Obituary

JACQUES MONOD, 1910-1976

Everything existing in the Universe is the fruit of chance and of necessity.

Democritus

With the death of Jacques Monod, one of the great scientists of the twentieth century has passed from the scene. He will always have an honoured place among the leaders of the second major revolution in the history of biology, which occurred almost exactly 100 years after the Darwinian one. Few of the protagonists were more conscious than Monod of the connections between the two revolutions, of the way in which he and his contemporaries had extended and deepened Darwin's concepts. His achievement thus far transcends the confines of our discipline, even though his specific contributions to microbiology were of the highest order.

Nature and nurture

The Monods, Swiss by origin and Protestant by religious conviction, have had an honourable place in the life of France for many generations; the family tree is heavily laden with pastors and professors, physicians and public servants. However, the father of Jacques, Lucien Monod, abandoned these well-trodden family paths to become a professional artist and art historian. He was also a music lover, and a man of great erudition; indeed, his admiration for the works of Darwin first aroused his son's interest in biology. Lucien Monod had abandoned the family faith; he was a free-thinker, imbued like many of his liberal contemporaries with a positivist belief in the joint progress of science and society. He married an American, the former Sharlie Todd MacGregor. Mme Lucien Monod's father was born in Scotland, a child of the manse, and emigrated to the States as a young man; her mother belonged to an old American family, established in New England since 1632. Jacques Monod accordingly had a Calvinist and puritan family background on the maternal as well as the paternal side.

Jacques Monod's childhood and youth were largely spent in Provence, since his parents moved from Paris to the south of France when he was seven. He was a third child, much younger than his brother and sister; both his parents were over 40 when he was born. Clos Saint Jacques, the family home in Cannes, provided an exceptionally favourable and protective environment for the development of a sensitive child who early displayed both intellectual and artistic gifts. Thanks to his mixed heritage, he grew up completely bilingual: he thought, talked and wrote with equal facility and distinction in French and English. An attack of poliomyelitis in childhood left him with one weak leg, and a slight limp. This did not prevent him from becoming a good rock climber and mountaineer. Later in life, he was an able and enthusiastic yachtsman. As a boy, Jacques learnt the cello, and participated in the chamber music which was a regular feature of life at Clos Saint Jacques. In Paris, he created a Bach choir and was seriously tempted for a time to make a career as a conductor.

Clos Saint Jacques always remained a precious refuge. In the last difficult years, when he was exhausted by illness and struggling to keep the Pasteur Institute afloat, he returned there whenever he could in search of spiritual and physical refreshment; and it was there that he died.

The making of a biologist

After completing his secondary education in Cannes, Monod came to Paris in 1928 to study at the Sorbonne. Three years of courses in general chemistry, general biology, zoology and geology made him a *Licencié ès Sciences*, but little else. Only somewhat later did he realize that most of the instruction he had received was decades out of date. His real scientific education was informal and was obtained from a group of slightly older men, most of

whom were then unconnected with the university. At the Marine Biological Laboratory in Roscoff, where many students from Paris went during the summer, he met four scientists, each of whom revealed to him a different facet of biology. As he later put it, he owed 'to Georges Teissier the taste for quantitative descriptions, to André Lwoff the initiation to the powers of microbiology, to Boris Ephrussi the discovery of physiological genetics, to Louis Rapkine the idea that only chemical and molecular descriptions can give a complete interpretation of the functioning of living organisms'.

