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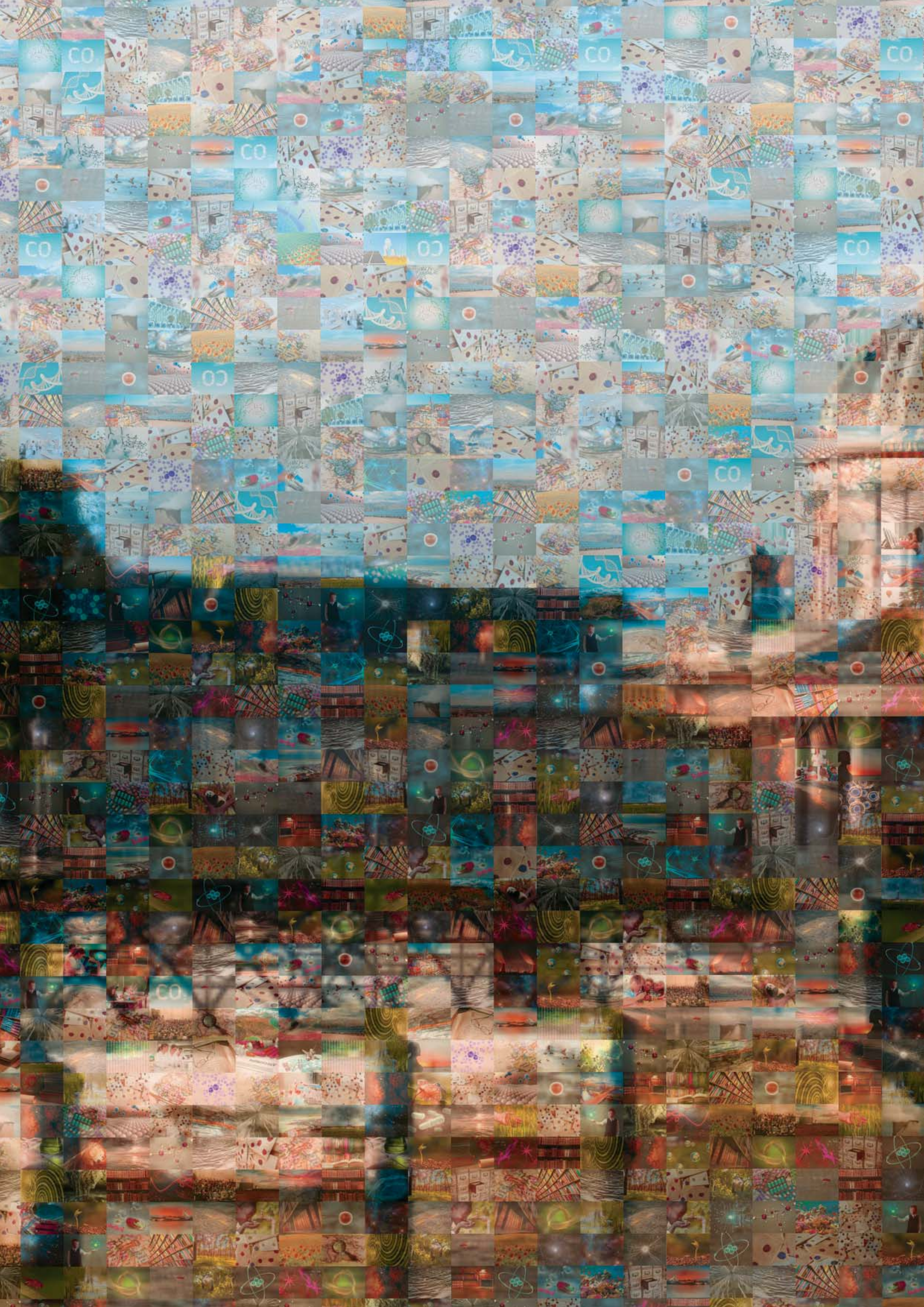
La Lettre

de l'Académie des sciences

SPRING-SUMMER | AUTUMN-WINTER 2016

350 years of science




350
INSTITUT DE FRANCE ACADÉMIE DES SCIENCES
1666
2016
ans
Académie des sciences



1666-2016: the solemn ceremony celebrating the 350 years of the Académie des Sciences was held under the Cupola of the Institut de France on 28 June 2016. Eight members of the Académie, from as many sections, briefly recounted the history of their disciplines, highlighting their important stages and paying tributes to the scientists who, whether they were French or from other countries, contributed the most to the progress, if not the revolution, that took place in their own disciplines. This special issue of *La Lettre de l'Académie des Sciences* presents the proceedings of this momentous one-day event dedicated to the history of science.

350 YEARS OF SCIENCE

Draw me an Académie!

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Bernard Meunier

President of the Académie des Sciences, Emeritus Senior Researcher at CNRS

One evening, as Louis XIV was falling asleep away from the crowd of his courtiers, he felt like a castaway in the middle of the ocean. Suddenly, a little voice woke him up and said to him: *Sire, please....draw me an Academy!*" The King listened to the Little Prince and said to him: "*But I already have an academy, which my father made in 1635; it takes good care of our beautiful French language.*" "*I know*", the Little Prince said, "*but another one is needed, to deal with science, with scientists telling us about the world, our planets, plants, animals, diseases and also machines that should be created to make your kingdom a bigger and stronger one.*" The King was convinced. This was the year 1666; he asked Colbert to engage the creation of the "Académie Royale des Sciences".

Recruiting for excellence

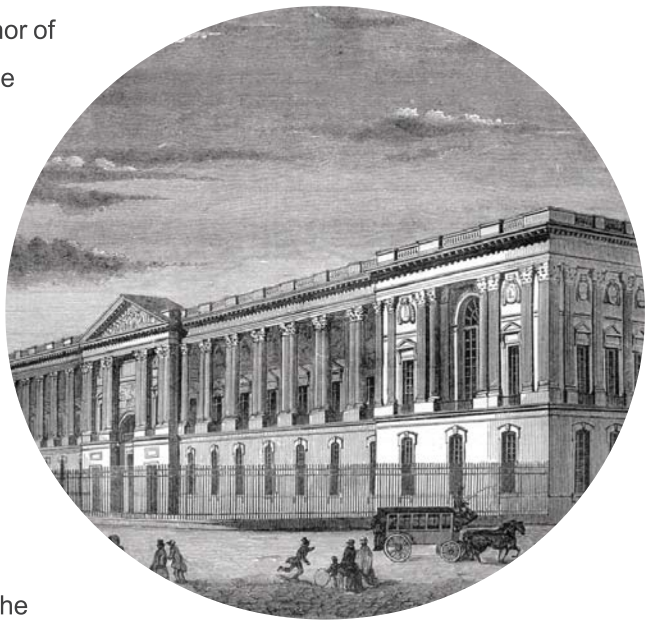
In fact, there are no historical documents recording how Louis XIV made his decision. One thing is certain: the "Académie des Sciences" has been there for 350 years! The young King, 28 years old in 1666, was concerned with France's influence, as is illustrated by his search for natural borders and his support for artistic creation, in all fields: architecture, painting, theatre and poetry. His early reign was still lacking a group of scientists able to develop mathematics and physics – this latter word covering, in the middle of the 17th Century, not only today's physics but also chemistry, natural sciences and medicine. French scientists such as Descartes and Pascal, who respectively died in 1650 and 1662, had not been replaced and England had recently created a scientific society, in 1660, immediately taking an important place in Europe: the Royal Society.

It was urgent for the French royalty to show France's precedence on the Continent. Colbert appointed his librarian, Pierre de Carcavi, a mathematician who had been trained by Pierre de Fermat, to recruit a scientist recognized by his pair in Europe and able to animate an academy of sciences in Paris. The choice would be Christiaan Huygens, a mathematician and astronomer from the Netherland, admired by

all in Europe and who had just been elected at the Royal Society in 1663. Christiaan Huygens negotiated attractive terms for his arrival in Paris: an apartment in the King's library and an annual pension of 6 000 pounds!

The recruitment of the first academicians started from May 1666. Seven names were selected from a short list: Christiaan Huygens, Adrien Auzout (astronomer), Jacques Buot (astronomer), Pierre de Carcavi, Bernard Frénicle de Bessy (mathematician), the abbot Jean Picard (astronomer) and Gilles Personne de Roberval – a mathematician who is still known to us for his double pan balance. This first group formed the Mathematics Section, and started to meet in the summer 1666 to observe two eclipses, that of the moon and that of the sun. They produced a report that reassured Colbert on their capacity to work together.

In October 1666, a second section was created, the Sciences of Observation section, with the help of Charles Perrault, who was a man of letters, Colbert's right-hand man and the author of the famous tales. Also recruited were: Marin Cureau de la Chambre (physician of the King), Claude Perrault (architect and Charles Perrault's brother – who conceived the colonnades of the east façade of the Louvre, which has since been an inspiration for many architects over the world), Samuel Cottereau du Clos (physician and chemist) and Louis Gayant (physician). Before December were added Claude Bourdelin (chemist), Jean Pecquet (anatomist), Nicolas Marchant (botanist) and Jean-Baptiste du Hamel – an Hellenist who would gradually grow a passion for anatomy and be the first "Secrétaire de l'Académie".



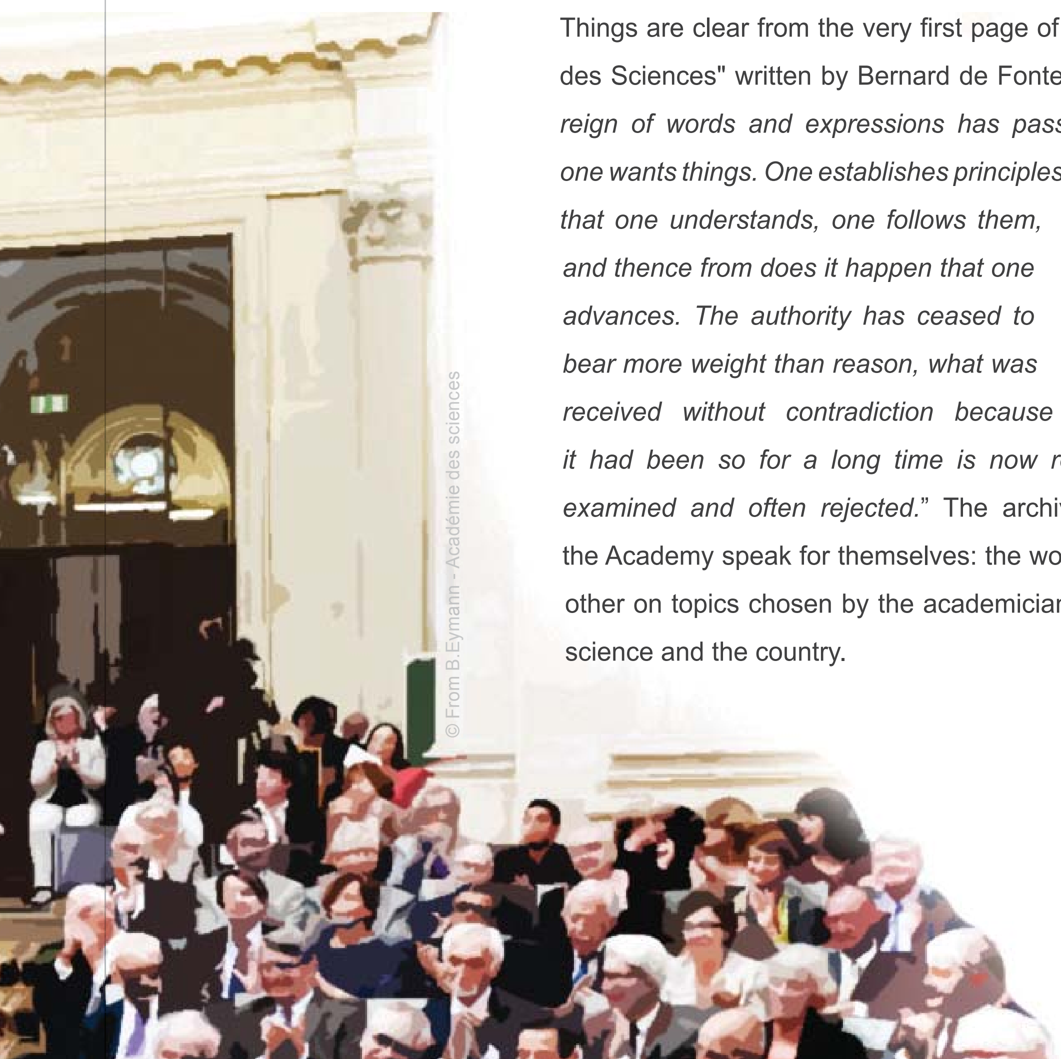
Claude Perrault's Colonnades of the Louvre

This list of personalities, selected for their expertise in their respective field, is not only a tribute paid to the first academicians, it is mainly the expression of a principle at the foundation of our institution. An academy should be an assembly of very high level scientists in their own discipline, in order to enable them to work together on topics whose consideration requires strong skills. The interaction between disciplines takes place smoothly and naturally, when it is deemed necessary, not forgetting that many problems find their own solution within one same discipline. Interactions between disciplinary fields should not be passively lived through, like an old song one sings more or less in tune to feel safe for lack of ideas; on the contrary, they should be voluntary and associate the skills of all to venture off into new horizons.

This conception finds itself clearly expressed in the very first page of the archives held at the Academy: "*On this 22 December 1666, it has been settled in the company that it would meet twice a week, on Wednesdays and Saturdays. [...] On Wednesdays, one shall deal with mathematics, on Saturdays, on shall work on physics. As there is a great connection between these two sciences, it was deemed fit that the company did not divide and that all gathered at the assembly on these same days.*"

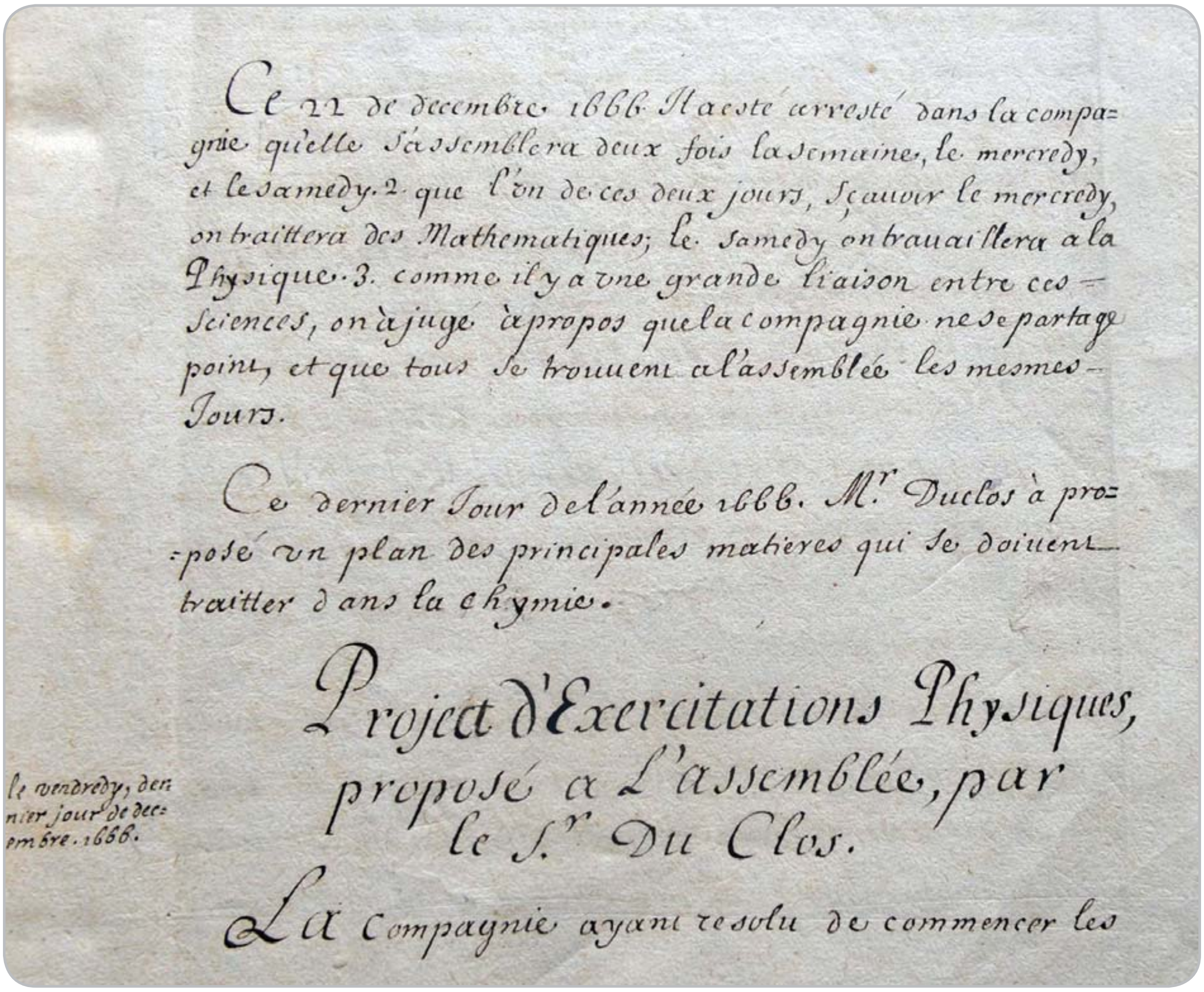
This new Academy thus met for the first time on 22 December 1666, in the King's library, rue Vivienne. This presentation before the King was the object of a magnificent painting by Henri Testelin, which may be seen at Versailles.

What place in the Nation?



Things are clear from the very first page of the history of the "Académie des Sciences" written by Bernard de Fontenelle: "*The reign of words and expressions has passed, one wants things. One establishes principles that one understands, one follows them, and thence from does it happen that one advances. The authority has ceased to bear more weight than reason, what was received without contradiction because it had been so for a long time is now re-examined and often rejected.*" The archives of the Academy speak for themselves: the working sessions followed each other on topics chosen by the academicians, protecting the interests of science and the country.

Bernard de Fontenelle
(1657 -1757)


le vendredy, dernier jour de decembre. 1666.

Ce 22 de decembre 1666 Il a esté arresté dans la compa=
gnie qu'elle s'assemblera deux fois la semaine, le mercredy,
et le samedy. 2. que l'un de ces deux jours, sçauoir le mercredy,
on traittera des Mathematiques; le samedy on trauaillera a la
Physique. 3. comme il y a vne grande liaison entre ces
Sciences, on a jugé a propos que la compagnie ne se partage
point, et que tous se trouuent a l'assemblée les mesmes
Jours.

Ce dernier Jour de l'année 1666. Mr. Duclos a pro=
=posé vn plan des principales matieres qui se doiuent
traitter dans la chymie.

Project d'Exercitations Physiques,
proposé a L'assemblée, par
le Sr. Du Clos.

La Compagnie ayant resolu de commencer les

Minutes of the very first session of the "Académie des sciences" (extract)

After such a good start, a few words to mention the resilience of the "Académie des Sciences": great academies are bound by the duty to stay on course, “reason against authority”. Over a period of 350 years, the Academy could have faltered, gone astray, forgotten its raison d’être, become a mere coterie of members enjoying its comfort. Such was not the case. It went through difficult times. Annoyed, indeed, by the adjective “royal”, the Convention decided to suppress all the academies on 8 August 1793. As they were involved in the "Comité d’instruction publique", Talleyrand in 1791 and Condorcet in 1792 proposed the creation of an institute grouping different academies and aiming at the advancement of science and arts. Unfortunately, this period of the French Revolution was not conducive to such a creation. The Terror was its height: “*The Republic does not need any scientists*”, so was it claimed to have been said in May 1794. Even if these words were not uttered, no doubt some revolutionists thought them very loud. A song was even written on this theme. Even today, many people question the value of scientific progress. We do not forget that the evolution of science is like a medal: there is always a flipside. Is this any reason to reject scientific creation? We do not have fond memories of the countries that, at some point in their history, tried to get rid of science and scientists. Very quickly, these societies found themselves on the path to social and cultural regression. Trying science is always preferable to maintaining ignorance.

The young Republic came back fast enough on this decision, taken in 1793, and acknowledged the work of scientists who were committed to the service of the Nation. In a law on the organization of public instruction, approved on 25 October 1795, the thermidorian Convention created an "Institut des Sciences et des Arts", aimed at "*perfecting sciences and arts by unremitting research, the publication of discoveries, correspondence with scientific and foreign societies.*" One may feel here the remains of a faint grudge against the period when work stopped at the Academy, and it may be noted there is an international dimension in this Institute consisting of 144 members, divided into three classes, the first being physical and mathematical sciences. This class became the "Académie des Sciences" by the Royal Ordinance of

21 March 1816. Two hundred years later, the Academy is still there, with the same title.

The next big step will be the celebration of the 400 years of the Academy, which our younger members will see in 2066. They will then be in a situation to say: "*I remember the 350 years of our young Academy*."

Tempus fugit, memoria manet.

Colbert introduces the members of the "Académie des Sciences" to Louis XIV : one may recognize the King at the centre, in red, with Colbert to his right and, facing him, the abbot du Hamel; Christiaan Huygens, who is represented full-face, is immediately placed behind du Hamel. A painting by Henri Testelin (1616-1695)

The march of knowledge

© B.Eymann - Académie des sciences

Catherine Bréchignac

Secrétaire perpétuel of the Académie des Sciences, Ambassador for Science, Technology and Innovation

"*All men naturally desire knowledge. An indication of this is our esteem for the senses; for apart from their use we esteem them for their own sake.*" Such is the beginning of Aristotle's first book of *The Metaphysics*, in which he examines the construction of knowledge from experience. He makes a distinction there between art, in its first sense of know-how, and science. "*Art is produced when, from many notions of experience, a single universal judgement is formed. Science [...] is concerned with the primary causes and principles.*"

More than two thousand years have passed and this reflection remains fully relevant. Aristotle dissociates the know-how, which is grounded on empirical knowledge, from science, which is based on theory. This distinction reflects the activity of the brains, which, besides emotion, works, to answer questions, either by comparison – it then draws analogies from all the experiences stored in its memory – or by theoretical deduction. It sometimes rely on a combination of the two. The comparative mode, often called "intuitive", is generally quicker than the deductive mode.

As far as we may trace back human knowledge, what progress has we achieved?

The rock paintings that have withstood tens of thousands years to reach us are as moving as paintings by Dufy, Kandinsky or Franz Mark; between them, no progress. Even if we did not knew their meaning, it is their ability to move us that matters. True, painting has a history. Over successive periods of time, artists have displayed on canvas their beliefs, environments, impressions, symbols, abstractions; such history is however not similar to progress. There is no doubt that the mastery of perspective allowed the Renaissance painters to perfect the representation of landscapes; nevertheless, in itself, this is no progress. There is no progress in art, because there is no progress in aesthetics: beauty remains a subjective value, a personal

The Council Held by the Rats, *a fable by La Fontaine, whose moral remains topical*

confrontation between one's sensitivity and a work of art, a landscape, a moment, a person.

Nor shall progress be mentioned in literature. Homer's Iliad and Odyssey, a poem by Ronsard, a fable from La Fontaine, or verses by Rimbaud or Rilke, resonate within us with the same intensity. This is what Victor Hugo reminded us in his book *William Shakespeare*, written in 1864: « *Does Shakespeare change anything in Sophocles? […] No. Poets do not climb over each other. The one is not the stepping stone of the other.*" In literature, what matters are the words, words that express, words that suggest, the power of words that triggers emotion. There is indeed an infinity of possibilities that move us at different scales.

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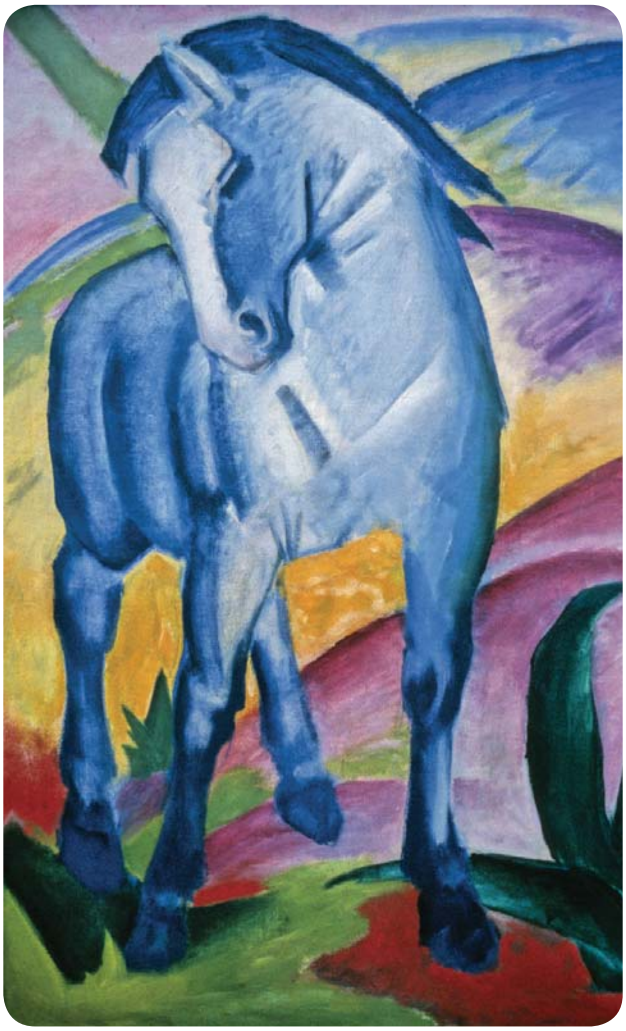
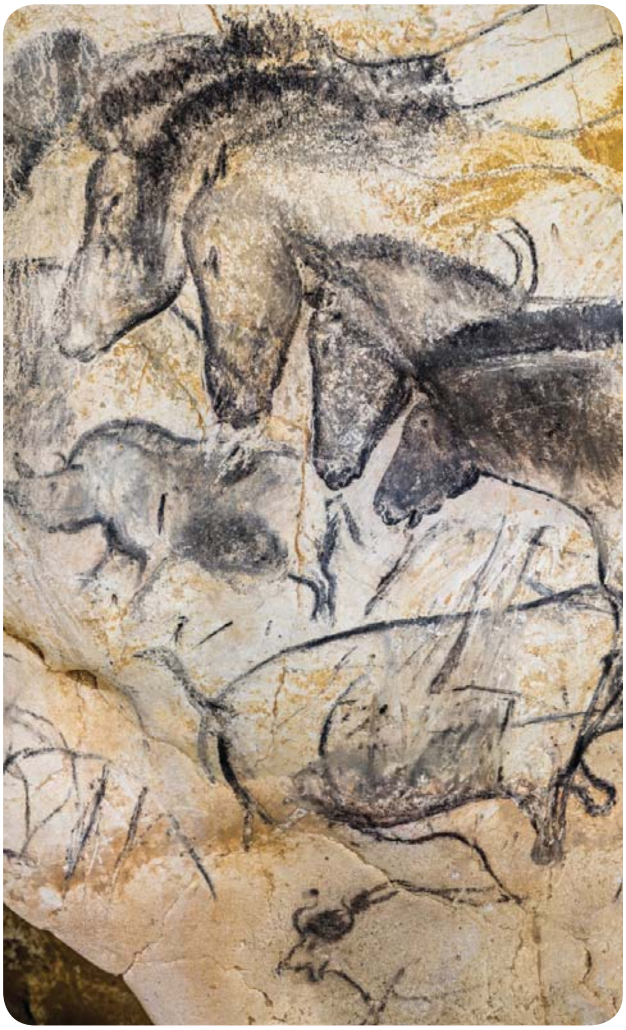
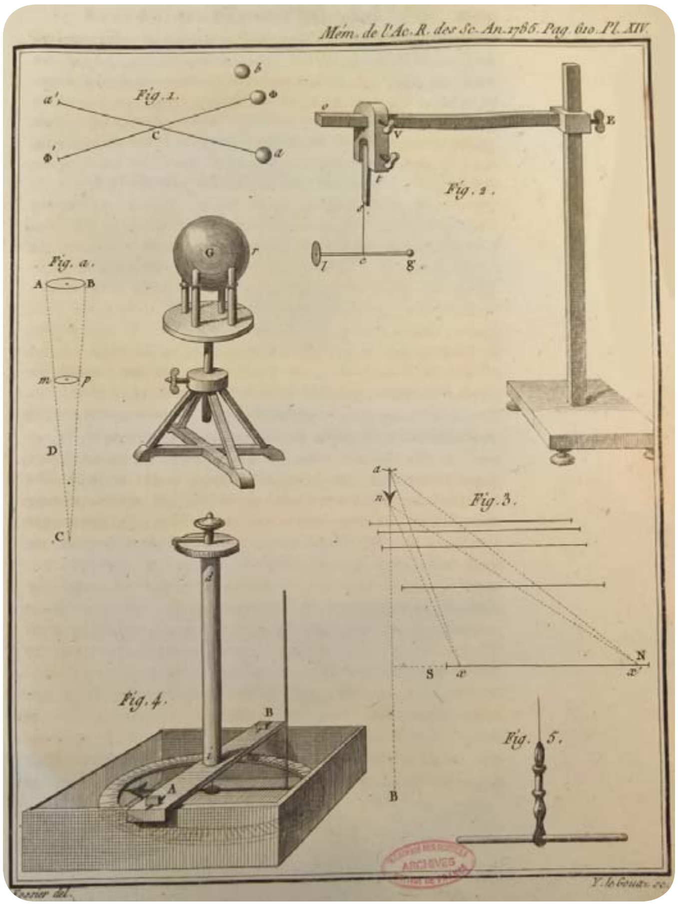


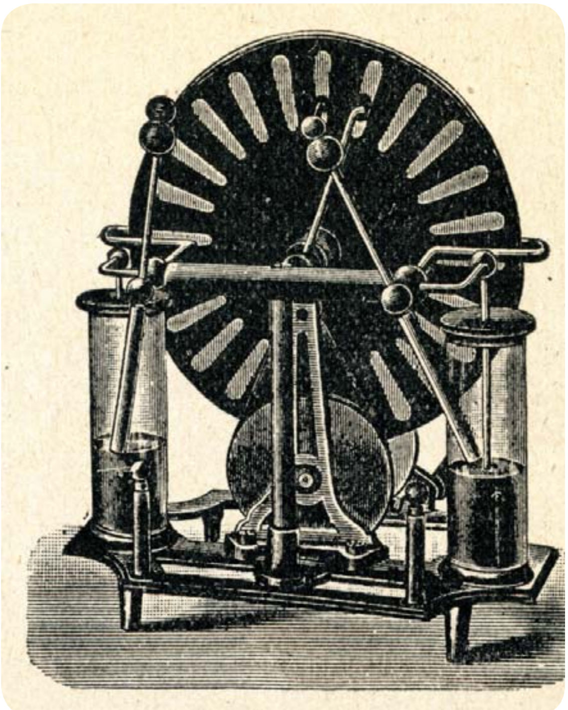


Several tens of thousands of years separate the rock fresco of the Chauvet Cave (on the right) and the Blue Horse painted by Franz Marc in 1911 (on the left).

