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Abstract – During the early 20th century the diverse practices of genetics were unified by the concept of the gene. This classical gene was simultaneously a unit of structure, function, mutation, and recombination. Starting in the 1940s, however, the classical gene began to fragment. Today when we speak of a gene for some malady, a regulatory gene, a structural gene, or a gene frequency, it is entirely possible that we are deploying different gene concepts even though we are using the same term. The problem of the gene addresses the fragmentation of the classical gene concept by asking to what extent a comprehensive and unifying gene concept is possible or desirable. Fully comprehensive gene concepts seem untenable today, but, within different disciplinary domains, unifying, but non-comprehensive, gene concepts can be epistemically worthwhile. The problem of the gene persists, however, not because of its epistemic value, but because of its political value. Using both the arguments for newly proposed gene concepts and the historical dispute over the classical gene, I argue that the desirability of gene concepts rests in part on the political ramifications of their deployment and contestation. © 2000 Académie des sciences/Éditions scientifiques et médicales Elsevier SAS

Résumé – La problématique du gène. Au début du XX^{e} siècle, les diverses pratiques de la génétique furent unifiées grâce au concept de gène. Le gène « classique » était à la fois une unité de structure, de fonction, de mutation et de recombinaison. À partir de 1940, le gène classique a commencé à se fragmenter. Aujourd'hui, lorsque nous parlons d'un gène impliqué dans une maladie, d'un gène régulateur, d'un gène structural ou de fréquences de gènes, il est tout à fait possible que, sous le même terme, nous fassions référence à différents concepts de gène. En quelle mesure un concept global et unificateur du gène est-il possible ou désirable? Il semble impossible aujourd'hui de proposer un concept global, mais la recherche, à l'intérieur des différents domaines disciplinaires, de concepts unificateurs peut être importante. Que la notion de gène reste un problème ne vient pas des ambiguïtés de son usage scientifique, mais des enjeux politiques qui y sont liés. En se basant à la fois sur les arguments qui ont été utilisés pour justifier une nouvelle définition du gène, et sur les controverses qui ont agité la génétique classique, je conclus que la nécessité de proposer de nouvelles définitions du gène vient surtout des conséquences politiques de son utilisation ou de sa critique. © 2000 Académie des sciences/Éditions scientifiques et médicales Elsevier SAS

1. Introduction

At the 100th anniversary of the publication of Gregor Mendel's paper, Milislav Demerec noted that during the first half of the 20th century the gene had been regarded as 'a unit of a genetic system, an indivisible entity in the processes of recombination, self-reproduction and mutation' [1]. Writing as he was in 1965, Demerec knew that the classical gene which had once unified structure, function, recombination, and mutation had been fragmented. Perhaps because his own work on mutability had reluctantly contributed to the dissolution of the classical gene concept, Demerec's commemorative essay makes its fragmentation an historical inevitability. Beginning with De Vries and Correns, Demerec argued that supposedly 'Mendelian' characters in plants were not always so well

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behaved. Citing later work on variegation in plants, including his own research, as well as research on step-allelism, Demerec documented the genetics community's growing doubts about the indivisibility of the gene. Of course, to Demerec's list of work undermining the classical gene, we could add H.J. Muller's work on the position effect and distribution of scute alleles, Richard Goldschmidt's attacks on the gene, and E.B. Lewis's work on pseudo-alleles such as the star, asteroid system [2–5]. In the intervening 35 years since Demerec wrote his essay, the classical gene concept has been buried in a proliferation of molecular genetic structures and processes. Phenomena such as the various kinds of regulatory elements, different forms of RNA splicing, satellite DNA, and pseudogenes seem to guarantee that we cannot return to a comprehensive gene concept [6–8]. Nevertheless, gene concepts still prove irresistible to biologists and philosophers of biology.