The quest for scientific identity

After a brief sojourn (1931–2) in Strasbourg where he worked on the differentiation of ciliates in the laboratory of Edouard Chatton, a leader of the then great school of French protozoology, Monod returned to Paris and to the Sorbonne. He spent several years in the search for a problem, before finding one to which he could devote himself wholeheartedly. The stages of this journey are marked by a few papers on axial gradients in ciliates, on galvanotropism, on the role of symbiotic algae in animals, and finally, as the search neared its goal, on the growth of the ciliate *Tetrahymena pyriformis*. In the summer of 1934, he joined a scientific expedition to Greenland on board the *Pourquoi Pas*, which resulted in the publication of a 'preliminary account' (destined to remain preliminary) of his natural historical observations. He was preparing to take part in a second expedition to Greenland on the *Pourquoi Pas* in 1936, when Boris Ephrussi persuaded him to embark on a different venture. Ephrussi was to spend a year with T. H. Morgan's group at the California Institute of Technology. He helped Monod to obtain a Rockefeller Fellowship, and they set off together to Pasadena. As fate would have it, the *Pourquoi Pas* was lost with all hands that summer on the Greenland coast. The attractions of genetics and the persuasiveness of Boris Ephrussi had saved Monod's life.

The year in Pasadena did not simply give Monod a solid knowledge of genetics. It also revealed to him an academic society wholly different from that which he had known in France. Life at the California Institute of Technology was characterized by friendly cooperation, vigorous critical discussions, free exchange of ideas, and easy personal relations between young and old. The lesson was one which he never forgot; the same spirit pervaded his research group and eventually his department, when he finally found a place at the Pasteur Institute. Furthermore, the French academic gerontocracy became a permanent object of his indignation and scorn, expressed with vigour and eloquence whenever an occasion, either suitable or unsuitable, presented itself. No other explanation need be sought for the fact that Monod was 49 before he became a professor at the Sorbonne.

The theme discovered

As already mentioned, Monod's search for a problem that he could make his own eventually led him to the analysis of growth. His first experiments on the effect of nutrient concentration on growth rate were conducted with a ciliate. Since André Lwoff was then working at the Pasteur Institute on the nutrition of protozoa, Monod visited him to discuss the results. Lwoff pointed out to him that a bacterium which could grow in a synthetic medium of simple composition would be a far more appropriate experimental object, and suggested the use of *Escherichia coli*. It was thus that Monod started to study the organism on which his life's work was to be based, after Lwoff had assured him that *E. coli* was not pathogenic.

Five years of work culminated in the preparation of a doctoral thesis, *Recherches sur la croissance des cultures bactériennes*, which is the classical and definitive treatment of the problem of microbial growth under conditions of eventual nutrient limitation. In it, Monod defined the two fundamental parameters, growth rate and growth yield; determined the dependence of growth rate on the concentration of a limiting nutrient, the organic carbon and energy source; and demonstrated the independence of growth yield from growth rate.

The young musician, *aet.* 18.

His conclusions were epitomized in an article which appeared in English in an early volume of *Annual Review of Microbiology*, bringing them to the attention of readers unable to cope with the longer original work in French.

A decade later (1950), Monod made a second major theoretical and technical contribution to the study of growth, by defining, independently of Novick and Szilard, the principle of continuous growth, and designing a fermenter, the 'bactogène', for the continuous culture of bacteria. He offered the use of the bactogène to colleagues at the Pasteur Institute who were engaged in the production of bacterial vaccines; but the offer was declined. They preferred to stay with Roux flasks.

Let us return to 1940. Having exhausted the possibilities of studying bacterial growth at the expense of one sugar, Monod decided to see what would happen when *E. coli* was presented simultaneously with two different sugars. To his surprise, he discovered that some binary mixtures give rise to two distinct cycles of growth, separated by a lag phase: the phenomenon which he christened *diauxy*. Once again, he consulted Lwoff, who suggested that diauxy might have something to do with 'enzymatic adaptation'. This was a subject of which Monod had not previously heard. Armed by Lwoff with Marjory Stephenson's *Bacterial Metabolism*, the best summary of information then available, he returned to the Sorbonne to continue his experiments; but not for long.

The nettle and the flower

Either our history shall with full mouth
Speak freely of our acts, or else our grave
Like Turkish mute, shall have a tongueless mouth.

