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Balorda, Vito

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Vito Balorda

ORCID 0000-0002-7928-7088
Department of Philosophy, Faculty of Humanities and Social Sciences, University of Rijeka (Rijeka, Croatia)
vito.balorda@gmail.com; vito.balorda@uniri.hr

Reductionism Debate in Molecular Biology: Max Delbrück's Complementarity Approach

Abstract

In this paper, I address Max Delbrück's conceptual and experimental importance for molecular biology (henceforth MB) origins. In particular, his complementarity approach and its anti-reductive implications on the (epistemic) reductionism debate in MB.

Regarding Delbrück's conceptual and experimental importance, I examine his influence on the development of MB by exploring a shift of his interests from physics to biology. Particularly, I outline his central role in "The Phage Group", an informal group of scientists examining the origin of hereditary life using bacteriophages as their experimental model of choice. Delbrück and "The Phage Group" greatly influenced

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the development of MB, which culminated with the shared 1969 Nobel Prize for the discoveries regarding replication mechanism and genetic structure of viruses.

Moreover, I examine Delbrück's complementarity approach towards biological explanations. The complementarity in biology assumes that "biological phenomena might require the employment of descriptions that are mutually exclusive yet jointly necessary for understanding life processes" (McKaughan 2011, p. 11). I explore Delbrück's complementarity approach, in particular the debate between the reductive and anti-reductive interpretations of it. I argue for the latter interpretation by suggesting that Delbrück advanced an anti-reductive view towards biological explanations by advocating for independent status of explanations of various biological disciplines. Furthermore, I address the complementarity approach in the light of the anti-reductive interpretation in the recent developments in MB, particularly, the potentiality of finding the complementarity approach in systems biology, epigenetics, and boundary selection.

Keywords: *anti-reduction, explanation, molecular biology, Max Delbrück, complementarity approach*

Debata na temat redukcjonizmu w biologii molekularnej: Podejście komplementarne Maxa Delbrücka

Abstrakt

W tym artykule omawiam koncepcyjne i eksperymentalne znaczenie Maxa Delbrücka dla początków biologii molekularnej (odtąd MB). W szczególności jego podejście do komplementarności i jego antyredukcyjne implikacje dla (epistemicznej) debaty redukcjonistycznej w MB.

Jeśli chodzi o konceptualne i eksperymentalne znaczenie Delbrücka, badam jego migrację od fizyki do biologii, a tym samym jego wpływ na rozwój MB. Podkreślam jego rolę jako centralnej postaci „The Phage Group", czyli nieformalnej grupy naukowców, która wykorzystywała bakteriofagi jako eksperymentalne

modele do badania pochodzenia i dziedziczności życia. Delbrück i „The Phage Group" wywarli ogromny wpływ na rozwój MB, którego kulminacją była wspólna nagroda Nobla w 1969 r. za odkrycia dotyczące mechanizmu replikacji i struktury genetycznej wirusów.

Ponadto badam komplementarność podejścia Delbrücka do wyjaśnień biologicznych. Komplementarność w biologii zakłada, że zjawiska biologiczne mogą wymagać stosowania wzajemnie wykluczających się opisów, ale wspólnie niezbędnych do zrozumienia procesów życiowych. Badam podejście Delbrücka do komplementarności, w szczególności debatę między redukcyjnymi i antyredukcyjnymi interpretacjami na jego temat. Opowiadam się za tą drugą interpretacją, sugerując, że Delbrück rozwinął antyredukcyjny pogląd na wyjaśnienia biologiczne, opowiadając się za niezależnym statusem wyjaśnień różnych dyscyplin biologicznych. Ponadto zajmuję się podejściem komplementarności w świetle antyredukcyjnej interpretacji ostatnich osiągnięć w MB, w szczególności możliwości znalezienia podejścia komplementarności w biologii systemowej, epigenetyce i selekcji granic.

Słowa kluczowe: *antyredukcjonizm*, *wyjaśnienie*, *biologia molekularna*, *Max Delbrück*, *podejście komplementarne*

1. Introduction

Molecular biology (MB) is a scientific discipline that investigates the molecular basis of biological activity and "the activation of genetic information residing in DNA" (Fox Keller 1990, p. 391). It is a relatively young discipline that originated in the first half of the 20th century and became institutionalized in the second one. MB rapidly evolves by the day, and today's world is greatly influenced and transformed by its discoveries, among others, by gene therapy, genetic engineering, cloning procedures, and complete genome sequences of various organisms (see Tabery, Piotrowska and Darden 2021).