The problem of the gene is rooted in the fragmentation of the classical gene concept and asks to what extent a comprehensive and unifying gene concept is possible or desirable. Hans-Jörg Rheinberger recently posed the problem of the gene as this question, 'Do molecular biologists need a unified and generalized gene concept?' [6]. Molecular biology is understood by Rheinberger as a hybrid array of experimental systems ranging from biophysics and biochemistry to evolutionary genetics and developmental genetics which produce a corresponding array of gene concepts. From his perspective, it is not 'necessary or even desirable to have a unified concept of the gene in order to tie all of these disciplinary specializations together and to develop them in a coordinated fashion'. In fact he argues that 'an attempt to do so today would produce nothing more than an exercise in rhetoric' [6]. From a conceptual perspective, Rheinberger is correct. A single comprehensive gene concept is not needed by molecular biologists or biologists in general. More specific gene concepts, such as a developmental gene concept or an evolutionary gene concept, are not valued because they are fully comprehensive. Nevertheless, they provide a means to unify or systematize circumscribed disciplinary domains. When considering the problem of the gene then we must drive a wedge between the scientific values of generality and unification. The problem of the gene should be decomposed into two problems: Is it necessary or desirable to have a comprehensive or generalized concept of the gene? and Is it necessary or desirable to have a unifying concept of the gene? Rheinberger and others have convincingly argued that we do not need a comprehensive gene concept. The case against generality does not extend to unification, however. Within different disciplinary domains unifying, but non-comprehensive, gene concepts can be epistemically worthwhile. The problem of the gene persists, however, not because of its epistemic value, but because of its political value. To paraphrase Pierre Bourdieu, epistemological problems are always, inseparably, political problems [9]. Using both the arguments for newly proposed gene concepts and the historical dispute over the classical gene, I argue that the desirability of gene concepts rests in part on the political ramifications of their deployment and contestation.

2. Unifying the gene

Part of the allure of the classical gene lay in its ability to unify significant aspects of the theory and practice of genetics in the early 20th century. In Thomas Hunt Morgan's *The Theory of the Gene*, for instance, genes are assumed to be stable, paired elements in the germinal material which follow Mendel's laws, exist in a linear order on the chromosome, and remain in tact during crossing over [10]. As such Morgan's gene becomes a common object for practices of determining patterns of transmission, inferring linkage, and mapping. Later, H.J. Muller and L.J. Stadler would make the gene the object of the study of mutation as well [11, 12]. Accepting the classical gene as a common object of research meant accepting that different aspects of genetics were in fact dealing with the same phenomena. In the eyes of philosophers such as Michael Friedman this is what makes unification valuable.

Although philosophers of science have typically discussed unification in conjunction with issues of explanation, Friedman motivates his theory of explanatory unification by appealing to phenomena. According to Friedman, 'science increases our understanding of the world by reducing the total number of independent phenomena that we have to accept as ultimate or given. A world with fewer independent phenomena is, other things being equal, more comprehensible than one with more' [13]. The key to Friedman's claim lies in defining what counts as independent phenomena. Being an analytic philosopher, Friedman quickly translates 'independent phenomena' into 'logically independent lawlike sentences' and proceeds with his argument. We can resist the urge to axiomatize, however, and allow that for practical purposes whether phenomena are independent or not depends on whether they are the common objects of different scientific practices or not. Scientific practices are operations involving theoretical and/or experimental systems. They can be individuated by noting differences in operations (constructing a model, running a simulation, performing an experiment) or in experimental systems (Drosophila population cages versus bacterial chemostats, for instance). Phenomena that form the common object of many different scientific practices offer the opportunity to find interconnections that will allow scientists to unify or systematize their beliefs more readily than if no such phenomena existed.

Consider a molecular gene concept recently proposed by Ken Waters. Waters suggests that we speak of a gene as 'a gene for a linear sequence of product at some stage of genetic expression' [14]. This definition allows Waters to circumvent problems posed by the existence of introns and mRNA splicing. Waters' gene concept applies both to the claim that there is a gene for a linear sequence of mRNA and that there is a gene for a linear polypeptide

sequence. So, systems with and without post-transcription modifications can be described using the same term. Waters' definition provides a gene concept that unifies our understanding of the gene as a coding region either with or without further modification.

Waters' gene concept has been criticized as doing nothing to clarify the use of the term within molecular genetics. While it may provide a more unified systematization of beliefs, Eva Neumann-Held has argued that we are better off describing the processes of polypeptide expression in the more precisely defined terms already in use with in molecular biology [15]. Neumann-Held's argument is motivated by her concern with what Waters left out. According to Neumann-Held, Waters' gene concept does not include regulatory regions, yet regulatory regions are necessary for his genes to produce any linear sequence. If genes are thought of as 'making a polypeptide', then Waters' definition leaves too much out. In its place, Neumann-Held offers her own more inclusive gene concept.

Neumann-Held proposes what she calls 'an expanded constructionist gene concept', which integrates DNA and its developmental context. Instead of viewing the gene as a DNA sequence, which is responsible for some linear chemical product, Neumann-Held suggests that genes be understood as 'processes, which under certain environmental conditions structure the DNA (and the mRNA) and result in a polypeptide' [15]. Although intentionally limited to processes which produce linear sequence products, this process view of the gene incorporates environmental and developmental components as well as DNA sequences, RNA sequences, and polypeptide sequences. To further emphasize the importance of process, in collaboration with Paul Griffiths, Neumann-Held rechristened her gene concept the 'molecular process gene concept' [16].