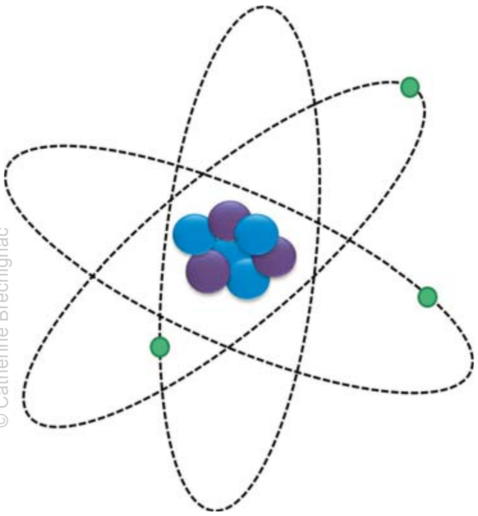


A plate from Charles Coulomb's First Memoir on Electricity and Magnetism *(1785)*

It is however customary to mention progress in science. It is because they are cumulative that sciences and technologies progress: to add a contribution to scientific knowledge, one must know all the links of the chain made of what was previously acquired. Let's take the example of electricity, which has now become indispensable in our daily lives. It was discovered very early in antiquity. The Greek word “electron” meant “yellow amber”, which was known for its electrostatic properties. The next step to better understand it was only taken in the early 18th Century with Charles Du Fay who, in the 1730s, dissociated two kinds of electricity, depending on whether it came from rubbing glass or rubbing amber. Soon afterwards, Benjamin Franklin called them “positive” and “negative”. Of the same sign, they repel each other; of opposite signs, they attract each other. In 1785, Charles Coulomb presented a memoir at the Académie des Sciences explaining the force between two electric charges. Such a force is proportional to the charges and inversely proportional to the square of the distance between them. Then came the electrostatic machines, made to generate current, which would bring about the birth of electric circuits. At the end of the 19th Century, J.J. Thomson demonstrated the existence and role of the electron, which, a few decades later, would prove to be one of the elementary particles that make up our universe. In December 1947, researchers at the Bell Telephone Company, in the United States, invented the transistor, which would be the root of electronics. Then, changing scales to reduce the dimensions of the transistor in the early 2000s, would emerge the paradigm



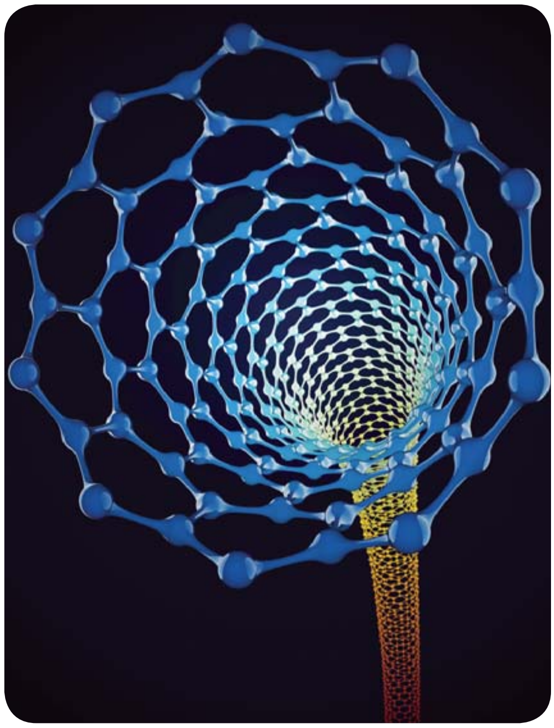
An electrostatic machine



A diagram of an atom: the core diameter is about 100,000 times smaller than the electron orbits.

of one-electron electronics. Such cumulative science is not constructed in a linear way but it progresses in steps often associated with paradigm shifts that always lead to gain more comprehension. Successive theories are but approximations of more general theories. “*Science is constantly removing itself*” wrote, once again, Victor Hugo.

Science differs from literature and arts. Scientific breakthroughs materialize when the acquired knowledge allows a deeper understanding to emerge. Men of science are, all levels being equal, interchangeable. Had Einstein not existed, another would have found relativity, perhaps not as fast, or maybe would it have been necessary to team up. In any case, building on general relativity, we would have developed our GPSs with as much precision.



Carbon nanotube

An outline of the principle of operation of GPS

Transmitting is urgent

The cumulative nature of science prompts us to adapt ourselves to the rapid increase of knowledge. Long gone is the time when Descartes used to advise the younger generation – and rightly so at the time – to free themselves from the dogma of the ancients, rediscover knowledge by themselves, taking a critical approach. As testified by François-Xavier Bellamy in *Les déshérités, ou l'urgence de transmettre* (Plon Ed., 2014), it is pointless today to let anyone believe that one can rediscover it all by oneself. Time is missing. In the century of the Enlightenment, any scientist could acquire and assimilate all the scientific knowledge that had been gathered at the time and what we now call interdisciplinarity could easily germinating in one brain. Things are quite different today, as none of us would be able to embrace everything and everyone must restrict themselves to acquiring one discipline. It is this segmentation of science, indeed, that we should connect in order to make the best use of knowledge.

This is the way science progresses, its cumulative nature beating the rhythm of the irreversibility that drives us. Such progress, however, does not exclude perverse results. Ignorance has always brought out beliefs from the shadows to help overcome fears for what seems mysterious because not understood. Some centuries ago, still, these ancestral fears were the same for all. But today, the knowledge that some have enables them to create and produce objects that seem magical to others. The latter do not understand how these work, or sometimes what their purpose is, and yet they use them. Such discrepancy between a minority of people, who have acquired deep scientific knowledge, and the vast majority, who does not make it their own, endangers the cohesion of our societies. It creates an expanding breach into which charlatans, ideologists and impostors rush, using a pseudo-rational language to take advantage of those for whom scientific knowledge remains an enigma. Like a spring that stretches and eventually breaks if one does not watch out, the mass of new scientific knowledge cannot draw away from our societies. Education and everyone's involvement in reflecting on the use of such knowledge are more than ever of prime importance. In his book *La pensée sauvage* (Plon Ed., 1962) – The Savage Mind, translated in 1966 by George Weidenfield and Nicholson Ltd, London –, Claude Lévi-Strauss invited us to let our two ways of thinking coexist, scientific thinking and savage thinking – the former is more abstract and considers the world from the outside, while the other is more concrete and considers it from the inside – because

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we cannot ask science to answer alone to all the questions our societies must face. It cannot do so and such is not its role.

The unprecedented increase in scientific and technological knowledge that has been taking place for the last two centuries has made us change our worldview. We apprehend the world differently from our ancestors. This produces some anxiety: the anxiety associated with what we will discover. What will the state of scientific knowledge be in a few hundred years, what shall we do with it? That's is where all artistic and literary creations find their potential, precisely because they are stable over time, because they do not progress – or maybe do they evolve, as men's emotions evolve.

It is this construction of science – science progressing through successive accumulation – that we shall visit, letting each field carry us along through the following pages. It reminds us, 350 years after the creation of our Académie, that the march of knowledge is inseparable from a certain idea of progress. The exercise our fellows have accepted to undergo is a difficult one. Well aware of how harsh it is, we thank them all the more for tackling such a task.

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The new microbiology

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Pascale Cossart

Secrétaire perpétuel of the Académie des Sciences, Professor at Institut Pasteur

The discipline of microbiology was born at exactly the same time as the Académie des Sciences. It is now in full “renaissance”, and even undergoing a revolution. Indeed, in the last twenty years, many new concepts have emerged; others are about to appear. This revolution will increasingly influence our daily lives, including our nutrition, medicine and many fields in biology, not forgetting the environment.

An historical perspective

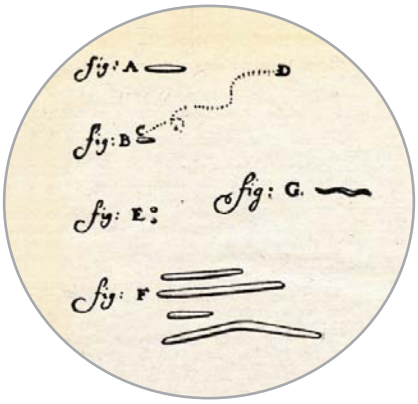
It all started in 1666 in Delft: the draper Antonie van Leeuwenhoek, then 34 years of age, used microscopes – which were far from resembling current microscopes – to ascertain the quality of his fabrics. He quickly grew a passion for microscopy and started making himself lenses, of a quality and a power that had never been reached before. This led him to observe the contents of blood, sperm and many other liquids, such as water from the ponds of his village and brought him to discover what he called “animalcules”, small organisms sometimes moving. These unicellular living organisms were able to divide in a binary way, thus giving rise to identical unicellular organisms: van Leeuwenhoeck had just discovered bacteria. He recorded his observations in letters he sent to the Royal Society as early as 1673. An important correspondence then followed, lasting until his death in 1723. The Royal Society elected him as a member en 1680, the Académie des Sciences admitted him as Corresponding Member in 1699.

Van Leeuwenhoek’s work long remained unknown, partly because this scientist had not shared his lense manufacturing technology with others, preventing his observations from being reproduced and his conclusions from being verified. A the time, research publications were not subject to the same rules as those which are imposed nowadays!

It is really to Louis Pasteur and Robert Koch that we owe the birth of microbiology in the late 19th Century.

Antonie van Leeuwenhoek (1632-1723)
and the beginning of microbiology

Replica of Leeuwenhoek's microscope



"Animalcules" detected in
human saliva, 1675

These two eminent scientists definitively rejected the spontaneous generation hypothesis and, with their many disciples, identified the agents responsible for diseases that had been devastating humanity for millenia, such as plague, cholera or tuberculosis. They paved the way for the development of various tools for diagnosis, therapeutics and, above all, prevention: vaccines.

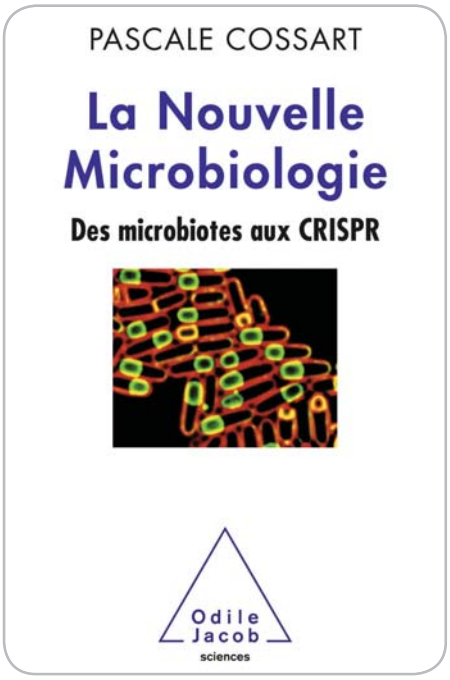
Louis Pasteur and Robert Koch, the fathers of microbiology

Louis Pasteur (1822-1895)

Robert Koch (1843-1910)

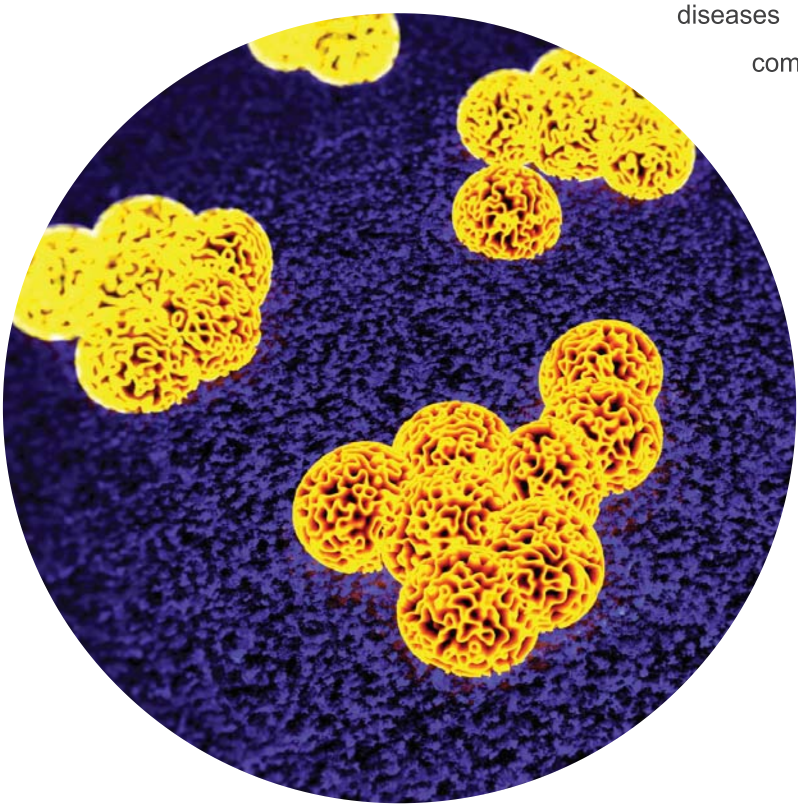
Their knowledge on infectious diseases, and particularly bacterial diseases, was of course quite empirical, and it is only with the discovery of DNA, the birth of molecular biology and its applications using non-pathogen bacteria, in particular the famous *Escherichia coli*, that a new period in the understanding of infectious diseases began at the end of the 1980s.

The virulence factors that pathogenic bacteria produce started to be identified, as well as how toxins act and how some bacteria enter the cells and disseminate in the tissues, developing an incredible variety of strategies to subvert the immune defenses of the infected host. Very quickly, cell biology and its various types of microscopy – fluorescence microscopy, electronic microscopy, video microscopy – enabled microbiologists to observe infections in real time. Needless to say that, to help in this molecular hunt, genomics entered just before the beginning of this millenium. The complete sequences of bacterial genomes of various species were published one after the other. These bacterial genomes displayed a great variability and their analysis highlighted the basis for bacterial



To better understand how microbiology has dramatically changed during the last decades (P. Cossart, Odile Jacob Éd., Paris, 2016) adaptability: bacteria are able, through various mechanisms, to receive or give, i.e. to exchange with other bacteria, genomic fragments that provide new properties – in particular that of resisting to antibiotics – and the ability to live in many environments.

Antibiotic resistance and the mondial panic



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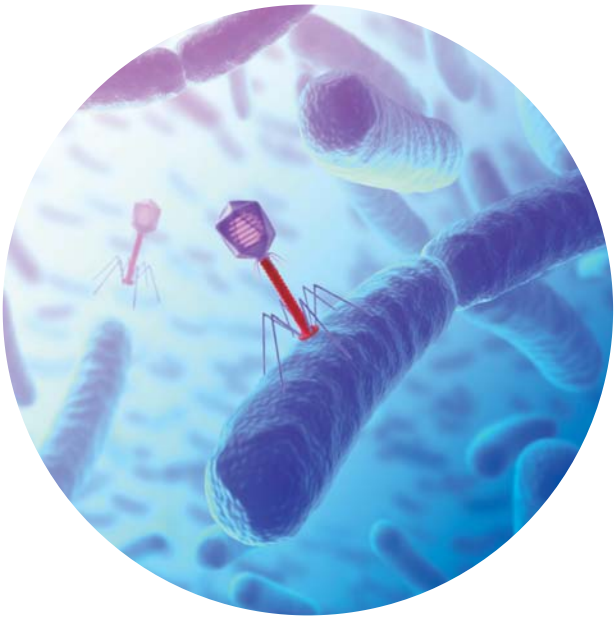
Superbug antibiotic resistant bacteria

In 2016, indeed, one can no longer mention bacterial infectious diseases without mentioning antibiotics. These compounds, which started to be used on a daily basis in the 1950s and predicted the end of infectious diseases, have, together with vaccines, significantly decreased mortality due to infectious diseases in developed countries. Sadly, the first resistances appeared in the late 1960s and such resistances have become so serious that they now lead to dramatic therapeutic dead ends, with a conspicuous return to the pre-antibiotic era.

What are these resistances due to? In great part to the gene transfers mentioned above, that make the bacteria able to alter the antibiotic and thus inactivate it, or to alter the target of the antibiotic, making the antibiotic ineffective. Resistance may also stem from the presence of a pump protein exporting the antibiotic after it has entered. Many bacteria have several resistance genes; they are called multi-resistant. Death prediction figures due to antibioresistance have become alarming: if we do not act now, by 2050 such deaths may every year rise to 10 million persons worldwide. Public authorities are on alert and strong measures will be needed at the global level to put an end to this situation, prevent the emergence of new resistance and produce new antibacterial agents.

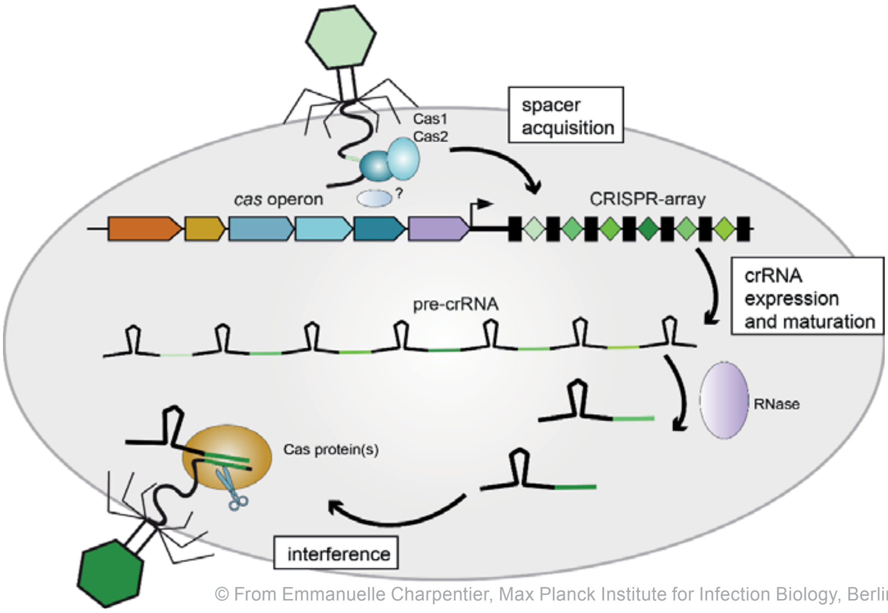
CRISPR/Cas9, the bacterial system that revolutionizes genetics

Antibiotics are not the only antibacterial agents. In nature, bacteria are, as we are, attacked by viruses called bacteriophages. These viral attacks take place in any environment but there are situations where they may have dramatic consequences, for instance in the dairy industry. Some dairy products, such as yogurts, are indeed made by specific bacteria selected for the aroma they bring to the final product. An attack by a bacteriophage may have desastrous economic consequences. One of the great breakthroughs of these recent years is the discovery that bacteria are able to immunize themselves against bacteriophages and possess a very efficient immune system.



Bacteriophage attacking a bacterium

When they encounter a virus, most bacteria may, right after the infection, that is, after the interaction of the virus with its receptor, integrate a small part of the viral DNA in a locus of their genome called CRISPR (*Clustered Regularly Interspaced Short Palindromic Repeats*). If these bacteria thereafter meet the same virus, they recognize it and are able to destroy it and prevent the infection. This destruction involves either several proteins, namely Cas (*CRISPR associated proteins*), or only one protein, Cas9. The efficiency of the CRISPR/Cas9 system is so impressive that, very quickly, emerged the idea to utilize this bacterial machinery to edit, in a targeted way, the genomes of all living organisms. This was successfully done. The technique is in the process of revolutionizing biology, as it enables genes to be studied in a targeted way, either by deleting them or by modifying them, opening therapeutic avenues that have never been explored before, incidentally raising at the same time important ethical issues.



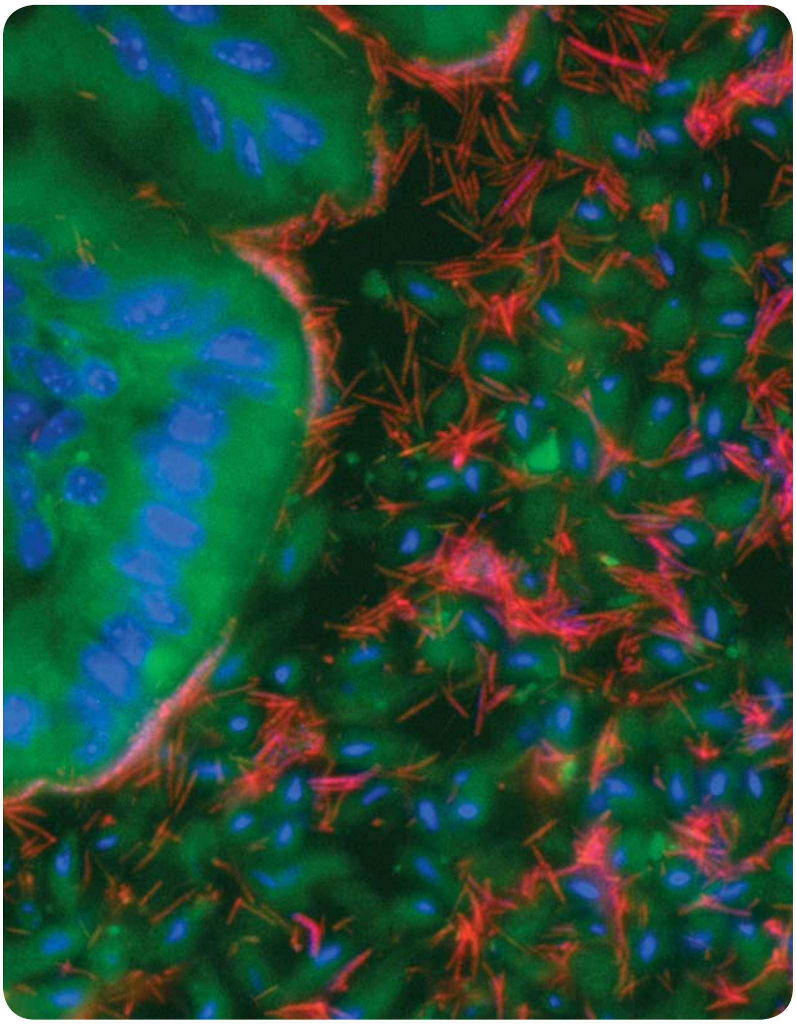
CRISPR = Clustered regularly interspaced short palindromic repeats
Cas = CRISPR-associated
CrRNA : CRISPR targeting RNA

The CRISPR/Cas system

Bacterial communities

One last aspect of microbiology that has to be considered is the new concept of "sociomicrobiology". Rarely does one find a bacterium which lives alone: bacteria live in groups, which can form as soon as one of them lays on a surface, inert or alive, adheres to it, multiplies, secretes a matrix which eventually structures a small community, protected from the external environment, that is called a biofilm. Such biofilms may be found everywhere in nature, but also on some parts of our bodies – teeth, in particular – in some industrial structures – such as water pipes – or, also, on some prostheses or catheters in the medical setting. In these biofilms, bacteria may stay for several years, sheltered from antibiotics and detergents, which raises serious medical and industrial concerns.

Other microbial assemblies, of a much larger size, may form in symbiosis with any living organism, and they are beginning to be extremely well-documented: these are microbiota. Who hasn't heard of the intestinal microbiota, formerly called the gut flora? Progress achieved in genomics and transcriptomics has enabled us to remarkably improve our understanding of how a crucial role this flora plays. It is now well established that in an organism, a microbiota harboring a great diversity of species is a signal of good health and that such diversity reduces with age, that the microbiota regulates our development in general, and in particular that of our immune system, protects us from pathogens and produces components that may migrate to our brain and affect our behaviour.



The intestinal microbiota

Microbiota and biofilms are *bona fide* societies, in which the members of a same species talk to each other in a specific chemical language, perceived by receptors that enable bacteria to appreciate the number of their sieblings present in their close environment and with which they can act together. This phenomenon is called *quorum sensing*: the objective of the group is to act together if the quorum is reached! For instance, a pathogen bacterium only produces its toxins if enough bacteria of the same species are present and have a good chance of succeeding an infection and subvert the immune defenses of the infected host. Bacteria are like academicians, they take important decisions only if they have a quorum!

From empirical medicine to precision medicine

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Alain Fischer

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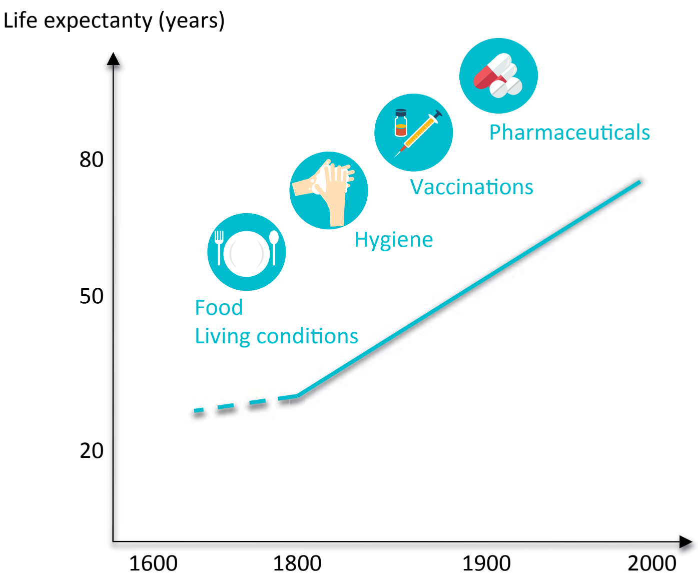
In 1666, Moliere staged *Le Médecin malgré lui* – The Doctor in Spite of Himself –, a satirical depiction of the state of medicine in his time. In the 19th Century, empiricism and the introduction of the experimental method both allowed curative medicine to progressively emerge. In the 20th Century, the upsurge of such sciences as mathematics (epidemiology), physics (imaging), chemistry (drugs) and biology (genetics, molecular biology) contributed to the progress of medicine, particularly through the adoption of a reductionist approach. Tomorrow, with the integration of health data, precision approaches will possibly develop, provided the human dimension of medicine remains steadfast and the concept of access to treatments for all is not mere words.

Difficult beginnings?

On the year of the creation of the Académie des sciences, *Le Médecin malgré lui* was one of the many opportunities for Moliere to mock the ineffectiveness of medicine. Nearly 150 years later, Pierre Simon Laplace, who was reforming the Académie, indicated: "*I do not place doctors at the Académie des Sciences because they are scientists but for them to be with scientists*" – a clear vision of medicine, as the future would tell, but also a cruel one, as it still remained hardly efficient. Evidence of this may be found in life expectancy, which remained pretty much stable from prehistory to the beginning of the 19th Century. Actually, the therapeutic era of medicine only started with penicillin and would only rise on the decline of the World War II, 70 years ago. S. Shryrock, an American expert in human sciences, wrote in 1947 that the medical 19th Century is characterized by therapeutic nihilism, which is bound to last until the half of the next century. Medical research had difficulty expanding in France. For instance, referring to a meeting he had after the war with the director of the French Institut national d'hygiène, François Jacob wrote, in



Evolution in life expectancy during the 350 last years in France, with the major causes of increase

The Statue Within: "*He could do nothing for me; besides, genetics did not interest him.*" Does this mean that medicine was really born but 70 years ago, and that the early days of medical research in France were painful?

© LACMA

Medical empiricism: Seated figure with sores (Mexico, Nayarit, 200 B.C.-A.D. 500)

A great deal of the answer is no, for many have contributed to making sure science met and fertilized medicine. The tradition of medical empiricism, the quality of observation – shared by Laennec, Bichat, Corvisart ("the School of Paris") – in the early 19th Century laid the foundations. Thus, as early as 1796, Jenner administered efficient vaccines against smallpox; in 1847, Ignace Philippe Semmelweis, who did not know microbes existed, understood that if doctors and midwives washed their hands after dissection and before delivery, the rate of puerperal fever and mortality associated to it would drop considerably, thus establishing on simple observation the foundations for hygiene. The 19th Century produced the essential concepts and the major discoveries that enabled medicine to rise in the 20th Century. Let's mention, obviously, how significant was the notion of experimentation introduced by Claude Bernard as he wrote, in *An Introduction to the Study of Experimental Medicine* (1865): "*Experimental medicine, like all the experimental sciences, (...) is (…) the science which tries to reach the immediate causes of vital phenomena in the healthy and in the morbid state*." He created the concept of physiology, while Gregor Mendel defined the laws of genetics and Louis Pasteur and Robert Koch discovered microbes.

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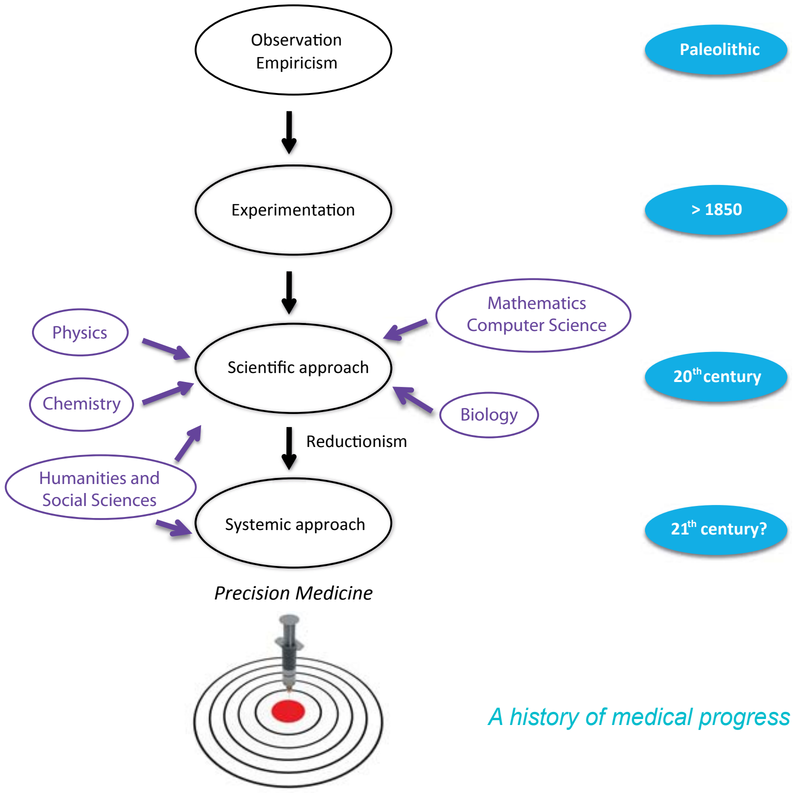
Claude Bernard by Léon Lhermitte (oil painting, 1889)

A scientific approach towards medicine

As a matter of fact, the progress of medicine since 1945 stemmed from the development of a scientific approach to medical issues, based on the input of sciences: mathematics then computer science, physics, chemistry and, obviously, biology. The latter, in this context, made it possible to study diseases at the molecular level, from a reductionist standpoint that proved fruitful.