Max Delbrück was one of the central figures in the development of MB. He was originally a physicist but later turned to biology. Delbrück is known as one of the founders of "The Phage Group", an informal group of scientists originating from various scientific fields, such as genetics, physics, microbiology, chemistry, etc. The group was named after the bacteriophages, experimental models, which were used to examine the origin and heredity of life. "The Phage Group" was responsible for numerous discoveries that made an impact on the development of MB.[1] However, perhaps their most notable accolade was the 1969 Nobel Prize for discoveries regarding replication mechanism and genetic structure of viruses. Max Delbrück, Salvador Luria, and Alfred Hershey shared the Prize.

Delbrück's turn to biology was highly influenced by Bohr's lecture from 1932 entitled "Light and Life". Bohr spoke about complementarity approach towards physics and biology.[2] The complementarity principle was formulated by Bohr to explain the fact that two theories, regarded as mutually exclusive, are required to explain a single phenomenon, for instance, in the quantum realm, the wave-particle duality (see Mazzocchi 2010). Bohr believed that the complementarity approach, as found in the study of quantum realm, could be found in the life sciences as well. Complementarity approach in biology indicates

> that no single technique or perspective allows comprehensive viewing of all of a biological entity's complete qualities and behaviors (Theise, Kafatos 2013, p. 11).

However, complementary perspectives would be necessary to understand the whole.[3]

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[1] For more discoveries made by "The Phage Group", see, in particular, Hausmann 2002, and Summers 1993.

[2] Some authors argue that Bohr was influenced by the Kantian teleo-mechanical tradition, and consequently advocated a complementarity view, which expected that purposive and functional aspects of biological phenomena could not be made understandable on a strictly mechanistic basis (for more information see Mazzocchi 2010, McKaughan 2005, and Roll-Hansen 2000). However, that discussion surpasses the scope of this paper, thus I am not addressing this issue further.

[3] I would like to point out that complementarity can be observed differently in physics and biology according to Rosenfeld 1961. Namely, in quantum physics complementarity considers the relationship between mutually exclusive concepts, in the sense that there is present an account of the properties of individual atomic systems, but also the description of the behavior of systems of large numbers of atoms. In biology, according to Rosenfeld (1961, p. 388), there is present another stage of complementarity, i.e., "on one hand, we have the complete description of organs in terms of physics and chemistry, and on the other, the functional mode of description, which will always be necessary for a complete account of such complicated arrangements of molecules as living beings".

Delbrück later described Bohr's lecture as an event that changed the course of his life and, consequently, motivated his interest in biology and shaped his research projects (see McKaughan 2005, p. 508). He followed Bohr's idea of complementarity between physics and biology, which appears as an anti-reductive idea, i.e., an idea that any biological explanation needs more than one perspective. Consequently, he migrated gradually from physics to biology. However, there is no clear consensus among scholars whether the complementarity, posited by Bohr-Delbrück approach, is confirmed, i.e., it seems that no biological phenomena have yet been discovered that cannot be, at least approximately, explained physically, namely, in the biochemical and physical terms (see Sarkar 1992, p. 71).[4] Moreover, the discovery of a double-helical structure of DNA by James Watson and Francis Crick showed that replication, mutation, and gene function could be explained biochemically. That discovery was in contrast with Delbrück's belief that replication could be the one area, where the complementarity approach might be realized in some nonbiochemical way (see Strauss 2017, p. 647). Delbrück immediately acknowledged and praised the scope of Watson-Crick discovery, which led to the decrease in interest towards his phage research, since he believed that the double-helical structure of DNA resolved the problem of explaining of replication. It did so insofar as it explained replication from one perspective – the biochemical one. Consequently, he directed his research towards the phototropism phenomenon in *fungi*, in hopes of finding the complementarity approach (see Strauss 2017, p. 647). Bohr-Delbrück's complementarity idea is addressed further on the following sections. In particular, I discuss the topic whether Delbrück held an anti-reductive view towards biological phenomena.

The structure of the paper is the following: in Section 2, I examine Max Delbrück, both his role in "The Phage Group" and his importance for the development of MB. In Section 3, I examine the complementarity approach and the debate between reductive and anti-reductive interpretations towards biological explanations advocated by

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[4] Although some authors argue that the complementarity approach might be found in systems biology (e.g., see Theise, Kafatos 2013), or in the discovery of alternative splicing and epigenetics (e.g., see Mazzocchi 2010). Those approaches are addressed in Section 4.

Max Delbrück. In Section 4, I examine the anti-reductive interpretation found in Delbrück's work in a more contemporary setting, that is, in the recent discoveries in MB.

2. Max Delbrück, "The Phage Group", and his conceptual and experimental influence on MB

Let us start this section with a brief history of Delbrück, particularly his early career and the migration from physics to biology. Afterwards, I turn to his work in "The Phage Group" and the overall importance of the group for the development of MB.

