NEW BIOLOGICAL BOOKS

The aim of this section is to give brief indications of the character, content and cost of new books in the various fields of biology. More books are received by The Quarterly *than can be reviewed critically. All submitted books, however, are carefully considered for originality, timeliness, and reader interest, and we make every effort to find a competent and conscientious reviewer for each book selected for review.*

Of those books that are selected for consideration, some are merely listed, others are given brief notice, most receive critical reviews, and a few are featured in lead reviews. Listings, *without comments, are mainly to inform the reader that the books have appeared; examples are books whose titles are self-explanatory, such as dictionaries and taxonomic revisions, or that are reprints of earlier publications, or are new editions of well-established works.* Unsigned brief notices, *written by one of the editors, may be given to such works as anthologies or symposium volumes that are organized in a fashion that makes it possible to comment meaningfully on them.* Regular reviews *are more extensive evaluations and are signed by the reviewers. The longer* lead reviews *consider books of special significance. Each volume reviewed becomes the property of the reviewer. Most books not reviewed are donated to libraries at SUNY Stony Brook or other appropriate recipient.*

The price in each case represents the publisher's suggested list price at the time the book is received for review, and is for purchase directly from the publisher.

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ONE, TWO (TOO?), MANY GENES?

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A review of

THE CONCEPT OF THE GENE IN DEVELOPMENT AND EVOLUTION: HISTORICAL AND EPISTEMOLOGICAL PERSPECTIVES. *Cambridge Studies in Philosophy and Biology.*

Edited by Peter J Beurton, Raphael Falk, and Hans-Jörg Rheinberger. Cambridge and New York: Cambridge University Press. $59.95. xvi + 384 p; ill.; index. ISBN: 0-521-77187-0. 2000.

Where once the question of whether the classical gene could be "reduced" to the molecular gene was all the rage among philosophers of biology, the tide has turned back toward a version of the ancient Greek conundrum about the one and the many. Although some motivation for this turn can surely be attributed to a growing appreciation of the complexity and diversity of meanings in use of the word "gene," one also sees the hallmarks of a changing *Zeitgeist.* The earlier debate grew out of the more ambitiously systematizing intentions of Logical Positivism and perhaps a more ideologically strident intellectual climate. Today's disposition reflects an enhanced sensitivity to empirical, historical, and rhetorical particulars (let alone the exponentially expanded domain of empirical particulars to be sensitive to), but also the interpretative influence of multiculturalism and metaphysical pluralism. Dupré (1993) provides a good example of one of the

more systematic expressions of this perspective in the philosophy of science.

This important collection of papers, derived from two workshops held at the Max Planck Institute for the History of Science, spans the distance from theoretical attempts to reconstruct a single, unified gene concept to historical, empirical, and epistemological arguments on behalf of an irremediable conceptual pluralism. I will attempt to bridge the chasm between the reductionist program of the past and the unity-versus-plurality standpoint of the present by offering, in some sense, to split the difference. Between the one and the many I will argue that there are not one and not many, but *two* fundamental gene concepts underlying current scientific usage. Far from attempting to absorb or assimilate one to the other, the real objective should be to disentangle the two, recognize their independent and nonoverlapping status, and thereby undercut misleading inferences derived from their unwarranted conflation.

Genes were, and continue to be, defined with respect to phenotype and are also defined at the molecular level with respect to DNA sequence. The difficulties of bringing these together is the basis of what Raphael Falk, in this volume, refers to as "a concept in tension" (p 317), and this distinction, and this tension, is conceptually critical to every article in the collection (and to my own argument as well).

We are all accustomed to common references to the numbers of genes in a sequenced genome. And in as much as no one yet even claims to know the phenotypic function of every gene in a genome, it would appear that such knowledge is not necessary for individuating and tallying up genes on the basis of molecular sequence data. So how is it done? What are the criteria that enable a genome project to tell us how many genes humans, flies, worms, yeast, or rice are endowed with? The collection begins with an outstanding analysis by Thomas Fogle that discloses how empirically problematic this actually is.