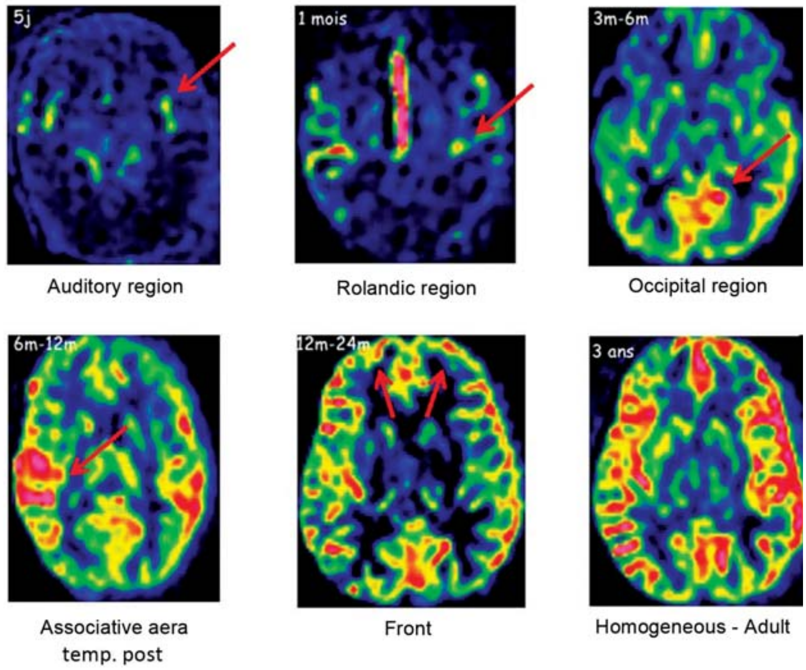
A history of medical progress

Epidemiology plays a central role in medicine as it identifies the factors that are responsible for diseases. It implies the use of models, whose first example may be found in Daniel Bernoulli's work[1]: he demonstrated as early as 1760 that the method of variolation (the inoculation of smallpox, or variola) was efficient in reducing the risk of variola. Since then, it became possible to model infectious and non-infectious diseases. Thus, the quantitative understanding of data replaced the "opinion" in the analysis of the causes and consequences of diseases.

As for physics, it made it possible, in particular, to develop medical imaging, which is now ever-present in medicine. It was a marvellous progression, from the first X-ray image of a hand, obtained by Wilhelm Röntgen in 1895, to the actual applications dominated by the many assets of magnetic resonance imaging, developed by Paul Lauterbach and Peter Mansfield (Nobel Prize 2003) who built Anatole Abragam's fundamental work on nuclear magnetic resonance. These approaches have disrupted medicine as they have allowed us to look into the interior of the body and

1 - See AJ Valleron. CR Acad Sci Paris, Sciences de la vie 2000, 323 : 429-33

Radiograph of the hand of Wilhelm Conrad Röntgen's wife



Brain imaging showing the functional regions activated during the brain development of a healthy child aged from 5 days to 3 years old

consider the volumes, shapes and some functional aspects – whether normal or pathological – of all the organs. Now combined with algorithmic science, using them is a key element in the development of digital medicine, which shall be mentioned further on.

The birth of organic chemistry at the end of the 19th Century, the concepts of enzyme/substrate, ligand/receptor (Paul Erlich) have been decisive. A new form of research was born, which, starting from the use of natural substances, had come to create chemical molecules used as drugs. As a consequence, the pharmaceutical industry has been booming for the last 70 years, and creating an impressive number and diversity of classes of active molecules: anti-infectives, anti-hypertensives, neuroleptics, analgesics, anesthetics, etc.

Biology, with the rise of molecular biology, genetics and cell biology – thanks, once again, to progress physics had made possible in the

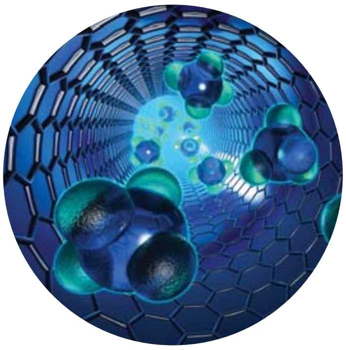
© Dan Race - Fotolia

elaboration of microscopes – has particularly fed development studies, immunology, neurosciences and physiology, resulting in the identification of many mechanisms of diseases. Studying genes has proved decisive, both in the identification of more than 3 000 monogenic hereditary diseases – enabling precise diagnoses and genetic counselling to be provided – and in the observation of acquired genetic disorders associated with cancer. For instance, the identification of a fusion transcript between the *BCR* and *ABL* genes – which gives birth to an aberrant kinase – made it possible to understand the physiopathology of one of the most common forms of leukaemia: chronic myelogenous leukaemia. This resulted, by 2000, in the development of a family of inhibitors against this kinase, whose use controls the disease (complete remission) and, sometimes, cures it. This is a most illustrative example of the power of the reductionist scientific approach to medicine as we have been observing it for the last 20 years. Let's also mention the development of anti-infective agents against viruses, and that of new hypertensive or new anticoagulant drugs.

On the whole, combining these approaches has expanded the therapeutic palette:

- Thanks to the nanotechnologies, drug vectorization makes it possible to improve drug availibility inside the cell, in particular.

- Biotherapies take an ever-growing part in the production of new drugs. Thus, the development of more and more elaborated and increasingly well-tolerated monoclonal antibodies (MAb) has contributed to the development of efficient treatment against chronic diseases – such as rheumatoid arthritis or Crohn's disease (anti-TNF MAb) – or lethal diseases – lymphomas (anti-C20 MAb), or several cancers whose prognosis until then was hopeless, as metastatic melanoma and some forms of lung cancer (anti-PD1, -PDL1, -CTLA4 MAb).



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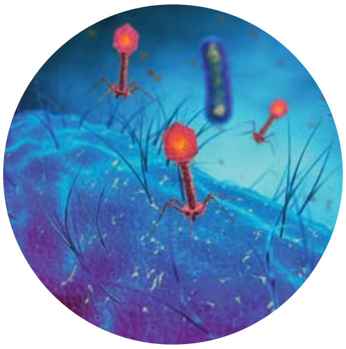
- Cell and gene therapies, for which first results have been obtained (hereditary diseases, some forms of leukaemia), may even enlarge the therapeutic arsenal.

- The development of medical devices – such as a sophisticated implant in ergonomic engineering research – is another source of progress, and so is minimally-invasive surgery, which draws on "augmented reality" obtained through the use of new software combined with robotics.



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And the results are here to see: life expectancy is ever-growing. In France, between 1990 and 2013, life expectancy in men thus passed from 73 to 78 years old, and in women from 81 to 85 years old. Such spectacular results are also due to social progress but medicine and especially improvements in perinatal medicine, preventive measures and policies – hygiene and vaccination – so as the effective treatment of many diseases, have been influential. The implications of such progress are twofold: the life expectancy in good health has increased (4 years gained for men and 3 years for women in France between 1990 and 2013) but, at the same time, a growing fraction of the population lives with one or several chronic diseases. Indeed, of the 60-69 years old age group, more than 75 % suffer from at least one disease and close to half of them have at least five. Combined with the ageing of the population, this situation is a health and economic challenge for our society.

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The challenges of tomorrow's medicine and health

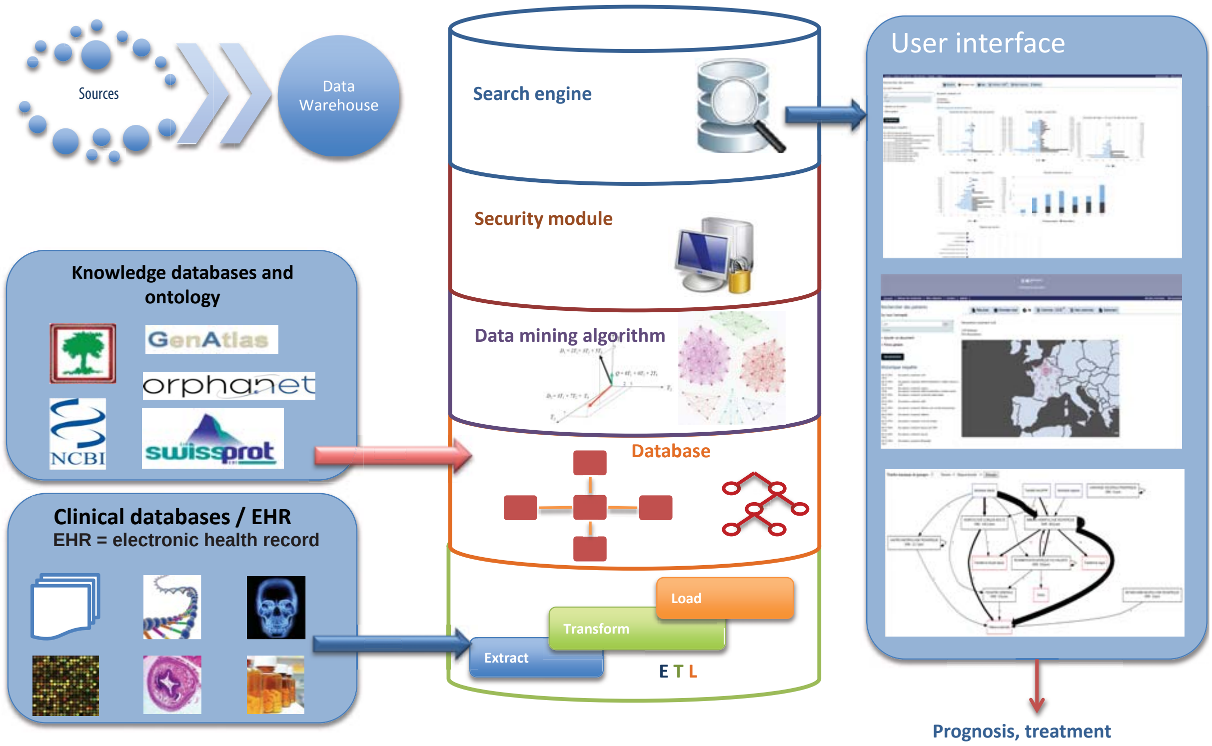
Despite spectacular breakthroughs, some fields of medicine have less progressed, as the questions they raise are more complex. Such is the case, in particular, with diseases that are neurodegenerative or sensory (deafness, blindness) and with mental health conditions. Changes in the environment and behavioural evolutions are at the source of some progressing conditions: obesity, diabetes, addiction, allergic or autoimmune diseases, bacterial diseases triggered by antibiotic resistance. Medical research, boosted by progress in fundamental research, should take this into account.

The complexity of living beings, including human being (whether in good health or ill), as illustrated by our 22 000 genes, the million regulation elements in our genome, the 3 x 10^{13} cells of our body, our cohabitation with 4 x 10^{13} bacteria in the intestine and more than 10^{15} viruses has to be taken into account, as well as time and individual and collective behaviours – how is it possible to grasp this complexity, to quantify it and extract useful elements for medicine to benefit from in ever-changing environment?

Quite logically, the number and types of available data for each individual increase rapidly, all the more so as “connected” devices are more and more used, making it easier to remotely extract many relevant parameters in the context of any given diseases (cardiac rhythm, glycaemia, etc.). A systemic approach to the individual, healthy or sick, is born. Thus, warehouses data are being built, often involving the individuals’ electronic medical files, which may, in turn, be associated to various biological pieces of information – genome, epigenome, proteome, metabolome, images, etc. The “intelligent” extraction of relevant data – a major development in algorithmic sciences – should logically drive progress in medical knowledge and become a major medical decision tool in what might be precision medicine. A serious issue will be our ability to link up the fruits of research that human and social sciences reap on health, as they will be crucial to understand the individual and collective human behaviours of those facing health issues.

Health is a social issue with an ever-prominent place; it is in direct contact with the progress of medicine, based on a scientific approach. Many questions call for an answer: how acceptable are preventive measures and policies, and potential forecasts, when health is the matter? Where should we draw the line? Efficient public health policies require quite sharp health training programmes for the people (and caregivers), especially on grasping a better notion of the different orders of magnitude of risk involved. How accessible is care? In France, despite a rather efficient redistribution system, health inequalities remain: there are life expectancy differentials, lethal diseases are diagnosed at more or less early stages, access to prevention is very diverse, etc.[2]

2 - O Nay, et al. Lancet 2016 , 387 : 2236-49



A medical data warehouse with relevant data extraction modules

The cost of innovative treatments – as illustrated in the recent period of time by the new anticancer drugs – is a factor weighing heavy on the risk that inequality of access to care may worsen. Such issues call for an in-depth ethical reflection, in order to make any progress in medicine the part of a human vision, draw the lines and prevent abuses. In this context, Nicolas de Condorcet's text – in *Outlines of an historical view of the progress of the human mind*, 1794 – proves widely prophetic: "*It is manifest that the improvement of the practice of medicine (…) must in the end put a period to transmissible or contagious disorders, as well to those general maladies resulting from climate, aliments, and the nature of certain occupations. Nor would it be difficult to prove that this hope might be extended to almost every other malady, of which it is probable we shall hereafter discover the most remote causes.*"

Nicolas de Condorcet (1743-1794)

On the path to discovering human beings and their brains

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Jean-Pierre Changeux

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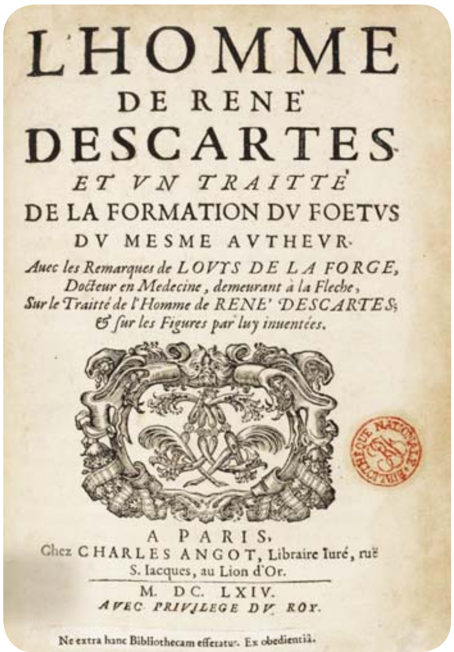
Descartes wrote about 1632 the *Treatise on Man*, which would only be published after his death, in 1664, two years before the first session of the Académie des Sciences was held. Although unfinished, this prophetic text anticipates, despite the inaccuracies, 350 years of research on the discovery of human beings and their brains. From the elementary structures of man's body – muscles, nerves "small and big pipes", and so on – he attempted to establish a causal link between the anatomy of this "machine" and its physiological functions, one level after the other, up to the "reasonable soul", with "its principal seat in the brain".

Here is the end of Descartes' treatise: "*In this machine (...) it is not necessary to conceive of (...) any other principle of movement or life, other than its blood and its spirits which are agitated by the heat of the fire that burns continuously in its heart, and which is of the same nature as those fires that occur in inanimate bodies.*" This proposition will be the backbone of my presentation on the successive steps by which our knowledge on human beings has progressed, from the chemistry of life to the higher functions of the brain.

Step 1: the chemistry of life

In 1661, the Irish Boyle, as a follower to Descartes' mechanistic philosophy, tried to explain the properties of matter from atoms he called "corpuscles". He also observed that pumping air from a closed vase extinguishes the flame of a candle and kills the animals placed inside it.

Lavoisier, the founder of modern chemistry, was interested in combustion. He demonstrated at the Académie des Sciences, on 26 April 1775, that the combustion of charcoal released "fixed" air, which resulted from



L'HOMME
DE RENE'
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ET VN TRAITTÉ
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Auec les Remarques de LOVYS DE LA FORGE, Docteur en Medecine, demeurant à la Fleche, Sur le Traitté de l'Homme de RENE' DESCARTES; & sur les Figures par luy inuentées.

A PARIS,
Chez CHARLES ANGOT, Libraire Iuré, ruë S. Iacques, au Lion d'Or.
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Descartes, in his Treatise on Man *(1664), anticipated the discoveries that would be made on the brain.*
*Pastel by Simon Vouet, from the collections of the Louvre. Identification of the model to René Descartes by Alexandre Marr (*In Times Literary Supplement*, 13 March 2015, pp 14-15). Thanks to Arnauld and Barbara Brejon de Lavergnée for transmitting this information.*

the combination of carbon with some gas, mysterious at the time: oxygen. A major step was taken when Lavoisier extended his chemical theory to the respiration of living beings. In cooperation with Laplace, he built the calorimeter to measure the quantity of heat that is released per unit of gas carbon produced either by a flame or by the respiration of a guinea-pig: the measurements being identical, Lavoisier concluded that "*respiration is combustion*", like the flame of a candle.

An experiment on a bird with the air pump – *Joseph Wright of Derby's painting, 1768 – recaptures the observation made by Boyle.*

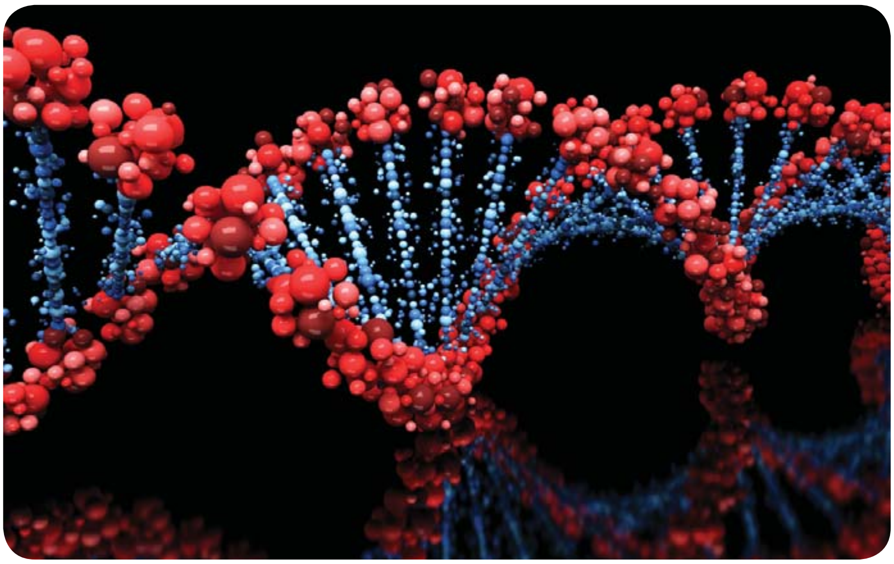
Fifty years later, the Swedish Berzelius built on Lavoisier's approach and proposed a theory according to which any chemical reaction resulted from the combination of groups of atoms that he called "chemical radicals". He even invented the term "catalysis" to describe the specific acceleration of a chemical reaction and called "polymers" the "organic" compounds that living beings produce from these very chemical radicals. A most animated debate then shook the scientific community. Could one believe in the vitalist theories that, invoking mysterious forces, claimed a difference between organic compounds – produced by living beings – and inorganic substances? The chemical synthesis of urea by Whöler, in 1825, brought a first demonstration that vitalism had failed; the many organic syntheses performed since then have confirmed such failure.

Jons Jacob Berzélius
(1779-1848)

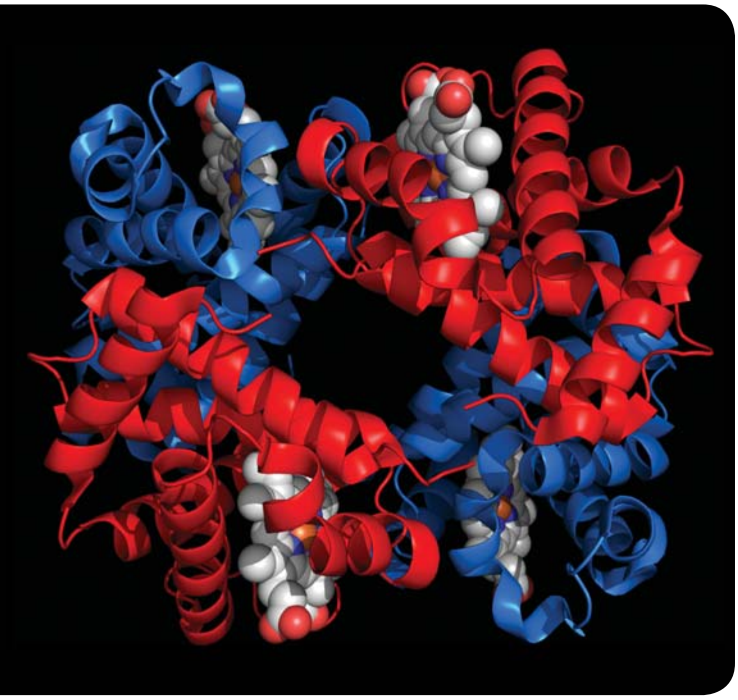
The repertoire of the molecules that constitute living beings comprises high-weight polymers, or "macromolecules", including in particular proteins – another term Berzelius coined – which result from the linear combination of 20 amino acids. Other macromolecules are formed from nucleotides – such as desoxyribo- and ribo-nucleic acids (DNA and RNA) – , sugars – for polysaccharides – and so forth. In 1833, it was observed that the enzymes catalyzing the chemical reactions that constitute living organisms were proteins. Finally, in 1897, Buchner demonstrated that the whole complex processes involved in alcohol fermentation could be obtained in vitro from an extract of yeast, in the very absence of any living yeast. The relevant set of enzymes and their substrates were enough. From then on, living beings – including human beings – would be understood as vast and complex chemical systems in which macromolecules would play a central role.

Throughout the 20th Century, and even today, research has been dealing with the fine structures, at the atomic level, of these macromolecules. Various physical techniques have been used, including X-ray diffraction. In 1953, it was the double stranded DNA model described by Watson, Crick and Rosalind Franklin that revolutionized our understanding of heredity. It would be followed, more recently, by the elucidation of

Francis Crick
(1916-2004)



Tridimensional structure of DNA by X-ray diffraction the complete chemical sequence of the 3.5 billion base pairs (which are of four types) of a human DNA. Each human being has now become "labeled" by his or her DNA sequence. In 1960, Perutz and Kendrew highlighted, on haemoglobin and myoglobin, the three-dimension folding of the amino-acid protein chain. Then followed the deciphering of the reconnaissance mechanism, enabling the proteins to recognize the small molecules they bind to: a specific complex forms, in which the ligand enters the protein just like a lock and key.



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Tridimensional structure of hemoglobin by X-ray diffraction

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Max Perutz
(1914-2002)

The chemical reactions that compose the living systems are not independent from one another but rather coordinated with one another. Specialized regulatory proteins, called "allosteric" proteins, act as biological switches, binding regulatory signals and biological actions together. A change in the conformation of the protein controls the coupling between distinct sites. Such was my thesis work at Jacques Monod's laboratory.

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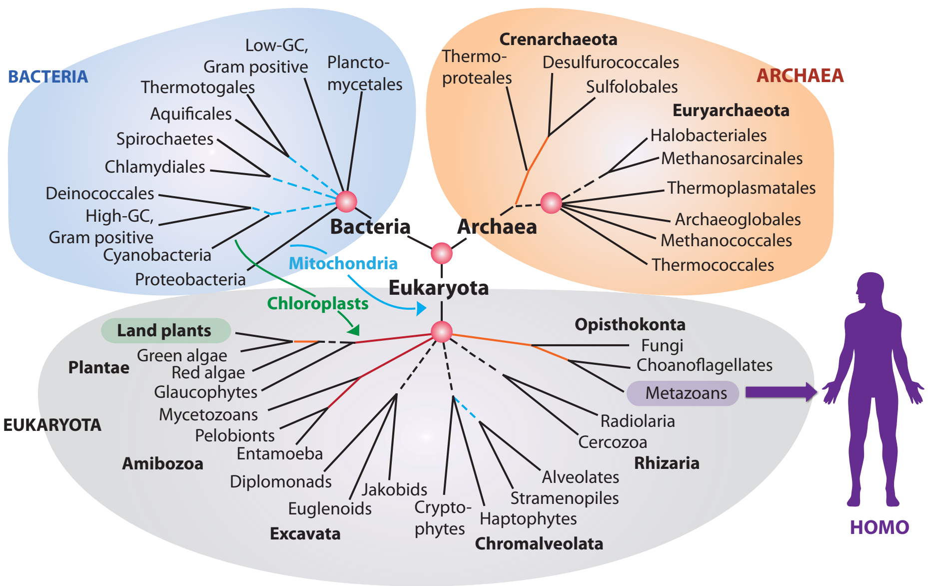
Step 2: cell biology and evolution

The living being is not merely a bag of enzymes: it has a shape and an organization. At the most elementary level is the cell, which accumulates proteins and nucleic acids. With higher organisms, a nucleus is to be found in each cell, inside a watery cytoplasm, circumscribed by a membrane made of lipids. "*Omnis cellula e cellula*" ("*Every cell [stems from] another cell*"), suggested Virchow as early as 1855. During the development of the embryo, not only do cells multiply, but they also differentiate into distinct types – muscular, hepatic and so on. This microscopic diversity is in line with a broader diversification, the diversification of the general shapes of living beings.

Starting with Aristotle, the description of species expanded in the century of the Enlightenments with the Swedish Linné and, in our country, with Buffon. These species were classified within a hierarchy in a table illustrating some "growing perfection" from one to the other. At the summit was seated "man", then the Creator above, responsible for this harmonious "*scala naturae*". The table is fixed and immutable. Until Lamarck, on 11 May 1800, in the opening speech of his course at the Muséum d'Histoire Naturelle, abandoned this vision of the world to the benefit of a revolutionary concept, the evolution of the species: species are not fixed, they "transform" themselves. Darwin, 59 years later, took over the transformism thesis but abandoned Lamarck's inheritance of acquired characters to the benefit of natural selection as the drive of evolution. Two centuries of biological research would validate this Darwinian model. The study of fossils has shown that species, or even entire groups, appeared and later, in great part, disappeared. Death has become the essential cog in the evolution of life. Unexpectedly, gene transfers occur between sometimes very distant species, and the tree of life becomes uncertain and irregular. It takes the shape of a bush, where *Homo sapiens'* ancestors appear on a lateral branch: human beings are not taking pride of place at the summit of the scale of beings any more.



Studying the genetic kinship of living species (based on ribosomal RNA) reveals a bushy tree of life in which man appears on a lateral branch.

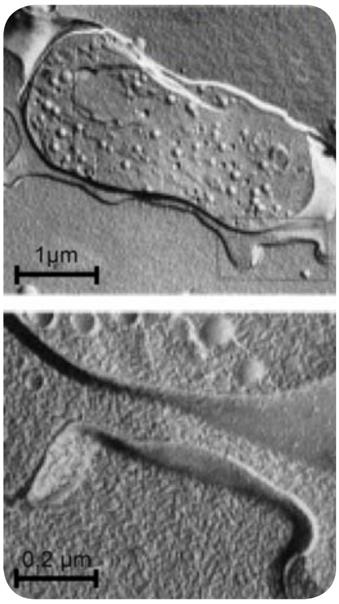
The developments of a new discipline, genetics, would reveal unbreakable bonds between evolution and development. As early as 1866, Mendel acknowledged the existence of stable and transmissible hereditary characteristics – such as the colour and form of the peas he cultivated in the garden of his monastery – which he ascribed to invisible "factors" that have been called "genes" since then. Morgan, in the 1920s, demonstrated, with the fly, that these genes are localized on the chromosomes, in each cellular nucleus. He considered they were likely to be modified by mutations that were transmissible through heredity. Molecular biology has established that each protein of the organism is encoded by a genetic sequence of DNA molecule and that mutations in such sequences are at the origin of many diseases in humankind. Besides, it is a fact that all the genes of our chromosomes do not express themselves at the same time during development. Tallying with the masterful demonstration Jacob and Monod made in 1961, specialized gene sequences, called "regulatory" sequences, control the diversification of cell lineages in the organism, and notably that of the nervous cell, the neuron.

The neuron appeared very early in the course of evolution, with the hydra and jellyfish. It ensures fast communication and coordination between the different parts of the organism. It individualises itself by the many prolongations, axon and dendrites, that come into contact with hundreds and sometimes tens of thousands of other cells. As Ramon y Cajal already suggested in 1890, neurons form discontinuous networks in which the membranes of the nervous cells are juxtaposed at synapses. Remarkably enough, the main anatomic and physiological features of the nerve cell are kept from the primitive species to human beings. Axons propagate electric signals that are entirely reducible to the transport of electrically-charged ions. At the synapse, chemical signals – neurotransmitters – take over, spread in the synaptic space and bind to receptors. As they convert chemical signals into electrical signals, receptors are part of the allosteric switches mentioned above. Already present in bacteria, these receptors impose irreducible constraints on the information processing performed by our brains. They are also the targets of many drugs. Our nervous systems are, as the rest of our organisms, vast physicochemical systems whose constituent parts have little changed in the course of evolution. What has changed is the organization.

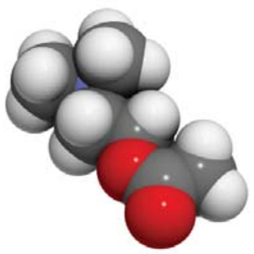
0,1 millimeter

Neuron (Santiago Ramon y Cajal, 1894)

micrometer

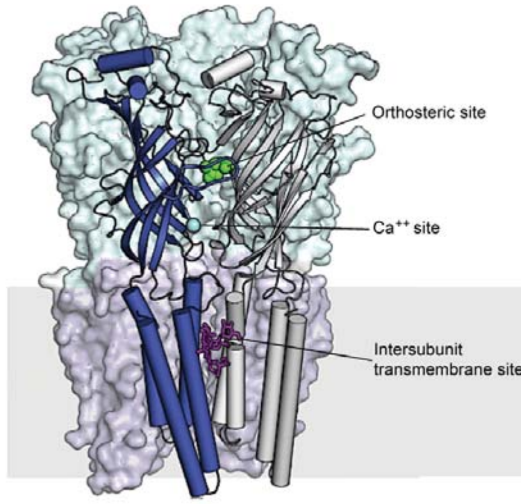


Neurotransmitter as a chemical signal

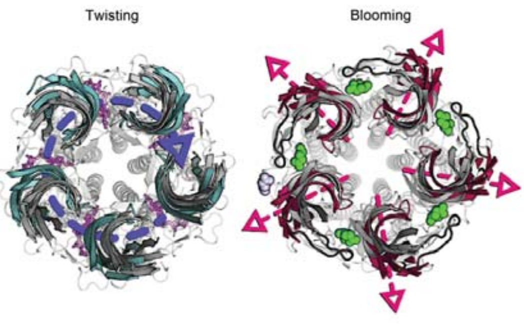


Acetylcholine

nanometer



Fine structure (atomic resolution) of a neurotransmitter receptor like the nicotinic acetylcholine receptor



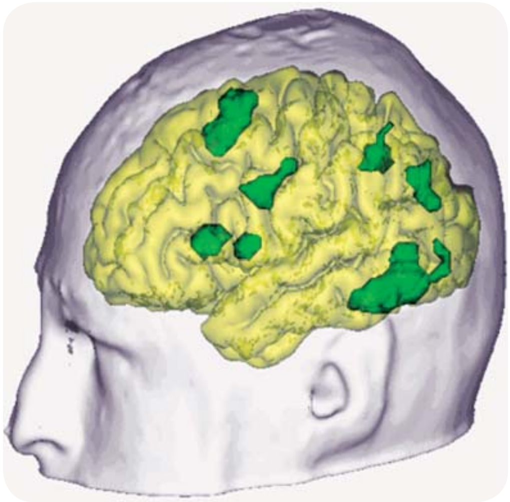
Allosteric transitition of a receptor like the acetylcholine receptor

The basic components of the brain: the nervous cell, synapse and molecule of the acetylcholine neurotransmitter with its receptor

Step 3: the evolution of the brain and the origin of culture

The brain evolved dramatically and differentially, both in size and complexity. Brain size increased, especially the surface of the cerebral cortex and more specifically its front part: the prefrontal cortex. Left/right hemispheric asymmetry developed. The number of brain neurons increased, from 50 million in mice to nearly 100 billion in humans. At the same times, new psychological functions appeared: self-awareness, our ability to consider others as oneself, symbolic life, with spoken and then written language. All these functions, defined as “cognitive”, now fall within the scope of the scientific method. To deal with them, several disciplines must converge: brain imaging, electrophysiology, psychophysics and computational modelling. Another revolution is underway: it stems from Socrates' "*Know thyself*" and even Descartes' "*Cogito ergo sum*"!