Griffiths and Neumann-Held want to make genes 'developmentally meaningful units'. Like Richard Goldschmidt in *Theoretical Genetics* [17], Griffiths and Neumann-Held argue that genes cannot be just DNA, because DNA can not do anything. For them, overlapping genes mean that a DNA sequence that functions as a promoter under one circumstance could function as part of a open reading frame in another. The function of a particular DNA sequence is thus determined by its role in a 'developmental system'. In their words, 'the gene is identified not with these DNA sequences alone but rather with the process in whose context these sequences take on a definite meaning' [16].

This gene concept, according to Neumann-Held, has the advantage that 'a research strategy is unsatisfactory which only identifies 'genes' (in the sense of DNA sequences), but neglects (or postpones) research into the mechanisms that make the 'genes' effective in connection with non-genetic…' [15]. Or, as Griffiths and Neumann-Held put it, because their gene concept emphasizes connections to everything influencing expression from a DNA sequence, their gene concept 'helps scientists bear in mind the easily overlooked fact that the production of this polypeptide product is the result, not of the presence of the DNA sequence alone, but of a whole range of resources affecting gene expression' [16]. As was her intent, the molecular process gene concept is a 'developmentally relevant gene concept' [15].

Insofar as the proposed molecular process gene subsumes a diverse array of phenomena, it is a unifying object of research. However, by focusing on the unifying power of these gene concepts I do not wish to suggest that the epistemic worth of a gene concept can be reduced to unifying power alone. Judgements of the epistemic worth of a concept, like judgements of the epistemic worth of a theory, incorporate and adjudicate between a variety of values and criteria of which unification is only a part. Nevertheless, part of Neumann-Held's motivation is to reclaim a small part of the 'Unity of Nature' by using a developmental systems approach. Griffiths and Neumann-Held are very clear that the molecular process gene concept is not a comprehensive gene concept: it does not apply to DNA sequences that do not contribute to a linear polypeptide and it is distinct from what they call the evolutionary gene concept. Nevertheless, it unifies a large array of phenomena (sequences with introns, exons, promotors, and other regulatory elements as well as sequences that must be processed and assembled). Indeed, the molecular process gene concept seems to cover the entire range of molecular phenomena that make up Petter Portin's nine-fold classification of the molecular gene [8]. This range is not accidental. Neumann-Held's constructivist gene concept was renamed the molecular process gene concept, because it was intended to replace more traditional molecular gene concepts, such as Waters', that do not seem to cover the diversity of phenomena associated with gene expression. Although presented as a philosophical argument concerning the epistemological value of a gene concept, Griffith's and Neumann-Held's targeting of the molecular gene and their advocacy of a developmental systems approach suggest an additional dimension to the appeal of gene concepts.

3. Genes and politics

Much to the chagrin of some analytic philosophers of science, scientists are rarely rational epistemic agents; by which I mean, scientists rarely make judgements regarding a theory, problem, or experiment on the basis of rational consideration of purely epistemic criteria. A host of non-epistemic concerns waits to complicate scientific decision processes and turn the philosophers' dream of logical clarity into a sociological entanglement of interests, enrolments, networks, values, and politics. A significant portion of the appeal of gene concepts is derived from this sociological context.

When Neumann-Held proposes her constructionist gene concept and defends its conceptual usefulness, she also engages in a struggle for authority in genetics that is almost as old as the gene concept itself [18, 19]. Ever since

Thomas Hunt Morgan argued for the separation of genetics and embryology, there has been a perception that geneticists have not taken developmental processes seriously enough [20, 21]. Neumann-Held's constructionist gene concept can be seen as an attempt to reorient genetics by making developmental biology a visible and essential component of the fundamental units of heredity. Instead of development being the 'black box' between the genotype and phenotype, the constructionist gene concept makes the process of expression as important as its inputs or outputs [16]. This redefinition creates the potential for a redistribution of who is considered competent to speak to fundamental issues involving the processes of expression; in effect, it legitimizes a developmental approach to the gene that would grant developmentally oriented molecular biologists greater scientific authority.

The struggle for authority underlies a great deal of the internal political struggle in science. A scientist acts or speaks with authority when she is judged to be both technically competent and socially powerful. According to Bourdieu, what is at stake in the competition for authority is the power to impose a definition of what will count as science. Naturally each scientist will prefer that definition which favors him or her the most; 'the definition most likely to enable him to occupy the dominant position in full legitimacy, by attributing the highest position in the hierarchy of scientific values to scientific capacities that he personally or institutionally possesses' [9]. Gene concepts, especially more comprehensive and unifying gene concepts, represent one means of defining the field of genetics; what problems it will consider important, what experimental systems and organisms will be used, and what assumptions will go unquestioned. As such the struggle over gene concepts often is also a struggle for scientific authority [19].