The ability to intelligibly discuss the number of genes in a genome, Fogle reveals, is based upon a methodological use of a kind of molecular-gene umbrella concept. This concept consists of "a collection of flexibly applied parameters derived from features of well-characterized genes" (p 3). Simply stated, investigators have abstracted from the features of particularly well-characterized molecular genes a set of criteria that are neither necessary nor sufficient, and which need not necessarily occur together, and by no means are exhaustive. Two of the most salient examples of such criteria would be evidence that the stretch of DNA in question serves as a template for the synthesis of an RNA transcript and the presence of an AT rich "TATA box" promoter site. The absence of a TATA promoter would be interesting, but it would not deprive a transcript producing sequence from being a gene. Nor, however, has the lack of a verified transcript prevented sequences that meet other gene parameters from being counted as genes in genomic analysis. Arguably, a flexible interpretative toolkit is not necessarily a bad thing, but what happens when empirical reality does not fit the canonical exemplar of what a molecular gene should look like? For example, what should one conclude when what one might want to call a single locus produces multiple different transcripts? The human dystrophin gene has seven different promoter sites that respond in tissue-specific ways to produce transcripts and polypeptides of different sizes. Is this one gene or seven? And what if there is one regulatory region, such as the Locus Control Region (LCR), that is involved in the regulation of a cluster of five related globin polypeptide gene sequences? Or cases where transcripts are derived from two entirely different chromosomal regions, yet come together to produce a single translation product? And what about cases where highly repetitive DNA generally regarded as "junk" DNA for its lack of apparent role in transcription (such as the ALU sequences) is found to give rise to some level of transcriptional activity?

The heuristics for naming and demarcating genes came about with a certain tacit preunderstanding about what the relationship of DNA structure to gene-function *should be,* which influenced the selection of the seemingly well-behaved cases that became exemplars. With the expectation of straightforward structure-function relationships no longer empirically tenable, two principal strategies

for reconstituting a gene concept present themselves. The first strategy, which Fogle has found represented in the leading molecular biology textbooks, is that of beginning with a functional outcome, typically a polypeptide, and backtracking to all of the DNA elements (coding and regulatory) that were necessary for its production. These are then included in what counts as "the gene" for this polypeptide. But the problems with this approach, Fogle explains, are legion. There is no clear way to demarcate those domains that are involved in transcription in some capacity from those that are not. There is no guarantee that the same domains will be involved in each instance of the transcription of the same polypeptide and there are also both coding and noncoding domains that are involved in the transcription of multiple polypeptides (e.g., the LCR regions discussed above). And if all the DNA elements that regulate transcription are included in the definition of the gene, why stop at just DNA sequences? On what basis, for example, would the DNA methylation patterns that regulate transcription be excluded? And what about all of the factors that are necessary for posttranscriptional processing, which have an enormous influence on the form of the polypeptide produced? This even more inclusive approach to defining a gene is exactly what is put forward by Griffiths and Neumann-Held (1999) and Neumann-Held (2001)—for a critique, see Moss (2001). Fogle convincingly emphasizes the complex integration of positional and contextual factors germane to any and all levels of functional analysis. Is it not, after all, the residue of Mendelian functional unit talk, projected onto DNA, that is at least *covertly* responsible for expectations about how DNA would be able to be parsed into phenotypically relevant units?

The second strategy, which Fogle favors, could be well described as a deflationary approach. Rather than attempting to fit the square pegs of the Mendelian gene into the round holes of the double helix, one can simply parse the DNA on its own terms, albeit shorn of phenotypic ascriptions. Fogle suggests that rather than label lots of loci as genes, it would be more useful to map different classes of domains that become functionally interconnected by way of multiple and complex interactions. What Fogle is calling for is a new vocabulary for the types of molecular interactants that come together contingently, in context-relevant ways, in the course of any actual transcriptional expression. He wants to avoid the bad habit of mistaking any of the interactants, before the fact, with the complex and contextually conditioned outcome of the process in which it participates. The gene, he suggests, "could become a quaint term of the past (at least in molecular biology circles) replaced by language that more accurately conveys relationships among domains contributing to phenotypic effects" (p 23). Now, of course, many of these domains already have names—promoters, enhancers, and silencers, among others. What lacks a deflationary appellation is the template-bearing regions of the DNA. For this, Fogle proposes the acronym DSAT for "domain set for active transcription." Of course, even with the benefit of its deflationary intentions, Fogle's DSAT would still have to grapple with the complexity of boundary ambiguities, a point that he readily acknowledges.

