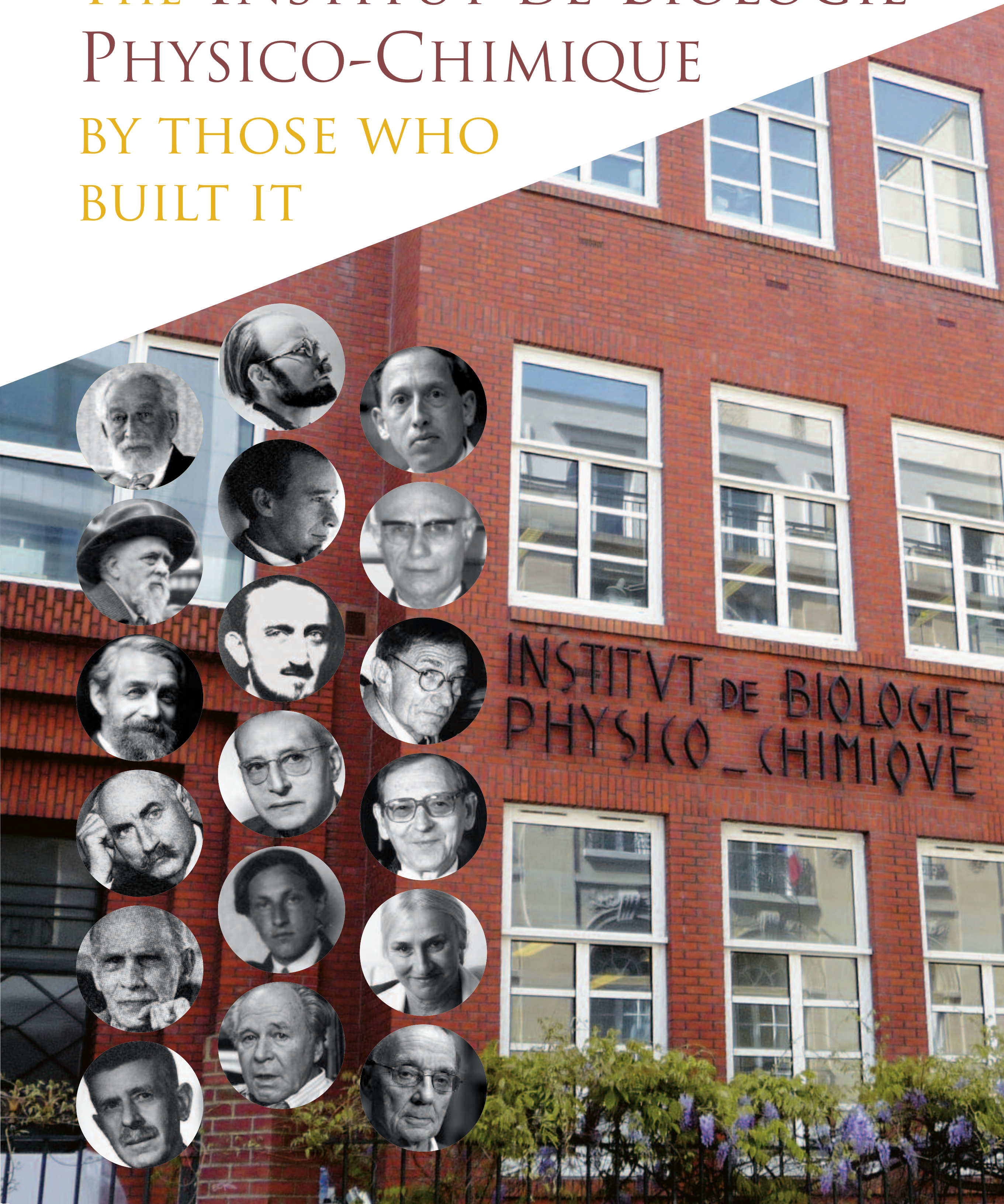
The Institut de Biologie Physico-Chimique by those who built it



FOREWORD

For a long time the IBPC was for me a beautiful château that you see from a familiar road and promise yourself repeatedly that you will visit while forever delaying the moment. For those interested in the history of science, the Montagne Sainte Geneviève has everything of the Loire Valley, with the Institut Curie and the Pavillion du Radium, the Ecole supérieure de physique et de chimie industrielles de la ville de Paris, the Institut océanographique, the Ecole normale supérieure and the Institut Henri Poincaré being so many tourist stops along the way.

A biologist by training, historian by adoption, and interested in French research during the 1930s and 1940s, I had often had the occasion to note the dual originality of the IBPC. A place where extremely innovative research in biology was conducted at a time when, in France, the discipline was in an advanced state of sclerosis. Also a place that was open internationally, welcoming in particular foreign researchers at a time when official xenophobia was raging.

My work as a journalist covering matters of scientific policy also caused me to realise to what extent, more than half a century later, the IBPC had lost nothing of its originality. Dedicated to the most fundamental research, it continued to pursue its work with seemingly little regard for the growing pressures to adopt the vain logic of short-term profit. A place also of reflection on the way the French research system was organised, defending with vigour "a certain idea of science," to paraphrase de Gaulle.

I therefore had no hesitation in accepting Francis-André Wollman's invitation to visit, when writing this little book, the intriguing and beautiful château, seeing in the enterprise a way of bringing together these two IBPCs that I had had the occasion to encounter. Francis-André wanted to compile a series of monographs presenting the personality as much as the work of the most eminent researchers to have worked at the IBPC. For my part, I wanted to look at the history of the IBPC as an institution. We readily reached agreement by organising our gallery of portraits in four sections. The first presents the five founders of the IBPC: Baron Edmond de Rothschild, who financed it, then Jean Perrin, Georges Urbain, André Mayer and Jean Girard, who organised its scientific activities during its first decade. The three subsequent sections combine a history of the IBPC, placed in the context of the progressive emergence of a national research policy, with monographs of the principal researchers of three periods: that of fertile intuition, extending from the IBPC's creation in 1927 to the major rupture of the Second World War; that of the birth of molecular biology, between 1945 and 1963; and finally the current period that is one of exploring the new questions posed by the paradigm of molecular biology. In perusing these four sections, it is an entire period of the history of modern biology that one is able to visit.

NICOLAS CHEVASSUS-AU-LOUIS

PREFACE

Any research institute seeks to promote its latest research. The laboratories of the Institut de Biologie Physico-Chimique, like laboratories all over the world, are engaged in the daily adventure of gleaning new elements of understanding from the world around us. The insert enclosed with this booklet is testimony to the fact. But few institutes take the time to look back at the work of past contributors, of those who shaped our ability to meet today's scientific challenges. Such is the purpose of this presentation of the scientific history of our institute, of 80 years that form an inextricable part of the history of the 20th century itself.

To present the Institut de Biologie Physico-Chimique through those who built it is to present a research institute as the unique meeting place of strong intellectual personalities whose interlocking destinies forge a shared scientific adventure.

The history of the IBPC, an institute founded in 1927 and inaugurated in 1930, illustrates one of the fundamental characteristics of the scientific research that flourished from the 18th century: the expression of a conceptual freedom to explore based on an experimental approach. It is an expression on which an institute must forever refocus its attention, such are the many constraints liable to intervene between the researcher and the exercise of his freedom of inquiry. Thus, the history of contemporary biology teaches us that certain places more than others lent themselves to this adventure. Microbiology and genetics developed largely outside the confines of the university, finding at the Institut Pasteur, for example, as at the IBPC, conditions more favourable to their development. Often independent of the major academic institutions, these places of discovery proved to be the crucible for a fruitful mixture of knowledge transmission and conceptual transgression. The dynamic co-existence of these two apparently contradictory processes resides entirely in the primacy of the logic of knowledge. Giving precedence to any other logic, whether administrative, accounting, strategic or political, always has the result of weakening the dynamic of discovery.

A philanthropic initiative such as that of Baron Edmond de Rothschild, who was no stranger to matters of the application of knowledge, enabled the "men of learning" in whom he trusted, such as Jean Perrin, to deploy their talents in total freedom in the study of the physico-chemical bases of life. Of course the philanthropist was acutely aware of the utility of science in developing the country, but he did not seek to impose the least "steering device" and simply placed the IBPC at the disposal of talented and imaginative researchers who were free to work in complete autonomy. The research device as conceived initially around the institute's four founders, or 'Tetrarchs', and that presided over the destiny of an institute employing full-time researchers driven by the sole desire to discover, was preserved in spirit over the years while evolving continuously in regard to the typology of the research undertaken. The fields of exploration, the challenges and the goals changed constantly as knowledge developed and new researchers arrived with new scientific concerns.

It was by welcoming successive waves of talented researchers with forever renewed centres of interest that the IBPC experienced a number of innovative periods. This was most certainly true at its inception when physicists, chemists and biologists were brought together to establish complementary methodologies to develop research in physiology. It was also the case in the immediate post-war period that saw the blossoming of non-Mendelian genetics – mitochondrial, bacterial and then chloroplastic – that made a crucial contribution to the birth of molecular genetics, or in the late 20th century that saw so many new lines of inquiry opening up, including bioenergetics, membrane biology, molecular modelling, structural biology and cryobiology.

The IBPC's relative share of research potential in physico-chemical biology is much more modest today than when it was founded. This is to be welcomed as it is evidence of the vigour with which research in biology developed throughout the 20th century. Yet it is a growth accompanied by increasingly complex administrative, technical and financial devices designed to meet the century's major methodological challenges. It is therefore all the more necessary to heed the demands of researchers for imaginative and conceptual freedom without which research would be no more than a translation of short-term innovation strategies rather than an aspiration to discovery.

In so far as its means permit, and limited as they are today, the IBPC still has the declared ambition to provide a framework dedicated entirely to shared scientific pleasure. The spirit of this "house", the one that every IBPC director seeks to promote, is an atmosphere of enthusiasm for research within the serenity of the conditions for exercising it. No doubt because it was also conceived by Jean Perrin, the CNRS that, at the time of writing, still embodies our country's passion for science, is most certainly continuing to carry the torch for the IBPC founders and their commitment. In assuming administrative and scientific responsibility for our institute in 1997, the CNRS, despite short-sighted pressures, changing fashions and superficial matters of image, has supported a scientific policy based quite simply on a demand for quality research pursued in total freedom by original researchers. The historical presentation of "*the IBPC by those who built it*" bears witness to the fecundity of this policy during the past 80 years. Of course we must adapt to a scientific and technical environment, as well as to an academic one, that has changed considerably during this period and especially in biology. But it is the same adventure that confronts us at the moving forefront of knowledge and by virtue of which it is an adventure forever renewed.

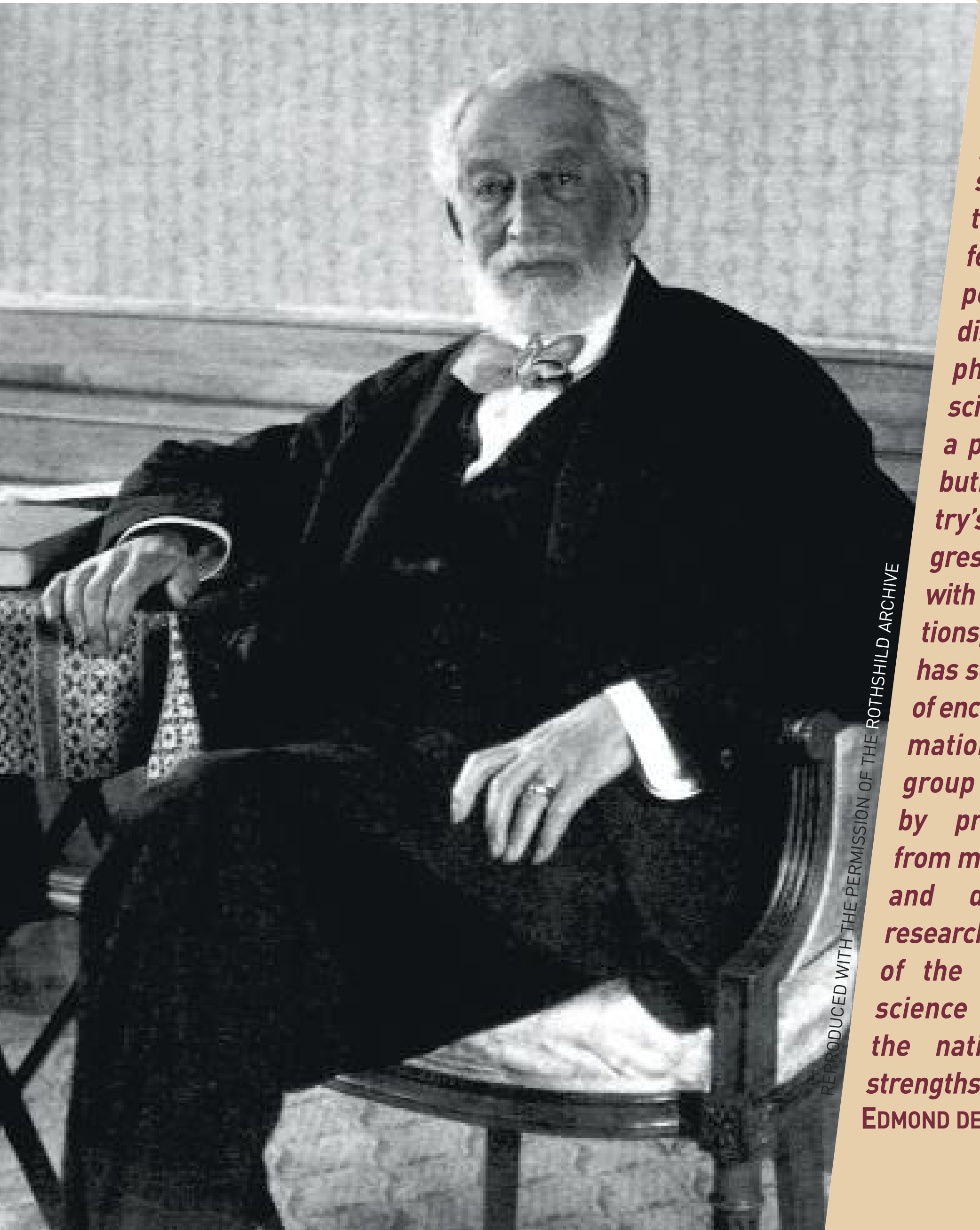
Paris, May 2010

FRANCIS-ANDRÉ WOLLMAN.
Director of the IBPC

Edmond de Rothschild

1845-1934

A philanthropist interested in science



"War showed that the contribution of the physico-chemical sciences was vital to national defence and that, in peacetime, the discoveries of the physico-chemical sciences can make a powerful contribution to the country's economic progress. In accordance with these considerations, the Foundation has set itself the goal of encouraging the formation of an elite group of researchers by protecting them from material concerns and directing their research in the direction of the applications of science in developing the nation's economic strengths."

EDMOND DE ROTHSCHILD

Grandson of the founder of the Rothschild dynasty and youngest member of the French branch of the family, in 1921 the banker Edmond de Rothschild created a Foundation dedicated to supporting scientific research. Among the first to benefit from its aid were Marie Curie, Paul Langevin, Georges Urbain... and Jean Perrin.

The latter forged a friendship with the philanthropic baron. When more than 80 years old, Edmond de Rothschild was a frequent visitor to Perrin's laboratory, located in the Sorbonne attic. A dark, steep and narrow staircase led to an area that impressed the baron by its bareness. The two men shared a common concern for France to catch up scientifically with Germany and at that time the baron was thinking mainly of closer contacts between researchers and industrialists. But Perrin's infectious enthusiasm convinced him of the importance of new physico-chemical approaches in biology. In his youth Edmond de Rothschild had known Claude Bernard and Louis Pasteur but, since then, he had *"lived in an age when research in biology had been largely abandoned, everybody turning to microbial studies." "It seemed to me a good thing and possibly useful to resume research in biology, but with the modern knowledge of physics and chemistry that has made the world of learning understand that in reality life, if not engendered by, is at least manifested by physico-chemical reactions,"* he wrote in 1927 to the mathematician Paul Appell, president of his foundation.

A second foundation was therefore created with a capital of 30 million francs (equivalent to 17 million euros in 2010). Its unique mission was to meet the operating and wages costs of an Institut de Biologie Physico-Chimique that would be built with a special donation from the baron. The foundation's statutes stipulated that the 24 members of its board of directors had to be chosen by the scientists. Only the founder, or his descendant, would be an ex-officio member. But when the IBPC opened its doors in 1930 the French research landscape was changing. The brand new Caisse nationale des Sciences now funded part of the costs of research grants and laboratory equipment, rendering the work of the first foundation less vital. In 1932 the two Rothschild Foundations therefore merged into a single foundation that financed the IBPC.

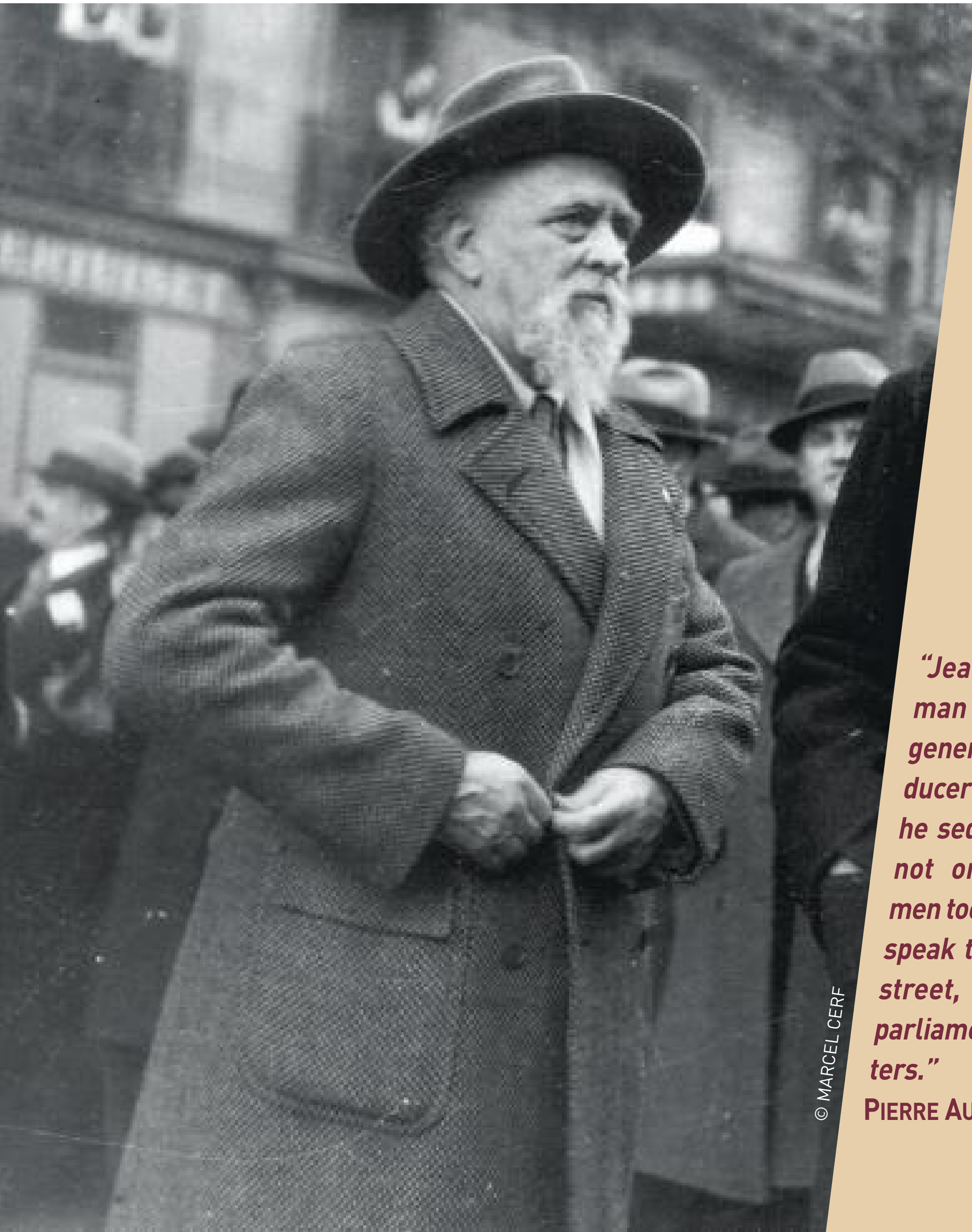
EDMOND DE ROTHSCHILD (1926-1997) COMMITTED HIMSELF FROM 1957 UNTIL HIS DEATH TO MANAGING THE IBPC TROUGH THE FOUNDATION SET UP BY HIS GRANDFATHER.

After his death in 1934, Edmond de Rothschild was replaced on the foundation's board of directors by his daughter Alexandrine, then by his son Maurice in 1952, and finally, from 1957, by his grandson Edmond. The latter was untiring in his commitment to managing the IBPC, filling the post of treasurer until his death in 1997. *"All members of the board of directors have ingrained in their memory the image of a stocky man with an impressive grey moustache who always said outright what he meant to say, a heavy smoker of gauloise cigarettes, a big eater and... Rothschild oblige! a great connoisseur of fine wines,"* remembers François Gros.◀

Jean Perrin

1870-1942

The poet of the atoms



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"Jean Perrin was a man of abounding generosity. A great seducer in every respect, he seduced everybody, not only women, but men too. He knew how to speak to the man in the street, to members of parliament and to ministers."

PIERRE AUGER

His hair stood on end like flames," said Paul Valéry, and it was as a Dionysus that he was portrayed by Georges Urban who sculpted a bust of his colleague and friend. Jean Perrin was physically imposing, a man with a presence. With his high forehead and clear eyes he embodied the unpretentious, absent-minded scientist, a man bursting with energy and passionately interested in all around him. *"If you want to understand Brownian motion, then you need do no more than to watch Perrin speak of it,"* the British physicist Ernest Rutherford said of him.

Born in Lille in 1870, where his captain father was garrisoned at the time, he entered the Ecole Normale Supérieure in 1891. It was there that he formed a lasting friendship with the mathematician Emile Borel and the physicist Paul Langevin and made the acquaintance of his elder, Pierre Curie. The Borel, Langevin, Curie and Perrin families were to remain linked by a close friendship. "Perrin's band," as they were described by their detractors, holidayed together at L'Arcouest in Brittany, nicknamed Sorbonne Beach, and brought up their children together, giving them all science lessons for example.

For his PhD in physics, in 1897 Perrin submitted a much noted thesis in which he describes the existence of a negative charge – the electron – within the atom. The next year he was appointed professor at the Paris Faculty of Sciences. His research into the discontinuous structure of matter earned him election to the Academie des Sciences in 1923 and then the Nobel Prize for Physics in 1926. He was also skilled at popularising science and in 1913 published *Les atomes* (1913), one of the first books to present modern physics to the general public. He was also interested in biology, this leading him to accept the IBPC presidency on its foundation in 1927. Astronomy was another passion, and it was Jean Perrin who demonstrated that the sun derives its energy from the fusion of hydrogen atoms

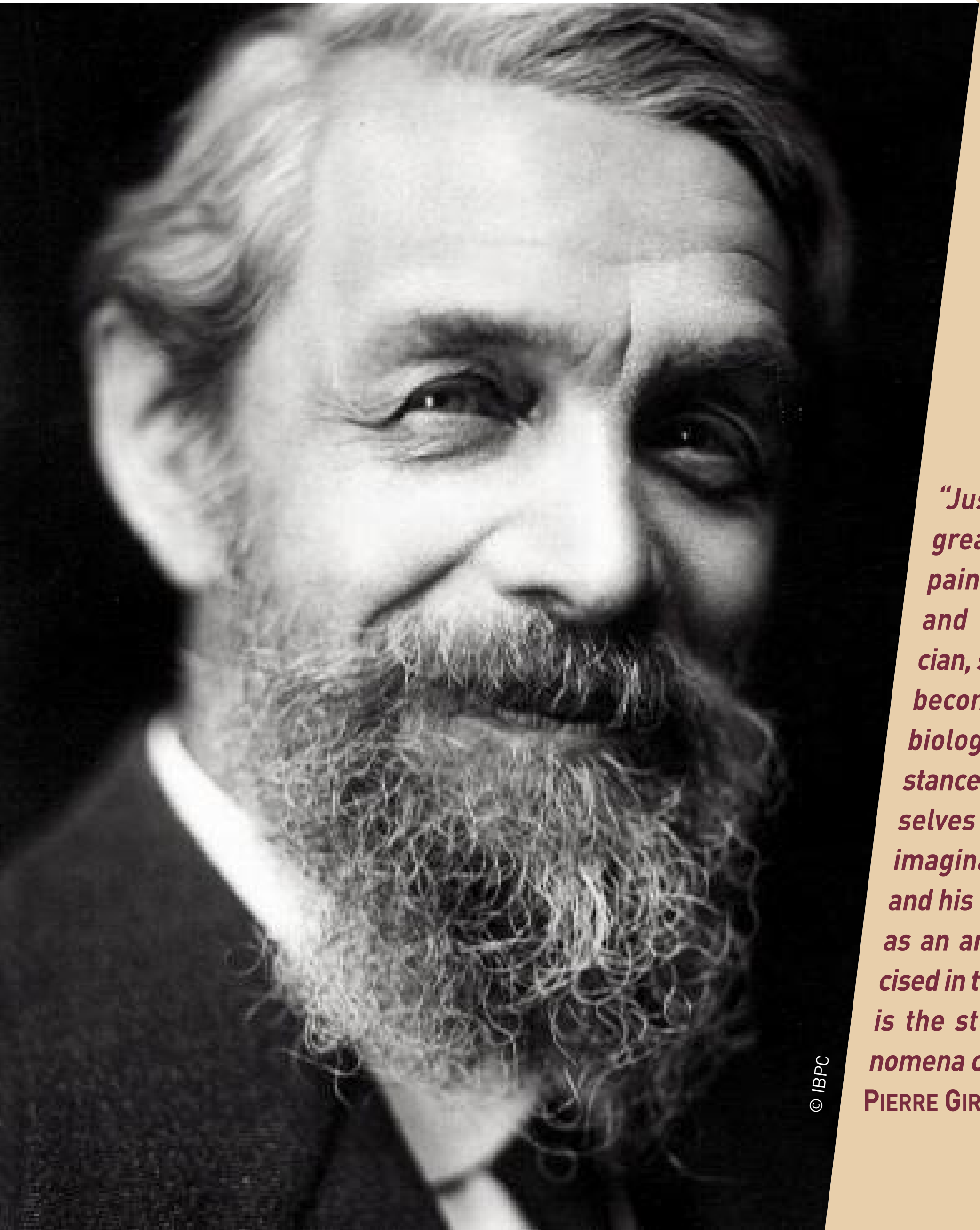
Like many of the elite Ecole Normale graduates of his generation, Perrin came to political commitment with the Dreyfus affair. A Dreyfusard from the outset, he established close contacts with the Human Rights League that lasted throughout his life. In 1930 he helped create the Union rationaliste and then the Comité de vigilance des intellectuels anti-fascistes. Close to the SFIO (French Section of the Workers International), he was on two occasions appointed junior research minister with the Blum government, initiating most notably the Palais de la Découverte science museum. He headed the CNRS when it was founded, in 1939. For this fervent positivist, scientific research and political commitment were closely linked: *"Rapidly, perhaps in the space of just a few decades, if we agree to the necessary slight sacrifice, men freed by science will live happily and healthily, developed to the limits of what their brains can give them... it will be Eden. Eden that we must situate in the future rather than imagining it in a past that was wretched,"* he wrote in *La Recherche scientifique* (1933).