King Henry V, Act I, Sc. ii

The conversation with Lwoff about diauxy took place in December 1940. Paris was under Nazi occupation; and Monod, married and the father of twin sons, had a Jewish wife. After finding a relatively safe refuge in the country for his family and taking his doctoral examination, he joined the underground resistance in Paris. This put an end to his work at the Sorbonne. However, between 1941 and 1944 he managed to do a few experiments during clandestine visits to Lwoff's laboratory at the Pasteur Institute.

Monod eventually reached a position of considerable responsibility in the resistance movement; he occupied a post from which his three predecessors had disappeared into the hands of the Gestapo, and he narrowly escaped the same fate. After the liberation of Paris, he joined the staff of General de Lattre de Tassigny, and was instrumental in the delicate and difficult task of integrating resistance forces into the regular army.

Characteristically, it was during the occupation that he chose to join the French communist party. This can be construed as an act of solidarity with fellow members of the resistance, rather than as an expression of Marxist faith. Not long after the end of the war, he broke publicly with the French communists, then totally subservient to Stalin, over the issue of their unquestioning support for the doctrines (if they deserve the dignity of that name) of Lysenko. The fact of having been a party member, which he did not attempt to conceal, was an inconvenience to Monod on his frequent post-war visits to the United States; he required a special clearance before a visa could be issued.

The path to the lac operon

The war over, Monod returned to the Sorbonne. Once again, he had to wash his glassware, and prepare and sterilize his media; no favours were shown to the study of bacterial growth in the Laboratoire de Zoologie. Once again, André Lwoff came to his rescue, this time with an invitation to enter the Service de Physiologie Microbienne at the Pasteur Institute, an offer that did not have to be made twice. At the age of 35, Monod at last found himself in a laboratory properly equipped for the kind of research on which he had embarked 10 years

earlier; he even acquired a technician, Madeleine Jolit, who continued to work with him until he became Director in 1971. Moreover, he was now surrounded by associates with whom a profitable exchange of ideas was possible. Pierre Schaeffer and Elie Wollman were already working in Lwoff's laboratory. Over the following years, Monod was joined by the collaborators destined to share various stages in the voyage of discovery which led to the *lac* operon. They were (more or less in chronological order) Annamaria Torriani, Mel Cohn, Germaine Cohen-Bazire, Georges Cohen, David Perrin, Adam Képès, Gérard Buttin and Agnes Ullmann. Temporary American visitors also helped greatly. They included Alwin Pappenheimer, William Sistrom, Howard Rickenberg, David Hogness, Arthur Pardee, Irving Zabin and Clyde Willson. A special place came to be occupied by François Jacob. With no background except his pre-war medical training and the 'Grand Cours' of the Pasteur Institute, he had joined the Service as Lwoff's student, and worked initially on phage. He went on, in collaboration with Elie Wollman, to elucidate the mechanism of conjugation and gene transfer in *E. coli*, and then brought his genetic experience to bear, with decisive results, on the problem of β -galactosidase synthesis. At this point, he and Monod became the joint leaders of the *lac* operon team. It proved to be one of the most productive collaborations in the history of biology.

In 1948, the conversation of December 1940 with Lwoff began to bear fruit. The information about 'enzymatic adaptation' had been carefully scrutinized, and a specific system had been selected for study; the induced synthesis by *E. coli* of the enzyme β -galactosidase, for which an easy and sensitive assay (hydrolysis of a chromogenic substrate, *o*-nitrophenyl- β -galactoside) had just been described by Lederberg. The isolation, purification and characterization of β -galactosidase was the first step. This also permitted the preparation of a specific antiserum, thus making possible the study of enzyme synthesis by a method independent of the measurement of catalytic activity.

It was soon demonstrated that induction leads to a total synthesis of the enzyme from amino acids; and that the enzyme protein, once formed, is stable *in vivo*. The belief, then prevalent, in the 'dynamic state of living matter' had been dealt a serious blow.

