts** appears like the Canon of acupuncture and moxibustion (**Mazliak, 2007; Pushina, 2023)**.

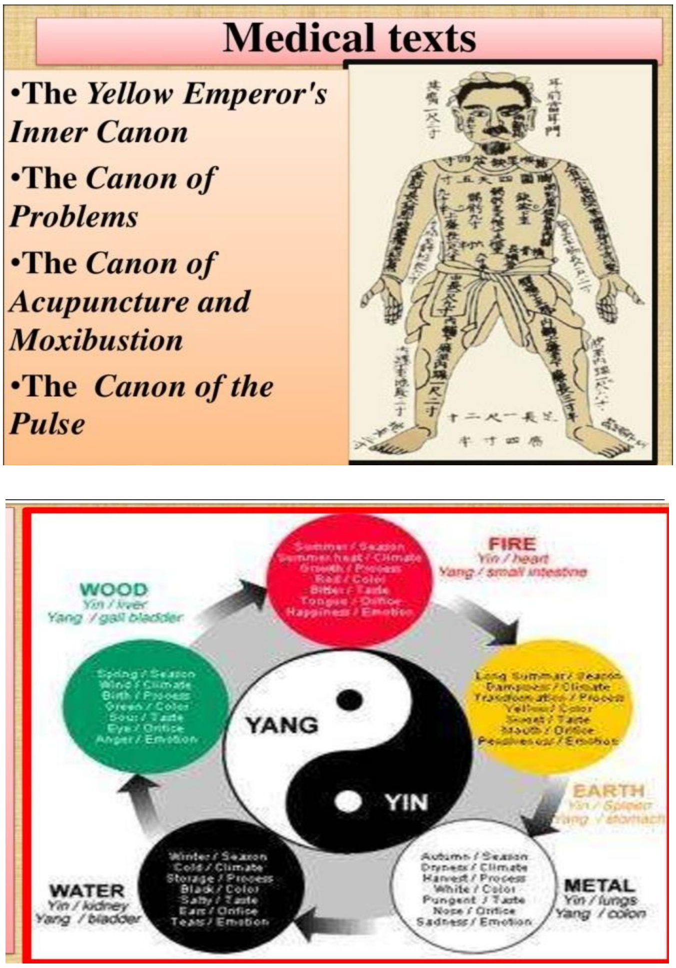


Fig. 10: Chinese medicine five elements and medical texts **(Pushina, 2023)**

1.4. Hindu Civilization

The so-called Indus Valley civilization is best known in the history of science due to the emergence of complex mathematics (or ganita). The decimal number of position, and the Indian numeral symbols, which will become the Arabic numerals, will influence the West considerably, via China and the Mongol invasions. Indians also mastered zero, negative numbers, trigonometric functions as well as differential and integral calculus, limits and series. The year had 360 days, 12-month to which was added when necessary a 30-day leap month and then 25 or 26. The days were divided into 30 moments (**Sénénchal, 2009**).

In India, texts describe some aspects of bird life. Alchemy developed aimlessly unlike the Chinese who sought immortality and later the Westerners who hoped to synthesize gold. An atomist theory appeared (**Chatelain, 2004**).

Medicine and more particularly surgery was advanced (removal of cataracts, cauterization,...). An effort of systematic classification of diseases was accomplished with a search of their origin in relation to the 5 elements of alchemy. The system of five elements are found in Vedas, especially **Ayurveda,** the pancha mahabhuta, or "five great elements", of Hinduism are: **earth, water, fire, air (or wind)** and **aether (space or zero or void**) (**Mazliak, 2007).**

According to ancient scriptures, the human body was maintained in the state of health by **three humors : kapha (phlegm),** composed of the elements earth and water, **pitta (bile)** which represents fire and water, and **vata (wind)** representing air and space. Many thought that illnesses resulted from an imbalance of these humors (**Chatelain, 2004;; Pushina, 2023)**.

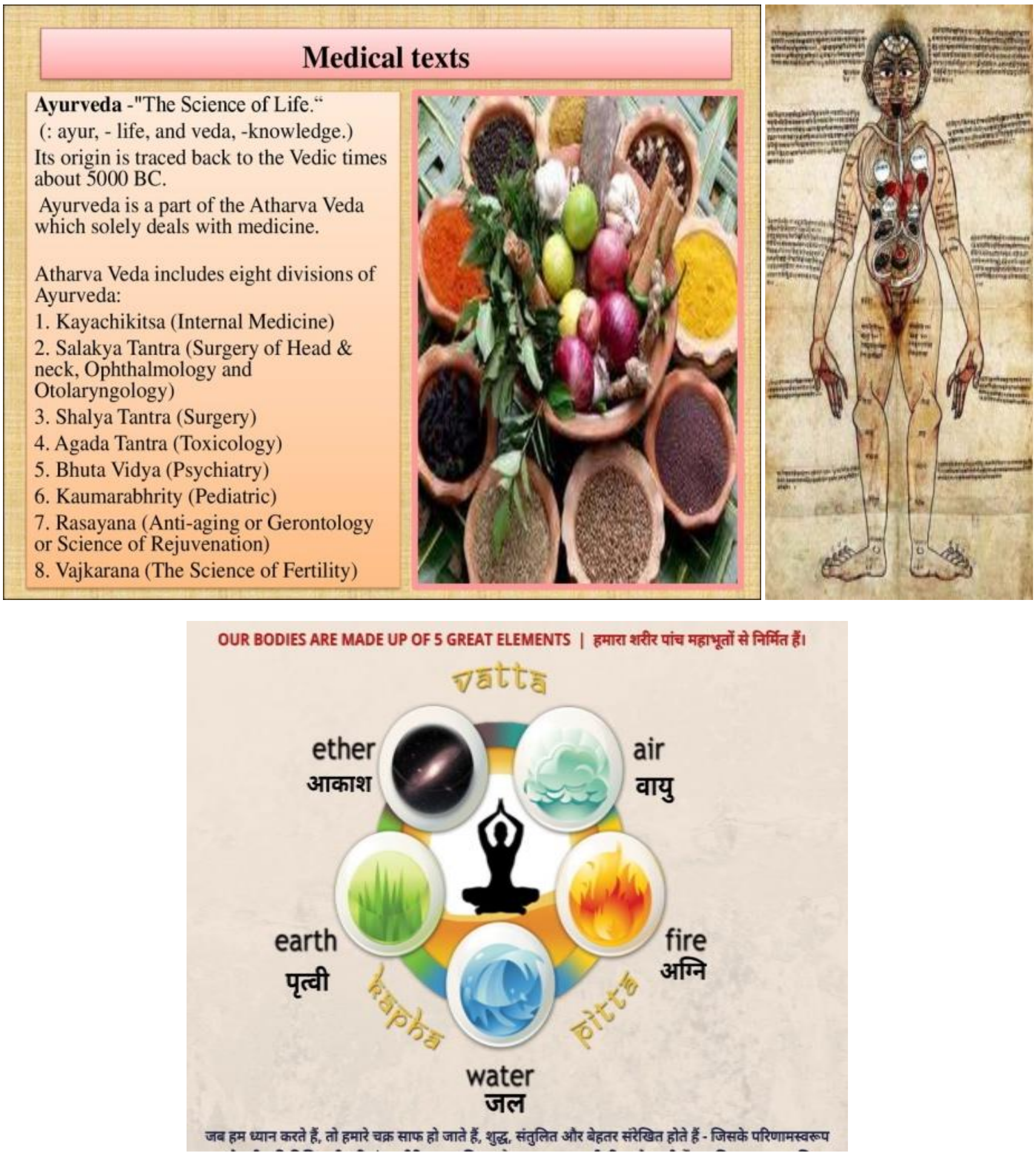


Fig. 11: The system of five elements and medical texts of Ayurveda **(Pushina, 2023)**

In post-vedic period, Medicine assumed a more rational approach under the gurus of Sushruta and **Charaka**. They listed many medicines. **Sushruta** wrote Sushruta Samhita, whose written versions describe more than 120 surgical instruments and 300 surgical procedures in the third century AD, classify human surgery into eight categories and introduce cosmetic surgery (**Pushina, 2023)**.

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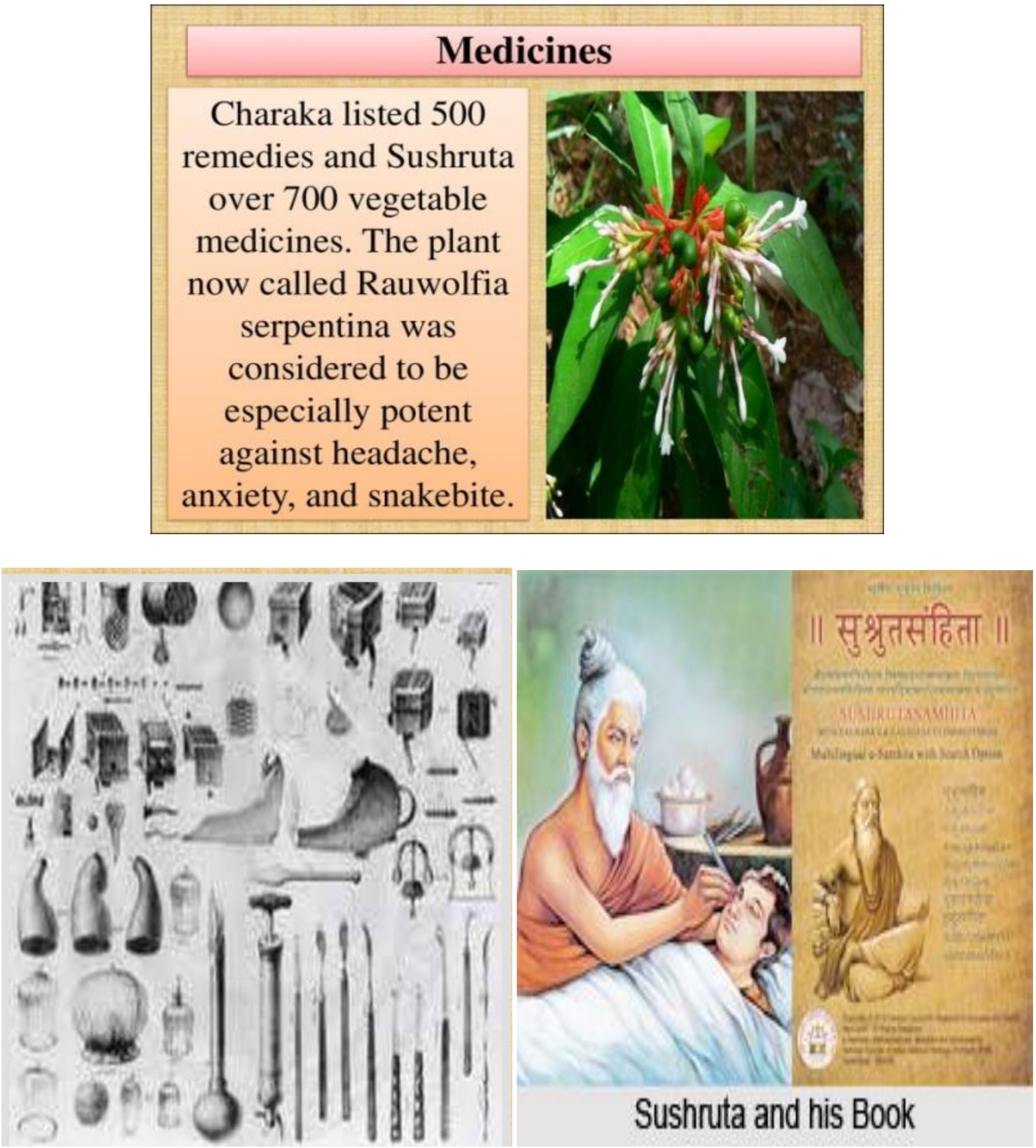

Fig. 12: Charaka and Sushruta medicines and surgical instruments **(Pushina, 2023)**

2. WESTERN ANTIQUITY

2.1. Ancient Greece

We will divide Greek science into three periods, corresponding to the epochs (1) archaic, (2) classical and (3) Hellenistic (**Sénéchal, 2009**).

2.2.1. Archaic period

The philosophers of this period are known as Pre-Socratic philosophers because they lived before or during the same time as Socrates (around 470–399 BCE).

They are the first to be interested in natural phenomena called physiologoi by Aristotle because they hold a rational discourse on nature and they investigate the natural causes of phenomena that become the first objects of method.

Thales of Miletus (c. 625-547 BC) and Pythagoras (v. 570-480 BC) mainly contribute to the birth of the first sciences such as mathematics, geometry (Pythagoras theorem), and astronomy.

There was a will to impute the constitution of the world to a unique natural principle

- **Thales** argues that life finds its origin in water,
- **Anaximandre** proposes a divine hypothesis,
- **Anaximene** air
- And fire for **Heraclitus**.

Xenophanes examined fossils and speculated on the evolution of life. c. 380 B.C (**Chatelain, 2004; Sénéchal, 2009).**

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2.2.2. Classic period

Socrates philosopher was very interested, in humain, morality and the process of knowledge; to the reason. His work is known to us by the dialogues of his disciple Plato. Socrate is well known its dialectical method of guiding the person to a rational conclusion rather than directly exposing ideas to the person.

Plato on the contrary is interested in the physical world and the means of knowing it, he attaches great importance to the study of geometry and stars, we see here the influence by the Pythagorean School and he founded the Academy.

Eudoxe of cnide, attached to the school of Plato, the greatest mathematician of the antiquity, its main contribution is the introduction of the concept of grandeur (**Sénéchal, 2009**).

ARISTOTE AND BIOLOGY

The most important contribution to science is that of Aristotle (384-322 BC), student of Plato, for 20 years. He founded his own school in Athens which was called the Lyceum (in competition with the Academy). He was later tutor to Alexander the Great. It formalizes deductive reasoning (all men are mortal; Socrates is a man so Socrates is mortal) (**Chatelain, 2004**).

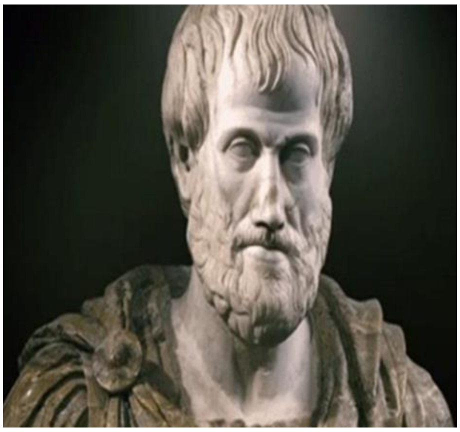


Fig. 13: Aristote (Britannica.com)

Life is born according to him from heat (fire element of which the man for example was constituted) and moisture (water, woman). Unlike Plato, Aristotle advocated experimentation (he practiced dissection systematically). He notes that organs are attributed only to animals that know how to use them. He studies reproduction and **admits spontaneous generation for lower life forms.**

Acquired heredity is generally accepted unlike **Hippocrates that wants to be preformator** (in sperm there are particles of all parts of the body), **Aristotle is epigenist** (he thinks that sperm contains in power all forms) (**Chatelain, 2004**).

He founded the teaching of natural history. Aristotle funds zoology. He describes 495 animal species (60 mammals and 160 birds) and has developed a simple taxonomic system (**Sénéchal, 2009**):

- **Animals with red blood (enaima)**
  a) **The viviparous quadrupeds**
  b) **The oviparous quadrupeds**
  c) **The birds**
  d) **The fish**
- **Animals without red blood (anaima)**
  a) **Soft-bodied animals (cephalopods)**
  b) **Scale animals (crustaceans)**
  c) **Shell animals (molluscs)**
  d) **Insects and worms.**

ARISTOTLE'S SUCCESSOR

Theophrastus (371-287 BC), pupil and successor of Aristotle at the head of his school (the Lyceum), was interested in botany, he observed scientifically and classified some 550 plant species.

Straton, who also directed the school, contests the existence of a natural upward movement of the light elements, the natural movement towards the bottom of the heavy elements sufficient to explain all physical phenomena (**Chatelain, 2004**).

CLASSICAL GREEK MEDICINE

During the classical period, two types of medicine were opposed in Greece: the medicine of temples and that of the different medical schools.

The medicine of the temples

The first is a magical practice, prosperous in Greece at the very moment of the birth of philosophy and rational science. The patient had to go to a special center, surrounding a **temple of the Greek god of medicine, Asclepius**.

The patient underwent a ritual treatment, consisting of a bath followed by a period of rest, called incubation, during which the patient dreamed. His dreams were then interpreted by the priests of Asclepius, who established a prognosis. In fact, the patient could hope to see his own healing (or the means to achieve it) in a dream.

Temple medicine made little use of drugs and did not practice surgery at all. In fact, the treatment was essentially psychological and rest was an essential part of it (**Sénéchal, 2009**).

Medical schools

Parallel to temple medicine were medical schools. These included the four main schools in the pre-classical period:

- **Pythagorean school**

whose main representative was **Alcméon de Crotone**. He distinguishes veins from arteries and discovers the optic nerve. According to this school, health is the result of a balance of different forces within the body. Pythagoreans had already identified the brain as the center of sensations.

- **Sicilian school**

represented by **Agrigento's Empedocles**. Empedocles introduced the concept of pneuma, or 'breath of life', which enters the body through the lungs. It also proposes a back and forth movement of blood between the heart and veins.

- **Ionian school**

where there was some dissection

- **Abdère's school**

where much emphasis was placed on health conditions: gymnastics and dietetics (**Sénéchal, 2009**).

Over time, two main schools survived: the Cnide school and the Cos school, located geographically very close to each other

- **The Cnide school** attached great importance to observations (for example, lung auscultation) but was reluctant to the theory.
- **In Cos**, on the contrary, we insisted on the importance of theory and reasoning: Cos' medicine is the first truly scientific medicine, although its theories seem very naive to us today (**Sénéchal, 2009**).

The most illustrious representative of the **Cos school is Hippocrates** (460/377). One of the most influentes theories of the Cos school is **the theory of moods**, according to which the human body consists mainly of **four types of liquids**, which must exist in balanced proportions so that the individual remains healthy:

1. Blood, associated with “dry” and produced by the liver.

2. Pituity, or flegme, or lymph, is the main element of nasal mucus, associated with moisture and produced by the lungs.

3. Bile, associated with “hot” and produced by the gallbladder.

4. atrabile or Black bile, associated with “cold” and produced by the spleen.

Diseases are caused by an imbalance of different moods and treatment must try to restore this balance (**Sénéchal, 2009**).

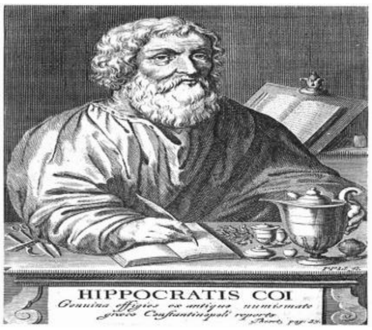


Fig. 14: Hippocrate (Britannica.com)

Diocles of carystus among Greek physicians second only to Hippocrates in ability and reputation. He was the first to write medical treaties in attic Greek, and wrote the first systematic textbook on animal anatomy. He was the first to use the word "anatomy" to describe the study, and wrote several medical books (**Britannica, 2023**).

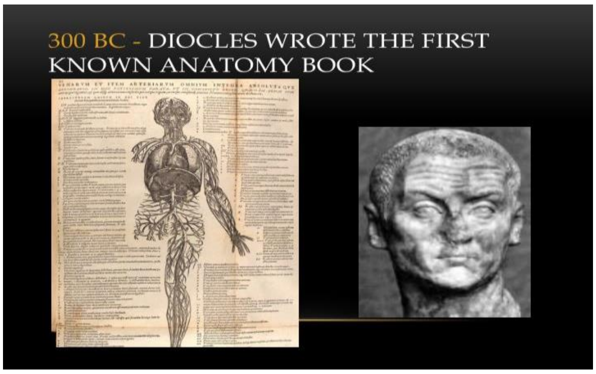


Fig. 15: Diocles of carystus (Britannica.com)

2.2.3. Hellenistic period

Greece will be conquered by Philip of Macedonia. The Macedonian Empire reached its extension with its son Alexandre Le Grand and Egypt under Macedonian dominance was ruled by the Ptolemaic dynasty. Greek science benefits from the ease of exchange with the non-Greek world. Some Hellenistic kings in particular the Ptolemy provide financial support for the exercise of science (**Chatelain, 2004**).