After the French Army's defeat in June 1940 he withdrew to the southern zone, leaving for the United States at the end of 1941. In New York he took over as head of the Ecole Libre des Hautes Etudes, a kind of university in exile set up by around 30 French researchers who were determined to maintain a high level scientific life across the Atlantic. In the US too, political commitment remained for Jean Perrin inextricably linked to research. *"As ultimately one must choose between France Libre and Vichy, we require that [those who belong to our school] should choose for France Libre,"* he said on the occasion of the school's inauguration, on 14 February 1942. His death two months later prevented him from pursuing this intellectual adventure that had attracted such notable figures as Claude Levi-Strauss and the philosopher of science Alexandre Koyré. Jean Perrin's ashes were transferred to the Panthéon in 1948.◄

Georges Urbain

1872-1938

A master of the chemistry of rare earths



"Just as he was a great chemist, a painter, a sculptor, and talented musician, so he would have become an eminent biologist if circumstances had lent themselves to his brilliant imaginative faculties and his exceptional gifts as an artist being exercised in this vast field that is the study of the phenomena of life."

Pierre Girard

The author of an *Introduction à la chimie des complexes* as well as an *Essai sur la musique*, a painter and sculptor but also coordinator of the two volumes of *La science, ses progrès, ses applications*, the discoverer of a new chemical element but also the founder of a laboratory for its industrial production, Georges Urbain was very much the Renaissance man, equally at ease in the sciences as in the arts.

The son of a chemist, Georges Urbain studied with Paul Langevin in preparing for the entrance exam to the Ecole Supérieure de Physique et de Chimie Industrielles de la ville de Paris, graduating in 1894. He then started work on a thesis devoted to the study of the series of rare earth elements. *"The prevailing opinion [...] was that the group of rare earths was to the other elements what the milky way is to the stars,"* he was later to say. He therefore developed new techniques, notably working with Pierre Curie in drawing on their magnetic properties to isolate one by one the members of this vast chemical family. This was research that led, in 1907, to the discovery of a new element that he named after his home town: lutetium (Z=71). His research on rare earths as a whole earned him several Nobel Prize nominations and, in 1921, election to the Académie des Sciences.

The First World War brought a major break in his career. Conscripted and, like most chemists, assigned to the production of combat gases, he witnessed the destruction of his laboratory and the loss of his collection of purified preparations of rare earths. He then turned to reflections on the philosophy of chemistry. His work on the subject was marked by hostility to atomic theory that caused him to see in the atom *"a work of art"*, that is, a pure concept without a physical reality. His thinking failed, however, to make a mark on the history of the discipline. On the other hand, his constant efforts to unify mineral chemistry – which he taught at the Sorbonne from 1908 – and organic chemistry proved to be remarkably trail-blazing. Long interested in biology, he replaced the chemist André Job, who died on 16 August 1928, as IBPC co-director. He ran its Department of Chemistry *"like a grandfather"*, as he liked to say, with his pipe in his mouth and his cane in his hand.

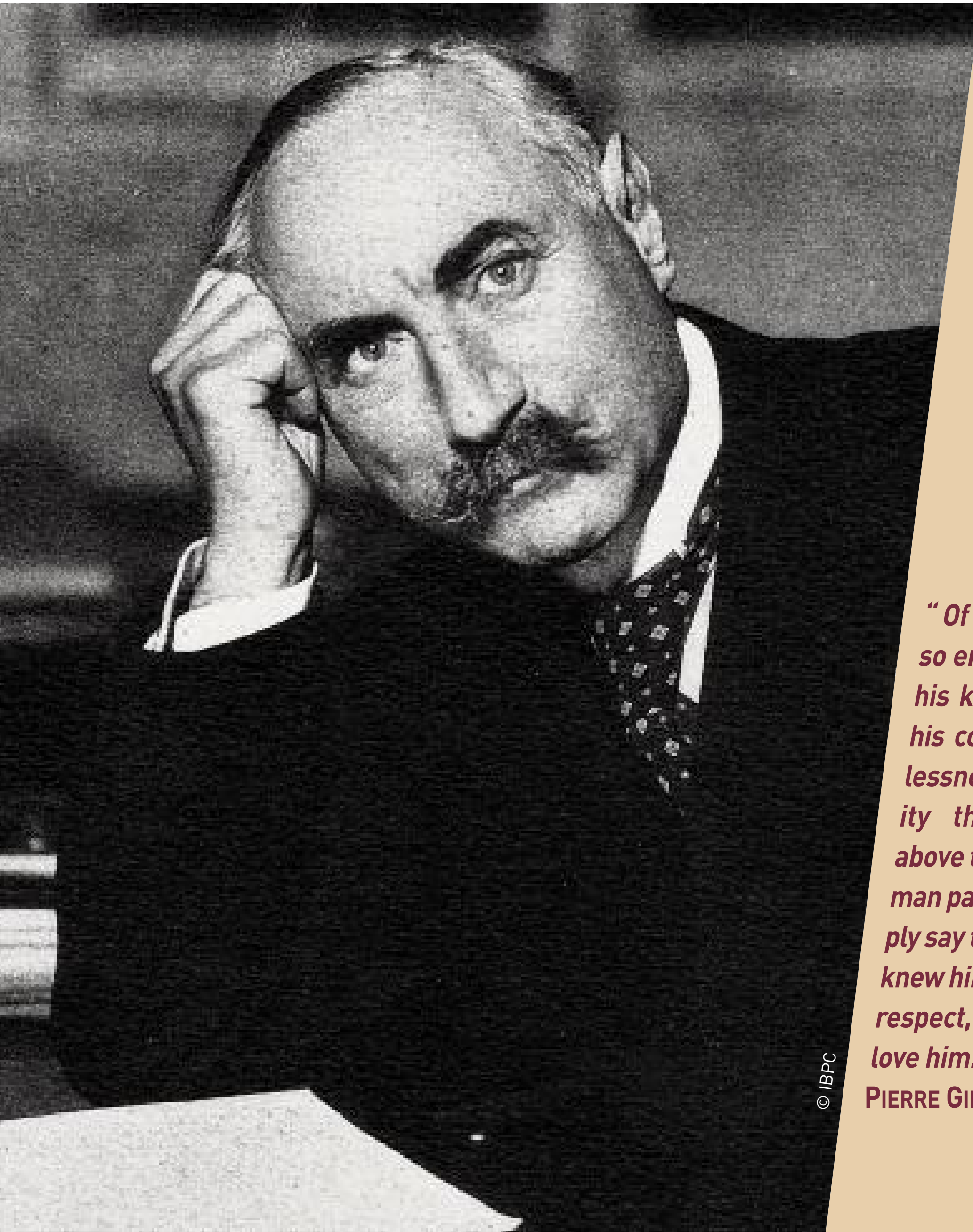
Highly critical of the academism of university teaching of chemistry, in 1928 he was also appointed head of a school of engineering, the Institut de Chimie de Paris (today the Chimie Paris Tech), where he developed research, the teaching of foreign languages and links with industry. This led him to create, in 1937, the Laboratoire des Gros traitements chimiques in Thiais, dedicated to the industrial production of rare earths. This is the ancestor of the present CNRS group of chemistry laboratories on the Vitry/Thiais campus.

A man of the left, Georges Urbain was a member with his friends Perrin and Langevin of the Comité de vigilance des intellectuels antifascistes and was president of the Comité Français pour l'accueil et l'organisation du travail des savants étrangers, founded in 1934 to aid scientists fleeing Nazism. In this connection he welcomed to his Department of Chemistry Otto Meyerhof, winner of the Nobel Prize in Physiology or Medicine. In delicate health, Urbain died on 4 November 1938, shortly after Meyerhof's arrival at the IBPC. ◄

André Mayer

1875-1956

Physiologist and international expert



" Of the man himself, so endearing through his keen intelligence, his courtesy, his selflessness and a serenity that placed him above the turmoil of human passions, I will simply say that all those who knew him could not fail to respect, to admire and to love him."

PIERRE GIRARD

It was while studying medicine at the Sorbonne, in the 1890s, that André Mayer first visited the laboratory of Albert Dastre, a former student of Claude Bernard. His doctoral thesis *Essai sur la soif, ses causes, et ses mécanismes*, which he published in 1901, shows the influence of Bernard's thinking. The work looks at the mechanisms permitting the homeostasis of osmotic pressure in animal organisms. The philosophers were enthusiastic in their reception of this first description of a sensation in physico-chemical terms. While working every morning as a surgeon at a clinic, Mayer embarked on research into the physico-chemistry of cells, leading him to describe the cytoplasm as a colloid whose behaviour can be modified by very small variations in chemical composition. In other words, he transposed to cell level Bernard's notions of the homeostasis of the internal environment.

Mobilised in 1914, he first served as a military surgeon before being assigned to research into defence against chemical attack. He was one of the inventors of the gas mask, for which he was rewarded with prestigious military decorations from all the allied armies. In 1919 he was appointed professor at the University of Strasbourg, which had just been returned to France, and three years later at the Collège de France, to the chair of experimental medicine formerly occupied by Claude Bernard.

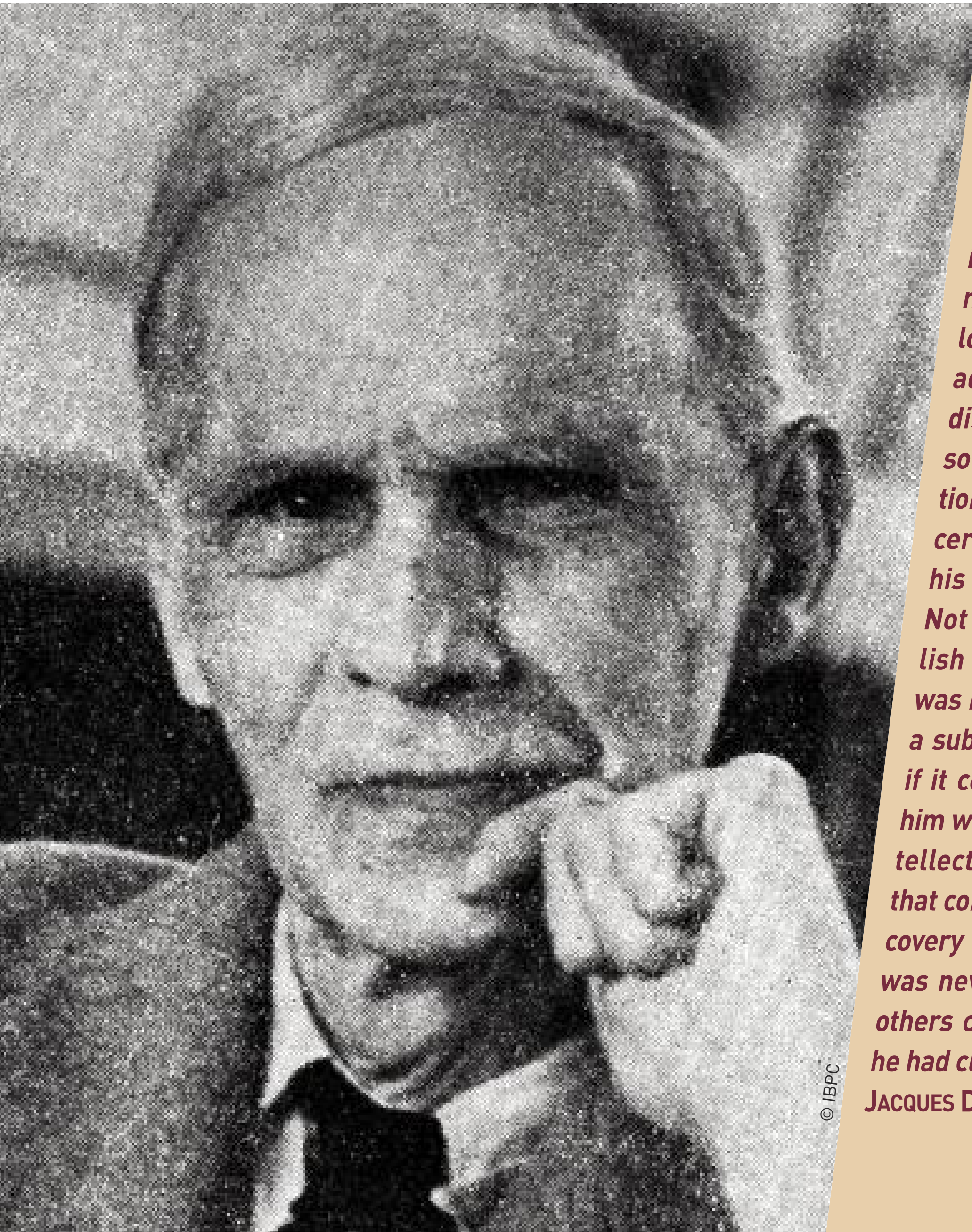
The laboratory he installed there became one of the principle sites of modern physiological research. Mayer devoted himself in particular to the study of mechanisms of thermogenesis and of nutrition while at the same time heading the IBPC's Department of Physiology where he encouraged research into genetics. It was his passion for research that caused him to refuse appointments to the highest administrative posts at the Collège de France and the Université de Paris. On the other hand, he did play an active role within various international bodies, heading the Red Cross Committee of Experts, campaigning for the Conference on Disarmament to ban chemical and biological weapons, and defending at the League of Nations the need for a policy to support agriculture to combat malnutrition.

When war was declared in 1939 he resumed his activities as scientific advisor to the military. Following defeat he moved to the unoccupied southern zone, deciding against returning to the Collège de France where he knew he would be in danger despite him being one of the 11 university teachers benefiting from exemption from the law excluding Jews from the teaching profession. In 1941 he travelled to the United States with an official mission to secure fresh supplies for the population of France. In New York he played an active role within the Bureau scientifique de la France libre. In this connection he submitted a memorandum to US President Roosevelt recommending, when peace returned, the creation of an agency responsible for questions of nutrition. He thus became the first president of the UN Food and Agriculture Organisation (FAO) after resigning his position at the IBPC. In 1950 he was elected to the Académie des Sciences. He died in Paris on 27 May 1956 after falling seriously ill while on an official FAO mission to Mali. ◄

Pierre Girard

1879-1958

The IBPC's first administrator



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"He was always independent and most of the time a loner with all the advantages and disadvantages associated with isolation. No career concerns ever dictated his line of conduct. Not seeking to publish a great deal, he was ready to abandon a subject immediately if it ceased to provide him with the kind of intellectual excitement that comes with the discovery of new facts and was never afraid to see others cultivate the field he had cleared."

JACQUES DUCLAUX

This expansion of the being, this need to dominate, this pride in subjugating the hostile forces of nature... the man of science can be prone to these but quite clearly also sees them as a rather puerile game, a kind of extension of childhood flights of fancy. He infinitely prefers, knowing them to be more noble and more beautiful, the joys of the mind's speculation. He is and remains, and that is the essential trait of his intellectual physiognomy, above all else an artist," writes Pierre Girard in his *Portrait de l'homme de sciences* (1937). Very much a self-portrait, it is a work in which this son and grandson of a painter, a man as discreet as he is secretive, reveals the reasons for his passion for physico-chemistry.

In half a century of research Girard tackled the most diverse problems. Trained, like André Mayer, in Albert Dastre's laboratory at the Sorbonne, he began as a neurochemist, writing his 1908 thesis on the chemical composition of bird brains. He then became interested in the electrical properties of membranes and introduced the notion of selective permeability, a subject on which he was rapporteur to the 1928 Solvay Chemistry Conference. Shortly afterwards he abandoned this promising subject and turned to the development of the instrumentation permitting the study of macromolecules. Girard was thus one of the first people in France to use methods of ultracentrifugation and electrophoresis. He left to others the task of applying them to biological problems, however, turning instead to research on the hertzian absorption spectrum of tissues, cells and biological molecules that was to occupy him until his death.

Deliberately avoiding academic and university honours, from 1927 Girard devoted himself to the administration of the IBPC that, following the death of his wife in 1935, virtually became his home. *"All those who saw him for so many years cross the lobby and take the lift up to his small office on the third floor will never forget his air of distinction. Very old school in his manners and his language, very human, he was interested in everybody, from the heads of department he visited in their offices to inquire about their problems, to the cleaning women to whom he addressed a friendly word in passing and who used to go to him to ask for advice,"* remembers Denise Levy-Astruc, IBPC general secretary during his time as administrator.

During the Occupation he showed admirable determination in confronting the threats to the IBPC in the form of aryanisation. *"Finding himself alone in assuming the heaviest responsibilities, he had to decide and organise everything. For a week, the fate of the institute and all it contained rested on him alone. Employees of the institute will never forget the courage he showed,"* declared the IBPC personnel in an address given on 10 July 1942 after Girard's efforts had made it possible to avoid the IBPC being requisitioned for the benefit of the foundation headed by Alexis Carrel. When peace returned, he set about restoring balance to the IBPC's accounts by diversifying its financing. This last of the founding fathers or Tetrarchs "*died on 5 November 1958, exactly 20 years after Georges Urbain. Everybody at the institute knew that it marked the end of an era. A new age was now beginning,*" remembers Denise Levy-Astruc. ◄

1927-1945
Fertile intuition

1927-1945
Fertile intuition

Between the wars, French science, and biology in particular, was in steep decline. Between 1901 – when the Nobel was created – and 1914, France totalled 11 laureates of one of the three science Nobels, compared with 13 for Germany which has one and a half times France's population. Between 1918 and 1939 a further five science Nobels went to France, compared with 20 for Germany.

The sorry state of public research; the disciplinary straightjacket: the founding of the IBPC was a response to these two difficulties.

In 1925, the French research budget was 11 million francs, equivalent to 8.5 million euros today. The next year, Parliament, prompted by a press campaign condemning the sorry state of French science, passed a bill introducing the "sou du laboratoire": a tax of 5 centimes on every 100 francs of wages paid in industry and services. This was a way of having the private sector, with its almost non-existent research effort, contribute to the cost of public sector research. The measure, initiated by the minister and mathematician Emile Borel, increased the public budget to just 25 million francs (14 million euros in today's money).

IBPC construction costs: 6 million francs (3.3 million euros 2009), financed directly by Baron Edmond de Rothschild.

The result was that researchers able to devote themselves full time to their work were far and few between. At the Natural History Museum, at the Collège de France, at the Sorbonne and at Strasbourg University (the only provincial university to be engaged in research), researchers had to devote an often considerable part of their time to teaching. This when university education was sclerotic. Locked into its narrowly disciplinary and seemingly immovable chairs, it seemed unable to keep pace with the progress of knowledge let alone participate in it. Quantum physics and formal genetics, for example, were ignored at the Sorbonne at a time when they were progressing in leaps and bounds in the Anglo-Saxon world. Three-quarters of a century after the publication of *The Origin of Species*, Darwin's theory of evolution was still not being taught in France.

The sorry state of public research; the disciplinary straightjacket: the founding of the IBPC was a response to these two difficulties.

PHILANTHROPY, IN THE ABSENCE OF GOVERNMENT

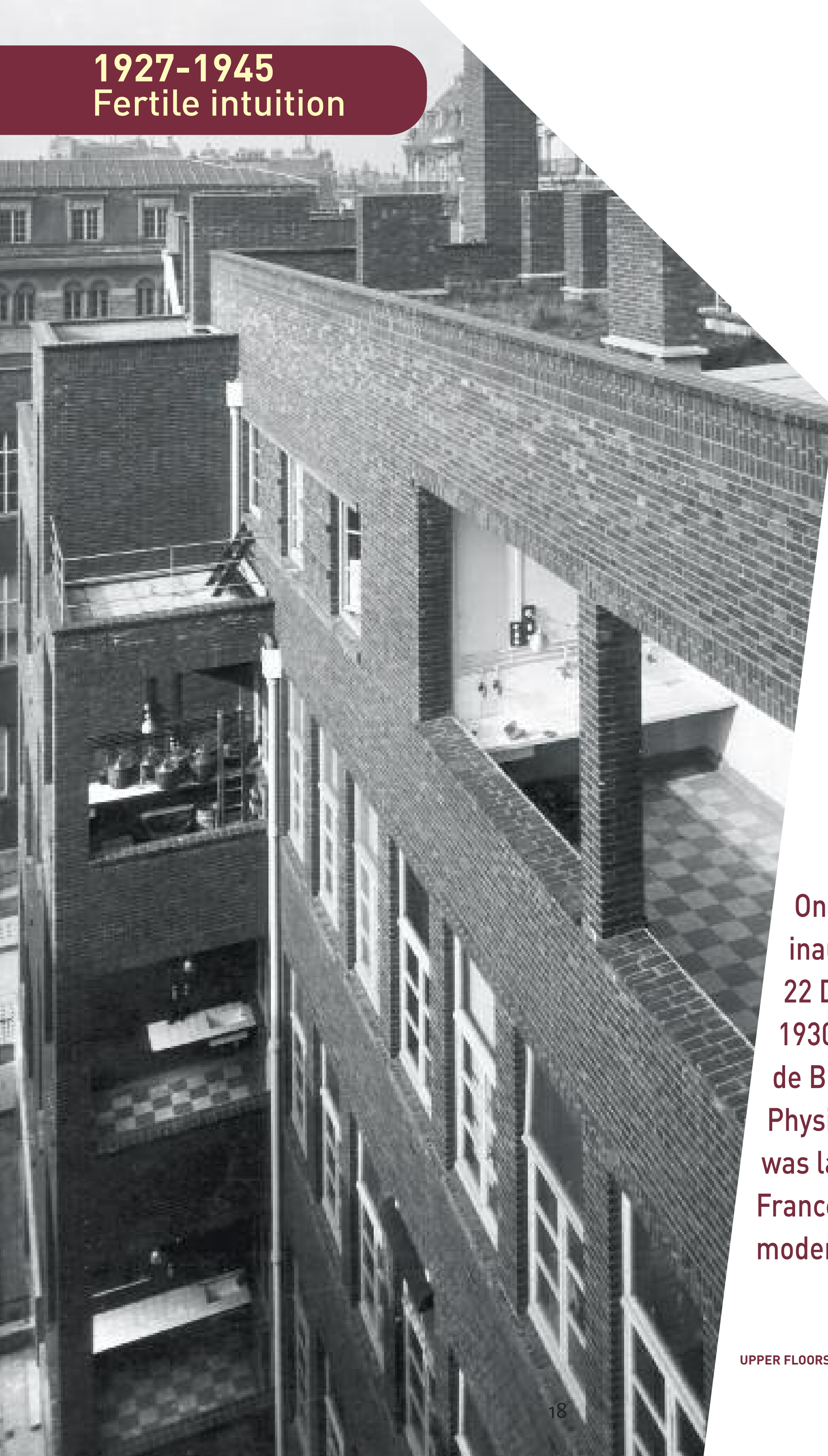
With government and industry showing no interest in science, philanthropy was the sole source of financing for new laboratories. In 1910, a Carnegie donation had already helped Marie Curie to open her Institut du Radium. After the First World War, the movement intensified. In the space of just a few years, three new modern research centres were built between the rue d'Ulm and the rue Guy Lussac. In 1920, a donation from Henri de Rothschild enabled Marie Curie to create the Curie Foundation where doctors and physicists could work on developing radiotherapy. In 1926, the Rockefeller Foundation, which was very active in its support of European research, financed the creation of the Institut Henri Poincaré, dedicated to closer contacts between mathematicians and physicists in the service of theoretical physics. It was this same desire for interdisciplinary rapprochement that was at the origin of the IBPC, founded following a donation from Baron Edmond de Rothschild.

THE HELIOSTAT SOLAR TOWER IN 1930

"This Institute will have the goal of researching into the physico-chemical mechanisms of the phenomena of Life, especially with a view to a better knowledge of the functioning of the human body; and this outside of microbiology so brilliantly studied and explored at the Institut Pasteur. To this end, adopting as general directives the doctrines of Claude Bernard on the physico-chemical determinism of Life, and seeking to continue the work of this great physiologist, the new institute will bring together physicists, chemists and biologists to study the problems posed by various physiological questions. This cooperation, often desired but to date not organised, will be the essential character of the Institut Edmond de Rothschild," the mathematician Paul Appell, president of the Edmond de Rothschild Foundation, announced at the Académie des Sciences on 2 May 1927.

"In no way is one scientific discipline subservient to another scientific discipline. In the present state of science, the biologist, the chemist and also, but to a lesser degree, the physicist, can no longer work in isolation."
Extract from the IBPC's 1931 report of activities.

1927-1945
Fertile intuition



On its inauguration on 22 December 1930, the Institut de Biologie Physico-Chimique was lauded as France's most modern institute.

UPPER FLOORS OF THE IBPC IN 1930

France's most modern institute

For the past six years, this foundation had financed grants and the purchase of scientific equipment. Edmond de Rothschild was now moving to an altogether different level: the creation of a genuine institute, financed by a foundation with a capital – 30 million francs – that was more than the annual budget for public research. At its head were four eminent researchers: Jean Perrin, Nobel Prize for Physics in 1926, heading the Department of Physics; Georges Urbain, professor at the Sorbonne, heading the Department of Chemistry; André Mayer, professor at the Collège de France, heading the Department of Biology; and the youngest of the four who would soon come to be known as the "Tetrachs", the physico-chemist Pierre Girard, who filled the post of administrator.