The next step was the demonstration that *substrate* and *inducer* are not necessarily synonymous. Experiments with a large number of synthetic and natural galactosides revealed that some substrates for the enzyme are unable to act as inducers; and conversely, that some potent inducers are completely devoid of affinity for the enzyme. Accordingly, induction was not triggered by a combination of the inducer with pre-formed enzyme molecules (as had been suggested earlier), but rather by an interaction of the inducer with some component, still mysterious, of the enzyme-forming system. This work also made possible, for the first time, a gratuitous induction of enzyme synthesis.

In the meantime, the chromogenic substrate had been used to detect and isolate a large number of mutants with altered abilities to synthesize β -galactosidase and utilize β -galactosides. These included, in addition to constitutive mutants, a puzzling class of 'cryptic' mutants, apparently capable of synthesizing β -galactosidase, but not of metabolizing galactosides. A comparison of the accumulation of radioactive thiogalactosides (gratuitous inducers) by cryptic mutants and induced and uninduced cells of the wild type led to the discovery of a second enzyme, also under inductive control: galactoside permease. Crypticity was the consequence of a mutation affecting the γ gene, governing synthesis of the permease, but not affecting the z gene, governing synthesis of β -galactosidase. The attempt (unsuccessful) to isolate the permease led to the discovery of a third enzyme associated with the metabolism of galactosides: galactoside transacetylase, controlled by the a gene. Another fact of great significance then emerged: the mutation to constitutivity is pleiotropic, and leads to simultaneous constitutive synthesis of β -galactosidase, permease and transacetylase. The products of the future *lac* operon were thus at last characterized; and the existence (though not yet the role) of another genetic component, the i gene, which governs inducibility had been demonstrated. In a sense a sideline on the path to the *lac* operon, the discovery

of galactoside permease opened up a new field of cell physiology. It had been shown for the first time that an inducible enzyme can mediate the specific transport and intracellular accumulation, in chemically unmodified form, of a nutrient. Georges Cohen soon established the fact that permeases have a general role in cellular metabolism by demonstrating that amino acid uptake is also mediated by a series of specific permeases.

The stage was now set for a genetic analysis. Wollman and Jacob had shown that conjugation in *E. coli* consists of the injection of the male chromosome into the female cell without cytoplasmic fusion, and that the entry process can be followed by kinetic analysis. Pardee, Monod and Jacob undertook a study of the expression of the z^+ and i^+ (inducible) alleles following their entry into a $z^- i^-$ female. They found that the z^+ gene is expressed very rapidly, β -galactosidase synthesis beginning at once and at maximal rate in the female recipient. This observation was crucial to the subsequent development of the messenger theory. They also found that the i^+ allele is dominant over i^- (constitutive) allele, but that dominance is expressed very slowly. This indicated that the product of the i^+ allele inhibits the synthesis of the enzyme; it was therefore christened the repressor. Negative control had been discovered: the role of the inducer was to inhibit the inhibitor (repressor) of enzyme synthesis. Once this essential point had been established, the existence of an operator gene had to be postulated, and was soon confirmed by the discovery of operator mutants; the *lac* operon had been born.

The next problem to be considered was the nature of the repressor. Since its role is to prevent expression of the operon, it appeared most plausible to assume that it acted at the level of DNA, blocking the function of the operator gene. This role could in principle be played by a direct product of the *i* gene, i.e. a polyribonucleotide. However, the inactivation of the repressor by inducers showed that it could also form a stereospecific complex with small molecules; this is a property of proteins, not of nucleic acids. Moreover, genetic experiments suggested that the active product of the *i* gene was a protein, which could combine both with the operator locus and with the inducer. It was left for others to confirm the validity of the specific hypothesis; but in the meantime the fundamental notion that it embodied became the source of Monod's second great contribution to biological theory.