Ptolemy I is the founder of the Museum, cultural and scientific institute inspired by the Lycée d'Aristote, but on a larger scale: the Museum included walks, classrooms, cells (offices), an observatory, dissection rooms, housing and even a zoological garden.

The Museum was flanked by a huge library, which counted several hundred thousand of volumes (in the form of rolls of papyrus). This institution was maintained by the kings (in particular by Ptolemy II who continued the work of his father) and then by the Roman emperors (**Sénéchal, 2009**).

Here are some of the outstanding figures of this exceptional period (**Chatelain, 2004; Sénéchal, 2009**):

- Philosophers: **Epicurus and Zeno of Kittion.**
- Mathematicians and mechanics: **Euclid, Archimedes, Appollonius of Perga, Heron of Alexandria.**
- Astronomers: **Aristarchus of Samos, Erathostenus, Hipparchus, Apollonius, Claude Ptolemy**.

LIFE SCIENCE AND MEDICINE

Life sciences declined after Aristotle and Theophrastus. Biological research specialized and focused on man. In zoology, the research gives way to the taste of the marvelous fed by the narratives of travelers and fables.

Posidonius (135-51 BC) bases ethnology (study of peoples, on its physical and psychological characters: he describes Celts and Germans as tall blondes and hyperemotional while the Mediterranean are smaller and dark are rational.

The most important Alexandrian doctors were:

Chalcedon's herophilus: famous for his contribution to anatomy through human dissection (he studies the nervous system, he distinguishes veins from arteries, he devoted a whole book to the eye), first doctor to have taken the pulse to his patients, he is also discoverer of the fallopian tubes.

Erasistrate de Céos first to have performed autopsies in order to know the cause of death, he distinguishes the sensory nerves from the motor nerves (**Chatelain, 2004**; **Sénéchal, 2009**).

Galien

Of all the Greek doctors, the most influant in the centuries that followed is undoubtedly Claude Galien. Galen was strongly influenced in his practice by the hippocratic school and in his physiological conceptions by Aristotle. It seems that Galen performed many dissections, but only on animals. Galen's designs on the vascular system are particular. Like Aristotle, Galen believes that it is the blood that nourishes and preserves the body (**Sénéchal, 2009**). .

Fig. 16: Galien (Britannica.com)

However, **the role of the heart** is rather curious: between the liver and the right ventricle occurs a back and forth movement of the blood, loaded with natural spirits from digestion. The left ventricle receives from the lungs the pneuma, which becomes a vital spirit, distributed by the arteries, after receiving a part of the blood, passed from the right ventricle to the left ventricle by the inter-ventricular septum, through invisible pores (**Sénéchal, 2009**).

Galen developed a theory of temperaments associated with different moods. According to Galen, human temperaments exist in four types, depending on the prevailing mood of each individual:

1. Blood type, warm and kind.

2. The phlegmatic, slow and calm type.

3. Angry or bilious type, quick and carried away.

4.The melancholic or atrabilary type, sad and withdrawn.

Galian medicine became a true dogma in the Middle Ages (**Sénéchal, 2009**).

2.2. Romain Empire

Rome has had many engineers, some of whom have a remarkable competence in both civil and military works, and who have built works whose scope is undeniable and still surprises us. On the other hand, if some scientists illustrated areas of the Empire (Alexandria in particular), these scientists were most often slaves or freedmen of Greek or Eastern origins.

The Roman mentality was not averse to intellectual work, reflection and study, but preferred practical application.

At the time when Rome became a great power, it received through conquered kingdoms everything it needs from science for practical jobs. But fortunately, the Roman Empire did not radically disdain anything that did not have a strictly utilitarian character.

The Romans, excellent engineers, left roads and sewers still usable after 2000 years, but their reluctance to speculative philosophy did not allow a real development of sciences (**Sénéchal, 2009**).

Among the Latin authors dealing with natural science :

Antonius Castor was a pioneering botanist and pharmacologist of ancient Rome who lived in the first century. He is several times quoted and mentioned by Pliny the Elder, who considered him the greatest authority on his subjects. Several of Castor's recommendations for herbal remedies are known. He suggested fennel root (ferula) to improve vision, the root of potamogiton (possibly *Hippuris vulgaris*) to fight goitre, and one of the two varieties of horehound (*Ballota spp. and Marrubium vulgare*) for abscesses and dog bites (**Sharma, 2023**).

***Naturalis Historia* of Pliny the Elder** (Gaius Plinius Secundus) was published in 37 volumes, a book which is the first **description of the remedies and their preparation**.

De universa medicina treatise in six books contains the description of six hundred medicinal plants, with the way to use them, and the list of diseases they cure.

He was the first to describe the role of lime water, copper sulphate, lead acetate, antimony, arsenic and sulphur in drug therapy. The last chapter of his treatise concerns venoms, poisons and counterpoisons (**Pietsch, 2012; Pelczar *et al.*, 2023**).

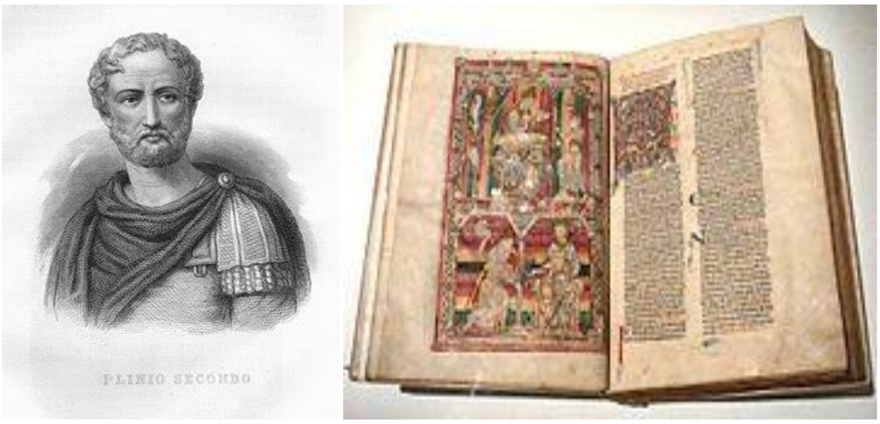


Fig. 17: Naturalis Historia of Pliny the Elder (Britannica.com)

Dioscoride's work, *De materia medica* written in Greek inspired Pliny and was widely quoted by Galen. Translated into Latin and Arabic, it influenced the Eastern and Western **pharmacopoeias,** and was commented in France until the late eighteenth century (**Chen *et al.,* 2023; Pelczar *et al.,* 2023**).

Fig. 18: *De materia medica* of Dioscoride (Britannica.com)

Lucius Junius Moderatus Columella was a prominent Roman writer on **agriculture** in the Roman Empire. His ***De re rustica*** in twelve volumes has been completely preserved and forms an important source on Roman agriculture, together with the **works of Cato the Elder and Marcus Terentius Varro**, both of which he occasionally cites. A smaller book on trees, ***De arboribus***, is usually attributed to him (**Cartwright, 2016; Pelczar *et al.,* 2023**).

The evolution of sciences :

Mathematics: Nicomede, Diocles.

Geometry: Hypsycles, Cleomede, Citium, Zenodore, Diophant Of Alexandria.

Physics: It was practically at a stagnant level (except applications by levers, pulleys and gears, the force of compressed or heated air, and steam).

Chemistry: in Alexandria, alchemy begins to develop in order to obtain gold from heavy metals.

Astronomy: Hipparque, Claude Ptolemee. Jules Cesar decided the abandonment of the old calendar of the king NUMA (which, with its year of 354 days shifted the seasons a little more each year). Rome appealed to an Alexandrine, SOSIGENE who was the creator of the Julian calendar 365 days in normal year and 366 every 4 years (leap years).

Geography and Cartography: Progress was very limited because the map of **Erathostene** already covered almost all the regions that formed the Roman Empire. It is enough to add to it some rectifications relating to the North of Gaul and Germania, and to Great Britain. The Romans knew that the world extended far beyond the mouths of the Ganges to the east, and the coasts of Africa to the south after the Strait of Gibraltar. Among the Roman geographers are **Strabo** and its geography of the Empire and MELA, which drew up the first map of the Baltic. In the 2nd century a cartographer of the Empire drew a very long and extremely deformed, very elongated in longitudes, and compressed in latitudes, but the road network which appeared there between the cities was exact and precise (distance between places of stages...).

Medicine, surgery: They mark no progress, even a certain regression, compared to those of the time, already distant, of Hippocrate (**Cartwright, 2016**).

MIDDLE AGES

IV. MIDDLE AGES

1. ORIENTAL (EAST) MIDDLE AGES

Arab-Muslim Civilization

The decline of the Roman Empire led to the disappearance or destruction of much knowledge, though physicians still incorporated many aspects of the Greek tradition into training and practice. In Byzantium and the Islamic world, many of the Greek works were translated into Arabic and many of the works of Aristotle were preserved.

Arabic science is not only the science of the Arab peoples, but science written in Arabic, which includes many Persian scholars and even non-Muslims (Jews). In fact, during the first century of Islam, the majority of scholars in Muslim territory are Christians. The Islamic religion was, to some extent, more favourable to the development of scientific knowledge than the Christian religion at the same time. Not only is astronomical knowledge important to precisely determine the beginning of Ramadan and the direction of Mecca, but the Koran encourages the study of Nature: The Greeks have greatly inspired the Arabs. We can consider, roughly, that Arab science is the logical extension of Greek science, or at least, of what remained of it in Roman times. However, the Arabs have a more practical mentality than the Classical Greeks and do not practice "science for science": practical applications are always present in their minds (**Sénéchal, 2009**).

Immediately after their conquest of the Middle East, the Arabs were open to existing cultures (Greek-Byzantine and Persian) and were able to assimilate the knowledge accumulated for centuries by these civilizations, without questioning their religion. The scientific texts of antiquity were translated from Greek into Arabic, often through Syriac (one of the late forms of Aramaic). Lecalife Al-Ma'mun (814/833) founded the Bayt al-Hikma ("House of Wisdom") in Baghdad, an institution responsible, among other things, for translating Greek texts. Many translators were Christians and the caliph imported the manuscripts from Constantinople when he did not have them in his possession (**Sénéchal, 2009**).

The development of Arab science is important especially from the 8th to the 11th century around Baghdad and from the 10th to the 12th century around Cordoba. Arab science stagnated and declined from the 14th century. The catastrophic Mongolian invasions are partly responsible for this decline, but also a change in religious attitude, which emphasizes more respect for the authority of ancient authors (**Sénéchal, 2009**).

BOTANY & ZOOLOGY (AGRICULTURE, VETERINARY)

Arabs are responsible for the extension of the cultivation of sugar cane and to lesser extent cotton. Their main achievement lies in the **creation of botanical gardens (Al-Andalus**), both places of acclimatization and study with an orientation towards medicinal plants. There is an extension of the growing area of some fruits (citrus fruits, bananas) and some flowers (*Crocus sativus* from which saffron is extracted). Thanks to the mastery of hydraulics and botany, Arab-Muslim agronomists have enabled Mediterranean agriculture to emerge from the ancient triad of wheat-vine-olive cultivation (**TeamCFL, 2023**).

From the work of selection of the Persian dynasty of the Sassanids, they will create the Arabian horses, the alezans, which will astonish the first crossed by their agility.

The creation of original races of pack camels will be an essential asset for the control of space.

Ibn Bukhtishu's Kitâb manâfi' al-hayawân is a treatise on the properties of animals. It describes the characteristics of each animal and the therapeutic uses of different parts of their bodies (**Walker-Meikle, 2023**).

Fig. 19: Book of Kitâb manâfi' al-hayawân (alamyimages.fr)

The book of **Zakarīyā Ibn Muḥammad al-Qazwīnī** is also known as **Ajā'ib al-makhlūqāt wa gharā'ib al-mawjūdāt**. It is a compilation of scientific and mythological information about the universe, the earth, animals, plants, and minerals. The book is written in a style that blends scientific explanations with stories and poetry to entertain readers (**Pashai, 2016**).

Fig. 20: Book of Ajā'ib al-makhlūqāt wa gharā'ib al-mawjūdāt (alamyimages.fr)

The **Andalusi agricultural corpuses** are texts of agronomic knowledge and sources for the history of agriculture in the Andalusi Iberian Peninsula. Agronomic advancement had deteriorated under Visigothic rule, but there are eight known agricultural treatises dating from the late 10th century to the mid 14th century, contributing to the Arab Agricultural Revolution. The Andalusi treatises follow the same pattern as Latin agronomic texts: a discussion of soil, water and manure followed by crop science, and sometimes notes on animal husbandry. Six of these are written between the 11th and 13th centuries.

The authors of this body of texts are **Ibn al-Wafid, Ibn Hajjaj, Ibn Bassal, Abū l-Khayr, Ibn al-'Awwam, Al-Tighnari and Ibn Luyun.**

The Arabic language agricultural corpuses were composed between the 11th and 14th century in Seville, Toledo, Granada and Córdoba (**Conan & Oaks, 2007**).

Abū l-Khayr's botanical work is the most complete Andalusi botanical text known to modern scholars, containing richer descriptions of plant morphology than other agronomy texts, and detailed information about habitat, plant phenology, uses, cultivars and geographical distribution (**Conan & Oaks, 2007**).

Ibn al-Awamm's *Kitab al Filaha* is considered the most important and encyclopedic of the medieval writings from the European west, but it was relatively unknown in Northwestern Europe until the 19th century when it was first translated into French and Spanish. It contains details on plants like "All plants planted in [the walnut's] vicinity show antipathy to it, with the exception of the fig". He quotes extensively from the *Nabatean Agriculture* and to a lesser extent from earlier Roman and Andalusi authors (**Zadoks, 2013**).

There is some information of how new species like the **Syrian pomegranate** were adapted to Al-Andalus. The Syrian pomegranate was brought to Al-Andalus by a returning ambassador where it was planted in Bunila (modern day Casarabonela, Malaga) in 780 AD.

The Book of **Veterinary** Art by **Ahmed Ibn Hosein ibn al-Ahnaf (Kitāb al-Baytara)** is an important work in the history of hippiatria which is a branch of veterinary medicine that focuses on the care and health of horses (**Elsayed, 2009**)

Fig. 21 : Book of Kitāb al-Baytara (bridgemanimages.com)

CONTRIBUTION TO MEDICINE

Maimonides (1135-1204), personal physician of the Ayyubid sultan Saladin, also influenced Arabic medicine, he wrote a treatise on poisons where poisonous plants and venimous animals are cited with the remedies to use (**Ferrario, 2017**).

A biomedical work by **Ibn al-Nafis,** adherent of experimental dissection. Who discovered the pulmonary circulation and function of coronary arteries, wrote Al-Shamil fi al-Tibb encyclopedia of 300 volumes (**Amr & Tbakhi, 2007**).

Anesthesia, practiced in ancient times by the ingestion of opium, mandrake or various other soporific substances, is perfected by the use of a sponge soaked by a mixture of these substances. Dried, this spongia somnifera as it will be called allows the surgeon to operate by subjecting the patient to the vapors of the moistened sponge before use and which plunged patients into a state close to general anesthesia, but which looks more like an analgesic state accompanied by loss of consciousness **(Öncel & Erdemir, 2007)**.

Hospitals served both as medical schools and as places of care, which corresponds to the invention of hospital medicine. The first hospitals opened, initially as a leprosarium, then evolved to treat diseases of the body as those of the spirit (**Tschanz, 2017**).

Ibn Sina (Avicenna)

Avicenna authored a five-volume medical encyclopedia: *The Canon of Medicine* (*Al-Qanun fi't-Tibb*). It was used as the standard medical textbook in the Islamic world and Europe up to the 18th century. *The Book of Healing*, a philosophical and scientific encyclopedia,

Avicenna's corpus includes writings on astronomy, alchemy, geography and geology, psychology, Islamic theology, logic, mathematics, physics, and works of poetry (**Nasser *et al.*, 2009**).

Fig. 22 : Ibn Sina (Avicenna) (alamyimages.fr)

Al-Razi

Contribute to medicine, chemistry and philisophy. First to isolate sulfuric acid and ethanol and initiator of the use of alcohol in medicine. Al-Rāzī’s two most significant medical works are the *Kitāb al-Manṣūrī,* which he composed for the Rayy ruler Manṣūr ibn Ishaq and which became well known in the West, and *Kitāb al-ḥāwī,* the “Comprehensive Book,” in which he surveyed Greek, Syrian, and early Arabic medicine as well as some Indian medical knowledge. Throughout his works he added his own considered judgment and his own medical experience as commentary. Among his numerous minor medical treatises is the famed *Treatise on the Small Pox and Measles* (**Britannica, 2022).**

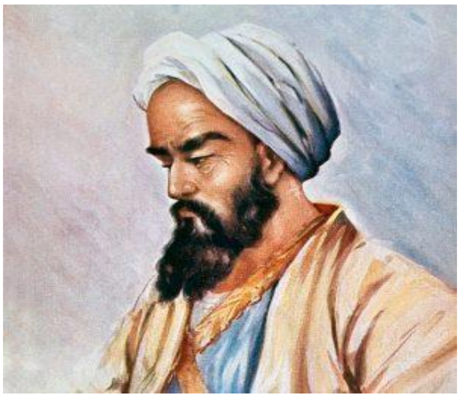


Fig. 23 : Al-Razi (alamyimages.fr)

Abulcassis

In the 11th century, the Andalusian Abu-l-Qasim az-Zahrawi (called in Western Abulcassis) wrote a reference book on surgery, kitab al-tasrif in 30 volumes (**Pekesen *et al.*, 2021**) .

Averroes (Ibn Rushd)

He was an Andalusian, polymath and jurist who wrote about many subjects, including philosophy, theology, medicine, astronomy, physics, psychology, mathematics, Islamic jurisprudence and law, and linguistics. The most famous book was *al-Kulliyat fi al-Tibb* ("The General Principles of Medicine", Latinized in the west as the *Colliget*) (**Ben Ahmed & Pasnau, 2021**).

Fig. 24 : Averroes (Ibn Rushd) (alamyimages.fr)

CONTRIBUTION TO CHEMISTRY, PHYSIC, OPTIC

The Arab-Muslim civilization has famous alchemists. While searching for gold, they work on other materials such as nitric acid and perfect distillation (**alembic** is a word of Arabic origin like **alcohol**, **syrup**). The Arabs translate the treatises of Dioscoride (*De Materia Medica*) and advance the pharmacopoei (**Ferrario, 2007**).

Chemistry experienced a decisive impulse with **Jâbir ibn Hayyân** (around 845) and distinguished itself with the handling of many mineral, plant and animal products. He discovered various **chemical bodies**: citric acid (at the base of lemon acidity), acetic acid (from vinegar) and tartaric acid (from winemaking residues) **(Biron, 2022)**.

The use of **alembic stills** developed in 800 AD by the Arab **alchemist Jabir ibn Hayyan,** makes it possible to **distil substances such as rose essence.**

Fig. 25 : Alembic stills (essentialoil.com)

Ibn Sahl gave the first mention of the **law of refraction**: considering the rectangular triangles, the ratio of the two hypotenuses is a constant of the system.

In ***De Gradibus,*** **Al-Kindi** attempts to apply mathematics to **pharmacology** by quantifying the strength of drugs. **Al-Kindî**, in studying the “fiery mirrors”, was the first to take an interest in the physical nature of light, to turn it into something material.

Hunayn Ibn Ishaq translator, scholar, physician, and scientist (ophtalmology). Study of the human eye can be traced through his innovative book, "Book of the Ten Treatises of the Eye"(Arabic: (كتاب الأطروحات العشر للعين is a 9th-century theory of vision **(Biron, 2022)**.