The refectory is a regular place for meetings. The simplicity and lack of hierarchy of the dialogue is in marked contrast to what is usually found at European universities. *"Me, having lunch with Jean Perrin! In Germany it would be inconceivable to eat at the same table as a boss!"* exclaimed the Yugoslav biologist W. Reich, who had worked previously in Germany.

On its inauguration on 22 December 1930, the Institut de Biologie Physico-Chimique was lauded as France's most modern institute. Its two buildings linked by a reinforced concrete walkway prompted André Mayer to note that: *"the impression is that of stylish factory."* With 3500 m^2 of laboratories boasting fade-resistant white ceramic walls to increase luminosity, an internal telephone network, anti-vibration system, central heating, high voltage cabin, and standardised furniture, doors and windows, the architect Germain Debré applied to the building all the precepts of the modernist movement. Careful attention was also paid to the scientific equipment, with X-ray generators for the physicists, gas and compressed air pipes in all the extractors for the chemists, animal house and aseptic operating theatre for the physiologists, heliostat and greenhouse for the botanists, and cell culture room for the biologists. In the basement, a vast workshop was set up to build the equipment that could not be bought.

THE MODERN LIFT IN THE IBPC ENTRANCE HALL, 1930

The IBPC was the only institute to employ full-time researchers engaged solely in advancing knowledge.

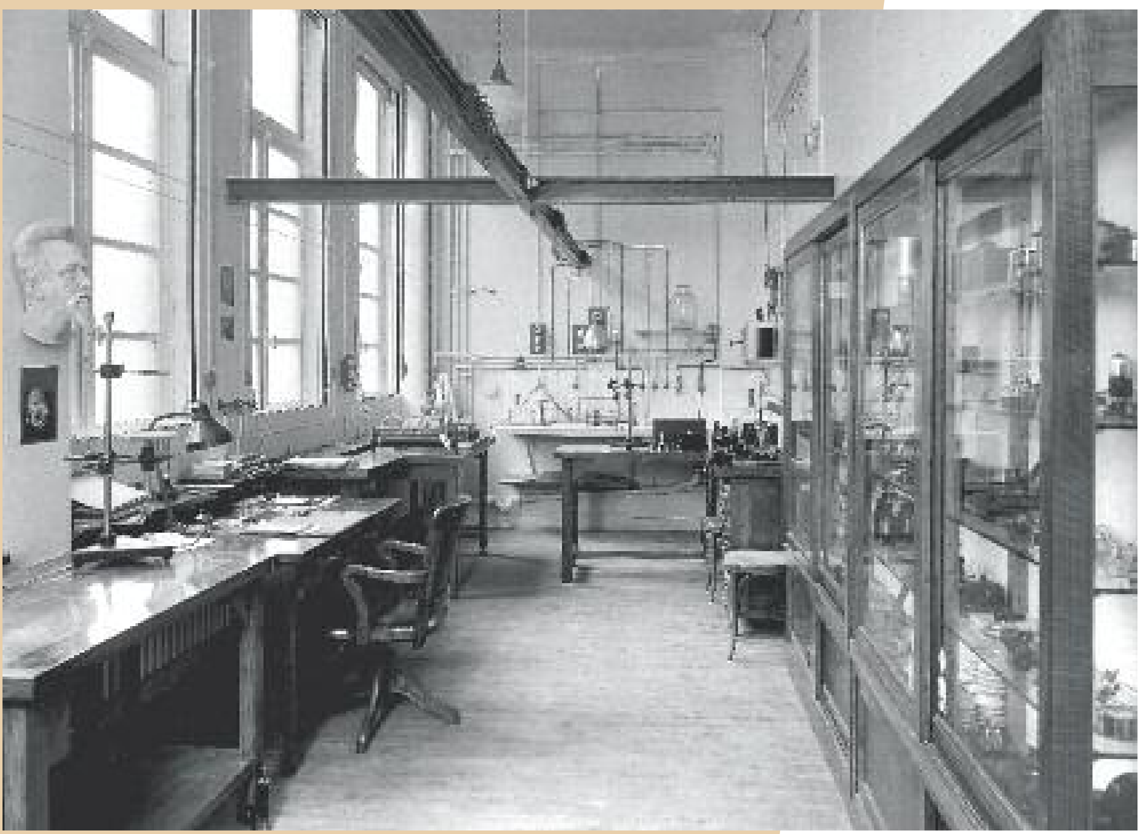
Unparalleled freedom

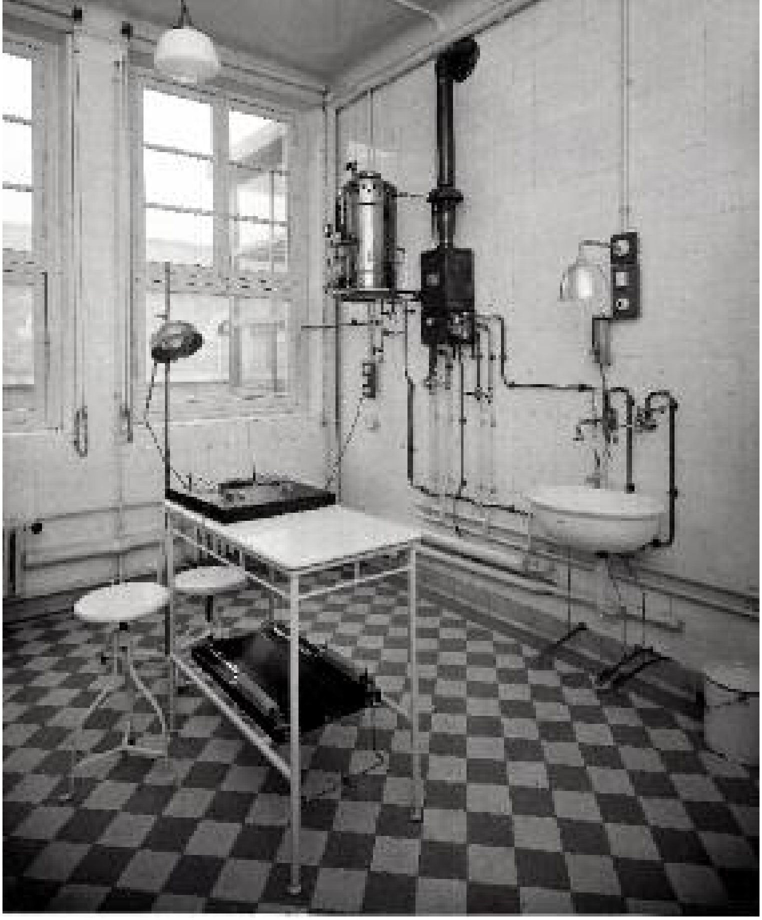
In the minds of the Tetrarchs, the IBPC was to serve as a testing ground for a global reform of French public research.

But the most notable innovation lay in the internal organisation. The IBPC was the only institute to employ full-time researchers engaged solely in advancing knowledge. From 1927, when the premises had not yet been built and research was starting up in the laboratories of the Tetrarchs, the Edmond de Rothschild Foundation was already paying in full the wages of around 30 technical staff and young researchers. Established researchers, who held university posts, received a supplement to their salaries.

The second notable innovation is that the IBPC was a place of freedom of exchange where the emphasis was placed on collective research, contrasting with the bureaucratic practice of chairs. *" From 3 March 1931, staff of the institute will be invited to meet*

A PHYSICS LABORATORY IN 1930
Note the bust of Jean Perrin, sculpted by Georges Urbain, on the left wall





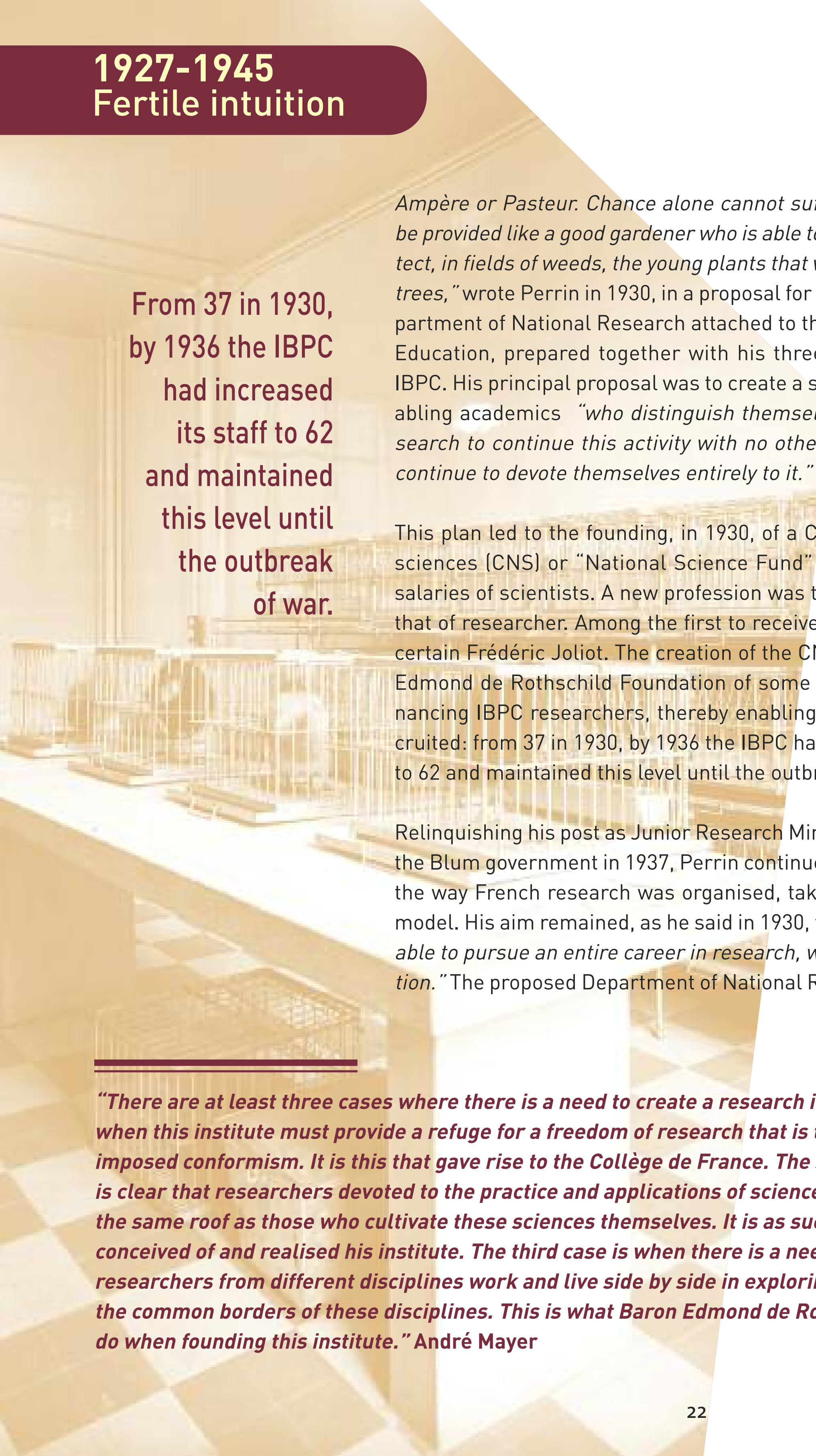
The IBPC was a place of freedom of exchange where the emphasis was placed on collective research, contrasting with the bureaucratic practice of chairs

ASEPTIC OPERATING THEATRE FOR ANIMAL PHYSIOLOGY EXPERIMENTS

for coffee in the library every Tuesday at 2 p.m. to talk among themselves, listen to any communications addressed to them and participate in discussions," was the message circulated by management. The subjects covered at these sessions included: the spontaneous evolution of forms of galaxies by Jean Perrin, the classification of biological species on the basis of their physical or chemical properties by Georges Urbain, the methods employed by Goethe in his scientific studies by Otto Meyerhof, the rhythmic nervous influxes in the nerves of crabs by Daniel Auger, and chain nuclear reactions by Francis Perrin. That was just on 6 May 1939!

THE CNRS MODEL

In the minds of the Tetrarchs, the IBPC was to serve as a testing ground for a global reform of French public research. The four men, and Mayer and Perrin in particular, were acutely aware of how much France was lagging behind internationally. They did not accept government leaving scientific modernisation entirely to the philanthropists. "*The whole problem of [our] scientific organisation lies in finding the young minds who will be able to become*



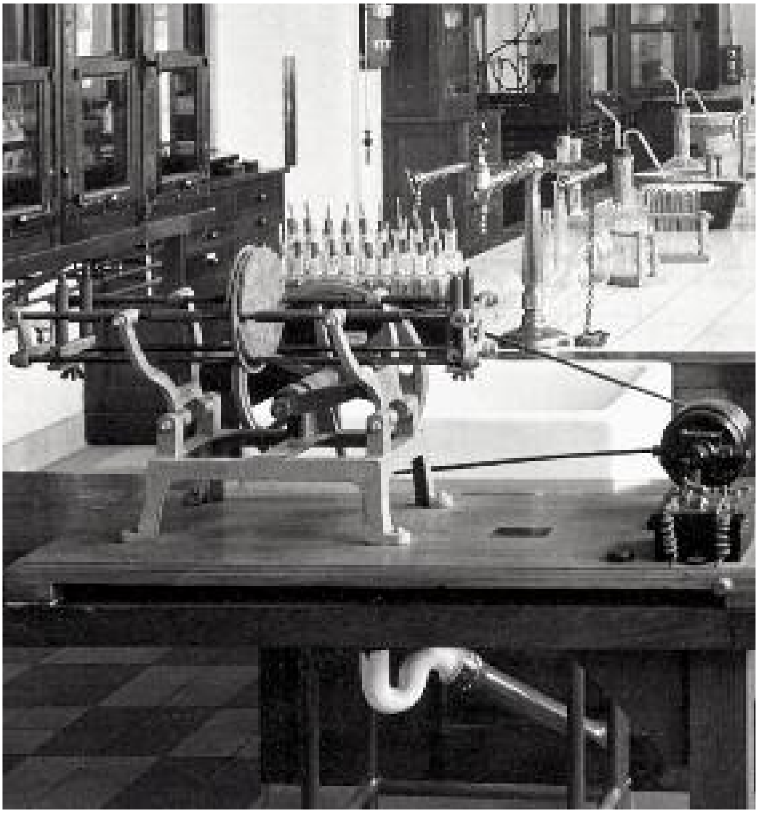
Ampère or Pasteur. Chance alone cannot suffice, and help must be provided like a good gardener who is able to recognise and protect, in fields of weeds, the young plants that will grow into strong trees," wrote Perrin in 1930, in a proposal for a bill to set up a Department of National Research attached to the Ministry of Public Education, prepared together with his three colleagues at the IBPC. His principal proposal was to create a system of grants enabling academics *"who distinguish themselves in scientific research to continue this activity with no other obligation than to continue to devote themselves entirely to it."*

This plan led to the founding, in 1930, of a Caisse nationale des sciences (CNS) or "National Science Fund" that would pay the salaries of scientists. A new profession was thus born in France, that of researcher. Among the first to receive a CNS grant was a certain Frédéric Joliot. The creation of the CNS also relieved the Edmond de Rothschild Foundation of some of the burden of financing IBPC researchers, thereby enabling new staff to be recruited: from 37 in 1930, by 1936 the IBPC had increased its staff to 62 and maintained this level until the outbreak of war.

From 37 in 1930, by 1936 the IBPC had increased its staff to 62 and maintained this level until the outbreak of war.

Relinquishing his post as Junior Research Minister with the fall of the Blum government in 1937, Perrin continued his reflections on the way French research was organised, taking the IBPC as his model. His aim remained, as he said in 1930, for a *"scientist to be able to pursue an entire career in research, with no other obligation."* The proposed Department of National Research would also

"There are at least three cases where there is a need to create a research institute. Firstly, when this institute must provide a refuge for a freedom of research that is threatened by an imposed conformism. It is this that gave rise to the Collège de France. The second is when it is clear that researchers devoted to the practice and applications of science must work under the same roof as those who cultivate these sciences themselves. It is as such that Pasteur conceived of and realised his institute. The third case is when there is a need to have researchers from different disciplines work and live side by side in exploring areas that lie on the common borders of these disciplines. This is what Baron Edmond de Rothschild wanted to do when founding this institute." **André Mayer**



contribute to the equipping, functioning and remuneration of the laboratory technical personnel. It would be headed by a *"jury with an incontestable authority, made up, for each science, of eminent figures of such number that every major scientific discipline would be represented, and accepting, without remuneration, in the sole interests of the Science of the Nation, to submit proposals."*

A staff of full-time researchers; well equipped laboratories; a learned assembly of scientists with full management responsibility: the three fundamentals tested at the IBPC that were subsequently incorporated within the Centre National de la Recherche Scientifique, the CNRS, which was founded on 19 October 1939 under the presidency of Jean Perrin.

A staff of full-time researchers; well equipped laboratories; a learned assembly of scientists with full management responsibility: the three fundamentals tested at the IBPC were subsequently incorporated within the Centre National de la Recherche Scientifique, the CNRS, which was founded on 19 October 1939

GREENHOUSE FOR GROWING TROPICAL PLANTS

In the summer of 1940 already, some of the researchers who had left at the time of the Exodus returned to the institute to resume their work. This marked the beginning of a high risk period for the institute.

The IBPC mobilized

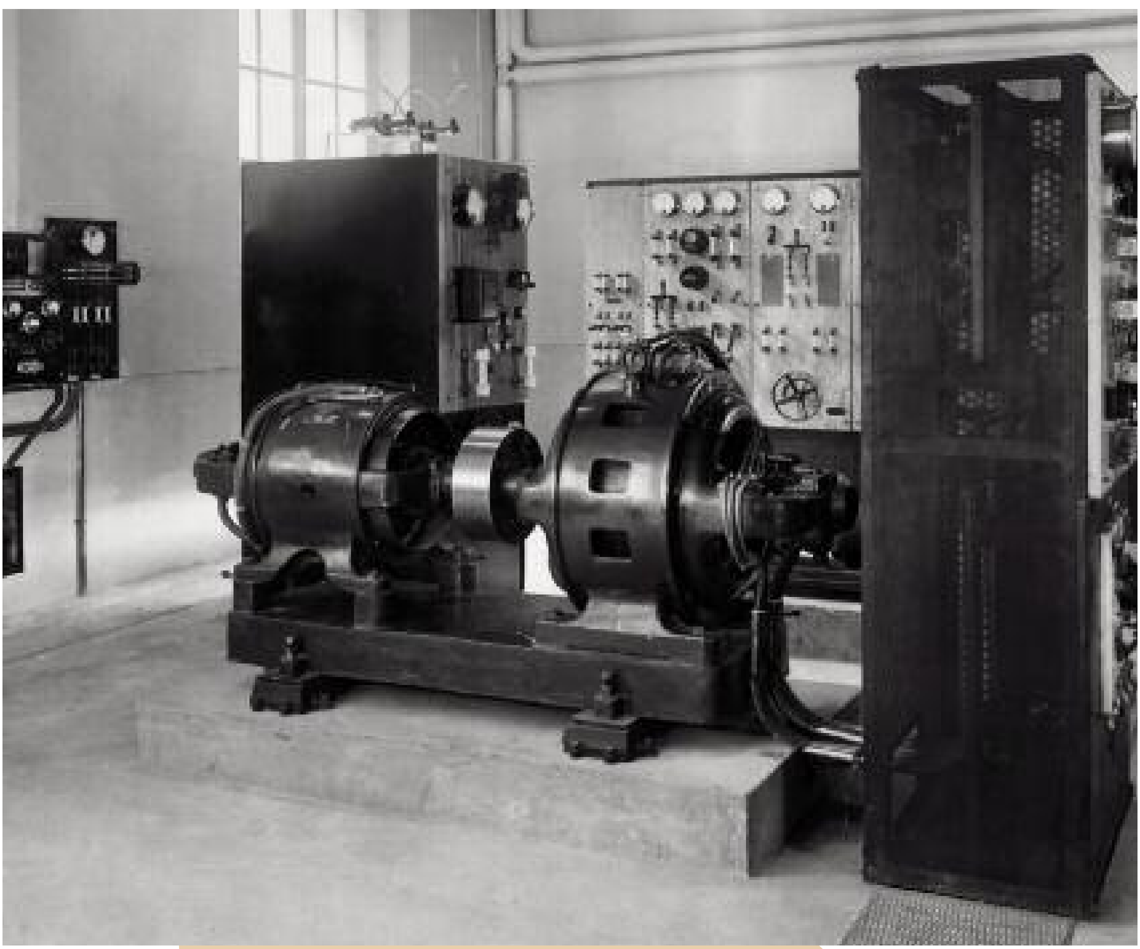
The first task the CNRS embarked on was to ensure that, unlike what had happened during the First World War, the skills of the scientists would be used to optimal effect by the national defence effort. At the IBPC, the 13 researchers eligible for military service were assigned to laboratories working for national defence. The physiologists André Mayer and Emmanuel Fauré Frémiet thus left for the Bouchet explosives factory to work on the biological effect of gases. About half of the IBPC personnel remained at the institute where research was redirected to possible military applications. Pierre Girard's department, for example, looked at ways of producing heparin – an anticoagulant much valued by military doctors – from beef livers.

On 10 June 1940, after the German armies broke through the front, the IBPC was evacuated. But, in the summer of 1940 already, some of the researchers who had left at the time of the Exodus returned to the institute to resume their work. This marked the beginning of a high risk period for the institute. The IBPC was vulnerable on two counts. On one hand, as a "Jewish" organisation by the terms of the Vichy regime's anti-Semitic legislation, because it was financed by the Edmond de Rothschild Foundation. The IBPC was therefore compelled to remove the name of its founder from all its official documents. On the other hand, as an institute of the Left, due to the support of its directors for the Front Populaire and the fact that the IBPC had welcomed Austrian and German scientists who had fled Nazism. Aware of these risks, some researchers, such as Jean Perrin and André Mayer, remained in the unoccupied southern zone where they rebuilt a laboratory at the University of Lyons. In 1941 they left for the United States where Louis Rapkine, who had been there since the summer of 1940, was instrumental in obtaining visas, grants and invitations to universities for them. Others, such as Boris Ephrussi and Pierre Auger, returned to the IBPC in November 1940, but only remained for a few months. The arrest by the Germans, on 9 November 1940, of Paul Langevin, a key figure in scientific circles of the Left, brought home to them the real dangers they were facing. They moved to the southern zone in the course of the following months and then they too sailed for the United States, also thanks to Rapkine's assistance.

With Urbain dead and Perrin and Mayer in exile, it fell to Pierre Girard to direct the institute during this difficult period. The IBPC had been deprived of its human capital. In 1941, only 33 people were left working there, half the number of the pre-war period. Rationing and other shortages slowed research. There was a lack of scientific equipment and frequent power cuts. On the roof of the main building, a vegetable garden was planted to help feed the staff. This was far from sufficient and the IBPC bought a site in the suburbs as an allotment that they planted with potatoes.

At the IBPC, the 13 researchers eligible for military service were assigned to laboratories working for national defence.

X-RAY GENERATOR IN THE IBPC CELLAR



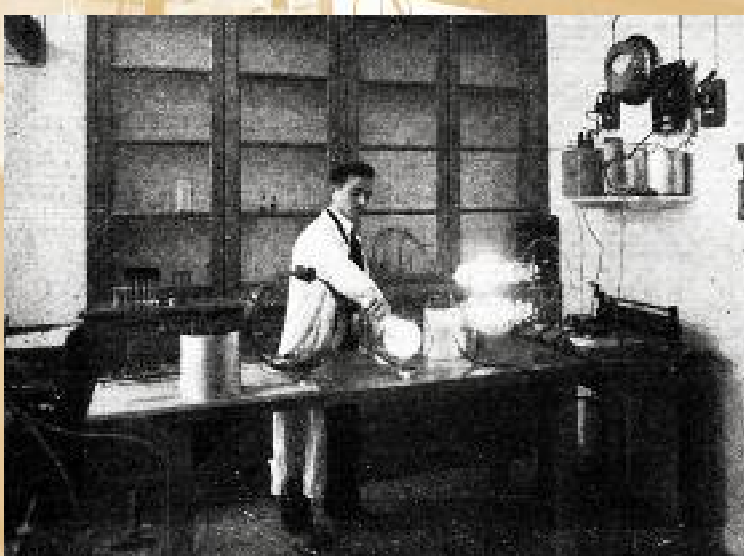
Threatened with requisition

Pierre Girard received the instruction that the IBPC buildings were to be requisitioned for the benefit of the Carrel Foundation.