Aside from skepticism about just how quickly the term gene could be relegated, even under the most enlightened of circumstances, to an innocuous dotage, there is still a serious shortcoming of Fogle's approach. He is quick to notice the uninvited presence of a Mendelian-like gene concept in his molecular soup, but pays it little more attention than just trying to shoo it away. Perhaps he thinks that it is already moribund, or that it is a pest that is simply best ignored, or maybe that it is just not his department to be concerned about it. But as I think other papers in the collection will bear out, this other sense of the gene is still alive and well, and the best way to guard against its intrusions is to give it its due while clarifying the nature of its proper boundaries.

When we refer to genes for phenotypes (e.g., genes for blue eyes, breast cancer, cystic fibrosis, or Marfan's syndrome), we use the term in a particular way. I call this sense of the gene, "Gene-P" (Moss 2003). A Gene-P is a phenotype predictor. It is defined by its phenotype, but is indeterminate with respect to

its nucleic acid sequence. How could this be? Surprisingly perhaps, this concept of a gene as Gene-P was understood by Wilhelm Johannsen, the very individual who coined the term "gene." In his 1923 paper, he told us that "[w]hen we regard Mendelian 'pairs', *Aa, Bb* and so on, it is in most cases a *normal* reaction (character) that is the 'allele' to an *abnormal*. Yellow in ripe pease is normal, the green is an expression for imperfect ripeness as can easily be proven experimentally e.g. by etherization" (Johannsen 1923:138). Johannsen got this right. Genes-P can serve as valuable predictors of a great many phenotypes because it is often the case that within some range of environmental and developmental contexts, organisms lacking a certain "normal" sequence will respond predictably. Genes-P are not defined by sequence because invariably there are many ways to lack or deviate from a norm. It continues to be useful in genetic counseling, and other areas, to speak *as if* (but only as if) a Gene-P determined the phenotype. But it does not—it merely predicts what the organism is likely to do. The "normal" BRCA1 (breast cancer) protein is a large molecule that is involved in transcriptional regulation events in many tissues at many times. It by no means constitutes instructions for making healthy breasts, nor does it even have a special relationship to this part of the anatomy. But given the context of a family with a history of breast cancer, there are many deviations of the BRCA1 sequence, the presence of which are highly correlated with the appearance of breast cancer at some point during a woman's lifetime. Breast cancer is one example, Marfan syndrome is another. There are at least 150 sequence deviations that will result in some version of Marfan syndrome. These are Genes-P. They do not constitute instructions for making tall, gaunt bodies (which is a complex developmental consequence of a failure to incorporate fibrillin into connective tissue microfibrills), but they are predictive of such.

Although Genes-P are defined by their predictive relationship to a phenotype and not by specific sequence, they are no longer purely classical as opposed to molecular. Molecular probes can, and are, being used to detect Genes-P such as those for cystic fibrosis and breast cancer. Although a negative test result could never rule out the possibility of a Gene-P for reasons just discussed, a positive test for the presence of an already characterized aberrant sequence can be used in the predictive capacity of a Gene-P. The explanatory "game" played by Gene-P is thus not confined to purely classical methods, which unfortunately has made it all the easier to conflate the meaning of this "gene" with the one I will refer to as "Gene-D."

Quite unlike Gene-P, Gene-D is defined by its nucleic acid sequence. A Gene-D is a developmental resource (hence the "D") which in itself is indeterminate with respect to phenotype. The sense of my Gene-D bears a striking resemblance to the intent of Fogle's DSAT. To be a Gene-D is to be a region on a chromosome within which is contained molecular template resources, used in the synthesis of various "gene-products." All of Fogle's provisos about context sensitivity and dependence apply. The very same Gene-D can be used for all sorts of different phenotypic end-products, both felicitously or aberrantly, depending upon the developmental or physiological context. Gene-P and Gene-D constitute qualitatively different kinds of explanatory concepts. There is no gene that is simultaneously a Gene-P and a Gene-D; to conflate them is just as much a conceptual category mistake as an empirical error. To see this clearly one need only consider a locus such as that associated with the Gene-P for cystic fibrosis. Considered as a Gene-D it constitutes template resources for a cellular transmembrane chloride ion channel protein that is contingently expressed at different times and in different places. As a Gene-D its significance is wholly determined by its context and dynamic history. Considered as a Gene-P, the presence of one out of over 900 possible deviations on each of the chromosomes provides a certain predictive power with respect to a complex pathophysiology of the lungs that involves the buildup of mucus and the inclusion of bacteria. Hyperbolic talk about genes as programs for phenotypes (let alone as the ontological groundwork of life itself) follows from the conflationary desire to have it both ways, Gene-P and Gene-D simultaneously, molecular templates that "code for"