The struggle for authority in genetics has been historically located by Jan Sapp in Morgan's theory of the gene. While Neumann-Held and Griffiths do not historically contextualize their process gene concept relative to Morgan, the historical narrative that follows represents an analogous situation in terms of the struggle for authority in genetics. In both the contemporary and historical cases, the problem of the gene is simultaneously an epistemic and political problem.

Morgan made the theory of the gene the central concern within Drosophila genetics in the early 20th century. Jan Sapp has interpreted Morgan's advocacy of the theory of the gene as a means of demarcating which topics should be considered to be legitimate topics for genetic research. As such, the classical gene concept became part of an early struggle for authority in genetics, according to Sapp. Recently, however, Sapp's analysis has come under attack from Jon Harwood and Robert Kohler. Harwood has argued that Sapp's interpretation is plausible but ultimately unconvincing because he does not develop his analysis of American scientific institutions [22]. I agree that more research on the American institutional context for genetic research is needed, but a full treatment of this history is beyond the scope of the present paper. Kohler has argued pointedly that Sapp's interpretation, as well as Garland Allan's interpretation [18], portray Morgan's Drosophila network as 'a 'hegemonic' establishment, from which genetics had to be liberated by people with a broader biological outlook' [21]. Kohler sees the choice made by Morgan to concentrate on transmission problems to be constrained by their own very successful experimental system and the difficulty of creating an equally successful system which would address problems in evolutionary and developmental genetics. In light of his own analysis of experimental practice, Kohler warns that 'we need to be less quick to impute to historical actors the contentious cultural politics of our own puritanical and sectarian age' [21]. Of course Kohler's warning is worth heeding; Morgan and his associates had enough contentious cultural politics without importing any of our own.

Consider, for instance, the interactions between Morgan's group and that of Richard Goldschmidt. Goldschmidt is remembered today largely for his 'heretical' rejection of the gene and his insistence on sudden evolution mediated by systemic mutations. In the early 20th century, Goldschmidt was head of a division of the Kaiser-Wilhelm Institute for Biology in Berlin and an influential geneticist in his own right. Goldschmidt had a history of encounters with Morgan and the fly group which concretely illustrate the struggle for authority in genetics and the role of gene concepts in that struggle.

From 1912 to 1936, Morgan's fly group managed the growing network of Drosophila researchers by managing the concepts and the specialized stocks of flies needed to do experimental work. In controlling the distribution of stocks, they controlled the distribution of problems, and the distribution of credit. As the group's founder and leader, Morgan maintained control well into the 1930s when it was handed over to Sturtevant. With a few famous exceptions, the fly group shared ideas and mutants freely. Indeed Kohler argues that this openness and cooperation were a result of the 'unspoken rules of etiquette' among the Drosophilists. These rules mandated reciprocity, 'the privilege of receiving stocks entailed the obligation to reciprocate'. They mandated disclosure, 'recipients of stocks were expected to tell donors what experiments they planned to do and to keep them informed of what the results were, especially if the results came a little too close to the donor's own line of work'. Lastly, they governed ownership, problems could be temporarily owned but tools could never be owned. In short, there were to be 'no trade secrets, no monopolies, no poaching, no ambushes' [21]. This system of etiquette enabled the Drosophilists to make such progress in genetics that by 1920 they dominated the field [23].

The Drosophila network was extended to Richard Goldschmidt's lab in Berlin when in 1926 Curt Stern literally brought back both stocks of *Drosophila* from Pasadena and the expertise to maintain and manipulate them. Up to this point Goldschmidt's reputation was based on his extensive work on the genetics of sex determination in the

Gypsy moth, Lymantria dispar. Underlying the course of Goldschmidt's research on sex determination from 1911 to 1934 was a theory of genetics that was physiologically oriented. Where many American geneticists during this time period, especially Drosophila geneticists, emphasized gene transmission, Goldschmidt emphasized gene action. In other words, Goldschmidt thought that the central question in genetics was the integration of the gene with the physiological processes of development [23–26]. Using *Drosophila*, Goldschmidt continued to develop a genetics that emphasized gene action.

