The Philosophy of Molecular and Developmental Biology

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Introduction

Philosophical discussion of molecular and developmental biology began in the late 1960s with the use of genetics as a test case for models of theory reduction. With this exception, the theory of natural selection remained the main focus of philosophy of biology until the late 1970s. It was controversies in evolutionary theory over punctuated equilibrium and adaptationism that first led philosophers to examine the concept of developmental constraint. Developmental biology also gained in prominence in the 1980s as part of a broader interest in the new sciences of self-organization and complexity. The current literature in the philosophy of molecular and developmental biology has grown out of these earlier discussions under the influence of twenty years of rapid and exciting growth of empirical knowledge. Philosophers have examined the concepts of genetic information and genetic program, competing definitions of the gene itself and competing accounts of the role of the gene as a developmental cause. The debate over the relationship between development and evolution has been enriched by theories and results from the new field of 'evolutionary developmental biology'. Future developments seem likely to include an

exchange of ideas with the philosophy of psychology, where debates over the concept of innateness have created an interest in genetics and development.

Review of Past Literature

Reduction of Mendelian to Molecular Genetics

According to the classical account of theory reduction, one theory reduces to another when the laws and generalizations of the first theory can be deduced from those of the second theory with the help of bridge principles relating the vocabularies of the two theories (Nagel 1961). In 1967, Kenneth Schaffner suggested that classical Mendelian genetics could be reduced to the new, molecular genetics in something like this way. In a series of papers, Schaffner outlined his 'general reduction model' and argued for its applicability to the case of genetics (Schaffner 1967; Schaffner 1969). Despite the fact that Schaffner's model of reduction was less demanding than the classical model and allowed considerable correction of the reduced theory to facilitate its deduction from the reducing theory, his proposal elicited considerable skepticism. David Hull argued that key terms in the vocabulary of Mendelian genetics – gene, locus, allele, dominance and so forth – have no unique correlate in molecular biology (Hull 1974). There is, for example, no single molecular mechanism corresponding to dominance. The phenotypic resemblance between heterozygote and dominant homozygote might be explained by the nature of the products of the two alleles, by gene regulation that compensates for the loss of one copy of an allele or by the existence of alternative pathways to the same outcome in morphogenesis. Definitions of dominance and other key Mendelian terms at the molecular level will be open-ended disjunctions of ways in which the Mendelian phenomena might be produced. Therefore, Hull and others argued, the generalizations of

classical genetics cannot be captured by statements at a similar level of generality in molecular biology. So the theory of classical genetics is irreducible to theories in molecular biology.

The same fundamental issues were still under discussion ten years later, when Philip Kitcher put forward his 'gory details' argument (Kitcher 1984). Kitcher argued that classical, Mendelian genetics offers explanations of many important biological phenomena which are complete in their own terms and are not improved by adding the 'gory details' at the molecular level. The Mendelian ratios, for example, are explained by the segregation and independent assortment of chromosomes. Any mechanism that obeyed these two laws would produce Mendelian ratios and so the details of how segregation and assortment are achieved, however important they are in their own right and as explanations of other facts, do not add anything to the explanation of Mendelian ratios. Kenneth C. Waters has rebutted this argument, arguing that classical genetic phenomena such as crossing-over in meiosis immediately raise questions that can only be addressed in a molecular framework, such as why recombination is more likely at certain points on the chromosomes. It is simply not plausible, Waters argues, to treat the relatively small number of exception-ridden generalizations identified by classical genetics as an explanatory framework that is complete in its own terms (Waters 1994a; Waters 1994b). Waters also proposes a definition of 'gene' designed to rebut the charge that Mendelian genes do not display a unity at the molecular level. A gene is any relatively short segment of DNA that functions as a biochemical unit (Waters 1994a: 407). Waters admits that this definition makes the gene a unit of indeterminate length and

that it is the specific research context that determines whether a particular utterance of 'gene' refers to a series of exons, an entire reading frame including both exons and introns, the reading frame plus adjacent regulatory regions or that complex plus other regions involved in regulating splicing and editing the transcript. Nevertheless, he argues, at the core of all these definitions of 'gene' is the basic concept of a sequence that is transcribed to produce a gene product. Other authors have argued that Waters's definition creates a merely verbal unity between 'genes' with different structures, different functions and different theoretical roles in molecular biology (Neumann-Held 1998). The empirical facts that underlie this dispute are that reading sequences – the structural basis of the classical molecular conception of the gene - can be used to make a variety of products depending on the cellular context which regulates their expression and cuts, splices and edits the gene transcript. Reading sequences can also overlap one another. All these phenomena were unanticipated by early molecular biologists, let alone by pre-molecular Mendelian geneticists. The magnitude of these theoretical developments in genetics makes it highly plausible that there have been changes in the concept of the gene, which is the central theoretical construct of that discipline. Whether such conceptual change would make reduction impossible is less clear.