Allostery

The role of the repressor outlined above implies that a small molecule, the inducer, can combine with the repressor protein in such a way as to alter its affinity with the operator, and thus trigger a very complex sequence of events: transcription of the *lac* operon, followed by synthesis of three different proteins. But if the repressor can behave in this fashion, why not other proteins? This led Monod to interest himself in the problem of the regulation of enzyme activity. Feedback inhibition of enzymes operative at early steps in biosynthetic pathways by the end-product had already been demonstrated by Novick and Szilard, Pardee and Umbarger; but no general explanatory theory had been developed. This Monod proceeded to do, together with Jacob and Changeux. The analysis of the properties of such regulatory enzymes as were then (1963) known, led them to conclude that in most cases regulation of catalytic function by effectors of low molecular weight involves stereospecific interaction with the enzyme molecule at a site different from the catalytic one, leading to a conformational change which changes the affinity of the catalytic site for the substrate. This was termed an *allosteric effect*, and the modification undergone by the enzyme molecule an *allosteric transition*. It is difficult at this point to avoid a direct quotation (Monod, *Science* **154**, 475–483, 1966):

‘By virtue of being indirect, the allosteric interactions do not depend on the structure or the particular chemical reactivity of the ligands themselves, but entirely on the structure of the protein, which acts as a relay. This is what confers upon these effects their profound significance. The metabolism, growth and division of a cell require, obviously, not only the

operation of the principal metabolic pathways – those through which pass the necessary energy and material – but also that the activity of the various metabolic pathways be closely and precisely coordinated by a network of appropriate specific interactions. The creation and development of such networks during the course of evolution obviously would have been impossible if only *direct* interactions at the surface of the protein had been used; such interactions would have been severely limited by chemical structure, the reactivity or lack of reactivity of metabolites among which the existence of an interaction could have been physiologically beneficial. The “invention” of indirect allosteric interactions, depending exclusively on the structure of the protein itself, that is on the genetic code, would have freed molecular evolution from this limitation.’

Thus far the general theory. Like most great scientific concepts, it formed in Monod’s mind in a sudden flash of insight; and he was not far from the truth when he told two of his collaborators: ‘I have discovered the second secret of life’.

It remained to find a physical interpretation of allosteric interactions in terms of molecular structure; and this Monod did in collaboration with Jeffries Wyman and Jean-Pierre Changeux. Their explanatory model, which proved to be applicable to many allosteric systems was simple in principle, being based on the following postulates. An allosteric protein contains several identical sub-units or protomers, arranged in such a way that none is distinguishable from the others; the protein therefore has one or more axes of symmetry. The protein can exist in two (or more) conformational states; and its conformational transitions tend to preserve molecular symmetry.

Chef de Service

By the early fifties, the attic which housed the Service de Physiologie Microbienne had become far too small for the manifold scientific activities which were going on in it. In 1953, Monod was made the head of the Service de Biochimie Cellulaire; and in 1955, he and his group moved into renovated quarters two floors below, while continuing to maintain close relations with the inhabitants of the attic. These new quarters also rapidly became overcrowded, and remained so until most of the group moved, in 1971, into a new building constructed to house the Departement de Biologie Moleculaire. By then, however, Monod was Director of the Pasteur Institute, and his career as an active scientist was over.

Teacher and writer

Monod contributed in several different ways to the development of biology in France. Shortly after the war, he organized the Club de Physiologie Cellulaire. This ‘club’ had neither rules, nor funds, nor regular members; but its monthly meetings served for a number of years as a focal centre for the exchange of ideas, and provided an occasion – then unique in France – for scientific beginners to meet informally the leading experimental biologists of the Paris region. The programme consisted of a seminar, often given by a foreign visitor, followed by dinner and further discussion in a nearby restaurant. A meal, paid for by the other diners, was the speaker’s honorarium.

