



ELSEVIER

Contents lists available at [ScienceDirect](http://www.sciencedirect.com)

Comptes Rendus Biologies

www.sciencedirect.com



Jacques Monod – A theorist in the era of molecular biology / Un théoricien à l'ère de la biologie moléculaire

Monod as the founder of a new discipline: Local and international contexts



Monod, fondateur d'une nouvelle discipline : contextes locaux et internationaux

Soraya de Chadarevian

Department of History, University of California, Los Angeles, 6265 Bunche Hall, Box 951473, 90095-1473 Los Angeles, USA

ARTICLE INFO

Article history:
Available online 7 April 2015

Keywords:
Jacques Monod
Molecular biology
Pasteur Institute
DGRST
Action concertée
Francis Crick

Mots clés :
Jacques Monod
Biologie moléculaire
Institut Pasteur
DGRST
Action concertée
Francis Crick

ABSTRACT

Monod gained stature as an experimentalist and theorist as well as a discipline builder. The essay reviews the intimate connection of the intellectual and institutional projects in his career. A brief comparison with the development of the new science of molecular biology across the English Channel highlights the commonalities and specificities of the disciplinary projects in France and Britain and the role that individuals like Monod played in their formation. The article argues that there was not a single path that led to the rise of molecular biology. Rather individual initiatives and historical contingencies very much shaped local outcomes.

© 2015 Académie des sciences. Published by Elsevier Masson SAS. All rights reserved.

RÉSUMÉ

Monod est considéré comme un expérimentateur et un théoricien aussi bien que comme l'architecte d'une discipline. Cet essai rend compte des liens intimes, dans sa carrière, entre les projets intellectuels et institutionnels. Une brève comparaison avec le développement outre-Manche de cette jeune science qu'est la biologie moléculaire souligne les points communs et les spécificités des projets disciplinaires en France et en Grande-Bretagne, et le rôle que des individus comme Monod ont joué dans leur formation. Cet article montre que le chemin menant vers l'émergence de la biologie moléculaire n'a pas été unique. Des initiatives individuelles et des contingences historiques ont bien souvent façonné des résultats locaux singuliers.

© 2015 Académie des sciences. Publié par Elsevier Masson SAS. Tous droits réservés.

1. Introduction

In his Nobel lecture, Jacques Monod described the decisive impact his stay as a young researcher at Thomas

Hunt Morgan's laboratory at the California Institute of Technology in 1936 had made on him. It was a “revelation of genetics, at that time practically unknown in France” and a “revelation of what a group of scientists could be like when engaged in creative activity and sharing in a constant exchange of ideas, bold speculations and strong criticism”. It was also a “revelation of

Email address: chadarevian@history.ucla.edu.

<http://dx.doi.org/10.1016/j.crvi.2015.03.003>

1631-0691/© 2015 Académie des sciences. Published by Elsevier Masson SAS. All rights reserved.

personalities of great stature”¹. By the time Monod was reflecting back on his formative years, it was amply clear that he had made these revelations very much his own.

Monod gained stature as an experimentalist and theorist as well as a discipline builder. The intellectual and institutional projects were intimately connected. By the 1960s, the Pasteur Institute, where André Lwoff, Monod, François Jacob and others were working, had become a centre for the “new biology” in Europe. While European scientists traveled to American laboratories to complete their formation, a growing stream of American researchers took advantage of the many new fellowship opportunities set in place after the surge in science funding following the Sputnik crisis to spend time in European laboratories. Those interested in the new biology visited the Pasteur Institute or the Laboratory of Molecular Biology in Cambridge – or both. A comparison of the development of the new discipline in these two places will highlight the commonalities and specificities of the intellectual and disciplinary projects in the two centres and the role individuals like Monod played in their formation. There was no obligatory path that led to the rise of molecular biology. Individual initiatives and historical contingencies very much shaped local outcomes.