complex phenotypes. Gene-P needs to be given its proper due, but be kept distinct from Gene-D. Uncontaminated by Gene-P, Gene-D is consistent with Fogle's deflationary intentions.

Where Fogle's analysis is wholly synchronic in nature, many of the articles address the theme of the book through analyses that are at least partially historical. Jean Gayon's contribution offers an epistemological periodization of the history of thinking about heredity going back a century and a half. He begins by distinguishing between two fundamentally different ways of physicalizing heredity, where heredity is conceived of as a physical force that, like other physical forces, could be measured in terms of magnitudes, versus heredity as based upon a physical structure. Mid-19th-century breeders and biologists "unequivocally" regarded heredity as a force. Common belief held that the longer a trait was reproduced in succeeding generations, the stronger its hereditary force would be—a doctrine known as the "constancy of race" (although unremarked upon by Gayon, one can quickly fathom the likely influence of these views on the rise of 19th-century racial degeneration ideologies, such as that of Gobineau, as well as upon the thinking of Nietzsche and late 19th century "Lebensphilosophie.")

Gayon schematizes the modern history of heredity into three phases that correspond to three different epistemological standpoints. Biometry (1870–1900) still conceptualizes within the framework of a hereditary force, but especially for Pearson, that which the biometrician measures and statistically analyzes is taken in a purely phenomenalist vein. There is no force that is being ontologized, only apparent patterns of inheritance that can be quantitatively described. In the second Mendelian-Chromosome Phase (1900–1950) heredity as a force gives way to heredity as structure, with its quantification denoting not magnitudes, but hypothetical entities. The ontological status of these entities was not at all clear, but this did not matter to the predictive power of the enterprise, thus leading to an operationalist or instrumentalist epistemological self-understanding on the part of the discipline. As Morgan is quoted as saying in his 1933 Nobel lecture—"it does not make the slightest difference whether the gene is a hypothetical unit or whether the gene is a material particle" (p 79). Finally, with the molecular phase beginning in the 1950s, the units of heredity (the molecular gene) are understood to be real. Now for Gayon, even if the edges are blurry, it is just intrinsically interesting that a science, genetics, could have gone through such philosophically distinctive phases: "I know of no other history of a modern biological discipline that could be reconstructed in terms of such successive epistemological shifts" (p 87). But Gayon's historical/epistemological periodization opens up another line of inquiry as well.

The operationalist/instrumentalist standpoint of the Mendelian phase gave rise to Gene-P. But what happens to the Gene-P concept when instrumentalism gives way to realism? The contribution by Sara Schwartz provides an opportunity to consider exactly this issue. Her contribution, The Differential Concept of the Gene: Past and Present, offers a historical story, but with a practical intent. She veers in the direction of a unificationist approach and of all the contributors comes the closest to trying to unify the gene under something close to a pure Gene-P concept. The differential concept that is constitutive of Gene-P served the instrumental purposes of its enterprise because it did not depend upon a one-to-one relationship between gene and trait. Classical genes and Genes-P are difference makers, and it is the predictability of some discrete phenotypic difference that counts. But how does one understand the role of the gene in relation to that difference? If one assumes a many-to-many relationship between genes and traits then one does not interpret a single gene, in a realist vein, as the cause of the trait associated with it. Indeed, Morgan had originally attempted to formulate a nomenclature using several letters to indicate that the appearance of a trait was not due to the difference maker, but rather to the "*residuum*—the factors left when this factor is missing" (p 29). But Morgan was soon to give up on this nomenclature and, for simplicity's sake, endorse the formalism of attributing the different phenotype to the "difference maker." Exactly when did the instrumentalist

and realist heuristics begin to become blurred? Is it the case that bringing the differential concept of the gene from Gayon's instrumentalist period to his realist period is precisely tantamount to the conflation of Gene-P and Gene-D? Schwartz would like to salvage the differential gene concept as an explanatory strategy that can survive the shift to molecular and even genomic paradigms, but she is not oblivious to the difficulties that have been encountered in attempting to do so.