Fig. 26: Illustrations of Hunayn Ibn Ishaq (agefotostock.com)

Ibn Al-Haytham's optics written in Egypt in the first half of the 11th century represented a theory of vision that went beyond Galen, Euclid and Ptolemy. This diagram of the two eyes seen from above, shows the principal tunics and humours and the optic nerves connecting the eyeballs to the brain (**Masic, 2008**).

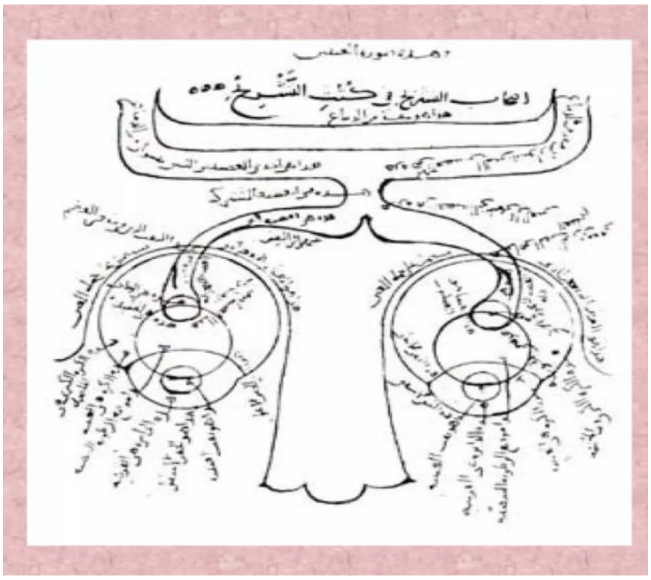


Fig. 27: Ibn Al-Haytham optic work (lomography.com)

2. OCCIDENTAL (WEST) MIDDLE AGES

Elementary prejudices towards the middle Ages describe it as a period of ignorance, if not barbarism and religious fanaticism. Nothing is more unfair and exaggerated. The Middle Ages is the period of European history that extends from the end of the Roman Empire (to the 5th century) to the beginning of the Renaissance (to the end of 15th century) (**Sénéchal, 2009**).

Western penetration of Greco-Arab science

Towards the end of the century, the West was clearly far behind the Byzantines and the Arabs in economic and scientific terms. Several westerners moved to the centers of Arab culture (Sicily, Spain) to perfect their education. They brought back works written in Arabic which were then translated into Latin for Western use.

Among those Westerners who studied in the Arab world, the most illustrious is the Frenchman **Gerbert d'Aurillac** (c.940/1003). He stayed in Spain (967/969) and devoured available scientific texts. He wrote a treatise on the astrolabe and built a sphere representing the movement of the stars. He is also reputed to have owned or built various automata, including a steam organ. The Englishman **Adélard of Bath** (1090/1160) travelled to the East (Damascus, Baghdad, and Jerusalem). He translated from Arabic into Latin the Elements of Euclid, the Almagest of Ptolemy and the treatise on arithmetic of Al-Khwarizmi.

The problem of translation was initially quite difficult, because several Arabic words did not have their equivalent in Latin. Thus the Latin language and later the French language imported a number of Arabic words. Translations were numerous at this time and often proceeded through a Jew who knew both Arabic and Latin, or at least knew both Arabic and the vulgar language (Castilian, French). The Jew Savasorda (Abraham bar Hiyya of Barcelona) translated several texts from Arabic to Hebrew for the Jewish communities of France and his collaboration with Plato de Tivoli made it possible to translate several of these texts into Latin.

In general, scientific knowledge of Western antiquity came through the Arabs before the 12th century. But early on, the original Greek versions were translated directly into Latin, which greatly improved the accuracy and fideliberation of the original (**Sénéchal, 2009**).

The universities and scholasticism

The rise of **European universities**, though important for the development of physics and philosophy, and had little impact on biological scholarship.

From the year 1000, the West saw the appearance of a few schools, most centered on a bishopric. The most famous is the Ecole de Chartres, founded in the early 11th century by Bishop Fulbert. The 13th century saw the development of universities. The oldest universities in Europe were:

1. Bologna (1119), specializing in Law.
2. Paris (Universitas magistorum et scolarium), founded about 1170;
3. Oxford (1133), founded by students dissatisfied with the teaching of Paris schools.
4. Cambridge (1209), founded by teachers and students expelled from Oxford.
5. Montpellier (1289). Medical and law schools already existed there in the 12th century.

The typical university has four faculties: Arts, Law, Medicine and Theology (**Sénéchal, 2009**).

By 1500, Europe had about 50 universities.

The student had to master the basic subjects, divided into two groups: *trivium and quadrivium. The trivium* had three elements: grammar, logic and rhetoric. The *quadrivium* had four elements: arithmetic, geometry, astronomy and music.

The term scholastic refers to the teaching conferred in the universities of the time as well as the method used:

- **Scholastic instruction consisted of several elements.**

✓ The first was the ***lectio*:** a teacher would read an authoritative text followed by a commentary, but no questions were permitted.

✓ This was followed by the ***meditatio*** (meditation or reflection) in which students reflected on and appropriated the text.

✓ Finally, in the ***quaestio*** students could ask questions (*quaestiones*) that might have occurred to them during *meditatio*. Eventually the discussion of *questiones* became a method of inquiry apart from the *lectio* and independent of authoritative texts. *Disputationes* were arranged to resolve controversial *quaestiones* (**Sénéchal, 2009**).

Roger Bacon and the scientific method

The above may suggest that medieval intellectuals were entirely absorbed by metaphysical considerations and had little interest in the physical world for themselves. This is not entirely true.

The Englishman **Robert Grosseteste** (1170/1253) was particularly interested in the physical sciences, especially optics. He read the works of Aristotle and Alhazen. He concluded that it was possible to enlarge and bring objects closer together using optical instruments. He stressed the importance of observation and experience.

However, it was his pupil, **Roger Bacon** (1214/1294), who was best known for his defense of the experimental method. Bacon was a precursor of modern scientists in that he believed in a universe governed by physical laws, expressed in mathematical language. Book about experimental science "Opus Majus".

Fig. 28 : Roger BACON (sciencephoto.com)

According to him, mathematics is "the door and the key to the natural sciences, the key to philosophy". In terms of concrete achievements, Bacon extended the work of his master Grosseteste in optics and saw the possibility of a lens-based magnification instrument, but there is no evidence that he made one (**Sénéchal, 2009**).

Hildegard of Bingen

Doctor of the church, she developed many talents, being at the same time abbess, mystic, visionary, illustrator, composer, poet. Works: The first, Physica, contains nine books that describe the scientific and medicinal properties of various plants, stones, fish, reptiles, and animals. This document is also thought to contain the first recorded reference of the use of hops in beer as a preservative. The second, Causae et Curae, is an exploration of the human body, its connections to the rest of the natural world, and the causes and cures of various diseases (**Acevedo Butcher, 2013**).

Fig. 29: Hildegard of Bingen (healthyhildegard.com)

Albertus Magnus

The German Albert the Great. He was primarily responsible for the introduction of Greek and Arabic texts to the University, particularly Aristotle (1240). Albert the Great was an open mind, a proponent of observation and criticized several points of Aristotle's physics.

He writes works of natural history (De animalibus and De vegetalibus). For him the heart is the seat of vital heat. He was interested in plant propagation and reproduction and discussed some detail the sexuality of plants and animals. He also practiced Alchemy. Albert the Great succeeded in preparing caustic potash, he was the first to describe the chemical composition of cinnabar, ceruse and minium (**Führer, 2022**).

Fig. 30: Albertus Magnus

Frederic II of Hohenstaufen

Emperor of the Romans from 1215 to 1250 under the name of Frederick II. He was also king of the Romans, king of Sicily, king of Provence-Burgundy (or Arles), and king of Jerusalem.

In 1241, Frederick II issued an edict authorizing the dissection of human corpses, thus opposing the Church, which, favoring the bodily integrity of the human being, hastened to cancel the edict at his death. At the end of an eventful life, Emperor Frederick II wrote a manual on falconry in Latin, entitled De arte venandi cum avibus (The art of hunting with birds: morphology, physiology… of various birds) (**Vagnoni, 2021**).

Fig. 31: Frederic II of Hohenstaufen (personality-database.com)

Medicine, Anatomy, Surgery

Mondino de Luzzi (c. 1270 – 1326), was an Italian physician, anatomist and professor of surgery, who lived and worked in Bologna. He is often credited as the restorer of anatomy because he made seminal contributions to the field by reintroducing the practice of public dissection of human cadavers and writing the first modern anatomical text, *Anathomia corporis humani*, written in 1316 (**Mavrodi & Paraskevas, 2014**).

Fig. 32: Mondino dissection, early 14th century (sciencephoto.com)

RENAISSANCE 15TH TO EARLY MODERN 16TH AND 17TH CENTURIES

V. RENAISSANCE 15^{TH} TO EARLY MODERN 16^{TH} AND 17^{TH} CENTURIES

Renaissance was a movement dedicated to the rediscovery and use of classical learning. It is considered to have originated in Italy.

Renaissance literally means 'rebirth'. It thinkers believed the period between themselves and the fall of Rome. Renaissance can also refer to the period between 14th and 16th century.

Its was a dynamic era, infact there was a lot of changes, as: European explorers "finding" new continents; the decline of feudalism; scientific developments, as the Copernican system.

In this period there was also the invention of printing (Johannes Gutenberg, 15th) with movable type. The first printer book was the Bible. The priting press was also developed, allowing Renaissance texts to be disseminated widely.

Classical culture had never totally vanished from Europe, and it experienced sporadic rebirths. Some historians argue that the Renaissance ended in the 1520s, some the 1620s. The Renaissance didn't just stop, but its core ideas gradually converted into other forms, and new paradigms arose, particularly during **the scientific revolution of the seventeenth century.**

Fig. 33: Renaissance gutenberg press (printmuseum.org)

Scientific revolution

This term refers to all scientific progress made in the **16th and 17th** centuries. It was at this time that **Western science** took off and surpassed all that had been accomplished by the Greeks or other civilizations. One of the main characteristics of this **scientific revolution** is the increasing use of mathematics in physics and the certainty, the precision that mathematical demonstrations bring.

- ❑ Progress in the description of human anatomy
- ❑ Publication of numerous illustrated works of zoology and botany
- ❑ And the encounter between alchemy and medicine

1. 15TH CENTURY ANATOMISTS

Antonio di Paolo Benivieni was a Florentine physician who pioneered the use of the autopsy and many medical historians have considered him a founder of pathology. He published a part of those writings calling them “Antonii Benivenii, De abditis nonnullis ac mirandis morborum et sanationum causis, Florentiae” (1507) (**Bambach, 2002**).

Alexander Achillinus was an Italian philosopher and physician. The “Anatomical Notes by the Great Alexander Achillinus of Bologna” demonstrate a detailed description of the human body. He was also distinguished as an anatomist, among his writings being *De humani corporis anatomia* (Venice, 1516–1524), and *Annotationes anatomicae* (Bologna, 1520) (**Bambach, 2002**).

Leonardo da Vinci

In about 1489 Leonardo da Vinci begins a series of anatomical drawings. Over the next twenty-five years he dissects about thirty human corpses, many of them at a mortuary in Rome - until in 1515 the pope, Leo X, orders him to stop. His drawings, amounting to some 750, include studies of bone structures, muscles, internal organs, the brain and even the position of the foetus in the womb and other vertebrates that he dissected. His studies of the heart suggest that he was on the verge of discovering the concept of the circulation of the blood (**Bambach, 2002**).

Fig. 34 : Anatomical drawings of Da Vinci (themarginalian.org)

Girolamo Fracastoro (1483-1553)

His studies of the mode of syphilis transmission are an early example of epidemiology.

In 1546 he proposed that epidemic diseases are caused by transferable tiny particles or "spores" that could transmit infection by direct contact, indirect contact, or even without contact over long distances, and propose that the very small, unseeable, particles that cause disease were alive. Considered to be able to spread by air, multiply by themselves and to be destroyable by fire and he was the first to promote personal and environmental hygiene to prevent disease.

Its importance in the history of medicine is due to its many natural and medical considerations, represented in "De sympathia et antipathia rerum", foreword to the "De contagione et contagiosis morbis et eorum curatione libri tres", which exposes an innovative theory of contagion **(Pesapane *et al.*, 2015)**.

2. MODERN ANATOMY AND PHYSIOLOGY

Vesalius and the science of anatomy

Galien's ideas, which became authoritative in the Middle Ages, were swept aside by the great Flemish anatomist André Vésale (1514-1564), who acquired knowledge of the many dissections he practiced at the universities of Padous and Bologna. During his many dissections, Vesalius realized that Galen's anatomical treatises were little reliable and that they most often represented the anatomy of a macaque and not that of a human! Vesalius openly deified the galenic tradition in 1539.

Vesalius sets himself the task of providing it, illustrated in a series of dissections and drawings. He has at his disposal a method, relatively new in Europe, of ensuring accurate distribution of an image in printed form - the art of the woodcut. His studies inaugurate the modern science of anatomy.

At Basel, in Switzerland, Vesalius publishes in 1543 his great work - De humani corporis fabrica (The Structure of the Human Body). There are seven volumes including numerous magnificent woodcut illustrations (**Sénéchal, 2009**).

Fig. 35: Woodcut illustrations of Vesalius (alamy.com).

Ambroise Pare (1510 – 1590)

Ambroise Pare is considered one of the fathers of surgery and modern forensic pathology. He was also an anatomist, invented several surgical instruments. Pare contributed both to the practice of **surgical amputation** and to the **design of limb prostheses**. He also invented some ocular prostheses

Pare discovered that the soldiers treated with the boiling oil were in agony, whereas the ones treated with the ointment had recovered because of **the antiseptic properties of turpentine.** He published his first book *the method of curing wounds caused by arquebus and firearms* in **1545.** Pare also reintroduced the ligature of arteries instead of cauterization during amputation. **For the ligature technique,** he designed the "*Bec de Corbeau*" ("crow's beak"), a predecessor to modern haemostats (**Hernigou, 2013**).

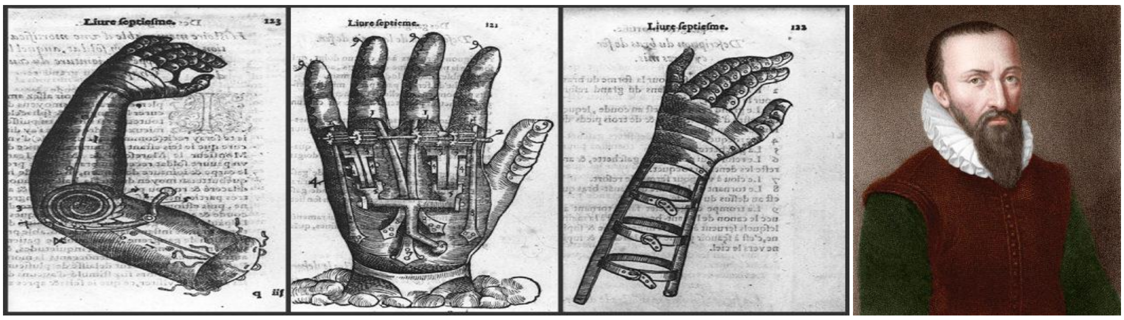


Fig. 36 : Limb prostheses of Pare (thevintagenews.com)

Michel Servet (1511 – 1553), had discovered the small circulation of blood (between the heart and the lungs).

Gabriel Falloppe (1523/1562), known for his study of the reproductive system and fetal development. He also studied structures as complex as the inner ear.

Volcher Coiter (1534/1576), performed numerous dissections on humans and animals, as well as vivisections on animals; his works were also magnificently illustrated. Coiter pioneered the comparative study of the anatomy of several species (comparative anatomy) (**Sénéchal, 2009**).

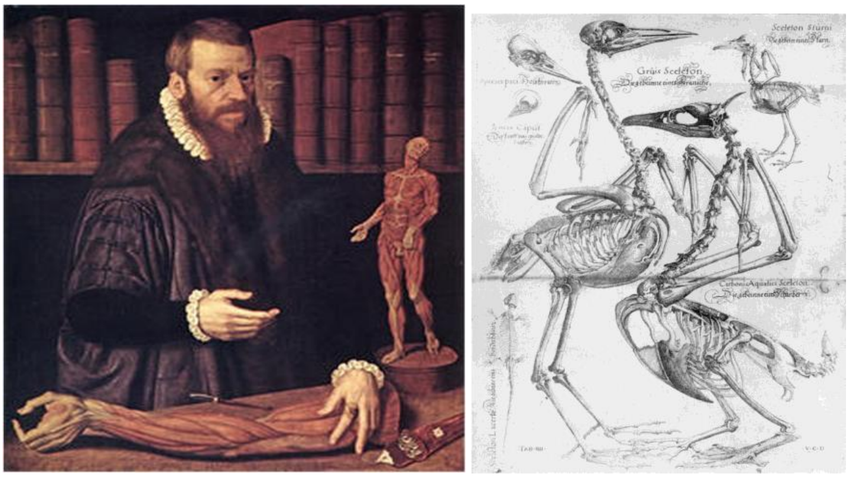


Fig. 37 : Volcher Coiter illustration (alamy.com).

Paracelsus (1493–1541), father of toxicology

He preached but he also pioneered the use of chemicals and minerals in medicine. His hermetical views were that sickness and health in the body relied on the harmony of man (microcosm) and Nature (macrocosm).

He took an approach different from those before him, using this analogy not in the manner of soul-purification but in the manner that humans must have certain balances of minerals in their bodies, and that certain illnesses of the body had chemical remedies that could cure them (**Rabinovich, 2008**).

Fig. 38: Paracelsus (britannica.com)

3. ZOOLOGY ILLUSTRATED BOOKS: 16TH CENTURY

Conrad Gessner contributed to the 16th century progression of Zoology •*History Animalum* is a 5 volume bibliography of his knowledge of plants and animals •He used the same method of classification as Aristotle by ordering data and observations on fish, insects, birds, etc. (**Pietsch, 2012; Ragan, 2023**).

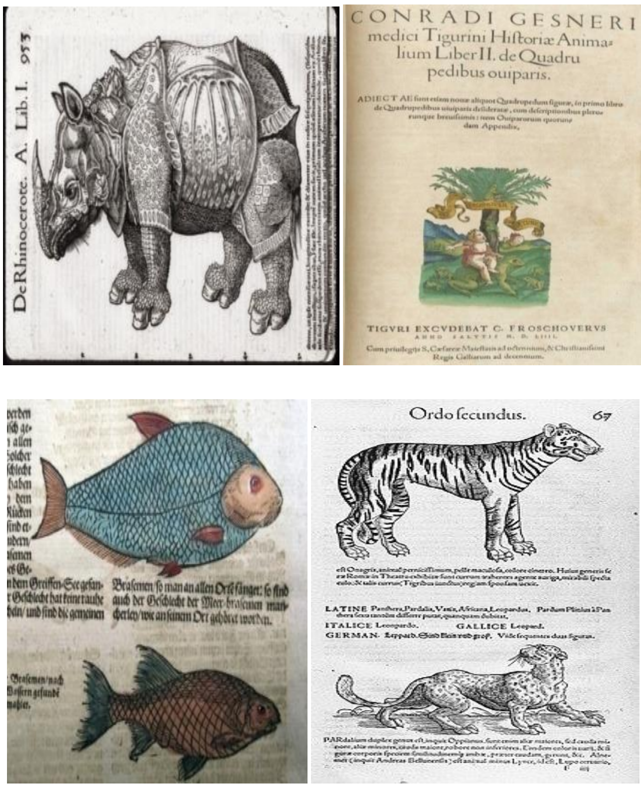


Fig. 39 : Conrad Gessner illustrations (alamy.com

Pierre Belon noted anatomical similarities between the human skeleton and that of birds, published La Nature et Diversité des Poissons (1551) that contained illustrations of his observations on fishes, marine mammals and birds (**Pietsch, 2012; Ragan, 2023**).

Fig. 40 : Pierre Belon illustrations (alamy.com)

4. BOTANIC ILLUSTRATED BOOKS: 16TH CENTURY

In the 16th century, scholars returned to direct observation of plants and animals for natural history.