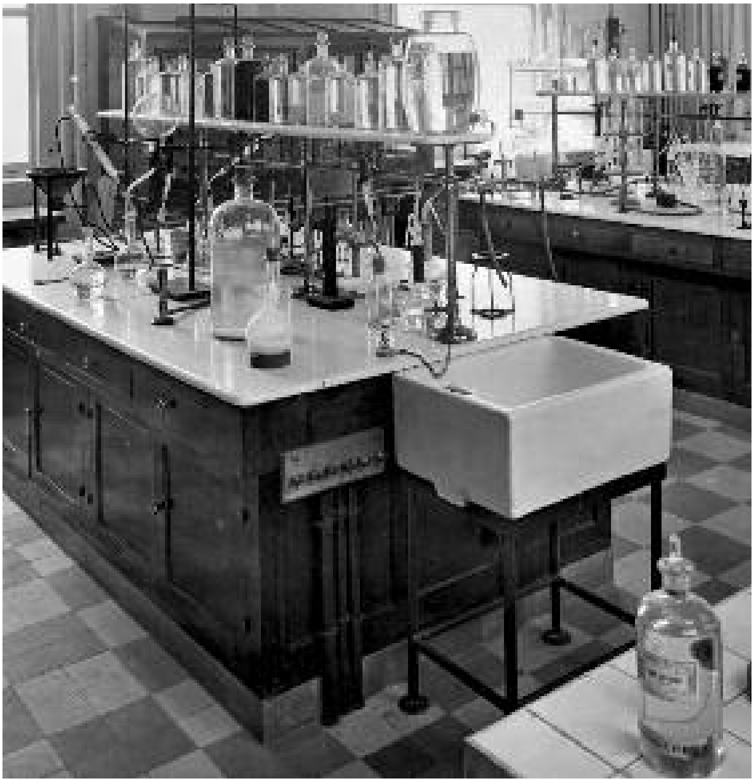
These everyday concerns were nothing compared with two much more serious threats. First there was the anti-Semitic persecution that led to the arrest of the chemist Osias Binder, who had worked at the IBPC since 1931 and had presented his engineering doctoral thesis there in 1935. Arrested during a roundup of Jews, he was deported to Auschwitz on 27 March 1942 after which no more was heard of him. Then there was the plan to requisition the entire institute for the benefit of the Fondation Française pour l'Etude des Problèmes Humains. Set up by the Vichy regime and allocated 40 million francs – double the CNRS budget – this scientific institute was headed by Alexis Carrel, winner of the 1912 Nobel Prize for Medicine or Physiology and a man close to the new regime. Demographists, biologists, nutritionists, sociologists and psychologists had all been recruited en masse... but it was in need of premises. On 22 June 1942 Pierre Girard received the instruction that the IBPC buildings were to be requisitioned for the benefit of the Carrel Foundation.

During the Occupation, the IBPC turned to applied research: the development of a vaccine against typhus and improved performances when preparing insulin from the pancreas.

RESEARCHER OPERATING AN ELECTROMAGNETIC WAVE GENERATOR



"It is with genuine stupefaction that, without any warning, without the least prior investigation into the nature and importance of the scientific activity of the Institut de Biologie Physico-Chimique, I receive from your services the requisition order [...] I am unable to believe that after so much effort and so many pains to maintain intact the activity of one of the most important and valued scientific centres in France or abroad, it



is from French quarters that suddenly I am given the order to abandon the pursuit of the scientific goals that constitute our activity and that are of such great social importance," Girard wrote to the Seine Prefect that same day.

Despite Girard's efforts, a second requisition order arrived on 30 June. It was executable within two hours. Acting quickly, some of the scientific equipment was concealed in neighbouring laboratories, in particular at the Ecole Normale Supérieure. Meanwhile the staff prepared for the worst. Girard, who was counting on support from the 10 members of the Académie des Sciences who sat on the IBPC Board of Directors, requested a meeting with Carrel. He finally obtained it on 4 July. Carrel agreed to cancel the requisition on the express condition that Alexis Lacroix, permanent secretary at the Académie des Science, make the request. The latter promptly did so. Carrel renounced the requisition. The IBPC was saved.

"With Chemin de fer de l'Est bonds in the name of the Edmond de Rothschild Foundation approaching maturity, the Compagnie de l'Est's legal department felt obliged to ask the Commissariat for Jewish Affairs for permission to pay the money. The deputy head of the Economic Aryanisation Department of the said Commissariat, having decided that the IBPC was a Jewish organization, notified the Compagnie de l'Est of this decision and that at his request a decision would be taken blocking all the institute's assets."

Extract from the minutes of the Board of Directors of 28 January 1943

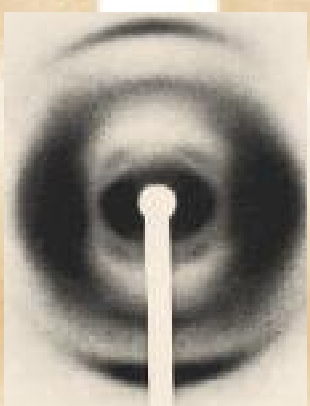
Georges Champetier described the macromolecular structure of cellulose, while Emmanuel Fauré Frémiet and Pierre Girard highlighted periodic structures in collagens and keratins

INTERDISCIPLINARITY ON A DAILY BASIS

Gene, macromolecule, coupling of oxido-reduction reactions, enzymatic kinetics, membrane... all familiar notions to any secondary school pupil taking science subjects today, but in the 1930s they were at the cutting edge of research. The IBPC played a leading role in this new endeavour of describing physiology and heredity in physico-chemical terms.

This new research programme required an instrumentation making it possible to prepare biological molecules and to analyse the properties. The IBPC physicists thus used the analysis of the diffraction diagrams of X-rays to study the structure of biological molecules. Georges Champetier described the macromolecular structure of cellulose, while Emmanuel Fauré Frémiet and Pierre Girard highlighted periodic structures in collagens and keratins. The concept of the macromolecule – a term that appears for the first time in French in 1936 in the writings of Champetier – was thus born. But how to separate these giant molecules? At the initiative of Jean Perrin and Nine Choucroun, electrophoresis was developed. At the mechanical engineering workshop, an ultracentrifuge reaching 100 000 revs a minute was built under the direction of Pierre Girard. Edgar Lederer, a young Austrian researcher who was fleeing Nazism, also brought to France a new technique to separate molecules: chromatography. This was used to prepare photosynthetic pigments.

Between 1932 and 1939, 22 theses for state doctorates were presented by IBPC researchers. Despite the restrictions, three others followed between 1941 and 1944.



FIRST SLIDE OF X-RAY DIFFRACTION OF COLLAGEN FIBRES OBTAINED AT THE IBPC IN 1938

The study of the mechanisms of photosynthesis is one of the priority fields in which physics and biology meet. The IBPC adopted it as a favoured research field from the moment of its foundation. In the 1930s, René Wurmser showed that the primary action of photosynthesis is to break down a water molecule into chloroplasts under the effect of light, eight quanta being needed to release one molecule of oxygen. The study of photosynthesis also served as a paradigm for anabolic reactions. "*The distribution between different points in the cell of successive stages in a chemical transformation is not particular to green cells. It is very general and it is this that reveals the singular nature of biological chemistry. This same condition of environmental heterogeneity and the action of coupled reactions is found when one studies the syntheses effected by organisms without chlorophyll,*" wrote Wurmser in 1930.

The description of the different oxidoreduction reactions of the cell metabolism occupies an important place in the research carried out at the IBPC during the 1930s. Eugène Aubel showed the pivotal role of pyruvate, both the final product of the breakdown of sugars, proteins and lipids and the point of departure for synthesis pathways. His research on redox balances in physiology had the unexpected consequence of initiating a series of experiments that led to a crucial discovery in genetics. It was by virtue of developing environments permitting tissue culture, for which the redox potential must be carefully fixed, that a young IBPC researcher, Boris Ephrussi, together with the American Georges Beadle, began experiments that culminated in the formulation of the gene/protein relationship.

The description of the different oxidoreduction reactions of the cell metabolism occupies an important place in the research carried out at the IBPC during the 1930s.

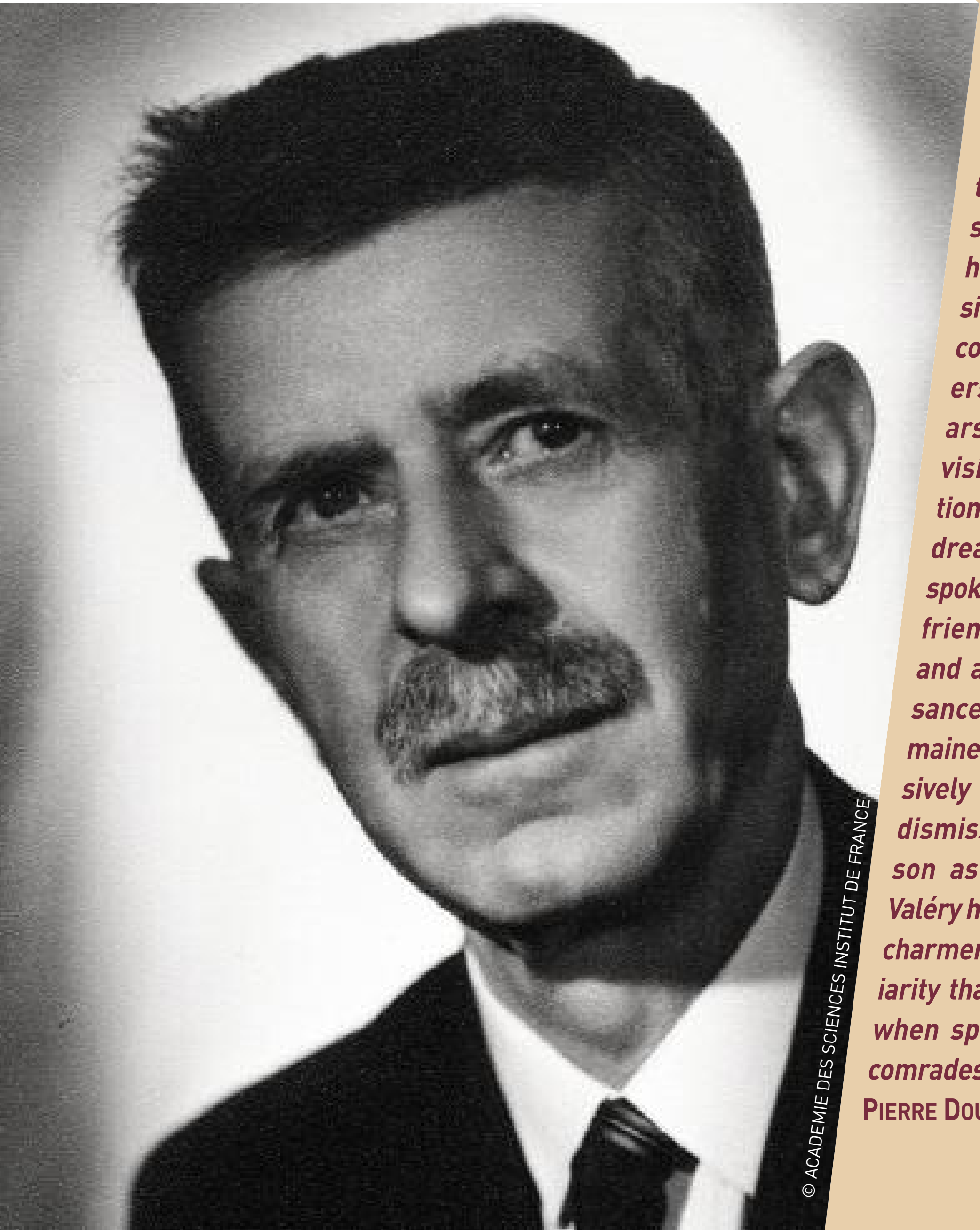
" On reading this report, one will be struck by the frequency of the cooperation between a biologist, a chemist and a physicist. It is increasingly rare for a researcher, especially if a biologist, to work alone. This is due to the rewards of sharing technical knowledge or methods of reasoning originating in different scientific disciplines. Very often a discovery or an invention results from considering the problem from an uncustomary angle. [...]; but no less often it originates in examples provided by neighbouring fields and the mental excitement engendered by the knowledge of brilliant successes in these fields. But it is not just a correct and fertile idea that has most chance of blossoming due to these exchanges, but also the technical invention, the new method, or the new means of inquiry that permits the discovery of unknown territories and that one always finds at the origin of major discoveries.
Nearly all major biological or medical discoveries – from Lavoisier's analytical methods to Roentgen rays or radium – were made by physicists or chemists. If nothing else, they provided the means to make them."

Extract from the 1936 report of activities

Jacques Duclaux

1877-1978

Introduction of the macromolecule to France



"Duclaux was among the last to have been associated with a high society consisting of a motley collection of writers, poets, scholars and artists, visionary revolutionaries and simple dreamers. Duclaux spoke of Péguy as the friend he once was, and also as the 'nuisance' that he remained, of Rodin incisively and then rather dismissively, of Bergson as a bore and of Valéry his neighbour as a charmer, with the familiarity that is appropriate when speaking of one's comrades."

PIERRE DOUZOU

The only truly scientific way of treating living matter would be to write beneath the title 'we know nothing' and refer the reader to the second edition that may appear 20 years or 50 years later," wrote Jacques Duclaux in 1910 in *La chimie et la matière vivante*. When he wrote these lines so typical of his keen critical sense and scathing irony, Duclaux was a young chemist at the Institut Pasteur known for his work on the chemistry of colloids. He demonstrated that colloidal solutions are conductors of electricity and that their osmotic pressure is not zero, contrary to what was believed at the time. Two results that did not go unnoticed by Jean Perrin who, in 1930, invited him to take over as head of a colloid laboratory at the IBPC.

Duclaux accepted without hesitation. At the Institut Pasteur he felt cramped and lacked facilities. This man with intransigent Protestant ethics also did not like being regarded there as the son of Emile Duclaux, the direct associate of Pasteur and his successor at the head of the institute. Above all, the research programme at the IBPC was in line with his own inquiries. He was convinced that *"the principal interest in studying colloidal substances is that it seeks to fill, at least in part, the gap that still separates physics from chemistry and biology."*

At the IBPC he set about applying his theories on the chemistry of colloids to macromolecules, a term recently introduced by the future Nobel for Chemistry, Hermann Staudinger. But at the time these macromolecules were still conceptual hypotheses rather than observable entities. Some chemists thus considered that the high molecular weights measured for proteins, starch or cellulose were no more than apparent values due to small molecules clustering to form colloidal particles. Working with the young German refugee Alma Dobry, who was to become his wife, he showed that the dilution of nitrocellulose in different solvents results in the same lower limit for osmotic pressure. This indirect argument in favour of the physical reality of macromolecules was completed a few years later when Georges Champetier obtained at the IBPC the first X-ray diffraction images of cellulose. In his lectures at the Collège de France, to which he was appointed in 1931, Duclaux also set about spreading the message of the new notion of the macromolecule.

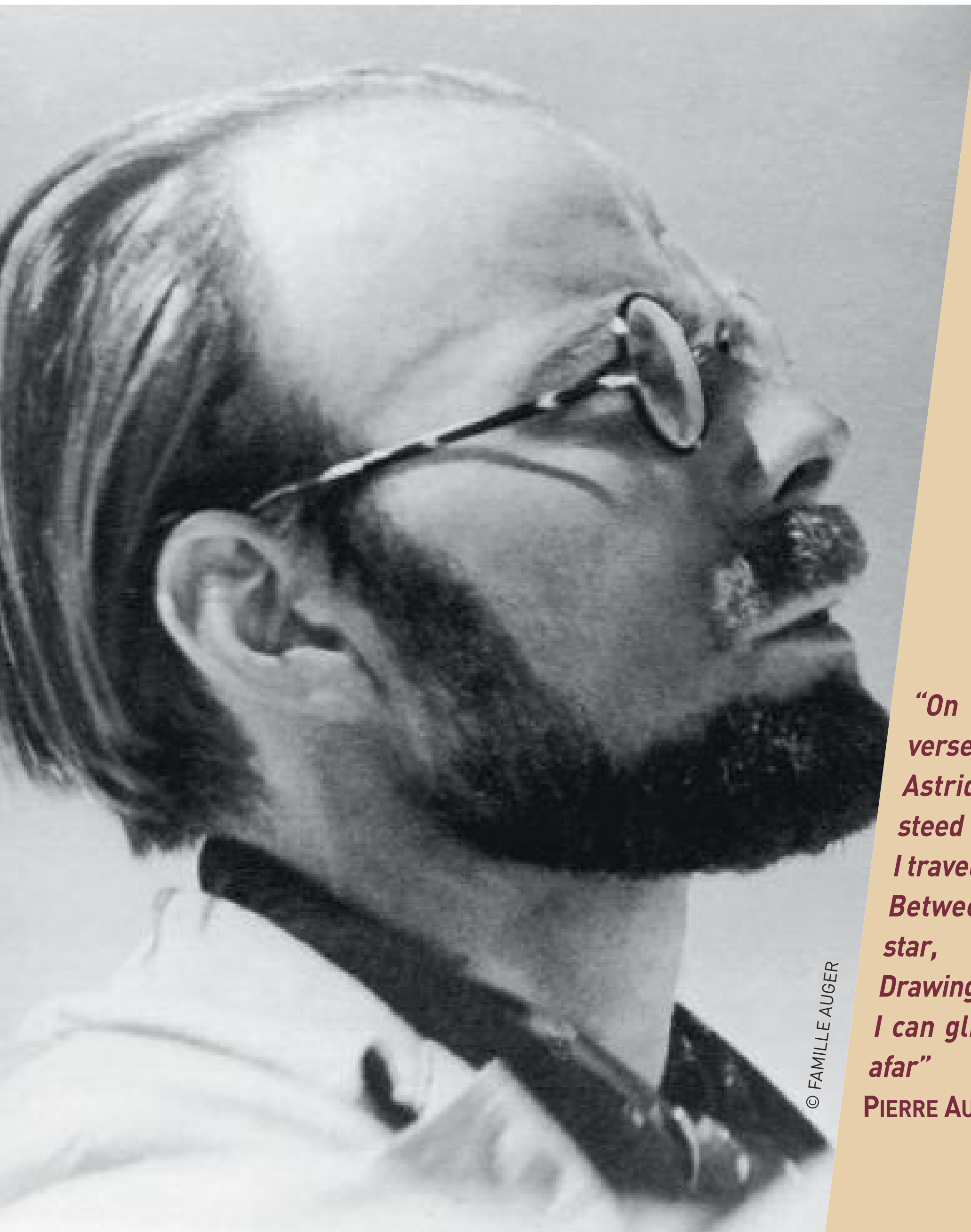
After the Second World War, Jacques Duclaux turned his attention to the philosophy of science while continuing as head of his department, renamed the Department of Macromolecular Chemistry in 1959 when he was succeeded by Alma Dobry. *"Resolutely anti-interventionist when it came to research, his overriding concern was to help creative minds. At the IBPC he was always ready to support initiatives that brought real innovation and individual researchers whose imagination impressed him,"* remembered René Wurmser. A member of the Académie des sciences, in 1976 Duclaux addressed to his colleagues a memo that was highly critical of the functioning of the venerable institution on the Quai Conti, expressing concern that *"they are discussing the colour of the fire extinguishers while the house is burning."* He was 99 years old at the time! ◀

1927-1945
Fertile intuition

Pierre Auger

1899-1993

The man who discovered high-energy cosmic rays



"On seven syllable verse
Astride my fine Arab steed
I travel my universe
Between the atom and star,
Drawing aside every veil,
I can glimpse you, from afar"

PIERRE AUGER

The son of a chemistry professor, Pierre Auger entered the Ecole Normale Supérieure in 1919 after taking the entrance exam in biology and left with an aggrégation in physics. He worked for his doctoral thesis on the photoelectric effect at Jean Perrin's laboratory at the Sorbonne. In 1923 he discovered the phenomenon that today bears his name. The Auger effect describes the emission, in certain cases, of an electron by an atom absorbing an X-ray quantum that possesses an energy that is characteristic of this atom, thereby enabling it to be identified. On receiving his doctorate he followed his master to the IBPC's Department of Physics while also teaching at the Sorbonne where, in 1937, he founded the first course on the experimental bases of quantum theory.

In the 1930s he identified, by connecting up a series of detectors placed on laboratory roofs on the Montaigne Sainte Geneviève, the first high-energy particles originating in cosmic rays. As these are more easily detectable at altitude, he transferred these experiments to the pic du Midi observatory and, above all, in 1938, to the summit of the Jungfraujoch in Switzerland, at an altitude of 3500 metres. It was there that he detected particles measuring 10^{15} eV, an energy that would not be achieved in accelerators until many decades later.

On the outbreak of war, in 1939, he created a documentation service at the CNRS so that the laboratories mobilised in support of national defence could continue to receive foreign scientific publications. Throughout the ensuring Occupation, this CNRS *Bulletin signalétique* was the sole link between French laboratories and international science, despite it having no legal existence. Auger himself left Paris in 1941, feeling threatened by the Nazis due to his links with the first stirrings of the Resistance. His international renown enabled him to obtain an invitation from the Rockefeller Foundation to travel to the United States. He worked initially at Chicago University, where Enrico Fermi was assembling the first nuclear reactor. As the United States prohibited French physicists from participating directly in the Manhattan project, Auger left for Canada to work with Jules Guéron and Bertrand Goldschmidt on the British nuclear programme. In 1944 the three men met General de Gaulle and informed him that the Americans were on the point of developing an atomic bomb.

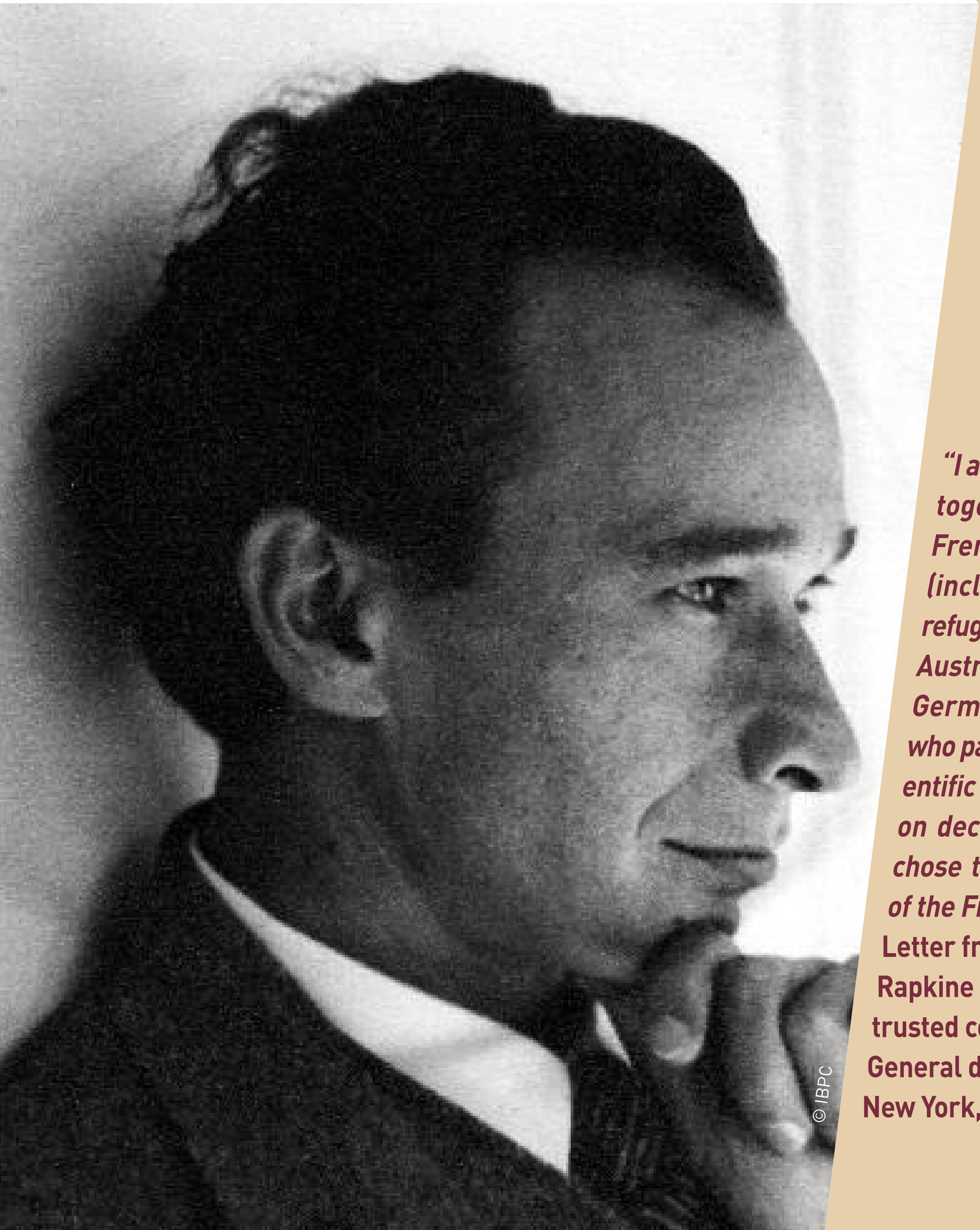
He returned to France after the Liberation and switched from scientific research to administration. Later describing himself as *"a creator who does not follow his creatures,"* Auger was the instigator of an impressive number of scientific institutions. As director of higher education at the Ministry of National Education, he created the network of Ecoles Nationales Supérieures d'Ingénieur while also, together with his close friends Frédéric Joliot and Francis Perrin, helping to set up the French Atomic Energy Commission. Drawing on his many international contacts, he headed UNSECO's science section until 1959. He subsequently helped found the European Centre for Nuclear Research (CERN) in Geneva. As first president of the National Centre for Space Research, he also developed European cooperation by creating the predecessor to the European Space Agency. The international observatory on the Argentinean pampas with 1600 detectors installed over an area 3500 km^{2}, which opened in 2008, today bears his name in homage to his major contribution to the discovery of cosmic rays. ◀

1927-1945
Fertile intuition

Louis Rapkine

1904-1948

A life committed to the service of scientists persecuted by fascism


© IBPC

"I am trying to bring together all the French scientists (including certain refugee Polish, Czech, Austrian, Italian and German scientists) who participated in scientific activity and who, on declaration of war, chose to share the fate of the French."

Letter from Louis Rapkine to René Pleven, trusted colleague of General de Gaulle, New York, 18 August 1941

Louis Rapkine was sensitive to the plight of refugees from a very young age, his parents having been forced to flee the pogroms of tsarist Russia in 1913. As a biology student at the Sorbonne, Louis himself experienced great hardship. Before receiving a grant from the Rockefeller Foundation in 1925, he worked at a shoe shop to make ends meet and ate just one meal a day. A meal he skipped once a week for a trip to the public baths. His material circumstances improved when he was taken on by the IBPC, at the time of its foundation, but this did not end the administration's xenophobic hostility. It was not until 28 September 1941, when the country was already at war, that he obtained the French nationality he had been seeking for the past two years.

The utmost discretion was therefore required when pursuing his activities in support of scientists threatened by fascism after Hitler came to power. While temperamentally inclined to discretion, his status of foreigner made it a necessity. A very shy man, in his 12 years at the IBPC he refused to give any lectures, despite the quality of his research into embryology that won him several prizes. Similarly, not one document produced by the Comité français pour l'accueil et l'organisation du travail des savant étrangers bears his name, despite the pivotal role he played within the organisation. Based at the IBPC and with Urbain as president and Perrin as vice president, this organisation was active, together with its British sister organisation, in assisting German, but also Spanish and Portuguese scientists who opposed fascism.