Eminent scientists have embarked on this path, such as Jouvet or Buser, Crick or Edelman. The strong idea behind it is that conscious processes, shared by all human beings, develop in common physical spaces of our brains. There, takes place the “global and unitary” synthesis of perceived exterior events and inner memories. Dehaene and I have suggested that neurons with very long axons might create interconnections between these different territories of the brain and contribute to building this conscious space. Such a network involves the prefrontal, parietotemporal and cingulate cortices, the latter being involved in emotions. It is possible within this neuronal space to make out the brain images obtained while visual processes are taking place, whether consciously or non-consciously.



Reading in a conscious way

Reading in a non-conscious way

Functional magnetic resonance imaging of a individual reading a word in a conscious or non-conscious way

No mysteries, but still a lot to discover!

Everyone might wonder what critical genetic modifications have led to the astounding increase in structural complexity entailed by such cognitive functions. In 1830, Geoffroy Saint-Hilaire suggested at our Académie that there was a unity of plan in the organisation of animal species. The central nervous system is on the front part of this plan. We now know, especially through Nüsslein-Volhard's pioneer work, that this plan is determined by a network of regulatory genes, called “homeotic” genes. Their mutations bring about spectacular changes, such as, in the fly, the substitution of an antenna for a leg.

These genes play indeed a role in the biogenesis of the brain. The recent deciphering of the complete genome, however, has created one more paradox. As a matter of fact indeed, if the genome of yeast contains about 6 000 genes against 13 000 for the drosophila, there is however no variation in the number of genes that code for proteins from mice to humans – about 25 000 – and, between chimpanzees and humans, the total sequences of coding genes only differs by 1.2 %! The anatomic and functional complexity of the brain thus increases much faster than the complexity of the genome. One first hypothesis is that this evolution may result from mutations in some critical regulatory sequences that control the development of the brain. Another lies in the process of postnatal development.

At birth, human cubs have brains that weigh five times less than the brain of an adult, and the period of maturation after birth is exceptionally long compared to other species – it lasts more than fifteen years. More than half of the synapses of the adult brain, of the order of one million billions, form after birth. During this period, fundamental learning takes place, such as the acquisition of walking, language or social interactions. Then phases of synaptic exuberance occur with maximal variability, followed by selection phases with the stabilisation of some connexions and the elimination of the others. The activity of the network, whether it be spontaneous or triggered by the environment, regulates this synaptic selection process, which is “Darwinian” but not genetic. Some variability even occurs between genetically identical individuals. As we have suggested with Courrège and Danchin, “*to learn is to eliminate*”. Due to this intense synaptic plasticity, cultures develop, pass from one generation to the other and distinguish social groups from one another. “Cultural pathways”, such as those taken by writing, reading, or even ethical rules, remain inscribed, as it were, in the brain. The brain of each individual “internalizes”, according to Vygotsky, the features of his/her physical, social and cultural environment. Thus develops the “human person” with his/her “*habitus*” associated to each individual’s story.

Would this physicalist approach – first Cartesian and then Darwinian – drive mankind to lose part of its humanity? This is far from certain. Here is indeed what Günther Anders tells us: “*Extend your representative capacity in order to know what you are doing*” (In *Nous, fils d’Eichmann, Rivages Ed., 1999*). The dispositions of our brains, that enable us to progress in the knowledge of what we are, leave us with a heavy ethical responsibility. It is for us to invent, with our brains, a future that will open access to, as Ricoeur put it, a “*good life with and for others, in just institutions*” (In *Soi-même comme un autre, Seuil Ed., 1990*) and, I should add, in a sustainable environment...

From the cell to the ecosystems

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Yvon Le Maho

Member of the Académie des sciences, Emeritus Senior Researcher at CNRS, Institut pluridisciplinaire Hubert-Curien, University of Strasbourg, also affiliated at the Monaco Scientific Centre

One way to explore the huge field for investigation that spans from the cell to the ecosystems is to consider the question of “animal models”. This is what we call animals by which we try to understand how our organisms function and how to fight more efficiently against diseases. In this context, animal biodiversity proves to be an amazing source of biomedical innovation. Now, Voyager, sail thou forth to seek and find…

Classical models VS exotic models

First stop: the Kalahari Desert, with a strange animal, the Damaraland mole-rat. In fact, it is neither a rat, nor a mole – it belongs to a family of animals close to the guinea pig. But as a model animal for biomedical research, it is undoubtedly an exotic animal. Indeed, the "standard" model is the mouse: it breeds rapidly and, being small, is quite cheap. We now have a whole range of genetically engineered mice, designed for all sorts of so-called "mechanistic" approaches. But the key issue is the relevance of the animal model that is being used. Because this was overlooked, tragic foetal malformations occurred after pregnant women took thalidomide.

But let’s get back to the family of mole-rats. All have high life expectancy, including the naked mole-rat. Less photogenic than its fellow creature from Damaraland, it may live 32 years, which is 16 times longer than a mouse. Now, we have discovered that it is provided with a mechanism, which the mouse does not have, preventing the proliferation of cancer cells. The editorial written by JM Sedivy, in the Proceedings of the National Academy of Sciences of the United States of America (PNAS, 2009), asked then whether and how it was relevant to devote virtually all the resources of research to the standard animal model: “*The situation is in some ways reminiscent of the old joke of the drunk looking for his keys under the street*

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The mole-rat, here from Damaraland, an exotic animal model

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Kalahari Desert
(South of Africa)

lamp. The currently mainstream biological model systems sure shine a powerful light, but the keys to some really interesting (and important) questions may simply not be found under it." However, we thought that the naked mole-rat was preserved from cancer, but tumours have just been discovered in animals kept in American zoos. It will obviously be very interesting to determine what elements led these animals to develop tumours, in order to possibly learn lessons for human health.

Research on mole-rats is conducted in the laboratory, but mechanisms developed by some exotic animals may only be studied in nature. Thus, one of the most remarkable model animals is the hibernating bear. Echocardiography performed on the bear show that its heart beats about 60 beats per minute - a rate that reduces to 5 or 6 beats per minute when the bear hibernates. What is extraordinary in this hibernation fasting is that the bear exclusively uses its own fat: it saves its muscles and all its other valuable body proteins, which explains why it does not urinate or defecate for the 5 to 6 months of its hibernation. Bears are among the only animals able to do so: men, as any other animals, with a few exceptions such as some bats, experience a reduction of their muscle mass when they fast. Indeed, in the treatment of severe obesity, even when there is still a lot of excess fat, very low calorie

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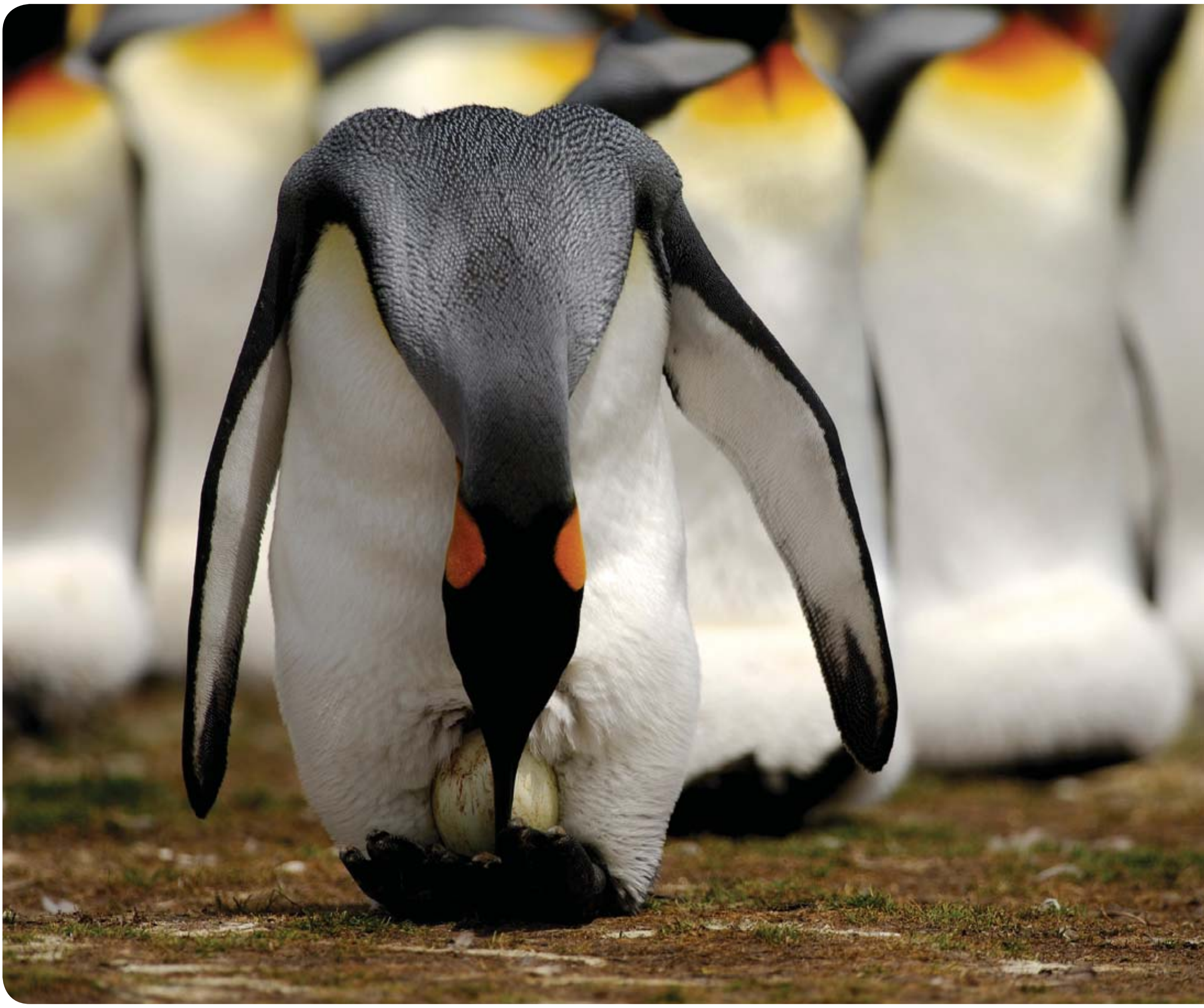
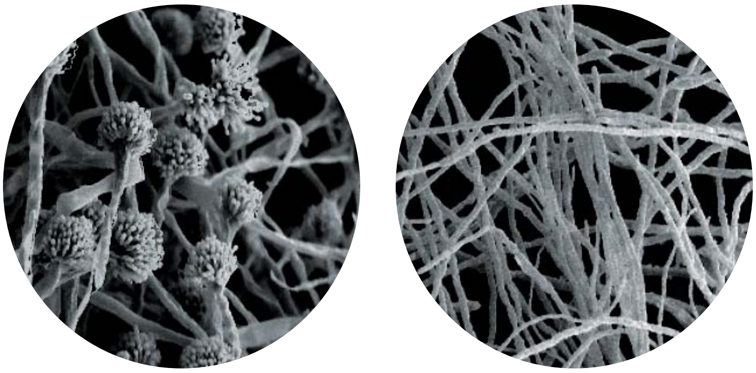
diets may not be extended beyond a certain period of time because they would result in a critical loss of muscles, and notably heart muscle. We therefore see how desirable it is to elucidate and mimic this mechanism in the treatment of severe obesity.

Another example of a physiological mechanism of interest that can only be studied in nature is that of the king penguin incubating its egg. Male and female feed at 300 to 400 km offshore; fasting is thus associated with incubation, for which they take turns on dry land. Usually, it is the male that performs the incubation during the last 2 or 3 weeks, with the female then coming back on hatching time to feed the chick. The female may however not come back in time, especially because of the warming associated with El Niño, whose effects are felt as far as the Southern Ocean, and may thus drive its prey even further away, over 200 km further south. It is remarkable that the male is then able to keeps its chick alive for a week, feeding it with marine prey it keeps intact during those two or three weeks into its stomach despite a temperature of 37-38° C. With the support of the Fondation de France, we have been able to associate this ability to preserve food with the presence of a small antibacterial and antifungal protein. Once its structure established and the synthesis of its molecule made, it has been shown it was very effective against two of the main agents



of nosocomial infections, *Staphylococcus aureus* and the pathogenic fungus responsible for aspergillosis. Moreover, this protein is very effective in saline environments – the salinity of the penguin's stomach is comparable to that of our eyes – unlike most antibiotics. Now, bacterial resistance to antibiotics has become an emerging major public health concern, and there is a dramatic lack of antimicrobial agents able to fight eye infections.



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Spheniscin, a peptide produced by the stomach of the king penguin, alters the growth of microorganisms – here, the growth of Aspergillus fumigatus *(left, control sample; right, with penguin peptide). From Thouzeau C,* et al. J Biol Chem *2003 ; 278 : 51023-8.*

Even with all the expertise in biology required to identify such a molecule and its structure, it would not have been enough. It took innovate new methods to collect microsamples of gastric content at the different stages of the incubation, in satisfactory asepsis conditions, and without, of course, disturbing the animals and cause reproduction to fail. If a penguin stops incubating, it stops keeping its food in its stomach and digests it. But how should we go about studying an animal in its environment?

Adapting research to the natural environment

For centuries, animals have been studied from their only remains brought from expeditions. The approach entailing the description of their ways of life and behaviours through undisturbed observation is a very recent one: it was made possible by the considerable progress that has been achieved in the last few decades in computing and electronic miniaturization.

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To identify each individual animal and locate it without disturbing it is not simple. For this to be done, we have used for a long time, in penguins, a metal band placed on a flipper of each penguin with numbers that were easy to read from a certain distance with binoculars. But how were we to make sure that the resulting hydrodynamic hindrance to the movement of the sea animal caused no injury? It took, in the early 1990s, the invention by Texas Instruments of RFID - radiofrequency identification - which uses electronic tags of less than one gram implanted under the skin, to have real control animals with no hydrodynamic hindrance. Thanks to the Bettencourt-Schuller Foundation, this technology, even before being marketed, enabled us to highlight the impact of a flipper band on the king penguin: compared to control individuals, the reproductive success of banded individuals reduced from 40% in ten years, and their survival from 16%. The chick survival after three years is halved when it has been wearing a band.

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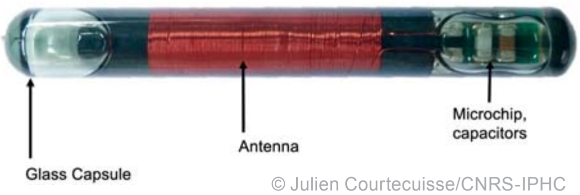

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A band, or even better an electronic tag, helps locate the penguins

This extreme miniaturization of electronic RFID tags is made possible because they operate without any battery. Power is supplied by an antenna when the "labelled" animal is less than 50 cm from it; in return, the antenna takes down the number corresponding to the label. It’s been 18 years since, within the framework of the Paul-Emile Victor Polar Institute, antennas have been buried on three passage points in a large area of the colony of Possession Island, in the Crozet Archipelago, allowing king penguins to be automatically identified on entering or leaving. This, however, does not enable us to locate them within the colony. In theory, it could be possible to identify and locate the individuals wearing electronic tags by roving around in the colony with a manual RFID reader containing the activation-sensor antenna. However, approaching each animal this way is out of the question as the resulting disturbance would be phenomenal.

Inspired in this by the exploration of Mars, and with means provided by the Total Foundation, we have had the idea of using rovers, that is to say remote-controlled vehicles. Incubating king penguins defend their territory against the rover in the same way as they do against their fellows that commute into the colony. By equipping king penguins with cardiac monitors of the type that is used for jogging, we do not observe the significant increase in the heartbeat rate that reflects stress caused by the presence of humans - stress that would make them leave their location in the colony - thus causing its disruption, with the risk of egg abandonment. At Kerguelen, we have already launched the operational phase.

With the emperor penguin, all turned out to be more complicated. Indeed, it does not defend any territory when incubating its egg or chick, as this would prevent it from huddling tightly with its fellows and thus reducing energy expenditure in the polar cold. However, if the rover is disguised with a fake little chick, the penguin allows to be approached at the right distance for electronic identification to take place. But the size of a rover under the disguise of a small chick is a limitation to the number of scientific instruments it can carry. Moreover, such a rover may only be used in the period of time when there are small chicks.

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Adult and chick emperor penguins even vocalize to communicate with the fake chick rover (Le Maho, et al. *Nat Methods 2014; 11: 1242-4).*

It was therefore necessary to build a fake adult emperor penguin. There is a big obstacle to it: it is impossible to maintain it in an upright position and make it move, as the speed of the wind often exceeds 100 km/h in Adélie Land. However, adults can be seen moving on their stomachs with the help of their flippers and legs: they are said to be "tobogganing". This is how our new project was born: within the international laboratory we have created with the Institut pluridisciplinaire Hubert-Curien de Strasbourg and the Monaco Scientific Centre, and once again with the support of the Total Foundation, a first prototype has been designed in Strasbourg. It was completed in mid-January and then sent to the Dumont d'Urville Station, in Adélie Land. Tests are currently underway in the colony, while engineers are working in Strasbourg on the articulation of its flippers and legs, which it is for now unable to move. Another hurdle: the servomotors that, until the present day, activate the robots may not be used because the sounds they make are within the vocalization spectrum of the penguins. New methodological innovation is needed.

© Marco Monticone

Precious information

Studying animals in their natural environments also provides more insight into environmental changes, especially into those related to variations in the climate. Thanks to the electronic monitoring systems that have been in place for 18 years with king penguins, it will be eventually possible to know, on the scale of a population, how climate variations, as they determine where and how abundant their marine prey may be, impact the reproductive success and survival of penguins.

In return, when wild animals are equipped with data acquisition systems coupled with carefully designed Argos beacons, data may be gathered on the ecosystems in which they live. This has been done, in particular, for the olive ridley sea turtle in Guyana, in order to measure how the salinity and temperature of its living environment vary at different depths.

In addition to the standard mouse and rat models, the so-called "exotic" animal models are still largely unexplored mines of information that enable us to highlight, from the cell to the ecosystems, mechanisms that are yet unknown and, at the same time, better understand our environment.

"Adult" rover in a colony of emperor penguins in Adélie Land (austral winter 2016)

Chemistry, the science of matter: to understand and create!

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Jacques Livage

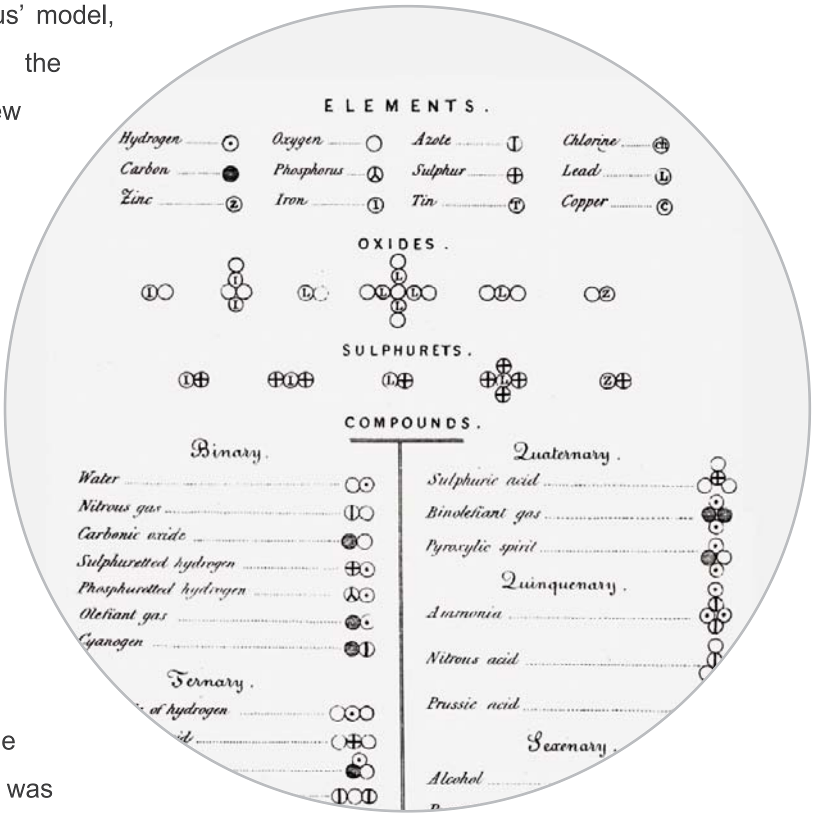
Member of the Académie des Sciences, Honorary Professor at the Collège de France

Chemistry, the art of transforming matter, played a key role in the history of humanity. With every progress achieved in extracting metals from their ores, another stage was reached in our development. Indeed, we have gone from the Age of stone to that of copper, then bronze and iron. Today, high-temperature silica reduction leads to the formation of silicon, which is at the origin of the development of all modern electronics.

Chemical Arts

Curiously enough, although "chemical arts" had been practised since earliest antiquity, chemistry as a science only rose in the late 17th century. As soon as it was created, in 1666, the Académie des Sciences appointed two chemists, Claude Bourdelin and Samuel Cottereau du Clos. As a matter of fact, neither was really a chemist: the former was an apothecary to the Duke of Orleans, and the latter was an ordinary physician to Louis XIV. At the time, chemistry was mostly about extracting active principles from plants or analyzing mineral water: it was part of medicine and pharmacology.

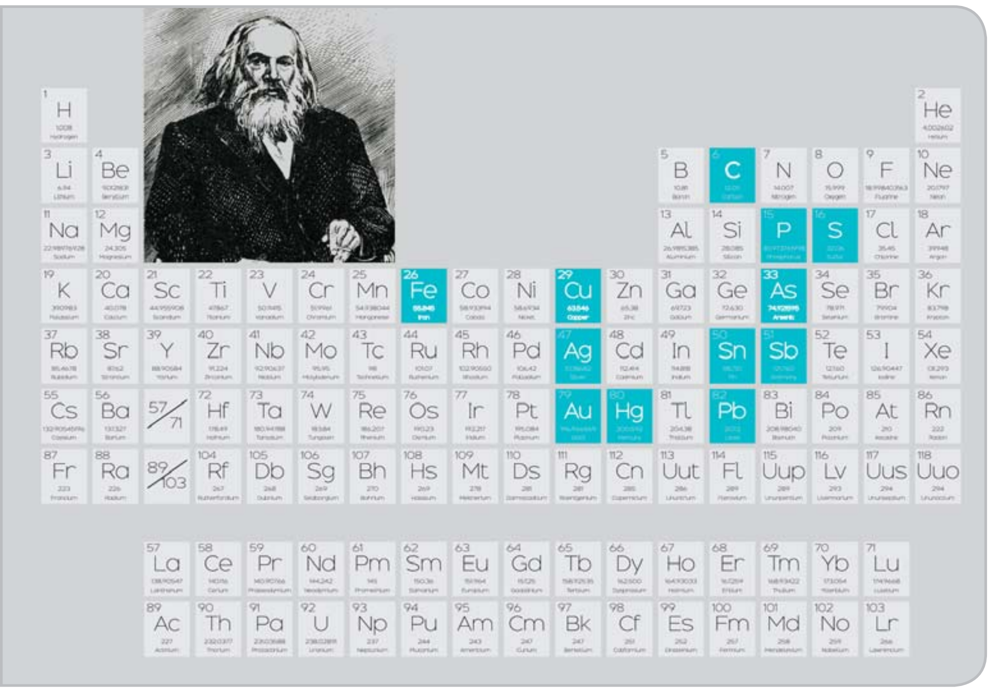
For chemistry, the science of matter, there was still a fundamental question to answer in the early 17th century: what is matter, what is it made of? The hypotheses propounded by the Greek philosophers of antiquity were still predominating. Democritus claimed that matter was composed of tiny grains (atoms), whereas Empedocles, Aristotle and Plato asserted that it was made of four elements: water, air, fire and earth – a model that alchemists would apply to their own ambition, transforming metals into gold... In the 18th Century, Ernst Stahl, to explain combustion, was still resorting to the element of "flame": it was the "phlogiston" theory, superseded by Lavoisier when he highlighted the role oxygen played in combustion phenomena. The publication of the Elementary Treatise of Chemistry, in 1789, marked the birth of a universal language - chemical nomenclature - that would be used by chemists worldwide! Shortly afterwards, John Dalton confirmed Democritus' model, drawing a distinction between the atom and the molecule. In his New System of Chemical Philosophy, published in 1808, he showed that air was made of a mixture of four gases: nitrogen, oxygen, carbon dioxide and water vapour! It was the birth of the modern atomic theory.



John Dalton's table of atomic symbols

From analysis to synthesis

The concept of atoms as the elementary compounds of matter was accepted, but it still remained to know what an atom was. In the early 18th century, only a dozen elements had been identified, such as gold, silver, mercury, lead, copper, sulphur and carbon. There still remained a hundred other elements to be found in order to know at last what matter was made of. Analysis thus became the chemists' first task: they discovered chromium and beryllium (Vauquelin), boron (Thénard), bromine (Balard) and silicon (Berzelius). About sixty chemicals were thus discovered over the following two centuries. They were listed in the periodic table published by the Russian chemist Mendeleev in 1869. This classification reveals how clever and sharp-eyed the chemists of the 19th century were. At the time, electrons and the structure of the atoms were still unknown, the latter being only described in 1913 by Niels Bohr. Each element was only defined by its mass and properties. Moreover, many elements were still to be discovered. It was thus necessary to leave blank spaces, which would, by some miracle, coincide with the elements that would be



The periodic table of elements, published by Dmitri Mendeleev in 1869, illustrates the essential contributions analytical chemistry made in the 18th century. However, at that time, only a dozen chemical elements (in blue) were known.

later discovered! The periodic table was probably one of the greatest scientific discoveries ever: it showed that no more than some tens of atoms constitute all matter in the universe. Incidentally, the very existence of atoms was not yet universally accepted: some chemists, such as Marcelin Berthelot, violently opposed the atomic theory!

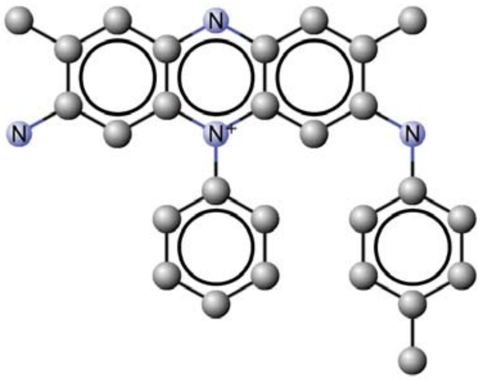
Marcelin Berthelot (1827-1907)

With analysis, chemists finally understood what matter was made of. In return, they could combine the elements in order to develop the most creative part of chemistry, synthesis. Chemists were becoming able not only to understand nature, but also to create new molecules. The synthesis of urea by Wohler, then that of acetylene by Berthelot, showed that it was possible to synthesize an organic compound without resorting to the "vital force". Marcelin Berthelot's work, *Organic Chemistry based on Synthesis*, published in 1860, triumphantly opened the pathway for organic chemistry.

William Henry Perkin (1838-1907)

Chemistry was a science but it was also an industry, which, relying on the new syntheses performed in the laboratory, would be a great contribution to the industrial revolution of the 19th Century. The synthesis of dyes – mauveine by Perkin, indigo by Baeyer, the 1905 Nobel Prize – enabled the organic industry to rise and companies such as BASF to be created, in 1865.

The synthesis of dyes launched the chemical industry era: here is mauveine, the first synthetic dye to be made (Perkin, 1856).



At the same time, inorganic chemistry was developing the manufacture of soda using the Leblanc process, replaced 50 years afterwards by the Solvay process. Technically ambitious and clever, the implementation of these processes is a model of what the chemical industry has been able to achieve.

In the 20th century, chemistry diversifies

With quantum theories developing and characterization techniques improving in the course of the 20th Century, chemistry experienced a rapid evolution. It conspicuously deepened and diversified at the same time. New disciplines appeared: catalysis, solid state chemistry, organometallic chemistry, computational chemistry, physical chemistry, biochemistry, geochemistry, etc. The discovery of radioactive elements - polonium and radium - by Pierre and Marie Curie marked the beginning of radiochemistry, with all its impacts on the fields of medicine, energy, and even weapons.

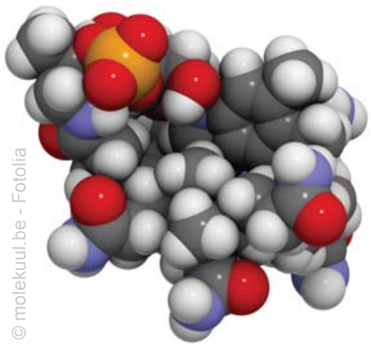
Pierre (1859-1906) et Marie (1867-1934) Curie

The quantum description of the electrons shed new light on their behaviours within matter. It became possible to provide a quantitative description of chemical bonding and of the electronic properties of molecules (Pauling, 1954 Nobel Prize; Ken'ichi Fukui and Hoffmann, 1981 Nobel Prize). Theoretical chemistry would play an ever-increasing role. It became predictive and would be rewarded with two Nobel Prizes, the first one being for quantum methods (Pople and Kohn, 1998) and the other one for multiscale methods, that allow the behaviour of a population of several hundred thousand atoms to be modelled (Karplus, Levitt and Warshell, 2013).