Max Delbrück was first attracted to astronomy, i.e., during his early studies. In the late 1920s, he was trained at Göttingen as a theoretical physicist. That period was exciting in physics, due to the development of quantum theory. After he received his degree in physics, in the early 1930s, he became a theoretical physicist in Lise Meitner's group in Berlin. His training included also a period of work in Copenhagen under the direction of Niels Bohr (see Strauss 2017). Inspired by Niels Bohr's 1932 lecture "Light and Life", Delbrück switched to biology later on, in order to investigate the applications of complementarity to biological phenomena.[5]

After his postgraduate work in Bristol and Copenhagen, Delbrück returned to Berlin. There, at his mother's house, he formed a circle of theoretical physicists, biologists, and biochemists, who discussed various contemporary topics concerning science. He describes this period of his life as follows:

> I don't know how this came about, but after a while there was a group of, as it were, exiled, internal exiled, theoretical physicists, I and five or six of them, who met fairly regularly and mostly at my mother's house to have private theoretical physics seminars among ourselves; at my suggestion we soon brought in also some other people, some biologists and biochemists. And one of the people we brought in was N. W. Timofeeff-Ressovsky (Harding 1978).

[5] Physicists' importance for the birth of MB, especially their contribution of technical and cognitive skills, and social authority and social authorization, is foregrounded in Fox Keller 1990.

In the quote, Delbrück mentions Timofeeff-Ressovsky, a Soviet geneticist, who at that time was a visiting scientist at the Kaiser-Wilhelm-Institut (Genetics Department) in Berlin. He was famous for his work in the field of radiation genetics. In collaboration with physicist Karl Zimmer, Timofeeff-Ressovsky studied the mutagenic effect of X-rays on *Drosophila* (Hausmann 2002, p. 56). Eventually, Delbrück joined them, and their mutual effort ended with the famous article nicknamed the "Three-Man-Paper" in 1935. The article advocated an interesting notion: mutations are brought about by modifications of a molecule, or, in other words, a gene was likely to be a molecule (see Strauss 2017).

In 1937, Delbrück earned a fellowship from the Rockefeller Foundation and worked at the California Institute of Technology (Caltech) in Pasadena (see Hausmann 2002, p. 58). Firstly, he joined the research group of Thomas Morgan, a famous geneticist, established at Caltech since 1928, which worked on the *Drosophila* experimental model (see Roll-Hansen 2000, p. 427). Morgan was hoping that a theoretician, such as Delbrück, would help improve his research on *Drosophila melanogaster* genetics. However, Delbrück soon regarded the *Drosophila* experimental model as being too complex, particularly in the sense that it could not adequately provide new insights to the physical nature of a gene. Subsequently, through the encounter with Emory Ellis, a biochemist, he learned about bacteriophages, an experimental model that was extensively used by Ellis in his research about carcinogenesis. Delbrück opted for bacteriophages as the "right organism for the job"[6] of resolving the principles of biological self-replication, mainly because of the astonishing rate of gene duplication found in bacteriophages and simpler understanding of the structure and function of the genes in contrast to the research on *Drosophila* (see Summers 1993, p. 255). Thus, he joined Ellis, who already extensively studied bacteriophages, and together they advanced the research culminating with a paper on "the so-called one-step-growth-experiment" in 1939 (see Hausmann 2002, p. 59).

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[6] At the time, there were two major views on the question whether bacteriophages were organisms, and according to Strauss (2017, p. 645): "the first was that the phage was a living organism, a virus that infected bacteria. The second was that phage was a product of bacteria that, when induced, produced enzymes that lysed the bacteria". This distinction surpasses the aim of this paper, so I do not explore it further. For more information, see Strauss 2017.

After Delbrück's Rockefeller fellowship expired, he accepted the position of assistant at Vanderbilt University (Nashville, Tennessee), and later on, in the early 1940s, collaborated quite successfully with microbiologist Salvador Luria. Their collaboration culminated in 1943 with publishing the famous paper entitled "Mutations of bacteria from virus sensitivity to virus resistance". The paper is usually cited as the start of microbial genetics. As Strauss (2017, p. 645) points out, "Delbrück's major experimental contribution to the development of MB consists of a series of articles during the war years". However, his most notable accolade was the 1969 Nobel Prize. This Prize was a culmination of collaboration between founders of "The Phage Group", namely, Max Delbrück, Salvador Luria, and Alfred Hershey. They shared the 1969 Nobel Prize, specifically because of their contribution to the field of replication mechanism and the genetic structure of viruses. Both Luria and Hershey were studying bacteriophage as an experimental model prior to meeting Delbrück (see Summers 1993). In the 1940s, Delbrück, Luria and Hershey started their fruitful collaboration and are considered founding fathers of the earlier mentioned "Phage Group". The central figure of the Group was Max Delbrück (see Summers 1993, p. 255).