The thirty-year debate between reductionists and anti-reductionists has been complex and wide-ranging and numerous authors not mentioned here have made important contributions. A more adequate, but still brief, survey can be found in (Sterelny and Griffiths 1999: Ch 6-7) and an extended treatment in (Sarkar 1998). For many philosophers the main lesson of the debate is that traditional models of reduction do not

capture the important role played in scientific progress by successful explanations of larger systems in terms of their smaller constituents (Wimsatt 1976). Even committed reductionists such as Waters have adopted models of reduction very different from those with which the debate began. Schaffner himself has continued to make some of the most sophisticated contributions to the development of adequate models of the relationship between molecular biology and theories of larger units of biological organization. His work has increasingly focused on the role of model systems and results of limited generality derived from the analysis of these systems (Schaffner 1993).

Developmental Constraints and Evolution

It is generally accepted that the 'modern synthesis' of Mendelian genetics and natural selection that put so many of the biological sciences on a common theoretical basis failed to include the science of developmental biology (Hamburger 1980). The synthetic theory bypassed what were at the time intractable questions of the actual relationship between stretches of chromosome and phenotypic traits. Although it was accepted that genes must, in reality, generate phenotypic differences through interaction with other genes and other factors in development, genes were treated as 'black boxes' that could be relied on to produce the phenotypic variation with which they were known to correlate. The black-boxing strategy allowed the two tractable projects – theoretical population genetics and the study of selection at the phenotypic level – to proceed. Selection could be studied at the phenotypic level on the assumption that variant phenotypes were generated in some unknown way by the genes and that phenotypic change would be tracked by change in gene frequencies. Population genetics, the mathematical core of the modern synthesis, could postulate genes corresponding to phenotypic differences and track the effect of

selection on these phenotypic variants at the genetic level. One effect of this strategy was to direct attention away from ideas that would obstruct these research practices. Amongst these inconvenient ideas was the view that development does not always permit the phenotypes that selection would favor. This idea was revived in the 'punctuated equilibrium' theory of Niles Eldredge and Stephen J. Gould (Eldredge and Gould 1972; Gould and Eldredge 1977). Traditional neo-Darwinian gradualism suggests that species evolve more or less continuously in response to local selection pressures. The fossil record, on the other hand, suggests that species remain largely unaltered for long periods of time and occasionally undergo dramatic periods of rapid evolutionary change. The punctuated equilibrium theory proposed that the fossil record be read at face value, rather than in the light of the gradualist model of evolution. The new theory needed an evolutionary explanation of this pattern and sought it in 'developmental constraints'. The range of variant phenotypes produced by genetic changes is constrained by the nature of the organism's developmental system so that selection is usually unable to produce dramatic reorganization of the phenotype. Conversely, a relatively small genetic change might, in the context of development as a whole, result in large phenotypic changes and very rapid evolution. Both possibilities can be understood using C. H Waddington's metaphor of developmental canalization (Figure 1.). Most small perturbations to the course of development are compensated so that the organism arrives at the same destination. Some, however, send development down an entirely new 'channel'.

Insert Figure 1 about here.

A second source of the renewed interest in developmental constraint was the debate over the limits of adaptive explanation. Stephen J. Gould and Richard Lewontin strongly criticized 'adaptationism' – the practice of seeking adaptive explanations for every feature of organisms. They suggested developmental constraint as one alternative explanation of biological form (Gould and Lewontin 1979). There are, for example, many viviparous snakes, but no viviparous turtles. Perhaps this is to be explained adaptively: any transitional form of turtle would be less fit that its fully oviparous competitors. The ease with which other groups, such as snakes and sharks, have evolved viviparous and quasi-viviparous species suggests an alternative explanation. Perhaps the developmental biology of turtles means that no mutation produces the transitional forms. Gould and Lewontin also revived the traditional idea of the *bauplan* (body plan) or 'unity of type' of a whole group of organisms. Crustaceans, for example, have the segmented body of other arthropods but are distinguished from other clades by the fusion of the first five segments to form a head. It seems unlikely that this character has been a critical component of the fitness of every crustacean, from lobster to barnacle, but it has remained stable through long periods of evolution. Perhaps this is to be explained by developmental constraint – the head is part of the basic body plan of this kind of organism - a highly canalized outcome of crustacean development.