2. Building a new science

Monod joined Lwoff’s laboratory, the Service de physiologie microbienne, at the Pasteur Institute in 1945². Early on, Lwoff and his colleagues were engaged in improving the status and funding of their research in bacterial genetics and biochemistry. Their aim was to achieve better research conditions at the Institute and to change the biological and medical curriculum in French universities, where genetics and biochemistry played only a marginal role. In 1954, a donation from the Rothschild family largely funded the establishment of a Department of Cellular Biochemistry at the Pasteur Institute, of which Monod became the head. Yet this was only a first step.

In 1956, a colloquium organized in Caen by outgoing Prime Minister Pierre Mendès France brought together left-wing scientists, business people and politicians to discuss measures to promote French research. The colloquium was instrumental in forging new links between the participants and in the formation of a science policy in France. As chairman of the committee on fundamental research and university teaching and co-author of the final report Monod played a prominent role in achieving these aims³.

¹ J. Monod, From enzymatic adaption to allosteric transformations, Nobel Lecture, December 11, 1965, p. 190; http://www.nobelprize.org/nobel_prizes/medicine/laureates/1965/monod-lecture.pdf, accessed 28 September 2014. [The Nobel Lecture is also reprinted in *Origins*; for quote see p. 297].

² For the reconstruction of the development of molecular biology in France, I rely on the work of Jean-Paul Gaudillière [1–3] as well as on the archival material available at the Fonds Monod at the Archives of the Pasteur Institute (AIP). For the development of molecular biology in Britain see [4]. For a comparison of the institutionalization of molecular biology in France, Britain, Germany, and Switzerland, see [5].

³ On the role of the scientists of the Pasteur Institute in these discussions see [1,6]. On the role of the 1956 colloquium in the formation of science policy in France, see [7].

The next opportunity for the Pasteurians to promote their institutional plans came a couple of years later, when an American delegation, headed by Democratic Senator Hubert Humphrey, came to Paris to discuss with them the plan of a European Institute of Molecular Biology. The project was to be part of an ambitious “Marshall Plan for Medicine” proposed by the American Senator to “immunize the World from War”. According to the Humphrey’s vision, American funds, funnelled through the National Institutes of Health, would allow scientists from across the iron curtain to cooperate in the field of medical research and provide global health solutions. Such a program would help overcome Cold War divisions and provide the basis for peaceful coexistence⁴. The plan followed on the heels of the Sputnik launch that had raised Cold War tensions and led to a steep rise of government funds for research in the US.

Monod was unable to attend the discussions, but Lwoff, Jacob, François Gros and George Cohen met with the American Senator. The scientists presented the Americans with a memorandum that was signed by Lwoff and apparently was drafted overnight⁵. Yet the proposal was based on long-standing discussions in the group.

The American initiative died before it came to the Senate floor. A European Laboratory of Molecular Biology would not be created before the mid-1970s. The plan was spearheaded by British molecular biologists – an ironic development considering their country’s difficult relationship to Europe. Although Nice was originally considered as a possible site for the new initiative, in the end the European Laboratory (EMBL) was built in Heidelberg [4,8]. Nevertheless, the effort the Pasteurians invested in the American initiative was not lost. Soon the plan for an Institute of Molecular Biology was resumed on a national level in France.

The occasion came in 1960, when President Charles de Gaulle created the Délégation générale à la recherche scientifique et technique (DGRST) as part of an ambitious effort to promote research in France. Molecular biology was designated as an area of special intervention. This was not an obvious choice, but it was made possible by the leading role of the biologists at the Pasteur Institute in the decision-making process and by the convergence of views between them and their political interlocutors that had been forged at the colloquium in Caen. As French historian Jean-Paul Gaudillière has argued, the designation of molecular biology, next to just a handful of other subjects, including oceanography, electronics, cancer research and nutrition, as an area of concerted action was not so much the choice of a discipline as the choice of a group of people that had acquired trust and authority in political and scientific circles [1]⁶. However, not just the Pasteurians were to profit. A first five-year plan foresaw the creation of

⁴ J.A. Shannon (Department of Health, Education and Welfare) to J. Monod, 14 October, 1958 and H. Humphrey, “Bold ‘Marshall Plan for Medicine’ ” proposed by Senator Humphrey to “immunize world from war”, attached to letter J. Cahn to J. Monod, 1 January, 1959; Fonds Monod, file EIMB, AIP.