The creation of transgenic knockout mice in order to identify the function of the gene knocked out has given rise to results notoriously counter to expectations based upon the differential gene strategy (for example, the deletion of genes such as "p53" and "src," which had been shown to be of importance in cancer and other studies, resulted in relatively normal mice). Likewise, the attempts to identify the function of unknown genes in yeast by deleting them and seeing what happens proved to be problematic. But should this really have been a surprise? These research strategies, focusing on analyzing Genes-D, are built on a Gene-P concept. The Gene-P idea arose at a time when discrete differences in phenotype were all that were available to work with. And as Johannsen (1923:140) presciently asked: "Is the whole of Mendelism perhaps nothing but an establishment of very many chromosomal irregularities, disturbances or diseases of enormously practical and theoretical importance but without deeper value for an understanding of the 'normal' constitution of natural biotypes?"

Genes-P represent a special group—the cases in which a deviation in a Gene-D results in a distinctive (and viable) phenotype (that for the sake of utility can be treated instrumentally as a direct causal consequence of that deviation). But there is no reason to assume that any or even most Genes-D would provide such an allelic deviation, but even more to the point there is no reason to believe that when they do, when there is a Gene-P phenotype such as cystic fibrosis, Marfan syndrome, or blue eyes, it provides an accurate impression of the histological or developmental scope of the respective Gene-D expression, or an accurate insight into the mechanisms of its activity. But if trying to turn every Gene-D into a realistically construed (i.e., *conflationary*) Gene-P is not the way to go then what alternatives are there? Perhaps an alternative model of the meaning of a Gene-D can be found in the expanding framework of the *developmental* gene concept.

Evelyn Fox Keller, Scott Gilbert, and Michel Morange contribute articles that are concerned in some way with genes and development. Although Keller's piece examines the distinction between the idea of a "developmental program" versus a "genetic program," Gilbert and Morange address, albeit in different ways, the notion of the developmental gene. Gilbert's paper turns on a very suggestive comparison of the gene of population genetics that was presupposed by the evolutionary Modern Synthesis and the gene of developmental genetics that is now being taken up by proponents of a new model of evolution based upon an evolutionary-developmental synthesis (evo-devo). Gilbert enumerates these differences as follows: Where the population (Pop) gene was an abstraction with no physical referent the developmental (Dev) gene refers to specific sequences of DNA that include not only coding regions, but regulatory regions such as promoters, enhancers, silencers, and introns, among others; Pop genes were picked out as difference makers, but Dev genes have been identified on the basis of their *similarity* across taxa; Pop genes were meant to explain mechanisms of selection and Dev genes explain the *constraints* that underlie phylogenetic patterns; Pop genes were assumed to pertain to changes in enzymes and structural proteins, and Dev genes are seen to encode proteins involved in *signaling and the regulation of processes such as transcription and splicing;* Pop genes were presumed to be active in adults fighting for fitness, but Dev genes are expressed during *organogenesis* by the embryo; and the Pop gene was conceived of as acting in a context-independent atomistic fashion, while the Dev genes are seen as *context dependent parts of a pathway.* Gilbert goes on to discuss the history and status of MyoD as an exemplar of a developmental gene, but numerous homeotic genes and many other examples could also have been used.