There is no doubt that developmental constraints exist (Maynard Smith, Burian et al. 1985). A constraint can be defined fairly uncontentiously as a bias in the production of variation in a population. But there is little agreement about the evolutionary importance of constraints. Even more importantly for philosophy of biology, there is little agreement about how their importance might be measured. At one extreme, 'process structuralists' like Brian Goodwin have argued that explanation in terms of natural selection have only a marginal role when compared to explanations in terms of developmental constraint (Goodwin 1984; Ho and Saunders 1984). The process structuralists sought to revive the nineteenth century project of 'rational taxonomy': a classification of biological forms in terms of the generative principles by which form is constructed. The fact that an organism has a particular form is primarily explained by its place in this system. In support of their position, the process structuralists were able to offer striking examples of this kind of explanation. There are only a few patterns of phylotaxis – the successive arrangement of radial parts in a growing plant – and these patterns are typically conserved within lineages of plant species. A general mathematical description of these patterns is available and models of growth that obey this mathematical description are biologically plausible (Mitchison 1977). If correct, this is an impressively general explanation of many biological traits in many species. The process structuralists also presented methodological arguments. Scientific explanations should appeal to laws of nature, not historical accidents. Explanations of form in terms of the mechanisms of growth are simply better explanations than those that rely on natural selection (Goodwin and Webster 1996). Most developmentalists have been less extreme than the process structuralists. They do not deny the importance of natural selection, but insist that the

course of evolution cannot be understood in terms of selection alone, only in terms of the interaction of selection with the constraints imposed on phenotypic change by development. At the other extreme, some biologists have argued that constraints can only ever be temporary, since evolution can reconstruct the developmental system of the organism so as to achieve whatever outcome is selectively optimal. Darwin himself expressed something like this sentiment when he remarked that his theory embraced both traditional forms of biological explanation, the 'unity of type' and the 'conditions of existence', but that the conditions of existence was the 'higher law' because it explains the origin of the types (Darwin 1964: 206). But there are many highly conserved features of biological lineages that are not plausibly explained by stabilizing selection, such as the fused head-segments of crustaceans mentioned above or the relative position of bones in the tetrapod limb. Something must explain the fact that these features have not been affected by random genetic drift and developmental constraint is an obvious candidate. William Wimsatt has offered a highly general argument for the view that developmental constraints will be harder for selection to remove than to construct (Wimsatt 1986; Wimsatt 1999). It is widely accepted that the ability of natural selection to create complex adaptation depends on the ability to create those adaptations cumulatively, adding features one at a time. Wimsatt argues that new adaptations will be constructed by utilizing existing developmental structures in the organism, so that the ability to develop the new feature is left dependent on the continued existence of the older features. Wimsatt calls this process 'developmental entrenchment' and argues that it will lead to features of the organism becoming progressively less open to selective modification in their own right as additional features are built 'on top'.

Another argument for the adaptationist perspective concedes the role of development as a *cause* of form, but questions its value as an *explanation* of form. One of the primary aims of biology is to explain the fact that organisms are well adapted for their conditions of life (Dawkins 1986; Dennett 1995). Naturally, there is a developmental explanation of how each organism is constructed, but this cannot explain the fact that organisms are well adapted. How could the developmental structure of organisms ensure in and of itself that organisms are well suited to the demands of their environment?

> 'Of course, large quantities of evolutionary change may be non-adaptive, in which case these alternative theories may well be important in parts of evolution, but only in the boring parts of evolution, not the parts concerned with what is special about life as opposed to non-life.' (Dawkins 1986: 303. *Some process structuralist targets of this remark are identified by name on 307*.)

Peter Godfrey-Smith has christened this view 'explanatory adaptationism' to distinguish it from the 'empirical adaptationist' view that almost every feature of organisms has an adaptive explanation (Godfrey-Smith 1999). For the explanatory adaptationist, the problem with developmental explanations is not that they are false, but that they explain the wrong thing.

Ronald Amundson has argued that adaptationists and developmentalists are to a significant extent talking past one another because they have very different concepts of developmental constraint (Amundson 1994). In developmental biology, a developmental constraint explains why certain phenotypes do not occur, either generally or in some

particular group of organisms. The fact that a feature conforms to a developmental constraint in this sense is consistent with it being perfectly adapted to its environment. In the study of adaptation, however, developmental constraints are postulated to explain why organisms are unable to construct the optimally adaptive phenotype. This, second understanding of constraint is manifested in another of Godfrey-Smith's categories: 'methodological adaptationism'. This is view that the best way to reveal developmental constraints is to build optimality models and look at how nature deviates from what is optimally adaptive. In this sense, constraint and adaptation are opposed to one another by definition. Like Godfrey-Smith's distinction between empirical and explanatory adaptationism, Amumdson's distinction between constraints on form and constraints on adaptation goes some way to explain why the debate between adaptationists and developmentalists has produced more heat than light. But even after these conceptual clarifications, there remain genuine empirical differences between the two views, as Amundson himself makes clear. The underlying empirical issue is how much of the space of possible biological forms ('morphospace') is ruled out by the fact that organisms built using the fundamental techniques shared by the earth's biota cannot develop in that way. One way to represent this disagreement is by different predictions about what would happen to a population of organisms in the absence of selection. The adaptationist 'null hypothesis' is that random variation would spread the population evenly through an increasingly large region of morphospace. The developmentalist 'null hypothesis' is that even without selection organisms would be found clustered in some regions of morphospace and excluded from others because of developmental constraints on the production of variants (Alberch 1982). Developing this theme, Paul Griffiths has argued