At the same time, the analysis tools and characterization techniques - X-ray diffraction, NMR, electron microscopy, scanning tunneling microscopy, etc. – provided a much finer picture of the structure of matter. The determinations of the structure of insulin (Sanger, 1958 Nobel Prize) and of the DNA double helix (Watson and Crick, 1962 Nobel Prize) were most significant examples of it.

The Watson-Crick model of the structure of DNA

With such new data, chemical synthesis encountered considerable developments. Chemists became more skilled at transforming matter to

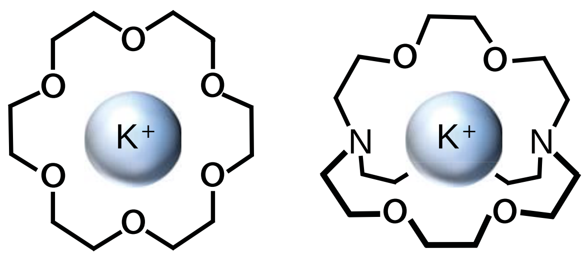


Vitamin B12 molecule

synthesize increasingly more complex molecules. Vitamin B12, in this respect, is quite exemplary. This molecule, which is vital to us, is synthesized naturally by microorganisms - bacteria, fungi, algae. It was an object of investigation for numerous studies, leading to four Nobel Prizes. Isolated in 1948, its structure was elucidated in the early 1960s. Its synthesis, published in 1973, was achieved through the use of the Woodward-Hoffman rules that describe chemical bonding in terms of molecular orbital symmetry.

Chemical synthesis had made it possible to move from atoms to molecules, and now to supramolecular chemistry, in which the molecules assemble into increasingly complex structures (Cram, Pedersen and Lehn, 1987 Nobel Prize). The issue was no longer to study the properties of a given molecule, but to consider the synergy their associations created. This blurred the borders between organic and inorganic chemistry. Organometallic compounds, coordination complexes and organic-inorganic hybrids developed, in which metal atoms are associated to organic ligands.

Jean-Marie Lehn



Supramolecular chemistry deals with the complex combinations that molecules form with one another: here, a cryptate, for whose discovery the Member of the Académie des sciences Jean-Marie Lehn was awarded the Nobel Prize in Chemistry in 1987.

During the second half of the 20th century, inorganic chemistry turned to the study of structure-properties relationships. Such research, primarily conducted on crystals, in close interaction with physicists, have led to the development of materials with remarkable physical properties - spintronics, semiconductors, magnetism, superconductivity, photovoltaics, etc. Quite memorable was the revolution brought about in 1986 by the synthesis of superconducting ceramics (Berdnoz and Muller,

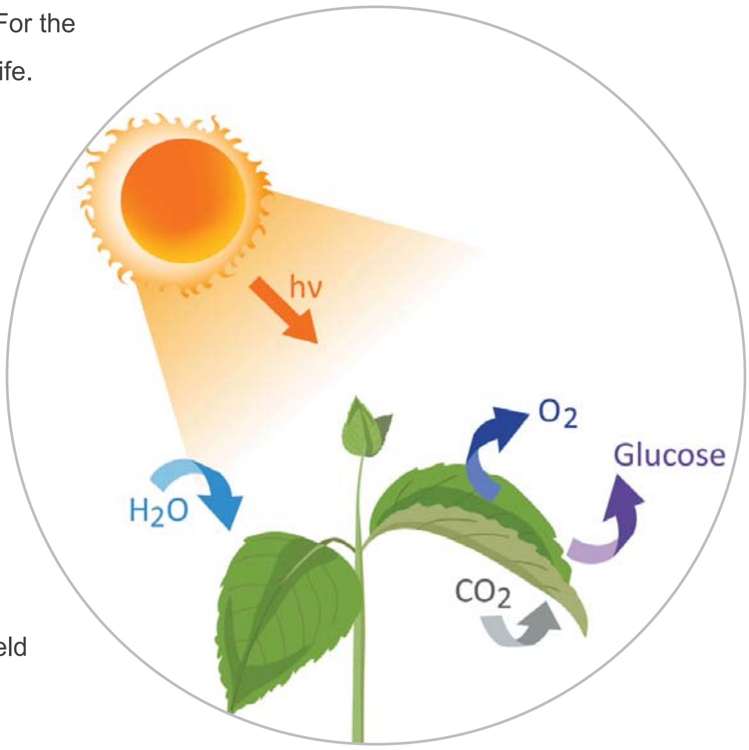
1987 Nobel Prize). Most of the new materials in current development in the industry are derived from such collaboration between chemists and physicists.

Polymer chemistry expanded rapidly after the First World War. Rubber production, spurred by military needs, led natural production to be replaced with chemical synthesis. Such work was at the root of the first syntheses performed on plastic materials, such as nylon during World War II. Research in macromolecular chemistry (Staudinger, 1953 Nobel Prize) brought the development of a new range of materials quickly achieving great industrial success. From structural polymers to functional polymers, they are still thriving and diversifying. At the same time, studies on "soft matter", with, here again, close cooperation between chemists and physicists (de Gennes, 1991 Nobel Prize), brought about important progress in the field of liquid crystals, emulsions and enhanced oil recovery.

21st Century: chemistry and sustainable development

It is often said that "chemistry is everywhere": it should thus be concerned with society's needs and be in line with sustainable development. The synthesis of chemical products, which are often opposed to natural products, draws an increasing part of its inspiration from biological processes. There are mentions of "soft chemistry", "green chemistry", or even "bio-inspired chemistry", which are rooted in the observation of living beings.

Global warming is one of the major concerns of our times. It is linked to the production of greenhouse gases, such as carbon dioxide, CO_2. What role may chemistry play in the capture, storage and recycling of CO_2? For the chemist, the CO_2 molecule is essential to life. Through photosynthesis and under the action of the sun's radiation, it reacts with water to form oxygen and the organic molecules – sugars, starch, cellulose, etc. – that are necessary for life to develop on Earth. Couldn't we imitate nature and develop "bio-inspired" chemistry that would use the photoreduction of CO_2 into CO, HCOOH or CH_3OH? This is a promising avenue of research, which relies on progress made in the field of catalysis.



CO_2 is a greenhouse gas, but it is also a molecule which, through photosynthesis, reacts with water to produce the whole organic matter essential for life.

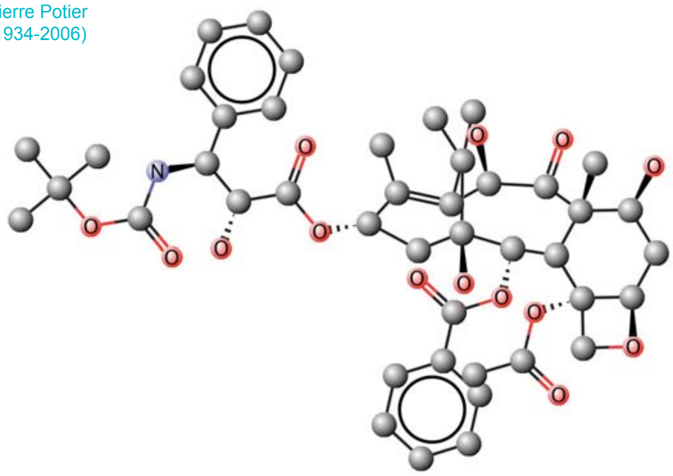
Solar energy may also be used to generate electricity. Conventional photovoltaic devices use semiconductor crystals to convert photons into electrons. But there are also cells in which such a transformation is performed in chemical dyes. Here again, chemistry offers new solutions and paves the way for much more flexibility in molecular electronics (Heeger, MacDiarmid and Shirakawa, 2000 Nobel Prize).

Solar power plant in Seville

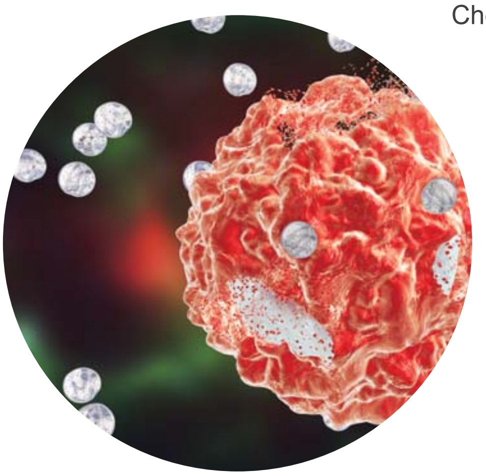
Energy transition aims to find new forms of renewable energy. The nuclear power plants currently developed in France involve sophisticated reactions to generate heat then transformed, that is to say converted – with a very low yield – into electricity. We do not know how to directly convert nuclear reactions into electricity. Any simple chemical redox reaction, though, implies a transfer of electrons between two elements; all it takes then is to capture these electrons to directly produce electricity: such is the secret of the battery invented by Volta, stacking copper and zinc discs. Building batteries is a way to simultaneously solve the problems raised by the production and the storage of electricity. Batteries are now under intense research, in which chemistry plays an essential role; their performances have been greatly improved over the past decade.

Pierre Potier
(1934-2006)

Taxotère®, synthesized by Member of the Académie des Sciences Pierre Potier and his colleagues, was a revolution in the world of cancer chemotherapy.

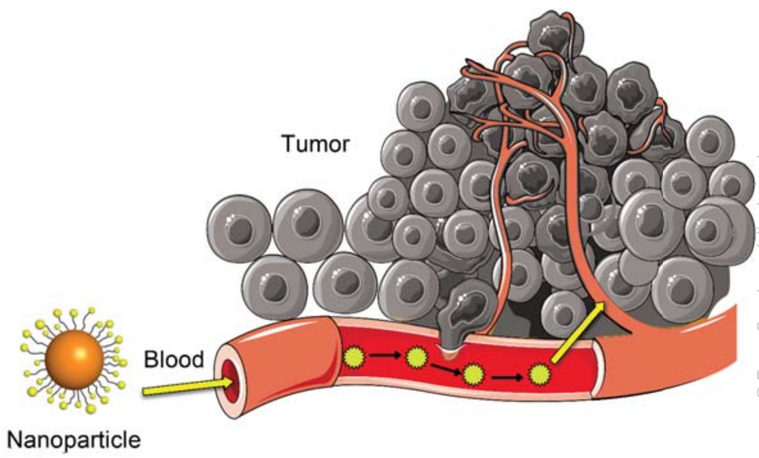


Chemists also play a fundamental role in the field of health. The synthesis of active molecules such as Taxol®, derived from the bark of the yew tree, significantly helped improve cancer drugs. Unfortunately, the production of Taxol® required a great number of trees to be removed. Research conducted at the French *Centre national de la recherche scientifique* in Gif-sur-Yvette has allowed an even more active compound to be identified – Taxotere® – which, since it received marketing authorization in 1995, has become the most used of all products against breast and lung cancer. Incidentally, chemistry and medicine often merge. The 2015 Nobel Prize in Chemistry has thus been awarded to the discovery of DNA repair mechanisms, while, the same year, the Nobel Prize of Medicine rewarded work conducted on the role of artemisinin and avermectin in the fight against parasitic disease. In both cases, chemistry was directly involved.



Chemistry is not only interested in discovering new drugs, it is also involved in drug delivery. The introduction of nanotechnology in pharmacology helps develop nanoparticles that can be used as vectors to transport active principles at the very heart of a cell. In the case of cancer, the drug is only delivered in its target – the cancerous tumour –, thus avoiding the well-known side effects of chemotherapy. Swift progress is being made, both in diagnosis and therapy, thus contributing to the development of nanomedicine.

A versatile molecular science, chemistry builds bridges between different disciplines – physics, biology, medicine, pharmacology, earth science, etc. Just as it was involved in the formation of the universe and the appearance of life, it will play a key role in the development of modern society.



In medicine, chemistry uses nanoparticles as vectors to transport drugs inside the tumor itself.

Planets and exoplanets

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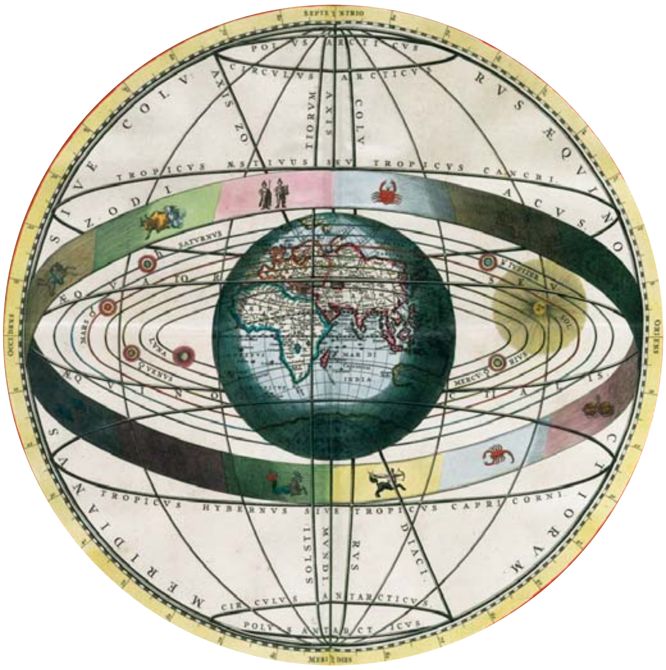
Anne-Marie Lagrange

Member of the Académie des Sciences, Senior Researcher at CNRS, Institut de planétologie et d'astrophysique of Grenoble

During the last centuries, our understanding of the world has considerably changed. Once Earth had lost the specific status the geocentric system provided it and once it had been recognised as one of the planets orbiting the sun, it became possible to examine the formation of the sun and its planets. Stars, comets, nebulae, galaxies were observed, identified, catalogued, studied with ever-increasing precision thanks to progress achieved in spyglasses, telescopes and other instruments, as well as in physics, chemistry and geology. The observable universe kept on enriching itself and growing. The possibility that planets were orbiting stars other than the sun – exoplanets – was considered but it would take until the end of the 20th Century for any to be detected and the detailed study of some known examples to begin.

The place of Earth in the Universe

In the 16th and 17th Centuries, the theological and philosophical conceptions that, since antiquity (Aristotle, Ptolemy), had been placing Earth at the center of the world gradually lost ground as progress was being made in the fields of celestial mechanics and gravitation. The works of Copernicus, then of Kepler, Galileo and Newton, would now place Earth, and then the planets, in orbit around the sun, moving in accordance with the universal laws of physics, which thus corroborated the intuition expressed by Aristarchus of Samos in the 3rd Century B.C. Science could now gain its independence from religion – an idea d'Alembert would cherish. The appetite for science grew, secular structures in which scientists would gather were created, such as the *Académie des Sciences* in 1666 and, one year later, the *Observatoire de Paris* as the workplace of the astronomer members of the Roi-Soleil's Académie.



Two systems describing the world : the geocentric system (Ptolemy, on the left) and the heliocentric system (Copernicus, on the right). The Harmonia Macrocosmica of Andreas Cellarius (1660).

The Century of the Enlightenment would resolutely feed a taste for scientific exploration, whether on Earth, sea or sky, and theories would follow to explain the observations of the great naturalists (Buffon, Lamarck), geographers (Von Humboldt), geologists (Hutton, Cuvier and, later, Brongniart) and astronomers (Cassini, Lalande, La Caille) of the time. It is established that Earth revolves around the sun or that it was not formed in six days some thousand years ago. Drawing on the study of the cooling time of metal spheres from various diameters, Buffon calculated that 10 million years was the age of our planet.

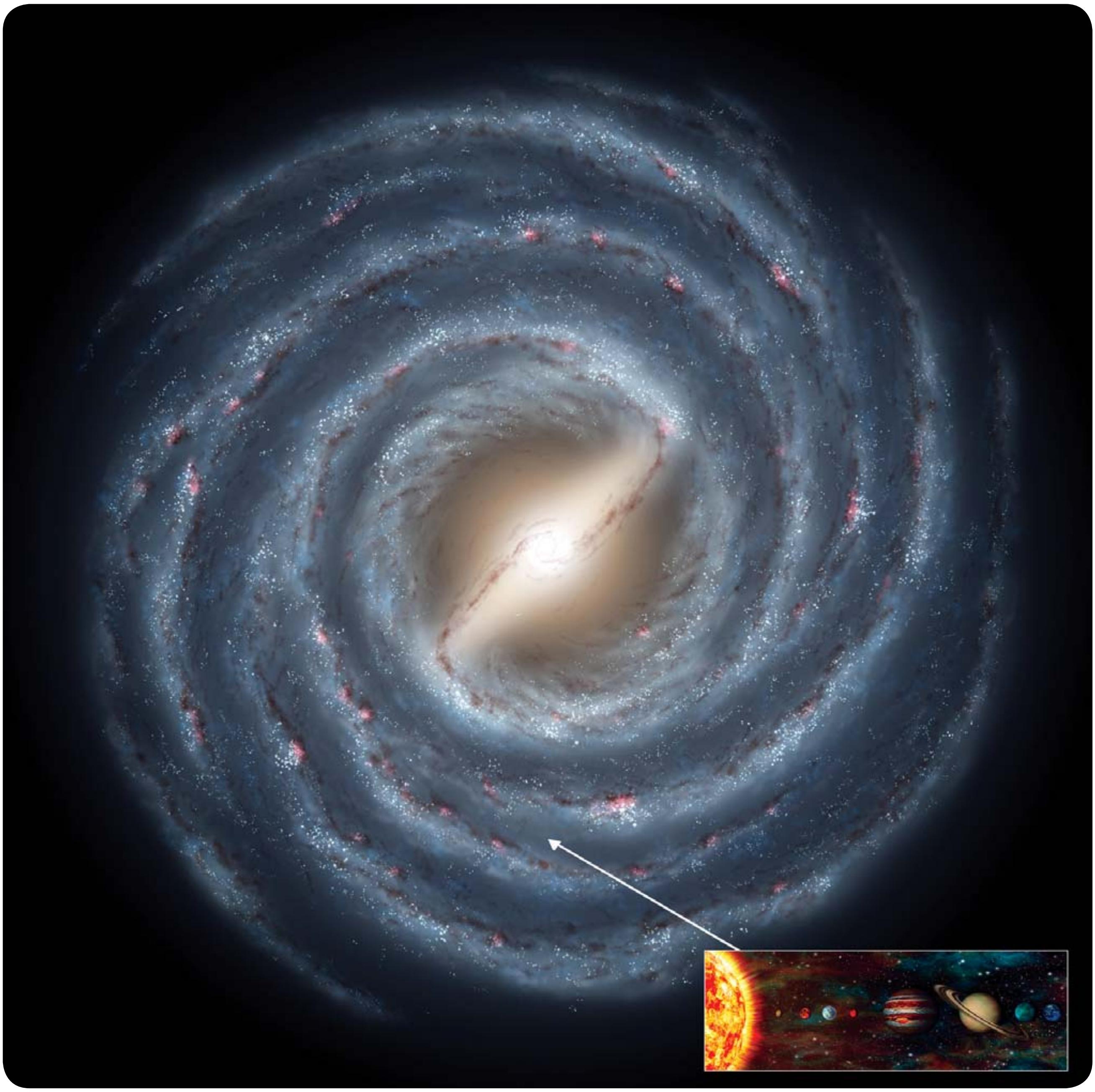
Astronomers built telescopes to probe the sky with ever-growing precision and sensitivity. The catalogues of the stars and nebulae, much in the way of the observation reports that naturalists compiled, became more and more detailed. They allowed Messier and Herschel to classify the stars with ever-increasing precision, which was a very useful preamble to physically understand them.

In the 19th Century, the theoretical and experimental works of Young, Fresnel, Foucault and Maxwell provided support for the wave-like nature of light that Huygens had put forward for consideration in 1670, and allowed for its speed to be measured. Fraunhofer invented the spectroscope and it became possible to study the chemical composition of the atmospheres of the sun, planets, solar system and, later, stars and galaxies. The Doppler-Fizeau effect made it possible to measure the speed of stars with reference to an observer located on Earth. This effect, indeed, would be decisive in showing that the galaxies moved away from each other and in establishing the expansion of the Universe during the 1920s as Lemaître and Hubble did, which Einstein's theory of general Relativity accounted for.

An image from the Hubble Ultra Deep Field

Nuclear physics and the study of radioactivity (Becquerel, Rutherford, the Curie couple) would, between 1850 and 1950, provide the bases for an explanation of the origins of the elements. The sun then became a star like the others, its energy deriving from reactions of nuclear fusion (Perrin, Eddington). Nucleosynthetis reactions became known to occur within the stars which, at the end of their evolution, were acknowledged to enrich the interstellar medium with heavier elements (Burbidge). The age of Earth was estimated, by means of natural radioactivity counting techniques, at 1 and then 4 billion years during the first half of the 20th Century.

At the end of such progress, it has been established that the sun and its train of planets are in motion in the Milky Way, our Galaxy, which comprises hundreds of billion stars more or less comparable to ours. The Milky Way has become but a galaxy among hundreds of thousand others within the expanding Universe (Shapley, Ross, Hubble).



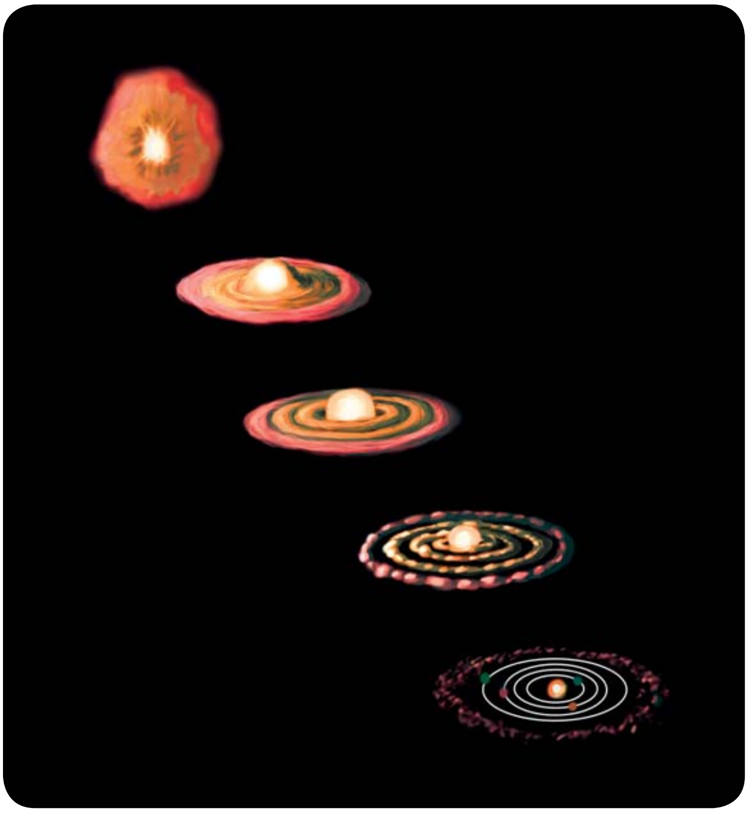
The sun inside the Milky Way (artist view)

The formation of the solar system

Georges-Louis Leclerc de Buffon (1707-1788)

Pierre-Simon de Laplace (1749-1827)

Once the sun and Earth freed from their specific status, it became possible to think about an origin that did not need the intervention of the hand of God. The first truly scientific theories appeared in Europe in the 18th Century with, notably, Buffon on the one hand, and Kant and Laplace on the other hand. Buffon suggested that Earth and the other planets are debris from the sun, teared off when a comet collided with it. In 1785, Laplace propounded the theory of the Primitive Nebula, a contracting and rotating gas cloud in which planets would form. He thus laid the foundation of the modern theory of the solar system formation. This scenario would be sharply refined and detailed in the course of the 20th Century, especially in what regards the initial physical conditions inside the protosolar nebula and the processes leading to the emergence of the two great groups of planets: the rocky planets, such as Earth, and the giant gas planets, such as Jupiter. We owe these improvements to progress achieved in ground observation tools, to space exploration, progress in terms of rock dating and to laboratory experiments designed to reproduce and thoroughly study some of the processes involved. We also owe them to the development of computers which have made it possible to simulate – although in an simplified way, obviously – the major steps of the solar system formation. The scenario that explains best the properties of the objects in the solar system predicts the formation of rocky or icy elements of some kilometers wide (planetesimals, comets) from the gas and sub-micronic grains of the interstellar medium. Those planetesimals then would agglomerate into cores, of a few Earth masses, in the cold part of the future solar system; such cores would then very quickly accrete enough gas to form giant planets. Closer to the sun, the rocky planets would form directly from planetesimals in some tens of million years. Some of the steps described here are still ill-understood : it is not possible to

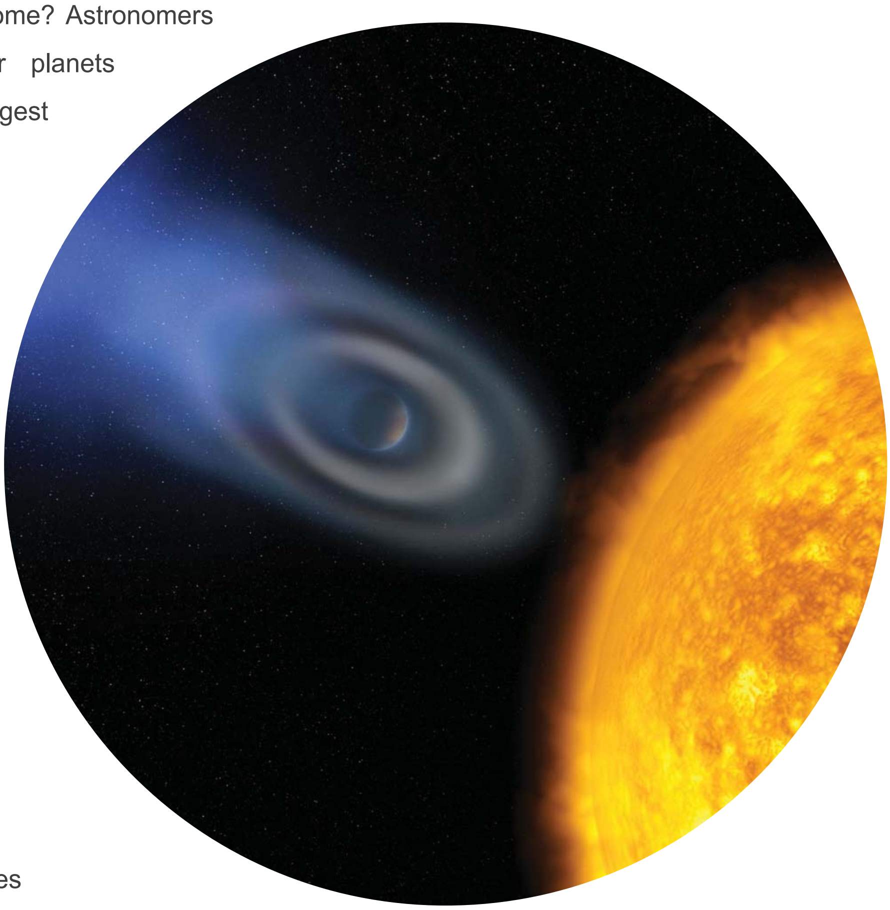


A sketch of the formation of the solar system, from the collapse of a molecular cloud and the formation of the Primitive Nebula : formation of a protostar and a protoplanetary disk, and formation of big solid bodies and structures in the disks. The solids called planetisimals are the building blocks of telluric planets and the solid cores of giant planets.

reproduce them in laboratory conditions, because our computational resources are not powerful enough to simulate them and because only scarce direct information is available on the physical, dynamic and chemical conditions in which the solar system formed.

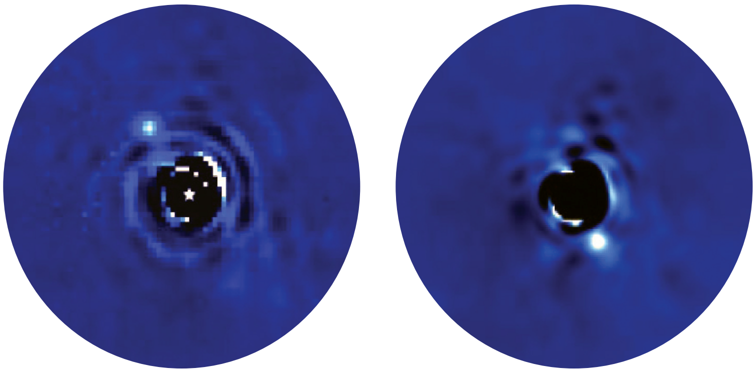
Exoplanets

Now that the sun had become one star among billion others, it was legitimate to speculate on the existence of other systems formed according to the same laws. Whether other worlds existed, however, remained an open question until the end of the 20th Century, as adequate observation tools were lacking. The announcement, in 1963, that a planet around the star of Barnard had been discovered, although disproved ten years later, launched the hunt for extrasolar planets. Such a hunt was based at the time on a methodology of indirect detection, intended to identify small perturbations of the stars induced by the presence of one planet or more orbiting around them. However, no planet was found before the 1990s. How come? Astronomers had started by searching for planets analogous to Jupiter, the biggest planet of the solar system. But such planets were too difficult to detect with the resources of the time. The first exoplanets discovered were as a matter of fact quite different from the expected planets. The first one was a planet revolving around a pulsar, which is the remnant of a stellar explosion; as for the second planet, its mass was indeed comparable to that of Jupiter but it was orbiting one hundred times closer to its star than Jupiter to the sun. The theories of the time did not expect the existence of such "Hot Jupiters" ("hot" because of their proximity to their stars), which however proved quite common thereafter. The first images of exoplanets were finally obtained in the 2000s through sophisticated technological developments.



Osiris, a giant planet near the star HD209458, in the constellation Pegasus. This exoplanet, which orbitS its star in 3.5 days, have an extended envelope of atomic hydrogen probably due to planetary evaporation (artist view).

Twenty years after those first discoveries, more than 3 000 exoplanets have already been identified; many await confirmation. Their characterization already reveals a vast range of masses (ranging from a few Earth masses to several Jupiter masses), radii and orbital properties (planets with inclined or retrograd orbits, or very remote ones), some of which have no equivalent in the solar system. Such a diversity may not be explained without considering the existence of several planet formation scenarios. Moreover, it appears that the individual and dynamic histories of young extrasolar planet systems may be very complex, even more than the history of the solar system: indeed, the orbit of an exoplanet, once the planet is formed, may be considerably altered due to interactions with the protoplanetary disk (which may account for the existence of "Hot Jupiters") or with other objects present in the system (which may explain why there are exoplanets with inclined or retrograde orbits).



The exoplanet β Pictoris b is a giant gas planet orbiting at about 9 au (1 au = the distance between Earth and the sun, which is 150 million kilometres) from its star (here represented as a star at the centre of the image). On the left, the image of the discovery of exoplanet β Pictoris b in November 2003 (light dot on the upper-left side of the image) ; on the right, 6 years later (in the bottom-right of the image).

