noder (1910–1976)

100 years ago, was one of the main founders of molecular biology. A quotation of Roger Stanier seems to advance to the topic of this meeting on “Chance and necessity in evolution,” dedicated to the works of Jacques Monod in his new Department, around 1958. The PaJaMo experiment (from Pardee et al. 1959.).

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In memoriam: Jacques Monod (1910–1976)

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onod, born 100 years ago, was one of the main figures of molecular biology. A quotation of Roger Stanier (Stanier 1977) about Monod is one of the most famous: “Jacques Monod was one of the great scientists of the twentieth century, will always have an honored place among the second major revolution in the history of biology, and will be remembered as the father of molecular biology. Monod’s scientific achievements and the connections between the two revolutions have had a profound influence on the progress of molecular biology.” (Stanier 1977).

Jacques Monod’s mother, Charlotte Todd Monod, was the daughter of a Scottish pastor, who had emigrated to the United States, was an American. In the Monod family, science was a tradition. As a boy, Jacques learnt the cello that he had wanted to play even later.

After completing his secondary education in 1929, Monod went to Paris in 1928 to study biology at the Sorbonne (the Paris University). In 1931, he obtained a bachelor’s degree (Licence) in science. At the age of 17, he had created a Bach choral group, “La cantate” and had even attempted for a time to make a career as a composer. In 1932, he made his first research experience, after having been awarded a grant, in Strasbourg in the laboratory of Edouard Chatton, where he worked on ciliates. In 1932, at the Sorbonne in the “Laboratory of organized beings” he continued research on ciliates, with more or less success. His true initiation to biology started when he met at the marine biology station in Roscoff: Georges Tessier, from whom he learnt genetics, André Lwoff, and Boris Ephrussi, who introduced him into the world of microbiology and genetics. Boris Ephrussi, who taught him the importance of the molecular descriptions of living beings (Monod 1972).

After several research projects on different organisms, Monod decided in 1934 to join a scientific expedition on Commander Charcot’s boat, the “Pourquoi-Pas?” in order to study the natural history of this region (figure 1). But first, however, he was about to take part in a new expedition organized by Boris Ephrussi. But Boris Ephrussi, who was to spend a year in Washington, had invited Jacques Monod to go off with him to learn...
Monod was born in Paris on February 9, 1910. At the years of the First World War, the Monod family, of Swiss Huguenot origin, fled to Switzerland to their cousins. In 1918, they moved to Cannes where they was to remain until 1928. Lucien Monod, was a painter, a rather audacious choice for some puritanical family that counted among its members, civil servants, pastors, and doctors (fig. 1).

he obtained for him a Rockefeller grant. Monod set off for Pasadena. That same year, Pourquoi pas? was shipwrecked in a storm off the coast, and its entire crew perished. Genetics saved Monod. Much to the regret of Ephrussi, of his time directing orchestras and choral groups, he got to the point where he was about to sign as head of the local orchestra. Even upon return...
to hesitate between music and science. He worked as an assistant, and music. He played a quartet and continued to direct the Bach choral in 1937, still at the Sorbonne, Jacques Monod worked on bacterial growth using *Escherichia coli*. From the very beginning of his research, he made an important discovery, the phenomenon of “diauxy,” growth observed when the medium contained a two sugars, one of them being glucose and the other lactose or maltose, for instance. His interpretation of diauxic growth phenomenon was that glucose (sugar used by the bacterium) inhibited the formation of the enzyme necessary for assimilating the second sugar (Monod 1941). The concept that would later come to be known as “induction time” of the enzyme was discovered.

Jacques Monod obtained his science doctorate in 1942, while World War II was devastating France was occupied by the Germans. The Germans occupied the underground movement. At the beginning of the war, he joined one of the most active armed resistance groups, and later he became Chief of the national stage representing the resistance in which his three predecessors had disappeared. Jacques Monod, several days before the arrival of the Allied forces into Paris, drafted the appeal to Parisians to mount the barricades. And later, following the liberation of Paris, he joined the First Army as a member of General de Lattre de Tassigny (fig. 3). It was discovered that Jacques Monod first entered into contact with American officers and was able to read some scientific publications. This was how he discovered the scientific library of the US army, the article on the nature of bacterial mutations (Luria and Delbrück 1943), and the historic publication by Avery, MacLeod, and McCarty, who identified the transforming principle as DNA (Avery et al. 1944).