Gilbert's comparison is offered in a descrip-

tive and pluralistic vein, but in this sense his analysis stops short of many of its own implications. This extended discussion could well begin by asking where, despite its 60 years of age, are the comparable exemplars of population genes that played the role in evolution that the Modern Synthesis ascribed to them? Gilbert's distinction between Pop genes and Dev genes map onto the Gene-P/Gene-D distinction with little remainder (and happily the Ps and Ds are already there). The gene of population genetics is a Gene-P. It is an abstract difference maker methodologically treated as an independent atomic unit. Population genetics took an instrumental construct and turned it into a mathematical formalism. The Modern Synthesis (or at least the Fisherian end of it) adeptly explained how evolution would work *if organisms were truly composed of Genes-P.* But they are not. The "Panglossian" adaptationism, famously criticized by Lewontin, Gould and others, is simply an implication that follows from a theory built on Gene-P, and hence the lack of examples. Gilbert points out that developmental genes are highly conserved across taxa—*but so are genes for structural and enzymatic proteins.* The fact that two species of bird have distinctly different beaks that serve distinctly different feeding habits does not mean that there needs to be gross differences in the molecular composition of the beak nor of their digestive enzymes (although fine-tuning differences could certainly be present). New evolutionary forms are built largely out of the same constituents by way of dynamic, developmental, and organizational innovations. There is no set of species-defining (structural and enzymatic) genes to fulfill the desideratum of the Modern Synthesis because at the level of the material reality of Gene-D there is no contrast class to those properties described by Gilbert under the heading of developmental genes.

Now this is not to say that developmental genes are immune to contamination and conflation with Gene-P. Quite the contrary. And it is very much to this point that Morange's article is addressed. The declaration that certain homeotic genes are "master-control genes" is nothing short of an attempt to pull them out of their context and declare them to be materialized Genes-P. In response to those who would drag developmental genes from being Genes-D to being little architects of the phenotype, Morange asks: "But it is also possible that the developmental genes are only the molecular components used to build the organisms: Their study will not reveal any principle of construction. Building of an organism is similar to the assembly of a nest by wasp colonies; it results only from the responses of individuals to local configurations and it is written nowhere" (p 207). Developmental genes are developmental resources (Genes-D) and there is no clear boundary between them and other Genes-D. The truth of this is further evidenced by Morange in pointing out that many "developmental genes" also serve as templates for proteins used in structural capacities (e.g., photoreceptors in *Drosophila*) and metabolic capacities (e.g., glycogen metabolism).

Metaphors matter, as Evelyn Fox Keller tells us here and in many of her other writings. The conflationary depiction of developmental genes as developmental blueprints that Morange challenges has another name—the genetic program. If the metaphorical appropriation of the computer model for thinking about development was inevitable, the particular formulation of it expressed as "the genetic program" idea was not. Rather than conceiving of the linear sequence of DNA as a program, it could also have been modeled as data. Indeed, an early attempt (Apter and Wolpert 1965) at bringing cybernetics to bear on the question of development assimilated, not the DNA, but the entire egg cell with all its maternal endowments to the function of a computer program: "In this kind of system, instructions do not exist at particular localized sites, but the system acts as a dynamic whole" (p 163). Keller exposes some of the contingent twists and turns that were taken by developmental biologists such as Bonner, and ultimately Wolpert himself, in endorsing the rhetoric of the genetic program, but her larger objective is to recover that earlier intuition. She cleverly gives phrase to this idea by bouncing off of a phrase of my own: "Supplementing Lenny Moss's observation that a genetic program is 'an object nowhere to be found' (Moss 1992, 335), I would propose the developmental program as an entity that is

everywhere to be found" (p 176). Keller's distinction between a genetic program and a developmental program partitions quite nicely as projections of the Gene-P/Gene-D distinction, respectively, onto development. Of course, the whole take-home of Gene-D would be that DNA has to be parsed *on its own terms* (very much as Fogle proposes with his desideratum for a new vocabulary) and functionally recontextualized among the myriad of other molecular resources of the cell. Gene-P councils one to always track causality back to the gene. Gene-D councils one to presuppose no constituent as causally privileged in advance but rather to elucidate the dynamics of living systems at the hierarchical level and from the point of departure that best befits the empirical demands of the inquiry. An attempt to provide experimental, historical, and philosophical perspectives consonant with this outlook can be found in the recent anthology, *Cycles of Contingency: Developmental Systems and Evolution* (Oyama et al. 2001).