⁵ A. Lwoff to J. Monod, 20 October, 1958 and “A European Institute for Molecular Biology” [undated, unsigned]; Fonds Monod, file EIMB, AIP.

⁶ On the initiative of the DGRST in molecular biology, see also [3].

a Center of Molecular Biology in Paris as well as a series of other initiatives in a number of laboratories around the country. Molecular biology was succinctly described as the study of the structure, function and biosynthesis of nucleic acids and proteins. The project proposed by the Pasteurians for their new centre focused on the question of biosynthesis, using microorganisms as research material⁷.

Despite governmental support, the realization of the proposed Center for Molecular Biology at the Pasteur Institute remained riddled with difficulties [1]. Monod assumed a central role in the protracted negotiations. The first plan to build the new centre with money from the DGRST, but on the grounds and with the support of the Pasteur Institute, was blocked by the Director of the Institute, who argued that molecular biology did not contribute to medical innovation and that the Institute was not there to step in for the inadequacy of the university in funding fundamental research. In his eyes, accepting the plan also meant giving up part of the autonomy that the Pasteur Institute enjoyed as a private institution. This situation led to a dramatic split among the prospective molecular biologists. Monod, reluctant to put at risk the significant state support, now suggested creating an Institute of Molecular Biology in the Science Faculty, turning it into a truly academic institution, even if preserving the interdisciplinary setup. Lwoff and Wollman and their respective groups decided against leaving the Pasteur Institute; the others opted to join the new venture.

The negotiations between the university, the Centre national de la recherche scientifique (CNRS) and the DGRST were still underway when structural changes at the Pasteur Institute resulted in more favorable conditions for establishing an institute for fundamental research on its premises. As an independent institute was still the preferred option, Monod and Jacob pulled out of the negotiations at the Science Faculty, having recruited others to pursue the cause there under slightly changed priorities. The Institute for Molecular Biology at the Pasteur Institute received final approval in 1965, just before the Nobel celebration for Lwoff, Jacob, and Monod. One year later, the Institute for Molecular Biology at the Science Faculty in Paris opened its doors. It later changed its name to Institut Jacques Monod in recognition of Monod's role in the creation of the institute and his intellectual contributions to the field.

A second five-year plan of special intervention in the field of molecular biology (1965–1970) was used as a launch pad to present molecular biology as the foundation for an encompassing understanding of all biological phenomena. Once more, the proposal presented was based on a preliminary report drafted by Monod. A few years later, Monod developed this vision in a book-length essay entitled *Chance and necessity* (French: *Le hasard et la nécessité*) that laid the philosophical foundation for a unified theory of life based on a molecular understanding of biological evolution. The essay also addressed the ethical

questions posed by the new science [9]. Widely read and hotly debated, the book was regarded as the philosophical manifesto of the new biology. It completed Monod's indefatigable efforts to establish the new science through research, teaching and institution building. Following the publication of the book, Monod's activity shifted increasingly towards the administrative side of scientific research, culminating in his nomination of director general of the Pasteur Institute in 1971, a position he occupied until his premature death in 1976. His nomination to the directorship reflected the recognition molecular biology and Monod personally had managed to achieve at the Pasteur Institute and beyond.

3. Multiple origins

How did these developments compare to developments across the English Channel?

Around the same time that the Pasteurians met with Senator Humphrey to discuss plans for a European Laboratory on the banks of the Seine, a group of researchers working on the molecular structure of biological systems in the Physics Department in Cambridge was involved in negotiations with the Medical Research Council concerning the creation of a Laboratory of Molecular Biology that would place their work on a safer institutional footing. What started off after the war as a small protein crystallography group, headed by the Austrian émigré Max Perutz, had grown into a cuckoo's egg that the new Cavendish Professor wanted out of the Physics department and that did not seem to find an institutional niche within the university. The proposed new laboratory, that opened its doors five years later, was to house three research groups under one roof: the protein crystallographers, including Perutz and his colleague John Kendrew; a molecular genetics group headed by Francis Crick and Sydney Brenner; and Fred Sanger's group, originally housed in the Department of Biochemistry, which worked on protein sequencing.