For many years, the beneficiaries of Monod’s remarkable gifts as a teacher were the small group of scientists and technicians associated with the research on β -galactosidase, and the post-doctoral visitors from other countries who had come to work for a time in the Service de Physiologie Microbienne or later the Service de Biochimie Cellulaire. Only after his appointment in 1959 as Professor of Biochemistry at the Sorbonne did he begin to attract French students. For the most part graduates of the Ecole Normale or the Ecole Polytechnique, two of the principal training grounds of France’s intellectual élite, they came to prepare doctoral dissertations in his laboratory at the Pasteur Institute. Endless time and patience were expended on their scientific training and on the planning of their future careers. An essential part of the programme was the arrangement of a lengthy post-doctoral sojourn

The end of the road. Photograph taken two days before
Monod's death, *aet.* 66.

abroad (usually in the United States), designed to avert the danger of the parochialism that was all too evident in many areas of French biology. The number of scientists who were directly trained by Monod is not large; but their quality more than compensates for the smallness of their ranks.

In 1967, shortly after he had received the Nobel Prize with Lwoff and Jacob, Monod was elected to a chair at that unique French institution, the Collège de France. Thereafter, his teaching took the traditional form of an annual series of lectures, open to anyone who cared to attend, on a subject that changed each year.

The inaugural lecture of a newly appointed professor at the Collège de France is a solemn and major occasion in the intellectual life of Paris. Monod used it to present a first sketch of his ideas on the philosophy of biology, subsequently expanded into a book, *Le Hasard et la Nécessité* (*Chance and Necessity*), published in 1970. He offered a materialist interpretation, which traced with skill and elegance the links between classical Darwinism and the deeper insights into the evolutionary process made possible by the molecular biological revolution. He also took the opportunity to attack both idealist and dialectical materialist interpretations, which he tarred with the same brush: animism. This generated considerable heat, notably among Marxist intellectuals, who have a prestige in the country of Descartes that Anglo-Saxons, with their long tradition of philosophical empiricism, find difficult to understand. To the surprise of everyone – not least of its author – *Chance and Necessity* became a best-seller both in French and in English.

Director of the Pasteur Institute

The prize of the general is not a bigger tent, but command.

Oliver Wendell Holmes, Jr

In April 1971 Monod became Director of the Pasteur Institute. A previous attempt to put him in this post had been blocked at the highest level, by President Pompidou, who had not forgotten some disobliging public criticisms offered by Monod a few years earlier. It is rumoured that Pompidou, who had modest literary pretensions and even more modest literary talents, relented as a result of the success of *Chance and Necessity*. Why did Monod accept this onerous and unrewarding task, which consumed the last years of his life? A profound sense of indebtedness was probably the key factor. Since 1945, the Pasteur Institute had given him the freedom to pursue his own work, without making other demands on his time. Now its very existence was menaced; and Monod believed that nobody else had the drive, ability and prestige to save it. As we shall see, he accomplished a great deal in five years; whether these reforms were sufficient to preserve the historical structure of the Institute still remains to be decided.

Monod's years as Director were shadowed by bereavement, sacrifice and illness. His wife, the former Odette Bruhl, an orientalist and the curator of the Musée Guimet, was gravely ill in 1971, and died early the following year. The projected sequel to *Chance and Necessity* had to be put aside, and work on it was never resumed. Experience soon convinced him that even the light duties of a professor at the Collège de France were incompatible with the directorship, and he resigned from his chair. He suffered a severe attack of viral hepatitis in 1972, and became ill again in October 1975. This time, the disease was terminal. He had developed an aplastic anaemia, but continued working to the end, kept alive (as he casually remarked one day) by the blood of others.

