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Summary

The aim of this article is to put the growing interest in epigenetics in the field of evolutionary theory into historical context. First, I assess the view that epigenetic inheritance could be seen as vindicating a revival of (neo)Lamarckism. Drawing on Jablonka's and Lamb's considerable output, I identify several differences between modern epigenetics and what Lamarckism was in the history of science. Even if Lamarckism is not back, epigenetic inheritance might be appealing for evolutionary biologists because it could potentiate two neglected mechanisms: the Baldwin effect and genetic assimilation. In the second section, I go back to the first ideas about the Baldwin effect developed in the late nineteenth century to show that the efficiency of this mechanism was already linked with a form of non-genetic inheritance. The opposition to all forms of non-genetic inheritance that prevailed at the time of the rise of the Modern Synthesis helps to explain why the Baldwin effect was understood as an insignificant mechanism during the second half of the twentieth century. Based on this historical reconstruction, in the last section, I examine what modern epigenetics can bring to the picture and under what conditions epigenetic inheritance might be seen as strengthening the causal relationship between adaptability and adaptation. Throughout I support the view that the Baldwin effect and genetic assimilation, even if they are quite close, should not be conflated, and that drawing a line between these concepts is helpful in order to better understand where epigenetic inheritance might endorse a new causal role.

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1. Introduction

Since the early 2000s, the new field of epigenetics has given rise to contrasting interpretations of the consequences of epigenetic inheritance for the theory of evolution. Some are claiming that Lamarckism, i.e. the inheritance of acquired characters, should be reassessed [1-3], whether others argue that the standard Modern Synthesis must remain unchanged [4]. Most evolutionary biologists, however, are somewhere in between these two extreme positions in trying to evaluate how epigenetic inheritance can impact evolutionary causality. The aim of this article is to put the growing interest in epigenetics in the field of evolutionary theory into historical context, in order to shed light on some of the stakes in the ongoing debate. Here, history of science is understood as a tool for conceptual clarification in contemporary science: concepts, like organisms and species, are historical entities. In order to better grasp their meaning, a historical and philosophical perspective is often useful.

This historical clarification will proceed in three steps. First, I assess the view that epigenetic inheritance vindicates a revival of (neo)Lamarckism. Based on the impressive theoretical body of work produced by Eva Jablonka and Marion J. Lamb since the late 1980s, my argument will emphasize what I see as differences between Lamarckism in its golden age (roughly, 1880-1920) and the present-day empirical and conceptual situation. In the next two sections, I turn to a related yet different issue: the possible re-appraisal of the efficiency of the Baldwin effect in natural conditions and/or of genetic assimilation. Both concepts were designed to explain the progressive genetic reinforcement of a phenotype that was first elicited by specific and unusual environmental conditions without the need for Lamarckian inheritance to occur. In the early conceptualizations of the Baldwin effect, which date back to the late nineteenth century, the efficiency of this mechanism was already linked with a form of non-genetic inheritance that James Mark Baldwin called 'social heredity'. The strong opposition to any form of non-genetic inheritance that prevailed at the time of the rise of the Modern Synthesis helps explain the reframing of the Baldwin effect by Simpson in 1953 into an almost insignificant mechanism, a view that prevailed during most of the second half of the 20th century. Based on this historical reconstruction, in the last section, I examine the contribution of modern epigenetics and investigate under what conditions epigenetic inheritance might be perceived as potentiating the Baldwin effect or genetic assimilation. I argue that the Baldwin effect and genetic assimilation are best conceived as two different concepts, which should not be conflated despite their similarities. In the Baldwin effect, the transient plastic response allows genetic evolution to catch up regardless the mechanistic basis of the final adaptation, whereas genetic assimilation is primarily a developmental theory where end-result genetic adaptations are conceived as stabilized plastic accommodations, both following the same developmental pathway (see sections 3(a) and 4.(a)). As this distinction, first elaborated by Paul Griffiths [5], is not the central subject of this paper and cannot be fully addressed in a short sub-section, I will mostly take it for granted and then detail why epigenetic inheritance, if widespread in natural populations, could enhance the efficiency of both mechanisms, yet for different reasons.