Leonhart Fuchs was one of the three founding fathers of botany, along with **Otto Brunfels and Hieronymus Bock.**

Bock in particular included environmental and life cycle information in his descriptions.

The first to make serious use of this opportunity is a botanist, **Otto Brunfels**, whose three-volume *Herbarum vivae eicones* (Living images of plants) is published in Strasbourg between 1530 and 1540. Another German botanist, **Leonhard Fuchs** whose *Historia Stirpium* (History of plants) is published in Basel in 1542 (**Dickman, 2013**).

Fig. 41 : *Historia Stirpium* of Leonhard Fuchs (mediastorehouse.com)

The first observations of plants under a microscope began and studies of plant anatomy underwent a great development, which was to exert a great influence on subsequent classifications (**Mason, 2016**). Observing leaves under a microscope, **Giovanni Alfonso Borelli** distinguished spots, veins, simple and starry bristles. Plant microscopy has achieved great interest and is considered **Robert Hooke and Nehemiah Grew, Marcello Malpighi and Antoni van Leeuwenhoek** as the most important representatives of this discipline in the last third of the seventeenth century.

5. ATTEMPTS AT CLASSIFICATION: 1583-1704

BINOMIAL CLASSIFICATION

Andrea Cesalpino, whose *De Plantis* of 1583 classifies plants according to the characteristics of their flowers, seeds and fruits. 1500 plants divided into 32 groups including umbelliferae and compounds.

Gaspard Bauhin described over 6000 plants, which he arranged into 12 books (*Phytopinax* 1596, *Pinax theatri botanici* 1623…) based on a wide range of common characteristics. He is the first to arrange plants in separate groups, or genera. Bauhin's work was the beginning of the binomial (two-name) system which subsequently prevailed in the classification of living organisms.

Guillaume Rondelet (1507-1566) was the first to use the binominal nomenclature. However, as the number of listed species increases, their classification requires them to be given longer and longer names.

Joseph Pitton de Tournefort. He proposes to limit the classification only to the actual physical traits of each species and, therefore, to group several according to the similarity of their characteristics. It also presents the idea of bringing certain genres into classes.

John Ray, publishes classifications of birds (1676), plants (from 1682), fishes (1686), land animals (1693) and insects (1705). The greatest achievement is Ray's own work on botany. The *Historia Plantarum* (1686-1704) describes some 18,600 plants, with establishing the monocot/dicot division (**Arber, 2010**; **Woodland, 2003; Cartier, 2023**).

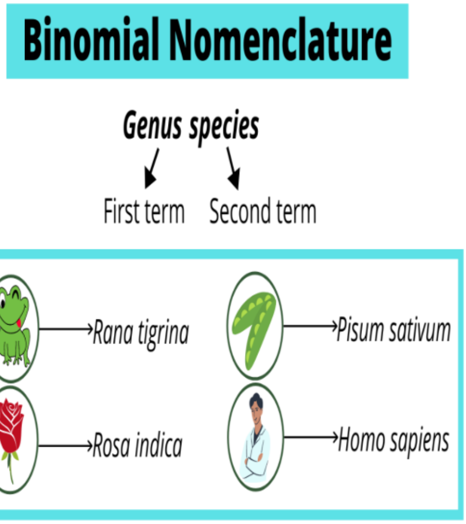


Fig. 42 : Binomial classification (neetexambooster.in)

6. SEVENTEENTH CENTURY

6.1. THE BIRTH OF THE EXPERIMENTAL METHOD

From the seventeenth century, when the minds are freed from the scholastic tradition and arguments of authority, the experimental method can develop freely.

The English lawyer Francis Bacon (1561/1626), was the most famous defender of the experimental method at the beginning of the seventeenth century. His main works are «The advancement of Learning (1605) and especially the Novum Organum (1620)», This last work is so called as opposed to the Organon of Aristotle, which he wanted to replace. Bacon attempts a new class of science, praises the merits of the experimental method and encourages amateurs to persevere.

Rene Descartes, (1596 - 1650) finds it entirely legitimate to justify a hypothesis by its consequences

A more careful point of view is exposed by Edme Mariotte (1620/1684), in his Essai de logique (**Sénéchal, 2009**).

Fig. 43 : Francis BACON and Rene DESCARTES (alamy.com)

6.2. CHEMISTRY

- **Isaac Newton**, universal law of gravity, formulates the three universal laws of motion.
- **Francis Bacon** in 1620, in the second part of the Novum Organum; describing the shape of the particles which constitute the texture of matter.
- **Pierre Gassendi** tried the first serious attempt to combine chemical conceptions with atomism.
- **Nicolas Lemery**, in his famous first chemical (Paris, 1675), conceived this specific chemical reactions in terms of particle shape and movement. While acids salts had a pointed shape which explained their sharp taste and their tendency to solidify by forming pointed crystals, alkalis were composed of a porous texture so shaped as to admit entry of the spike particles of acid (**Beretta, 2008**).
- **Robert Boyle**

Chemistry was not distinguished from the latter until the 17th century, notably by the work of Robert Boyle who applied the scientific method to his experiments. The publication of his famous Sceptical Chymist in 1661 is sometimes considered in the Anglo-Saxon world as the starting point of modern chemistry.

A master of considerable wealth, he devoted it to the advancement of the natural sciences. He meets Robert Hooke, who helps him build an air pump that Boyle needs for gas research. He thus polemicized with Thomas Hobbes about the existence of emptiness (**Amendolare & Roberts, 2023**).

Fig. 44 : Robert Boyle (alamy.com)

6.3. OLDEST CONCEPT GENERATION

From the outset, two ideas arise as to the origin of life: on one hand, according to the proponents **of spontaneous generation**, life can appear spontaneously from inert matter. As it is obvious that the higher animals only appear by reproduction from other living beings, the hypothesis of spontaneous generation is applied only to **lower animals**: worms, insects and vermin. **Aristotle** believed that some lower animals and plants can appear spontaneously from the earth and water, without the need for a seed (**Sénéchal, 2009**).

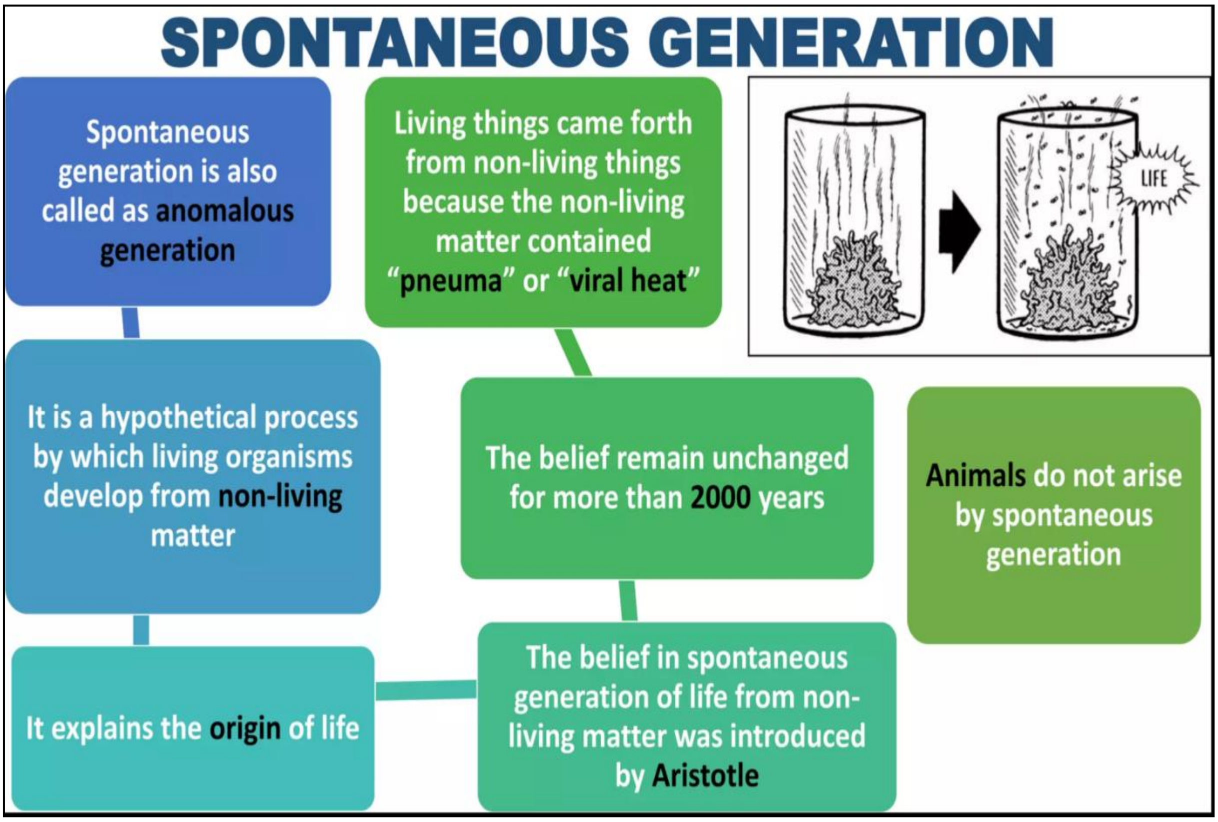


Fig. 45 : Spontaneous generation theory (Sreenivas, 2023)

17th, *omne vivum ex vivo*

In the seventeenth century, the thesis of *omne vivum ex vivo* is opposed to spontaneous generation according to which every living being comes from another living being and is ultimately created by God.

Francesco Redi (1626/1697) conducts an experiment on the putrefaction of meats. He concludes that the worms did not appear spontaneously, but were laid by insects that entered the fiole in the meantime (**Sénéchal, 2009**).

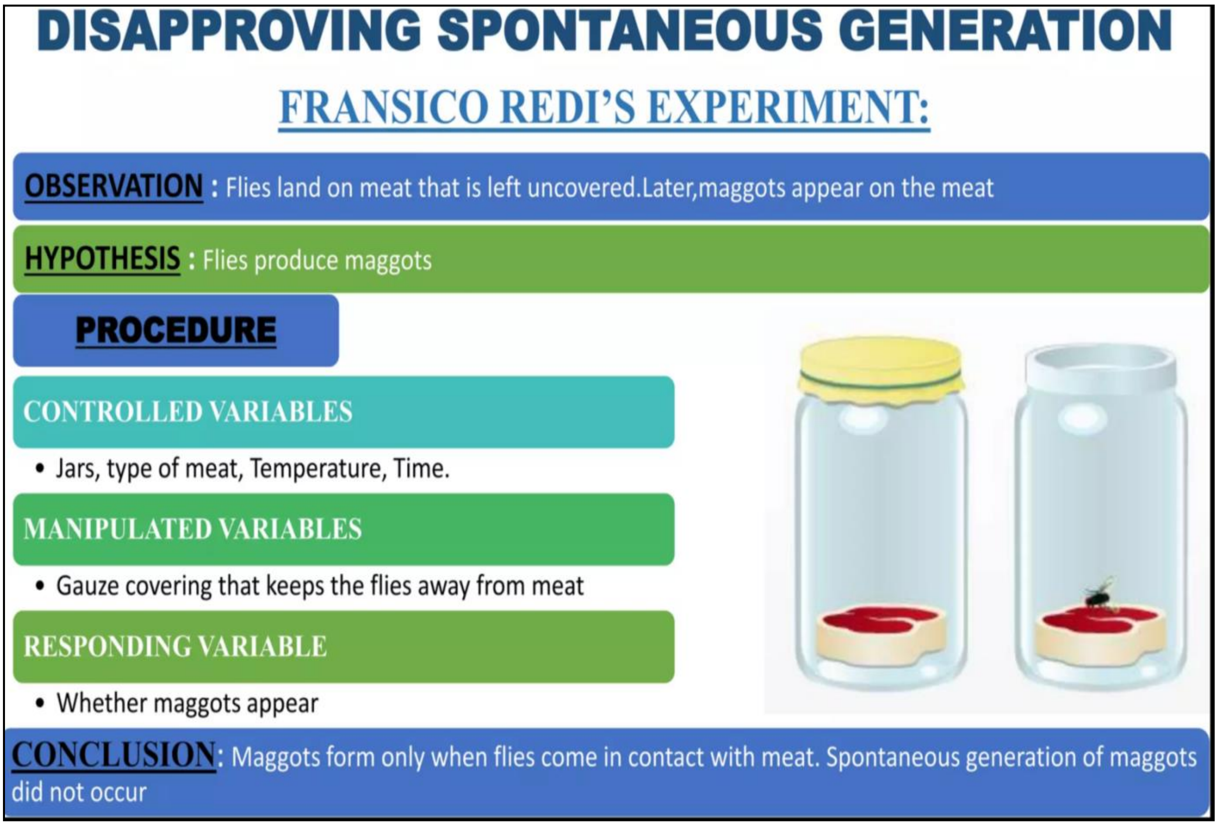


Fig. 46: Francesco Redi experiment's (Sreenivas, 2023)

6.4. PREFORMATION AND EPIGENESIS (HIGHER ANIMALS)

Hippocrates believes that an animal (the human being in particular) develops within its mother from a preformed germ, which already contains all parts of the adult. The development of the embryo is only a gradual magnification. This is the thesis of preformation.

As for Aristotle, he believes rather that the sperm of the male is homogeneous, although it carries in itself the potentiality of all the organs; the female, it, provides only the nourishing matter necessary for the development. This is the thesis of epigenesis: organs, limbs, etc., appear gradually during the growth of the embryo, but are not present in a microscopic form in the seed.

The idea of preformation became popular again in the 17th century. It seems reasonable, since some plants have a kind of pre-formed “germ” or “sprout” that only waits until the following year to hatch and flourish.

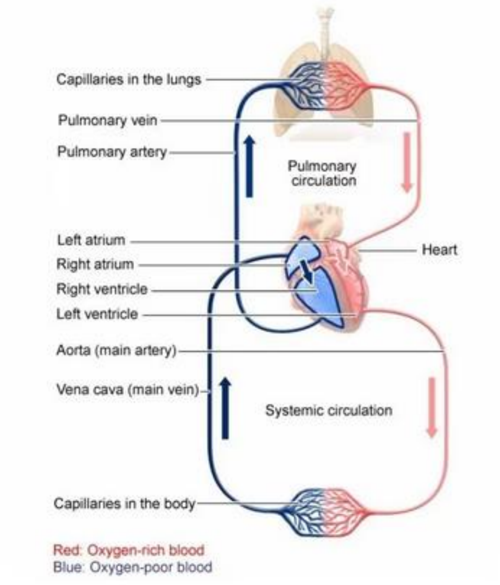
Supporters of animal preformation divided into two camps: some believed that the preformed germ was contained in the egg and were consequently nicknamed ovists, while others believed that the germ resided in the spermatozoid (discovered by Leeuvenhoek) and were nicknamed sperm or animalculists. The more complex reality of the union of male and female gametes was far from suspected.

In 1694, Rudolf Jakob Camerarius (1665/1721) discovers the sexuality of plants, amputating stamens in hermaphroditic plants and separating the sexes in sexual plants (**Sénéchal, 2009**).

6.5. HARVEY AND THE CIRCULATION OF THE BLOOD: 1628

The **Englishman William Harvey** (1578/1657), in his work *Exercitatio anatomica de motu cordis et sanguinis in animalibus* ('The Anatomical Function of the Movement of the Heart and the Blood in Animals), published in 1628, but resulting from discoveries made as early as 1616. He demonstrates beyond any reasonable doubt an entirely new concept Harvey concludes that blood circulates throughout the body, and the heart acts like a pump and that the action of the heart valves leads inevitably to the following scenario: the blood from the vena cava enters the right atrium, from where it is pushed towards the right ventricle which, when contracting, pushes it to the lungs through the pulmonary arteries. Venous blood, aerated in the lungs, returns to the left atrium through the pulmonary veins and then into the left ventricle, from where it is pushed into the aorta. There is therefore no back and forth movement, but a unidirectional circulation of blood. The blood must go through a full cycle before returning to the heart. (**Sénéchal, 2009**).

The only part of this cycle missing from Harvey, who did not have a microscope at the time, was the play of capillary vessels, where arterial blood, having delivered oxygen back into the veins.. (It is not till four years after his death that Marcello Malpighi observes the **capillaries.** And Harvey is unable to explain why the heart should circulate the blood. That explanation will have to await the discovery of **oxygen)**.



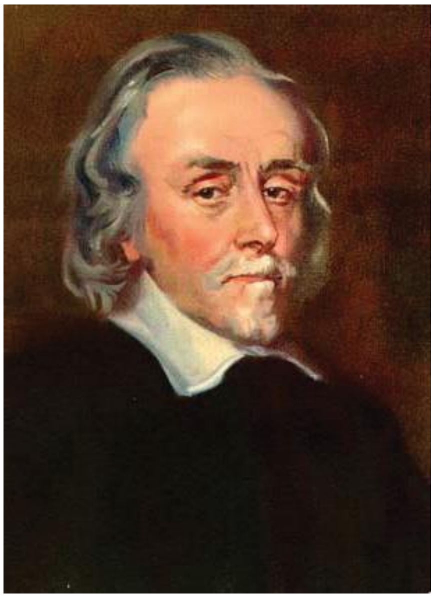


Fig. 47 : William Harvey and the circulation of the blood (irishtimes.com)

6.6. MICROSCOPY

Zacharias Janssen in 1595, the first optical telescope and/or the first truly compound microscope.

Galileo developed an occhiolino, a microscope consisting of a convex lens and another concave in 1609.

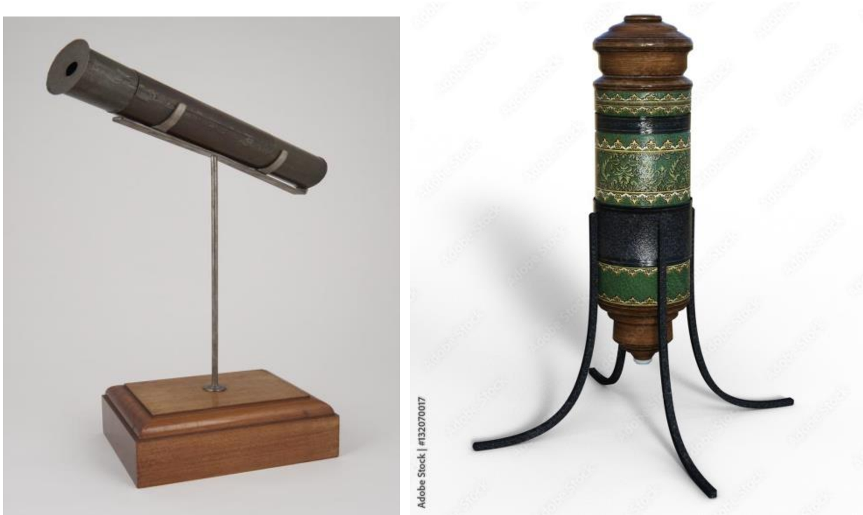


Fig. 48 : Telescope of Janssen and occhiolino of Galileo (stock.adobe.com; collection.sciencemuseumgroup.org.uk)

Antony van Leeuwenhoek invented the microscope in about 1650 opened up the micro-world of biology (some of them providing a magnification of 300x). In 1674 he is the first scientist to give an accurate description of red blood corpuscles. In 1677 he observes and depicts spermatozoa in the semen of a dog. In 1683 he provides a drawing of animalculae (or bacteria) seen in saliva and dental plaque. His researches demonstrate for the first time that the tiniest living things have a life cycle and generative systems like any larger creature **(Rhoads, 2007)**.

Robert Hooke built a microscope around 1660. Its intruder was coupled to a light source concentrated by a lens and would only be a modest enlargement (a few dozen times). Hooke used it to study the world of insects and plants and in 1665 published a collection: the Micrographia. Looking at a piece of bark under a microscope, Hooke discovered that the wood was actually formed from a multitude of adjacent rectangular cavities, evoking the cells of a monastery. The word cell has remained to designate the fundamental unity of the living **(Rhoads, 2007)**.