Once the war ended, Jacques Monod returned to Paris, this time as head of a laboratory in André Lwoff’s department at the Institut Pasteur. This department was located in a veritable attic, where Monod’s working space provided, as Melvin Cohn recalls, in an entry in the Adaptive Enzyme’s College of Cohn, Pollock, Spiegelman, and Stanier (Cohn et al. 1949).

From the very beginning, Monod was interested in the study of bacterial growth, which was already a part of his doctoral thesis. Later, considering bacterial growth as a method for the study of bacterial population biochemistry, he defined its quantitative analysis as growth phases, growth rates, and growth yields (Monod 1949). He also made an important and theoretical contribution to the methodological study of bacterial growth. He defined and utilized a constant rate in a chemical and physical state (Monod 1950). The experimental potential of this method are wide; besides the possibility of studying microbial growth rates without modifying either the composition of the medium or the temperature, it provides a means, for example, today, to select specific mutants. Melvin Cohn described the birth of the first device, called “bactoglider,” for continuous cultures. For a given experiment

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"Portrait of J. Monod by his father, Lucien Monod, 1940."
small rooms with wooden workbenches, which he shared with his technician Madeleine Jolit and an chemist, Annamaria Torriani. Gradually, the tiny lab expanded with the arrival of Alvin Pappenheimer udent, Melvin Cohn, an immunologist, as well Cohen-Bazire and David Hogness. Within this up, Jacques Monod devoted most of his time to enzymatic adaptation,” choosing as a model idase. One of the questions that had to be first was whether the enzyme was made de novo after or from precursor subunits, as postulated earlier. the first time isotope labeling, they showed that te was made from amino acids de novo after in a maximum rate (Hogness et al. 1955). This led formulate a new parameter, differential rate of nthesis, ΔZ/ΔB, called later “Monod plot” (Z stays :osidase and B for bacteria). Next, they decided to a number of lactose analogs; some of them (i.e., galactosides) turned out to be excellent inducers, ring hydrolyzed by the enzyme; they were called inducers. Others were shown to be substrates ny inducing activity. As Melvin Cohn noted, ence of nonsubstrate inducers had a profound cal impact, for, like Ionesco, Monod had created of absurd. A bacterium growing on succinate was useless enzyme, β-galactosidase, in response ate it could not metabolize” (Cohn 1976). Monod illusion and his immediate answer was: “Each of onquests is a victory of the absurd.” Nevertheless, inducers became important tools in biological around this period that Monod decided to other Lamarckian term “enzymatic adaptation” id use “induced enzyme synthesis,” which was to dilute the bacterial cultures every hour growing continuously. He then wrote: “I de ning to simply set up an automatic system for removal of culture. Since I had a liter of culture diluted, with a liter of medium every hour, I simply per hour of fresh medium and siphoned off a per hour continuously. To my surprise, the back to keep up and the density of the culture fell. I ain’t I could not feed more than 690 ml/hour output with this paradox, obviously upset, Jac with me and asked if I had any idea why I had more than 690 ml/hour when I expected it. ’T may sound wild to you, Jacques, but I think ered that bacteria, like men, have a biological He smiled patiently and said, ‘You have disco In 2 = 0.69. Think about that’. The next day had the detailed theory of continuous cult much the thing the bactogène (Cohn 1976).

To better understand the nature of enzymes Jacques Monod realized that, first of all, he study the relationships between gene and 1946 on, he isolated lactose− and lactose E. coli. Later, among a number of mutants isolated, several seemed to be lactose− and to synthesize β-galactosidase. The explainatio terious mutants, referred to as “cryptic,” was such mutants were lacking a specific protein, type bacteria, had the ability to accumulate. This protein was named “galactoside perme gene, which commanded it, was called “y, the gene for β-galactosidase, referred to as” et al. 1956). The two proteins were induced by the β-galactosides. A new category a “pump” responsible for accumulation of so
Monod in his new Department, around 1958.

...teria, was born. Several years later, a galactosidase (coded by the $a$ gene) and induced at the as $\beta$-galactosidase and permease, was discovered facilitating later studies on the genetic determination (Zabin et al. 1962). The physiological transacytase remains unknown to this day.

Galactosidase and acetylase led to any important discovery. Mutants were found in three proteins, $\beta$-galactosidase, permease, and acetylase were simultaneously constitutive, that is, synthesized in the absence of inducer. The constitutive named a genetic factor, which could exist in two corresponding to inducibility and $i$ corresponding activity. Genetic analysis revealed that the $i$ gene is d to the $z$, $y$, and $a$ genes (Jacob and Monod 1959). Jacques Monod was made head of a new department called Cellular Biochemistry and at about the same time François Jacob and Elie Wollman, in Lwoff’s elucidated the mechanisms of bacterial conjugation transfer, thus providing new and powerful tools to the problem of genetic regulation (Jacob and Wollman 1956). This was undertaken by Jacques and François Jacob during a long and fruitful collaboration was carried out with the well-known success.