At first sight, the institutional plans of the French and Britain groups could appear strikingly similar. Both groups came up with the same name for their projects. Both had problems finding a niche in the disciplinary setup of the university. And both institutional initiatives took place in the context of growing state funds for fundamental research and growing competition between European science and the United States.

However, a more attentive reading reveals that the definition of the new science and the actual proposals differed in decisive details and were, in fact, closely tailored to the experiences, projects and needs of the two groups.

According to Lwoff's memorandum prepared for the American sub-commission and repeated in the following proposals, the new science of molecular biology was based on recent advances in genetics, cell physiology and biochemistry that resulted in these formerly separated fields merging. This view of a fusion of disciplines reflected the actual dynamics at the Pasteur Institute, where Jacob, working on bacterial genetics, and Monod, working on the regulation of enzyme activity, two traditionally quite

⁷ "Rapport préliminaire sur la situation présente et les actions concertées à envisager dans le domaine de la biologie moléculaire" [draft, 1961] and "Projet de centre de biologie moléculaire à l'Institut Pasteur;" Fonds Monod, file IBM/IP, AIP.

separate fields had recently initiated a collaboration to study the mechanism and regulation of gene activity, combining the two approaches. Technologies and skills like X-ray crystallography or protein sequencing that the Cambridge molecular biologists saw as fundamental for the study of the structure and function of DNA and proteins were hardly mentioned in the French proposal. The terms of “structure” and “function” used by both teams thus acquired quite distinct meanings.

Besides differences in experimental approaches and in the way the new science of molecular biology was delineated, there were also differences in the strategies pursued to build the new science. From the beginning, the Pasteurian researchers acted on a national political level while the Cambridge researchers negotiated with the MRC for a local solution. As a consequence, the Institute of Molecular Biology at the Pasteur Institute was just one of several institutions funded simultaneously under the concerted action for molecular biology in France. The Pasteurians dominated the state-directed plan of intervention politically and conceptually – and in this sense defined a “French tradition” –, but on the national level biochemists were the ones who benefited most from the new state funds under the *action concertée* for molecular biology⁸. This is markedly different from the British situation where, throughout the 1960s, biochemists complained that the funding of molecular biology happened to their detriment [11]. In Britain, for a long time, molecular biology was nearly synonymous with the Laboratory of Molecular Biology in Cambridge. A first Department for Molecular Biology was created in Edinburgh in 1968, while in Cambridge such a department does not exist to this day.

The question remains why both groups chose the term molecular biology for their proposed institutes. The term was around but not at all common. The Cambridge project had already been discussed and in principle accepted by the MRC before the French drafted their plan. But this news was hardly public and there was not much interaction between the Cambridge and Paris groups until before some years later. Yet as one participant commented: “It was no chance that the term was adopted by people in Cambridge and Paris at about the same time. Even if not formally agreed, it was commonly assumed that molecular biology stood for the ‘new biology’ against the ‘classical biology of the universities’ ”⁹. Rather than delineating a specific research program, the term thus marked a territory that could be occupied by different groups in different ways.

As the brief comparison between the French and British case suggests, what molecular biology was always depended on the people involved, their respective research programs and the institutional strategies pursued. Competing origin accounts laid claim to these respective histories and historians do well in acknowledging them¹⁰.