Apart from numerous discoveries that made an impact on the development of MB,[7] the Group had an enormous influence on the new scientific generation. Specifically, by starting the phage course in Cold Spring Harbor in the summer of 1945. The course attracted many scientists and was held regularly for more than 20 years. According to Hausmann (2000, p. 64): "it became the foundation of the phage school, which, in its turn, wielded a crucial influence at the onset of MB – less for key experimental discoveries than for its refreshing mentality, pointing out innovative directions of thinking".[8]

"The Phage Group", through the work of Max Delbrück, considered the complementarity approach, according to which, different perspectives are necessary to explain biological phenomena. Delbrück's work was, as already mentioned, highly influenced by the anti-reductive approach

[7] For more discoveries made by „The Phage Group", beside the ones already mentioned in this section, see, in particular, Hausmann 2002, and Summers 1993.

[8] It is also worth mentioning that James Watson was mentored by Salvador Luria.

towards biology. In the next section, I address that issue in more detail. Additionally, I delineate the consequences of Delbrück's approach for the reductionism debate.[9]

3. Delbrück's complementarity approach

The principle of complementarity emerged from quantum physics. The idea of complementarity first appeared in the so-called 'Como paper'. Niels Bohr delivered the paper at the Alessandro Volta commemoration conference in 1927. 'Como paper' was later published and entitled "The quantum postulate and the recent developments of atomic theory" (see Domondon 2006, p. 436). Bohr formulated the principle "to explain the fact that, in quantum physics, two theories regarded as mutually exclusive are required to explain a single phenomenon" (Mazzochi 2010, p. 339). In Bohr's case, he dealt with the wave-particle duality, namely, with the fact that light exhibits different properties depending on the means of observation (see Mazzocchi 2010, p. 339).[10]

As already mentioned in the previous section, Max Delbrück migrated to biology, in part, influenced by Bohr's 1932 lecture "Light and Life". In that lecture, Bohr elaborated on the idea that the complementarity approach could be potentially found in biology. Delbrück was impressed by Bohr's idea, which could be essential to make progress in the central issues of biology, such as heredity (see Roll-Hansen 2000, p. 423). To further explicate, according to Roll-Hansen,

> Bohr apparently held that not only classical mechanical physics and chemistry, but also quantum mechanics, could not give a complete description of the physical basis of biological phenomena (Roll-Hansen 2000, p. 423).

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[9] Throughout the paper I consider epistemic reduction. In the reductionism debate, there are present following three types of reductionism: ontological, epistemic, and methodological. Epistemic reduction concerns the reduction between different levels of scientific body of knowledge, i.e., usually higher level processes can be reduced to lower level processes that are deemed fundamental. For more information on different types of reductionism see Brigandt and Love 2022.

[10] For the purposes of the present paper, I do not address Bohr's complementarity approach in physics further. For an updated introduction to the topic, see Plotnitsky 2013.

The quote from Bohr (1933, p. 457) states in that regard:

> The question at issue, therefore, is whether some fundamental traits are still missing in the analysis of natural phenomena before we can reach an understanding of life on the basis of physical experience. An answer to this question can hardly be given without an examination of the meaning to be given to physical explanation still more penetrating than that to which the discovery of the quantum of action has already forced us.

According to this quote, it seems that Bohr believed in the idea that the complementarity approach could be potentially applied in the life sciences as well.[11] The complementarity in biology can be understood in the following way:

> Biological complementarity would indicate that no single technique or perspective allows comprehensive viewing of all of a biological entity's complete qualities and behaviors; instead, complementary perspectives, necessarily and irrevocably excluding all others at the moment an experimental approach is selected, would be necessary to understand the whole (Theise, Kafatos 2013, p. 11).

Alternatively, McKaughan nicely constructs it in the following way:

> Biological phenomena might require the employment of descriptions that are mutually exclusive yet jointly necessary for understanding life processes (McKaughan 2011, p. 11).

I address the above question by using Sahotra Sarkar's (1992) categories of reductionism, which are construed in general terms. For the purposes of this paper, I examine one model of epistemic reduction, i.e., theory reductionism, since the following paragraphs deal with the relation between different scientific disciplines and the possibility of reducing theories of one discipline to another.[12] According to Sarkar (1992),

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[11] Furthermore, some authors argue that Bohr's complementarity could be applied to several disciplines, beyond physics and biology. For more information, see Bala 2017.

[12] Besides the category of theory reductionism, there are also present explanatory reductionism and constitutive reductionism. However, in this paper, I exclusively deal with theory reductionism.

theory reduction includes that the concepts, explanations, and methods of one scientific discipline are subsumed to the concepts, explanations, and methods of another scientific discipline. According to theory reductionism, one can reduce a whole scientific discipline to another scientific discipline. Theory reductionists believe that the reduction of one theory to another implies that the reducing theory explains the reduced theory, for instance, that the explanations from Mendelian or classical genetics are reduced to those from molecular genetics.[13]

Now, let me address the discussion whether Bohr-Delbrück's complementarity approach, as applied to biology, could be interpreted either in reductive or anti-reductive view. By anti-reductive, I mean the opposite of the reductive view mentioned above, i.e., that one scientific discipline, namely its concepts, explanations, and methods cannot be reduced to another scientific discipline. Roll-Hansen (2000) believes that Bohr held a reductive view on the relation between chemical and physical theory. He believes so because

> Bohr, and other theoretical physicists at this time tended to view chemistry as a discipline with little or no autonomy relative to physics (Roll-Hansen 2000, p. 424).