He was in London, where he worked as a statistician with the French mission for the purchase of coal, when Germany invaded France. He very quickly decided to draw on his international contacts to help scientists who had remained under the Nazis' heel. Accompanied by Henri Laugier, director of the CNRS who had been stripped of his post by the Vichy regime, he set sail for New York where he urged the Rockefeller Foundation to finance a programme to welcome French scientists. After tireless efforts in appealing to universities and Jewish charitable organisation, Rapkine managed to get 52 researchers out of France, nine of them from the IBPC: Pierre Auger, Théophile Cahn, Nine Choucroun, Boris Ephrussi, André Mayer, Jean and Francis Perrin, René and Sabine Wurmser.

11 December 1941, the day the United States entered the war, brought official recognition for these efforts he had pursued amid the utmost discretion so as not to upset the Vichy authorities with which Washington retained diplomatic relations. General de Gaulle founded the Bureau Scientifique de la France Libre and appointed Rapkine as its head. For the remainder of the war he devoted all his energies to ensuring that the bureau's members were employed to the best of their abilities in the service of the allied cause. In this he met with more success in the British than in the American camp.

These scientists trained in Anglo-Saxon methods went on to play a leading role in rebuilding France's national research system following the Liberation. Rapkine himself left the IBPC to head the cellular physiology section set up especially for him at the Institut Pasteur. He died suddenly from lung cancer at the age of 44, 18 months after being awarded the Légion d'honneur and before being able to resume his research activities. ◀

1927-1945
Fertile intuition

Francis Perrin

1901-1992

A founding father of the French electronuclear programme

"Contrary to what some believe, atheism does not lead to despair or anguish, but to great serenity, to full appreciation of the value of existence and a high conception of the dignity of man who is responsible to himself alone for his life and his actions. For me, life is all the more precious for being unique and fleeting. The joy of living seems to me the most essential virtue, despair the gravest crime against the spirit."

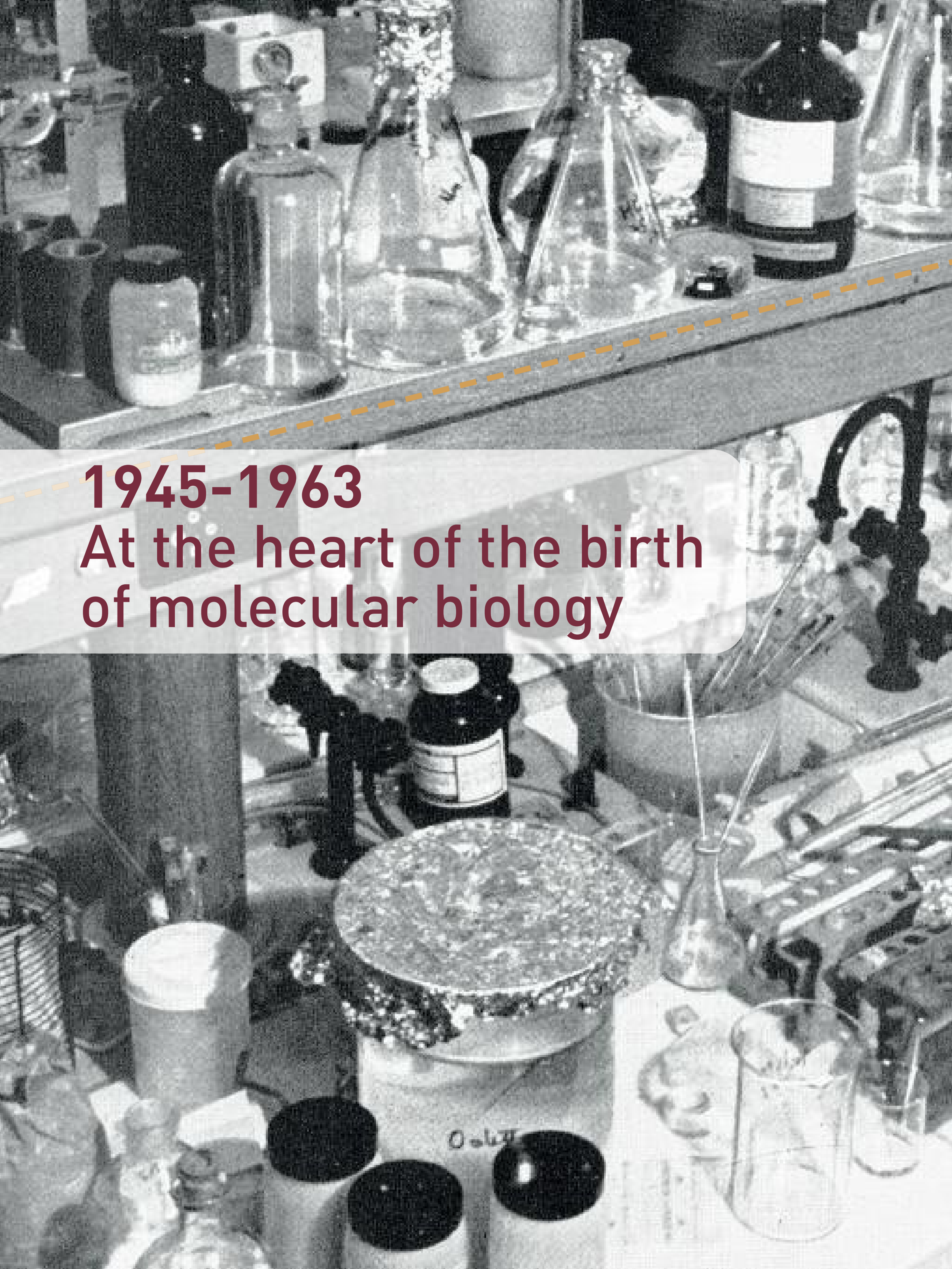
FRANCIS PERRIN

Brought up with the children of the Curie and Langevin families in a kind of school cooperative where they were taught by their parents, the son of Jean Perrin did not attend school until the preparatory year for lycée entrance. A fellow student of Pierre Auger at the Ecole Normale Supérieure and whose sister he married, in the 1920s he embarked on two theses, one a physics thesis at his father's laboratory, and the other a mathematics thesis under the supervision of Emile Borel. He joined the IBPC on its foundation, his subsequent research into theoretical physics leading him to postulate the existence of the neutrino, a particle of zero mass that would not be observed until many decades later.

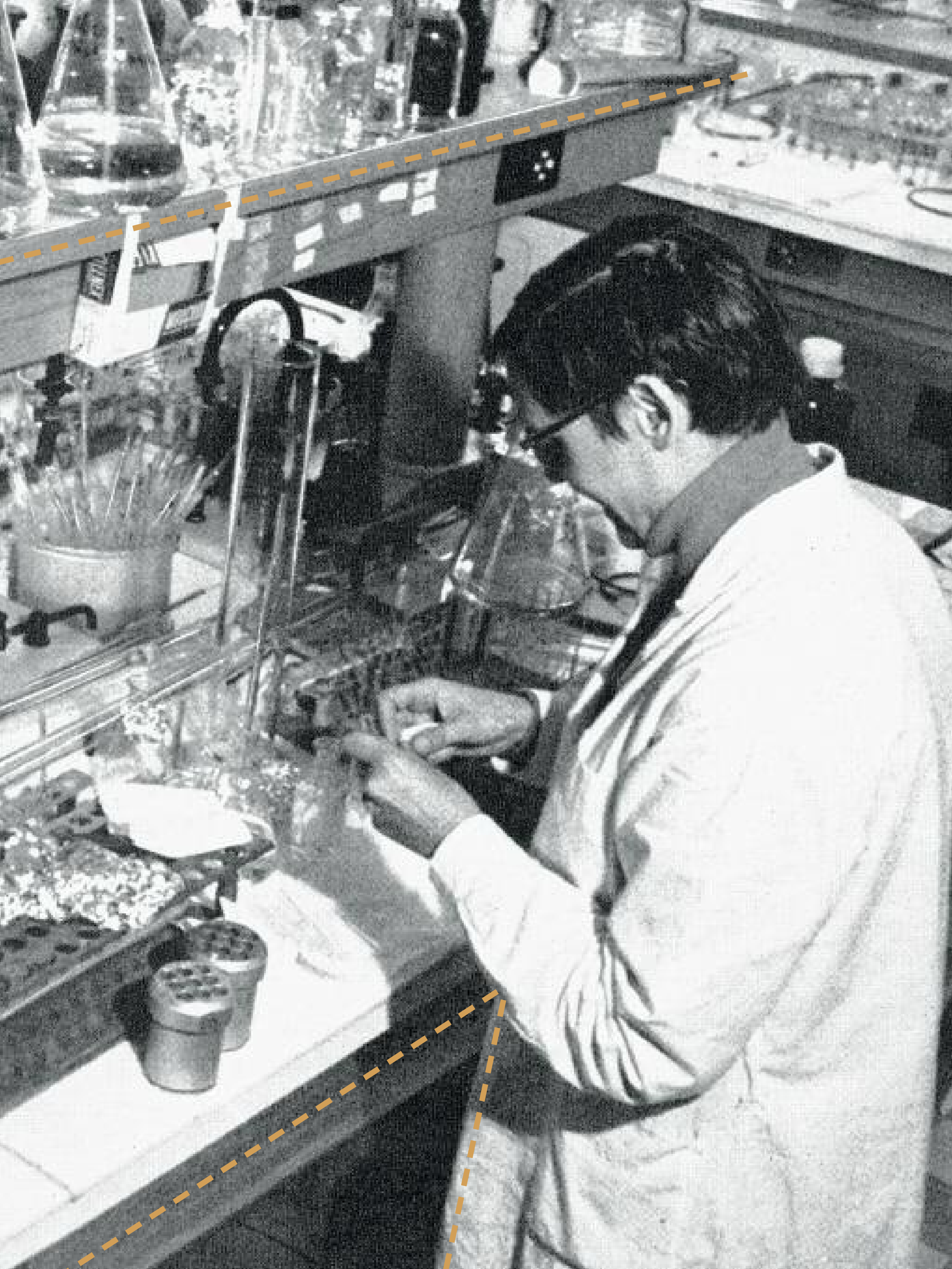
This interest in nuclear physics caused him to gravitate to the group centred around Frédéric Joliot at the Collège de France, a world leader in nuclear fission research at the time. As a mathematician, in 1939 he introduced the concept of the "critical mass" needed to trigger a chain reaction and that he estimated to be 40 tons of uranium. There were only two tons of uranium in the laboratory at the time but the group was convinced that command of fission energy was within reach. Five patents were registered – co-signed by Perrin – in 1939 and 1940, relating to civil as well as military applications.

War interrupted his research as he was conscripted to man an anti-aircraft battery. Frédéric Joliot was the only one of the Collège de France team to remain in Paris. Francis Perrin arrived in the United States with his father in December 1941. It was the intervention of his former colleague at the IBPC, Louis Rapkine, that served to dispel the initial reservations of the Rockefeller Foundation that agreed to finance the move to the US of this man of the Left who had visited the USSR in the 1930s. "*I was able to attend lectures accompanied by Fermi or Teller, great physicists who contributed to the development of the atomic bomb, but I was not able to make contact with those working on uranium fission and the chain reaction as I was a foreigner and had refused to adopt US nationality. I was nevertheless able to work a little on military applications, on bomb guidance systems for example. I also pursued, dare I say it, political activities and was bureau member of a Free French association known as France Forever,*" he explained. It was a commitment that led to his appointment by General de Gaulle as representative to the Consultative Assembly of the Free French in the United States.

After the Liberation he was appointed professor at the Collège de France. In 1950, the dismissal for communist sympathies of Frédéric Joliot from the post of high commissioner for nuclear energy presented him with a difficult choice: could he agree to replace his friend, whose pacifist convictions he shared? After considerable hesitation, he accepted the post and headed the Commissariat à l'Energie Atomique until 1970, developing research activities in fields outside of energy. President of the Edmond de Rothschild Foundation between 1955 and 1975, he emerged occasionally from retirement to defend the civil use of nuclear energy, to support Sakharov and the Soviet dissidents, and to defend the cause of atheism. ◄



1945-1963
At the heart of the birth of molecular biology

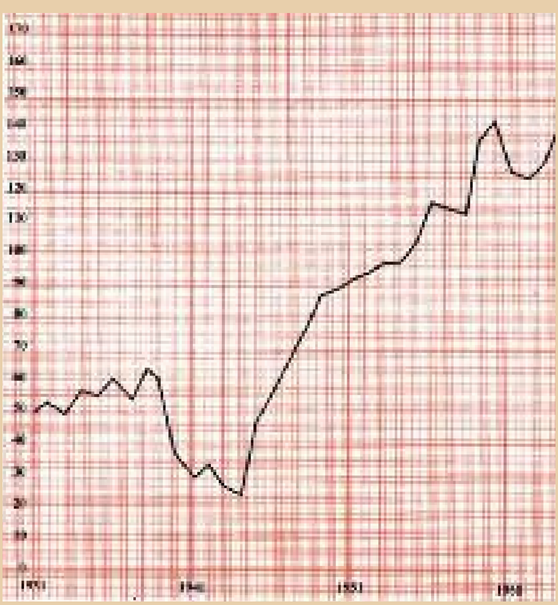


1945-1963
Molecular biology

In June 1948, Boris Ephrussi and André Lwoff organised, thanks to financial support from the Rockefeller Foundation, the first molecular biology conference in France, entitled "Biological units endowed with genetic continuity".

By 1947, the IBPC had regained its pre-war level of activity in terms of staff numbers and the annual rate of publications. Nonetheless, the Nazi occupation marked an important break in the institute's history. After the deaths of Urbain and Perrin and the departure of Mayer to take up a position with the FAO, Girard remained alone of the IBPC's helm. The man was anything but an autocrat, however, and in 1946 he had the six IBPC heads of department join the Edmond de Rothschild Foundation Board of Directors. A new more collegial style of management was gradually put into place. Its task was to rethink the IBPC's place within a French scientific landscape that was undergoing major changes. In the space of just a few years several large public research bodies had appeared in the wake of the CNRS: the Institut national d'hygiène – predecessor of the Inserm – in 1941; the Commissariat à l'énergie atomique (CEA) in 1945; the Institut national de la recherche agronomique in 1946. They all employed full-time researchers. They all pursued research involving a physico-chemical approach to the phenomenon of life. The model proposed by the IBPC in the 1930s had triumphed.

AFTER SLOWING DOWN DURING THE OCCUPATION, THE IBPC'S SCIENTIFIC ACTIVITY RAPIDLY STARTED UP AGAIN WITH THE LIBERATION



NUMBER OF SCIENTISTS

NUMBER OF PUBLICATIONS

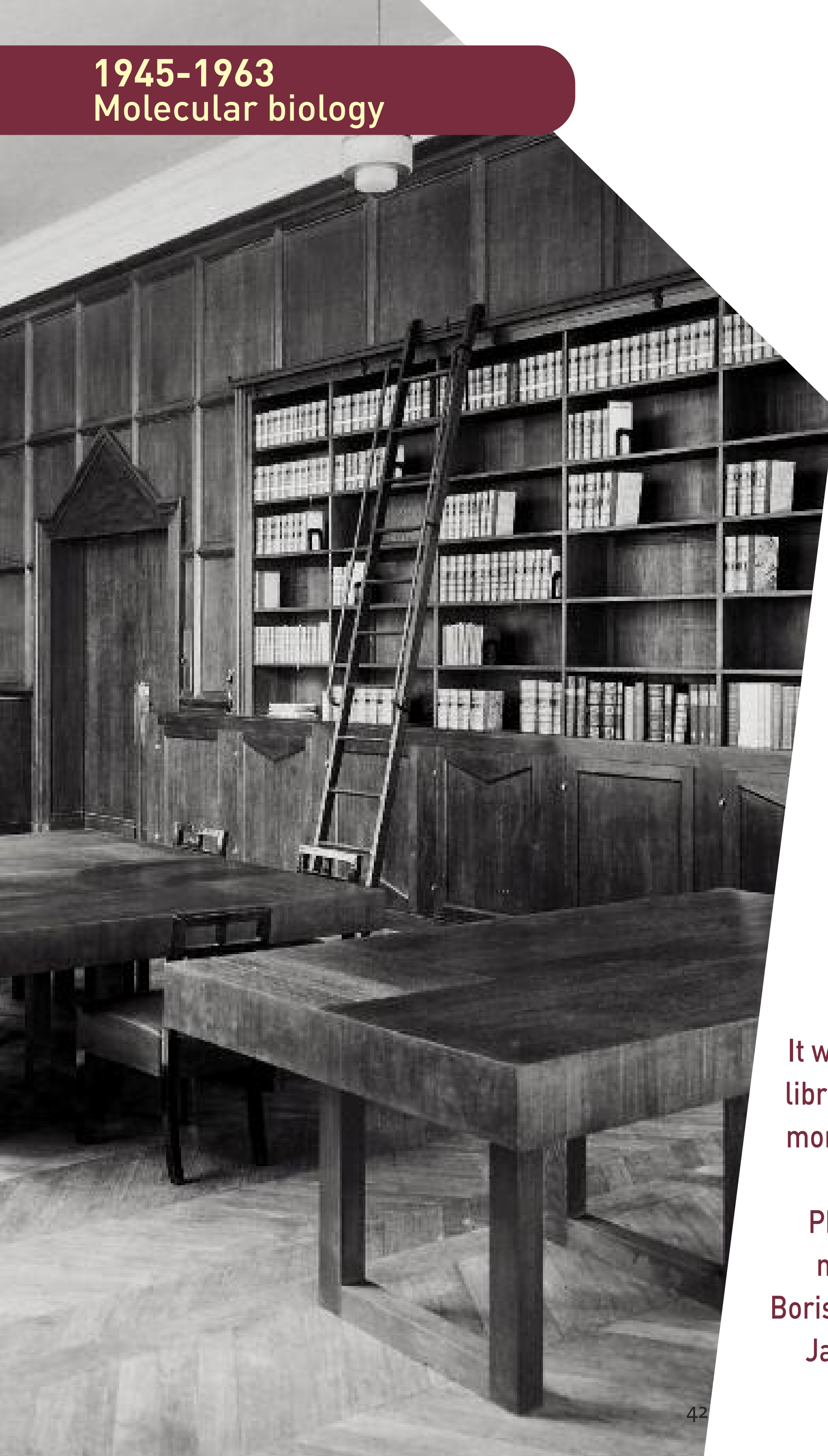
Refocusing on biology

Another break that coincided with the period of occupation was the loss of the physics department. Jean Perrin died and Pierre Auger and Francis Perrin, his principal colleagues, left the IBPC. At the same time, many US physicists started to become interested in biology, following the example of Erwin Schrödinger whose famous *What is life?* was published in 1944. Many of them, such as Léo Szilard, had worked on the Manhattan programme to build the atom bomb. Turning to biology was also a way for them to escape a physics that was too closely tied to military interests. A quite different situation prevailed in France, where many brilliant physicists, including Auger and Perrin, on the contrary became involved in creating the CEA and turned away from biology. With the departure of the physicists, an essential component of the interdisciplinarity sought by the IBPC's founders had been lost. The list of IBPC departments after the Liberation reflects this refocusing on biology:

Physiological physical chemistry, headed by Pierre Girard – Genetics, headed by Boris Ephrussi – Biophysics, headed by René Wurmser – Animal physiology, headed by Théophile Cahn – Biochemistry, headed by Eugène Aubel – Colloids, headed by Jacques Duclaux

In the space of just a few years several large public research bodies had appeared in the wake of the CNRS: the Institut national d'hygiène – predecessor of the Inserm – in 1941; the Commissariat à l'énergie atomique (CEA) in 1945; the Institut national de la recherche agronomique in 1946. They all employed full-time researchers. They all pursued research involving a physico-chemical approach to the phenomenon of life. The model proposed by the IBPC in the 1930s had triumphed.

CEA SCIENTIFIC COUNCIL IN 1946. TWO FORMER IBPC MEMBERS ARE PRESENT: PIERRE AUGER (LEFT) AND FRANCIS PERRIN (RIGHT) NEXT TO THE JOLIOT CURIE COUPLE IN THE FRONT ROW



It was in the IBPC library that, every month from 1947, the Cellular Physiology Club met, headed by Boris Ephrussi and Jacques Monod.

This internal organisation remained virtually identical until the death of Pierre Girard in 1958, the only change being the creation, in 1952, of a department specialising in the chemistry of natural organic substances, headed by Edgar Lederer.

The Molecular Biology Club

DISCOVERER OF ACETYLENE SYNTHESIS, PAUL LEBEAU SUCCEEDED JEAN PERRIN TO THE PRESIDENCY OF THE EDMOND DE ROTHSCHILD FOUNDATION IN 1943

"There were two major currents in pre-war biology: the geneticists who ignored totally the molecular nature of phenomena, and the physico-chemists who were interested in colloids and macromolecules. Molecular genetics was born of the coming together of these two currents: the study of structures on one hand, and the study of functions on the other," explained Piotr Slonimski. In other words, molecular biology was born of the study of biochemistry according to methods and approaches originating in other disciplines, other fields, other cultures, and in physics and genetics in particular.

By virtue of its history, the IBPC was at the centre of this convergence. Biochemistry had been studied there since its foundation and the departments headed by Eugene Aubel and René Wurmser were continuing research in this field. The IBPC also possessed, with Boris Ephrussi's department, one of just two genetics laboratories in France, the other being at the ENS and headed by Georges Teissier. As to methods of physical analysis, such as ultracentrifugation and electrophoresis to separate biological

THE PHYSICIST FRANCIS PERRIN WAS PRESIDENT OF THE EDMOND DE ROTHSCHILD FOUNDATION FROM 1955 TO 1975

"An impressive array of famous figures passed through the Cellular Physiology Club that met at the IBPC in the 1950s. At times there was a feeling of surprise when neither the figure nor the face of the man was how you had imagined them from the writings. Very often also a sense of exaltation and of plenitude at the sheer brilliance of a conference or the success of a research project. As when witnessing any very great performance, be it by an athlete, an actor or a musician. In short, any time that, in any field whatsoever, you are struck by the undeniable perfection."
François Jacob

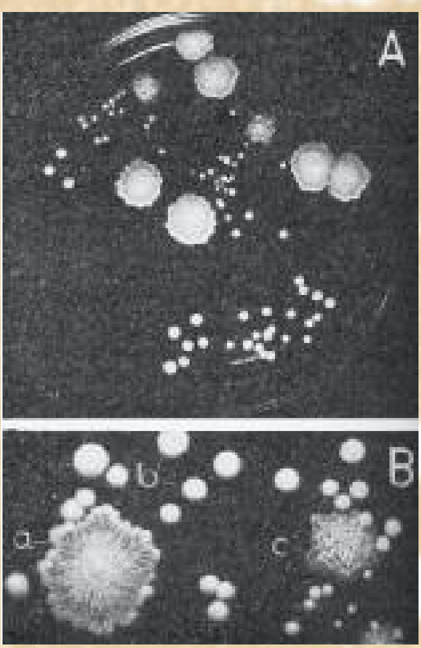
1945-1963
Molecular biology

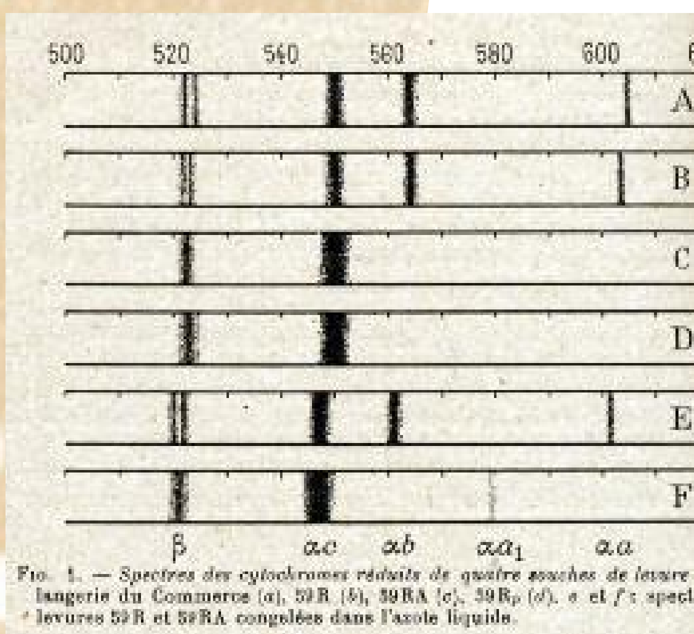
In the 1950s, Edgar Lederer's laboratory described a biosynthesis pathway unique to mycobacteria that are able to synthesise fatty acids of 80 carbon atoms in length, which is four times more than conventional lipids.

macromolecules and spectroscopy to measure nucleic acids, the IBPC had practiced these techniques since the 1930s. These high-tech methods became common practice in the 1940s when the necessary equipment started to become available commercially. In 1946 the IBPC acquired a Spinco ultracentrifuge thanks to aid from the Rockefeller Foundation and subsequently provided a home for the CNRS's first ultracentrifugation unit.

In the 1940s and 1950s, the IBPC – described by the biologist Vittorio Luzzati as a *"haven of interdisciplinarity where the emerging sciences were destined to flourish"* – drew on its interdisciplinary tradition to find itself at the heart of the emerging molecular biology. It was in the IBPC library that, every month from 1947, the Cellular Physiology Club met, headed by Boris Ephrussi and Jacques Monod. These informal meetings where discussion was freer than at official seminars were usually followed by a dinner in the Latin Quarter. All members of André Lwoff's department at the Institut Pasteur attended and the list of those invited to address the club members included all the big names from the nascent molecular biology: Max Delbrück, Francis Crick and Linus Pauling, to cite only the Nobels.

IN 1949, BORIS EPHRUSSI AND PIOTR SLONIMSKI DISCOVERED YEAST PETITE MUTANTS (LEFT) AND SHOWED THAT THEIR SLOWED GROWTH IS DUE TO MUTATIONS OF THEIR CYTOCHROMES (RIGHT)





Non-Mendelian genetics

The turning point for molecular biology is inextricably linked to the choice of a micro-organism model that lends itself easily to genetic analysis by virtue of its rapid growth. At the California Institute of Technology, Max Delbrück opted for bacteriophage. At the Institut Pasteur, with its microbiological tradition, André Lwoff concentrated on the bacteria *Escherichia coli*. The IBPC chose a eukaryotic organism: the yeast *Saccharomyces cerevisae*.