4. Theoretical dominance of the field: Crick and Monod

Although the Paris and Cambridge groups submitted their respective institutional proposals around the same time, there was rather little contact between them until about 1960. In that year, Monod visited the Cricks and on that occasion told Crick and Brenner about some puzzling results obtained in recent experiments performed by Arthur Pardee, Jacob, and himself in Paris [16]. Some months later, Jacob visited Crick and Brenner in Cambridge. Discussing once more what became known as the Pajama (or Pajamo) experiment, the three researchers assembled in Cambridge realized that an unstable RNA, later renamed messenger RNA (mRNA), rather than the ribosomal RNA as hypothesized before, was “the messenger” that regulated the synthesis of gene products in the cell. In the following summer, Jacob and Brenner met at Caltech and together with Matthew Meselson proved the presence of mRNA, while François Gros and James Watson pulled off a similar feat at Harvard. A couple of years later, Monod formulated the theory of allosteric change in proteins, building on Perutz’s observation of a structural difference in the oxygenated and the reduced form of haemoglobin. Monod’s theory proved useful for Perutz’s interpretation of the changes occurring in the haemoglobin molecule [17,18]. Some of the key concepts of the new science of molecular biology thus built on the extraordinary confluence of skills and ideas of the Paris and Cambridge groups.

In later years, Monod had cordial contacts with Brenner. At some point, he complained that Brenner never came to Paris and invited him to speak about “the worms, or for that matter, on any other subject, scientific, philosophical or esoteric”¹¹. Around that same time, Jacob tried to introduce the nematode *C. elegans*, which Brenner had established as a versatile laboratory organism for genetic and developmental studies, at the Pasteur Institute – an attempt that eventually failed. In the late 1960s, Monod tried to recruit Brenner to head the University Institute of Molecular Biology in Paris.

Yet Monod had the closest and most extended interactions with Crick. The two researchers shared several traits, including their laughter, their intolerance of sloppy thinking and their tendency to tell fellow scientists the real meaning of their work. These interventions were sometimes welcome, sometimes less so [19,20]. Both Crick and Monod were non-resident fellows at the Salk Institute. Between 1962 and 1973, they would meet regularly in the Californian winter. The two also sailed together, although Monod was by far the better sailor. Crick was the only scientist from the Cambridge group who contributed an essay – “Sailing with Jacques” – to the commemorative volume published in Monod’s honour [16].

Both scientists respected each other deeply. Monod suggested Crick for the Nobel Prize. If Crick returned the favor we do not know. Crick commented at length on

⁸ On the ‘French School’ of molecular biology, see also [10].

⁹ Interview with E. Wollman, Institut Pasteur, Paris, 26 June 1996.

¹⁰ For competing origin accounts see [12–14]. Every single one of these accounts was contested. On the functions of origin accounts for the consolidation of a discipline see [15].

¹¹ J. Monod to S. Brenner, 21 April and 5 May 1966; Cold Spring Harbor Laboratory Archives, SB/1/1/431. Online at Wellcome Library, Codebreakers: Makers of Modern Genetics; accessed 4 October 2014.

Monod and Changeux's draft paper on the proposed allosteric change in protein molecules¹². Crick also commented on the first draft (in English) of *Chance and necessity*. He spent several days discussing the book with Monod at his house in Cannes but found the final edition not much changed compared to the original version [16].

Crick and Monod also shared an anti-religious stance, but Crick was more conservative politically. Politics became a topic the two avoided. In contrast to Monod, Crick was also not interested in disciplinary politics. He shunned committees, did not take on teaching appointments and did not engage in institution building (later in life he did agree to fulfil a brief stint as President of the Salk Institute, but stepped down after a few months). In the Cambridge group this role was filled by Perutz and, in a significant but perhaps underestimated way, by Kendrew who, in 1957, founded the *Journal of Molecular Biology*, which to a significant extent created the field, and who promoted the new science in various governmental committees. He also became the driving force and, eventually, the first director of EMBL. Yet by this time he had left active research behind him [4]. Both Monod and Crick are credited with having dominated the field of molecular biology intellectually, but for Monod, intellectual mastery went hand in hand with institution building.

5. Conclusion

Monod combined many attributes of a discipline builder. He mastered the field intellectually, was dedicated to teaching, was deeply involved in institutional politics and provided a philosophical foundation for the new science. The blend of practice and theory, politics and philosophy was specifically adapted to the French situation, but Monod's intellectual contributions and disciplinary commitments, together with those of his close colleagues at the Pasteur Institute, undoubtedly shaped what molecular biology became, in France and beyond.