that what appear to be conceptual or methodological differences between process structuralists and extreme adaptationists may in reality be manifestations of this empirical disagreement (Griffiths 1996). The empirical disagreement produces conflicting intuitions about whether development or natural selection is more explanatory because a request for explanation presumes a contrast between the state of affairs to be explained and other possible states of affairs (Van Fraassen 1977). The question 'why is this organism *here* in morphospace?' implies the contrast 'as opposed to some other region of morphospace'. Because process structuralists think most regions of morphospace are developmentally impossible they will see an explanation of how the organism develops its actual form as highly explanatory. By explaining how this form is possible it contrasts it with the forms that are impossible. The adaptationist assumes that almost all forms are developmentally possible, so learning that the actual form is possible does not explain the contrast between this form and the adjacent forms.

Biocomplexity and Self-organisation

Support for the idea that selection is not the only factor determining biological form was provided in the 1990s by the new sciences of complexity (Burian and Richardson 1990; Bechtel and Richardson 1993). Some complex systems possess an intrinsic tendency to occupy highly ordered states, so selection is not the only possible source of order in living systems (see also Riedl 1977). Stuart Kauffman's simulations of networks of 'genetic' elements suggested that basic biological phenomena such as autocatalytic cycles required for the origin of life or the array of cell-types required for the emergence of multi-cellular life are highly probable outcomes of random variation in complex chemical

or, later, genetic networks (Kauffman 1993). This is in striking contrast to the traditional view that such complex outcomes are highly improbable and must be explained by cumulative selection of many, much smaller increases in order. Kauffman's simulations also suggested that selection is relatively ineffective when the 'genetic' elements are strongly interconnected so that the activity of one depends on that of many others, something that is probably true of actual genes. Because Kauffman's work suggests that order may be generated without selection, and that selection may not be able to overcome the intrinsic tendencies of systems, he has sometimes been seen as providing support for the process structuralist position (Goodwin, Kauffman et al. 1993). But other elements of Kauffman's work do not lend themselves to this interpretation. Self-organisation and selection can reinforce one another: self-organisation can enrich the input to selection and selection can 'tune' developmental parameters to encourage the production of complex variants (Depew and Weber 1995). In recent years even highly adaptationist authors such as Daniel Dennett have made use of Kauffman's work (Dennett 1995).

Current status of Problems

Genetic Information

There is an 'interactionist consensus' in the life sciences that all traits are dependent on both genetic and environmental factors in development (Sterelny and Griffiths 1999: 13-17). The consensus emerged from early twentieth-century critiques of the concept of instinct and from parallel critiques of the concept of innateness in early ethology. But this is consistent with the view that genes cause development in a radically different way from other, 'environmental' factors. Genes are widely believed to contain a program that guides development and to contain information about the evolved traits of the organism.

Despite the ubiquity of talk of genetic information in molecular and developmental biology, the predominant view in recent philosophical work on this topic has been that 'genetic information' and 'genetic program' have a precise meaning only in the context of the relationship between DNA sequence, RNA sequence and protein structure (Sarkar 1996; Griffiths and Knight 1998; Godfrey-Smith 1999; Kitcher In Press). In their broader applications these ideas are merely picturesque ways to talk about correlation and causation.

The obvious way to explicate information talk in biology is via information theory. Information in this sense is the systematic dependence of a signal on a source, a dependence that is created by a set of channel conditions. In the case of development, the genes are normally taken to be the source, the life-cycle of the organism is the signal and the channel conditions are all the other resources needed for the life-cycle to unfold. But it is a fundamental feature of information theory that the role of source and channel condition can be reversed. A source/channel distinction is imposed on a causal system by an observer. The source is one channel condition whose current state the signal is being used to investigate. If all other resources are held constant, a life-cycle can give us information about the genes, but if the genes are held constant, a life-cycle can give us information about whichever other resource we decided to let vary. So far as causal information goes, every resource whose state affects development is a source of developmental information (Johnston 1987; Gray 1992; Griffiths and Gray 1994; Oyama 2000a).