Two of the editors, Beurton and Rheinberger, provide the yin and yang of the one versus the many question with their respective contributions to the anthology—Rheinberger on behalf of pluralism, Beurton on the side of unity. Rheinberger builds a defense of pluralism about gene meanings on an epistemology of scientific knowledge that is informed by the conceptual tools of textual criticism. Science, we can agree, is realized and constituted in practices and "[t]he practices in which the sciences are grounded engender epistemic objects" (p 220). The gene is an epistemic object. An epistemic object is not some brute fact of the matter, but rather a kind of focused learning space, a niche in the complex nebulae of epistemic practices in which the nucleus of an object of inquiry proceeds to take shape. An object whose shape is formed along the contours of an epistemic possibility space is thus a "boundary object." Now much of Rheinberger's message is to say that the contours of the boundary space should not be sanded into smoothness by philosophical (or other) presuppositions about the (epistemic) virtues of clarity or sharpness. Where one must grapple with real complexity, it will be the fuzzier boundary object that better suits the epistemic needs. Rheinberger offers the postulate of colinearity between DNA and code as an example of a fuzzy boundary object that was productive, not only despite but perhaps because of its fuzziness.

Although this thesis of colinearity ultimately proved to be untenably simplistic, along the way to finding its limits it enabled the fleshing out of a theory of "code" to take place. Is it the case then that attempting to make distinctions and to hold concepts to standards of logical and empirical accountability is just the wrong way to go? Rheinberger's answer to this appears to be, well, fuzzy: "The gene has been a powerful epistemic entity in the history of heredity, in all the vagueness that is characteristic for such entities. It is tempting to generalize this statement and assume that fruitful scientific concepts are bound to be polysemic. I will resist this temptation and assure my critics that I do by no means deny the value of precision in science. But precision itself has historically changing boundaries" (pp 235–236).

But consider what appears to be Rheinberger's summary statement about the main topic of the book: "You may expect me to come up with a nice solution to the meandering story of the gene at the end. As far as the scientific story goes, there is none. As to an epistemological take-home lesson, I have one. Alas, it is a very disappointing message for nondeconstructivists. I might say . . . [a] gene is a gene is a gene. This is a strong claim. . . . Taken seriously, it means that in science every presumed referent is turned into a future signifier" (p 235). Now what does this mean? The boundary object that is formed in the practical/discursive scientific nebula is a referent. That conceptual space, that *is* the boundary object, takes itself to be pointing to, or perhaps engulfing, something in nature and giving it definition. As it obtains definition it likewise becomes part of the signifying nebula and semantically shapes the space in which new objects can be referred to and allowed to show up (or not). Gene-P, epistemologically qualified as an instrumental construct by Johannsen, and at least the early Morgan, was a permissive signifier. But when it got taken up by population genetics and

hardened into the Modern Synthesis, and then materialized into a conflationary Gene-P/Gene-D, it became rather imperious and unforgiving.

The prevailing conflationary gene concept of much of the last 50 years was surely fuzzy in many (including some productive) ways and yet it was also sharp enough to cut the entirety of developmental biology out of the mainstream of evolutionary thought, to dismiss the majority of the constituents of a cell from the study of heredity, and to draw a narrow preformationist line in the sand between cultural studies and putatively natural sciences of man. Critiques of the gene concept, here and elsewhere, have been motivated by a desire to release the straightjacket, not to tighten the strings. Rheinberger wants to advocate the epistemic value of the local, situated, engaged standpoint. But where are the presumed philosophical critics standing at a distance and demanding clarity for its own sake? Critical distinctions can well open up the space for many new and productive lines of inquiry. Blanket advocacy for pluralism may overlook epistemically stifling collusions at the roots. Because the standpoint of epistemic fuzziness does not seem to offer the resources for making distinctions about distinctions, this might well suggest that it is the deconstructionist who is in danger of trying to legislate from afar.

At the other end of the unity-plurality spectrum, Peter Beurton offers what may read like a heroic last chance attempt to reconstitute the unified gene. Granting that molecular biology has debunked the idea that DNA consists of discrete functional genetic units (Genes-P) to offer natural selection as its input, Beurton tries to turn the model upside down and argue that such discrete functional genes are what natural selection produces as its output. The argument begins with the claim that although the DNA that provides the wherewithal for any particular transcriptional event may be scattered about, natural selection will still pick out differences in distributed patterns of DNA that make a difference. "I suggest that such an array of non-localized DNA variations, whose reproduction comes to be controlled by some such an adaptive difference large enough for natural selection to detect, begins to qualify as a gene. Hence, a gene need not be located in any one place. All those DNA variations that, due to this common guidance (because they all share in the production of *one* adaptive difference), spread at the same rate in a population qualify as a single gene irrespective of location. It is this *sameness of reproductive rate* by which these DNA variations begin to meet the standards of being one single gene. Such a gene lacks physical discreteness but nevertheless acquires some distinctness as the smallest unit of selection. This is, I suggest, the unifying element in genes, the near-invisibility of which has been constantly bedeviling us. This element possesses the potential to bring together a variety of divergent gene concepts and to synthesize them into one common view of the gene" (pp 299–300).