A brief historical introduction is necessary to explain the multiple problems which confronted Monod in 1971. The Pasteur Institute had been created by subscription, the result of a wave of public enthusiasm, following Pasteur's development of a rabies vaccine; the original building is still called 'le Bâtiment de la Rage'. A special law gave it the status of a private foundation recognized to be of public utility, making it one of the very rare scientific institutes in France largely independent of governmental control. Despite this, the Institute has always played a national role of fundamental importance: it is the central microbiological reference laboratory of France, the repository of nearly all national culture collections, and a major teaching centre for microbiology and immunology. Since its foundation, the Institute has engaged in the production of serums, vaccines and other biological products, on the sale of which its financial independence was originally based. Only after 1945 did this source of revenue begin to be supplemented to a significant degree by state support, which thereafter took an increasingly important place. The sources of state support were multiple and, in part, indirect; for example, many of the scientists and technicians who

work at the Institute are employed by governmental organizations, such as the Centre National de la Recherche Scientifique.

The infusion of funds from external sources for some time prevented recognition that the Institute's industrial operations had been going downhill for many decades, as a result of antiquated production methods, failure to develop new products and improve old ones, and the absence of cost accounting; in short, a complete lack of sound business practice. Competition from private industry had made serious inroads into the traditional markets, both domestic and foreign. The gravity of the situation was further concealed by the absence of any overall control of the Institute's finances: nobody seemed to know where the money came from or where it went, and deficits were met by the dissipation of endowment funds. By 1971, however, it had become clear that bankruptcy could not be far away. The state would at that point intervene, to maintain those activities which it deemed essential; but the independence of the Institute would be lost. Monod assumed the directorship to try and avoid this outcome.

He had no previous administrative or business experience, and it took him some months to grasp the parameters of the problem. He then acted with energy and firmness. Since it was evident that the Director could not simultaneously head a research institute and run a business, a subsidiary company – Institut Pasteur Production – was created, and its key officers were recruited from private industry. Monod's success in staffing the new company with men who were able, devoted and loyal says much for his powers of persuasion; objectively, he had very little to offer them. The slow and painful task of revitalizing the industrial activities of the Institute was thus begun. However, financial projections revealed that even under the most optimistic assumptions, the Institute could not hope to attain financial equilibrium from this source; increased state support was indispensable. Monod therefore appealed to the government. A special commission was created to study the situation, and shortly before his death, the government agreed to help out.

Needless to say, the building up of the scientific activities of the Institute was also on Monod's agenda when he became Director. But when the financial preconditions were on the way to fulfilment, his time had run out. By an irony of fate, Monod will be remembered among the directors of the Pasteur Institute for his financial and administrative reforms, not for his role in determining its research programme.

The outer and the inner man

The attempt to sketch a likeness of Jacques Monod is perhaps foolhardy; it would tax the powers of an observer as subtle and perceptive as Henry James. For this, there are several reasons. First, his many-sidedness; scientist, teacher, musician, writer, sportsman, administrator and public figure. Second, his deeply ingrained sense of privacy; he kept his associations well compartmentalized, and few (if any) of his friends had more than a partial knowledge of the various facets of his life. The greatest difficulty of all stems from the complexity of his character, with its seeming contradictions: he could be considerate or brutal; courteous or rude; contemptuous of authority, or eager to exercise it.

In the personality of Monod, it is possible to perceive three superimposed and often incompatible elements. The most obvious personage was the liberal cosmopolitan, cultivated, urbane and ironical, equally at ease in two languages and three cultures. His familiarity with Anglo-American speech and folkways trapped many English-speaking acquaintances and friends into imagining that he was, at heart, one of them. Nothing could be further from the truth. Under the cosmopolitan facade, Monod was quintessentially French: a patriot and a conscious representative of a very distinctive sub-culture, the Protestant *grande bourgeoisie*. Failure to recognize this led to misunderstandings, made easier by Monod's overt behaviour, notably his oft-expressed admiration for some Anglo-Saxon attitudes, and his trenchant criticisms of the defects, as he saw them, of French society. This behaviour did not reflect a sense of estrangement from his own country and culture,

but a passionate desire, almost Gaullian in its intensity and arrogance, to improve that country and culture.