The fact that causal information conforms to this 'parity thesis' is now quite widely recognized (Godfrey-Smith 1999; Sterelny and Griffiths 1999; Maynard Smith 2000; Kitcher In Press). A common response has been to analyze genetic information using teleosemantics, the philosophical program of reducing meaning to biological function (teleology) and then reducing biological function to natural selection (Millikan 1984; Papineau 1987). In his version of the teleosemantic approach, John Maynard Smith compares natural selection to computer programming using the 'genetic algorithm' technique. The genetic algorithm programmer randomly varies the code of a computer program and selects variants for their performance. In the same way, natural selection randomly varies the genes of organisms and selects those organisms for their fitness. Just as the function of the selected computer program is to perform the task for which it was selected, the biological function of successful genes is to produce the developmental outcomes in virtue of which they were selected. Such genes are intentionally directed onto, or about, those effects. The defective haemoglobin gene in some human populations, which has been selected because it sometimes confers resistance to malaria, carries teleosemantic information about malaria resistance. However, teleosemantic information is fundamentally unsuited to the aim of avoiding parity. The most fully developed teleosemantic account of developmental information is the 'extended replicator theory' (Sterelny, Dickison et al. 1996; Sterelny 2000), which recognizes from the outset that teleosemantic information exists in both genetic and in some non-genetic developmental causes. Griffiths and Russell Gray argue that teleosemantic information exists in an much wider range of developmental causes (Griffiths and Gray 1997). Teleosemantic information exists in any inheritance system that is a product of evolution,

including epigenetic inheritance systems. The term 'epigenetic inheritance system' is used to denote biological mechanisms which produces resemblances between parents and offspring and which works in parallel with the inheritance of nuclear and mitochondrial DNA (Jablonka and Szathmáry 1995). Every organism inherits a great deal besides its DNA. To develop normally the egg cell must contain features such as: basal bodies and microtubule organising centres, correct cytoplasmic chemical gradients, DNA methylation patterns, membranes and organelles, as well as DNA. Changes in these other resources can cause heritable variation that appears in all the cells descended from that egg cell. Differences in methylation, for example, are important in tissue differentiation during the lifetime of a single organism, but they can also pass between the generations. Methylation patterns are often applied to the DNA in a sperm or egg by the parent organism. DNA methylation inheritance has excited a great deal of interest because of it is easy to see how it could play a role in conventional, micro-evolutionary change. Wider forms of epigenetic inheritance include the inheritance of symbiotic microorganisms, habitat and host imprinting, and the care of offspring. All these mechanisms are candidates for evolutionary explanation - they did not come about by accident. This means that the physical traces by which these inheritance mechanisms influence the next generation have biological functions and thus, on the teleosemantic approach, that these traces contain information. The widest form of epigenetic inheritance is 'niche construction'. Many features of an organism's niche exist only because of the effects of previous generations of that species on the local environment (Laland, Odling-Smee et al. 2001). However, despite the evolutionary importance of niche construction, the

collectively constructed features of a species' niche are not adaptations of the *individual* organism, and hence probably cannot be assigned teleosemantic information content.

Genetic Program

The concept of the genetic program has proved as controversial as that of genetic information (Keller 1995). Its critics have questioned whether development is more program-like than any other law governed physical process. There is a sense in which the planets compute their courses around the sun, integrating the forces that act on them to determine the trajectory they will follow. If the idea of a genetic program comes to no more than this, then it is of little scientific value. Some historians of molecular biology have argued that the history of the genetic program concept in molecular biology is one of retreat from literal hypothesis to guiding metaphor to mere tool for popularization (Chadarevian (1998) see also Sarkar (1996)). In contrast, Alexander Rosenberg has defended the view that the study of development is the study of how the embryo is 'computed' from the genes and proteins contained in the egg cell (Rosenberg 1997). Rosenberg's argument is that striking recent successes in developmental molecular biology have concerned genes which switch other genes on or off in hierarchical cascades of gene activation. What, he asks, could be a more powerful vindication of the idea that the genes contain a self-executing program for development? Evelyn Fox-Keller has rejected this interpretation of the science, arguing that gene activation in the developing embryo is precisely *not* like the unfolding of a stored program, but instead like distributed computing, in which processes are reliably executed by local interactions in networks of simple elements (Keller 1999). The mathematician Henri Atlan adds another perspective to this debate, arguing that if there is a program for development in any sense analogous

to programs in computer science, then the program is not in the genome. Atlan argues that a rigorous deployment of the analogy identifies DNA sequences with the data accessed at various times whilst a program is running. The program itself is running on the cellular mechanisms that transcribe and process DNA (Atlan and Koppel 1990).