In turn, biologists and biochemists complained that physicists were arrogant and ignorant towards biology and biochemistry, since they pointed out only the material as a fundamental basis of life (see Roll-Hansen 2000, p. 426).[14] Delbrück carried the suspicion towards biochemistry in his scientific research. That is particularly evident when, according to Strauss,

> somewhere around 1950, Delbrück started to lose interest in the details of the phage experiments, possibly because

[13] However, I would like to point out that there was present a clear anti-reduction consensus upon the issue whether Mendelian or classical genetics is reduced to molecular genetics (see Waters 1990). Furthermore, Dupre (see 2021, p. 3) highlights that, in recent years, many philosophers tend to reject reductionism on the issue whether biology is reduced to physics.

[14] Kornberg 1987 highlights the complicated relationship between chemistry and biology. He points out that, although biochemistry as a discipline was expected to bridge differences between two fields, it nonetheless failed in doing so and he argues that it is being pulled apart by both biology and chemistry. However, that debate surpasses the scope of this paper, so I am not addressing it further.

> the results required introduction of biochemical detail (Strauss 2017, p. 647).

After 1950, he published two more experimental papers regarding phages.[15]

On the other hand, Domondon (2006, p. 439) offers a different perspective on "Bohr's reason for rejecting chemistry as a means to explain life". Domondon believes that the rejection "did not arise directly from its early twentieth-century status as a science lacking in rigor when compared to physics", but he thought that, "a chemical explanation is insufficient because the chemical composition of a living organism is in constant flux by virtue of its interaction with its environment" (Domondon 2006, p. 439). Furthermore, Domondon argues that Bohr suggested that chemistry does not provide more insights than "the mechanical models explaining the nature of life" (Domondon 2006, p. 439). However, he argues that Bohr held an anti-reductive view on biological explanations, because Bohr believed that taking a reductive approach is problematic and that this difficulty has no analogue in physics, because if one ignores complementarity in examining atomic phenomena, then one might misunderstand the character of the phenomena in question.

I argue that Bohr and, more importantly for the origins of MB, Delbrück held an anti-reductive view on biological explanations.[16] Recall that theory reduction implies that the concepts, explanations, and methods of one scientific discipline can be subsumed to the concepts, explanations, and methods of another scientific discipline. According to reduction of a theory, one can reduce a fragment of a theory, to another fragment of a theory. However, I believe that Delbrück held

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[15] The 1951 paper is entitled "Mutual Exclusion between an Infecting Phage and a Carried Phage", written jointly with J. Weigle, and the 1953 paper "The Mechanism of Genetic Recombination in Phage", written with N. Visconti. For more information about the specifics of Delbrück's research history, see Strauss 2017.

[16] McKaughan 2011 also argued that Delbrück was an anti-reductionist, but on the basis that Delbrück followed an "empirical anti-reductive" research program. However, contrary to McKaughan, Roll-Hansen 2011 argued for a reductionist approach towards Delbrück's research program by drawing connections between the interpretation of Kant's teleological approach and consequently Bohr's complementarity approach leading to Delbrück's biological research program.

an anti-reductive view on explanations regarding biological phenomena. In my view, the following Delbrück's claim points in that direction:

> All of natural history operates with a system of concepts which has very little contact with the physical and chemical sciences. The habits of animals and plants, their reproduction and development, their relations to their symbionts and to their enemies, can all be described and analyzed with very little reference to the concepts of physics and chemistry. Perhaps the most notable of these independent branches of biology is genetics, which in its pure form operates with "hereditary factors" and "phenotypic characters" in a perfectly logical system, as an exact science without ever having to refer to the processes by which the characters originate from the factors: The root of this science lies in the existence of natural units of observation, the individual living organisms, which in genetics play somewhat the same role as the atoms and molecules in chemistry. (Delbrück 1949, p. 6)

Delbrück argued for an independent status of explanations of various disciplines, such as, for instance, genetics, rather than the view which perceives explanations from biology reduced to those from chemistry or physics. In other words, according to him, there are some biological concepts, such as "hereditary factors", that have little reference to concepts of physics and chemistry. Therefore, he followed the complementarity approach, an anti-reductive idea, that is, the idea that biological phenomena could be explained differently by adopting more than one perspective. I believe that complementarity is linked to the epistemic anti-reductive approach primarily, because complementarity approach in biology assumes that different perspectives are needed to comprehensively examine biological entities with their complete qualities and behaviors. The anti-reductive approach advocates for a view in which, to examine a biological entity, one does not limit oneself to a single perspective, but requires rather more than one perspective to explain phenomena. Also, as it can be observed in the above-mentioned Delbrück's quote; according to him, biology cannot be exclusively explained in physical and chemical terms, rather, as it is seen in genetics, other concepts play role in explanations as well.