In Beurton's first step, the diachronic mind's eye perspective of the evolutionist must be able to look into the genome of an organism and see what the synchronic view of the molecular biologist cannot. This critical first move turns on a couple of presuppositions the empirical plausibility of which Beurton does not explicate. Beurton is positing a gene, or really a proto-gene, on its way to becoming a gene. What gives the proto-gene its coherence is that no matter how it is distributed in the genome it is just that, and distinctly that, which is responsible for exactly one phenotypic trait whose adaptive advantage results in a uniform rate of selection wherever it is present. Now if one does not presuppose the existence of discrete functional genes to begin with, *and Beurton claims that he cannot,* then what exactly is the basis for believing that adaptive advantages are realized in discrete differences in traits (as opposed to complex differences in the performance of the whole organismic system)? And likewise, if he is not presupposing that end result he is trying to derive, on what basis is he warranted to abstract out only the dispersed segments of DNA from all of the molecular machinery which is actually involved in the processes that may result in adaptive advantage? And, finally, given the real heterogeneity of organisms, how plausible is it that Beurton's envisaged array of DNA will rise above the variable genomic, dynamic,

and biochemical contexts in which it is embedded and distinguish itself as a discrete unit of selection by way of its relatively context independent affect on reproductive rate?

Surely there are organisms with differences in DNA sequences here and there, and different reproductive rates, but unless these three assumptions are tenable, then the units of evolution become nothing short of the whole *developmental system* (Griffiths and Gray 1994). But let us provisionally grant the possibility of Beurton's initial move and consider the next step. Beurton believes that given this first condition, natural selection would then act to bring these dispersed units together into a physically discrete gene: "To say such an adaptive difference causes the origin of a new gene is to say that a genomic overall difference *between* individuals causes via its adaptive effect and the good offices of natural selection the emergence of a gene *inside* individuals in a process of downward causation (or genomic compartmentation, or genic individuation). This is how some specific genomic difference hardens into a single gene" (p 302).

But why should we believe that the force of evolution is toward the condensation of DNA segments into discrete units associated with discrete traits? Why cannot the opposite direction of movement be just as likely? Biologists such as Nina Federoff (1999) and James Shapiro (1999) have suggested that the restructuring of genomes, possibly through a kind of regulated use of transposon activity, has played a central role in generating evolutionary diversity. Would this not constitute a force in the opposite direction? The complexity and diversity of binding motifs, and the roster of transcriptional factors involved in the formation of regulatory complexes, has increased not decreased with the evolution of more complex life forms (International Human Genome Sequencing Consortium 2001). How can we rule out the possibility that natural selection has selected for more complexly dispersed genomic architectures in the case of more complex, phenotypically plastic organisms? Beurton seems to take it that the condensation of DNA into discrete atomic units constitutes some kind of attractor state in evolution. We can give this attractor state a name: it is Gene-P. Where a materialized misconstrual of Gene-P had served as the point of departure for the Modern Synthesis, Beurton now wants to insinuate Gene-P back as the very telos of evolution. In the absence of a prior assumption of the conflationary Gene-P/Gene-D gene, both steps of Beurton's model are problematic and his attempt at a grand unification of the gene founders.

The Concept of the Gene in Development and Evolution also includes articles by Fred Gifford, Michael Dietrich, James Greisemer, and Frederick Holmes, as well as an overview (which I have referred to) by Raphael Falk. It constitutes the first multidisciplinary collection of studies on the concept of the gene, and is thus long overdue. It is a very well-edited volume that could serve as a valuable nucleus for a seminar on a timely topic and a point of departure for both biologists and philosophers grappling with the meaning of *the gene*.

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