Fig. 49 : Microscope of Van Leeuwenhoek and Hook (alamy.com)

Marcello Malpighi use of the microscope in biology, in 1661, he uses the setting sun as his light source, shining it into his lens through a thin prepared section of a frog's lung. In the enlarged image it is clear that the blood is all contained within little tubes. Malpighi thus becomes the first scientist to observe the capillaries, the tiny blood vessels in which blood circulates through flesh. The animal comes from the egg the fertilization is made between the spermatozoid and an egg in the fallopian tubes **(Rhoads, 2007)**.

AGE OF ENLIGHTMENT 18TH AND 19TH CENTURY

VI. AGE OF ENLIGHTMENT 18 TH AND 19 TH CENTURY

1. IN THE 18TH CENTURY

Many fields of science including botany, zoology, and geology began to professionalize, forming the precursors of scientific disciplines in the modern sense (though the process would not be complete until the late 1800s).

1.1. CHEMISTRY AND PHYSIOLOGY

Antoine LAVOISIER

Father of modern chemistry, changed chemistry from observations to measurements, dertermined that oxygen is needed to burn, found and named elements, wrote textbooks, law of conservation of matter, made very precise balance, great lab and collaborated scientifically witgh peers (**Sénéchal, 2009**).

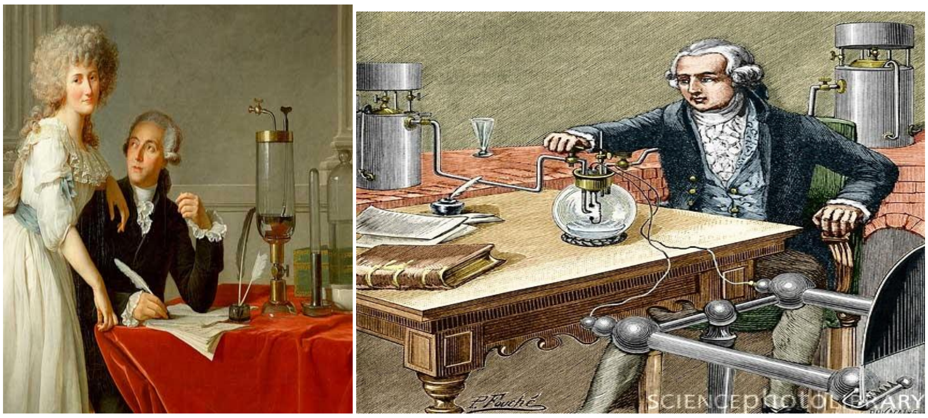


Fig. 50 : Antoine Lavoisier (herodote.net)

In 1727, Stephen Hales successfully established plant physiology as a science. He published his experiments dealing with the nutrition and respiration of plants in his publication entitled *Vegetable Staticks.* He developed techniques to measure area, mass, volume, temperature, pressure, and even gravity in plants (**Pelczar *et al.*, 2023; Richman, 2023)**.

Later part of the eighteenth century: **Joseph Priestley** laid the foundation for the chemical analysis of plant metabolism. Joseph Priestley published his works as Experiments and Observations on Different Kinds of Air in 1774 (**Rook, 1964).** The published paper demonstrated that green plants absorb “fixed air” (carbon dioxide) from the atmosphere, give off "gas" or "dephlogisticated air", which is now known as oxygen, and that this gas is essential to animal life **(Pelczar *et al.,* 2023)**.

In the middle of the 18th century the French physicist **René Antoine Ferchault de Réaumer** demonstrated that the fermenting action of stomach juices is a chemical process.

1.2. CLASSIFICATION OF SPECIES

The Linnaean system

The Swenish botanist **Carl von Linné**, is an obsessive classifier. Outside his own field of natural history he tries his hand at organizing a system of minerals and even of diseases. But his fame derives from his having finally put in place, at the end of an experimental period lasting nearly two centuries, the method of classification in the plant and animal kingdoms which still prevails today. In 1735 Linnaeus publishes Systema naturae (System of nature), in which he proposes a system capable of classifying all living things. It is based on the twin categories genus and species, pioneered by Bauhin and developed by John Ray **(Rhoads, 2007)**.

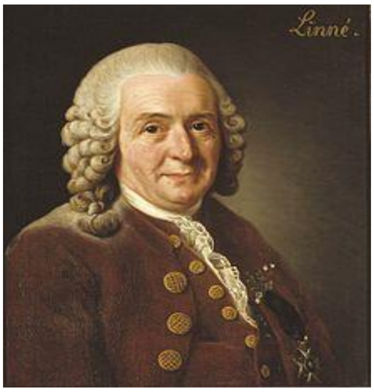


Fig. 51 : Carl von Linné (global-geography.org)

- ✓ Linnaeus tried to classify species in the "most natural way possible", mainly based on anatomical similarities.
- ✓ The hierarchy of categories is as follows, from the most specific to the most general**:** **variety or race → species→ genus→ family→ order →class →phylum → kingdom**

Fig. 52 : Systematic of *Mentha aquatica* (*inpn.mnhn.fr)*

Georges louis leclerc Buffon

Linnaeus's systematic classification is based on the principle, fundamental to him, that species and genera have an objective existence, that they are well-defined.

The French naturalist Buffon takes a contrary view by opposing even the notion of species. Buffon believes that "genus, orders, classes exist only in our imagination" and "there are only individuals in Nature".

Buffon places the human being among other animals.

Fig. 53 : Georges Louis Leclerc Buffon (alamy.com)

2. 19TH CENTURY: EMERGENCE OF BIOLOGICAL DISCIPLINES

By 1900, much of these domains overlapped, while natural history and (and its counterpart natural philosophy) had largely given way to more specialized scientific disciplines: cytology, bacteriology, morphology, embryology, geography, and geology.

Many naturalists began to reject essentialism and seriously consider the possibilities of extinction and the mutability of species. These developments, as well as the results of new fields such as embryology and paleontology, were synthesized in Darwin's theory of evolution by natural selection.

The end of the 19th century saw debates over spontaneous generation and the rise of the germ theory of disease and the fields of cytology, bacteriology and physiological chemistry, though the problem of inheritance was still a mystery.

2.1. NATURAL HISTORY AND NATURAL PHILOSOPHY

Widespread travel by naturalists in the early- to mid-nineteenth century resulted in a wealth of new information about the diversity and distribution of living organisms.

Into the 19th century, explorer-naturalists such as **Alexander von Humboldt** tried to elucidate the interactions between organisms and their environment, and the ways these relationships depend on geography - creating the foundations for biogeography, ecology and ethology.

Fig. 54 : Alexander Von Humboldt (alamy.com)

George Cuvier

founder of paleontology in the 19th century, believed in species fixism and their complete and sudden disappearances during disasters (catastrophism), after which new species are formed, either by spontaneous generation or by divine action (Cuvier does not pronounce categorically) (**Sénéchal, 2009**).

Evolution

The first to propose an evolutionary theory was Jean-Baptiste Lamarck (1744/1829); based on the inheritance of acquired characteristics (an inheritance mechanism that was widely accepted until the 20th century), it described a chain of development stretching from the lowliest microbe to humans.

Darwinism

The first is a partial explanation of evolution in his book On the Origin of Species by Means of Natural Selection. This book is extremely well documented: Darwin took 20 years to develop it. According to Ernst Mayr, Darwin's theory can be summarized in five points (**Sénéchal, 2009**):

Evolution: the world is old enough to allow the evolution of species.

Common ancestry: all species, all living organisms, have a common ancestor. The further back in time, the more we discover a kinship with many species.

The multiplication of species: a species can give birth to species that evolve differently because of geographical isolation.

Gradualism: evolution is a slow and progressive phenomenon. Natura non facit saltum (nature does not jump).

Natural selection: in an animal or plant population, the most suitable survive best, reproduce with more probability and their characters are transmitted preferably.

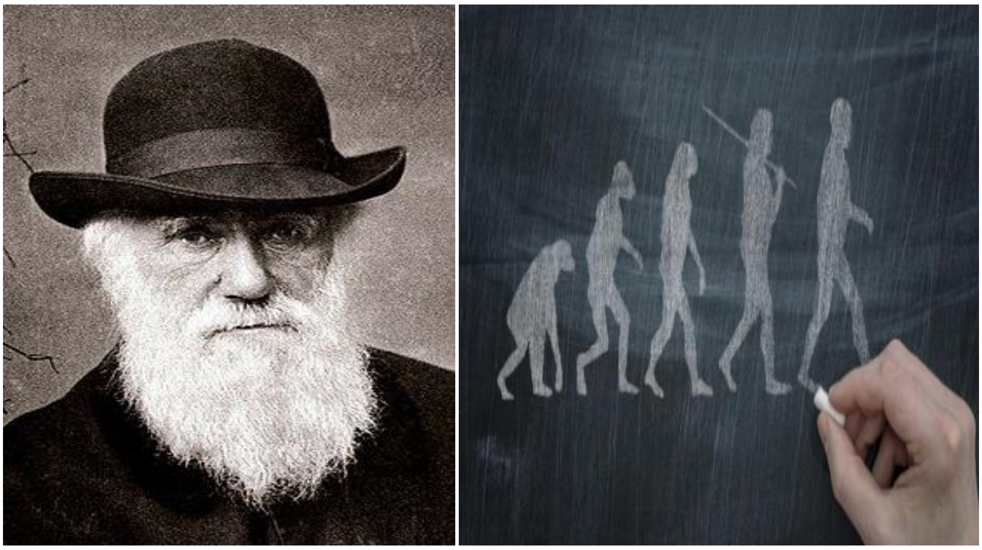


Fig. 55 : Charles Darwin (alamy.com)

In the 19th century, some, including Alfred Wallace, exaggerated the efficacity of natural selection and envied to claim that all characters must be useful, since they are the fruit of natural selection.

2.2. CELL THEORY

Robert Hooke first used the word cell while observing the cork.

In France around 1800, the autopsy allows a detailed examination of the organs, notably by Xavier Bichat (1771-1802), who identifies 21 types of tissues, thus basing the histology whose objects of study are the constituent elements of the organs.

The cell theory was developed between 1824 and 1830 by the French Turpin, Brisseau and Mirbel. But it is with the development of the achromatic microscope around 1830 by Ernst Abbe and Carl Zeiss that are formalized from 1838 the ideas of the cell theory with in particular:

Mathias Schleiden (1804/1881) discovers in 1837 that the plants are entirely formed of units which he calls cells, according to Hooke.

Two years later, his fellow zoologist Theodor Schwann (1810/1882) came to the same conclusion by observing animal tissues (**Sénéchal, 2009**).

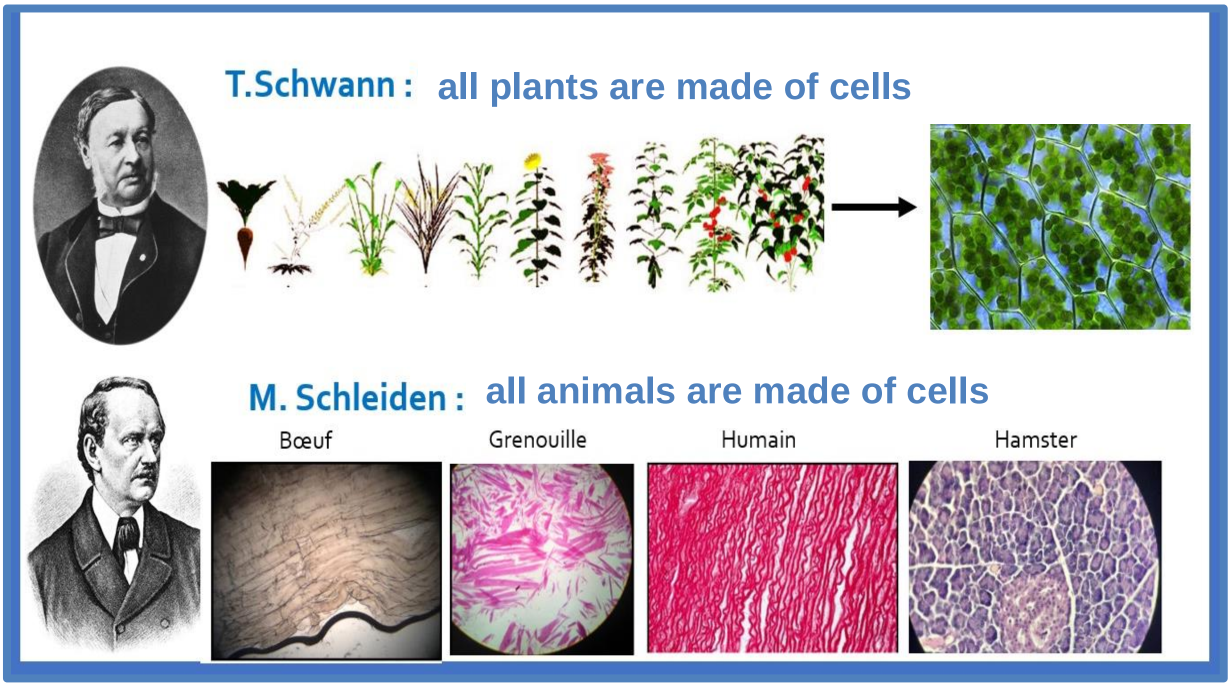


Fig. 56 : Observations of Schwann T. and Schleiden M (thibault-svt.fr)

The cell theory, according to which the cell is the atom of the living", the basic unit, is established in 1858 with the work of Rudolf Virchow (1821/1902), who believes that every cell comes from another cell (omnis cellula e cellula) and are not created by any isolated chemical process as was then thought.

Claude Bernard (1813-1878) studies the cell and its relationship with body fluids and drew upon both the cell theory and knowledge of chemistry to develop the concept of the stability of the internal bodily environment, now called homeostasis.

2.3. MICROBIOLOGY

Microbiology is a very old subject. Microbiology as a field in the biological sciences saw the light of the day because of several innovative research and experiments by pioneers in this field. The serendipitous discoveries and scientific inventions and breakthroughs of these notable microbiologists/scientists contributed immensely to making the subject/study of microbiology what it is today. The study of microbiology will be incomplete without a touch on the founding fathers of this important field of biological sciences (**Ezemba & Ezeuko, 2022**).

Several scientists/microbiologists in time past contributed tremendously to the development of microbiology; and the notable works of these famous microbiologists in time past have continued to impact and give impetus to the modern day microbiology that we now have at our hands. Though research all over the world is now going molecular and high-tech, it will be a disservice not to mention and elaborate on the serendipitous and innovative works and inventions of these legendary microbiologists whose research works and scientific findings have helped the field of microbiology to blossom to what it is today.

Microorganisms are ancient forms of life that are by and large too small to be seen with the naked eyes. The field of microbiology is exclusively dedicated to the studying and harnessing of these small forms of life which have immense impact on practically every spheres of life including plants, animals, humans and even the inanimate aspect of the earth. Microbiology which is both an applied and basic biological science demonstrates in every respect the fundamental principles that align the biological discipline, thus making it the foundation and a center-piece of the biological sciences. The study of microbiology cum microbes actually began and gained prominence with the discovery of the microscope, a metallic piece of instrument which is used to see microorganisms (**Ezemba & Ezeuko, 2022**).

The first person to postulate the existence of microorganisms was **Aristotle** in 4 B.C. He suggested that living organisms are made up of cells. It was only until 13th century when people realized that ground pieces of glass provided a greater magnifying power. They were able to see tiny objects that they could otherwise not see through their naked eyes.

Following these developments, **Roger Bacon** postulated that invisible living creatures cased diseases.

In 1530, **Fracastoro of Verona** coined the term syphilis to describe an outbreak that ravaged Europe in the 1400's when the returning French soldiers spread the disease. He called the disease agent "seminaria morbi" (living germs) that spread 'contagium vivum' (via contact with an individual with the germ). In 1658, **Athanasius Kircher** defined the invisible organisms found in decaying bodies, meat, milk, and secretions as worms.

Even before microorganisms were seen, some investigators suspected their existence and responsibility for disease. Among others, the Roman philosopher **Lucretius** (about 98–55 B.C.) and the physician **Girolamo Fracastoro** (1478–1553) suggested that disease was caused by invisible living creatures (**Ezemba & Ezeuko, 2022**).

The earliest microscopic observations appear to have been made between 1625 and 1630 on bees and weevils by the Italian **Francesco Stelluti**, using a microscope probably supplied by Galileo. **Robert Hooke** (1635-1703) was actually the first to use the microscope to view the unseen forms of life (particularly the fruiting bodies of moulds), making him the first to describe microorganisms. In 1665, the first drawing of a microorganism was published in Robert Hooke's Micrographia.

However, Antonie van Leeuwenhoek (1632-1723), who is widely regarded as the father of the field of microbiology, was actually the first microbiologist to see and describe bacteria. i.e To experiment on microscopic organisms (for example, bacteria). Beginning in 1673, Leeuwenhoek sent detailed letters describing his discoveries to the Royal Society of London. It is clear from his descriptions that he saw both bacteria and protozoa. Therefore, the development of microbiology as a biological science depended on the availability of the microscopes in addition to the ability of microbiologists to isolate and grow pure forms or cultures of microorganisms in vitro and in vivo.

There is plethora of microscopes today ranging from simple light microscopes to even complex electron microscopes that give better perspectives about the microbial world. These pieces of equipment allow microbiologists to gain better understanding of microbial cells at the cellular and molecular level.

As important as Leeuwenhoek's observations were the development of microbiology essentially languished for the next 200 years. Little progress was made primarily because microscopic observations of microorganisms do not provide sufficient information to understand their biology.

For the discipline to develop, techniques for isolating and culturing microbes in the laboratory were needed. Many of these techniques began to be developed as scientists grappled with the conflict over the Theory of Spontaneous Generation. This conflict and the subsequent studies on the role played by microorganisms in causing disease ultimately led to what is now called the Golden Age of Microbiology (**Ezemba & Ezeuko, 2022**).