2. A return of Lamarckism?

The past 20 years or so have witnessed a significant surge of the terms 'Lamarck' and 'Lamarckism' in scientific literature, in connection with the growing field of epigenetics. By far the most elaborate argument in support of a Lamarckian reading of the evolutionary consequences of epigenetic inheritance has been produced by Eva Jablonka, often in close collaboration with Marion J. Lamb. Since the late 1980s [6], they have published an impressive body of work at the crossroads of theoretical biology, philosophy and history of science [7-9]. Their 1995 book – *Epigenetic Inheritance and Evolution, The Lamarckian Dimension* – stands out by its scope and was an important step in the rise of the collective project of an "Evolutionary Extended Synthesis" [10].

Since the beginning, Jablonka and Lamb have acknowledged and embraced the highly controversial dimension of the term 'Lamarckism', deciding to stick to it [11, p. vii]. Their definition of Lamarckism is a very broad and inclusive one, which is why they often favor terms like 'Lamarckian dimension' [7] or 'Lamarckian problematics' [12]. In short, they emphasize the relevance of

developmental change in evolutionary theory [12, p. 145], an aspect that was indeed absent in the standard version of the Modern Synthesis.

Undeniably, terms 'Lamarckism' and 'Neo-Lamarckism', which were first coined in the mid-1880s, have come to mean many things for many people in the course of the history of biology, allowing room for interpretation and various appropriations. Yet, the fact also remains that despite this polysemy, 'Lamarckism', in opposition to Weismann's neo-Darwinism, was in the first place thought to designate an evolutionary theory where a physiological process of inheritance of acquired characters has the leading role (Bowler, 1983), a significantly narrower definition than the one currently used by Jablonka and Lamb. Considering some of the main versions of Lamarckism that flourished around 1900, I would like to emphasize several differences between the 'golden age of Lamarckism' [13] and the present day (for another critical evaluation of a Lamarckian account, see especially [14]).

(a) "Multiple inheritance systems"

Jablonbka and Lamb have always paid special attention to the conceptualization of potential reciprocal relationships between what they term "epigenetic inheritance systems" (developmental systems that could have heritable effects like DNA methylation, histone marks, RNA interference, self-sustaining loops, etc.) and the genetic system. This is why they devoted the concluding chapter of their 1995 book to this specific issue, a central aspect in their theoretical endeavor. This highly fecund area of conceptualization also defines the historical originality of the present-day situation: genetics has to be taken into account. In contrast, past Lamarckians thought of inheritance of acquired characters as the main mode of biological heredity, if not the only one (see for instance Ernst Haeckel's famous hypothesis of the "perigenesis of the plastidules" [15]). Even after 1900 and the rediscovery of Mendel laws, Lamarckian biologists tried to marginalize genetics because it would have only concerned secondary traits that could be neglected from an evolutionary perspective [16].

A point at stake now is how epigenetic inheritance could interact with genetic inheritance and thus have a causal intergenerational role, a mostly unprecedented discussion in the history of biology.

(b) Epigenetic inheritance: an evolved product of natural selection

Another remarkable difference, from a historian's perspective, lies in the fact that all these epigenetic systems are themselves understood as evolutionary constructions, i.e. products of natural selection [17]. In contrast to what was thought in past Lamarckian theories, the possible inheritance of acquired characters based on epigenetic mechanisms can no longer be seen as the ancestral condition of all living things that would have been efficient since the beginning of life. Put it briefly, inheritance of acquired characters has to be explained by natural selection and cannot be taken for granted. This constitutes another epistemological difference between current knowledge and what Lamarckism was in the history of science.

(c) Is epigenetic inheritance an autonomous driver of adaptive evolution?