Goldschmidt's first published paper using *Drosophila* landed like a bombshell within Morgan's fly group. Although Goldschmidt's 1929 paper did not mark his first run in with Morgan, it was his first attempt to make a claim using Morgan's experimental system [24]. In his paper, Goldschmidt announced that he had been able to induce massive mutations using temperature shocks administered during early development [27]. At this time X-ray radiation was the only known means for artificially inducing mutations. Goldschmidt's paper set the fly group into a frenzy as they tried to replicate his results. At six different laboratories, Alfred Sturtevant, Jack Schultz, Helen Redfield, Theodosius Dobzhansky, Harold Plough, Milislav Demerec, H.J. Muller, A.S. Serebrovsky, L. Ferry, N. Shapiro, and B. Sidoroff all followed Goldschmidt's procedures as closely as possible, but were not able to produce the effect [28, 29].

In a fashion typical of the Morgan's Drosophila group, the data from three of the replications were funneled via Sturtevant to Jack Schultz who was given the job of writing up the results [28]. Schultz's paper was short and to the point. After describing the pains taken to replicate the experiments and the negative results, Schultz concluded that Goldschmidt's experimental mutations were in fact experimental errors [30].

The concern with these failed replications was not expressed to Goldschmidt directly but to Curt Stern [31]. Schultz kept Stern well informed of the progress or lack of progress of the American Drosophilists but as he was preparing his rebuttal to Goldschmidt in January of 1930 a telegram from Stern arrived. It read: "Goldschmidt mutations proved withhold manuscript" [32]. Victor Jollos had replicated Goldschmidt's results [33]. Schultz did withhold the manuscript, but, according to Franz Schrader, a cytologist close to the fly group and a close friend of Stern's, not all of the Drosophilists appreciated Stern's warning. In a letter to Stern, Schrader wrote:

'It has become known that you warned Schultz not to publish his anti-Goldschmidt findings in re [sic] the temperature mutations. The general opinion at Woods Hole last summer [the summer of 1930] was that that was not exactly the right thing to do, in view of the loudly voiced conviction of the Pasadena people that Goldschmidt has done very bad work on it. I think myself that you should have let them go right ahead and make damn fools of themselves. They have come around to so many of Goldschmidt's views after laughing at him that I think a good fall is just about coming to them' [34].

Schultz never published his manuscript, but Demerec who had sent his data to Schultz did arrange for all of the data to be exhibited (probably as posters) at the International Congress of Genetics held in 1932 in Ithaca, NY [35]. Undoubtedly, the overwhelming number of negative replications created the impression that Goldschmidt's original experiments were questionable as were Jollos' replications. This is precisely what Schultz and the Drosophilists wanted, although even Schultz hesitated to say so directly. Schultz's reply to Demerec's query about exhibiting the results ends with the statement, 'From what you write, I suspect that there will be a representative collection of negative experiments ... in this field'. Schultz had crossed out his original conclusion which read, 'From what you write, I suspect that there will be a representative collection of negative experiments against which the others will seem wr[ong] ... ' [36].

Goldschmidt's dramatic entrance into the world of Drosophila genetics is significant because this episode ultimately questioned his technical competence. While he may not have ever been popular among all of the members of the fly group, in the 1920s and 1930s, he did have their respect due in large part to his extensive research record and his position in Germany. The temperature shock experiments began to erode Goldschmidt's authority within the fly group. This process was hastened when Goldschmidt was forced to immigrate to the United States in 1936 and announced loudly and often that the theory of the gene was dead. Goldschmidt reports that his opponents did not refrain from stating, often in his presence, that he had gone crazy [37–39].

Goldschmidt's rejection of the classical gene was the result of his strong belief in the power of position effects combined with his own research on spontaneous mutation. A position effect occurs when the location of a piece of genetic material alters the effects of that material. Position effects were problematic for the classical theory of the gene because it meant that the function of a gene did not fully reside within the gene itself.

Typical of Goldschmidt's papers attacking the classical gene was a short article published in the *Proceedings of the National Academy of Sciences* [40]. In this paper, Goldschmidt used results from his experiments on spontaneous mutability in Florida stocks of *Drosophila* to argue against the existence of the gene. In a letter to L.C. Dunn, Goldschmidt admitted that the article would make him 'an outcast in genetics', since he 'now stated in writing, as before only orally, that there is no such thing as a gene. Horror!' [41]. Goldschmidt's view was that the burst of mutations he and others had witnessed were the result of chromosomal rearrangements, not gene mutations.