Fig. 57 : Microbiologists of Transition Era (Sreenivas, 2023)

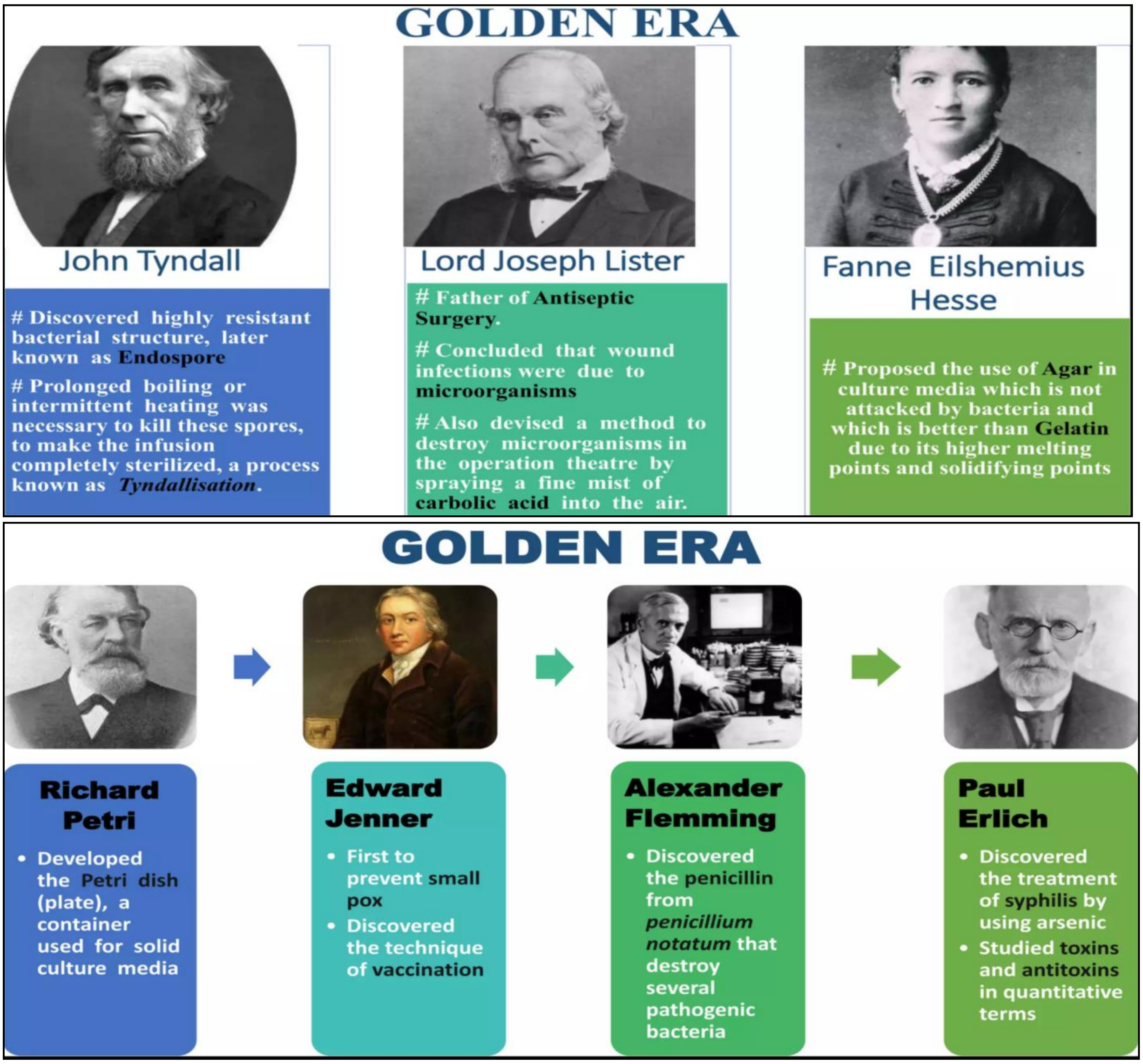


Fig. 58 : Microbiologists of Golden Era (Sreenivas, 2023)

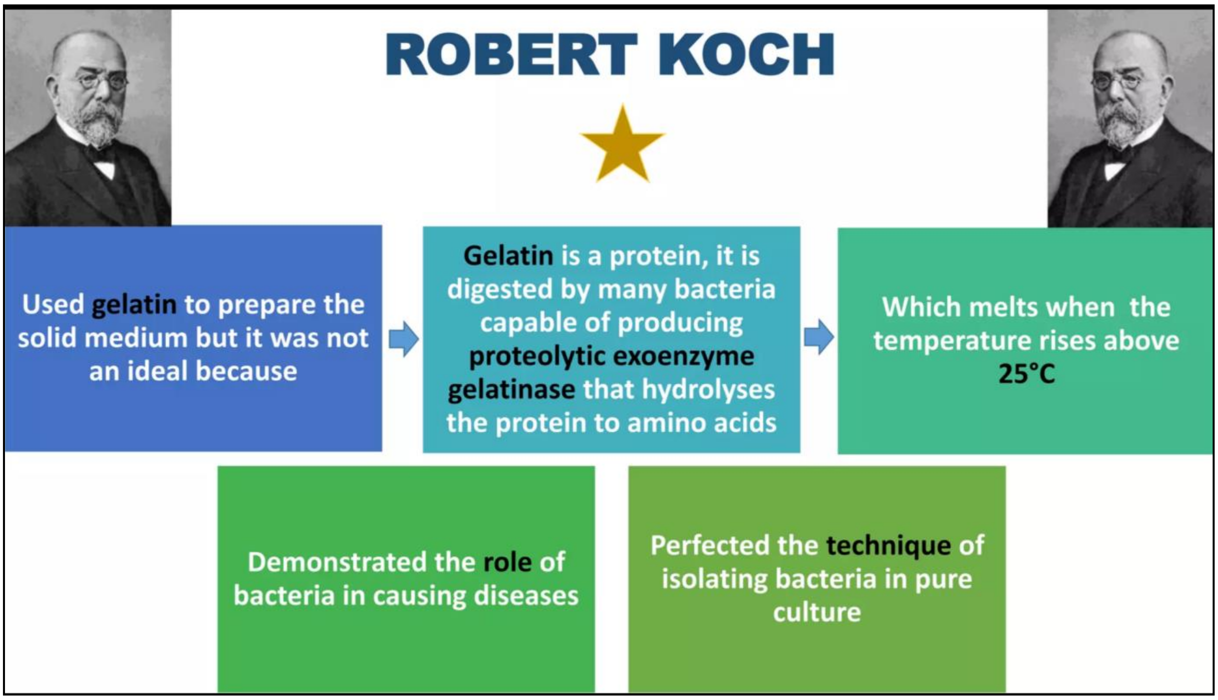


Fig. 59 : Works of Louis Pasteur and Robert Koch (Sreenivas, 2023)

Table 1: Modern era, nobel laureates (Sreenivas, 2023)

YEARS	NOBEL LAUREATES	CONTRIBUTION
1901	VON BEHRING	DIPTH ANTITOX
1902	RONALD ROSS	MALARIA
1905	ROBERT KOCH	TB
1908	METCHNIKOFF	PHAGOCYTOSIS
1945	FLEMMING	PENICILLIN
1962	WATSON & CRICK	STRUCTURE DNA
1968	HOLLEY & KHORANA	GENETIC CODES
1997	PRUISNER	PRIONS
2001	BRENNER,HERVITZ	GENETIC REGULATION OF ORGAN DEVELOPMENT & CELL DEATH

2.4.EMBRYOLOGY, FECONDATION, MULTIPLICATION

Charle Bonnet (1720-1793) discovered the parthenogenesis of aphids.

In 1759, caspar Friederich Wolff negates the efforts of preformationists by showing under microscope the gradual formation of organs during the development of the chicken embryo.

Lazarro Spallanzani carries out the fertilization of frog eggs and the artificial insemination of a dog. He also claims that air is at the origin of life. Hypothesis dismantled by Franz Schultze (born 1815).

the German physician Caspar Friedrick Wolff; and the Prussian-Estonian scientist Karl Ernst, Ritter von Baer, who proved epigenesis with his discovery of the mammalian ovum (egg) in 1827. Other pioneers were the French scientists Pierre Belon and Marie-François-Xavier Bichat.

Decisive arguments were made towards the end of the century by embryologists who, after having demolished the theory of the preformation of the fetus, highlighted the role played by sperm (Oskar Hertwig and Hermann Fol in 1876) in the egg development process.

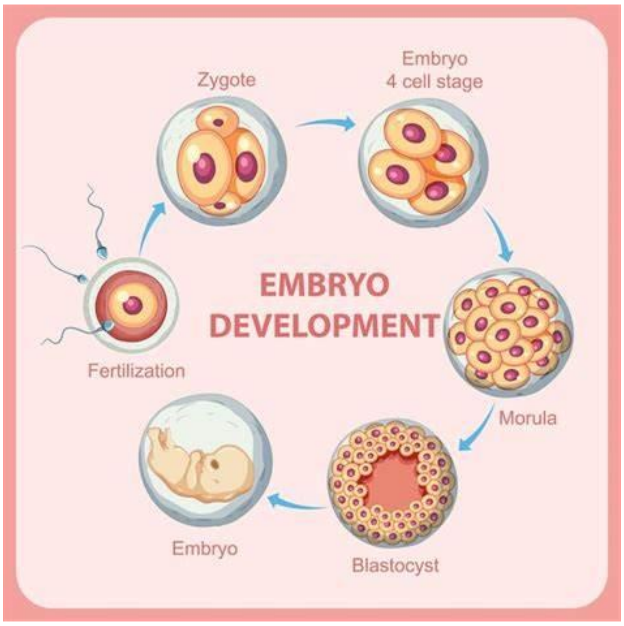


Fig. 60 : Formation of Zygote During Embryo Development (collegedunia.com)

The cytologist **Walther Flemming** in 1882 was the first to demonstrate that the discrete stages of mitosis for animals were not an artifact of staining, but occurred in living cells, and moreover, that chromosomes doubled in number just before the cell divided and a daughter cell was produced. **Eduard Strasburger** (1844/1912) also demonstrate mitosis in plants.

In 1887 **August Weismann** proposed that the chromosome number must then be halved in the case of the sexual cells, the gametes. This was shortly proved to be the case and the process of meiosis began to be understood. In 1891, **Henking** discovered chromosome X.

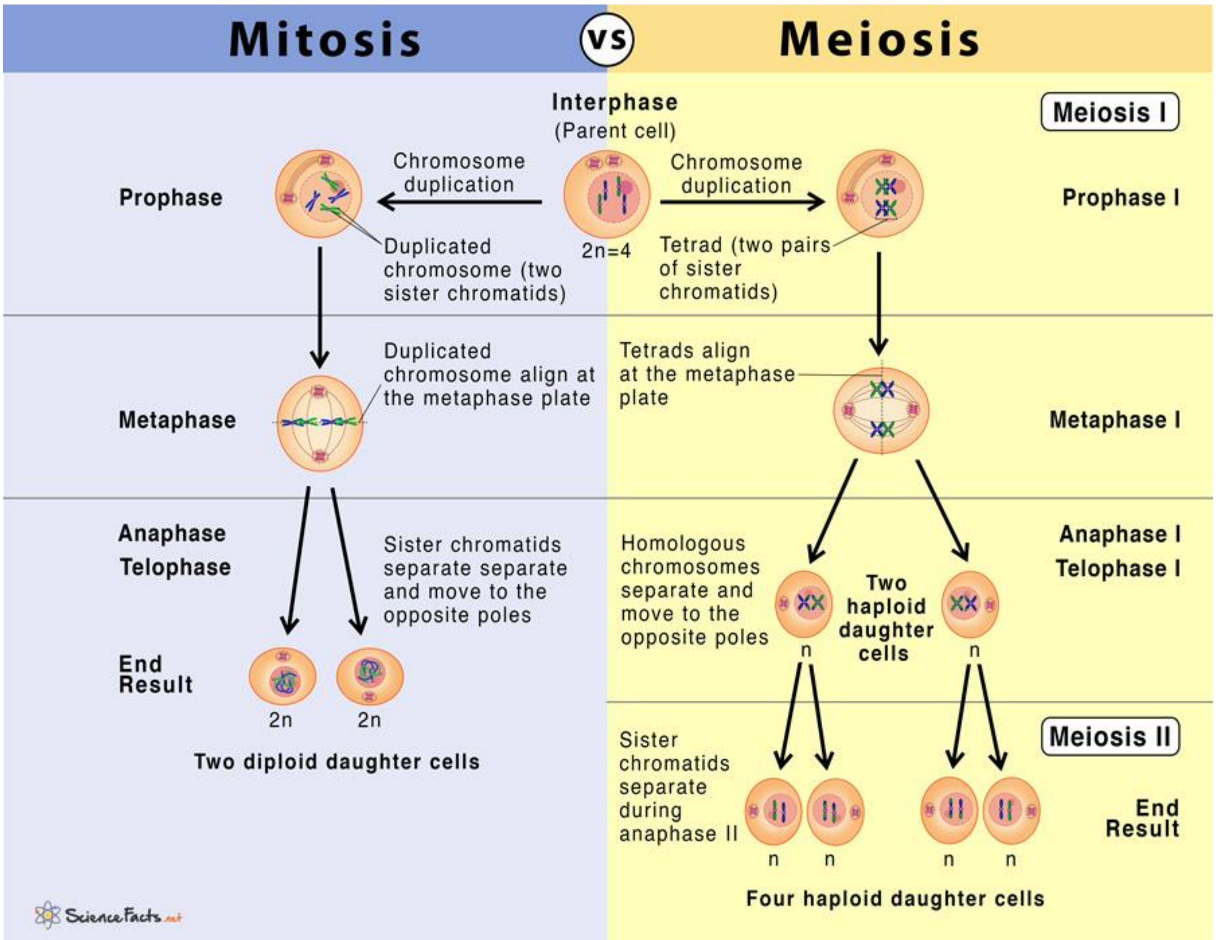


Fig. 61 : Mitosis VS Meiosis (Sciencefacts.net)

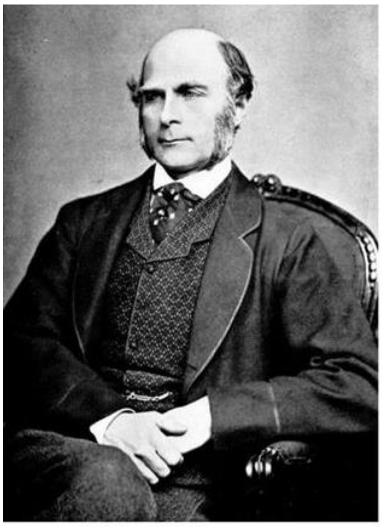
2.5.HEREDITY AND DEVELOPMENT

Francis Galton: Pioneer of heredity and biometry

The study of scientific study of heredity grew rapidly in the wake of Darwin's On the Origin of Species (1859) with the work of Francis Galton.

Galton believe that evolution of human could not proceed by the small steps envisioned by Darwin, but must proceed by discontinuous changes. Galton's book Natural Inheritance (1889)

Francis Galton was the founder of the statistical approach to heredity, now commonly called the "**biometric approach**" and first to study **fingerprints** and classify them for filing (**Gillham, 2015**).



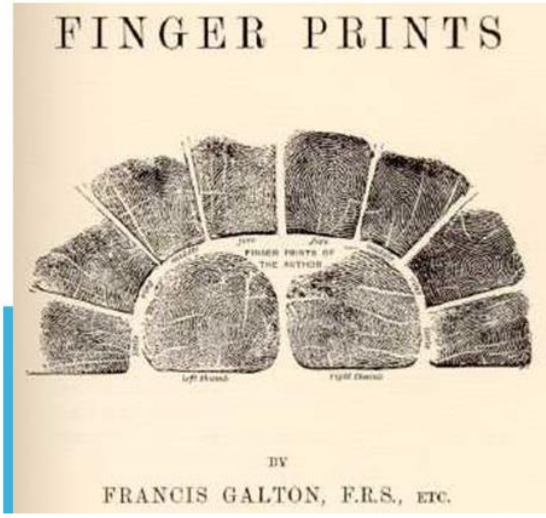


Fig. 62 : Francis Galton and fingerprints (galton.org)

Gregor Mendel

The origin of genetics is usually traced to the 1866 work of the Austrian monk Gregor Mendel, who in the years 1850-1860 made a series of experiments on the heredity of plants (The pea), distinguish recessive and dominant hereditary characters. It should be noted that, for Mendel as for his rediscoverers, the notion of gene is abstract and does not correspond to any identified physical object. One can only imagine that "something" is passed on from one generation to the next, without knowing exactly what it is.

Gregor Mendel specifically chose pea plants for a number of reasons including their availability in various varieties, self-pollination capabilities, short life cycles, ease of cultivation, and distinct characteristics. Mendel focused on studying seven specific traits in pea plants: seed shape, seed color, flower color, pod shape, pod color, flower position, and stem height.

Mendel conducted two main experiments, monohybrid and dihybrid crosses, to determine the laws of inheritance (**Tamang, 2023**).

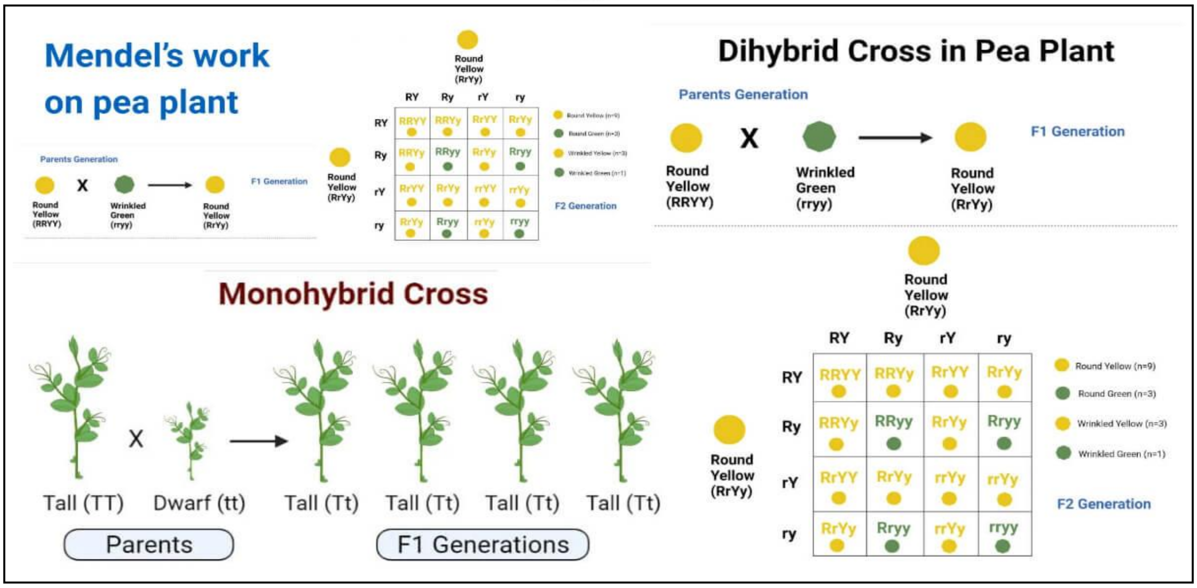


Fig. 63 : Mendel's experiments on the heredity of pea (microbenotes.com)

Ernst Haeckel

Embryology and ecology also became central biological fields, especially as linked to evolution and popularized in the work of Ernst Haeckel : General morphology, 1866, the book contains the first occurrence of the word «ecology» ; History of the creation of beings organized according to natural laws, 1868.

Schematically, Haeckel simply proposes an adaptation of the pre-existing classifications, with some modifications, in the form of «family trees» that we would now call phylogenetic trees (**Levit & Hossfeld, 2019**).

Fig. 64 : "Art Forms of Nature", The Ernst Haeckel Collection (Flickr.com)

TWENTIETH AND TWENTY-FIRST CENTURIES

VII. TWENTIETH AND TWENTY-FIRST CENTURIES

In the early 20th century, the rediscovery of Mendel's work led to the rapid development of genetics by Thomas Hunt Morgan and his students, and by the 1930s the combination of population genetics and natural selection led to the "neo-Darwinian synthesis" and the rise of the discipline of evolutionary biology.

New biological disciplines developed rapidly, especially after Watson and Crick discovered the structure of DNA in 1953. Following the cracking of the genetic code and the establishment of the Central Dogma, biology has largely split between : organism biology: consisting of ecology, ethology, systematics, paleontology, evolutionary biology, developmental biology, and other disciplines that deal with whole organisms molecular biology: including cell biology, biophysics, biochemistry, neuroscience, immunology, and many other overlapping subjects.

1. ELECTRON MICROSCOPE

The first prototype electron microscope was built in 1931 by Ernst Ruska and Max Knoll.

Two years later, Russjai built an electron microscope that exceeded the possible resolution of an optical microscope. Reinhold Rudenberg, the scientific director of Siemens, patented the electron microscope in 1931. Siemens produced the first electron microscope marketed in 1938. The first American electron microscope was built at the University of Toronto in 1938 by Eli Franklin Burton and students Cecil Hall, James Hillier and Albert Prebus. The first transmission electron microscope was built by Siemens in 1939. A high-resolution electron microscope was only possible after Hillier invented the stigma in 1946 (**Smith, 2018**).

Fig. 65 : Electron microscope (uts.edu.au)

2. GENETIC

A prerequisite for the rise of genetics in the 20th century was the abandonment of the idea of heredity of acquired traits, proposed by Lamarck and even accepted by Darwin. Once this idea is set aside, all characters are considered inherited from parents and studying characters over several generations can teach us something important. The early 20th century saw the rapid development of the chromosome theory of heredity, according to which genes are physically located on specific sections of chromosomes in the cell nucleus. In 1906, the Englishman W. Bateson introduced the word genetic to designate precisely the study of the transmission of characters (**Sénéchal, 2009**).

2.1.Gene location

In 1903, the American Walter Sutton (1877/1916) shows that Mendel's factors could be chromosomes. The American Thomas Hunt Morgan (1866/1945) and his large team of collaborators will carry out a series of researches confiring the chromosomal theory of heredity and even allowing to confirm that chromosomes are a sequential assembly of genes. Morgan discovered in 1909 that certain factors (or characters) were linked to the sexual chromosome (X or Y).

