C. R. Biologies 338 (2015) 380–384

Contents lists available at ScienceDirect

Comptes Rendus Biologies

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

Monod and the spirit of molecular biology

Monod, et l'esprit de la biologie moléculaire

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ARTICLE INFO

Article history:
Available online 15 April 2015

Keywords:
Allostery
Darwinism
Max Delbrück
Finality
Karl Popper
Symmetry
Modern synthesis

Mots clés :
Allostérie
Darwinisme
Max Delbrück
Finalité
Karl Popper
Symétrie
Synthèse moderne

ABSTRACT

The founders of molecular biology shared views on the place of biology within science, as well as on the relations of molecular biology to Darwinism. Jacques Monod was no exception, but the study of his writings is particularly interesting because he expressed his point of view very clearly and pushed the implications of some of his choices further than most of his contemporaries. The spirit of molecular biology is no longer the same as in the 1960s but, interestingly, Monod anticipated some recent evolutions of this discipline.

RÉSUMÉ

Les fondateurs de la biologie moléculaire partageaient certaines vues sur la place de la biologie parmi les sciences, aussi bien que sur les relations de la biologie moléculaire avec le darwinisme. Monod ne faisait pas exception, mais l'étude de ses écrits est particulièrement intéressante, car il exprime son point de vue avec une grande clarté et pousse les conséquences de ses choix plus loin que la plupart de ses contemporains. L'esprit de la biologie moléculaire actuelle n'est plus le même que celui des années 1960, mais, de manière intéressante, Monod a anticipé quelques-unes des évolutions récentes de cette discipline.

1. Introduction

It is not necessary to refer to the Vienna Circle to acknowledge that there is no such thing as "a spirit of molecular biology". Not only because a discipline has no spirit, but also because molecular biology was in permanent transformation, and because the molecular biology of the 1960s was not that of the 1980s or of today.

This did not prevent many of the founders of molecular biology, those who participated in its rapid development between 1940 and 1960, from sharing common ideas about the place of biology within the sciences, and the role of evolutionary theory in the explanation of biological facts. Among these shared conceptions, I will successively consider the project to "naturalize" life, the vision of physics as a multidimensional model for the biological sciences, the complex relations that molecular biologists had with Darwinism, and the evolutionary synthesis.

In most cases, the conceptions of Jacques Monod were those of the majority of molecular biologists. The clarity with which he expressed them, as well as the way he pushed them to their ultimate implications, can help to outline the "spirit" of molecular biology, as well as

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http://dx.doi.org/10.1016/j.crvi.2015.03.005
1631-0691/

eventually to understand how Monod's ideas could be distinguished from those commonly held.

2. The project to "naturalize" life

Monod often stated that his motivation for doing biological research originated in the flavor of metaphysics that still pervaded biological explanations when he was a student. For him, as for many molecular biologists, natural explanations had to be found for biological phenomena, just as had been done for physical phenomena centuries before, with the rejection of the physics of Aristotle during the scientific revolution, and the theories of Galileo and Newton.

The core of the issue was the place of finality in biology. Not only did the structures of organisms seem to be perfectly adapted to the functions they fulfilled, and to the environment in which the organisms lived, but the embryological development of multicellular organisms also seemed to be directed towards an end, the construction of an adult organism belonging to a well-defined species.

The first form of finalism had been attacked head on by Darwin, and the emergence of the evolutionary synthesis in the 1940s signed its death warrant among biologists. As Monod would express later, this apparent finality of the structures and behaviors of organisms is the simple consequence of the "chance and necessity" to which organisms are subject [1].

The second expression of finality, in embryological development, dates back to Aristotle, but was resurrected by the eminent German embryologist Hans Driesch at the beginning of the 20th century [2]. In experiments in which he perturbed the early phases of embryological development, he observed the extraordinary capacity of organisms to adapt to these perturbations, and to restore normal embryological development. He became convinced that the only possible explanation of this capacity was the existence within organisms of a principle that orients the developing organism towards the form that it must adopt at the adult stage, to which he gave the name of "entelechy".

The influence of Driesch had been considerable among embryologists. This was in part due to the reputation he had acquired as an experimenter, but also to the fact that the mechanisms of development were beyond the reach of the techniques and concepts available to biologists at that time. Since the time of Claude Bernard, a natural explanation for finality had been sought in the existence of regulatory mechanisms controlling the functions and the embryological development of organisms. This explains why the discovery of allosteric regulation – a process by which enzymatic activity is controlled by molecules whose structure is unrelated to that of the substrates – and the elaboration of models explaining the allosteric behavior of proteins were so important for Monod. The fact that he called the discovery of allosteric regulation that of the "second secret of life" [3] – the first being the double helix structure of the genetic material – was not a sign of pretention, but the conviction that the huge possibilities of regulation offered by allosteric regulation were precisely what had previously been missing from attempts to eject finality from biology. The value of allosteric regulation came from its partial independence of the thermodynamic relations that constrain the living world.

3. Physics as a multidimensional model

To naturalize life and biological phenomena meant mimicking what physicists have done. For that reason, and also because physics had experienced hugely successful transformations at the beginning of the 20th century – with the rise of quantum and relativity theories – and had attracted a lot of attention, physics appeared as a model for the biological sciences to follow. This was not a new phenomenon. The rise of physiology in the middle of the 19th century and the development of experimental embryology at the end of the same century were previous efforts to align biological sciences with physics, by shifting the activity of biologists from observation to experimentation.

The type of physics that might be useful for biologists was not obvious. Quantum theory was appealing for good, but also for bad reasons: it had successfully challenged some of the characteristics traditionally attributed to reality – such as the possibility of distinguishing the observer from the object that is observed. But a full understanding of quantum physics called for mastery of mathematical tools unfamiliar to most scientists, including many physicists and all biologists. The success of quantum physics was due to the pedagogical talent deployed by some of its protagonists to popularize it, notably Werner Heisenberg, Niels Bohr, and Erwin Schrödinger. The latter two were particularly important, because they both suggested that the solution to the mystery of biological phenomena would be found in quantum physics. For Bohr this would be done by applying an epistemological principle deriving from quantum physics – the principle of complementarity. Schrödinger favored a more direct approach through description of the specific characteristics of biological components that gave them special quantum properties [4]. Both were wrong, and quantum physics has not so far played an important role in biological explanations. The branch of physics that was important for the development of the new technologies that permitted the description of macromolecules and that accompanied the development of molecular biology – ultracentrifugation, electrophoresis, X-ray diffraction – was "classical" physics, optics, mechanics. This did not prevent many young physicists, trained in the new quantum physics, from turning to biology and playing a major role in the development of molecular biology. The emblematic example is Max Delbrück (1906–1981), a quantum physicist who was convinced by Niels Bohr to orient his research towards biology after his thesis, and who played a major role in developing a simple experimental system – the bacteriophage and its host, the bacterium. This system became the focus of a large part of the young community of molecular biologists. Nevertheless, Max Delbrück always remained in search of "something else" to explain biological phenomena, and was disappointed that the