On his return from the United States after the war, Boris Ephrussi set about selecting a wide range of biochemical mutations of yeast. He obtained them by using acridines as the mutagenic agent. In 1946 he wrote that *"there seems to be every indication that nucleic acids play an important role in the gene reproduction processes and there is reason to believe that the action of acridines distorts this process and leads to the formation of defective genes, thus of mutations."* One of these mutations caught his attention: that which forms reduced size colonies in an aerobic environment, hence the term "petite mutant" used in international literature.

This opened up two avenues of research. The first, developed by his pupil Piotr Slonimski, concerned the biochemical characterisation of this mutation, which proved to be due to a mitochondrial oxidase cytochrome deficiency. The second, explored by Ephrussi, involved identifying its curious properties of hereditary transmission. When a petite mutant is crossed with a wild-type

Non-Mendelian genetics has been studied at the IBPC, where it was discovered, since 1949.

Continuing their work on blood conservation, which they had begun in 1939 when science was mobilised for the war effort, in the 1950s René Wurmser and Sabine Filitti-Wurmser purified an antibody present only in individuals of blood groups A and O: anti-B isohemagglutinin. By refining their research at the genetic level, they isolated, with the anti-B of individuals A1O, the first human protein that is characteristic of the heterozygotes.

PHOTOSYNTHESIS LABORATORY. IN THESE EXPERIMENTS, OXYGEN PRODUCED BY CHLOROPHYLLIAN ASSIMILATION IS DOSED

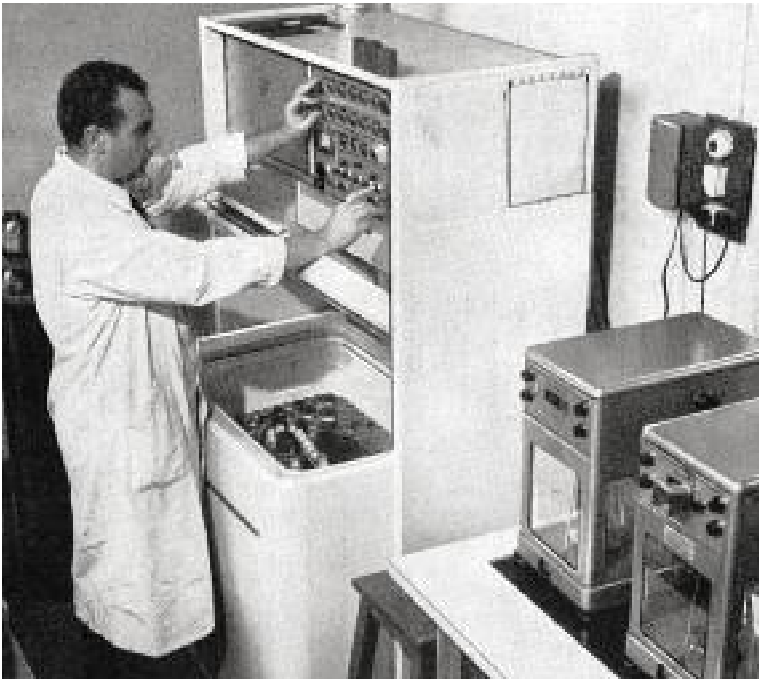
ISOLATION OF A MESSENGER RNA IN THE MICROBIAL PHYSIOLOGY LABORATORY DURING THE 1960S

strain, the result is 100% wild-type phenotype spores and not half petite and half wild-type as the Mendel laws would dictate. A non-Mendelian transmission of the sensitivity of fruit flies to carbon dioxide is also described at this time in Ephrussi's laboratory by Philippe L'Héritier. From 1949, Ephrussi and Slonimski brought together these two approaches, writing that *"the petite mutant colony differs from the normal form in the loss of the autoreproductive cytoplasmic particles essential to the synthesis of a group of respiratory enzymes."* This marks the beginning of non-Mendelian genetics that the IBPC studied continuously over the next 50 years, first in mitochondria and then in chloroplasts.

THE BIOCHEMISTRY OF NUCLEIC ACIDS

Parallel to this research in genetics, the IBPC biochemists were studying the structure of different nucleic acids and in particular of DNA that, in the 1940s, was revealed as being the biochemical support for heredity. In 1950, thus three years before its double helix structure was identified, Jacques Tonnelat's group prepared DNA from a calf thymus by ultracentrifugation and studied the light diffraction properties of the molecule to conclude a very long shape. The biochemists working with Eugène Aubel and René Wurmser were interested in ribonucleic acids (RNA) at a time when these acids were conceived as small tetramers consisting of four bases. These researchers showed that their high molecular weights are incompatible with this structure and that the double correspondence between A-T and G-C, already observed by Erwin Chargaff, continues to be respected. These observations helped in drawing up the double helix model of DNA.

From 1953 Pierre Joliot built devices at the IBPC making it possible to monitor the speed at which oxygen is formed during photosynthesis. These technical breakthroughs made it possible to describe the mechanism of water photolysis and to characterise the role of chlorophyllian pigments.



DEPARTMENT OF BIOCHEMISTRY. USING A PACKARD SCINTILLATION COUNTER TO MONITOR ENZYME ACTIVITY WITH TRACERS MARKED BY MEANS OF CARBON AND PHOSPHOROUS RADIOISOTOPES

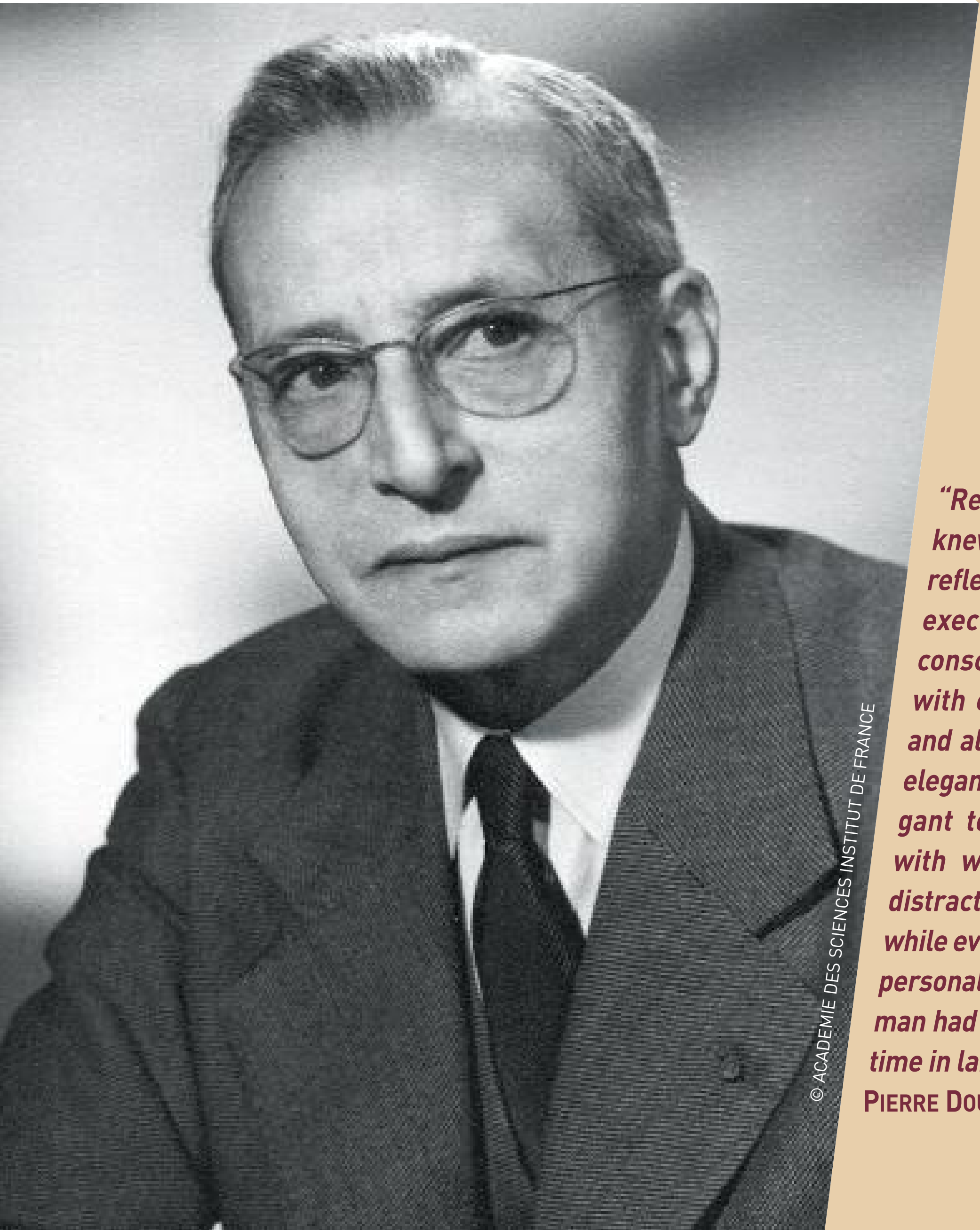
This research intensified in 1955 when Marianne Manago returned from her postdoctoral training at the Severo Ochoa laboratory in the United States. She brought back to the IBPC the polynucleotide phosphorylase that she had isolated. At this time researchers were just beginning to develop the idea that short-lived RNA (today known as mRNA) serves as a template for protein synthesis. It was possible to test this hypothesis by virtue of the ability to produce - thanks to polynucleotide phosphorylase that catalyses the polymerisation of diphosphate nucleosides - as much RNA with a statistically controlled nucleotidic composition as required. Marianne Manago's group thus showed that codons that contain only As and Cs code for threonine and asparagine when it was believed at the time that all codons contained uracil. The IBPC thus contributed to the deciphering of the genetic code that was completed in 1966. The development of systems for *in vitro* protein biosynthesis sparked a new interest in the small stable nucleic acids that are vital to the translation: the transfer RNA, whose structure Yvonne Khouvine's group set about describing using the methods of physicists.

The IBPC contributed to the deciphering of the genetic code that was completed in 1966.

René Wurmser

1890-1993

A bridge between biophysics and molecular biology



"René Wurmser knew how to listen, reflect and reply. He executed his tasks conscientiously and with comprehension, and always with great elegance. He was elegant to his fingertips with which he picked distractedly at his food while evoking surprising personal memories. This man had not spent all his time in laboratories."

Pierre Douzou

When he came to the IBPC in 1927, René Wurmser already had to his credit nearly 15 years of research into photosynthesis at the Sorbonne, first at Victor Henri's laboratory and then with Jean Perrin. In his thesis, submitted after his demobilisation in 1921, he applied the most modern ideas in physics to the study of chlorophyllian assimilation. Shortly afterwards, he showed that the initial event in this process is the photolytic breakdown of water and not, as was believed at the time, the reduction of carbon dioxide. Within the IBPC's Department of Biophysics he pursued, with his future wife Sabine Filitti, research in the field of bioenergetics and, more specifically, into the metabolic reactions of oxidoreduction.

The outbreak of war interrupted his promising career. During the years when science was mobilised for the war effort (1939-1940), he worked on a process for conserving blood that was long used by transfusion doctors. Of Jewish origin, he was one of the 15 academics exempted from the anti-Semitic exclusion laws due to the importance of his work. Aware of the dangers, he nevertheless went into hiding in Paris before leaving for Brazil with his wife in 1941 where he was welcomed at the University of Rio de Janiero by his former pupil Carlos Chagas. He became friends with Georges Bernanos during his Brazilian exile before returning to London in 1944 where he joined his former assistant Louis Rapkine at the scientific office of France Libre.

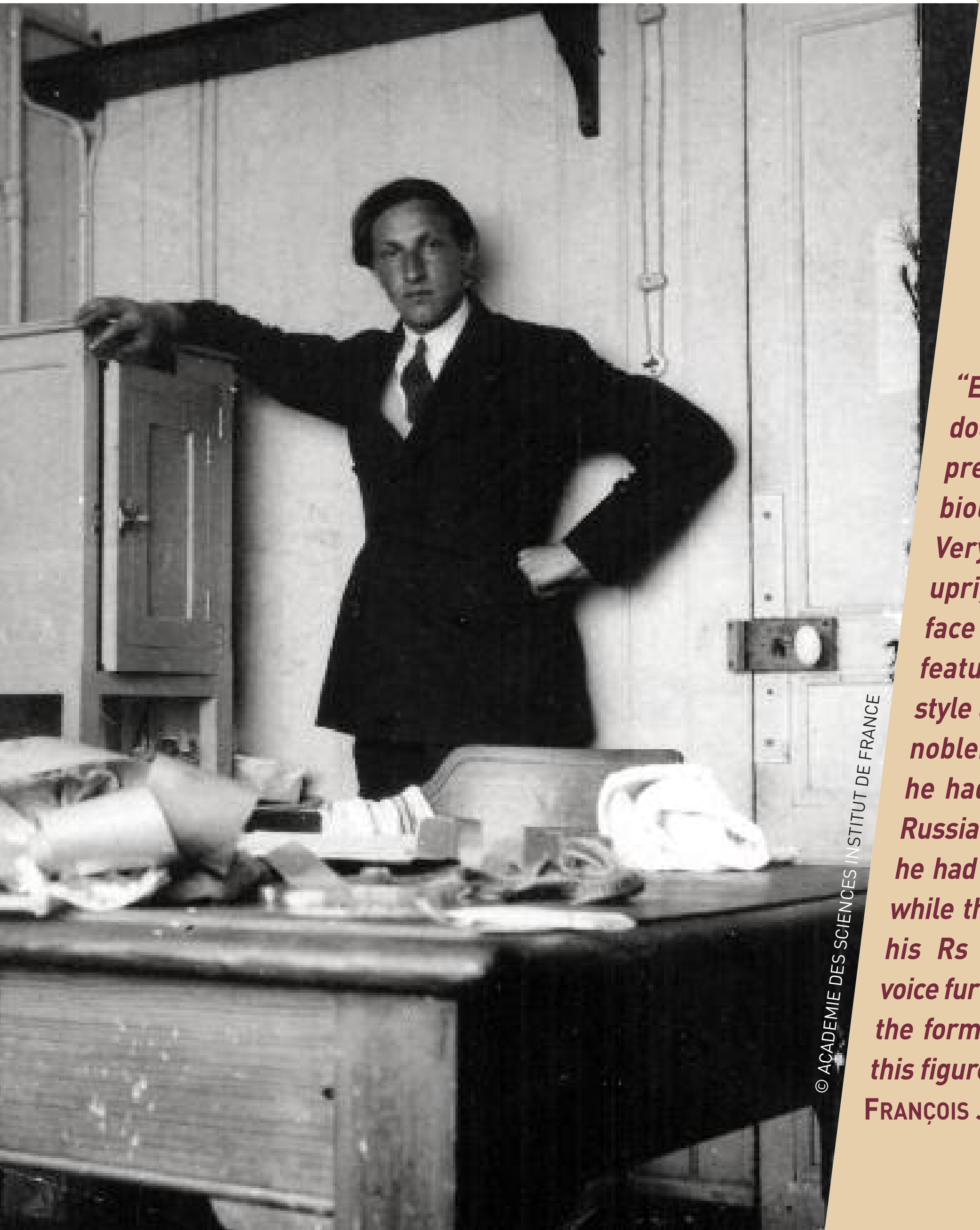
After the Liberation, he was elected to the chair of physico-chemical biology at the Sorbonne. François Jacob retained fond memories of his lectures: *"René Wurmser showed such ingenuity in explaining the formulas of physical chemistry, he described them with such passion, illustrated them with such pleasure with examples drawn from his own research that his lectures finally took on the air of a detective novel."* At the IBPC, he pursued, again with his wife, the study of the thermodynamics of the antigen/antibody interaction-link while at the same time heading the Department of Biophysics. *"René Wurmser believed that a director of research must enable young researchers to express their own originality, leading him to grant them great freedom of initiative. René Wurmser was nevertheless always available to give us his assistance but refused obstinately to impose his own ideas. This is perhaps the sole criticism I would allow myself to make of my master as sometimes I was too late in discovering certain visionary aspects of his work,"* remembers his principal pupil, Pierre Joliot, who continued his research into photosynthesis.

Following the death of Pierre Girard, in 1958 he became the IBPC's second administrator and began to work on its reorganisation. *"By virtue of his age, clearly René Wurmser could be no more than a transitional pope. In fact he was the John XXIII of our institute. Just a few years after the birth of modern molecular biology he had understood the importance of centring the IBPC's activity on this line of research,"* remembers Bernard Pullman. When the latter succeeded him as IBPC administrator in 1963, Wurmser concentrated on the work of the Molecular Biology Committee at the DGRST (Directorate General for Scientific and Technical Research) that he had chaired since its creation. Ceding his place to Jacques Monod in 1966, he set about creating a molecular biology section at the Académie des sciences. This discreet and reserved man remains one of the principal architects of the institutionalisation of this discipline in France.◀

Boris Ephrussi

1901-1979

The pioneer of genetics in France



"Ephrussi was no doubt the most impressive figure in biology in France. Very tall, thin and upright, with a long face and chiselled features, he had the style and bearing of a nobleman. Although he had left his native Russia at the age of 15 he had kept his accent, while the way he rolled his Rs in his gravelly voice further accentuated the formidable aspect of this figure."

FRANÇOIS JACOB

Born in Russia to a prosperous Jewish family, Boris Ephrussi arrived in Paris after the October Revolution. At the Sorbonne he made friends with André Lwoff and was a frequent visitor to the marine biology station in Roscoff. It was there that he took the sea urchin's egg as the model for studying the development of the embryo. In 1927, Emmanuel Fauré-Frémiet, professor at the Collège de France, employed him as an assistant at the IBPC where, in 1932, he submitted its first state thesis. The title was: "Contribution to the analysis of the first stages in the development of the egg. The action of temperature."

The attention this thesis attracted enabled him to obtain a grant from the Rockefeller Foundation. In 1934 he worked at Thomas Morgan's fly lab at the California Institute of Technology (CIT), the Mecca for genetics at the time. This was the first in a long series of stays in the United States. Together with George Beadle, he conducted, first at the CIT and then at the IBPC, a series of experiments on the fruit fly using micrografting techniques borrowed from embryology that led ultimately to the formulation of the principle of one gene/one protein. When this discovery was rewarded with a Nobel for Physiology or Medicine in 1951, many believed Ephrussi deserved to be co-laureate.

The war forced him into exile in the United States. On his return to France in 1945 he went back to the IBPC. At the Department of Genetics, which he managed with an iron hand, "Prince Boris", as he was nicknamed by André Lwoff, discovered with his pupil Piotr Slominski the non-Mendelian genetics of yeast. "*A brilliant and critical mind, with a liking for great syntheses and unexpected connections, Ephrussi was an exceptional lecturer and conversationalist. An excellent actor also. When he wanted to seduce he knew how to use his Slavic sweetness and charm and to tell his stories all night long. In the space of a few minutes he could switch from anger to gentleness, from reasoning to joking, from exaltation to melancholy. There was something of the Ivan Karamazov about him,*" remembers François Jacob.

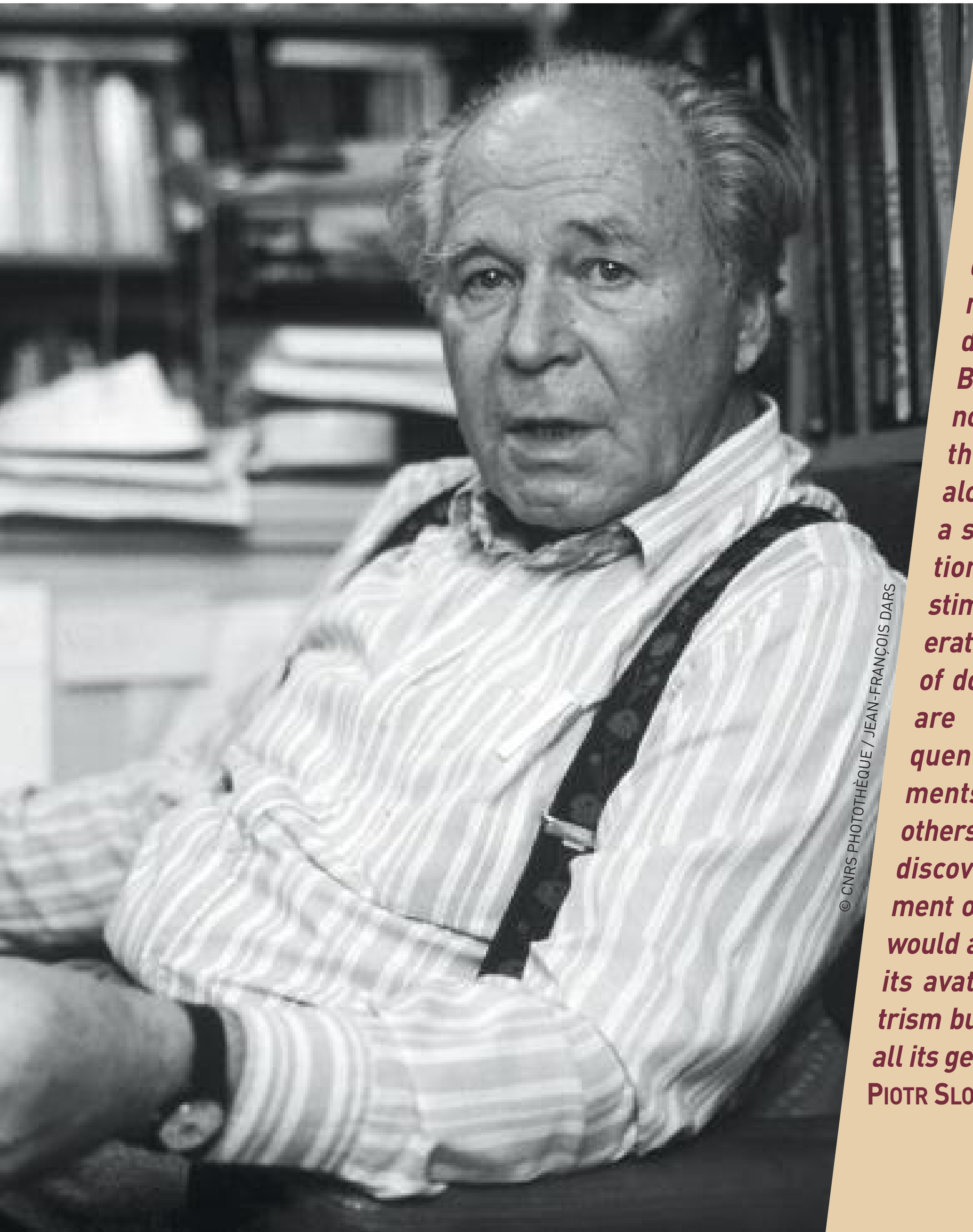
In 1945 also, he was elected to the chair of genetics that the Sorbonne had just created, the first in France. With the backing of the mathematicians and the physicists, but not most of the biologists, most of them being hostile to genetics. The new discipline did, however, have the support of the youthful CNRS and Rockefeller Foundation. In 1949 the latter was becoming concerned at the influence of the ideas of Lysenkoism in France. Ephrussi was sent by the CNRS to the United States to defend the cause of French genetics. "*As I look back on our conversations, I still feel that I presented to you as honestly as possible my opinion concerning the risks of leftist Lysenkoism, but I am not quite sure that I emphasized sufficiently the dangers to French genetics coming from the representatives of the still traditional French Lamarkism, more frequently associated with political ultra-conservatism,*" he wrote to representatives of the Rockefeller Foundation in 1950.

In 1959 he left the IBPC to take over as head of the Institute of Genetics that the CNRS had just founded in Gif-sur-Yvette. Awarded the médaille d'or from the CNRS in 1968, he continued his work there, on the subject of the genetic mechanisms of cellular differentiation during embryo genesis, until his death just a few months after his election to the Académie des Sciences.◀

Piotr Slonimski

1922-2009

The founder of mitochondrial genetics



"Why fundamental research? As far as I am concerned the answer is short: quite simply, I do not know how to do anything else. But this answer is not satisfactory. In this complex alchemy, curiosity, a spirit of competition, ambition, the stimulation of cooperation and the sense of doing useful work are the most frequently cited elements. But there are others: the pleasure of discovery and an element of play, to which I would add passion, with its avatars, its egocentrism but also and above all its generosity."

PIOTR SLONIMSKI

Paris, October 1985: Hubert Curien awarded the CNRS médaille d'or to Piotr Slonimski. The latter commented: *"With this medal, my dear minister, you have rewarded an exemplary thematic immobility and totally gratuitous research on a subject of minor importance."* It is an anecdote that demonstrates all the irreverence and outspokenness, lucidity and humour of Slonimski, a man much loved by a generation of researchers trained in the M. Phil in molecular genetics that he founded at Paris VI University.