Developmental Systems Theory

Developmental systems theory (DST) is an alternative account of the relationship between genes and other factors in development. It has its roots in a longstanding tradition of dissatisfaction with the concepts of instinct, innateness, genetic information and genetic program amongst workers in comparative psychology and developmental psychobiology (Gottlieb In Press). When used with care, ideas of instinct, innateness, genetic program and genetic information constitute a kind of 'methodological preformationism' in which biological form is treated *as if* it was transmitted intact to the next generation so as to avoid the need to deal with the complexities of development. Very often, however, these concepts are treated as if they were substantial explanatory constructs, leading to the illusion that no developmental explanation is needed for traits that are 'innate', 'hardwired' or 'in the genes'! In place of these ideas, DST argues for a thorough-going epigenetic account of development. Biological form is not transmitted intact, or as an intact representation of that form, but must be reconstructed in each generation by interaction between physical causes. Moreover, there is no one element that controls development or prefigures its outcomes. The term 'developmental system' refers to the system of physical resources that interact to produce the life cycle of a particular evolving lineage. A lineage is redefined as a causally connected sequence of similar individual life cycles and inheritance is redefined as the reliable reproduction of

developmental resources down lineages. This definition includes all the mechanisms of epigenetic inheritance, as well as niche construction and the mere reliable persistence of features upon which the developmental system can draw. Natural selection becomes the differential reproduction of heritable variants of developmental systems due to relative improvements in their functioning, a process which leads to change over time in the composition of populations of developmental systems (Griffiths and Gray In Press).

The book that drew the developmental systems tradition together and gave it a definitive name was Susan Oyama's *The Ontogeny of Information: Developmental Systems and Evolution* (Oyama 2000a), first published in 1985 at around the same time as several of Oyama's important papers (Oyama 2000b). Philosophers of biology began to discuss these new ideas in the 1990s, some aiming to develop and extend Oyama's approach (Moss 1992; Griffiths and Gray 1994) (Griffiths and Gray 1997) and others to critically evaluate it. Cor van der Weele has argued that the criticisms of contemporary neo-Darwinism offered by DST are almost completely orthogonal to those of the process structuralists (Van der Weele 1999). DST could potentially treat developmental resources atomistically and rely on selection as the primary explanation of biological form. In reality, however, most DST authors have been sympathetic to the idea that developmental constraints and emergent developmental organization are real and play a role in evolution. Kim Sterelny and others have accepted some of the critical points made by DST, but argued that these do not justify abandoning the replicator in favor of the developmental system as the unit of evolution (Sterelny, Dickison et al. 1996). Epigenetic inheritance can be accommodated by enlarging the cast of replicators to include some

inherited non-genes. The fact that replicators require a specific context in order to exert the causal influence can be handled in a manner similar to earlier critiques of the dependence of single genes on their genetic contexts (Sterelny and Kitcher 1988). Schaffner has argued that most work in molecular developmental biology conforms to the strictures about the distributed control of development and the context-sensitivity of genetic and other causes. He also argues that a certain instrumental privileging of genetic causes is a justifiable part of research practice (Schaffner 1998).

The most thorough presentation of DST and its application to date is (Oyama, Griffiths et al. 2001), a volume that also contains critical contributions by some of the authors mentioned here.

Analyses of Gene Concept

Controversies about the role of genes in development in evolution have generated controversies about the definition of the gene. These have not been sterile debates over the 'right' definition. The debates have concerned how genes are actually defined by various kinds of biologist, what this indicates about their thinking and whether genes so defined can bear the theoretical weight placed upon them. An excellent introduction to recent debates over the concept of the gene is (Beurton, Falk et al. 2000). There has been a great deal of criticism of the evolutionary gene concept of George C. Williams according to which a gene is *any* sequence of DNA 'which segregates and recombines with appreciable ' (Williams 1966: 24). Many authors in the philosophy of evolutionary biology have discussed whether change over time in populations of evolutionary genes can explain change at the phenotypic level (Sterelny and Griffiths 1999: 77-93). In the

philosophy of developmental and molecular biology, however, the central issue has been the relationship between genes and phenotypes. The classical molecular gene concept, which emerged in the 1960s and is still orthodox in textbook presentations of genetics defines a gene as a stretch of DNA that expresses a particular polypeptide via transcription and translation. This identifies an individual gene by a particular, minimal 'phenotype' to which it gives rise. As mentioned above, Waters still defends something close to this concept of the gene as both central to and adequate for the practice of molecular biology and his account has been criticized by Eva Neumann-Held (Waters 1994; Neumann-Held 1998). Griffiths and Neumann-Held have argued that the development of gene concepts from the turn of the century to the present day has been driven by the twin desires to find a structural unit in the DNA itself and to have that unit make some constant contribution to development (Griffiths and Neumann-Held 1999). They argue that current knowledge about the multiple functions of many genes makes this difficult if not impossible and suggest (but do not endorse) identifying a sequence of DNA with a unique norm of reaction of gene products across cellular contexts. Their own proposal is to identify a specific gene with a DNA sequence plus the context needed to pin down a single gene product in the manner of the classical molecular concept.