In controlled conditions, it is now possible to produce durable epigenetic variation within "epigenetic recombinant inbred lines" (epiRILs) which show a phenotypic diversity solely based on epimutations that could be faithfully transmitted for at least eight generations [18]. In such experimental systems, epimutations, like standard genetic mutations, are not intrinsically adaptive, and even if they are widespread in nature, natural selection would still be necessary to build evolutionary adaptations on such grounds. Here it is crucial to recall that Modern Synthesis [19-21] was developed before the rise of molecular biology, i.e. before genes were equated with DNA sequences. Population genetics is not concerned by the material basis of genes and could easily integrate epimutations in its formalizations. During the interwar period, the first models of population genetics assumed much higher mutation rates than those subsequently measured, rates closer to those applying to epimutations.

In the history of science, I argue, "Lamarckism" refers primarily to the idea that the inheritance of acquired characters is efficient enough to be responsible, in its own right, for building adaptations. This was already the case in Lamarck's original understanding [22], where the inheritance of acquired characters was for the first time a means of accounting for unlimited organic change [23]. It was also the case after Lamarck, regardless of what specific theory was being examined (Darwin's pangenesis, Haeckel's "perigenesis of the plastidules", etc.).

Thus the central question that remains is whether epigenetic inheritance could underline adaptation under natural conditions. This is difficult to answer because the frequency and stability of epigenetic inheritance are strongly related to the kind of organism in question: epigenetic inheritance might be relatively frequent in groups like plants and especially in unicellular organisms, but much rarer in higher vertebrates where epigenetic reprogramming mechanisms that efficiently remove epigenetic marks from DNA each generation have been selected [24,25].

The most challenging aspect would be to document empirical cases where epigenetic variations are both meiotically inherited and adaptive, i.e. not random regarding fitness. Until the mid-2010s, the few results available [26], often cited, were also highly controversial [27]. Yet, recent discoveries in *Caenorhabditis elegans* [28], if confirmed, strongly suggest that in some cases, RNA-mediated inheritance could be very close, in its functioning, to a genuine Lamarckian process [29,30]. It remains to be known how frequent this mode of inheritance could be beyond the specific case of *C. elegans*.

(d) A discontinuous history

The last case that could be made against Lamarckian accounts of modern epigenetics is that they are retrospective reinterpretations of a history that owes nothing to either Lamarck's own "*Philosophie zoologique*" [31] nor to the standard Lamarckian theories of the period 1880-1920 [13,32,33]. On the contrary, current understanding of the molecular mechanisms of epigenetic inheritance comes from the research program of standard molecular biology. The first epigenetic mechanisms were identified in the 1950s, when it was understood that under specific circumstances, some enzymatic systems might produce positive feedback loops that mimic genetic transmission [34]. Later, in the 1970s and 1980s, other molecular mechanisms, like DNA methylation, were first postulated and then characterized [35,36].

Molecular biology has since its inception been strongly opposed to any form of Lamarckian conception of life, a very sensitive topic at the time of 'Lysenkoism'. After World War II, the rise of agronomist Trofim Lysenko in the Soviet academic system was based on his unfailing support to the Marxist dogma and to his complete opposition to genetics, caricatured as an idealistic "bourgeois" science. According to Lysenko, organisms could easily be changed for the better by the right environment. With Stalin's support, he was able to almost entirely eradicate genetics in the USSR [37]. In reaction, during the "Cold War in genetics" [38] the growing field of molecular biology avoided any possible interpretation in terms of inheritance of acquired characters [39]. Thus, on the scale of the history of science, the reframing of molecular knowledge on epigenetic inheritance within a Lamarckian framework happened very recently. There is no such thing as a Lamarckian tradition, which would have silently developed in parallel with standard Darwinian biology. There are only specific outcomes of molecular biology that are sometimes reinterpreted in terms of Lamarckian heredity.

3. Looking for a third way: some landmarks in the history of the Baldwin effect

Arguing that epigenetic inheritance is substantially different from what Lamarckian inheritance was in the history of science is not tantamount to claiming that it could have no impact on our modern understanding of evolutionary causality. It has been noted for years that epigenetic inheritance could enhance the efficiency of the Baldwin effect and of genetic assimilation [40], two evolutionary mechanisms that were neglected during the second half of the twentieth century. In this section, my

aim is to show that initially (1896-1902), the Baldwin effect was already closely connected with non-genetic inheritance and that Simpson's 1953 standard and oversimplified account ignored this conceptual aspect.

