Logic and Philosophy of Science: Review of *Genetics and Philosophy: An Introduction*

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Paul Griffiths and Karola Stotz, ***Genetics and Philosophy: An Introduction***. New York: Cambridge University Press (2013), 270 pp., $29.99 (paper).

This is an important book. In it Paul Griffiths and Karola Stotz present a wide perspective on the issue of inheritance and its meaning for both the experimentalist and the philosopher. So extensive and challenging a text makes one wonder whether a less specific title, such as *Heredity and Philosophy*, would be more appropriate. The book provides a comprehensive analysis of classical genetics and the biology of heredity as well as a thorough and wide-ranging examination and assessment of much of the modern literature on molecular and postgenomic research. In addition, it presents the reader with meticulous philosophical discussions thereof. Griffiths and Stotz's presentations and conclusions are impressively well-grounded, even when the latter may appear at times difficult to accept.

Readers might wish to start with the final chapter of the book, "Four Conclusions" (221–28), which presents in a nutshell the major issues discussed—the identities of the gene, molecular epigenesis, genetics and reductionism, and nature and nurture. These pages summarize clearly, even in their relative extent, the subjects discussed in this book.

Griffiths and Stotz are actually among the banner carriers of "genetic system-analysis" that has been formulated in recent decades. As they make clear in their book, they continue to accept the important analytical value of *methodological reductionism*, while rejecting it epistemologically. Methodological reductionism states that the most fruitful investigative strategy is the decomposition of systems into their component parts. But a more in-

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tegrative approach is needed if the extraordinary amount of knowledge now available about living systems at the molecular level is to add up to an actual understanding of how those systems work. As Griffiths and Stotz note, this is because "biological specificity is distributed across the genome and its regulatory mechanisms, and . . . those regulatory mechanisms involve many factors 'outside the genome', including aspects of the environment and of experience. . . . These factors are not merely permissive, but instructive" (134).

The authors actually juxtapose three concepts of the units of reference of the science of heredity—that of Mendel's *Faktoren* (rather than "Mendel's Gene," as the authors named their chap. 2); that of Johannsen's *gene*, discriminating between genotype and phenotype; and that of Crick's conception of *molecular information*: "The molecular gene had a new role, very different from that of the Mendelian gene. Its primary role was to specify the linear order of elements in cellular products" (4). The emergence of Crick's 'informational specificity' or sequence specificity becomes the key property of the molecular gene.

> We argue that informational specificity or Crick information—the ability to causally specify the linear sequence of gene product—is not located solely in coding sequences of DNA, but is distributed between the coding sequences, regulatory sequences and their RNA and protein products, and the environmental signals. . . . These other factors help to determine the specificity of gene products through the activation and selection of coding sequences . . . a profoundly non-reductionist account of gene function which we refer to as 'molecular epigenesis'. The way in which genes in combination with other actors determine the activity of cells is mechanistic, but it is not reductionistic. (5)

Transfer of information is one of the most important, repeatedly discussed themes in the postgenomic era. Crick information, analogous to information carried by a computer tape, allowing "the ability to causally specify the linear sequence of gene product," is just one kind of information discussed (153). Of the two senses in which biologists talk of 'genetic information', information in genes and information about genes, only the first sense is considered here (144).

Thus, although the gene today is best conceived of as a set of contextually activated representations, it is still an instrumental unit for genetic analysis, and it is also a reasonably clearly defined structural unit used in annotating genomes. But the molecular gene, according to Griffiths and Stotz, is not a continuously evolving integral product of the gene concept. They conceive of all genetics prior to the 'molecular gene' as preparatory work: contrary to many older philosophical analyses that tried to understand a less adequate

theory called Mendelian genetics as one that was reduced to a newer more adequate theory called molecular genetics, the current authors deny such reduction, even though "when Mendel talked of 'factors' and Johannsen introduced the term 'gene' they were both, without knowing it, referring to the molecular gene" (31).

Oddly enough, the authors miss Beadle and Tatum's "one gene—one enzyme" notion of the early 1940s (1941a, 1941b), which was clearly a forerunner of the current authors' "Crick information" concept and directly instigated intragenic analyses and linear mapping of genes (see, e.g., Lewis 1951; Pontecorvo 1952), thus making the transition to the molecular gene concept less dramatic. This is not to underappreciate that "it was Francis Crick who in his famous 'Central Dogma' of molecular biology and 'sequence hypothesis' made the transition away from stereochemical specificity to informational or sequence specificity" (40). "The Central Dogma and sequence hypothesis certainly marked the beginning of a paradigm shift in genetics, and Crick's insights . . . were nothing less than visionary" (41). Crick "introduced a new way of thinking about biological specificity, a way of thinking that underpinned not only a new conception of the gene, but also the new technologies that would flow from molecular biology" (42). In the 1960s the two identities of the classical gene, the instrumental Mendelian and the hypothetical material, seemed to have converged nearly on a single well-defined entity—the classical molecular gene.