Other authors have argued that two distinct notions of gene play a role in molecular biology: 'structural' genes that code for polypeptides used to make structural proteins and 'regulatory' or 'developmental' genes are involved in developmental signaling (Morange 2000). The most famous examples of developmental genes are the homeobox genes – highly conserved sequences that are involved in segmentation in arthropods and in

forming the axes of the vertebrate embryo. Developmental genes have become the favored example of both the friends and enemies of the genetic program concept (Gilbert 2000). Those critical of the concept take the facts about developmental genes to show that the same sequence can have a radically different effect in a different context. Advocates of the program concept are impressed by how much of the developmental process can be 'controlled' by a few genes.

Lenny Moss has criticized both Waters' analysis and the analysis of Neumann-Held and Griffiths and argued that the very same genes are both multi-potential in the manner of the 'developmental gene' and, in another context, defined by a determinate phenotypic effect (Moss 2001; Moss In Press). Moss proposes that the whole range of uses of the gene concept in contemporary biology can be reduced to two competing conceptualizations of the gene that, he argues, were implicit from the earliest days of genetics. The first way of conceiving of a gene, which Moss calls 'Gene-P', is a manifestation of the instrumental preformationist research strategy discussed above. In research contexts in which scientists are interested in establishing or exploiting gene-phene correlations it makes sense to treat genes as if *as if* they were defined by their association with a certain phenotypic outcome. Blue eyes occur if a gene involved in the synthesis of the brown protein is damaged in some way. What makes a DNA sequence a gene for blue eyes is not any particular sequence nor any knowledge of the developmental pathway that leads to blue eyes but only the fact that the presence of this gene can be used to predict blue eyes. That example comes from classical Mendelian genetics, but contemporary molecular genetics also makes use of the Gene-P concept.

BRCA1, the gene for breast cancer, is treated as a Gene-P. Moss's other gene concept (Gene-D) is defined by its molecular sequence. Gene-D is a developmental resource that can make any of a multitude of different contributions to development in different contexts. Moss uses the example of the N-CAM gene, the gene that produces the so-called 'neural cell adhesion molecule'. The N-CAM gene is a specific nucleic acid sequences from which any of 100 different isoforms of the N-CAM protein may potentially be derived. This protein is expressed in different tissues at different developmental stages in many different forms.

> "So where a Gene-P is defined strictly on the basis of its instrumental utility in predicting a phenotypic outcome and is most often based upon the absence of some normal sequence, a Gene-D is a specific developmental resource, defined by its specific molecular sequence and thereby functional template capacity and yet it is indeterminate with respect to ultimate phenotypic outcomes." (Moss 2001: xxx)

Moss argues that many uses of molecular findings that have been criticized by, for example, the developmental systems theory, arise from taking findings that make sense using the Gene-D concept and interpreting them as if they involved the Gene-P concept. For example, Moss would see it as inappropriate to describe one of the classical developmental genes – sequences used in the control of gene expression in many parts of many distantly related species – as a 'gene for' the large section of the phenotype of one of those species in whose development it is implicated.

Evolutionary Developmental Biology

One of the most exciting trends in recent biology has been the emergence of 'evolutionary developmental biology' – the integrated study of evolution and

development (Raff and Raff 1987; Hall 1992; Raff 1996). Evolutionary developmental biology simultaneously explores the impact of development on the evolutionary process and the evolution of development. A common philosophical interpretation of this trend in biology is that the 'molecular revolution' has 'opened the black box' created as part of the modern synthesis. What were previously two kinds of empirical work that led to very different and conflicting pictures of life – evolutionary genetics and developmental biology - can now be empirically integrated so as to yield a single picture (Burian 1997). Waddington's notion of developmental canalization, for example, has been interpreted as the result of the ubiquity of negative and positive feedback loops in the regulation of gene expression (Freeman 2000). The developmental concept of a 'morphogenetic field' has been reinterpreted as an emergent phenomena resulting from gene regulation (Gilbert, Opitz et al. 1996).

A central issue in the older debate between developmentalists and adaptationists was the extent to which phenotypes are holistic entities in which change in one part affects every other. Part of Gould and Lewontin's critique of adaptationism was that it assumes an implausibly atomistic phenotype. Many traits of organisms, they argued, cannot be optimized by selection because they are developmentally linked to other traits. In reply, adaptationists accused their critics of having an implausibly holistic conception of the phenotype. After all, the documented examples of natural selection, to say nothing of artificial selection, demonstrate that many traits can be altered without causing any dramatic reorganization of the phenotype. The argument, mentioned above, that developmental constraints are created by evolution and can therefore be dissolved by

evolution was also used to support the adaptationist position. Work in developmental evolutionary biology has helped to make this debate more tractable and progressive. A key concept in evolutionary developmental biology is 'developmental modularity'. A developmental module is a set of developmental processes that strongly interact with one another and interact only weakly with processes outside the module (Müller and Wagner 1991). Modules can be the result of the same pattern of connectivity holding within the genome, so that the developmental module corresponds to a 'genetic module'. Alternatively, developmental modularity can be an emergent phenomena resulting, for example, from the emergence of physical boundaries in the embryo. Existing knowledge in developmental molecular biology strongly suggests that development is modular and models of the evolution of development suggest that selection will favor the emergence of modularity (Wagner, Booth et al. 1997).