(a) Baldwin's Baldwin effect and 'social heredity'

The concept of what would later be called the 'Baldwin effect' was almost simultaneously formed by James Mark Baldwin, Conwy Lloyd Morgan and Henry Fairfield Osborn in 1896 [41]. Baldwin was the most concerned by the explanatory power of this "new factor in evolution" [42], whereas Osborn was skeptical about its scope of application from the start [43]. Baldwin made a huge effort to elaborate on the concept, resulting in a 400-page book entitled *Development and Evolution*, published in 1902 [44]. The book presents the first comprehensive and detailed theorization of the Baldwin effect and is the focus of the present sub-section.

Basically, the Baldwin effect is the idea that individual and plastic accommodations to new environmental conditions, while not heritable by themselves, can allow populations to survive and for genetic evolution to 'catch up'. Adaptations, at first strictly phenotypic, will in the end be genetically encoded, but not for Lamarckian reasons. This is how Simpson framed the issue in the 1950s (see section (b)). Baldwin's original publications are much more difficult to interpret because they were written before the rediscovery of Mendel's laws and the emergence of population genetics, and because Baldwin changed his mind about the conceptual content of what he termed "organic selection" [45]. Yet, there is no doubt that he thought of something close to the previous definition: "The present writer considered this function to be probably a case in which natural selection has put a premium upon the acquisition of adjustments which would keep a creature alive and give the species time to acquire the congenital mechanism for the same functions – illustrating what is called, below, 'organic selection'." ([44, p. 28]; for a more detailed account, see pp. 137-138).

But what is usually neglected is that Baldwin, since the first publication, linked the efficiency of this mechanism to a form of non-genetic inheritance that he termed 'social heredity' [42, pp. 537-539,45]. 'Organic selection' was indeed part of a bigger theoretical picture termed evolution by 'orthoplasy', i.e. a hypothetical explanation of some trends in macroevolution. These trends were seen as the long-term effect of the interrelationship of organic selection and social heredity. As a psychologist, Baldwin was especially concerned with behavior and, to him, plasticity was mainly about behavioral plasticity. 'Social heredity' or 'tradition' was the intergenerational 'social transmission' [44, chapter 7] of specific behaviors resulting from learning. Social heredity was pivotal in allowing individuals to enhance their survival in new environments, which increases the efficiency of organic selection and thus the hereditary "acquisition" of new adaptations [42, p. 541]. Social heredity and organic selection were self-reinforcing processes, producing orthoplasy at the macroevolutionary scale [44, p. 104, p. 173].

It is quite easy to translate these outdated concepts in a modern framework: to Baldwin, epigenetic inheritance worked along the same lines as individual plasticity because these two interacting phenomena allow populations to temporarily survive environmental changes. The epigenetic transmission of a new phenotype reinforces the efficiency of the Baldwin effect by increasing the amount of time available for the occurrence of 'coincident' mutations (see 4(b)).

(b) Why was the Baldwin effect marginalized at the time of the Modern Synthesis?

After initially eliciting extensive debates regarding its efficiency and scope, the Baldwin effect was rather quickly eclipsed around the late 1900s and very rarely mentioned or discussed during the thirty years that followed. It re-emerged as a topic of interest only in the late 1930s, first in the Russian school of evolutionary biology led by Gause, Kirpichnikov, Schmalhausen and others [46-48]. Approximatively at the same time, the Baldwin effect also became a central topic for some French biologists, especially zoologist and cytologist Raymond Hovasse, who wrote a book devoted to it during WWII ([49], followed by a more detailed synthesis [50]).