References

- [1] J.-P. Gaudillière, *Biologie moléculaire et biologistes dans les années soixante : la naissance d'une discipline. Le cas français*, [Ph.D. Thesis], Université Paris-7, Paris, 1991.
- [2] J.-P. Gaudillière, *Molecular biology in the French tradition? Redefining local traditions and disciplinary patterns*, *J. Hist. Biol.* 26 (1993) 473–498.
- [3] J.-P. Gaudillière, *Inventer la biomédecine : la France, l'Amérique et la production des savoirs du vivant (1945-1965)*, La Découverte, Paris, 2002.
- [4] S. de Chadarevian, *Designs for life: molecular biology after World War II*, Cambridge University Press, Cambridge, UK, 2002.
- [5] B.J. Strasser, *Institutionalizing molecular biology in post-war Europe: a comparative study*, *Stud. Hist. Phil. Biomed. Sci.* 33 (2002) 515–546.
- [6] J.-P. Gaudillière, *Molecular biologists, biochemists, and messenger RNA: the birth of a scientific network*, *J. Hist. Biol.* 29 (1996) 417–445.
- [7] F. Jacq, *The emergence of French research policy: methodological and historiographical problems 1945-1970*, *Hist. Technol.* 12 (1995) 285–308.
- [8] J. Krige, *The birth of EMBO and EMBL*, *Stud. Hist. Phil. Biomed. Sci.* 37 (2002) 347–364.
- [9] J. Monod, *Chance and necessity: essay on the natural philosophy of modern biology*, Alfred A. Knopf, New York, 1971.
- [10] M. Morange, *History of molecular biology*, Harvard University Press, Cambridge, MA, USA, 1998.
- [11] P.G. Abir-Am, *The politics of macromolecules: molecular biologists, biochemists, and rhetoric*, *Osiris* 7 (1992) 210–237.
- [12] J. Cairns, G. Stent, J.D. Watson (Eds.), *Phage and the origins of molecular biology*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1966.
- [13] J.C. Kendrew, *How molecular biology started*, *Sci. Am.* 216 (1967) 141–144.
- [14] A. Lwoff, A. Ullmann (Eds.), *Origins of molecular biology: a tribute to Jacques Monod*, Academic Press, New York, 1979.
- [15] P.G. Abir-Am, *Themes, genres and orders of legitimation in the consolidation of new scientific disciplines: deconstructing the historiography of molecular biology*, *Hist. Sci.* 23 (1985) 73–117.
- [16] F. Crick, *Sailing with Jack*, in: A. Lwoff, A. Ullmann (Eds.), *Origins of molecular biology: a tribute to Jacques Monod*, Academic Press, New York, 1979, pp. 269–275.
- [17] A.N.H. Creager, J.P. Gaudillière, *Meanings in search of experiments or vice-versa: the invention of allosteric regulation in Paris and Berkeley, 1959-1967*, *Hist. Stud. Phys. Sci.* 27 (1996) 1–89.
- [18] H. Buc, *Interactions between Jacques Monod and Jeffries Wyman (or the burdens of co-authorship)*, *Rend. Fis. Acc. Lincei* 17 (2006) 31–49.
- [19] M. Pollock, *An exciting but exasperating personality*, in: A. Lwoff, A. Ullmann (Eds.), *Origins of molecular biology: a tribute to Jacques Monod*, Academic Press, New York, 1979, pp. 77–80.
- [20] J. François, *The switch*, in: A. Lwoff, A. Ullmann (Eds.), *Origins of molecular biology: a tribute to Jacques Monod*, Academic Press, New York, 1979, pp. 117–132.

¹² See Papers on allostery: F. Crick and J. Wyman, 'A footnote on allostery' [1965] and J. Monod, J. Wyman and J.-P. Changeux, 'A third power footnote about allosteric transitions', as well as extensive notes (including some calculations) and some correspondence between the authors; Crick Papers, PP/CRI/H/3/19/1, box 84. Online at Wellcome Library, Codebreakers: Makers of Modern Genetics; accessed 4 October 2014.