The concept of developmental modularity can be used to reexamine some of the older issues concerning developmental constraints. Developmental modules represent a natural partition of the phenotype in units whose evolution can proceed relatively independently. An accurate model of evolutionary dynamics must incorporate the fact that the evolving phenotype is neither atomistic nor holistic, but modular. It is far from obvious that this fact should be interpreted as showing the importance of what Amundson has termed 'constraints on adaptation' (Amundson 1994). If developmental modules are the real biological characters of which organisms are composed then saying that selectionnis constrained by having to act on modules is nearly as odd as saying that it is constrained by having to act on features of the phenotype. Philosophers of biology are starting to

rethink issues in evolutionary theory in terms of the modularity concept and the results promise to be of the highest interest (Brandon 1999).

Future Work

The debate over the role of information concepts in biology is in full swing at present and likely to continue. The renewed contact between the philosophies of evolutionary and developmental biology is also likely to occupy many writers for some time to come. One developmental concept that seems likely to be revisited after some years of neglect is that of innateness. In developmental biology 'innateness' seems as charmingly old-fashioned a theoretical construct as 'instinct' and equally peripheral to any actual account of gene regulation or morphogenesis. In behavioral ecology some authors regard the innateness concept as irretrievably confused and a term that all serious scientific workers should eschew (Bateson 1991) whilst others claim that the popular demand to know if something is 'in our genes' is best construed as a question about whether a trait is an adaptation (Symons 1992: 141). In cognitive psychology, however, whether a trait is innate in its traditional sense – coming in some sense from 'inside' rather than the 'outside' - is still a key question, and the subject of heated debate (Cowie 1999). Some philosophers of biology have tried to bring work in developmental biology to bear on the psychological debate (Ariew 1999) and judging by recent conference presentations more work of this kind can be expected.

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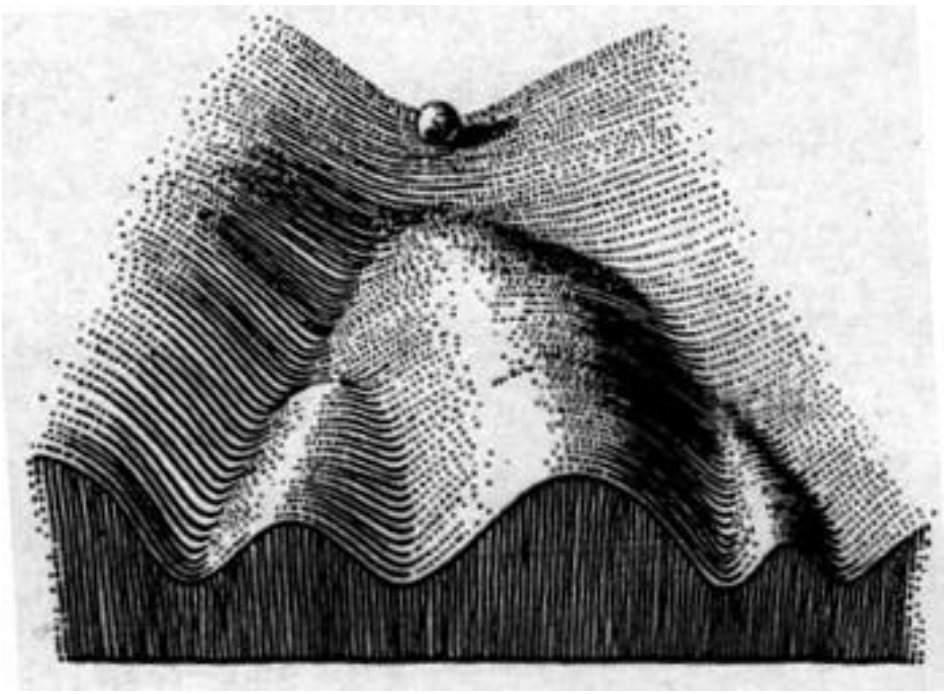

Figure 1. Canalisation of development. The development of the organism is represented by the trajectory of the ball when it is releases and the developmental structure of the organism by the surface. Mutations alter the height of points on this surface, generally with little effect on the trajectory of the ball, but occasionally with dramatic effect (Waddington 1957: 36).