Furthermore, following Delbrück's quote, I want to emphasize one more important aspect of the anti-reductive stance proposed by him. I would like to point out the link between his view on the anti-reduction of theories and the later vivid debate on the topic whether Mendelian or classical genetics should be reduced to molecular genetics. I try to show that he anticipated an anti-reductive stance towards the later issue, i.e., whether Mendelian genetics is reduced to molecular genetics.

Let me briefly address the issue mentioned above. According to Kenneth Schaffner (see 1993), the successes in MB show that Mendelian genetics is in the process of being reduced to molecular genetics, and consequently, to biochemistry. Schaffner believes that, even though this reduction is still not complete, it is in principle possible, and will occur eventually. He argues that MB analyzes the foundations of processes previously studied by Mendelian genetics, therefore, one can reduce Mendelian genetics to molecular genetics.

Schaffner's position was challenged by several authors. For instance, David Hull (1976) argued that classical genetics was being replaced by molecular genetics instead of being reduced to it. Namely, by pointing out the differences between Mendelian and molecular genetics, i.e., by outlining that molecular genetics, contrary to Mendelian genetics, "sets out in detail the molecular structure of genes and proteins" (Hull 1976, p. 668). Furthermore, William Wimsatt (1976) argues for a different version of reduction, namely for an explanatory reduction of Mendelian genetics to molecular genetics. He advocates for reduction as a causal explanation of an individual event, rather, than reduction regarding generalities, i.e. reduction of a higher level state of affairs to its component parts. Moreover, Philip Kitcher (1984) argues that Mendelian genetics did not have laws that could be reduced to molecular genetics, and discarded the reduction proposed by Schaffner. He argues that Mendelian genetics is difficult to axiomatize because the statements found in that genetics are too specific to be a part of a general theory. Mendelian genetics is a set of heterogeneous statements and thus Kitcher argues against Schaffner's reduction. Sarkar (1992) argues that at least the structure of explanations in MB is reductionist.[17] For the purposes of this paper, I am not examining the mentioned authors'

[17] For a brief overview of the critiques made towards Schaffner's theory reduction model, see Brigandt and Love 2022.

approaches to the issue, however, I emphasize one approach, that is, Lindley Darden's (2005) approach on the issue. I do so because I believe that her approach is, at least to some extent, anticipated in Delbrück' above-mentioned quote.

Recall that in his quote, Delbrück highlights hereditary factors and phenotypic characters as the concepts which are used in genetics. He points out that geneticists use those concepts in a perfectly logical system without having to refer to the processes by which the characters originate from. Obviously, at Delbrück's time of research work, molecular genetics was in its beginnings, thus, he could not address the issue of the reduction between the two fields of genetics at the time. However, I offer an interpretation that Delbrück anticipated the independent status of Mendelian genetics in respect to the molecular genetics by linking his approach to genetics with the later approach proposed by Darden (2005).

In her paper, Darden (2005) argues that Mendelian genetics has not been reduced to molecular genetics, nor been replaced by it. According to her, Mendelian genetics and molecular genetics are best characterized as two fields "investigating different, serially integrated hereditary *mechanisms*" (Darden 2005, p. 349). Those mechanisms operate at different times and are composed of different working entities. She argues the following:

> The working entities of the mechanism of Mendelian heredity are chromosomes, whose movements serve to segregate alleles and independently assort genes in different linkage groups. The working entities of numerous mechanisms of molecular genetics are larger and smaller segments of DNA plus related molecules. (Darden 2005, p. 349).

Darden (2005, p. 368) points out that "one does not always make progress by moving to lower size levels." Although molecular genetics, along with its discoveries of DNA mechanisms, filled black boxes left by Mendelian genetics, chromosomal mechanisms of meiosis still explain the regularities captured in Mendel's law of segregation. Thus, Mendelian genetics is not reduced, nor replaced by molecular genetics, rather, they are both autonomous in their own rights. I believe that Delbrück, by highlighting hereditary factors and phenotypic characters as the concepts that fit perfectly in a logical system used by geneticists that do not have to refer to the processes, by which the characters originate from, anticipated the possibility that the Mendelian genetics is an autonomous discipline.