Given this renewed interest in the Baldwin effect (see also for instance [51, p. 304]), the tense context of Lysenkoism and Waddington's new research program [52,53], Simpson thought it necessary to bring clarity in this debated and complex issue, where so many terms were used more or less as synonyms ('organic selection', 'coincident selection', 'post-adaptation', 'stabilizing selection', etc.). In a famous 1953 article, published in *Evolution*, Simpson offered a welcome clarification of the process as well as a new and definitive term to designate it: 'The Baldwin effect'. This is how he reframed the steps of the mechanism [54, p. 112]:

"(1) Individual organisms interact with the environment in such a way as systematically to produce in them behavioral, physiological, or structural modifications that are not hereditary as such but that are advantageous for survival, i.e., are adaptive for the individuals having them.

(2) There occur in the population genetic factors producing hereditary characteristics similar to the individual modification referred to in (1), or having the same sorts of adaptive advantages.

(3) The genetic factors of (2) are favored by natural selection and tend to spread in the population over the course of generations. The net result is that adaptation originally individual and non-hereditary becomes hereditary."

This new formulation was acknowledged as a helpful clarification of the Baldwin effect mechanism by the other architects of the nascent Modern Synthesis (see for instance [55, p. 610]). In comparison to the complex and sometimes obscure theorizations that had prevailed until then, this new definition was without a doubt a clarification. But, at the same time, it was also a simplification and an impoverishment of the causality involved in the process, especially when one compares Simpson's Baldwin effect and the mechanisms developed by Baldwin, Schmalhausen and Waddington.

Most importantly the reciprocal relationship between non-genetic inheritance and the Baldwin effect as elaborated by Baldwin is simply missing from Simpson's account, and as a consequence, it was never discussed again in the second half of the twentieth century. It is difficult to establish if this omission by Simpson was deliberate or not and to which extent it might have been caused by the lack of clarity of Baldwin's own writings. But the fact is that in such a simplified form, the Baldwin effect was both fully compatible with the Modern Synthesis and of little interest [54, pp. 115-116], a viewpoint that quickly become standard [55, pp. 610-613] and has remained so since [56].

4. Epigenetic inheritance and the efficiency of the Baldwin effect and genetic assimilation

Now that Lysenkoism is no longer a threat and that a less dogmatic understanding of the Modern Synthesis might be prevailing in the wake of the debate regarding a possible "Extended Synthesis", the issue of the link between epigenetic inheritance and the Baldwin effect should perhaps be reconsidered in a more positive light [57]. In this section, I propose a distinction between at least three types of causal links between epigenetic and genetic inheritance within the frameworks of the Baldwin effect and of genetic assimilation.

(a) The Baldwin effect and genetic assimilation: two different evolutionary mechanisms

To begin with, it is important not to conflate the Baldwin effect and genetic assimilation. The *theory* of genetic assimilation, independently elaborated by Waddington and Schmalhausen in the mid-twentieth century, is far more complex than the mechanism summarized in Simpson's 1953 formula (for a retrospective perspective, see [58,59]). Several conceptual criteria can be used to draw a distinction between the Baldwin effect and genetic assimilation [60], but for the sake of brevity, I will focus on one here, first highlighted by Paul Griffiths [5]: the Baldwin effect is concerned only with fitness, i.e. it is neutral regarding mechanisms, whereas genetic assimilation is a developmental theory where end-result genetic adaptations are conceived as stabilized plastic accommodations, both following the same developmental pathway [48,61]. This means that, in the Baldwin effect framework, there is no need for the final genetically-encoded adaptation to be homologous to the initial plastic

accommodation, as long as it is able to increase fitness. This conceptual aspect is unambiguously present in Simpson's standard formulation, in which the new genetic characters must only have "the same sorts of adaptive advantages" as the initial plastic variations. This had already been clearly stated by the most prominent figures in the history of the Baldwin effect, like Baldwin [44, p. 143] or Hovasse [50, p. 17]. The terms "coincident variations" (Lloyd Morgan) and "coincident selection" (Russian school) both emphasize the idea that, regardless of the mechanistic basis involved, the pivotal aspect is that genetic adaptations and plastic accommodations have to *coincide* in terms of functional/adaptive outcomes.