In 1911, Morgan published his theory of stepping (cross-over), according to which the two homologous chromosomes can exchange some of their segments during meiosis.

From 1910 to 1922, Morgan and his team were able to pinpoint hundreds of genes along the chromosomes of Drosophila by studying different degrees of genetic linkage (**Sénéchal, 2009**).

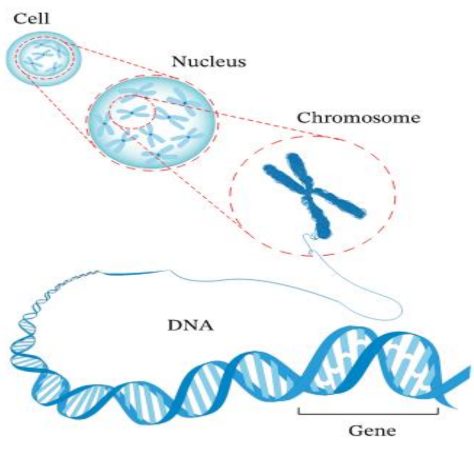


Fig. 66 : Gene location **(nagwa.com)**

2.2.Genetic mutations

The Dutchman Hugo de Vries (1848/1935), is best known for the discovery of the phenomenon of sudden genetic mutation in animals and plants.

Mutation is a change in a character that suddenly appears, without this character being present in previous generations, change subsequently transmitted to descendants.

In 1926, H.J. Muller, one of Morgan's collaborators, showed that exposure to X-rays increased the probability of mutation. It will later be discovered that not only radiation, but also certain chemical compounds can cause mutations. Most mutations render part of the cell's metabolism inoperative (**Sénéchal, 2009**).

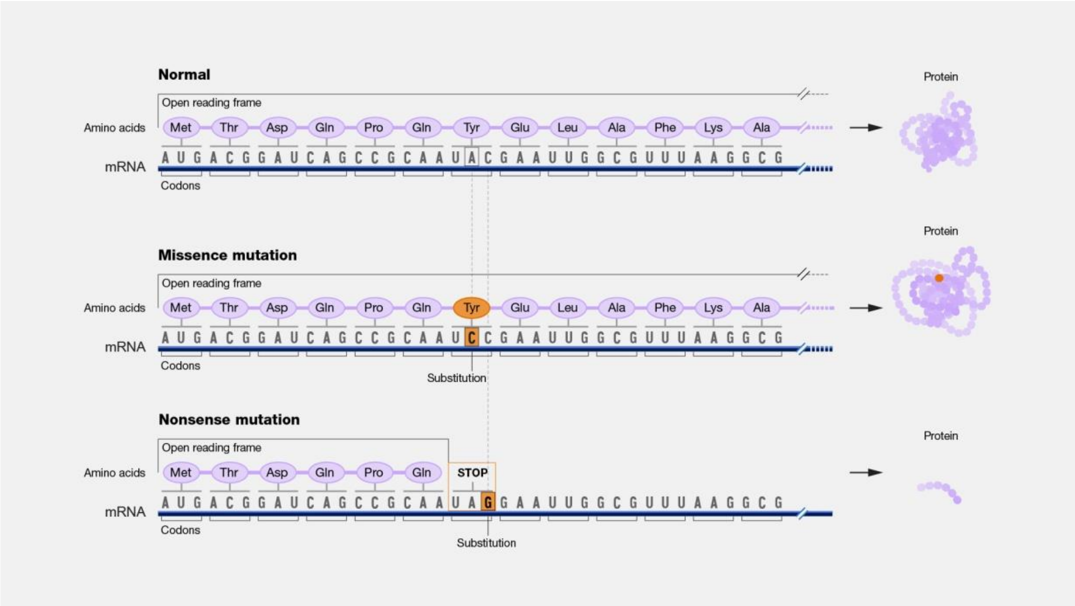


Fig. 67 : Genetic mutations (genome.gov)

2.3.Structure of ADN

In 1869, Friedrich Miescher isolated the chemical substance from which the nucleus is mainly constituted and called it nuclein.

Later, we will distinguish chemical varieties of this substance: deoxyribonucleic acid (DNA) and ribonucleic acid (RNA), without knowing its functions.

It was only in 1944 that Oswald T. Avery, C. Macloed and Mr. McCarty concluded that it is DNA that carries the genes, they also showed that injecting DNA with a bacterium can change its genetic type (**Sénéchal, 2009**).

One of the experiments leading to this conclusion had already been carried out in 1926 by the British geneticist Fred Griffiths. A more decisive experiment took place in 1952.

American biologists Alfred Hershey and Martha Chase marked a virion – the infectious part of a virus, made up of protein-covered DNA – with a radioactive isotope. To track DNA replication. In short, he showed that it was the DNA of the virion that was physically transferred to the bacterium and that caused its metabolism to change (**Sénéchal, 2009**).

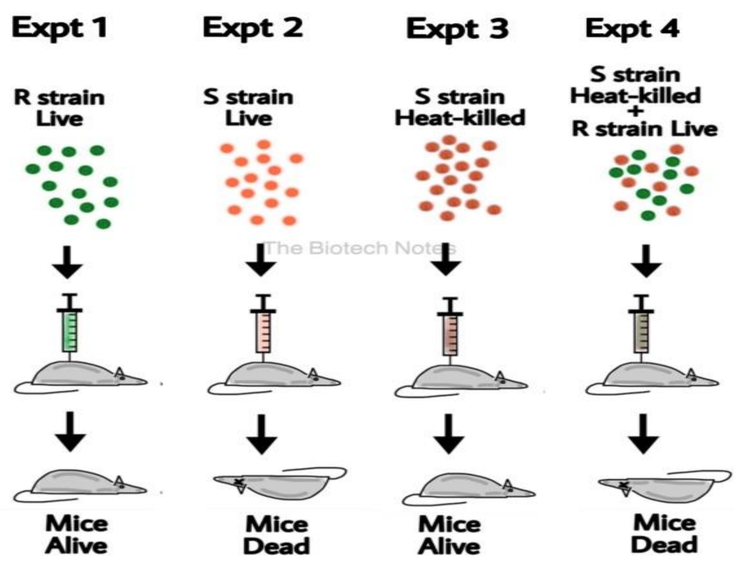


Fig. 68 : Fred Griffiths experiments

2.4.Double helix

It was known by chemical analysis that DNA was composed, in addition to phosphate and deoxyribose, of four bases or nucleotides: adenine (A), cytosine (C), guanine (G) and thymine (T). The so-called puric bases (A and G) are complementary to pyrimidic bases (C and T). Erwin Chargaff showed in 1950 that the concentrations [A] and [T] were identical, like the concentrations [G] and [C].

On the other hand, the DNA molecule had been isolated, crystallized and studied by X-ray difraction. This method, discovered by the physicists W.H. Bragg and W.L Bragg in 1912, was gradually developed to the point of recognizing the spatial structure of complex molecules (**Sénéchal, 2009**).

Indeed, in 1960, X-ray analysis, is generalized under the impulse of Max perutz which determines the three-dimensional structure of hemoglobin. W.L. Bragg founded a molecular biology laboratory in Cambridge where the structures of many proteins were discovered.

An important part of the DNA mystery was lifted by James Watson and Francis Crick in 1953, discovering the double helix structure wrapped around each other in DNA (**Sénéchal, 2009**).

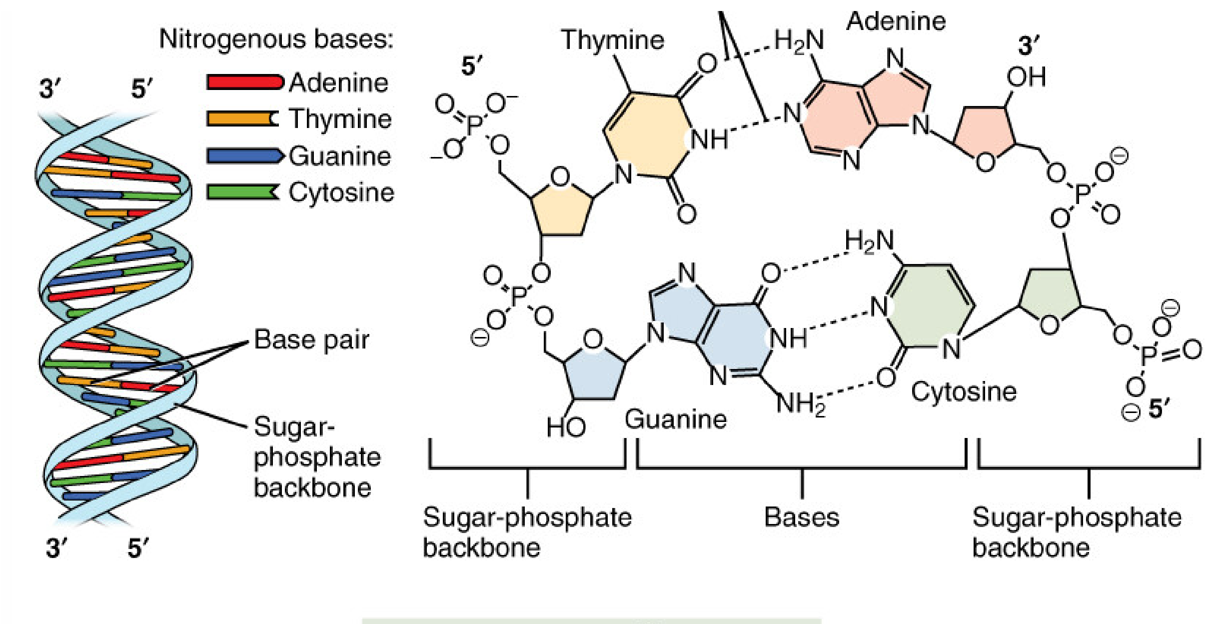


Fig. 69 : Double helix structure of DNA (storymd.com)

2.5.The genetic code and protein synthesis

It has gradually become apparent, especially since the experiments of Beadle et al., that each gene actually contains the information needed to make a specific protein.

Gene expression mechanisms are determined by François Jacob, André Lwoff and Jacques Monod. Indeed, their fundamental discovery is that information related to protein synthesis is transcribed from DNA onto an mRNA molecule (RNA-messenger). This transcription process is continuously followed during metabolism through the RNA-polymerase enzyme (**Sénéchal, 2009**).

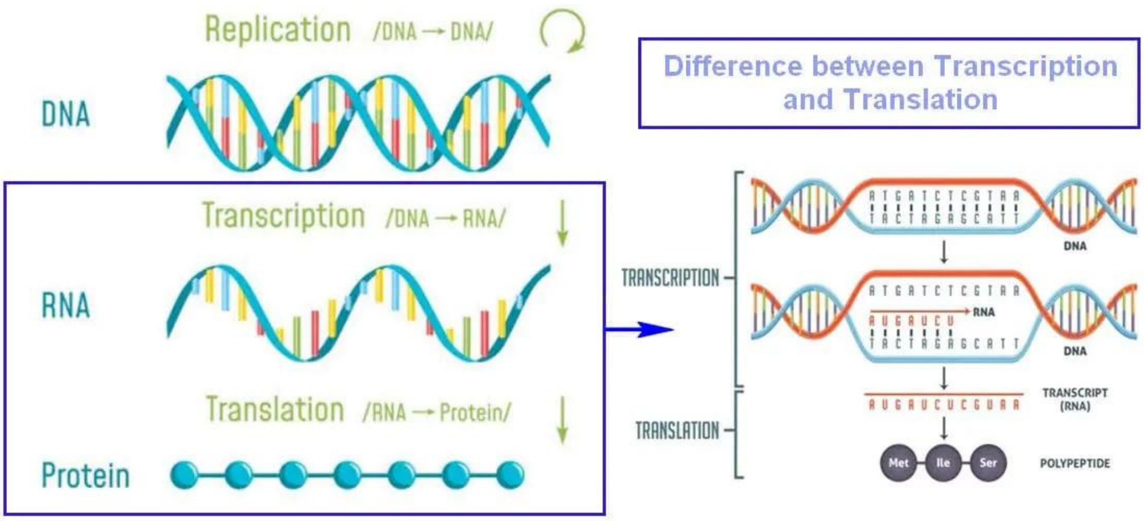


Fig. 70 : Transcription and Translation (technologynetworks.com)

3. THE REFORM OF DARWINISM

In the 1920s and 1930s a synthesis of Darwinism and more recent discoveries of genetics was formed. Darwin gives no mechanism for the variability of characters within a population. However, since the work of the Dutchman Hugo de Vries (1848/1935) and the American Thomas Hunt Morgan (1866/1945), we know that fortuitous changes of character, called mutations, can occur from one generation to another. These incidental mutations, in addition to the mixing of genes related to sexual reproduction, would cause random variability within a population and natural selection would serve as a guide to the evolution of the genetic heritage of this population. This 'updated' version of Darwinism is called **the synthetic theory of evolution or neo-darwinism (Sénéchal, 2009).**

4. EVOLUTION AND PHYLOGENETIC CLASSIFICATION

New theoretical and experimental approaches have allowed the recent explosion of research on evolution and classification, leading to the classification we know today as phylogenetic classification. This classification, whose bases were laid by the German entomologist Willi Hennig (1913-1976) is based on the principle of grouping organisms that derive from the same common ancestor according to the characteristics they share rather than the absence of shared characteristics, a principle once favoured by scientists.

The contemporary era: the contributions of genetics

Subsequently, the rise of molecular biology and the improvement of sequencing techniques allowed to deepen the theories in place and refine the different classifications.

In 1962, the American biochemist Linus Pauling (1901-1994) and the Austro-American biologist Emile Zuckerkandl (1922-2013) propose a hypothesis that genetic mutations in species accumulate at a constant rate over time, thus allowing to calculate when two species diverged. As a result, the use of genetic data is seeing a new way of classifying. From now on, science will be based on a method of genetic similarity providing a refinement of the classification of species. Thus, thanks to the studies of the French zoologist and marine biologist Édouard Chatton (1883-1947), living organisms were divided into two major groups: Prokaryotes (bacteria and archaea) and Eukaryotes (organisms with nucleus cells).

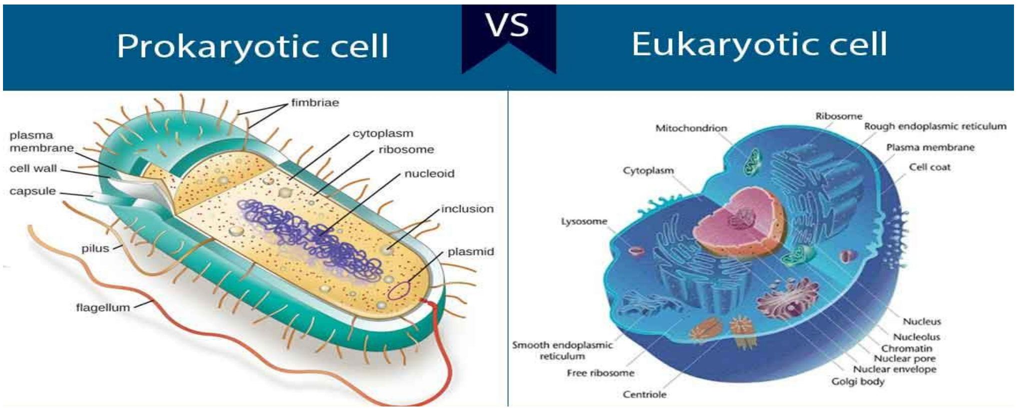


Fig. 71 : Prokaryotes VS Eukaryotes organisms (sciencefacts.net)

A little later, the American ecologist and botanist **Robert Harding Whittaker** (1920-1980), proposes to group the **fungi** until considered as plants into a separate kingdom and thereby classifies the world of life into five groups:

- **Protista (Protiste, unicellular organism)**
- **Monera (Monère, bacteria)**
- **Fungi**
- **Plantate**
- **Animalia**

In 1977, the American microbiologist **Carl Richard Woese** (1928-2012) developed a phylogenetic analysis technique that allowed him to discover a new field: **the Archaea, procaryotic unicellular microorganisms, but which, unlike bacteria, have no organelles**.

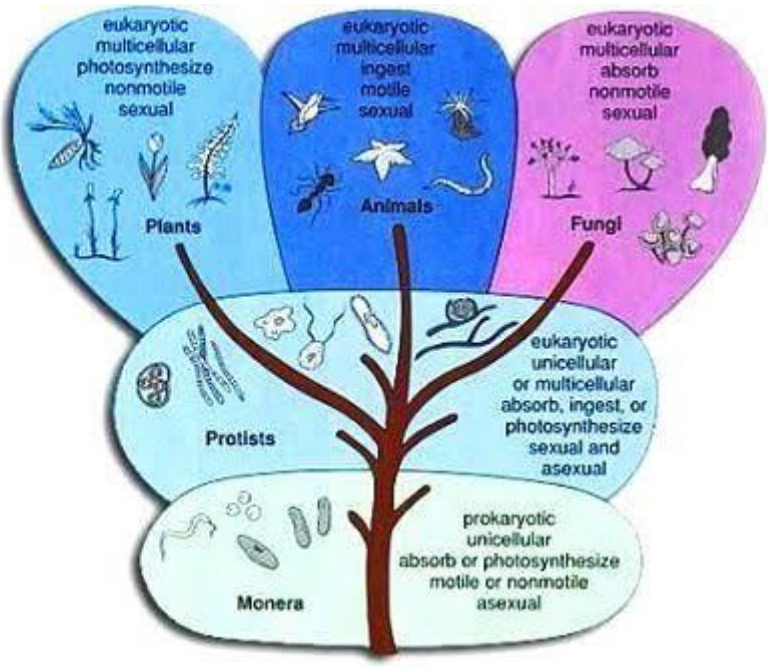


Fig. 72 : Classification system of Robert Harding Whittaker (dobggc.blogspot.com)

5. BIOCHEMISTRY

Frederick Gowland Hopkins (1861-1947) discovered that amino acids, essential for the body, cannot be synthesized there and must be provided by the diet (vitamins).

From 1890 to 1925, the nature and role of enzymes were explored, with von Liebig and Wohler in particular, and until 1960, researchers were particularly interested in their structure.

Wöhler showed In 1828 that organic molecules, such as urea, can be created by synthetic means that do not involve life, and thus provided a powerful argument against vitalism. The first enzyme, diastase, was described in 1833, and scientists began to explore connections between chemistry and biology. In 1847, the process of photosynthesis was first elucidated by Mayer. However, the exact and detailed mechanism remained a mystery until 1862.

In 1925, Theodor developed the ultracentrifuge to measure the molecular weights of proteins, revolutionizing the discipline. In 1940, the chromatography discovered in 1906 by Mickael Tswett was used. In the mid-1940s, the theory of Linus Pauling (1901-1994) and Robert Corey, proposed in the 1930s, was verified, according to which proteins are wound on themselves in the shape of a helix. By the end of the 19th century all of the major pathways of drug metabolism had been discovered (**Vennesland & Stotz, 2023**).

In the early decades of the twentieth century the role of minor components of foods in human nutrition, the vitamins, began to be isolated and synthesized. Then in the 1920s and 1930s the metabolic pathways of life, such as the citric acid cycle and glycolysis, finally began to be worked out by biochemists. This work continued to be very actively pursued for the rest of the century and into the next. During 1939-1941 Fritz Lipmann showed that ATP is the universal carrier of energy in the cell and then in the mid-1950s the power generators of the cell, the mitochondria, also began to be understood (**Vennesland & Stotz, 2023**).