Born into a middle class family of Jewish intellectuals in Warsaw, Piotr Slonimski fought during the war with the Polish Secret Army. It was an adventurous life and he narrowly escaped death on several occasions, while all the while pursuing his medical studies. His vocation as a researcher was sparked by a book he found on the body of a German soldier: *Theoretical biology* by Ludwig von Bertalanffy. *"After the war, having lost my loved ones in Poland, I had decided to emigrate. I did not want to go to Germany for obvious reasons and in Bertalanffy's book I had come across a note referring to the work of Beadle and Ephrussi on fruit fly genes. Beadle was in California which was rather far, so I set my sights on Ephrussi."*

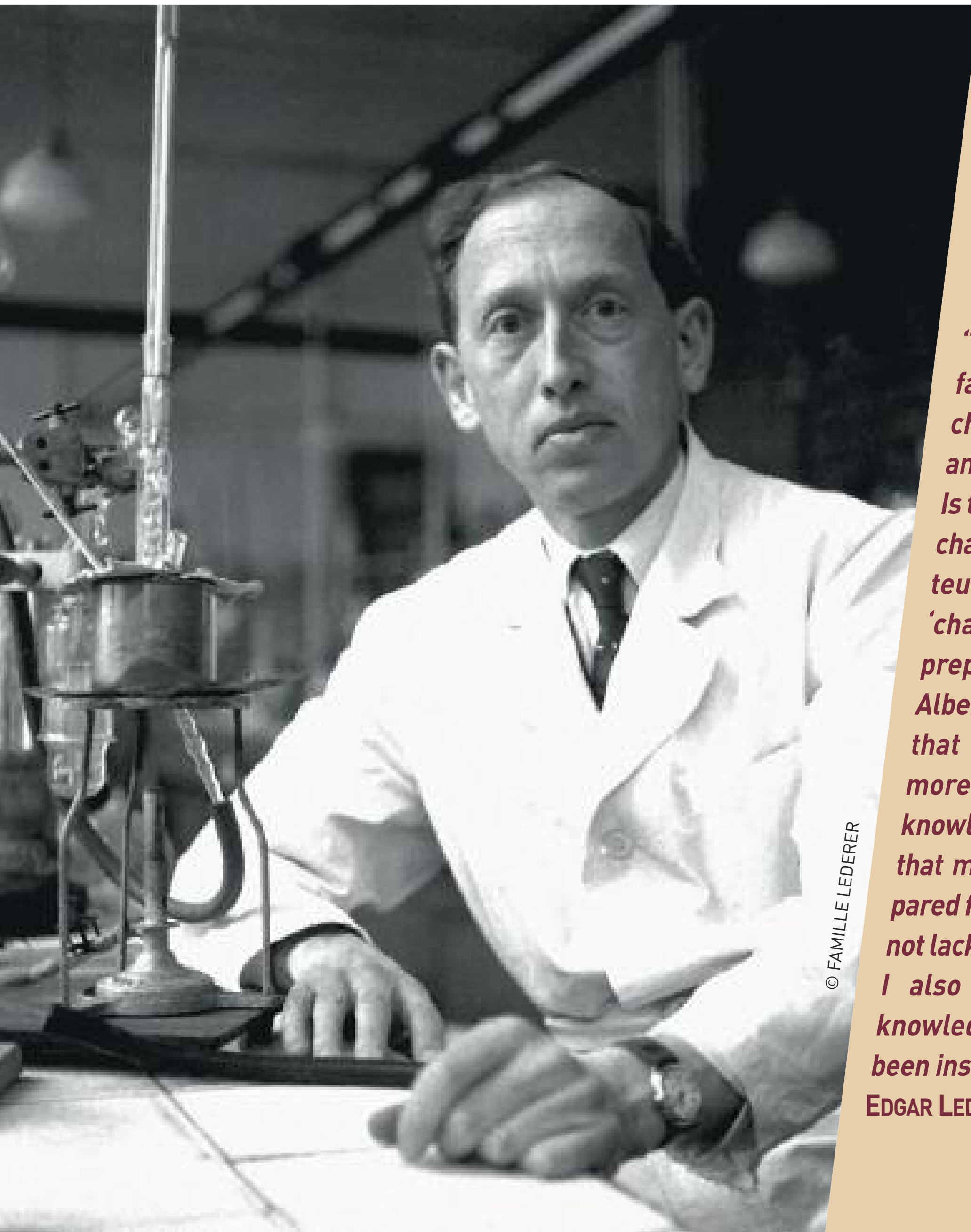
A fruitful cooperation developed between the two men at the IBPC, beginning in 1947. Slonimski earned the nickname of *"resistant mutant"* for his rare ability to cope with Ephrussi's authoritarian nature. The latter had just discovered the slow-growing "petite" mutants in yeast and charged Slonimski with explaining the phenomenon. *"One fine day I decided to measure the respiration of my strains, just to see. A stroke of luck! I found a 100% difference between the mutants and the wild-type strains. Clearly my first reaction was that the manometer was playing up, that there must be a leak somewhere. I repeated the process. The result was incredible! Who would have imagined that a simple mutation can occur in a process as fundamental as cellular respiration? I had discovered that the mitochondria of 'petite' mutants did not contain cytochromes."*

This discovery was the subject of his science doctoral thesis that he submitted at the Sorbonne in 1952 and that was to open the door to a career at the CNRS. At the Physiological Genetics Laboratory in Gif-sur-Yvette, which he headed from 20 years from 1971, he explored every aspect of the structure and functioning of mitochondrial genes. *"How the two types of genetic information that coexist within a eukaryotic cell are structured, how they function and inter-communicate, how they evolve, how the synthesis of energy production enzymes is regulated and, finally, why there are mitochondrial genes. We asked these same questions tirelessly while changing the techniques and trying to imagine new experiments with the benevolent participation of a single organism, always the same, baker's yeast."* In retirement, this Académicien devoted his energies to running the European consortium that in 1998 determined the first complete sequence of the eukaryotic genome... the yeast *Saccharomyces cerevisae.* He continued to work on his computer until the end of his life, this representing his new laboratory on which he sought to reveal the secrets of genomes. ◀

Edgar Lederer

1908-1988

A great chemist of natural substances



"I have always felt favoured by chance in my life and in my research. Is there a reason for chance? Louis Pasteur said that 'chance favours the prepared mind' and Albert Einstein added that 'imagination is more important that knowledge'. I suppose that my mind was prepared for it and that I did not lack imagination, but I also know that my knowledge has always been insufficient."

Edgar Lederer

Edgar Lederer prefaced his autobiography with this quote from Elias Canetti : *"You carry certain wounds with you until you die and all you can do is to hide them from the eyes of others."* This was a discreet way of expressing to what extent he was marked indelibly by the loss of the world of his childhood, that of the cultivated and polyglot Jewish bourgeoisie of Vienna, first ruined by the First World War and then eliminated by Nazism. As an undergraduate, Lederer chose to study chemistry *"because it was the only science at that time that could provide nourishment for man."* But anti-Semitism rendered impossible any university career in Vienna that he left in 1930 to settle in Heidelberg. In Richard Kuhn's laboratory he developed the use of chromatography to study natural substances, a lifelong speciality for Lederer.

When the Nazis came to power in Germany, he was once again forced into exile. He moved to Paris with his French wife and joined the IBPC where he introduced chromatography, unknown to French chemists at the time. *"It must be said that biological chemistry, or the chemistry of natural substances, was very much lagging behind. In 1935, I prepared to sit degree exams. For the biochemistry degree I had to learn the quantity of copper contained in the leaves of plants, of potassium in snails, etc. It was crazy. By contrast, there was no enzymology, and even no analysis of constituents more evolved than metal traces."* His meagre research grant was not enough for him to keep his wife and two children. Attracted by communism, he left for Leningrad in 1935 to head a laboratory working on the chemistry of vitamins. Two years later he suddenly left the USSR at the time of the Stalinist purges and returned to the IBPC. In 1938, it was there that he submitted his French doctoral thesis, subsequently joining the CNRS on receiving French citizenship. In 1941 the Vichy government's anti-Semitic legislation forced him to leave. *"Stupidly optimistic"* and *"quite tired with all these changes since 1930,"* he refused Louis Rapkine's offer of exile in the United States and spent the war in Lyons living under an assumed identity and working in the perfume industry.

It was only after the Liberation, at the age of 36, that he was finally able to pursue his scientific career without having to worry about the future. In 1952, he was appointed head of department at the IBPC where he worked on the chemistry of natural substances, becoming an internationally recognised expert on such subjects as carotenoïds, bacterial cell wall compounds and vegetal extracts. He was also interested in the nascent molecular biology that he liked to describe, citing his compatriot Erwin Chargaff, as *"the illegal exercise of essentially the practice of biochemistry without a license."*. He was also one of the few IBPC researchers to establish partnerships with the medicines and perfume industries that were both interested in his know-how.

He left the IBPC in 1960 to head the Institute of the Chemistry of Natural Substances that the CNRS had just set up in Gif-sur-Yvette, while continuing to teach biochemistry at the Paris and then Orsay universities. He retired in 1978, four years after being awarded the médaille d'or from the CNRS and four years before being elected to the Académie des Sciences. ◀

Since 1963
Biology: a free space for research and knowledge


INSTITVT DE BIOLOGIE-
PHYSICO-CHIMIQVE

With the founding, in 1960, of two major CNRS institutes in Gif-sur-Yvette, one for molecular genetics and the other for the chemistry of natural substances, the IBPC had again served as a template.

In 1963, when Bernard Pullman became the IBPC's third director, he knew that the institute was at a decisive moment in its history.

Once again, the model of which it had been the sole example in the 1930s showed its pertinence. With the founding, in 1960, of two major CNRS institutes in Gif-sur-Yvette, one for molecular genetics and the other for the chemistry of natural substances, the IBPC had again served as a template. These new institutes were headed by two researchers who had spent the greater part of their careers at the IBPC: Boris Ephrussi at the former; Edgar Lederer at the latter.

What is more, the principal concepts of molecular biology - in particular the existence of a unidirectional information flow from DNA to proteins by way of messenger RNAs - were now acknowledged and the new discipline firmly established at the IBPC. Pullman's predecessor in the post of administrator, René Wurmser, aged 73, created two new departments that he entrusted to the rising stars of the new discipline: Marianne Manago and François Gros. He also brought in from the Sorbonne a young professor of quantum biochemistry, Bernard Pullman. On becoming the IBPC's third administrator at the age of 44, it was Pullman who raised a number of questions. What new directions should the IBPC take? How to give new impetus to the initial ambition of developing a physico-chemical approach to life when, with the advent of molecular biology, it seemed to have become hegemonic?

STRATEGIC CHOICES

The context in which these strategic questions were raised was very favourable. Since General de Gaulle had become president in 1958, public support for research had become the major priority that Jean Perrin and André Mayer had advocated back in the 1930s. The new Délégation Générale à la Recherche Scientifique et Technique (DGRST), which reported directly to the prime minister, was the armed wing of government intervention in scientific policy. The DGRST's priorities included molecular biology and membrane biology, two subjects to which the IBPC was committed.

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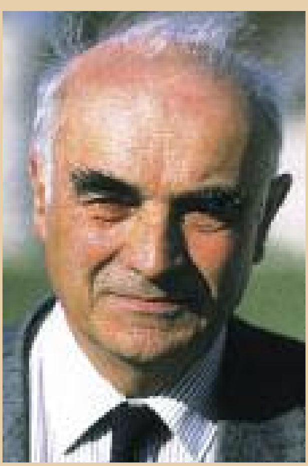
IN 1967, THE RUE PIERRE CURIE BECAME THE RUE PIERRE ET MARIE CURIE. THE FOLLOWING YEAR IT WAS AT THE HEART OF THE STUDENT RIOTS.

The IBPC was not spared the 1968 student revolt, lying as it does at what was the geographical epicentre of the nightly riots. The criticism of the old guard struck a chord among some of the technical staff and researchers at the institute whose day-to-day management was in the hands of a permanent five-member committee (Jacques Duclaux, René Wurmser, Bernard Pullman, Francis Perrin and Jacques Trefoüel, honorary director of the Institut Pasteur), with an average age of 71. Bernard Pullman responded by holding an internal referendum in June 1968 proposing the election to the permanent committee of representatives of heads of department, researchers and technicians. The proposal was adopted by 116 votes to 14 (7 spoiled votes and 2 blanks). This marked the beginning of the democratisation of the IBPC's management structures.

In 1959, the DGRST contributed to the renovation of the IBPC's buildings and financed the construction of high-tech biophysical equipment.

In 1959, the DGRST contributed to the renovation of the IBPC's buildings and financed the construction of high-tech biophysical equipment for the study of photosynthesis that Pierre Joliot had initiated when working in René Wurmser's laboratory. It also facilitated the arrival at the IBPC of Pierre Douzou, a biophysicist from the Armed Forces health service who was appointed head of a biospectroscopy department. Finally, the DGRST charged the IBPC with holding regular seminars on molecular biology, these replacing the informal cellular physiology club that had been meeting there since 1947. Its aim was to disseminate the new molecular approach within the community of French biologists. Jean Pierre Changeux, a young biologist who had begun his career at the IBPC before joining Jacques Monod's laboratory at the Institut Pasteur, was charged with organising these seminars.

Following the reorganisation initiated by Wurmser and then by Pullman, the IBPC thus had five departments. Four of these were in totally new disciplines: molecular biology (Marianne Grunberg-Manago and François Gros), theoretical biology (Bernard Pullman) and biospectroscopy (Pierre Douzou). The fifth had been a part of the IBPC since its foundation: the Department of Biophysics, headed by Sabine Filitti-Wurmser. The IBPC also had four laboratories. Two had been present since the beginning: macromolecular chemistry (Alma Doby-Duclaux) and physiology (Théophile Cahn, then Jacques Houget). Two others were for new disciplines: cellular chemistry (Donald Hayes) and photosynthesis (Pierre Joliot), the latter evolving into a department in 1974, thereby setting the seal on the IBPC's long tradition of research in this field.



TWICE APPOINTED RESEARCH MINISTER BY FRANCOIS MITTERAND, THE CRYSTALLOGRAPHER HUBERT CURIEN BECAME PRESIDENT OF THE EDMOND DE ROTHSCHILD FOUNDATION IN 1975

Progressive integration within the CNRS

Another challenge awaiting the new administrator Bernard Pullman was the management of the IBPC finances. Since the late 1950s the institute had been running at a loss, dipping into the Foundation's capital to make ends meet. What is more, it was a capital being eroded by inflation. At the same time, research was becoming increasingly expensive, especially the cost of major equipment. Pullman therefore set about looking for partners. He persuaded the Armed Forces health service to finance the con-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GALA DINNER IN 1977 TO MARK THE IBPC'S FORTIETH ANNIVERSARY ATTENDED BY THE ADMINISTRATOR BERNARD PULLMAN (TURNING HIS HEAD, WEARING GLASSES), ALBERTE PULLMAN (TO HIS LEFT), FRANCIS PERRIN (TO HER LEFT) AND RENE WURMSER (OPPOSITE, WITH GLASSES)

"The idea of bringing together biologists and physico-chemists was new 50 years ago. It is now widespread, much more widespread even than its implementation. Over and above the intentions and the statements, multidisciplinarity only bears fruit if the marriage between the disciplines is effectively consummated. If we have the weakness of thinking that, in this institute, the marriage has been fertile, we can also affirm without embarrassment that it was a happy one."
Hubert Curien, on the occasion of the ceremonies to mark the IBPC's 50th anniversary (1977).

struction of an Electron Paramagnetic Resonance device and to assign some of its staff to its operation, including Pierre Douzou. He also obtained major financing from the CNRS and INSERM.

Public research bodies had grown stronger under De Gaulle. In 1965, the CNRS launched its first associated laboratories, with the aim of giving new impetus to university research. The IBPC also benefited from this and its laboratories became units associated with the CNRS. This institutional transformation simply formalised what was already a reality as, since the late 1940s, the salaries of researchers had already been paid by the CNRS. The IBPC was also the victim of its success, its buildings designed for around 60 researchers now having to accommodate twice

THE BUILDING, IN 1983, OF LABORATORIES AND OFFICES LINKING THE TWO IBPC BUILDINGS

that number. It was therefore becoming essential to enlarge and modernise the IBPC. However, between 1968 and 1974 the institute experienced a serious financial crisis that was only resolved when the DGRST intervened directly to bail it out through the CNRS. The director general of the CNRS at that time was Hubert Curien who, in 1976, when Francis Perrin retired, became president of the Edmond de Rothschild Foundation. He was instrumental in negotiating a new stage in the coming together of the IBPC and the CNRS when, in 1978, the latter started to pay the salaries of staff previously paid by the Foundation.
The latter nevertheless continued to fund a part of the IBPC's activities. Baron Edmond de Rothschild, grandson of the founder, was

thus involved in organising the ceremonies for the institute's 50th anniversary, marked by an international conference on the "new frontiers in physics and chemistry". In 1982 he also financed the building modernisation programme. The walkway linking the two buildings was demolished and replaced by a two-storey building with laboratories and offices.

When he retired, in 1989, Bernard Pullman thus left behind him a modernised IBPC that was very active scientifically. But one that was facing seemingly insoluble financial difficulties. His successors who followed in rapid succession, including Claude Paoletti who died in 1992 shortly after being appointed administrator, did not have time to get to grips with the real issues. It therefore fell to Pierre Joliot, appointed IBPC administrator in 1994, to undertake the ultimate mission of negotiating a new administrative organisation that would make it possible to complete a modernisation that the Edmond de Rothschild Foundation could no longer finance on its own. In January 1997, the Edmond de Rothschild Foundation ceded the buildings to the CNRS for a period of 50 years. The IBPC thus became an inherent part of the CNRS for which it had been the testing ground in the 1930s. The

In January 1997, the Edmond de Rothschild Foundation ceded the buildings to the CNRS for a period of 50 years. The IBPC thus became an inherent part of the CNRS for which it had been the testing ground in the 1930s.

THE FIVE IBPC RESEARCHERS ALSO MEMBERS OF THE ACADEMIE DES SCIENCES, IN 1977. FROM LEFT TO RIGHT: PIERRE JOLIOT, BERNARD PULLMAN, MARIANE MANAGO, RENE WURMSER AND PIERRE DOUZOU

THE IBPC LABORATORIES
IN THE 1980s

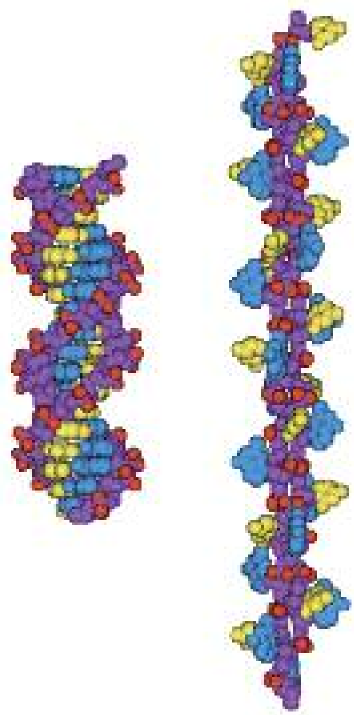
IBPC departments became research units of the CNRS coordinated within an Institut Fédératif de Recherche (IFR) with Pierre Joliot as the director. He was succeeded in this post by Jean Pierre Henry from January 2001 to December 2006 and then by Francis-André Wollman.

After molecular biology

"*Research on nucleic acids during the 1960s was like the tube at rush hour,*" commented Michael Michelson, the English biochemist who joined the IBPC in 1963 and was soon appointed head of the Department of Physical Biochemistry. It was during these early 1960s that molecular biology matured to the stage of being a "normal science" with the progressive building up of knowledge without any real conceptual breaks. With the beginnings of genetic engineering in the early 1970s it subsequently became the crucible for biotechnologies and their many applications in the field of medicine or agriculture. Remaining true to its fundamentalist tradition, the IBPC did not participate in these economic and technological developments. On the contrary, its research turned to an investigation of the *infra* and *meta* molecular phenomena at work in living organisms._

The IBPC's research turned to an investigation of the *infra* and *meta* molecular phenomena at work in living organisms.

Inframolecular phenomena, in the sense that the study of biochemical reactions that began in the 1930s with the isolation of the first enzymes turned towards an even more detailed level of organisation. *"At a time when in biology one swore by molecules alone (any reference to the molecular brought you consideration and money), I dreamed of mechanisms. This well oiled molecular machinery with so much potential had a future that very few researchers concerned themselves with,"* explained Pierre Douzou. The most ambitious progress in this field was made by Alberte and Bernard Pullman's group that was devoted to the application of quantum chemistry to biomolecules, following directly on from Jean Perrin who had transposed to biology his discoveries on Brownian motion. This very innovative approach opened the way to the development of theoretical methods for the elucidation of the conformation of macromolecules and of nucleic acids in particular. Similarly, the precise description of enzymatic reactions thanks to techniques for slowing down reactions at low temperatures developed by Pierre Douzou's group was at the origin of major progress in enzymology by making it possible to study metastable reaction intermediates. This approach consisting of looking *"under the bonnet"* of molecules, as Douzou expressed it, remains today the approach adopted by



STRUCTURE OF THE SAME DNA MOLECULE WITH TWO FORMS: ON THE LEFT, THE DOUBLE HELIX OF DNA-B, ON THE RIGHT, THE NEW STRUCTURE, KNOWN AS DNA-P, DEDUCED BY MOLECULAR MODELLING

DISSECTING THE TETRAD OF THE ALGAE CHLAMYDOMONAS REINHARDTII TO SEPARATE THE FOUR CELLS PRODUCED BY MEIOSIS WITH THE AIM OF CARRYING OUT A GENETIC ANALYSIS

GENETIC TRANSFORMATION OF THE GREEN UNICELLULAR ALGAE CHLAMYDOMONAS REINHARDTII BY MICRO-BOMBARDMENT WITH TUNGSTEN BALLS COATED IN DNA

laboratories of theoretical biochemistry and of the physico-chemical biology of membrane proteins as well as of the common crystallography department created at the initiative of Jean-Luc Popot and inaugurated in 2003 which is open to the neighbouring teams on the Montagne Sainte Geneviève.

Metamolecular phenomena, in the sense that, after a physico-chemical reductionism stage, it becomes necessary to return to the study of higher organisational levels, such as the organelles (ribosome, mitochondria, chloroplast, etc.), the micro-organism or the eukaryotic cell. The department headed by François Gros between 1963 and 1969 initiated this progressive return to physiology by developing the study of the various stages of the translation – interaction between codon and anticodon, elongation, start-up and termination

"If, reproducing the ideas of the liberal society, the researcher is given the ultimate aim of becoming a manager or boss at the head of a group of executives engaged in merciless competition, I do not see what could attract a young and talented student to our profession."
Pierre Joliot

factors – and their regulation with a view to cellular differentiation. After François Gros left to join the Institut de Biologie Cellulaire (now the Institut Jacques Monod), this approach was continued in the department headed by Marianne Manago and her pupils within the present laboratory of microbial genetic expression.

The same move in the direction of physiology is apparent in the study of membranes. After a period of very physical description started by Pierre Girard in the 1930s, interest shifted to questions of fluidity that are so important for intercellular communication: secretion, exocytosis, synapse construction. Similarly, the study of photosynthesis initiated by René Wurmser continued with Pierre Joliot in the 1950s and 1960s with the biophysical description of the mechanisms for converting luminous energy into chemical energy. During the 1970s, Joliot's pupils such as Pierre Bennoun and Francis-André Wollman extended this to the characterisation of biochemical compounds and the genes that synthesise them, incorporating as they did so the research tradition on cytoplasmic heredity started by Boris Ephrussi. The Photosynthesis Department subsequently turned to the *in vivo* study of isolated algae or chloroplasts. "*The in vivo approach had been ignored during the decades of necessary reductionism. It is now vital to return to it to understand the functioning of the photosynthesising device as a whole, this made possible by our spectroscopic devices that are 50 times more sensitive than those of other laboratories,*" remarked Pierre Joliot

Spanning three-quarters of a century, the history of the IBPC is marked by great continuity. The approaches and study methods may change but the themes remain. New disciplines, computer modelling in particular, have confirmed the rich potential of the interdisciplinary approach sought by its founders whose ambition to describe the mechanisms of life in physico-chemical terms is today shared by all biologists.

In 1980, the heirs of Nine Choucroun, fellow worker of Jean Perrin and IBPC researcher, founded an annual prize for doctors aged under 30 working in the field of physico-chemistry. The 5,000 euros prize is awarded by a jury set up at the IBPC's initiative.

Spanning three-quarters of a century, the history of the IBPC is marked by great continuity. The approaches and study methods may change but the themes remain.

1963-...
A free space

Bernard Pullman

1919-1996

A pioneer of quantum biochemistry

"Bernard Pullman, with the haughty air of a British officer, cared little for passing fads or what people would say. He advanced methodically and nothing and nobody was going to impede his progress. I often admired his understanding, his patience and, in a word, his diplomacy. I also came to appreciate his human qualities beneath the rigidity of the soldier he had been in the desert sands when our destiny was at stake."
Pierre Douzou

"I did not come to quantum chemistry out of a sense of vocation but through marriage," said Bernard Pullman. His life is indeed inseparable from that of his wife and lifetime colleague, Alberte, whom the young Polish student met while studying at the Sorbonne Faculty of Science in 1938, shortly after coming to France. But war was to separate the couple who were engaged to be married. Bernard joined the Free French Forces in London and participated in campaigns in Africa and Syria as an engineering officer. Alberte remained in France where she worked as a calculator at the Institut Poincaré while starting work at the Institut du radium on her thesis that she submitted in 1946. Entitled *"Contribution to the study of the electronic structure of organic molecules. Special study of carcinogenic hydrocarbons,"* it was the first thesis in the field of quantum chemistry to be submitted in France. Two years later Bernard Pullman submitted his physics doctoral thesis on the rules governing the effects of substitution on polycyclic aromatic hydrocarbons.

At the Institut du radium the couple went on to deepen their research on forecasting the carcinogenic character of a molecule on the basis of its structure. In 1952 they published *The electronic theories of organic chemistry* with a preface by Louis de Broglie. Two years later Bernard Pullman was appointed professor of quantum chemistry at the Sorbonne. He joined the IBPC in 1958, heading the Department of Theoretical Biochemistry.

In 1963, Alberte and Bernard Pullman published *Quantum Biochemistry*. This came to be regarded as a reference. To the quantum chemistry specialists, it revealed the problems posed by the structure of biological macromolecules, a fast growing field of research at the time. To the biochemists, it showed how quantum mechanics could help resolve problems of the structure and action of biological molecules. The advent of computers – Pullman's department at the IBPC acquired its first IBM in 1961 – changed the situation entirely. For his thesis, Alberte Pullman had to draw on tracing paper the 649 mesomer forms of naphtacene, incredibly painstaking work that obliged him to consider the molecule as isolated. With the increased calculating power it became possible to study molecules in their environment, and the hydration of proteins, nucleic acids and other biological macromolecules in particular. *"The beginning of our work in biochemistry and quantum biophysics came shortly after the birth of molecular biology. It was the discovery of the structure of nucleic acids that had a decisive effect on the direction of our research. It seemed obvious to me that, by becoming molecular, biology necessarily opened its doors to the entry of quantum theories as the properties of molecules are determined largely by the distribution of their electronic clouds for the study of which ondulatory mechanics is recommended,"* he explained. Resolutely theoretical, Pullman's work also influenced pharmacology following the symposiums co-organised by Bernard Pullman and Ernst Bergmann in Jerusalem between 1967 and 1995.