The variety of architectures of the extrasolar planet systems is probably the most surprising result obtained in exoplanetology so far. It is probable that the interiors and atmospheres of the exoplanets, which we have only started to probe, will also prove very diverse. The proprieties of the forming atmospheres result from the capture of the gas present in the Primitive Nebula but also from outgassing that occurs on the forming planets, and from potential external inputs (asteroids, comets) and complex and multiple physico-chemical processes. Their evolution depends on many factors (volcanism, light gases escape, stellar radiation, etc.) – as many circumstances that are difficult to foretell and variable parameters that make it very tricky to formulate any prediction. Since the atmospheres play fundamental roles on the conditions in which life appears and develops, considerable efforts, in particular with the James Webb Space Telescope, the successor to the Hubble Space Telescope, and with the future Extremely Large Telescopes, will be devoted in the years and decades to come to probing the atmospheres of giant, and then telluric, exoplanets.

The Primitive Earth (artist view)

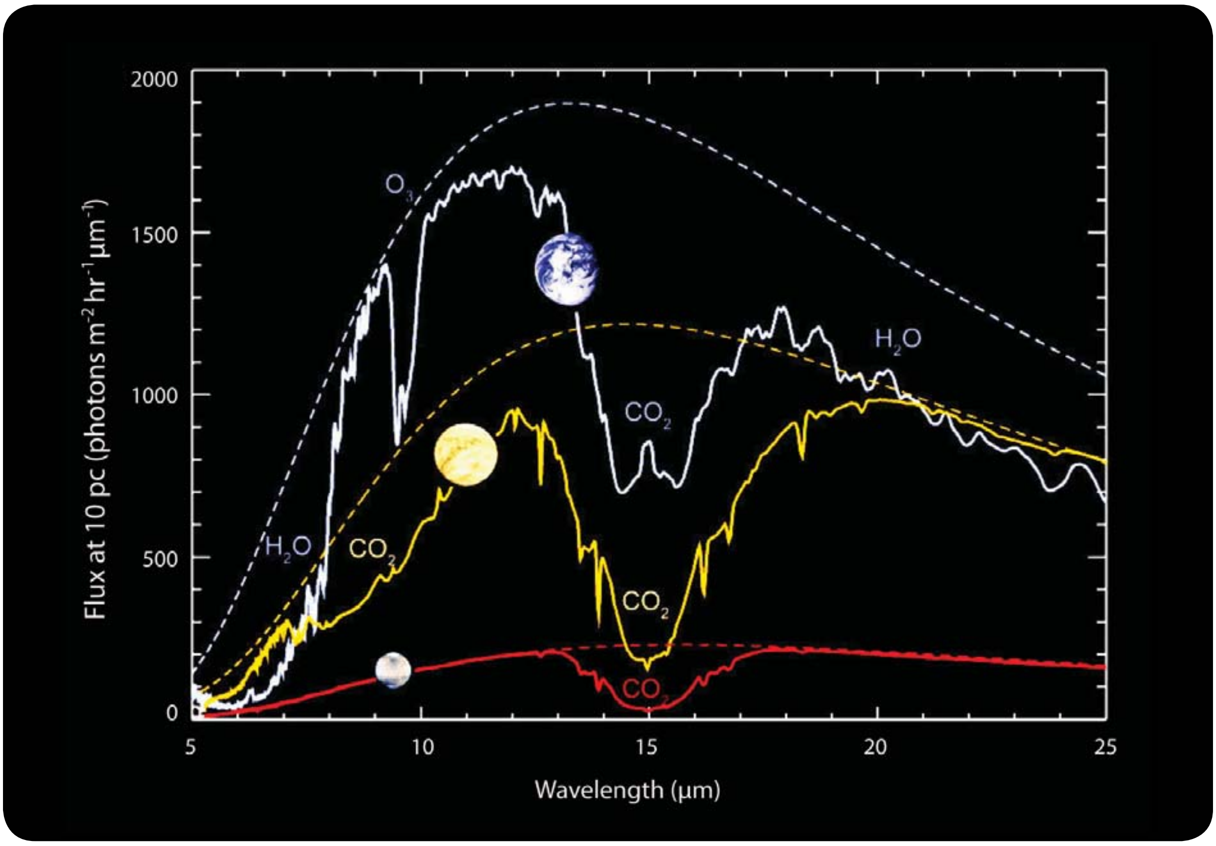
Given that close – not mentioning *in situ* – explorations are impossible, it is the detailed study of the atmospheres that will probably allow for the first signs of life to be detected on exoplanets. The first step is to identify which exoplanets are most fit for the development of life. Drawing on an analogy with Earth, a preference is given to telluric planets located at such distance to their stars as to allow liquid water to be on the surface. The presence of liquid water is assumed to be a necessary condition for life to appear on our planet. Yet it is probably not sufficient. Other factors indeed may have played an important, or even necessary, role for life to develop, including: the proprieties of the sun itself, moon, comets, asteroids, magnetic field of Earth, intern activity of our planet (volcanism, outgassing), composition of the atmosphere (greenhouse effect).

What signatures of life are to be looked for on the exoplanets? This question is highly complex. Drawing on an analogy with our planet, one preferred criterion is the presence of dioxygen (and ozone, which derives from it) in an atmosphere that would moreover have proprieties quite similar to those of Earth. The presence of dioxygen in our atmosphere results indeed from photosynthesis and it would not be possible to explain it by simple physical ou chemical abiotic processes. However, is this criterion still valid in the case of the atmosphere of an exoEarth bearing a different physico-chemical history, and orbiting a star that is different from the sun?

Whether Earth should play a potential role as a reference model is indeed a very central question. So is our ability to apprehend the variety of atmospheres on the exoplanets, imagine other possibilities and formulate, on the sole basis of theoretical considerations and with the help of simulations and laboratory experiments, original and coherent scenarios on the formation and development of life, in conditions that differ from those of Earth.

A grain of sand in a very wide Universe

The explosion of knowledge that occured during the 350 last years, the emergence of various disciplines now called physics, geophysics, chemistry, life sciences and, more recently, computer science have brought about a sharply new perspective on Earth and the solar system, that are regarded now as tiny pieces in a very wide Universe. The question whether other worlds exist is now raised in scientific terms. The first extrasolar planet systems were only discovered recently, in the 1990s. After 20 years of study, we observe there is a wide variety of exoplanets and we may have only caught glimpses yet of such variety. The hunt for exoplanets is not over: we have not explored all the diversity of systems – we do not know, for instance, if systems analogous to the solar system exist and only the close neighbourhood of the sun has been investigated. The atmospheres of the exoplanets also remain widely unexplored and their study, will probably be the only way to detect signatures of life. However, in the present state of knowledge, to establish the probable existence of life on another planet appears to be a very long term objective.
The solar system, in this context, is a valuable and indispensable element of comparison, even though we must remember it is but one case, and not necessarily a representative one, among a population of systems whose diversity appears greater every day.



The spectrum of the Earth differs from that of the two other telluric planets Mars and Venus, in particular due to the presence of oxygen that derived from life on Earth. The study of the atmospheres of exoplanets will probably be the only way to detect signatures of life.

From Huygens' waves to Einstein's photons: strange lights

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Alain Aspect

Member of the Académie des Sciences, Emeritus Senior Researcher at CNRS, Professor at the Institut d'optique and at the École polytechnique

350 years ago, Colbert invited the great scientists of the time to join the Académie des sciences. One of the most eminent of them, Christiaan Huygens, born in 1629 and raised in the Netherlands, had studied Descartes, Pascal and Fermat, and already produced major results in mechanics, mathematics and astronomy. He accepted to come and settle in Paris where he would dwell until Colbert's death and the revocation of the Edit de Nantes – events that led him to return to his native land, to spend there the rest of his life.

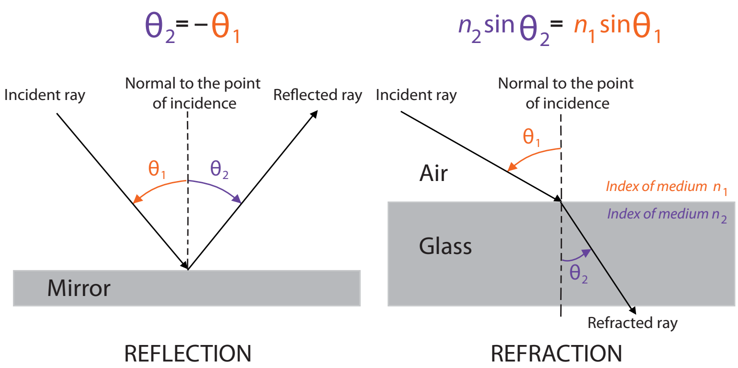
Emergence of a wave model of light

In 1672, Huygens discovered Newton's work on the corpuscular model of light. At the time, the major problem was to find a model that would justify the laws of reflection and refraction independently formulated by Descartes and Snell. It is easy to understand that a bouncing corpuscle is a good model to describe the fact that a ray of light is reflected in a symmetrical way with respect to the normal, but the challenge is to understand why the refracted ray comes closer to the normal when it passes from air to a denser medium, such as water or glass. Newton explained it by invoking the attraction of the denser medium: the particles of light are accelerated perpendicularly to the interface, and the trajectory is therefore closer to normal. But Huygens was looking for a model that would account for all known phenomena and in particular the phenomenon of double refraction that is observed with some crystals, such as calcite. He discovered in 1678 that a wave model of light would meet this requirement, while Newton's corpuscular model did not.

Despite its value, Huygens' wave model, described in full detail in 1690 in his *Treatise on Light*, was ignored by most scientists for more than a century. If they adopted the corpuscular model, it was because of the tremendous prestige conferred upon Newton, who had managed to explain the motions of planets

Christiaan Huygens (1629-1695)

Christiaan Huygens soon looked into the question of light beam reflection and refraction.



through his law of universal gravitation. It took more than one century before Thomas Young, in England, and Augustin Fresnel, in France, developed the wave model of light, as the only one able to account for the phenomena of interference and diffraction, that they carefully studied in remarkable experiments.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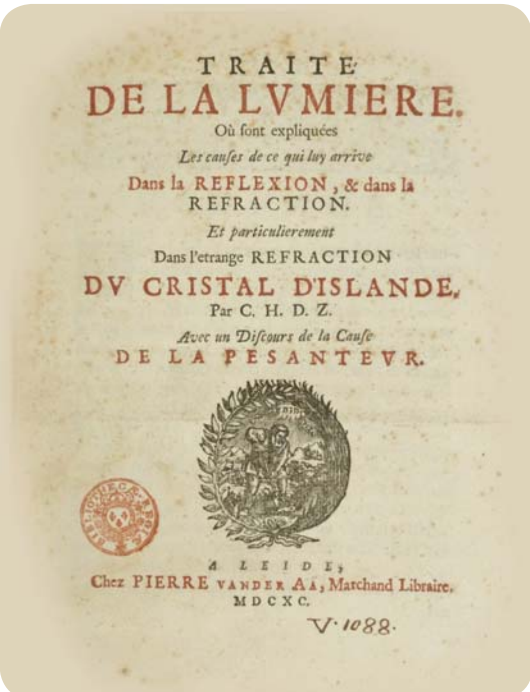
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Où ſont expliquées
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DV CRISTAL D'ISLANDE,
Par C. H. D. Z.
Avec un Diſcours de la Cauſe
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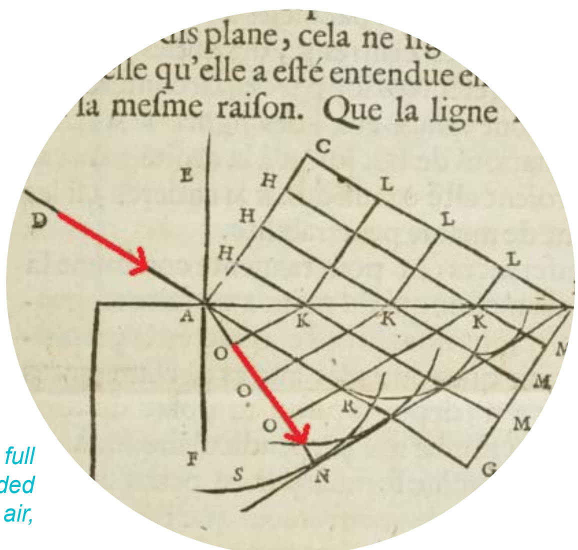
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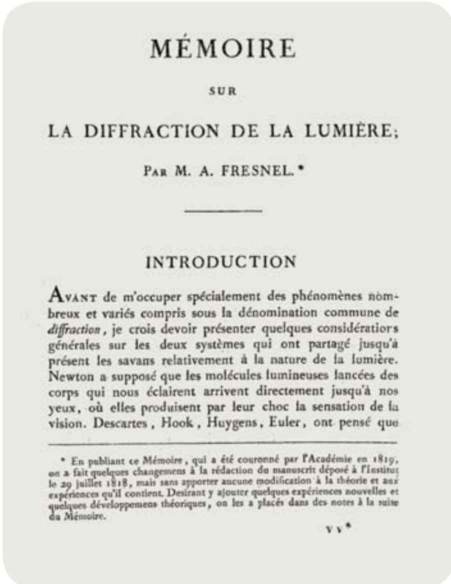
Huygens' wave model, expressed in 1678 and described in full in his Treatise on Light (1690), accounts for refraction provided that the speed of light is slower in the denser medium than in air, in contrast to Newton's corpuscular theory.

Wave VS corpuscular theories

Young and Fresnel had to fight to impose this model, as evidenced by the story of Poisson's bright spot, which introduces members of the Académie who were most... bright.

1819 was the year, and the Académie des Sciences had sponsored a contest on the diffraction of light, in other words, on the fact that, in the zone of transition between the shadow of a screen and an illuminated zone, fringes are observed, that is, alternating shadows and light. Fresnel, a young and brilliant mind educated of the École polytechnique, and who was a student of the member of the Académie Arago, presented a memoir describing his experiments and giving the problem a complete mathematical

Augustin Fresnel
(1788-1827)



MÉMOIRE

SUR

LA DIFFRACTION DE LA LUMIÈRE;

PAR M. A. FRESNEL.*

INTRODUCTION

AVANT de m'occuper spécialement des phénomènes nombreux et variés compris sous la dénomination commune de *diffraction*, je crois devoir présenter quelques considérations générales sur les deux systèmes qui ont partagé jusqu'à présent les savans relativement à la nature de la lumière. Newton a supposé que les molécules lumineuses lancées des corps qui nous éclairent arrivent directement jusqu'à nos yeux, où elles produisent par leur choc la sensation de la vision. Descartes, Hook, Huygens, Euler, ont pensé que

* En publiant ce Mémoire, qui a été couronné par l'Académie en 1819, on a fait quelques changemens à la rédaction du manuscrit déposé à l'Institut le 29 juillet 1818, mais sans apporter aucune modification à la théorie et aux expériences qu'il contient. Desirant y ajouter quelques expériences nouvelles et quelques développemens théoriques, on les a placés dans des notes à la suite du Mémoire.

V V*

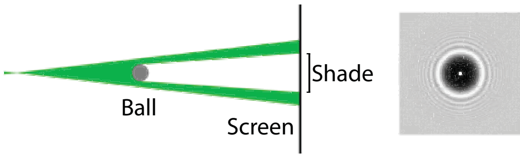
In France, Augustin Fresnel developed the wave model at a contest launched by the Académie des Sciences. In parallel, Thomas Young conducted his work in England.

treatment, based on a convincing wave model. Many members of the Académie, though, were eminent scientists, whose works were based on Newton's mechanics, and they would not admit that Fresnel questioned their hero, even in a field other than mechanics. Siméon Denis Poisson, one of the

Thomas Young
(1773-1829)

Siméon Denis Poisson
(1781-1840)

die-hard Newtonians and a sophisticated mathematician, discovered a surprising consequence of Fresnel's equations: if a light source is placed on the axis of a circular obstacle that blocks light, the theory predicts there will be a bright spot behind the screen, at a place where common sense tells us utter darkness reigns. Does it not show that Fresnel's theory is absurd? This is when the events took a surprising turn that the history of physics still remembers: Arago decided that an experiment should be conducted, and, to the amazement of Poisson and the Newtonians, the bright spot was indeed observed. The story has it that the Académie then shifted in favour of the wave theory, awarding Fresnel the prize of the competition and soon admitting him as a new member.



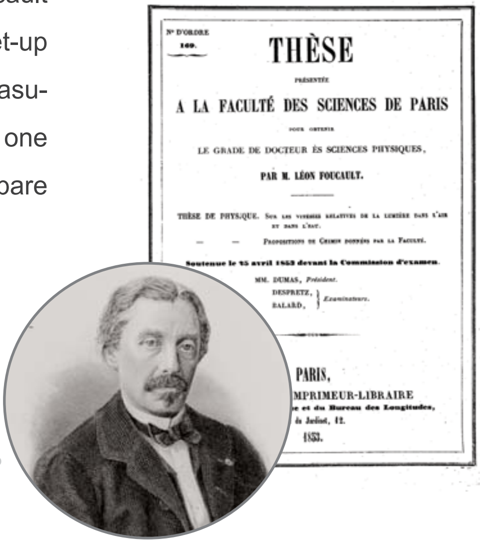
The Poisson's bright spot: Fresnel theory predicts the existence of a bright spot in the middle of the shade. The observation of that counter-intuitive feature played an important role in the success of Fresnel wave-theory of light

Some historians of science claim that the story has been embellished and that the conversion to wave theory was far from being so massive. As a matter of fact, explained for example Dominique Pestre (citing John Worrall), Poisson was dazzled by the elegance and mathematical consistency of Fresnel's theory, and was waiting only to welcome him at the Académie, while being at the same time not really convinced Newton's optics should be rejected. One cannot fail to notice, indeed, that the followers of the corpuscular theory remained active in the subsequent years until a new episode would clear the debate. Arago – him again – once more played a key role in 1838 when he proposed a crucial experiment to settle the argument between Newton's corpuscular theory, then called the "system of emission", and Fresnel's wave theory, called the "system of undulations". All it takes, he explained, is a comparison between the speed

of light in air and in a refractive medium such as water. One remembers, indeed, that, in Newton's theory, light accelerates when it penetrates a denser medium; on the contrary, according to the wave theory of Huygens and Fresnel, light goes slower in the denser medium.

In 1849, Fizeau measured the speed of light between Montmartre and the Mont-Valérien, near Paris. The website of the Observatoire de Paris presents a remarkable explanation of these experiments, which were repeated in 2005 with a laser beam. In 1850, Foucault improved the experimental set-up and was able to realize the measurement over a distance of only one meter. He could then directly compare the speed of light in air and water. The thesis of the future member of the Academy is only 35 pages long and it plainly concludes: "*Always, light is delayed as it passes through the most refractive medium. The final conclusion of this work thus consists in declaring the system of emission incompatible with the reality of the facts*." The last followers of the wave theory then surrendered or passed – is it not a saying that new theories do prevail only when their detractors have passed?

Hippolyte Fizeau
(1819-1896)



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THÈSE

PRÉSENTÉE

A LA FACULTÉ DES SCIENCES DE PARIS

POUR OBTENIR

LE GRADE DE DOCTEUR ÈS SCIENCES PHYSIQUES,

PAR M. LÉON FOUCAULT.

THÈSE DE PHYSIQUE. Sur les vitesses relatives de la lumière dans l'air et dans l'eau.

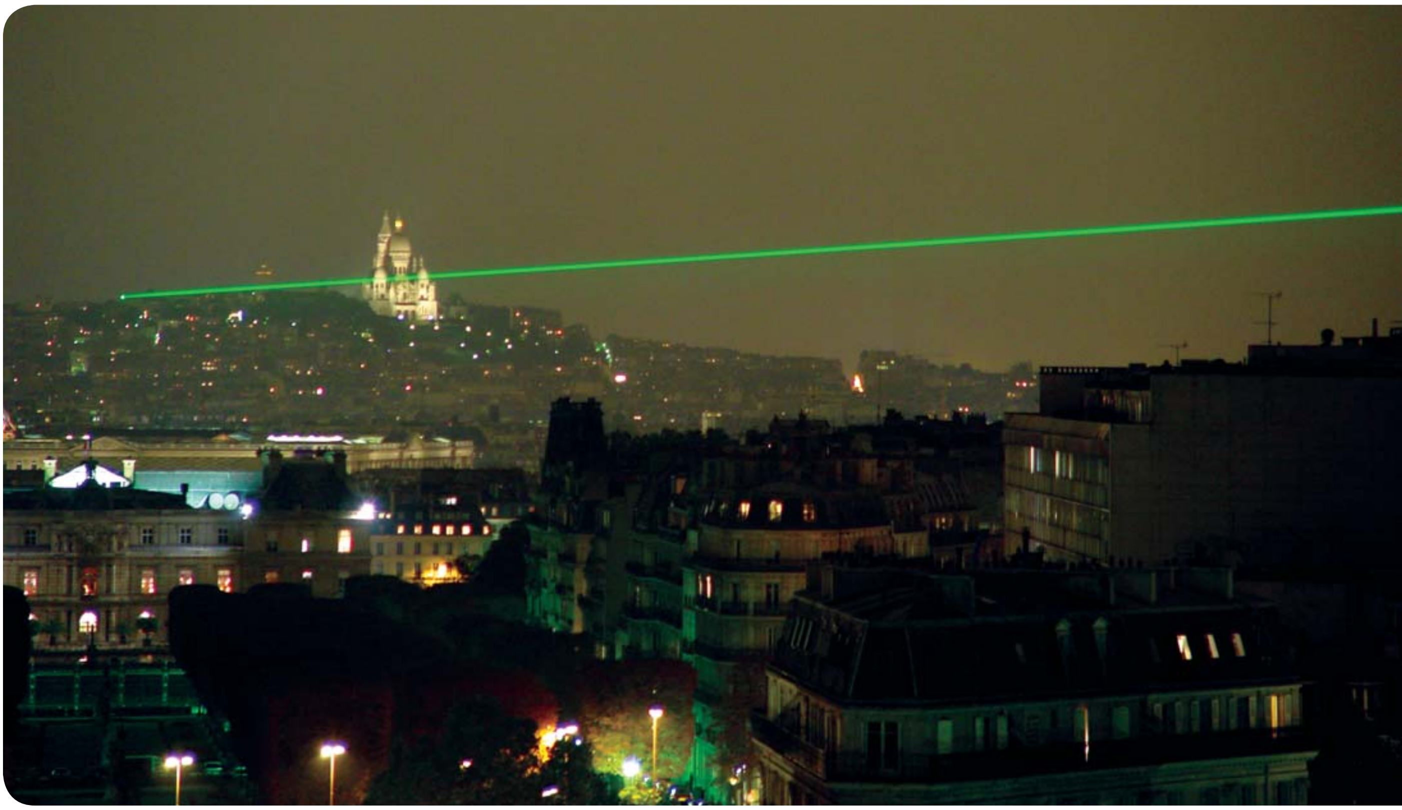
— — Propositions de Chimie données par la Faculté.

Soutenue le 25 avril 1853 devant la Commission d'examen.

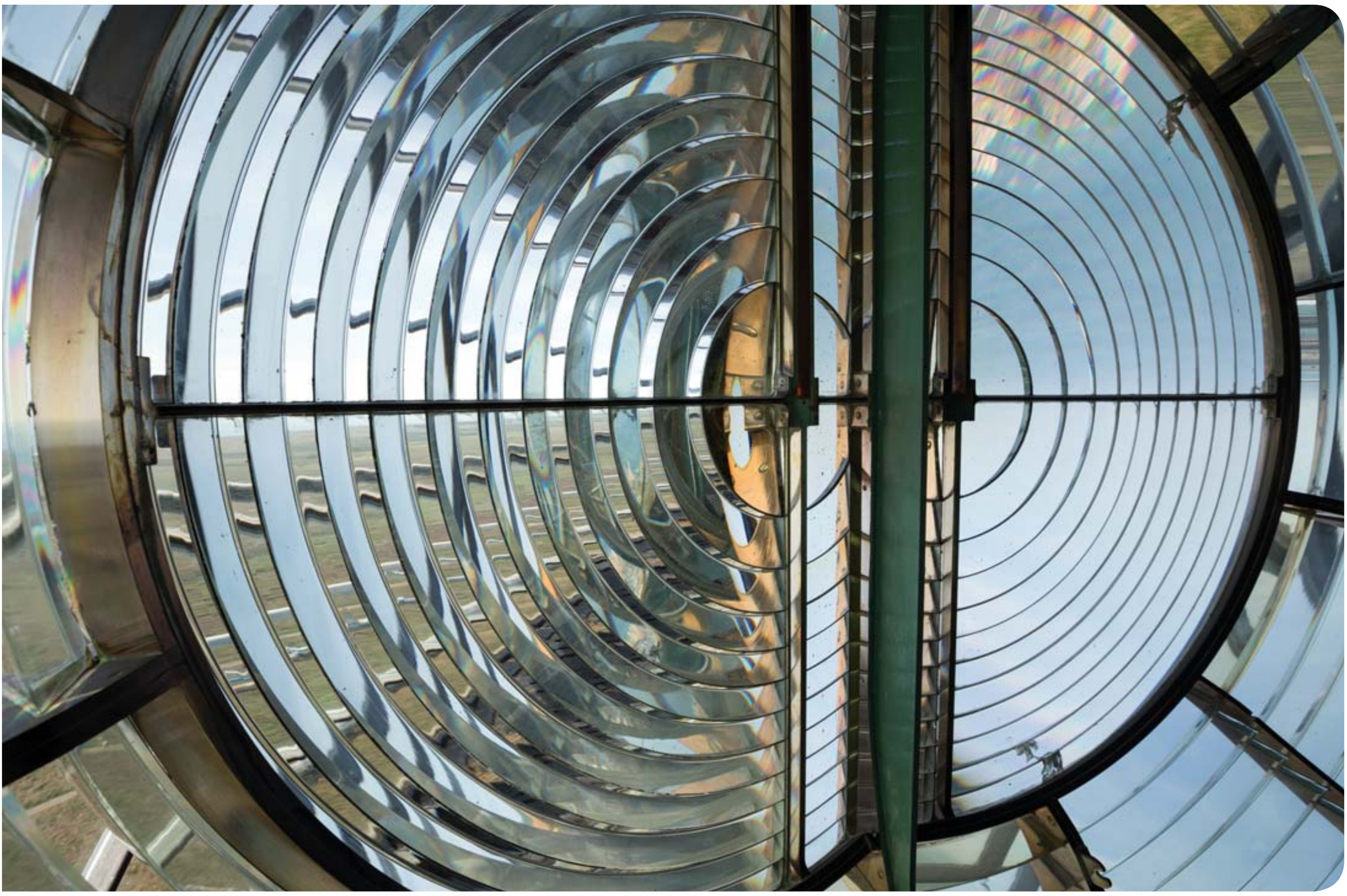
MM. DUMAS, *Président.*
DESPRETZ, BALARD, *Examinateurs.*

PARIS,
...MPRIMEUR-LIBRAIRE
...e et du Bureau des Longitudes,
...du Jardinet, 12.
1853.

Sur les vitesses relatives de la lumière dans l'air et dans l'eau. *The doctoral thesis Léon Foucault (1819-1868) presented to the* Faculté des sciences de Paris*, 1853.*



Measuring the speed of light between the Observatoire de Paris and Montmartre, in 2005



Huge Fresnel lens in a lighthouse

In these times of debate and sometimes opposition between fundamental research and applications, it should be pointed out that the theoretician Augustin Fresnel was also the father of all modern lighthouses, that he contributed to conceive them as an engineer of the corpse of the Ponts et Chaussées, and that they are equipped with the marvellous Fresnel lenses. As for his theory of wave optics, it is so perfect that we may continue to use it without making any change to it. But in 1818, Fresnel still lacked the answer to this question: what is the nature of this quantity that vibrates as it propagates?

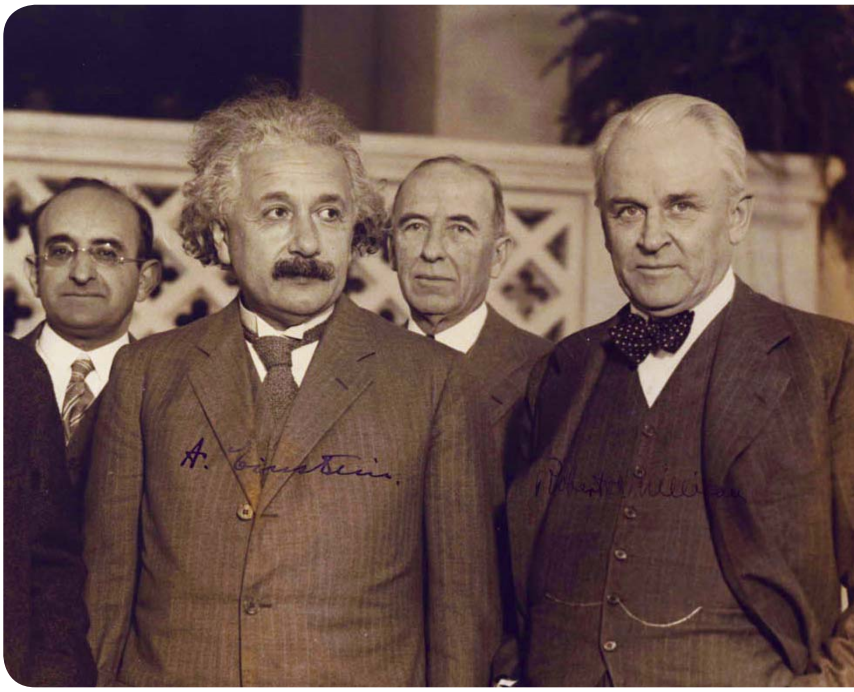
James Clerk Maxwell
(1831-1879)

It was the great Scottish genius James Clerk Maxwell who gave the answer, in 1864. He had written equations enabling to describe the whole set of facts that were known at the time in the fields of electricity and magnetism. In any true physical theory, equations imply more than what has been built into them; they have unexpected solutions whose traces may be looked for through experimental observation. In the case of Maxwell's equations, their novelty was impressive: some solutions of the equations indicated waves propagating at a speed Maxwell calculated. And he concluded: "*This speed is so close to that of light that it seems we have good reason to conclude that light itself [...] is an electromagnetic disturbance in the form of waves propagating through the electromagnetic field according to the laws of electromagnetism*."

The case thus seems settled: light is now known to be an electromagnetic wave, in other words, electric and magnetic fields vibrating in harmony, perpendicularly to the direction of propagation. That is to say they are transversal waves, as Fresnel's waves, and we can describe these waves with a comprehensive theory to which no phenomenon seems to be able to escape. Is it the end of theoretical research in physics, and is there nothing for physicists but to refine their measurements, as the American optics scientist Michelson reportedly put it? Surely not. In 1900, the great Kelvin caught sight of two "clouds above the dynamical theory of heat and light" (Lord Kelvin. *Nineteenth century clouds over the dynamical theory of heat and light. Philosophical Magazine Series* 6 1901 ; 2 : 1-40). Such two clouds, which Kelvin described as "very dense", would lead Einstein to lay the foundations of the two revolutions of the 20th Century physics: relativity, obviously, but also quantum physics, in the emergence of which he would play a key role.