Goldschmidt was right about the reaction he would get. In a letter to Demerec, Theodosius Dobzhansky wrote:

"I have just read Goldschmidt's paper in PNAS. This is all we need. But what a series of illogical statements! Even assuming that his facts are straight (and I am personally

more inclined to think that he has a wholesale contamination of cultures) his conclusions absolutely do not follow! I am really sorry for the old man, because I have a liking [sic] and respect for him" [42].

Not being a shy person, Dobzhansky let Goldschmidt know what he thought of this and other papers attacking the classical gene. Goldschmidt being who he was, did not stop publishing his views, although he did modify them [23]. In correspondence, Demerec and Dobzhanksy discussed how best to respond to Goldschmidt's challenge. Dobzhanksy rejected the idea of treating Goldschmidt's views with a 'conspiracy of silence', because he liked Goldschmidt and continued to admire him, which he says made it unpleasant for him to listen to Sturtevant and others in the fly group 'who have nothing but contempt and ill will for the old man' [43]. Nevertheless, Demerec and Dobzhanksy did draft a paper responding to Goldschmidt's attack on the gene. Although it was never published, it reveals much about how Demerec and Dobzhanksy viewed the classical gene.

In their manuscript, The Validity of the Gene Theory, Demerec and Dobzhanksy claim that 'by far the most important among the doctrines on which is founded the edifice of modern genetics is the theory of the gene'. Likening the gene to molecules, atoms, protons, and electrons in physics and chemistry, they argued that the gene was the 'fundamental biological unit'. Indeed, they argue that 'it was the advent of the gene theory that has permitted the transformation of genetics from a descriptive to an exact science'. Given such a build up, you would think that Goldschmidt's views would be in for rough treatment. Demerec and Dobzhanksy reject Goldschmidt's attacks on the gene, but they do it in a very careful way. They claim that something as important as the theory of the gene needs to be carefully evaluated from time to time so that it can be improved and strengthened. For many years, they claim, the gene has had no serious challengers, but, in their words, 'quite recently ... a person so authoritative as Goldschmidt ... has flatly denied the reality of the existence of genes'. They go on to say they believe that Goldschmidt has a done 'a service to genetics', but that the gene will emerge from this trial 'unscarred' [44].

At the time Demerec and Dobzhanksy were writing this manuscript, other members of the fly group were reviewing Goldschmidt's submissions to *Genetics* and rejecting them [23]. Even Goldschmidt's friend, Curt Stern, had serious doubts about Goldschmidt's work and its effects on his standing in the field. In a letter to L.C. Dunn asking about a paper Goldschmidt had submitted to *Genetics*, Stern wrote, 'It is indeed a very painful experience for me to read this paper and it makes one strongly doubtful of many things. I am quite of your opinion that the publication of this paper would harm the author very much and I agree with you in trying, at least, to avoid this .... My first reaction regarding this paper was to write a frank letter to Goldschmidt and tell him how he made people wonder about his recent work. However, I agree with you that the style of this paper shows so definitely that outside criticisms would not be effective that I feel much at a loss and don't know what to do.' [45]. Dunn decided not to publish the paper and it is not clear that Stern ever wrote his letter to Goldschmidt.

These episodes reveal the extent to which certain players within the genetics community considered the personal and political ramifications of Goldschmidt's attack on the gene. Goldschmidt himself was willing to gamble his standing in part be cause he thought he would eventually be shown to be right, in part because his style of research was to theorize first and experiment later, and in part because he keenly felt his own loss of status when he was forced to leave Berlin for Berkeley [23]. Demerec, Dobzhanksy, and Stern saw the Goldschmidt's attack on the gene as a strategy which would further degrade the perceptions of his competence and authority within Drosophila genetics and genetics in general. Indeed as Goldschmidt persisted and expanded his views in the 1940s, Dobzhanksy's responses became less charitable. Dobzhanksy's response to Goldschmidt's *The Material Basis of Evolution* (1940), for instance, was much more pointed and was undoubtedly partly a result of the fact that Goldschmidt had chided Dobzhansky in print for his unwillingness to give up the particulate gene [46]. In fact, an important facet of Goldschmidt's argument rested on a systematic reinterpretation of Dobzhansky's research as it was presented in his *Genetics and the Origin of Species* (1937).

In terms of the classical gene concept, these responses to Goldschmidt's attacks reveal the place given to the gene as a fundamental feature of genetic research among the members of the fly group. Morgan's control over the distribution network may have regulated experimental practice, but his theory of the gene helped regulate the conceptual frameworks that were simultaneously being deployed. Morgan's success at making the gene foundational is evidenced by how quickly Demerec, Dobzhanksy, and Stern saw the political consequences when Goldschmidt questioned its existence. Questioning the gene, questioned the conceptual framework for Drosophila genetics. In doing so it questioned Morgan's authority and the authority of his successor (Sturtevant) and his associates to conceptualize the field.