Underlying the cosmopolitan and the Frenchman was a third persona, recognition of which is essential to an understanding of the man. Although separated by at least one generation from Protestant religion, Monod was imbued with the sternest and most pitiless version of the Protestant ethos: at heart, he remained a Calvinist. The novels of André Gide, another distinguished and wayward product of French Calvinism, provide a useful literary guide to this aspect of his character. Since France is still largely permeated by the Catholic ethos, Monod's Protestant conscience, important in determining both his own destiny and his relations with others, was not clearly recognized by many of his compatriots, who remained perplexed by its manifestations. This component of Monod's character was without question a fertile source of conflicts, internal and external, sometimes painfully overcome, sometimes unresolved.

An anecdote permits a glimpse of one internal conflict, which was overcome. Shortly after his arrival in Lwoff's attic, Monod had collaborated with Elie Wollman in a study of the effect of phage infection on β -galactosidase synthesis. Some time later, when the work on β -galactosidase had run into temporary difficulties, he confessed to one of his co-workers that he had been strongly tempted to work on phage, but had resisted the temptation 'parce que j'en avais trop envie' ('I wanted too much to do it'). It would be difficult to find a better illustration of Samuel Butler's aphorism about the Protestant ethos, that virtue is the condition in which the pain precedes the pleasure!

Pitiless with himself, Monod could also act harshly towards others, particularly when his conscience told him that he was right. This led him into many needless difficulties, particularly during his years as Director. For example, having decided to retrench by abolishing some small research units, mostly of mediocre quality and peripheral to the main interests of the Institute, he arbitrarily forced their heads into premature retirement, when half an hour of sympathetic discussion would in many cases have elicited a voluntary retirement. One of the individuals so affected had accompanied Monod to Greenland on the *Pourquoi Pas* in 1934, and had watched Monod's subsequent rise to fame with admiration and affection. He had served the Institute well in the past, but he was permitted to leave the scene of his life's work without a word of thanks from the Director.

Although Monod could be authoritarian and inflexible, he could also act with great generosity and kindness. The scientists, technicians and secretaries who worked with him could always count on his sympathy, advice and support; in return, he received an unreserved loyalty and devotion from nearly all of them. His time, his prestige and his personal fortune were freely used to aid humanitarian causes and individuals. Although the fact never became public knowledge, several victims of both fascist and communist tyranny owe their escape and opportunity to make a new life in the free world to him. As a leader of the movement (finally successful) to legalize abortion in France, Monod often received anguished private letters appealing for his help. He always responded in the only way possible before the law had been changed: by sending money.

One common French quality which Monod did not share was the Latin brand of sentimentality. It differs from the English one in being lavished not on animals, but on national shibboleths and (in lesser measure) on fellow humans. Desperately searching as Director for solutions to the problems of the Institute, he hit on the notion of rebuilding it on the suburban campus at Garches, financing the operation by the sale of the very valuable land which it occupies in Paris. One day while he was expatiating on the virtues of this solution (never, of course, put into effect), the author of this memoir asked him what he proposed to do about the tombs of Pasteur and Roux, both on the Paris campus. 'No problem', he replied, 'We'll dig them up and take them along with us'. Fortunately, no French colleagues were present to hear him utter this blasphemy!

If Jacques Monod's faults have been evoked here, that is because one cannot write

other than honestly about such a man. At the risk of eliciting sniggers from readers for whom the very notion of the hero is a medieval anachronism, it must be said that he was of heroic stature. I hope this is evident from the preceding account of his life. It is no accident that an epigraph from Henry V surfaced during the preparation of this memoir. Shakespeare's soldier-king and our departed friend and leader had, when one thinks about it, a good deal in common.

André Lwoff kindly put at my disposal the manuscript of the memoir of Jacques Monod which he has prepared for The Royal Society. It provides by far the most authoritative account of Monod's scientific career; and since it will be accompanied by a full bibliography, I have not listed Monod's publications here. My wife, Germaine Cohen-Bazire, helped me to reconstruct the early years of work on what later became the *lac* operon. I am deeply indebted to both of them.

R. Y. STANIER