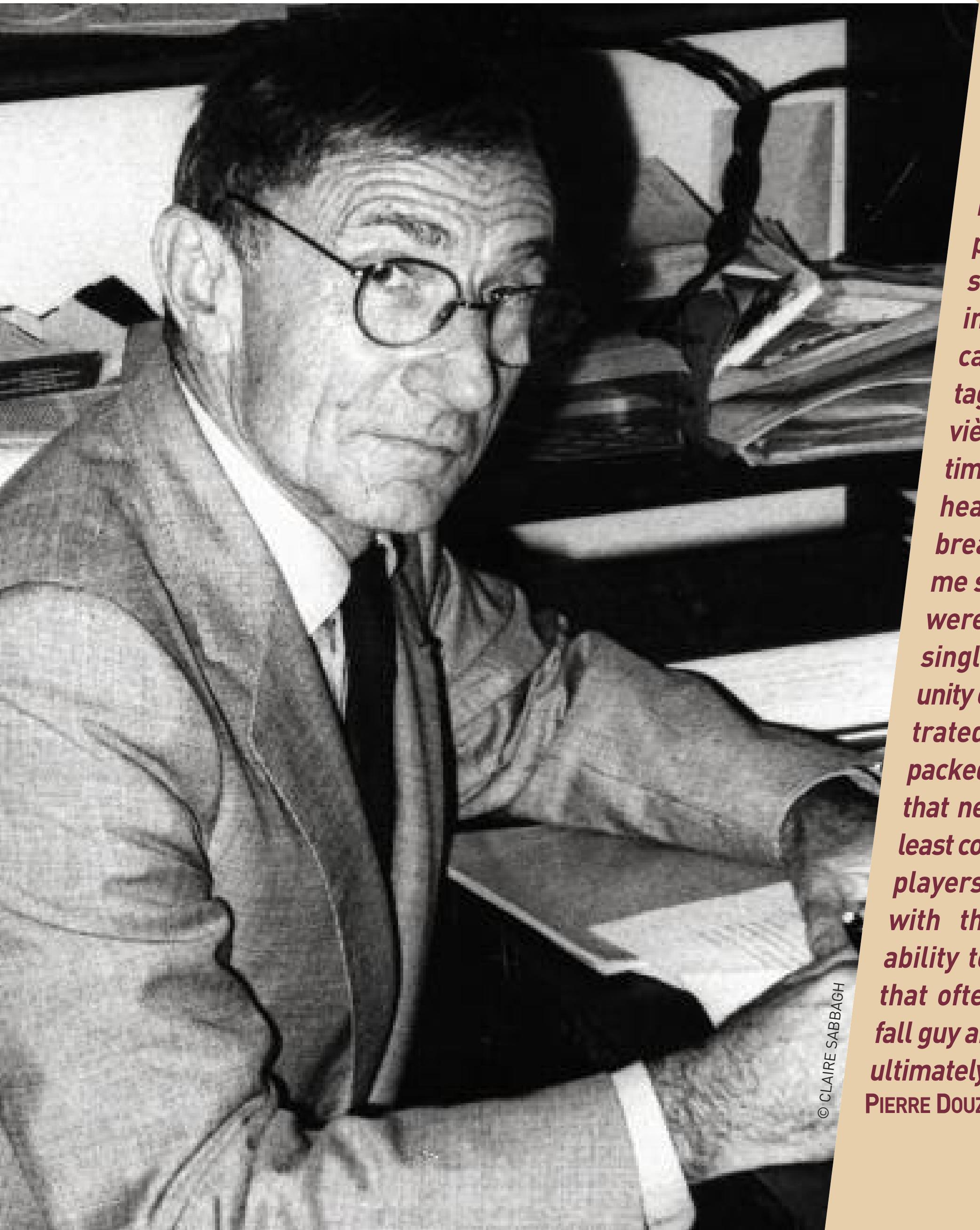
While pursuing a career as researcher recognised by his appointment to many institutions – including the Académie des Sciences in 1979 - Pullman was the administrator at the IBPC between 1963 and 1989. On his retirement he set to work on a vast study of the history of the atom since Antiquity. ◄

1963-...
A free space

Pierre Douzou

1926-2000

The inventor of cryo-enzymology



"My career conformed to the famous rule of three unities. Firstly, unity of place: I remained seated on the inspirational volcano of the Montagne Sainte Geneviève. Then unit of time: 20 years of rehearsals without breaks and that to me seemed like they were packed into a single day. Finally, unity of action: concentrated in a test tube packed full of intrigues that never came to the least conclusion. With as players the molecules with their marvellous ability to improvise and that often made me the fall guy and of which I was ultimately the prisoner."

Pierre Douzou

Son of a glove maker from Millau, Pierre Douzou joined the Armed Forces health service in 1947, seeing it as the only way of financing his studies. After qualifying as a pharmacist he was sent to work at the Val de Grâce military hospital. His army work nevertheless left him time to attend the Institut du radium where he worked on the effects of radiations on water molecules.

He submitted a physics thesis in 1958 and two years later joined the CNRS to work with Charles Sadron at the Museum on biological polymers. But without leaving the army. *"The most difficult thing was to conform to the image that society expected of the military man, by 'playing dumb' in your own circles and advertising the fact outside of it. [...] Pursuing simultaneously two vocations that were by definition opposed to one another, the vocation of researcher supposing intelligence, was an exciting but difficult exercise [because] there could be no confusing of roles in either of the two duly compartmentalised circles."*

In the early 1960s he worked with Max Delbrück on the use of ultraviolet rays for inducing mutations. A great experimenter who liked to build and regulate his own devices, he developed new spectroscopic methods for analysing macromolecules and was passionately interested in molecular phototransformations. His talents as a biophysicist were noticed by Bernard Pullman who in 1965 invited him to head a department at the IBPC. His research concentrated on describing transient molecular intermediates at the time of enzymatic reactions. He tried obstinately to slow their kinetics by reducing the ambient temperature.

For many years he endeavoured to develop antifreeze solvents, lowering the freezing point of reactions without distorting the molecules. *"The profession of researcher involves more transpiration than inspiration. The respective percentages of these two requirements of course vary between individuals, but the inspired researcher must be as wary of facility as of the plague. Facility is to the researcher what boredom was to the soldier: the avowed and mortal enemy."*

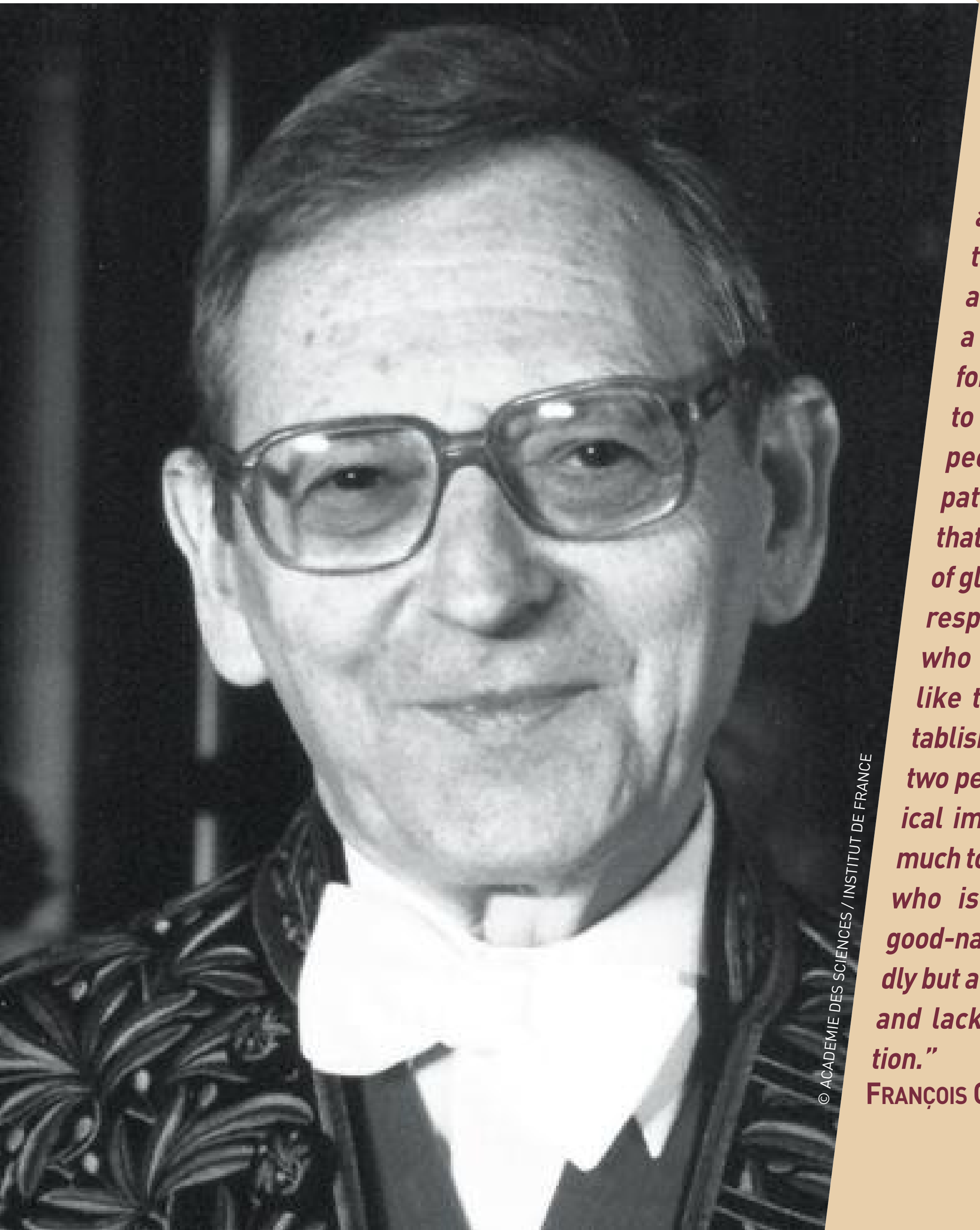
In 1970 he finally succeeded, by a series of cooling and heating processes, in "slicing", to use his expression, the breakdown of oxygenated water by means of peroxydase action, i.e by isolating the reactive intermediates. The following year Pierre Douzou abandoned his military career to head an Inserm unit at the IBPC and also a laboratory at the Ecole Pratique des Hautes Etudes. He was elected to the Académie des Sciences in 1979. While continuing to develop cryo-enzymology he explored the applications of freezing methods, especially in agronomy, which led to his presidency of the National Institute for Agronomic Research between 1989 and 1991. ◀

1963-...
A free space

François Gros

Born in 1925

One of the discoverers of messenger RNA



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"I inherited from my mother a certain happy-go-lucky attitude, a heightened sensibility, a certain fatalism, a great attraction for those referred to as the 'common people'. As to the paternal instinct, that made me a kind of glutton for work, a respecter of rules who does not much like to upset the established order. These two perfectly antinomical impregnations did much to shape someone who is both basically good-natured and friendly but also at times rigid and lacking in imagination."

François Gros

When he joined the IBPC in 1963 to set up the Department of Cellular Physiology, François Gros was already a renowned molecular biologist. His first stay in the United States, in 1953, had been a *"cultural shock"* for someone who had known only the rigidity of the teaching at the Sorbonne, where he had obtained his science degree in 1946, and the ill-equipped laboratories at the Institut Pasteur where he had presented his thesis the previous year. At the University of Indiana and then at the Rockefeller Institute he discovered the biochemistry of nucleic acids. On his return to the Institut Pasteur he showed, at Jacques Monod's laboratory, that the blocking of protein synthesis in *Escherichia coli* is accompanied by an accumulation of ribonucleic acids. This was the first indirect argument in support of the idea that RNAs act as intermediary between DNA and proteins. With the Japanese researcher Shiro Naono he went on to demonstrate that 5 fluorouracil, an uracil analogue that is known to be characteristic of RNAs, inhibits protein synthesis. This provided the second indirect argument. Shortly afterwards, when working at James Watson's laboratory at Harvard University, he used the phosphorous 32 radioactive marking of phosphorous 32 to identify a rapidly renewable RNA population. Published in *Nature* in 1961, this experiment, which is now taught routinely to students of molecular biology, provides one of the first indirect arguments to support the existence of messenger RNA.

His department at the IBPC was concerned with the mechanisms for regulating the gene expression. He isolated the factors involved in starting up the translation and that permit the positioning of ribosomes at the end of the RNA chain. He showed that the induction of the expression of certain bacterial genes is explained by the removal of the permanent inhibition of their transcription. With Philippe Kourilsky he studied the early stages in the transcription of bacteriophage genes – a model he established at the IBPC – following the induction of bacterial lysis. A young chemist from Israel, Moshe Yaniv, started the sequencing of transfer RNA. *"Sometimes I say to myself that I was more of a competent impresario than an ideas man,"* said François Gros with a smile. *"In the late 1960s my laboratory was like an open house. It was easy to enter due to my (genetic) inability to say 'no' to anyone who turned up to offer their services. This meant that the work spaces became increasingly cramped. The place was packed! Although this promiscuity was all very friendly, the limited space necessarily gave rise to certain conflicts when competition for 'territory', equipment or biological reagents became too fierce."*

Feeling cramped at the IBPC, François Gros left in 1968 for the new Institut de Biologie moléculaire that had just started up at the Faculty of Science, where he was appointed professor. Four years later he was appointed to the Collège de France. But the 1970s saw him leave, without regret, *"the world of labour of researchers surrounded by other researchers, like me busy with their pipettes, their flasks, their reagents and their machines"* to take up senior posts, first as director of the Institut Pasteur from 1976 to 1981, then as scientific advisor to the prime minister until 1985, and finally as permanent secretary at the Académie des Sciences between 1991 and 2000. He never severed his connections with the IBPC, however, and remained there until 1997 as a member of the board of directors. ◄

1963-...
A free space

Marianne Manago

Born in 1921

The first woman president of the Académie des Sciences

"I think that the fact of being a woman worked rather to my advantage. My discovery of PNPase came just at the right time, when people were beginning to understand the importance of women. That is how I came to be chosen to teach at Harvard University, specifically because I was a woman and this may have perhaps played a part in other presidencies I exercised."

MARIANNE MANAGO

Architect? Literary critic? Or archaeologist? Obtaining her baccalaureate at the age of 17, Marianne Manago envisaged all these professions before discovering research. *"When I was a girl I never thought at all in terms of 'making a career' but rather of finding what interested me. My parents were Russian immigrants, I had the feeling that you could never predict the future and I did not worry about it,"* she explains. It was during the Nazi occupation when she acted as a replacement teacher while studying for her science degree that she discovered biology. At the Roscoff marine station first of all. Then at the IBPC, which she first entered in 1942. Five years later, it was there that she presented her state thesis on the action of oxygen on strict anaerobices, having worked on it in Eugene Aubel's Department of Biochemistry.

Her post-doctoral period in the United States marked a turning point. It was while working in Severo Ochoa's laboratory that, in 1954, she isolated PNPase, an enzyme that catalyses the formation of ribonucleic acid polymers. For the first time, the *in vitro* synthesising of synthetic polynucleotides was possible, a development that permitted the deciphering of genetic codes. Ochoa was awarded the Nobel Prize for Physiology or Medicine for this discovery. Does she feel any bitterness at not having herself been a laureate? *"Not really. First of all, I was young. Also, everybody knew my contribution to this research."*

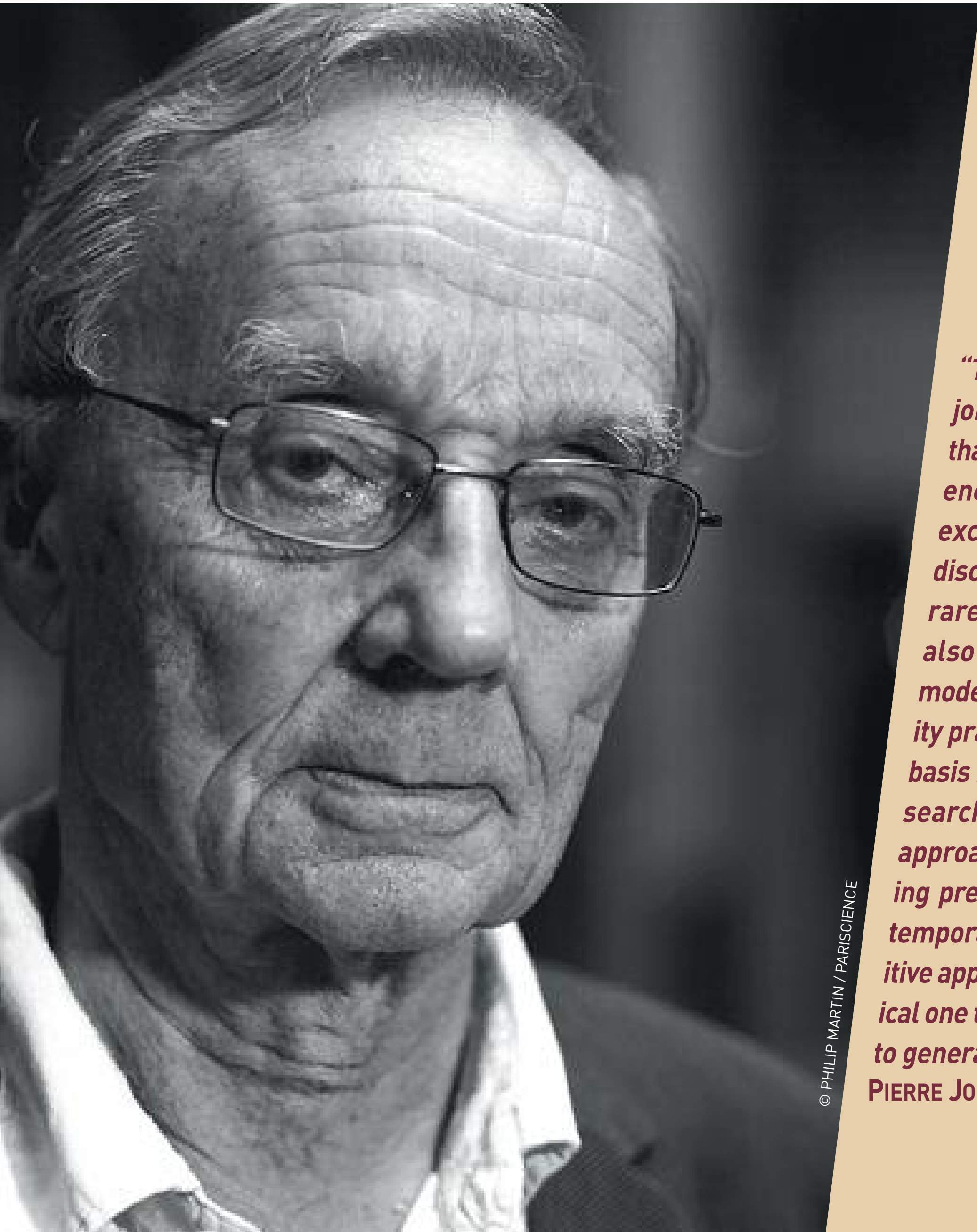
The Department of Biochemistry she headed at the IBPC from 1959 played a leading role in the rise of molecular biology. An entire generation of French molecular biologists, including Antoine Danchin, Mathias Springer and Richard Buckingham, trained there. *"Her office was open to everyone. A strange office moreover, with its chaotic piles of manuscripts in the process of being written, laboratory notes, sundry correspondence, bills and order forms in an inextricable disorder, and taking pride of place as if in an art gallery the many works by her husband, a painter of the naïve school. The visitor was struck by the constant buzz of voices and machines, the continuous coming and going of researchers seeking advice or wanting to show the results of experiments,"* remembers François Gros.

As a sign of her international renown, Marianne Manago was elected to the US National Academy of Science in 1982 and served as president of the International Union of Biochemistry from 1985 until 1988. In 1985 she became president of the Académie des Sciences, the first woman to hold the post in the 328 years of its history. ◀

Pierre Joliot

Born in 1932

The co-discoverer of the photosynthetic mechanism of oxygen emission



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"The beauty of our job lies in the fact that progress in science does not rest exclusively on the discoveries of a few rare geniuses, but also on the more modest creative activity practiced on a daily basis by very many researchers. A creative approach involves giving preference, at least temporarily, to an intuitive approach over a logical one that is rarely able to generate new ideas."

PIERRE JOLIOT

"I occupied every possible post at the IBPC, from an unpaid intern to director," says Pierre Joliot with a smile. This long career began in 1953 when the young biology student entered the office of René Wurmser, then head of the institute's Department of Biophysics. He left it with a white coat and a subject for a thesis on photosynthesis. At that time it was unexplored territory with as starting point Wurmser's affirmation that the primordial stage is the breakdown of water under the effect of light. During his thesis, Joliot developed original methods for the amperometric detection of oxygen that made it possible to correlate photosynthetic oxygen production with the properties of excitation light. After a break for military service during which he served as an officer in Algeria, he returned to his research with a passion. *"My principal contribution is to have shown in the late 1960s that plants can count to four! In other words, that four electrons must be removed in succession from the water molecule by photons for an oxygen molecule to be released."* It is a phenomenon known today as the "Kok-Joliot model". *"I carried out decisive experiments and my colleague, friend and rival Bessel Kok provided the correct interpretation. It is indeed the proof that a certain ethics is possible within international competition."*

This discovery earned him sudden international recognition: election to the National Academy of Science in 1979, to the Collège de France in 1981, and then to the Académie des Sciences the following year that also saw him awarded the médaille d'or from the CNRS. "*It was just as I was receiving this international recognition that I realised I was losing my originality. That is why I regularly change my field of investigation so as to once again confront my ignorance."* Within the Department of Photosynthesis that he headed at the IBPC he continued to diversify his biophysical methods of approach, designing new spectrophotometers with impulse detection for the *in vivo* study of photosynthesis, regarded as an energy conversion system integrated in its cellular environment. Going against the trend for increasingly reductionist approaches, he thus developed the approach of the physiologist. With André Verméglio and Jérôme Lavergne he introduced the concept of supramolecular compartmentalisation, today the focus of attention for a growing community. He incorporated his own research in a multidisciplinary study of photosynthesis by gathering around him a small number of colleagues, such as Pierre Bennoun, Bruce Diner and Francis-André Wollman, who introduced progressively biochemical, ultrastructural and genetic approaches to the study of photosynthetic proteins.

Despite his institutional responsibilities at the CNRS, the Ecole Normale or the IBPC - where, between 1994 and 1997, he was the last administrator and then the first director – Joliot continued to pursue his own research, accompanied by his wife Anne. *"The only time I stopped conducting experiments was in 1985 and 1986 when I was scientific advisor to the prime minister. I endeavoured, nevertheless, to come and lunch at the IBPC as often as possible to draw sustenance from the contact with researchers."* After he retired he continued to carry out his personal experiments on the most varied photosynthetic organisms. *"It is like a video game. You carry out experimentation, reflection and interpretation in parallel. It is this rapid activity of the mind, this research in real time, that I like in biophysics."* ◄

BIBLIOGRAPHY

Jacques Boyer, "Le nouvel institut de biologie physico-chimique de Paris," *La Nature*, May 1931, pp 398-400

Richard M. Burian, Jean Gayon and Doris T. Zallen, "The Singular Fate of Genetics in the History of French Biology, 1900-1940," *Journal of the History of Biology* (1988), 31 : 357-402

Micheline Charpentier-Morize, *Perrin. Savant et homme politique*, Belin, 1997

Antoine Danchin, "Physique, chimie, biologie. Un demi-siècle d'interaction 1927-1977," in *Fondation Edmond de Rothschild, Cinquantième anniversaire de l'IBPC*, Paris, 1977

Claude Debru, "La photosynthèse : Victor Henri, Otto Warburg, René Wurmser, in *Les Sciences biologiques et médicales en France, 1920-1950*, CNRS Éditions, 1994

Pierre Douzou, *Vous cherchez quoi au juste ?*, Odile Jacob, 1994

Diane Dosso, *Louis Rapkine (1904-1948) et la mobilisation scientifique de la France Libre*, doctoral thesis, Université Paris 7, 1998

Hélène de Hauss, *La vie quotidienne à l'IBPC de 1959 à 1983*, manuscript kept at the IBPC library.

Jean-Paul Gaudillière, *Biologie moléculaire et biologistes dans les années soixante : La naissance d'une discipline. Le cas français*, doctoral thesis, Université Paris VII, 1991

François Gros, *Mémoires scientifiques. Un demi siècle de biologie*, Odile Jacob, 2003

François Jacob, *La Statue intérieure*, Odile Jacob, 1987

Pierre Joliot, *La recherche, passionnément*, Odile Jacob, 2001

Edgar Lederer, *Itinéraire d'un biochimiste français*, Publibook, 2007

Denise Lévy-Astruc, *Histoire officielle, officieuse et marginale de l'IBPC, d'avril 1927 à décembre 1958*, manuscript kept at the IBPC library

André Mayer, "L'institut de biologie physicochimique," *Paris médical*, 21 February 1931

Michel Morange, *Histoire de la biologie moléculaire*, La Découverte, 2004

Michel Morange, "L'Institut de biologie physico-chimique de sa fondation à l'entrée dans l'ère moléculaire," *La revue pour l'histoire du CNRS,* 2002 accessible on-line http://histoire-cnrs.revues.org/538

Jean-François Picard, *La République des savants. La recherche française et le CNRS*, Flammarion, 1990

Jean-François Picard, *La fondation Rockefeller et la recherche médicale*, PUF, 1999

Jean-François Picard, *Témoignages pour l'histoire du CNRS* http://picardp1.ivry.cnrs.fr/memoirecnrs.html

Jean-François Picard, *L'histoire de la génétique à Gif-sur-Yvette racontée par ses acteurs*,
http://picardp1.mouchez.cnrs.fr/histoire_de_la_genetique.html

Marian Schmidt, *Hommes de sciences. 28 portraits*, Hermann, 1990

Yvonne Khouvine, "The institute of physico-chemical biology in Paris," *Journal of Chemical Education*, May 1930, pp 1051-1057.

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