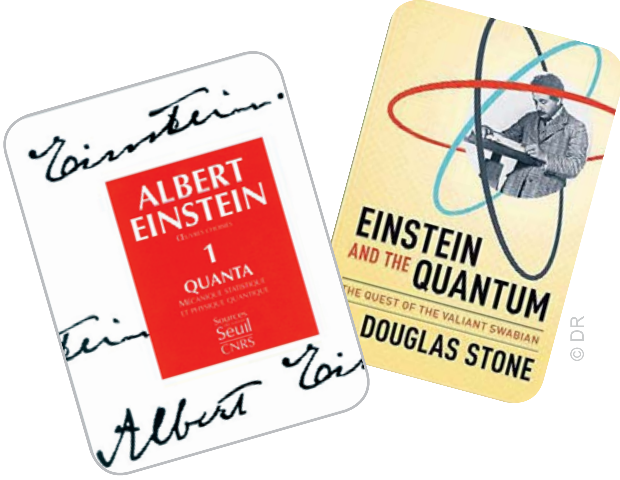
The wave-particle duality

Einstein's first article on quantum physics was published in 1905. It propounds a drastic hypothesis: light is formed of grains, the LichtQuanten, with a very specific energy and momentum, depending on the constant introduced by Planck in 1900. Today, these quanta of light are called photons. Drawing on this model, Einstein interpreted the photoelectric effect – in other words the ejection of electrons from matter under the effect of light – as a photon-electron collision and thus deduced what was the energy of the ejected electrons. Among the works Einstein published at that time, this article is certainly the least appreciated of all, as can be seen from a negative comment in the report which would however lead to his election at the Prussian Academy of sciences in 1911. Yet it was this article that caught the attention of the Nobel Committee, awarding him the Prize in 1922 after Millikan' experiments confirmed Einstein's predictions on the photoelectric effect – a confirmation "*contrary to all my expectations*", said Millikan in his memoirs (R.A. Millikan. *Albert Einstein on His Seventieth Birthday. Rev Mod Phys* 1949 ; 21 : 343).



With Albert Einstein (1879-1955), 1905 marks the revival of the corpuscular theory of light, allowing him to make predictions on the photo-electric effect confirmed by experiments of Robert Millikan (1868-1953) in 1915.

The corpuscular model was back on track. But then, how could one account for interferences, diffraction or double refraction, as Young and Fresnel showed they could only be consistently explained through the wave model? How could one make this corpuscular model compatible with Maxwell's description of light as an electromagnetic wave? Einstein, an admirer of Maxwell, could not ignore the question and provided a masterful answer to it on his first appearance at a scientific conference, the conference of German physics that held in Salzburg in 1909. Einstein developed there a series of arguments and concluded: "*I only wanted to briefly illustrate the fact that the two structural properties (wave structure and quantum structure)…should not be seen as incompatible*." At the end of each argument, Einstein's conclusion was the same: light is both wave and corpuscle. It would take fourteen years before Louis de Broglie would express this wave-particle duality, this time not for light but for material particles.



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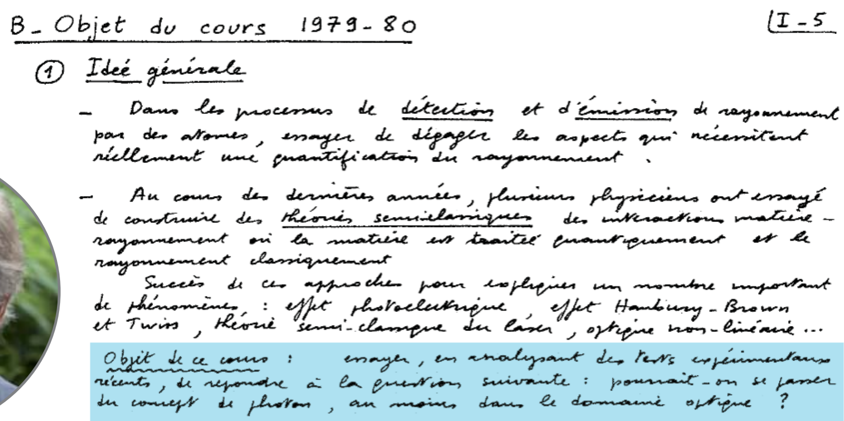
The major role of Einstein in the emergence of quantum theory is highlighted in "Albert Einstein, Œuvres choisies (French translations), Tome 1: Quanta. Texts selected and presented by Françoise Balibar, Olivier Darrigol and Bruno Jech. Seuil and Éditions du CNRS", *and in* "Einstein and the Quantum, A. Douglas Stone, Princeton University press, 2014".

With wave-particle duality, modern quantum physics was born. Optics would continue progressing all over the 20th Century, notably with the invention of the laser, and the French scientists, perpetuating the tradition of their predecessors, would take an eminent stand there, supplying our Académie with important battalions. But the wave-corpuscle duality of light still remained quite mysterious, as is apparent from the questions of the future Nobel laureate Alfred Kastler, then a high-school professor in Bordeaux in 1932; such questions led him to discover optic pumping with Jean Brossel. "*If this synthesis satisfies the mathematician*", Alfred Kastler wrote, "*it continues to worry the physician, who shall not be content with abstract formulas. To him, the duality between the wave aspects and the corpuscle aspects of light remains an unresolved mystery...*" (Les propriétés corpusculaires de la lumière, In *Procès-verbaux des séances de la Société des sciences physiques et naturelles de Bordeaux*, 1931-1932, pp 32-58)

Thirty two years later, as a student in upper sixth at the Lycée of Agen, I asked the same questions to a professor who was hard put to answer it, despite his huge capacities. It would take me fifteen more years to find, as many of my contemporaries, illuminating answers at Claude Cohen-Tannoudji's course at Collège de France, as he clarified such questions and thus enabled the French School of Quantum Optics to exert a radiant influence throughout the world.

Fruitful questioning: "Object of this course: to try […] to answer the following question: could we do without the concept of photon, at least in the field of optics?". Claude Cohen-Tannoudji, course at Collège de France, 1979


B_ Objet du cours 1979-80 (I-5

① Idée générale

– Dans les processus de détection et d'émission de rayonnement par des atomes, essayer de dégager les aspects qui nécessitent réellement une quantification du rayonnement.

– Au cours des dernières années, plusieurs physiciens ont essayé de construire des théories semiclassiques des interactions matière-rayonnement où la matière est traitée quantiquement et le rayonnement classiquement

Succès de ces approches pour expliquer un nombre important de phénomènes : effet photoélectrique, effet Hanbury-Brown et Twiss, théorie semi-classique du laser, optique non-linéaire...

Objet de ce cours : essayer, en analysant des tests expérimentaux récents, de répondre à la question suivante : pourrait-on se passer du concept de photon, au moins dans le domaine optique ?

© DR

Claude Cohen-Tannoudji

Machines and information

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Gérard Berry

Member of the Académie des Sciences, Professor at the Collège de France

Mechanics, applied mathematics, computer science, control theory and signal processing: all those domains of the *Mechanics and Computer Science Section* of the Académie des sciences are obviously not 350 years old. Modern applied mathematics and computer science were only born in the 20th Century. Yet they are moved by a common thought and action: the invention and optimization of all sorts of machines that are at the core of successive industrial revolutions, from the motor to the computer, including the train, automobile, airplane, machine-tool, etc.

Matter and energy formed the bedrock of science and technology until the middle of the 19th Century. Mechanical machines, and then electric ones, used energy to transport and work on matter, or also convert one form of energy into another; the whole great industrial revolution that appeared in the 18th Century completed the bedrock triangle and made it possible to connect men to one another without any material support.

Until the middle of the 20th Century, information was not really an explicit notion, although it already played a very central role. Progress indeed constantly built on ever more precise measurements of such natural phenomena as the balance of forces, friction, combustion and radiation, leading to conceive better models for nature and improve machines by means of superior architectures and plans. Measures, models, calculations, architectures and plans all pertain to the field of information, stored and transmitted via standard material supports such as books, blackboards and pieces of chalk. With modern computing, information and the algorithms that manipulate it now play a much wider role, to such an extent that we now live on a tetrahedron and not on a triangle any more. Let it be mentioned, incidentally, that the algorithmic methods are ancient, dating further back in time than mechanics, mathematics and even writing. The very word "algorithm" comes from the name of the great Persian scientist Al Khwārizmī, while "algebra" derives from Al Jabr, which is the name of his treatise on solving equations through calculation.

Al Khwārizmī (c. 783- c. 850), at the origin of the word algorithm

Mechanical science evolution

Once the first connections between mechanics and calculation were established by Galileo and Descartes, Newton laid out the fundamental principle or dynamics. Huygens developed the pendulum clock and he and Papin experimented on the driving force of steam. D'Alembert published his *Traité de dynamique* in 1743, which served as a basis for Lagrange's treatise, *Mécanique analytique*, in 1788. In 1765, Watt's steam engine, which was reliable because it was adequately regulated, created the first industrial revolution. Then, in 1824, Sadi Carnot understood the conversion of heat in mechanical energy and introduced the notion of cycle of work production. His intuitions paved the way for the second principle of thermodynamics and the introduction of a fundamental notion: entropy.

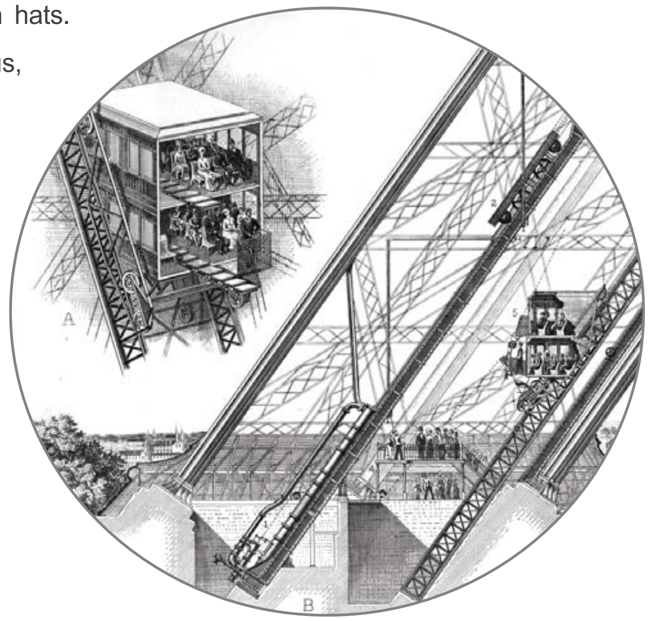
Denis Papin (1647-1713) and his digester (1679), an ancestor of the pressure cooker

Mechanics extended to deformable solids with Caucher and Navier's general theory of elasticity in 1821. Poisson then studied the equilibrium of elastic bodies, the behaviour of strained beams and pressure vessels. The development of perfect fluid

mechanics, initiated by Euler, d'Alembert and the Bernoullis, was taken over by Navier and Stokes in the 19th Century, who modeled viscous stress and wrote their famous equations.

Laplace and Fourier transforms were from the same period of time. Extracting fundamental information from signals, Fourier Spectral Analysis, which was extended by Wiener in 1930, became the key instrument for studying waves and vibrations in mechanics, acoustics and all the fields of physics. The first Fourier analysers/synthesizers, which were mechanical and then electronic, were replaced in 1965 by the computer implementation of the Fast Fourier Transform, or FFT. It was extended more recently by wavelet analysis, which is far more precise.

In those times, it was quite difficult to distinguish scientists in mechanics from mathematicians, as those researchers wore both hats. Newton and Leibniz created the differential calculus, Cauchy holomorphic analysis and functions, Euler and Lagrange the calculus of variations. Progress in mechanics was brightly illustrated in 1889 by the construction of the Eiffel Tower, a monument that required very complex calculations, and then in



The Eiffel Tower elevator in 1889


EDITION SPECIALE

Le Matin

LE FRANÇAIS BLÉRIOT VIENT DE TRAVERSER LA MANCHE EN AÉROPLANE

DOUVRES

DÉCLARATIONS de M. Millerand

1909 when Louis Blériot made the first flight over the Channel. His airplane and engine were far more efficient than his competitors', thus demonstrating the still unfailing strength of the French aeronautic industry.

During the whole period of time we have just mentioned, calculation was lengthy and tedious, performed by hand with help of logarithmic tables, slide rules and, later on, mechanographic machines. But there were also older attempts to build calculating machines, from Pascal to Babbage…

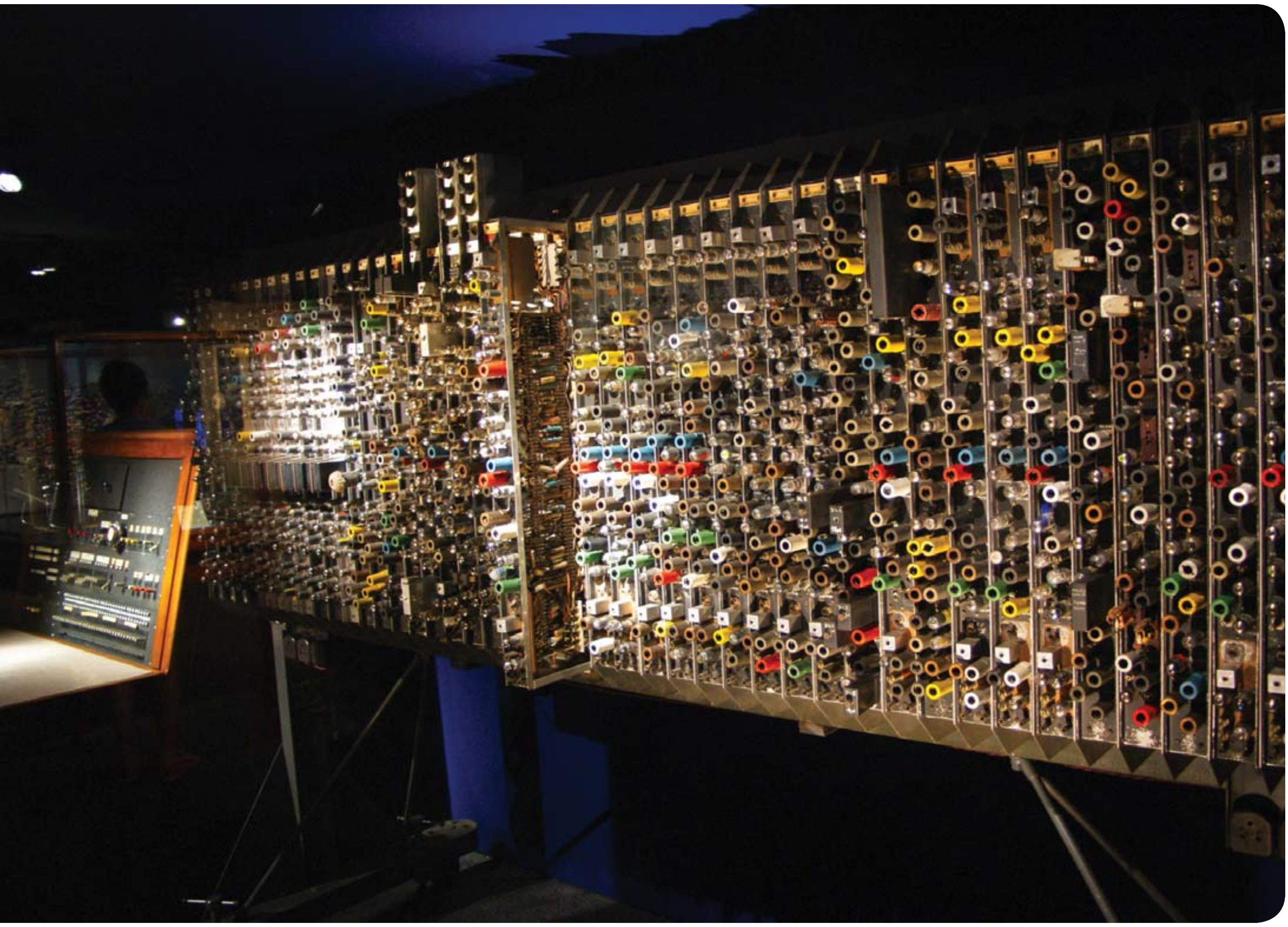
The Pascaline, an adding/substracting machine invented in 1642 by Blaise Pascal

Information science development

Alan Turing
(1912-1954)

Modern information and computation sciences were born from the invention of the computability theory by Alan Turing in 1936. In a visionary article, Turing presents his machines, composed of a tape on which characters may be written, a read/write head and a mechanism that decides whether the character that is being read must be replaced by another or the tape shifted. Turing first showed that these extremely simple machines could perform any known calculation; he then established two fundamental results, the existence of universal machines able to compute from a program that is recorded on the tape next to its data, and the impossibility to compute in finite time whether a given machine will or will not stop on a given data. Thus, at the very moment he defined the notion of calculability, did he set its limits. The same year, Alonzo Church introduced the λ-calculus, a logical language still used as the basis for modern programming languages, and showed it has the same expressive power as Turing machines. He stated the thesis that any formalism of effective computation to come would also be equivalent to them – a thesis that has never been contradicted.

But it was not until the end of World War II that the first computers were built, immediately followed by a surprising and still topical discovery: the difficulty to write and develop programs given the gap



The Automatic Computing Engine (ACE) is the prototype of the first computer built in the UK, developed in 1950 from Alan Turing computer project.

that separates men, who are intuitive but slow and not very rigorous despite their efforts, and hyperfast computers, which are unable to make mistakes but lack common sense and intuition. In computer science, bugs are failures from the programmers, not from the programs themselves. Turing himself wondered then how to bypass this difficulty, either by mathematically proving that programs are correct – and we have improved, there – or by using software able to confer some form of intelligence to computers: strength is always in the software, no on the bare circuit board.

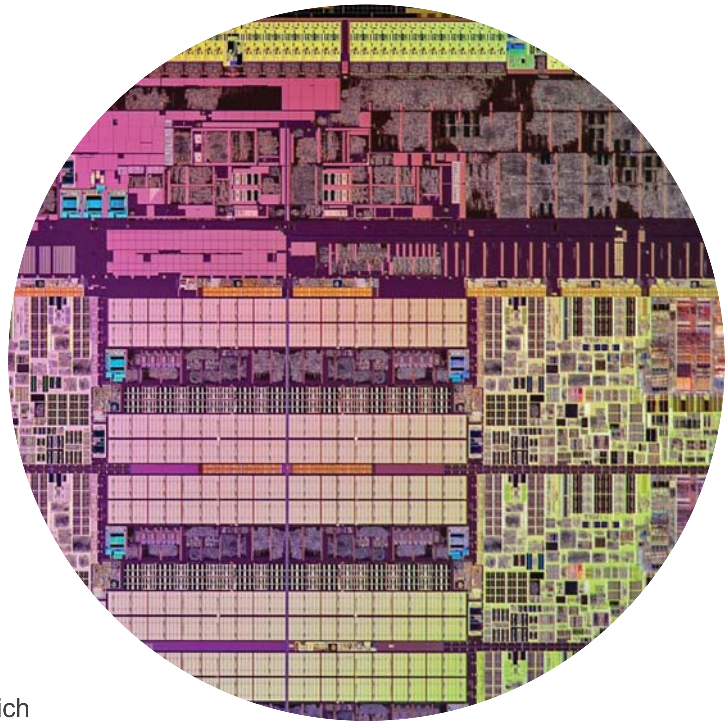
At the beginning of the 1950s, other conceptual revolutions occurred. We owe to Claude Shannon the revolution of the theory of information. First aimed at understanding and optimizing the transportation of information on noisy telephone lines, this theory has become of major importance in many fields: telecommunications, sound and image compression, general signal processing, optimization of major networks such as the Internet, etc. At the same time, process control was born as a new science devoted to analyzing and controlling physical systems. Maxwell and Wiener were its pioneers, and it has been well illustrated by our fellow Pierre Faurre on both its research and industrial sides. And Jacques-Louis Lions' exceptional personality honoured our company by giving rise to the use of numerical analysis to solve more and more complex equations and by promoting all forms of applied mathematics.

Claude Shannon (1916-2001)

Informatics in the industrial era

The industry of computers really started booming at the beginning of the 1970s with the use of the transistor and then the invention of the integrated circuit and the implementation of Moore's law, which expresses the concerted decision of the industry to double the number of transistor per surface unit more or less every two years. Indeed, there was quite a move from the 17 500 vacuum tubes of ENIAC in 1946 to the 2 250 transistors of Intel 4004 in 1971, and then to the billions of transistors inside the microchips of today's computers. This exponential law is getting weaker, though, for reasons certainly physical but most of all economic: even though it produces tiny objects, the industry of circuits has become the heaviest in the world in terms of costs of production factories as well as research and development. So far, we have never needed to leave the world of electronic circuits etched onto silicon wafers. Other technologies are finally being liberated and might take over – physicists to the rescue!

The Electronic Numerical Intergrator Analyser and Computer (ENIAC)



Intel® Core™ i7-5960X Processor

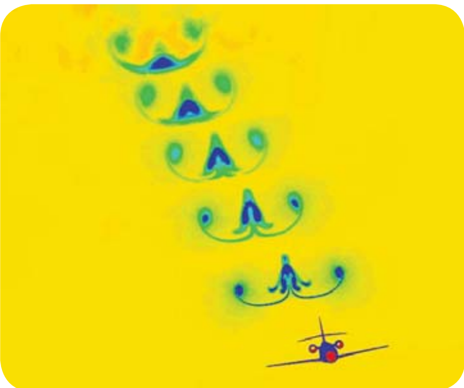
Computers have been progressively connected to one another and networked, so much so as to form the actual Internet, which connects billion machines and will still grow enormously as all sorts of computerized objects will connect. But the amount of data to be processed is expanding at even faster a speed, whether because of human interaction or because measurements and experiments have induced progress in all fields of science and medicine. It is said that, over the last two years, more data has been produced than since the birth of mankind. Processing such this data deluge is key for the future.

© Oleksandr Delyk - Fotolia

In today's digital world, computer science and applied mathematics have played and keep on playing a role that is as central as the power increase of computers. In computer science, algorithms have flourished, driven by more and more diverse applications (images, sounds, videos, etc.) but also by such internal reasons as the conception and production of circuits, networks, software and operating systems. Algorithmic complexity, a theory which was born in the 1970s, studies the performances of algorithms and optimizes them. Since the same period of time, our understanding of the mathematical foundations of programming has gradually improved, first as regards syntax, with the theory of languages in which our fellow Marcel-Paul Schützenberger has illustrated himself, then regarding the formal semantics of programming languages, which led to more compact and safer languages and to formal verification techniques for program correctness.

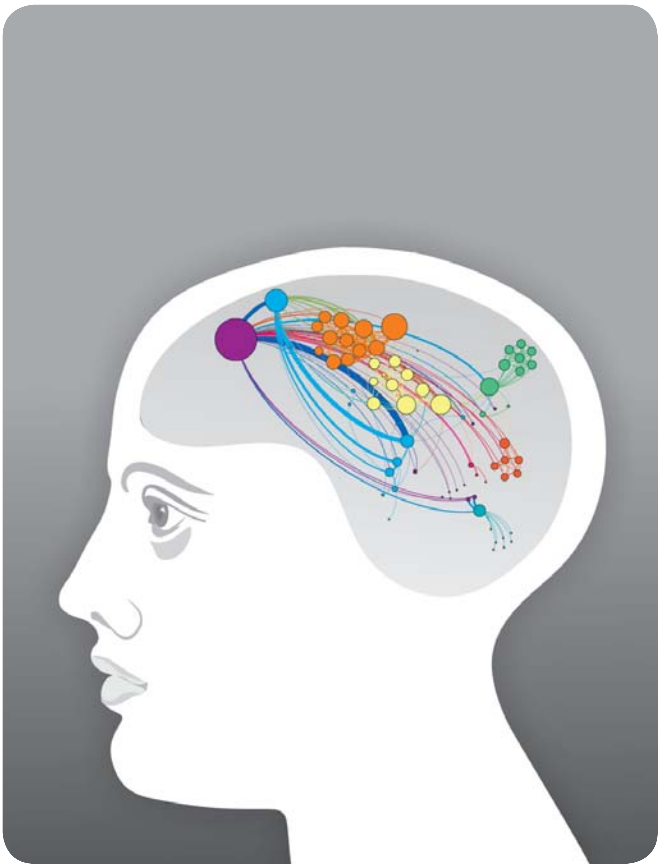
We witnessed the creation of databases with their fast indexing mechanisms, the development of modern man-machine interfaces and the standardization of communication protocols efficiently connecting machines within the networks. We then saw drastically new ideas come out, such as Web search engines, which we cannot do without any more, or the systematic use of probability in algorithmics. Recently, older ideas burst out: they were triggered by artificial intelligence but had to wait for very high computing power to be available. Deep neural network-based learning now causes great disruption in as various fields as Go game, the recognition of faces or objects in images, speech recognition, automatic language translation, and the analysis of scientific data. If we bear in mind that the new and efficient methods of multilingual translation use only few linguistic concepts, we do grasp a notion of how far it remains possible for progress to go. Yet essential fields are still ill-understood. The most critical of them is certainly that of computer security, where craft has reached its limits: it now requires science, at the highest levels of theory and practice.

It is important to point out that, in the 21st Century, mechanics, applied mathematics, control theory and computer science are increasingly entwined into one another. Such is directly the case in the theories of turbulence that lie at the core of modern mechanics and require large computer simulations. More generally, computer-aided design is replacing paper documents and physical prototypes with three-dimensional computer models, which also make it possible to simulate the effects of the control theory-based software that drives the objects depending on their interactions with the environment. The image provided here concerns the aerodynamics of an airplane, a field in which our colleague Paul Germain has distinguished himself. Other examples include Computer Numerical Control (CNC) machines, robotics, 3D printing, etc.



A modeling of airplane wake turbulence

Finally, the algorithmic concepts and tools of information science are now taking a prominent part in our understanding of the most complex of natural phenomena, from the formation and evolution of galaxies to the in-depth understanding of the living, for which we draw progressive models of proteins, cells, organs, organisms, populations and eventually – who knows? – the brain. After the power of physical levers, which are various and quite well known to us, now comes the power of information, as a unique lever that is only starting to amaze us.



Mathematics: to understand and predict

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Cédric Villani

Member of the Académie des Sciences, Professor at the University Claude-Bernard Lyon 1, Director of the Institut Henri-Poincaré (UPMC, CNRS), Paris

It was in a state of mathematical frenzy that the Académie des Sciences was founded in 1666. The movement of Greek science rediscovery was still recent; for instance, the translation of the writings of Diophantus, "the father of algebra", was achieved hardly forty years earlier. A generation of bold and prolix mathematicians had just passed away, yet an extraordinary one was preparing to take over in the four corners of Europe.

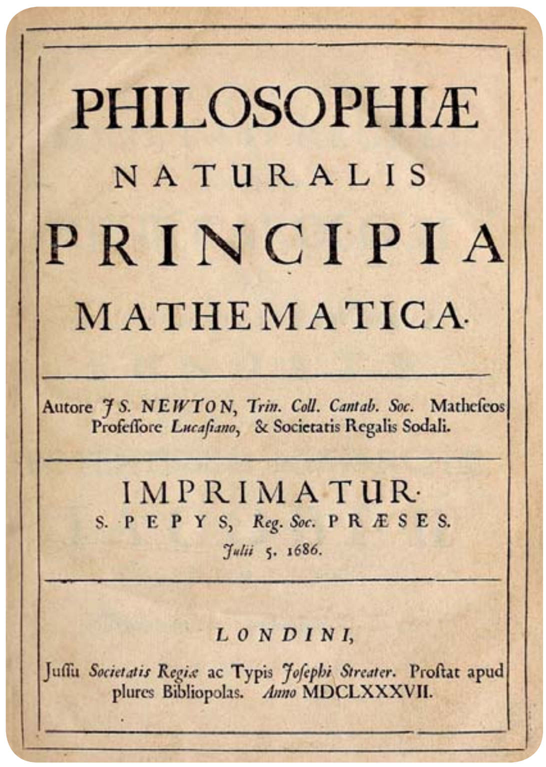
Gone were Mersenne, Descartes, Pascal, Fermat: they had laid the foundations for the theory of numbers and analysis, built bridges between geometry and algebra, initiated the calculus of probability and of variations, deciphered the laws of optics and acoustics and even built the first calculating machines. In each and everyone of them, there was this double movement of mathematical ideas: towards the inside, on the one hand, with the study of mathematical concepts and objects in themselves, and towards the outside, on the other hand, in a perpetual struggle to describe, understand and predict the phenomena of nature – as a matter of fact, of physics.

Those who were about to follow the steps of these giants would not be less bright. At the University of Cambridge, a student named Isaac Newton was making the best impression: influenced by Wallis and Barrow, he had also read Fermat and Descartes with enthusiasm. Forced out of class by a plague epidemic, he worked on – among other topics – a new theory of gravitation. A somewhat younger student from Leipzig, Gottfried Leibniz, had just become Doctor of law; he refused a teaching position to continue the intellectual exploration that would make him one of the most universal spirits of his times. In Basel, a rich merchant, Nicolaus Bernoulli, was raising his son Jacob in the hope that he would take the family business over, far from suspecting he would become the first of the most famous dynasty of mathematicians ever. Now, at the time, in Paris, the most acclaimed mathematician was the Dutchman Christiaan Huygens, who was in his thirties and had been educated at The Hague, Paris and London. His work on the pendulum clock was a revolution in how we measure time, although that was only one of the feats that brought him to be chosen among Colbert's very first recruits at the Académie des Sciences.

Huygens, Newton, Leibniz, the Bernoullis: those would become the most famous heroes of the mathematical revolution that would break out in this second half of the 17th Century. Strong personalities who would influence one another, join forces, tear one another to pieces, challenge and sometimes insult one another in letters almost only them could fully appreciate; within a few decades, they would produce several treatises that count among the most important of the history of science.

Emblematic of this period was Newton's *Philosophiae Naturalis Principia Mathematica*, a work published in 1687 that, as its title foretells, aims at developing the mathematical foundations underlying our knowledge of the world. Such an ambitious programme would make its author one of the most influential men of all times. As emblematic was the birth of infinitesimal, differential and integral calculus, a very powerful tool with major applications in modern analysis, allowing the variations of functions to be quantified. And no less emblematic was the ferocious quarrel that opposed Newton and Leibniz on the first paternity of differential calculus – a preamble to the relative isolation in mathematics from which Great Britain would suffer for two large centuries; more dramatically, in France, religious persecution resumed and it would eventually drive Huygens away from this country.