In the same 1953 issue of *Evolution* where Simpson published his seminal article, Waddington strongly opposed the possible conflation between genetic assimilation and the Baldwin effect [62]. One of his arguments was that, in his mechanism, there is a causal link between steps 1 and 2 of Simpson's scheme (see above 3(b)), but that the link in question is non-Lamarckian [62, p. 386]. Waddington singled out genotypes as having the ability to respond adaptively to new environmental stimuli to be selected in the building of evolutionary adaptations. This is why he was so concerned by the fact that plasticity is itself a genetic property, and as such a character upon which natural selection can act [63].

(b) Buying (more) time: the Baldwin effect

Epigenetic inheritance could enhance the efficiency of the Baldwin effect in a straightforward manner, by extending the time period of the transient plastic response to new environmental challenges. Since Baldwin [42, p. 445] and throughout the twentieth century [50, p. 12], the Baldwin effect has been primarily about "buying time" [64], especially when environmental conditions are changing too fast for the standard mutation/selection process to adequately respond. This extra amount of time is supposed to have two roles.

The first, as we have already seen, is to increase the probability of occurrence of the "good" mutations, the ones that pave the way to the new fitness peak. Because mutations remain random, the more a population is able to survive in a new environment, the more its allelic pool will get the opportunity to be enriched with adaptive variants.

In the traditional 'Simpsonian' account, the Baldwin effect is reduced to a "breathing space" during which good mutations can occur [65], and as such could be understood as a minor process in adaptive evolution. Yet, I argue that this classical account is an oversimplification, because it says nothing about the fact that plastic adaptations create a new ecology and thereby new selective pressures that could causally produce genetic adaptions. After Simpson, it took time to fully acknowledge this dimension of the Baldwin effect and to conceptualize it in the terms of niche construction theory [45,65,66]. Nonetheless, careful reading suggests that the idea was already formulated in Baldwin's writings, albeit often rather cryptically [44, p. 150]. In more recent literature, it is not difficult to find much more explicit instances [50, p. 128].

This second, sometimes neglected, evolutionary role of plastic accommodations is fully in accordance with the idea put forth in the previous section that the Baldwin effect is neutral about mechanisms. By definition, the polarization of selective pressures by individual plastic responses maximizes fitness, regardless of the mechanisms that could be used in the process. Epigenetic inheritance could be important there not because the final adaptation would be a genetically stabilized form of the initial plastic accommodation but because, by helping to maintain new selective pressures over several generations, it would favor the path towards a new adaptive peak.

This aspect also highlights a theoretical problem inherent in the Baldwin effect itself: the evolutionary impact of the plastic response. It remains an open question whether plasticity, in creating a new ecology, enhances selection pressure, or, on the contrary, because it masks genetic polymorphism, slows gene-level evolution. This issue has been raised explicitly at least since the 1990s [67,68]. The impact of plasticity on genetic evolution appears to depend on several parameters, including the cost of plasticity and the complexity of the fitness landscape [69].

(c) Stabilizing the epigenetic landscape: Genetic assimilation

If one accepts the demarcation between the Baldwin effect (a fitness based argument) and genetic assimilation (a developmental based argument) sketched above, then it follows that epigenetic inheritance might not play the same role in genetic assimilation. In the original Waddingtonian framework, genetic assimilation is about channeling and stabilizing, in the epigenetic landscape, developmental pathways already involved in the initial plastic response. Between the genotype and the phenotype, in contrast to the Modern Synthesis, Waddington put the emphasis on a third intermediate entity, namely the epigenetic landscape. This developmental phase-space is rooted in the genome and causally produces the phenotype. However, the complexity of these relationships, especially the systemic functioning of the genome, tends to thwart any sort of reductionist understanding of phenotypical characters in terms of additive gene actions [5,70]. For Waddington, the epigenetic landscape has a life of its own, an idea conceptualized in the notion of canalization [52,53,59,61].

Therefore, any mechanism that tends to increase the robustness of a developmental path would immediately favor genetic assimilation, as has been theoretically demonstrated [71]. This is precisely where transgenerational epigenetic inheritance could have a causal role: it would respond more quickly than the genome in stabilizing/canalizing the new adaptive developmental path, paving the way for the genetic architecture of the character to be reframed. Whereas in the Baldwin effect, epigenetic inheritance would have a selective-ecological impact (its evolutionary causality is outside the organism), in genetic assimilation it would have a mechanistic-developmental one (its evolutionary causality is inside the organism).