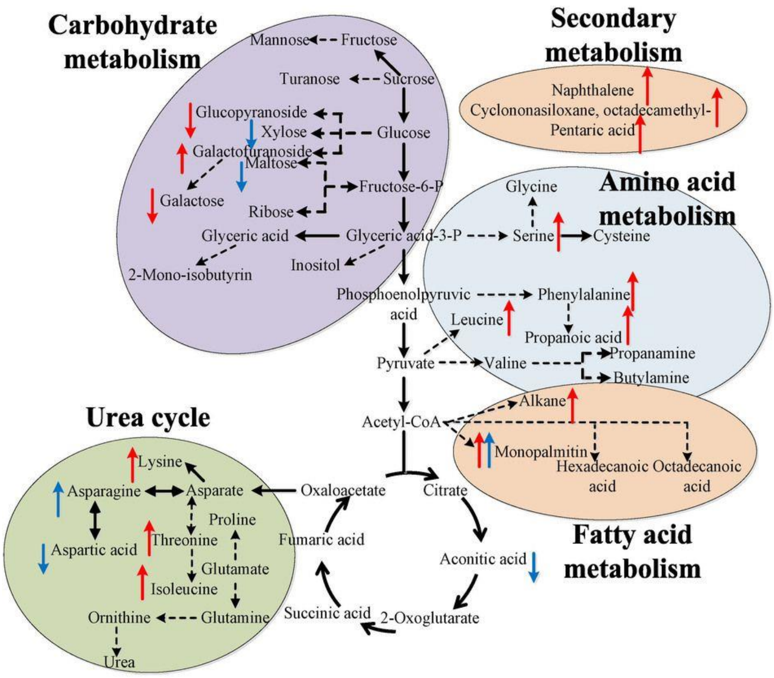


Fig. 73 : Metabolic pathways of life (vrogue.co)

6. CLONING

Cloning is the identical reproduction of a cell or living organism, one of its parts or one of its genes. Cloning mainly refers to two processes. It is on the one hand the natural or artificial identical multiplication of a living being, which is to say with exact preservation of the same genome for all the descendants (clones). It is also the induced multiplication of a fragment of DNA via a microorganism (**Rugnetta, 2024**).

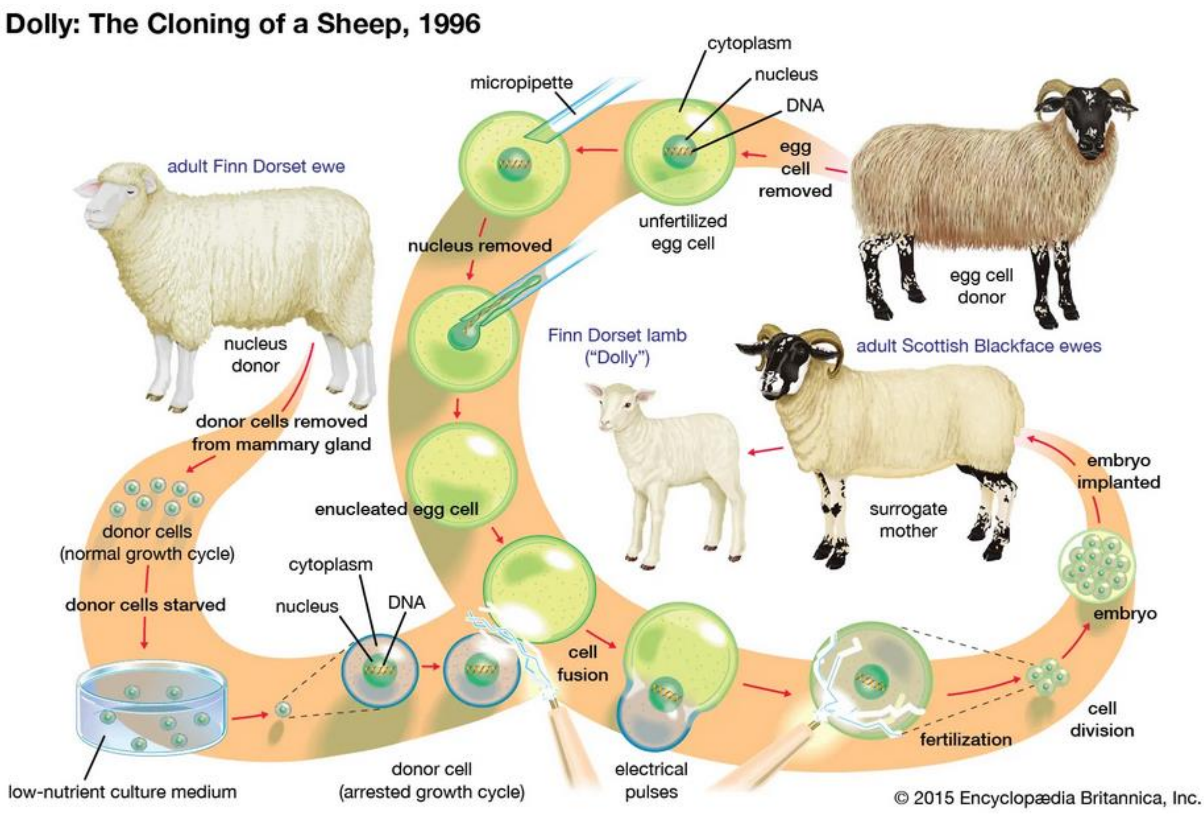


Fig. 74 : Birth of Dolly, the sheep cloned from a mammary gland cell (encyclopedia Britannica.com)

Table 2 : Timeline of cloning history (***infoplease.com)***

1903	**Appearance of the word «clone»**	Botanist H.J. Webber.
1935	**First evocation of a core transfer**	Nobel Prize in Physiology and Medicine Hans Spemann
1939	**Artificial parthenogenesis initiated in the rabbit**	The work of Pinkus and Shapiro
1952	**Cloning of frogs by embryo cell nucleus transfer**	Americans Robert Briggs and T.J. Kings
1962	**Cloning of frogs by transfer of nucleus of adult cells**	British biologist J.B. Gurdon
1963	**Cloning of carp by nucleus transfer of differentiated cells**	Chinese embryologist Tong Dizhou
1970	**Gurdon reproduces his experience of cloning a frog by transferring differentiated nuclei**	J.B. Gurdon
1979	**First attempt at human cloning**	The American L.B. Shettles

1981	**Attempt to clone mice by embryo cell nucleus transfer**	German Karl Illmense and American Peter Hope
1984	**Cloning a sheep by separating the cells of an embryo**	The English Steen Willadsen
1994	**Four calves cloned by separation of cells from an embryo**	Dr Neal from the University of Wisconsin
	New human test on non-viable embryos	American Robert Stillman
	First laws of bioethics	The French Parliament adopts a bill on bioethics, which condemns in particular human reproductive cloning.
1996	**Birth of Dolly, the sheep cloned from a mammary gland cell**	Ian Wilmut and his team from the Roslin Institute, Scotland,
1997	**Birth of Polly, cloned and transgenic sheep**	Ian Wilmut and his team
	Birth of two cloned rhesus monkeys	Don Wolf's team in Oregon,
1998	**Birth of Marguerite, the first cloned French cow**	Marguerite, the first cloned French cow, was born on a INRA farm.
	First mouse clones	The team of Dr Yanagimachi of the university
1999	**New essay on man**	Korean researchers
2000	**First clones of pigs**	The first pig clones are obtained in March 2000 There are 5, Millie, Christa, Alexis, Cassel and Dotcom represent a hope for xenografts.
	Obtaining a monkey clone by embryo splitting	American scientists from the Oregon Regional Primatology Centre
	Birth of Starbuck II, first cloned bull.	teams from the Faculty of Veterinary Medicine of the Université de Montréal and the alliance Boviteq inc.
2001	**First cloned transgenic pigs**	PLL Therapeutics
	New attempt in humans	Advanced Cell Technology
	Birth of Copy Cat, first cat clone	In Texas, Max Westhusin and his team
	Cloning of the first endangered species	in the laboratories of Trans Ova Genetics
	Cloning of bulls	Professor Lawrence Smith,
2002	**Announcement of the first human clone by the Raelian sect.**	
	INRA announces the birth of 6 young rabbits by cloning	Jean-Paul Renard's team at INRA
2003	**Draft revision of bioethics laws**	The draft revision of the bioethics laws was adopted at first reading in the Senate in January and voted at second reading in the National Assembly in December.
	Birth of Fut heifer, Africa's first	Born in South Africa, it is the first cloned animal in

	cloned animal	Africa.
	Birth of the foal Prometheus, first cloned horse first cloned animal carried by its genetic mother	Italian born
	Birth of three cloned mules	
	Cloning of a deer	
	First successful cloning of a rat	laboratory of Dr Renard at INRA in Jouy-en-Josas in collaboration with the company genOway.
	Death of the Dolly sheep	
2004	**Cloning a commercial cat**	Genetic Savings and Clone
	Adoption of the bioethics bill	The senate voted in second reading the law on bioethics of August 6, 2004 which prohibits therapeutic and reproductive cloning in France but makes possible research on supernumerary embryos.
2005	**Cloning a fruit fly**	Vett Loyd and Andrew Haig of Dalhousie University in Halifax
	Cloning of a dog	the highly controversial Professor Hwang. These results have been confirmed by independent studies conducted notably by the NIH (National Institutes of Health)
2007	**First cloning of a primate**	The American team of Shoukhrat Mitalipov from the University of Oregon
2008	**Obtaining the first human blastocysts by cloning;**	At Jolla, in the United States, the companies Stemagen corp and the Reproductive Sciences Center

7. GENE THERAPY

Gene therapy uses nucleic acids (DNA or RNA) to treat or prevent diseases. Depending on the pathology, this objective can be achieved by delivering to the cells a functional gene that replaces the defective gene at the origin of the disease (transgene), a gene with therapeutic action, or RNA capable of regulating or partially blocking the expression of an altered gene **(Galy, 2017)**.

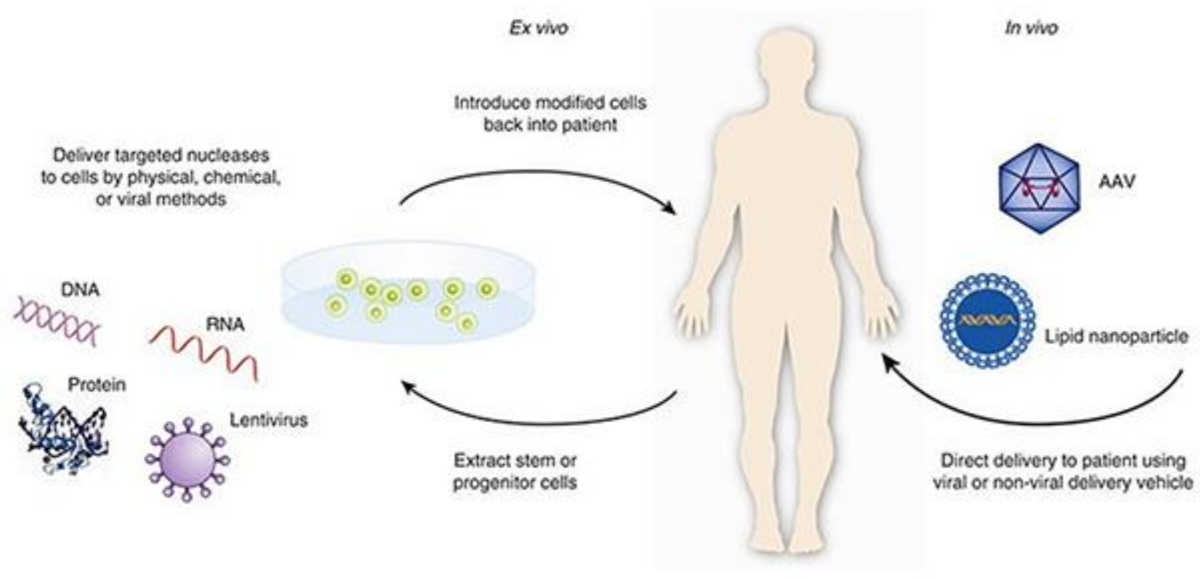


Fig. 75 : Gene therapy (fda.gov)

Historical :

The concept of **gene therapy dates back to the 1950s but it really materialized in the 1990s**, with the first trials conducted in humans. In 1990, the American Steven Rosenberg tried a first trial of gene therapy in humans, a trial based on the injection of genetically modified T lymphocytes in cancer patients. The beginning of a great adventure. After a **Milanese team** attempted the first genetic stem cell transplant in immunocompromised patients in 1995.

The first reproducible therapeutic victories in children with severe combined immunodeficiencies (SCID X1 and ADA-SCID) were not seen until the 2000s. A first trial is carried out in Paris by **the teams of Salima Hacein-Bey Abina, Marina Cavazzana and Alain Fischer** (Inserm 768 unit, Necker hospital), others in Milan and London: doctors collect immune stem cells from children's bone marrow, genetically modify them with a vector carrying a copy of the therapeutic gene, and then re-inject them into the bloodstream of patients. If more than ten years after the pioneer trial, eight of the nine «bubble children» treated in France are alive and follow a normal schooling, the success of this world premiere is marred by the occurrence of leukemia in several treated children

Trials conducted between 2007 and 2013 show that gene transfer therapy stops the progression of these progressive diseases. **The French teams**, notably attached to Inserm, are often pioneers in this field **(Galy, 2017)**.

An integrated clinical investigation centre for biotherapy is established at **Necker Hospital (Paris).** By collaborating with this structure, **Nathalie Cartier and Patrick Aubourg** showed for the first time the possibility of stopping by gene therapy, in some patients, the evolution of a neurodegenerative disease: adrenoleukodystrophy.

A treatment developed by **the teams of Philippe Leboulch and the investigation clinic Center 1416** has also allowed a patient with beta-thalassemia to interrupt his weekly blood transfusions for five years now.

To date, more than **1,800 gene therapy trials are underway**, including 65% in cancer, 10% in cardiovascular, 10% in monogenic diseases (where the results are often the most spectacular) and the rest in other very varied indications such as infectiology (tetanus, AIDS), neurodegenerative diseases (Alzheimer's, Parkinson's, multiple sclerosis, etc.) or ophthalmology (retinitis pigmentosa, glaucoma, age-related macular degeneration, etc.) **(Galy, 2017)**.

Despite this profusion, only **few gene therapy drugs are currently available**:

- **Gencidine**, intended for the treatment of neck and head tumors, has been marketed in China since 2004.
- **Oncorine** Released in China in 2005. It is used in combination with chemotherapy for the treatment of refractory nasopharyngeal cancers.
- **Glybera** has been available in Europe since late 2012, to treat a hereditary lipoprotein lipase deficiency.
- **Imlygic** in 2015 in the United States and Europe, It is indicated in adults with non resectable melanoma.
- **Strimvelis:** It was approved in Europe in 2016. Indicated in ADA-SCID,
- **Zalmoxis:** Indicated against bone marrow transplant rejection since 2016 in Europe
- **Kymriah and Yescarta:** Approved in 2017 in the United States,) to treat resistant forms of acute B-cell lymphoma.
- **Luxturna** : indicated in retinal dystrophy linked to the RPE65 mutation. It was approved in the United States in late 2017 **(Galy, 2017)**.

8. HUMAN GENOME PROJECT

The largest, most costly single biological study ever undertaken, the Human genome project began in 1988 under the leadership of James Watson, and a first draft of the human DNA sequence was announced in 2000. By 2003 99% of the genome had been sequenced to an accuracy of one part in ten thousand.

The HapMap project to determine patterns of differences in the human genome began in 2002 and by 2005 completed its first phase work by of discovering on the order of one million SNPs in 270 people sampled from four distinct populations of people: Han Chinese, Japanese, Yoruba Nigerians, and Northern Europeans (**Gannett, 2008**).

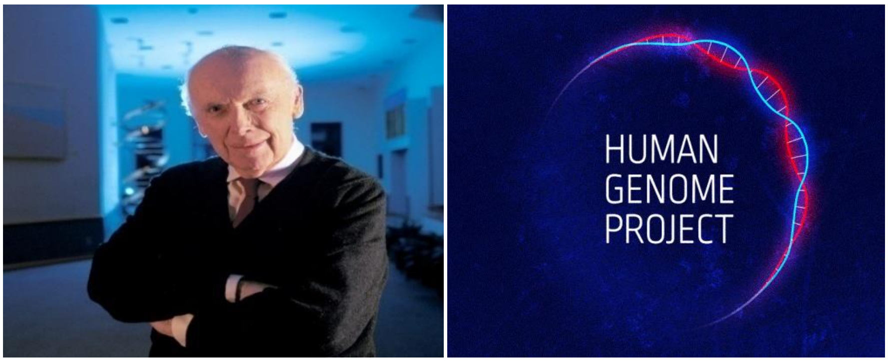


Fig. 76 : James Watson the leadership of the Human genome project **(labxchange.org)**

The advent of whole-genome sequencing and surveys of their variation in different populations (races), together with new statistical methods, permitted researchers by 2006 to systematically identify candidate loci for recent natural selection during evolution in humans. Some of these genes were also shown to be ancestry-informative markers which came to be used in genealogical studies and to understand ancient human migrations. The first genome of a plant model organism, *Arabidopsis thaliana* was sequenced in 2000. Dozens of bacteria, the mouse, the nematode *Caenorhabditis elegans* and other model organisms were sequenced and their genes mapped, often by large international collaborations (**Gannett, 2008**).

9. PROTEOMICS, COMPUTATIONAL BIOLOGY AND BIOINFORMATICS

The first decade of the twenty-first century saw the rise of proteomics, computational biology and bioinformatics, with an emphasis on huge databases of experimentally derived data, all connected by the Internet and available to researchers everywhere, which has fundamentally changed the structure of the science of biology itself.

Proteomics is the systematic study of the many and diverse properties of proteins in a parallel manner with the aim of providing detailed descriptions of the structure, function and control of biological systems in health and disease. Advances in methods and technologies have catalyzed an expansion of the scope of biological studies from the reductionist biochemical analysis of single proteins to proteome-wide measurements. Proteomics and other complementary analysis methods are essential components of the emerging 'systems biology' approach that seeks to comprehensively describe biological systems through integration of diverse types of data and, in the future, to ultimately allow computational simulations of complex biological systems (**Patterson & Aebersold, 2003)**.

Bioinformatics is an integral part of proteomics research. It is an interdisciplinary field that takes insights from a range of subjects (statistics, biology, mathematics, computer science, chemistry, etc.) to create tools and approaches to understand biological data.

Bioinformatics is inherently an innovative field that is situated at the limit of life and computer sciences that allowed new technological advances in genome sequencing, data processing, predication and simplified the treatment of complex and huge data.

This field is related on two common approaches namely; *in silico* and molecular docking-dynamic experimentations to improve and clarify the scientific perception of ligand-receptor interactions, especially of those molecules involved in the drug elaboration process. This discipline has emerged to replace the traditional approach of drug discovery which was very limited, very expensive, and didn't always provide the expected results (**Mitra *et al.*, 2022**).

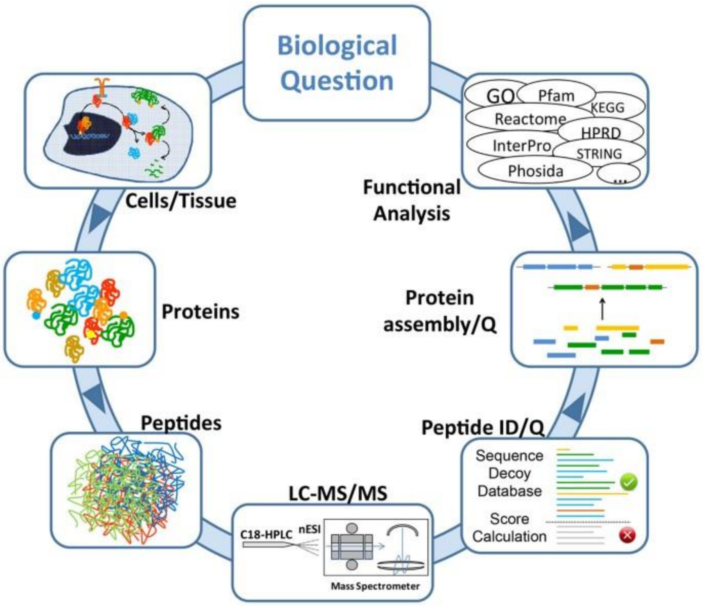


Fig. 77 : Bioinformatic analysis of proteomics data (bmcsystbiol.biomedcentral.com)

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