4. Conclusion

An important part of what makes a comprehensive or unifying gene concept attractive is that it makes a certain set of disciplinary concerns central to everyone who then uses the concept. Concepts which are comprehensive or which unify large domains become obligatory points of passage if they are accepted. As such, gene concepts can be very powerful tools for defining a field or at a minimum having a significant impact on a field's conceptual framework. This does not mean that they are necessary or universally desirable. Molecular biologists seem to be in no way hindered by the absence of a unifying gene con-

cept. Nevertheless, Neumann-Held and Griffiths find value in offering a molecular process gene concept. This gene concept is not meant to be comprehensive. Its more limited scope grants it a modest unifying power. The real impact of the molecular process gene lies in its conceptual reorientation – it would force us to shift our focus from genetic structures to developmental processes. The value of this reorientation is currently being debated and as a result we still face the problem of the gene. But even if the discussion of the molecular process gene concept were to end tomorrow, we would continue to face the problem of the gene as new gene concepts are proposed and debated.

The problem of the gene resists attempts at resolution by conceptual means, because it is not a wholly conceptual problem. Deploying a gene concept is also exercise in scientific authority. The classical gene concept embodied Morgan's authority as well as his ability to manage his network of researchers and impose his definition of science upon the field. Goldschmidt's attack on the classical gene was in part an attack on the authority of the fly group. In attacking the gene, Goldschmidt sought to reorder the field conceptually and politically. While today's struggles over gene concepts are not nearly as dramatic as Goldschmidt's, they are similar enough to suggest that we will continue to confront the problem of the gene for as long as there are struggles for authority which use gene concepts to attempt to realign the problems and practices of genetics.

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References

[1] Demerec M., Properties of genes, in: Brink R.A., Styles E.D. (Eds.), Heritage from Mendel, University of Wisconsin Press, Madison, 1967, pp. 49–61.

[2] Carlson E.A., The Gene: A Critical History, Iowa State University Press, Ames, 1966.

[3] Raffel D., Muller H.J., Position effect and gene divisibility considered in connection with three strikingly similar scute mutations, Genetics 25 (1940) 541–583.

[4] Goldschmidt R., On some facts pertinent to the theory of the gene, in: Science in the University, University of California Press, Berkeley, 1944, pp. 183–210.

[5] Lewis E.B., Pseudoallelism and gene evolution, Cold Spring Harbor Symp. Quant. Biol. 16 (1951) 159–174.

[6] Rheinberger H-J., Experimental complexity in biology: some epistemological and historical remarks, Phil. Sci. 64 (1997) S245–S254.

[7] Fogle T., The dissolution of protein coding genes in molecular biology, in: Beurton P., Falk R., Rheinberger H.J. (Eds.), Gene Concepts in Development and Evolution, Preprint 123, Max-Plank-Institute für Wissenschaftsgeschichte, 1999, pp. 69–88.

[8] Portin P., The concept of the gene: short history and present status, Q. Rev. Biol. 56 (1993) 173–223.

[9] Bourdieu P., The specificity of the scientific field and the social conditions of the progress of reason, Soc. Sci. Inform. 14 (1975) 19–47.

[10] Morgan T.H., The Theory of the Gene, Yale University Press, New Haven, 1926.

[11] Muller H.J., Artificial transmutation of the gene, Science 66 (1927) 84–87.

[12] Stadler L.J., Mutations in barley induced by X-rays and radium, Science 68 (1928) 186–187.

[13] Friedman M., Explanation and scientific understanding, J. Phil. 71 (1974) 5–19.

[14] Waters C.K., Genes made molecular, Phil. Sci. 61 (1994) 163–185.

[15] Neumann-Held E., The gene is dead – long live the gene! Conceptualizing genes the constructionist way, in: Koslowski P. (Ed.), Sociobiology and Bioeconomics: The Theory of Evolution in Biological and Economic Theory, Springer Verlag, Berlin, 00, pp. 105–137.

[16] Griffiths P.E., Neumann-Held E., The many faces of the gene, Bioscience 49 (1999) 656–662.

[17] Goldschmidt R., Theoretical Genetics, Univ. of Washington Press, Seattle, 1958.

[18] Allen G., T.H. Morgan and the split between Embryology and Genetics, 1910–1935, in: Horder T.J., Witkowski J.A., Wylie C.C. (Eds.), A History of Embryology, Cambridge University Press, Cambridge, 1986, pp. 113–146.