A crucial experiment, which marked the beginning of a new era later to become known as molecular biology, was carried out by Jacques Monod, François Jacob, and Arthur Pardee, who was a sabbatical year in Paris in Monod’s laboratory at Pasteur. This experiment involved measuring the $f$ $\beta$-galactosidase in zygotes resulting from the $z$ of male bacteria carrying the $z^{+}$ and $i^{+}$ genes, carrying $z^{-}$ and $i^{-}$ genes. In the absence of the parents are able to synthesize the enzyme because of the absence of inducer and the cause of a defective $z$ gene. Crossing the two strains, enzyme synthesis began within a few minutes. If the $z^{+}$ gene entered the recipient, but after the enzyme synthesis stopped. When inducer was added, enzyme synthesis resumed, suggesting that the $i^{+}$ gene was becoming gradually expressed as z became phenotypically inducible (fig. 5). This experiment remains a landmark and is generally referred to as one of the three scientists who performed it: PaJaMo, scientific jargon, just simply “pajama” (Pardee 1959).

The PaJaMo experiment was the point of departure for proposing a model of negative regulation: the inducer produces a substance called “repressor” that blocks expression of the $z$ gene. A previous hypothesis that this was achieved by provoking enzyme synthesis had to be abandoned; it acts by “inhibiting an inhibitor” of enzyme synthesis.

Two other concepts of utmost importance came from those experiments: that of messenger RNA and the operon. The model of genetic regulation (the operon model) proposed by Jacques Monod and François Jacob, in a series of articles that have since been summed up as follows (Jacob and Monod 1961).

First of all, they defined two categories of the structural and regulator genes. Structural genes ($l$ genes) govern the capacity to synthesize $\beta$-galactosidase, permease, and transacytase; $lac$ is a regulator gene for a regulator protein, the repressor. The structural genes are found in a single genetic entity, and Monod called the “operon.” According to the model, the repressor acts upon a single receptor site named the “operator.” The repressor–operator complex blocks expression of structural genes. The repressor inactivated in the presence of the inducer, allowing the proteins of the operon are synthesized.

Fig. 5.—The PaJaMo experiment (from Pardee et al. 1956).
transcription, which is the first step, operon genes in a single messenger RNA with a short life span. In the second step, this messenger RNA is translated into proteins via the ribosomes (fig. 6).

Beginning of the 1960s, the molecular mechanisms—inducer and repressor-operator recognition—were already resolved. However, the isolation of the repressor—such interactions account for a great number of allosteric interactions during evolution opened the possibility of a great number of possible regulations. As for the bacterial regulatory theory was substantial, virtually nothing was known at the time.

The prion theory, which implies a transmission of a conformational change between identical protein molecules across species, was inspired from the allosteric concept.

As Monod pointed out, the “invention” of allosteric theory was substantial, virtually nothing was known at the time. Boris Magasanik pointed out to Jacques Monod a prion that is the product of an allosteric interaction during evolution opened the possibility of a great number of possible regulations. As for the bacterial regulatory theory was substantial, virtually nothing was known at the time. Boris Magasanik pointed out to Jacques Monod a prion that is the product of an allosteric interaction.

The concepts that Jacques Monod developed in the lac operon model, formulated 50 years ago, were the most important elements of the biotechnical revolution and proved to be correct.
Pinpoints Minimum Requirements for Auxin Distribution during Fruit Opening

A Vroomans · Samantha Fox · Athanasius F. M. Marée
[Nobel prize for André Lwoff, Jacques Monod and François Jacob in 1965 for discoveries on the geneti...]

July 1969 · Wiadomości lekarskie (Warsaw, Poland: 1960)

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**Article**

Jacques Monod, 1910-1976: His life, his work and his commitments

March 2010 · Research in Microbiology

Agnes Ullmann

Even today, the concepts developed by Jacques Monod during the course of his career remain at the core of modern biology. Looking back, Jacques Monod stands out as one of the giants who most strongly marked twentieth century science. He was endowed with intelligence, rigor, creativity, a relentless sense of deductive reasoning and a love of scientific elegance. His name will remain intimately ... [Show full abstract]
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