But Griffiths and Stotz's intent goes much further: as appropriately phrased on the cover, "By examining the molecular biology of the 'environment', they situate genetics in the developmental biology of whole organisms, and reveal how the molecular biosciences have undermined the nature/nurture distinction." They make explicit and emphasize their position as belonging to those who transformed the science of genetics from a distinct reductionist branch of biology into one of systems research. Indeed, a great part of the book, especially chapters 4–6, is devoted to the evolution and development of heredity of living beings as systems.

Chromatin renders DNA inaccessible to the transcriptional machinery; therefore, eukaryotes have no default or constitutive transcription: all gene expression needs to be regulated. As a first step, transcription factors must recruit a chromatin-remodeling complex to cleave the DNA away from the nucleosome: these are the so-called epigenetic mechanisms (53). Thus, the 'postgenomic era' in molecular biology has given rise to a 'systems-biological' outlook that seeks to reassemble these components and to learn how they interact to form complex living systems (71). And in variance to the classical molecular conception of the gene as a sequence with distinctive structure (promoter, ORF [open reading frame], adjacent regulatory regions) that performs the definite function of the gene, a postgenomic gene is

a collection of sequence elements that are the 'image' of the target molecule (the product whose activity we wish to understand) in the DNA, however fragmented or distorted that image may be (75). The nominal gene reduces to its RNA image. Accordingly, Scherrer and colleagues suggested that at the DNA level one may identify what they call the *genomic footprint*, that is, the fragments at the DNA level out of which the functional sequence is assembled during the expression process (Scherrer and Jost 2007, 2009; Stadler et al. 2009; see also Falk 2010). Without mentioning Scherrer's or Stadler's notion, Griffiths and Stotz develop quite adjacent notions: there is a built-in conflict in the changing concepts of genetics and its molecular views. The idea of specificity has been the touchstone of molecular biology. It transformed our understanding of biological mechanisms from a highly fluid and interactive process into an assembly of pieces each with its own specific and restricted part to play. But the idea of the DNA sequence as the sole source of specificity does not seem to capture how complex organisms are regulated and organized (84). These findings appear to support three interrelated theses: "genetic underdetermination and amplification, distributed causal specificity by means of regulated recruitment and combinatorial control, and molecular epigenesis" (98). A less metaphorical way to describe the situation is 'molecular epigenesis', following Waddington's 1950s notion (100).

This is not a return to preformationism: the structure of the body parts is not preformed, even though the structure of the molecular parts, proteins, is preformed in the DNA (100). But, as the authors argue, this is not molecular preformationism. Rather, "multiple factors, none of which contain a full representation of the molecule, are brought together in a process regulated by the larger system of which they are part. The Crick information manifest in a biomolecule is produced by an 'ontogeny of information'" (101), as suggested in Oyama (1985) and qualified by Griffiths's notion of the 'parity thesis' asserting "that the roles of causal factors in development do not fall neatly into two kinds, one role exclusively played by DNA and RNA sequences, and the other role exclusively played by elements other than nucleic acids" (160).

Thus, the move toward systems biology, from reduction to integration, may be better described as 'integrationist' rather than as 'holistic' (103). "Epistemic anti-reductionism is not an ontological claim. It is a family of claims about the relationship between different scientific domains and their bodies of knowledge" (104). Up-down causation is identified with the constraints (and possibilities or promises) placed on the behavior of parts by their interaction with the other parts of the system that contains them. "A set of sequences [becomes] a gene because of the way in which it is used by the cell, not because of its intrinsic structure" (106).

Regulated expression of the genome depends on many other factors apart from the DNA sequence. The environment, acting through the regulatory mechanisms described, plays an instructive role in regulating gene expression (109). This interaction undermines the common oppositions between nature and nurture, innate and acquired, biology and environment.

The only obvious way in which a sequence of DNA can possess intentionality is that embraced by Maynard Smith, deriving the intentional properties of DNA sequences from their design by natural selection. This is known as 'teleosemantics' because it seeks to derive semantic properties from the evolutionary design of the system that produced it (162). "If genes carry teleosemantic information because they have been designed to influence the development of offspring, then anything else designed to do that must also carry teleosemantic information. . . . The distinction between genetic, informational causes and environmental, merely physical causes is replaced by a distinction between causes which are designed to carry out developmental information and causes which are not designed to do this" (163). Work on epigenetic inheritance made increasingly significant the concessions that some nongenetic resources carry teleosemantic information (163). As put by Lewontin, "organisms fit the world so well because they have constructed it" (209). According to 'Niche construction' theory, environments are the agents that select, rather than induce, variations (210).

For a long time the science of inheritance had been captive of the Weismannian conception of segregation of soma and germ lines or, in cellular terms, of cytoplasmic and nuclear domains. Remarkably, it prevailed over the Mendelian notion that methodologically the essence of heredity may be profitably analyzed by selecting appropriate discrete characters that define discrete unit factors of the organism. Thus, in the first half of the twentieth-century genetic reductionism prevailed, and the dialectic was between a conceptual reduction of genes as units of heredity and a material reduction to such gene units. It took molecular genetics to challenge these concepts and establish a systems conception of inheritance.

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