[19] Sapp J., Beyond the Gene: Cytoplasmic Inheritance and the Struggle for Authority in Genetics, Oxford University Press, New York, 1987.

[20] Morgan T.H., The theory of the gene, Am. Nat. 51 (1917) 513–544.

[21] Kohler R., Lords of the Fly: Drosophila Genetics and the Experimental Life, University of Chicago Press, Chicago, 1994.

[22] Harwood J., Styles of Scientific Thought: The German Genetics Community, 1900–1933, University of Chicago Press, Chicago, 1993.

[23] Dietrich M.R., On the mutability of genes and geneticists: the 'Americanization' of Richard Goldschmidt and Victor Jollos, Perspect. Sci. 4 (1996) 321–345.

[24] Allen G., Opposition to the Mendelian-chromosome theory: the physiological and developmental genetics of Richard Goldschmidt, J. Hist. Biol. 7 (1974) 49–92.

[25] Richmond M., Richard Goldschmidt and sex determination: the growth of German genetics, 1900–1935, Ph.D. dissertation, Indiana University, 1986.

[26] Gilbert S., Cellular politics: Ernest Everett Just, Richard B. Goldschmidt and the attempt to reconcile embryology and genetics, in: Rainger R., Benson K., Maienschein J. (Eds.), The American Development of Biology, Rutgers University Press, New Brunswick, 1991, pp. 311–346.

[27] Goldschmidt R., Experimentelle Mutation und das Problem der sogenannten Paralleinduktion. Versuche an Drosophila, Biol. Zbl. 49 (1929) 437–448.

[28] Demerec M. to Sturtevant A.H., 14 November 1929, J. Schultz Papers, American Philosophical Society Library, Philadelphia, PA.

[29] Ferry L., Shapiro N., Sidoroff B., On the influence of temperature on the process of mutation, with reference to Goldschmidt's data, Am. Nat. 64 (1930) 570–574.

[30] Schultz J., Temperature and experimental mutations, unpublished manuscript, no date, Jack Schultz Papers, American Philosophical Society Library, Philadelphia, PA.

[31] Schultz J. to Stern C., 16 October 1929, Curt Stern Papers, American Philosophical Society Library, Philadelphia, PA.

[32] Stern C. to Schultz J., 1 January 1930, Jack Schultz Papers, American Philosophical Society Library, Philadelphia, PA.

[33] Jollos V., Studien zum Evolutionsproblem. I. Über die experimentelle Hervorrufung und Steigerung von Mutationen bei Drosophila melanogaster, Biol. Zbl. 50 (1930) 541–554.

[34] Schrader F. to Stern C., 14 March 1931, Curt Stern Papers, American Philosophical Society Library, Philadelphia, PA.

[35] Demerec M. to Schultz J., 29 January 1932, Jack Schultz Papers, American Philosophical Society Library, Philadelphia, PA.

[36] Schultz J. to Demerec M., no date, Jack Schultz Papers, American Philosophical Society Library, Philadelphia, PA.

[37] Stern C., Richard Benedict Goldschmidt (1878–1958): a biographical memoir, Experientia Suppl. 35 (1980) 68–99.

[38] Goldschmidt R., In and Out of the Ivory Tower, University of Washington Press, Seattle, 1960.

[39] Dietrich M.R., From gene to genetic hierarchy: Richard Goldschmidt and the problem of the gene, in: Beurton P., Falk R., Rheinberger H.J. (Eds.), The Concept of the Gene in Development and Evolution, Cambridge University Press, Cambridge, 2000, pp. 91–114.

[40] Goldschmidt R., Spontaneous chromatin rearrangements and the theory of the gene, PNAS 23 (1937) 621–623.

[41] Goldschmidt R. to Dunn L.C., 3 November 1937, L.C. Dunn Papers, American Philosophical Society Library, Philadelphia, PA.

[42] Dobzhanksy T. to Demerec M., 28 December 1937, Milislav Demerec Papers, American Philosophical Society Library, Philadelphia, PA.

[43] Dobzhanksy T. to Demerec M., 19 January 1938, Milislav Demerec Papers, American Philosophical Society Library, Philadelphia, PA.

[44] Demerec M., Dobzhanksy T., The validity of the gene theory, unpublished manuscript, no date. Milislav Demerec Papers, American Philosophical Society Library, Philadelphia, PA.

[45] Stern C. to Dunn L.C., 6 June 1938, Curt Stern Papers, American Philosophical Society Library, Philadelphia, PA.

[46] Dietrich M., Richard Goldschmidt's 'heresies' and the evolutionary synthesis, J. Hist. Biol. 28 (1995) 431–461.