Moreover, as we have already seen, Delbrück followed the idea that different kinds of explanations, beyond the physical one, are possible. He believed that the replication was the one area where Bohr's complementarity concepts might find its realization in some nonbiochemical way, but the discovery of the DNA double-helical structure proved otherwise, and for the coming decades biology became more and more explained by biochemistry (see Strauss 2017, p. 647). Delbrück was not interested in the biochemical research. Thus, he had to turn his attention to other research programs in biology, beyond the explanation of replication through his work on phages. He still searched for the application of the complementarity concept, which is evident from his letter written to Niels Bohr in 1954. Delbrück states that he might find a biological system that "will run into a paradoxical situation analogous to that in to which classical physics ran in its attempt to analyze atomic phenomena" (see Fischer, Lipson 1988, p. 242). In the letter, he proceeds by emphasizing that this was his "secret" motive in biology from the start, that is, finding an alternative, complementary explanation of biological phenomena that would capture a different perspective on biological phenomena.

Thus, even though there are reductive interpretations of Bohr's and Delbrück's views, I argue that we can classify Delbrück's position as an anti-reductive one towards explanations in biology. This can be primarily seen in his strong commitment to the complementarity approach and the possibility that there is a different perspective on the explanation of biological phenomena, as suggested in his remarks addressed above. In the following section, I examine the presence of Delbrück's anti-reductive view in some recent debates. In other words, I investigate whether complementarity idea is alive in the 21st century MB.

4. The post-Delbrück complementarity approach

In the 20th century, notions of simplicity and linearity had a significant impact on MB. According to Mazzochi (2010, p. 340), "DNA structure is an essentially linear representation of genomic information; the genetic code is linear although redundant; and the central dogma of unidirectional information flow is also simple and linear". Moreover, the operon model of gene expression examined the idea that the complexity of biological systems could be explained by interactions at the molecular level, although it introduced control genes and feedback loops (see Schaffner 2002). However, Mazzocchi (2010, p. 342) points out that life cannot be explained at the molecular and genetic level only, and that one needs to look beyond the genome. He proceeds to mention the following quote from Strohman (1997):

> Gene management involves interactive cellular processes that display a complexity that may be described only as trans calculational […]. This interactive complexity is epigenetic in nature; it involves open networks of genes, proteins, and environmental signals that may turn out to be coextensive with the cell itself.

It seems that the above-mentioned epigenetic networks display a nonlinear behavior. For instance, recall that the central dogma of MB is perceived as a linear explanation of biological phenomenon. However, epigenetics apparently challenges the central dogma insofar as biological information flows in more than one direction. As commonly understood, epigenetics is a discipline that examines heritable changes in gene expression, but ones that do not involve modifications to the underlying DNA sequence. Epigenetic change happens naturally and could be affected by several factors, such as, among others, age, environment, and lifestyle. Moreover, multiple pathways, as well as feedback circuits, are embedded into epigenetic networks. Thus, it seems that the behavior of biological systems cannot be explained by theories invoking notions of linearity. In order to accommodate the need for a different explanation towards the epigenetic challenge, Mazzocchi (2010. p. 342) provides different theoretical frameworks.[18]

As to the 21st century development of MB, according to Theise and Kafatos (2013), systems biology is arguably biology of the present century. It could be a potential candidate for examining whether complementarity approach is alive in the 21st century biology. Systems biology is an approach, by which life scientists try to understand

[18] For more information on the different theoretical frameworks regarding non-linearity and complexity, see Mazzocchi 2010; Theise, Kafatos 2013.

an organism or a cell, by putting its parts together. In contrast to the reductive approach,[19] one can potentially characterize systems biology as a holistic approach[20] focusing on reassembling of all the data obtained by taking biological structures apart to better understand a biological entity as a whole (see Theise and Kafatos 2013, p. 12).[21]

Moreover, according to Theise and Kafatos (2013), boundary selection posits a challenge for the reductive approach towards biological explanations. Another possible evidence for the complementarity approach in the life sciences derives from quantum physics. According to them (2013, p. 15), "like quantum uncertainty, any attempt to study a system will necessarily change the nature of the system being studied, either by experimentally/physically abstracting it from its larger context or by conceptually isolating it from some of its inputs by drawing restrictive boundaries around the system in the process of modeling". Bohr pointed out that, by studying a biological organism one changes its nature inevitably insofar as it breaks up its parts and organization. By analyzing stem cells, Theise and Krause (2002) have come to similar conclusions by stating the principle that "any attempt to analyze a cell

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[19] In this paper, I take reductive approach to be as it is described by the following Rosenberg (1997, p. 464) quote: "all biological properties are realized by combinations – sometimes vastly complex combinations – of molecular properties".

[20] I would like to point out that systems biology is not consensually characterized as a holistic approach (see, in particular Mazzocchi 2012). Moreover, O'Malley and Dupre' (2005, p. 1271) distinguish between 'pragmatic systems biologists' and 'systems-theoretic biologists'. Former examine systems biology as "the study of interacting molecular phenomena through the integration of multilevel data and models" and the latter examine "systems as systems, and not as mere collections of parts in order to understand the emergent properties of component interactions".