(d) From epimutations to mutations for molecular reasons: a theoretical novelty

With the recent advances of the growing field of epigenetics, another possibility has been put forth: that epimutations might preferentially be converted at the same or neighboring sites in the same genes [40]. This is why the 'pseudoassimilation model' recently designed and supported by Laura Fanti, Sergio Pimpinelli and colleagues [72,73] might be regarded as a new proposition in the history of the theoretical relationships between adaptability and adaptation. In this model, the fixation of a new phenotype is the consequence of the selection of *de novo* mutations. Another key aspect of the model is that it makes mechanistic assumptions about a possible connection between the epigenetic production of phenocopies and an increased mutation rate in the corresponding loci in the germ line. According to the authors, "if the same epigenetic modifications that induce phenocopies make the corresponding loci more susceptible to DNA alteration caused by transposon insertions or DNA rearrangements, it is possible to envisage a mechanism that increases the probability of pseudoassimilation of the phenocopies" [72].

This hypothesis is a new possibility that differs from those discussed in the two previous sections. It differs from the traditional Baldwin effect framework because the replacement of epimutations by mutations has, in this case, a structural basis: it is the same DNA sequence that is subject to epimutations and mutations. Yet it also differs from genetic assimilation strictly speaking because it does not need to take into account the intermediate level of the epigenetic landscape. At this point, a distinction should be highlighted between two interpretations of genetic assimilation. It seems that Waddington himself sometimes balanced between two substantially different understandings of his evolutionary mechanism. The first is still a structural/mechanistic but non-radical one (with respect to the Modern Synthesis): it consists in explaining genetic assimilation at the level of individual genes. By selecting the fittest genotypes in stage 1 (the plastic response), stage 2 will be more genetically accessible until reliable genetic control of the characters involved (stage 3). It is assumed that the same set of genes is responsible for the initial plastic response and the final adaptation. In this framework, genetic assimilation is reducible to threshold selection, an explanation favored by some members of Waddington's research group [74] and by the founders of the Modern Synthesis [55, p. 190]. If this interpretation of genetic assimilation is favored, then a possible causal molecular link between epimutations and mutations would greatly reinforce its efficiency in making accessible new variants of the genes already recruited in the phenotypic stage.

A much more radical understanding of genetic assimilation makes such assumptions problematic because the genome is seen as a complex network of interactions where it is almost impossible to individualize the causal role of a specific allele on the phenotype [61]. Accordingly, natural selection in a new environment cannot be reduced to gene selection [48]. What is selected is a new epigenetic landscape, a new developmental space, and because of canalization, it could have multiple genetic bases [60]. This concept of genetic assimilation would not be directly impacted by the molecular transition epimutations → mutations. Epigenetic inheritance potentiates its efficiency only as long as it helps stabilize the new form of the epigenetic landscape (4(c)).

5. Conclusion

My aim in this paper was to evaluate what epigenetic inheritance can bring to the picture of evolutionary theory, where "evolutionary theory" is itself understood as a historical entity, i.e. with the benefit of hindsight. As a historian of science, I am especially interested in conceptual change and in the intrinsic challenge of writing the history of evolutionary theory since Darwin published *On the Origin of Species* in 1859.

My claim is twofold: (1) given present-day knowledge, epigenetic inheritance would be better conceptualized as something different than a modern instance of Lamarckism, (2) epigenetic inheritance could help reconsider the scope of two neglected evolutionary mechanisms, namely the Baldwin effect and genetic assimilation. Throughout, I have supported the view that the Baldwin effect and genetic assimilation, even if they are quite close, should not be conflated. Drawing a distinction between these two mechanisms allows to develop a more precise understanding of the evolutionary steps where epigenetic inheritance might have a causal role, as I have tried to give a historically informed characterization.

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Competing Interests

I have no competing interests.