Here is a famous excerpt from a letter Newton wrote to Leibniz, in a time when they were not so cross with each other: *6accdae13eff7i3l9n4o4qrr4s8t12ux*. That is how Newton, a true amateur of mysteries, had encoded the Latin and hardly less mysterious sentence "*Data aequatione quotcunque fluentes quantitates involvente, fluxiones invenire; et vice versa*", for which the mathematician Vladimir Arnold suggested the following free translation: "*It is useful to solve differential*



PHILOSOPHIÆ
NATURALIS
PRINCIPIA
MATHEMATICA.

Autore *J S.* NEWTON, *Trin. Coll. Cantab. Soc.* Matheseos Professore *Lucasiano*, & Societatis Regalis Sodali.

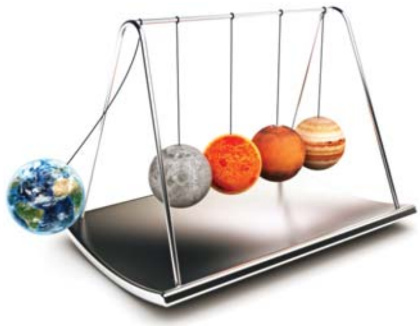
IMPRIMATUR.
S. PEPYS, *Reg. Soc.* PRÆSES.
Julii 5. 1686.

LONDINI,
Jussu *Societatis Regiæ* ac Typis *Josephi Streater*. Prostat apud plures Bibliopolas. *Anno* MDCLXXXVII.

Philosophiae Naturalis Principia Mathematica *(1687) would make Isaac Newton (1642-1727) one of the most influential men of all times.*

equations”. Nowadays, such secrets may seem childish but the invention of the differential calculus was an unprecedented revolution, inasmuch as it made it possible to translate into equations all sorts of physical problems based on tendencies and variations. Did Albert Einstein himself not declare this was the most important step ever taken in physics?

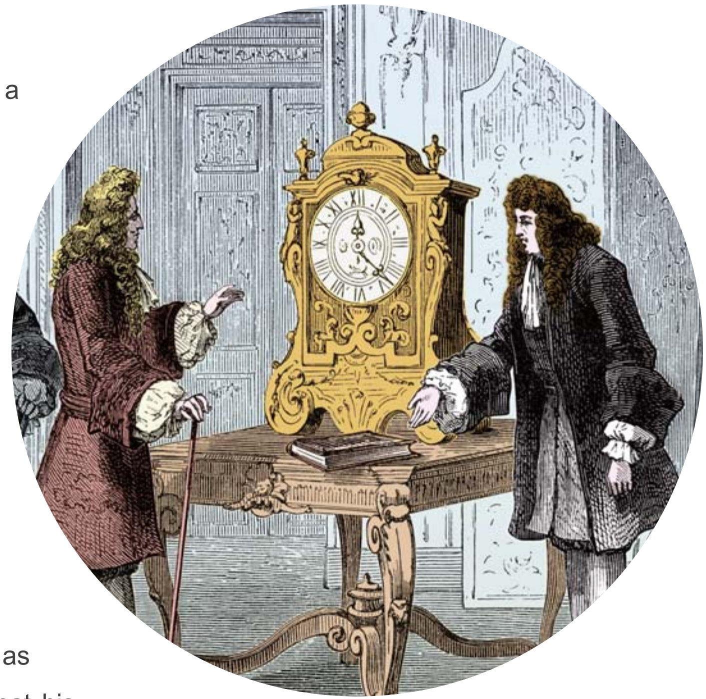
The differential calculus: promises kept



One famous example of it is the stability of the solar system: knowing the equations that describe the motions of stars, is it possible to predict whether the solar system will stay as we know it or, on the contrary, be devastated by a major cataclysm, such as a collision between two planets? Thanks to differential equations and Newton’s law – the sum of gravitational forces is equal to mass times acceleration – the problem could now be translated into mathematics. From then on, everything would go very fast. Ninety generations had passed since Thales and his disciples dreamt of mathematizing the motions of planets; yet, once differential equations discovered, it would take less than 12 generations to send a human being on the moon; and two more for a machine to land on a comet and transmit us a wealth of information. Each step of the way, though, was fraught with obstacles and unexpected developments, and involved the parallel efforts of an ever-growing number of scientists.

Let’s consider one of those innumerable stories that have been initiated by our heroes of the 17th Century. It started with a familiar object, the pendulum: a mass suspended at the end of a thread. Pendulums have always been there, under one form or the other; yet, apparently, only circa 1600 did they start to be really observed, with Galileo. The illustrious Italian remarked, and rightly so, that the oscillation period does not depend on mass, but varies according to the amplitude of the motion. When it came to using the regularity of pendulum oscillations to build clocks, such a variation limited accuracy. Huygens then had a purely mathematical question: is it possible to constrain the motion of a pendulum by a well-chosen curve, so as to make its oscillation period independent from its energy? The solution was no other than the famous cycloid, i.e. the curve described by a

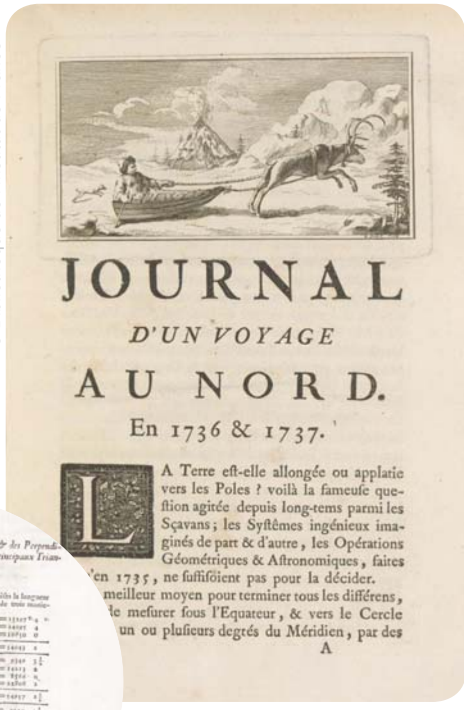
Galileo (1564-1632) observing the oscillation of a hanging lamp in the Pisa Cathedral (Fresco by Luigi Sabatelli, circa 1840) marked point on a rolling wheel. Indeed, if a pendulum is constrained by two “cheeks” of cycloidal shape, then the mass describes a trajectory that is itself cycloidal; and, remarkably, the oscillation period will be rigorously invariant. This enabled Huygens to build the first mechanical precision clock, with an error inferior to one second per hour.



Christiaan Huygens (1629-1695) presents his pendulum clock to Louis XIV.

However, the pendulum was far from saying its last word. In 1673, the astronomer Jean Richer, who had been recruited as "élève académicien" in 1666, discovered that his pendulum ticked a bit slower in Cayenne than in Paris. Huygens and Newton deduced from this trivial observation that the Earth, subject to a centrifugal force, is slightly flattened at the poles: a theory that would remain controversial for half a Century, until a famous measurement campaign in Lapland that the Académie des Sciences entrusted to Maupertuis.

Pierre Louis Moreau de Maupertuis (1698-1759) and the campaign to Lapland



JOURNAL
D'UN VOYAGE
AU NORD.
En 1736 & 1737.

LA Terre eſt-elle allongée ou applatie vers les Poles ? voilà la fameuſe queſtion agitée depuis long-tems parmi les Sçavans ; les Syſtêmes ingénieux imaginés de part & d'autre, les Opérations Géométriques & Aſtronomiques, faites en 1735, ne ſuffiſoient pas pour la décider. ... meilleur moyen pour terminer tous les différens, ... le meſurer ſous l'Equateur, & vers le Cercle ... un ou pluſieurs degrés du Méridien, par des

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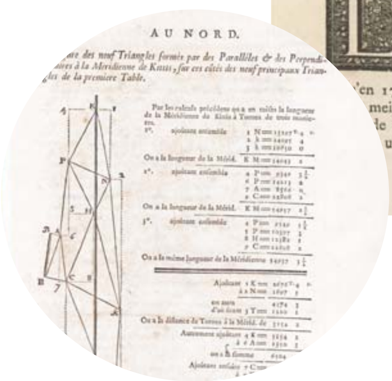


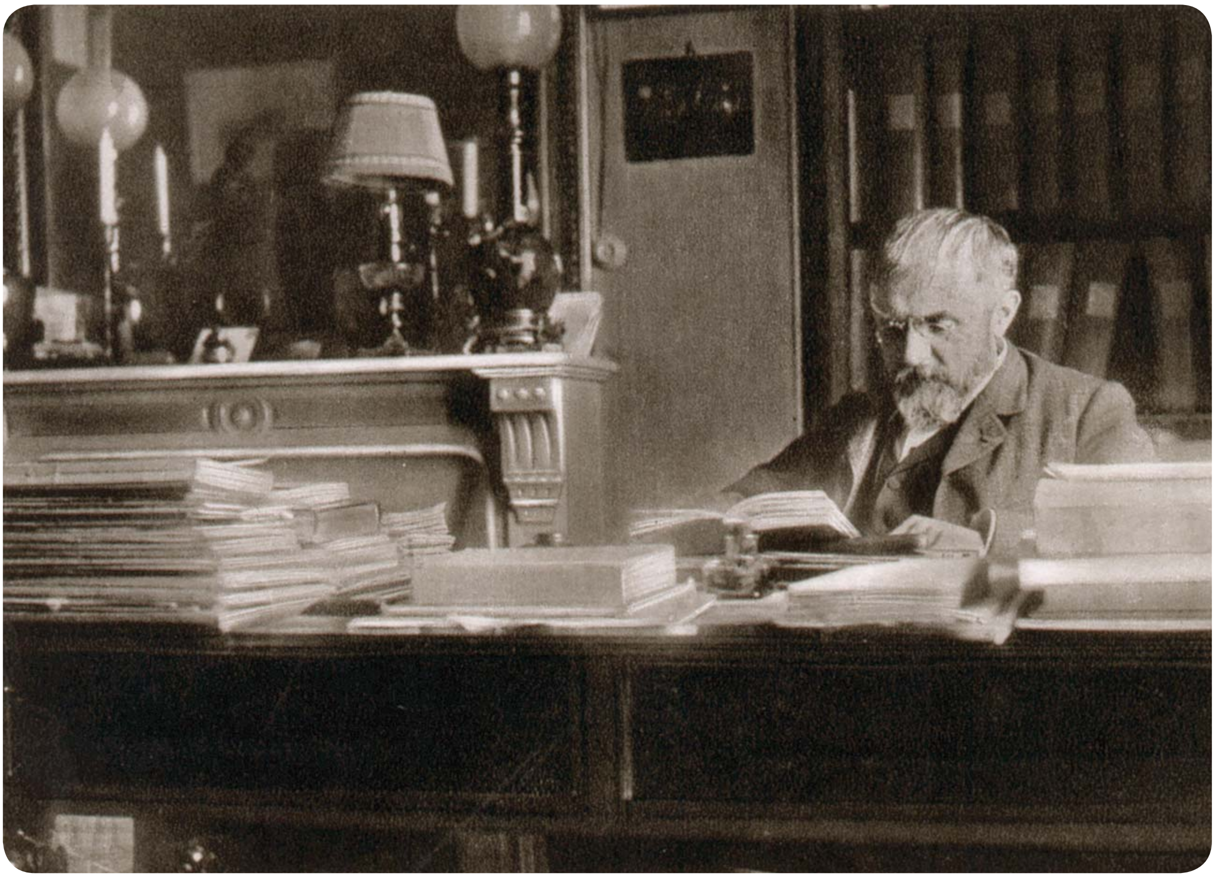
Journal of the campaign, by the abbot Outhier and Maupertuis, Paris, 1744

Thus, within this pendulum lie the seeds of two great scientific epics. One is the technology of precision clocks, whose most colorful moment was Harrison’s 1765 chronometer, a real wonder that would not lose more than one second per month and made it possible, through the calculation of time difference, to take precise bearings at sea. The other is the discovery of the precise shape of the Earth, whose most dramatic chapter was the heroic effort Delambre et Méchain made on the wake of the French Revolution to measure the Earth and thus provide the world with a truly universel unit, the metre.

Adventures like these, with their share of surprising observations, unexpected developments and conceptual revolutions, became more numerous in the following decades and centuries. One after the other, problems would wind up into mathematical hands. In the 18th Century, Euler, Bernoulli and d'Alembert sought to conquer the ungraspable fluids; it took almost one century before the Navier-Stokes equations finally won recognition. With Condorcet, then, it was time to explore votes and systems of decision, and with Laplace, the statistical fluctuations of stochastic events, and with Monge, such operational problems as the displacement and rearrangement of matter at the least expense, and with Sophie Germain, the oscillations of membranes, and with Fourier, the propagation of heat. As Fourier's motto puts it: "*Et ignem regunt numeri"* – even fire is ruled by numbers, by equations.

Mathematical refoundations and revolutions

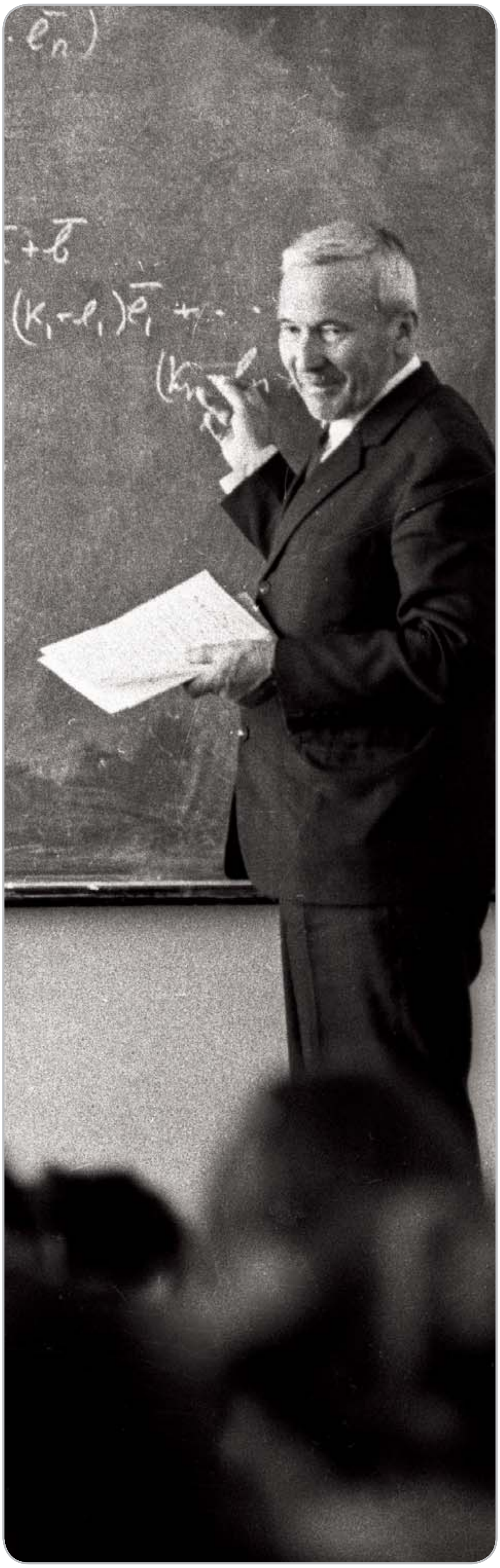
To be more efficient, the discipline also had to improve its own structure and tools. Throughout the 19th Century, concepts were refounded, one after the other, by Gauss, Legendre, Cauchy, Jacobi, Abel, Galois, Dirichlet, Riemann, Weierstrass, Cantor, Poincaré, to name but a few of them. Analysis was redefined, as well as algebra and the very concept of number; non-Euclidean geometry was founded, and topology, and the notion of set. The theory of complex functions provided for a systematic research of solutions, while at the same time algebra was used to demonstrate that some problems are not solvable. With his theory of dynamical systems, Henri Poincaré introduced a vast programme of qualitative study on the solutions of differential equations, which shed new light on Newton's mechanics.



Henri Poincaré (1854-1912)

The beginning of the 20th Century also had its train of revolutions. Measure theory, and probability theory, were refounded by Borel, Baire, Lebesgue and Kolmogorov. Statistical physics, quantum mechanics and even finance: all received their own personalized mathematical expression. But the most amazing of such scientific storms took place in logic, questioning the very foundations of the discipline – what is a reasoning, what is a proof, which are the problems that have a solution and those that do not? And what does this mean: “1+1=2”? A source to the *Principia Mathematica* written by Russell and Whitehead (a volume of which ends up, after nearly 400 pages, to the eventual proof that 1+1=2!), and to the works of Hilbert, Church, Gödel and others, such an abyss of perplexity eventually spurred Von Neumann, Turing and Shannon on to imagine computers, as logical machines able to perform any mathematical operations. Interestingly enough, one of the first motivation of these pioneers of computer science was the systematic study of differential equations – definitely a universal topic.

It is impossible here for me to pay tribute to the mathematical development of the 20th Century, which may have been the richest of all. Beside the new conceptual feats achieved by the great Bourbaki, Weil, Noether, Banach, Wiener, Riesz, Atiyah, Cartan, Hardy, Ramanujan, Littlewood, Chern, Grothendieck, Cohen, Leray, Hironaka, Itô, Serre, Gel'fand, Schwartz, Hörmander, Carleson, Nash, De Giorgi, Solovay, Malliavin, Gromov, Langlands, Thurston, Varadhan, Wiles, Perelman and so many others, hundreds of new topics emerged. I shall mention only one, which is



Andrei Kolmogorov (1903-1987)

dear to me: in 1933, Torsten Carleman conducted the first mathematical study on the Boltzmann equation, describing and predicting the statistical evolution of a gas that experiences unceasing collisions; today, the mathematical literature on this topic is tens of thousand of pages long.

And mathematicians may now be counted by hundreds of thousand, operating within highly organized research systems and publishing more than ever – and probably too much – in hundreds of specialized journals, most of the time in collaboration with others; they gather all over the world, in a relentless ballet of conferences, symposia and emails. The roles of mathematicians within the industry has been acknowledged; they have been praised and reviled, and by times called criminals. The time of craft, of Newton and his colleagues, is far away; and yet their questions are still ours, so as their unremitting desire to understand and predict the phenomena, with is sometimes fulfilled, other times held in check.

Thus, to the question raised by Newton – Is the solar system stable? – after three hundred and fifty years of work, the introduction of linear algebra, dynamical systems, probability theory, chaos theory, perturbed Hamiltonian systems, symplectic schemes and the contributions of such sacred monsters as Laplace, Lagrange, Poincaré and Kolmogorov – to this question, we may now confidently answer: "*Perhaps*!"

This "perhaps" is nothing we should be ashamed of, as it may be quantified in probability terms, and as we know it is not possible to do better: the outcome of the universe is ruled by a set of probabilities, for lack of an infinite, unreachable precision. Ultimately, in Newton's problem, we are faced with two well-known conceptual monsters: chance and the infinite. Prediction and unpredictability are two themes entwined in each other throughout this long story, which is not unlike a great novel, with its share of ironic twists and turns. Indeed, when Gauss managed to find the lost orbit of the asteroid Ceres, then to master Vesta's, its little sister, the world seemed most predictible; yet, some two centuries later, our fellow Jacques Laskar would demonstrate the perturbing effect Ceres and Vesta has on the whole solar system, forbidding any prediction beyond 60 million years. And as for

Carl Friedrich Gauss (1777-1855)

Artist's view of Ceres

the measurement of time, let us say that the programme initiated by Huygens progressed to such an extent, with every scientific opportunity, that the best modern clocks would not vary more than one second in a billion years.

Above all, heartbeats, one-week weather forecasts, electrical influx in our neurons, the growth of a tumor, or a rumor – all and more have been translated into equations to be understood and predicted. The mathematical science is thus proud to participate, in harmony with other sciences, to some of the great technological adventures of our time, as with the algorithms that feed the artificial heart developed by our fellow Alain Carpentier, those that coordinate the electric supply of intelligent grids, or even analyzing measures taken by gravitational wave detectors. Disciplines widely blend together, now more than ever, at the image of what we observe in our Academies, and in our world.

The Academie des Sciences, a forward-looking institution

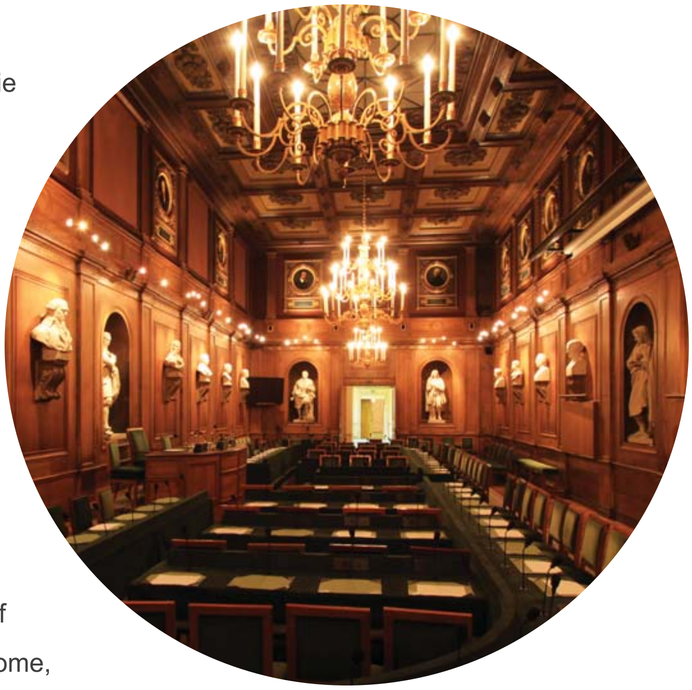
Originally under the protection of the King, the Académie des Sciences today has the status of a 'Public Legal Entity' under the protection of President of the French Republic. As an independent institution, the Académie performs an advisory role to the decision-makers. Enriched by its 259 members, 138 foreign associates and 88 corresponding members[1] — who rank among the most prestigious scientists of their time in the whole range of scientific disciplines including the most emerging ones —, the Académie composes reports, advice notes and recommendations, all acting as decision aid tools. Members are peer-elected from the eight sections of the Académie, but they work in multidisciplinary standing committees which are the cornerstones of the Académie's expertise.

Five missions

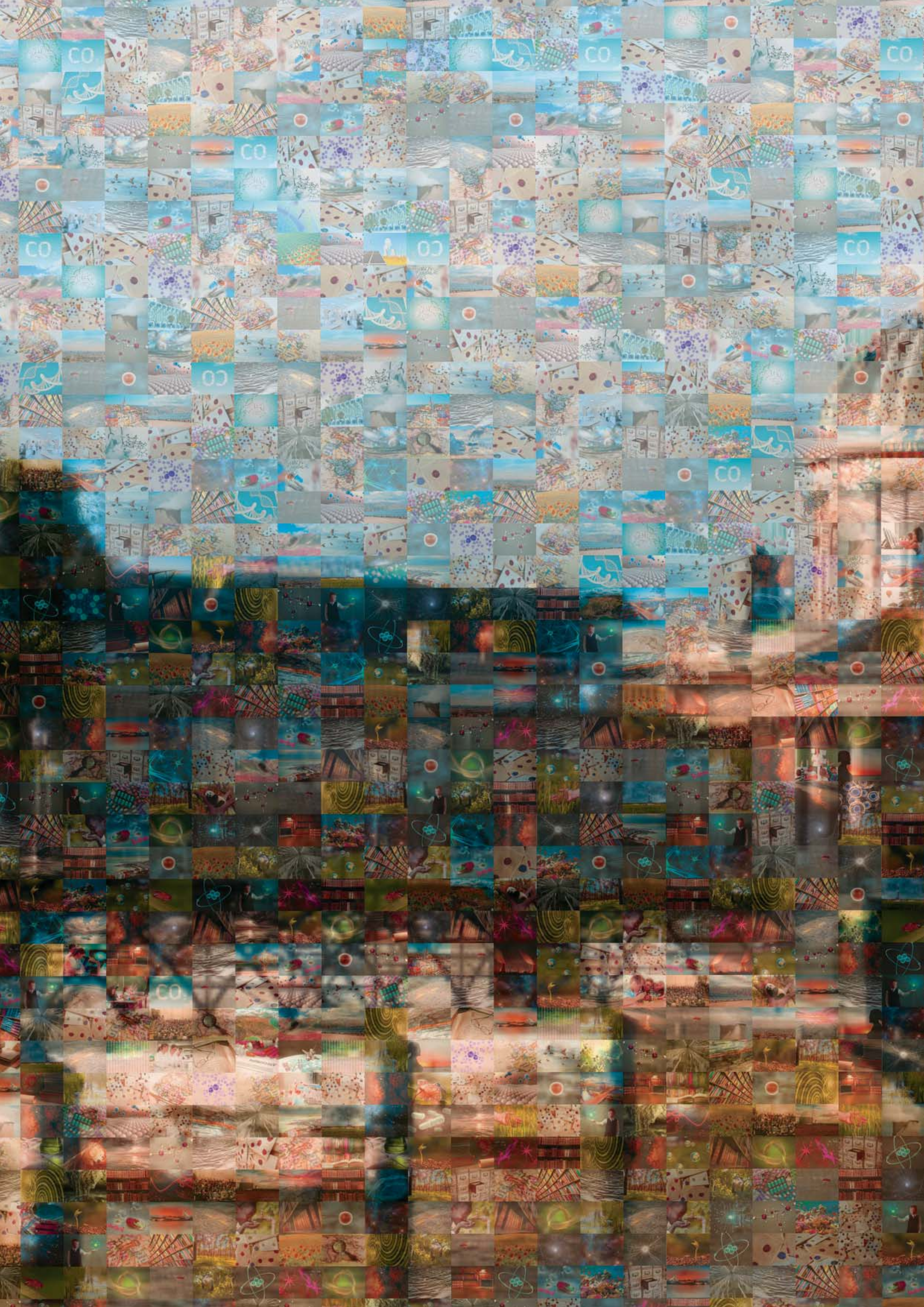
- Encouraging the scientific community: Scientific conferences and colloquia, Prizes and medals, *Comptes Rendus de l'Académie des sciences*.
- Promoting science teaching: Scientific teaching at school, Standing committee for science education and training, Museums.
- Transmitting knowledge: Public scientific sessions, Website, Biannual letter, Twinning scientists with MPs programme, Archives.
- Fostering international collaboration: Interacademic networks, Bilateral cooperation.
- Performing the role of an expert and advisor: Standing thematic committees, Reports, Advice Notes and Recommendations.

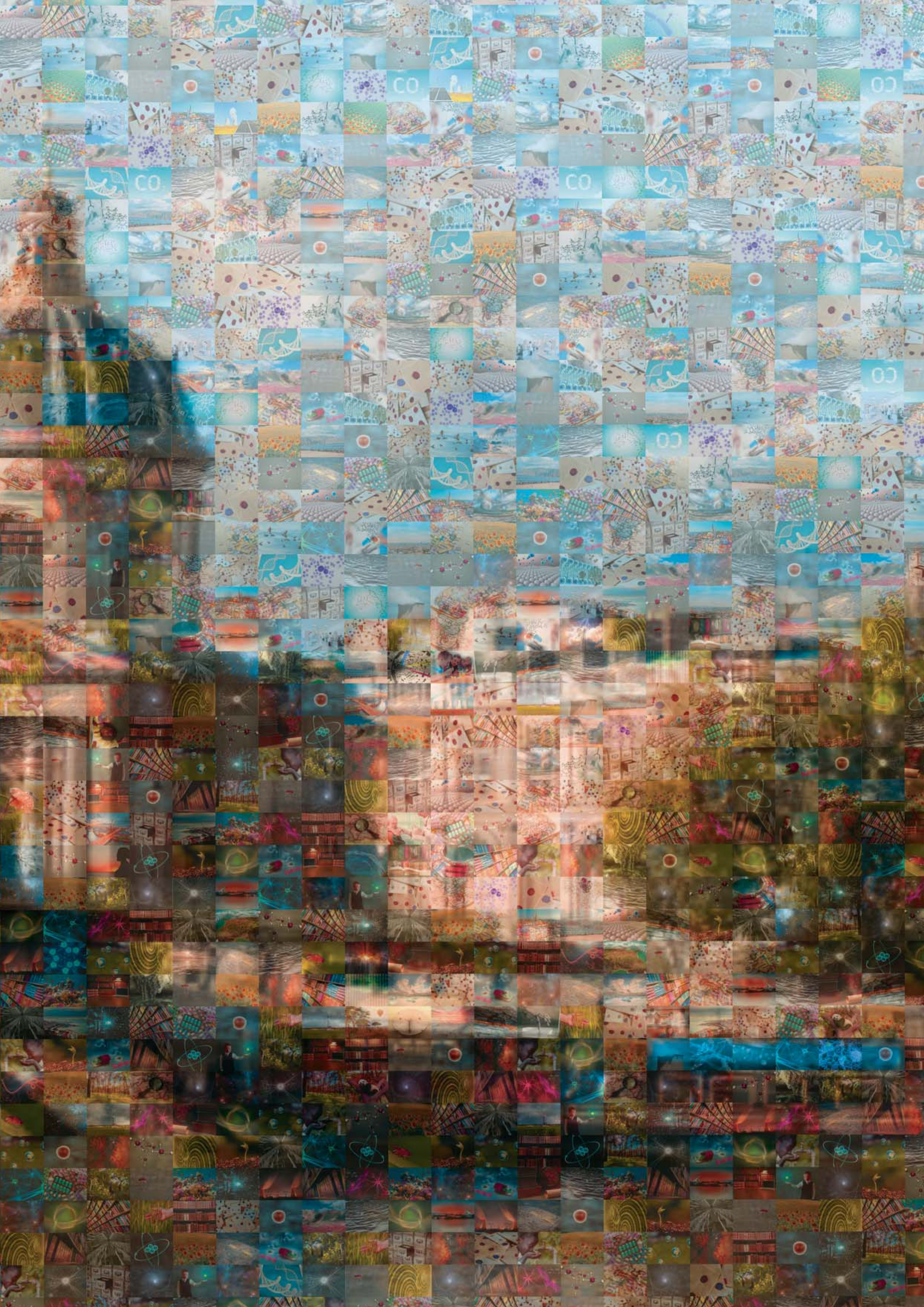
1 - As of 1 September 2016

As provided by the new statutes the Académie adopted in the early 2000s, half of the newly elected members are less than 55 years old. This is a worthwhile asset in keeping the Académie focused on the future and allowing it to always provide up-to-date and appropriate answers to the questions society may have on the development of science and its applications.



Since the founding of the very first academy of sciences — the *Accademia Dei Lincei*, in Rome, 1603 —, the number of national academies rapidly expanded, first in Europe and then worldwide. In addition to the role they play in their own countries, these academies, linked in interacademic networks, express their opinions on global issues. Its renown and 350 year-long expertise still make the French Académie des Sciences an essential partner for international scientific diplomacy.





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ISSN 2102-5398

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