[21] According to Theise and Kafatos (2013, p. 14), "the centrality of classical cell theory, as the foundational doctrine of Western biology and medicine, is the first victim of the recognition of biological complementarity". Classical philosophical debate was concerned "whether a body is an endlessly divisible fluid continuum or made of a finite number of indivisible subunits". After the discovery of microscope, the cell theory was born. However, one can drill down and discover another level at which cells do not contain defined or unitary existence. Thus, it is possible that there is present an alternate, equally verifiable, and potentially powerful model of the body, namely, the classical fluid model. Such a model might be beneficial to explain biological phenomena that remain unexplained by cell theory. For instance, Theise and Kafatos (2013, p. 14) proceed to give an example of acupuncture, a method for which no anatomic correlates to meridians and acupoints have been identified.

necessarily alters the nature of the cell at the time of isolation, thereby altering outcomes of subsequent differentiation events."

Marie Kaiser (2011) in the similar fashion mentions the issue of exploring properties of parts of a system *in vitro* and *in situ*. She argues that there is a limit of reductionism since the reductive method of analyzing parts by decomposing a system and studying it in isolation (*in vitro*) can lead to a limiting understanding of a complex system and its organization and interaction between parts *in situ*. That is particularly the case when referring to integrated systems that are organized in a complex sense, namely, the parts and interconnections are co-determined by the system's organization (see Bechtel and Richardson 2010). Thus, Kaiser (2011) argues that the more complex organization of a system is, i.e., the parts are more integrated and dependent on each other, the more limited reductive method is in investigating those systems in isolation. In that sense, it seems that another perspective is needed when examining systems, especially the complex one, and the above-mentioned examples provide a serious challenge to the reductive approach.

Let me now return to Delbrück's and formerly Bohr's complementarity approach. The examples provided above are connected to the views that were offered by Delbrück. In that sense, I present the following quote:

> Just as we find features of the atom, its stability, for instance, which are not reducible to mechanics, we may find features of the living cell which are not reducible to atomic physics but whose appearance stands in a complementary relationship to those of atomic physics. This idea, which is due to Bohr, puts the relation between physics and biology on a new footing. Instead of aiming from the molecular physics end at the whole of the phenomena exhibited by the living cell, we now expect to find natural limits to this approach, and thereby implicitly new virgin territories on which laws may hold which involve new concepts and which are only loosely related to those of physics, by virtue of the fact that they apply to phenomena whose appearance is conditioned on not making observations of the type needed for a consistent interpretation in terms of atomic physics (Delbrück 1949, p. 8).

As it is evident, Delbrück claimed that one should look beyond molecular physics and at the phenomena exhibiting in the living cell. In other words, that one should look for new concepts that are somehow connected to those concepts found in physics, but different. It seems that Delbrück believed that there are concepts, or rather different perspectives, that would be complementary and ultimately provide biological explanations. In that sense, the previously mentioned examples of epigenetics, systems biology, and boundary selection are related to the complementarity approach offered by Delbrück.

Although concepts from epigenetics, systems biology, and boundary selection are still developing, it will be interesting to observe the possibility of finding complementary approach in biological explanations. It seems that the search for complementary concepts and different perspectives on biological explanations is still ongoing. Delbrück's complementarity approach and, as I argued, his anti-reductive stance towards biological explanations, still provides an inspiration for scholars.

5. Conclusion

In this paper, I examined the origins of MB by addressing the conceptual and experimental influence of Delbrück in the development of MB. In particular, his migration from physics to biology, and his scientific work in biology. I emphasized his role in "The Phage Group" as a founding member and a central figure of the group. I explored Delbrück's search for complementarity approach in biology, greatly influenced by Bohr's complementarity approach found in physics. I addressed both reductive and anti-reductive interpretations on Delbrück's view on the nature of biological explanations. Particularly, by examining the theory reduction, i.e., the reduction including that the concepts, explanations, and methods of one scientific discipline are subsumed to the concepts, explanations, and methods of another scientific discipline. I argued for the anti-reductive interpretation by claiming that Delbrück argued for an independent status of explanations of various disciplines, such as, for instance, genetics. In that regard, I proposed that he anticipated an anti-reductive view on the topic whether Mendelian genetics is reduced to molecular genetics. Furthermore, I examined Delbrück's anti-reductive interpretation in the contemporary setting. In that sense, I offered the examples of epigenetics, systems biology, and boundary selection. Those fields potentially posit a challenge to the reductive approach. In other words, the complementarity approach, characterized by Delbrück, could still be alive. However, those fields, along with their ideas and concepts, are still developing. Nonetheless, Delbrück's idea that there are concepts, or rather different perspectives, that would be complementary and ultimately provide biological explanations is still alive and the search for those concepts is ongoing.

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