AN INTERPRETATION OF BIOLOGICAL DEVELOPMENT

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ABSTRACT

The research programs and practices used to address biological problems are often grounded in the way one interprets biological organisms. There is a practical motive to explain organismic development in terms of genes and the environments in which genes are expressed. This interpretation presupposes that organisms are simply gene environments. In this way, genes either control the outcome of development or contain information that specifies particular outcomes. In either case, development is basically a problem to be resolved through an increased understanding of genes and the ways genes are expressed. This interpretation fails to adequately explain the process by which complex form is generated. Therefore, there are grounds for rejecting it. An approach centred around the whole organism directs attention towards its many constituents and requires that one take seriously the role of multiple organismic elements in order to adequately explain development.

PREFACE

The basis for my research on the topic originally stemmed from both my interests in practical biology and a growing awareness of the importance of philosophy for science in general and biology in particular. I have noticed the divorce that has occurred between academic science and academic philosophy, where it is usually accepted that the former can do without the latter and that students of the latter should engage in different kinds of problems than those emerging from within the scientific disciplines. Beyond this, I find there is a tendency among both academic scientists and popular writers to interpret complex functioning organisms and their reproductive and developmental life cycles solely in terms of modern technological innovations. Such innovations usually emerge from molecular biology and genetics and are deemed important because they produce immediate practical results. In accepting the importance of such innovations for development, one implicitly prefers the practical output of technology over a careful philosophy of nature. Few practitioners in either science or philosophy seem to familiarize themselves with the traditional philosophical problems surrounding things like explanation in embryology or the role of teleology or function in biology. These problems I bring to bear on my research on the interpretation of development.

None of the efforts put forward here would be possible were it not for the loving support of my spouse and frequent encouragement from my parents. I also wish to thank my supervisor, Richard Arthur, for his continual engagement, advice, and patient support throughout this process; Rama Singh, for his

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TABLE OF CONTENTS

Introduction……..1

1 Development as Genetic Control 14

2 Development as Genetic Revelation 35

3 An Organism-Centred Approach 52

3.1 Function and Explanation in Biology..... 53

3.1.1 Objections to the problem of form 54

3.1.2 Objections to anti-reductionism 67

3.2 The Whole Organism in Development..... 76

3.3 The Whole Organism and the Problem of Constraints..... 83

Conclusion…….89

Bibliography……..97

INTRODUCTION

One of the most controversial problems in the philosophy of biology is that of interpreting how development occurs in living creatures. Although the mechanical details of developmental processes are the subject of numerous studies, these studies are often stilted because they are conducted in a gene-centred framework. The reason this is seen by many as problematic is that it portrays development as a bottom-up phenomenon, in which a range of outside events provide the key to understanding how inherited elements at the bottom are causally linked to fully-formed adult phenotypes. No one denies that DNA continually interacts with environmental factors at every stage of development.[1] But a method that merely abstracts away genes from organisms has troubling implications for the study of development, which interprets the formation of embryos to be mostly about genes and their environments.

One might reasonably ask whether genes ought to have primacy in the interpretation of development. Observing that organic form both varies and repeats itself in development and evolution leads to the view that gene-centred explanations are too simplistic. While it is sometimes appropriate to separate genes from trait-bearing organisms, I contend that much of what one observes in biology makes sense only if one begins with the whole organism rather than with any of its elements. Therefore, the current strategy to take genes and environments as the central dichotomy of development should be rejected. The

[1] Personal Communication with Rama Singh, June 27, 2019.

same sentiment is given by Jason Robert in his book *Embryology, Epigenesis, and Evolution*, in which he argues that

> organisms are more than epiphenomena of genomes, more even than epiphenomena of genomes in particular structured environments. For a genome is in no sense prior to or separate from an organism….[2]

It is this view of genes as 'prior to' and 'separate from' organisms that is often taken for granted and which makes it possible to relate genes to organisms in a 'bottom-up' way, with genes as primary in explaining the structures of organisms, which are 'epiphenomenal'. In this way, genes are the primary causal determiners of organisms, which emerge in an unfolding process. One version of this emphasizes *both* notions of 'prior to' and 'separate from'. It takes for granted that inherited genes are preformed parts of organisms and are, thus, prior to organisms whose form they produce. Genes are also separate from organisms in the sense that genes are interpreted as unique. Specifically, they contain unique information specifying organic form. This information is revealed when genes are activated during development. Another version merely emphasizes the *separation of* genes from organisms, focusing on how environments reveal the unique effects of genes over the course of development.

Robert attributes such attitudes about the status of genes to what he terms the Modern Consensus, according to which early competing theories of preformation and epigenesis are standardly combined in the modern literature. On this approach, whatever is inherited is preformed, and whatever is preformed

[2] Robert (2004), p. 129.

is revealed through those factors that regulate its expression. Such an approach involves three central commitments: genetic informationism, genetic animism, and genetic primacy. Informationism holds that, while information abounds throughout the organism, it is "specifically genetic information [that] is useful in explaining development."[3] This is because genes "specify the adult structure of the organism."[4] Contra all other information, genetic information is *intended for* a particular phenotypic outcome. And so, it follows that understanding how the effects of intentional genetic information are revealed is the goal of development. Genetic animism holds that genes specify "a programme containing the plans for building an organism."[5] Because genes specify plans, they are active, executive directors of outcomes. And genetic primacy holds that

> the gene is the unit of heredity, the ontogenetic prime mover, and the primary supplier and organizer of material resources for development, such that the phenotype is the secondary unfolding of what is largely determined by the genes.[6]

And so, the first version of preformed, separate genes commits itself to all three of informationism, animism, and primacy, which has some relevance today, particularly in the field of molecular and developmental genetics. Genes, on this view, contain unique information which specifies programs that causally generate particular structures. The second version commits itself mainly to genetic informationism and primacy, in which less emphasis is placed on the internal

[3] Robert (2004), p. 43.
[4] Ibid, p. 44.
[5] Ibid, p. 49.
[6] Ibid, p. 39.

programmatic and regulative function of genes and greater emphasis on their unique informational content, which contain effects that are revealed in the context of necessary environments.

Both accounts fail to interpret genes in terms of whole organisms. Rather, they begin with genes in an organismal context and emphasize the primary role of genes in development. Many who oppose the stronger claim accept the weaker one by asserting that while genotypes do not map directly onto phenotypes, genes still contain specific effects that are revealed within specific organismal environments. The alternative is often favoured because it explains why genetic variation is not always revealed in phenotypic variation and why phenotypic variation is sometimes revealed without variation in genes. Environmental factors take on a necessary role in determining the effects of genes on phenotypes. And yet, the dichotomy between genes and environment gives genes primacy, while the environment merely reveals the effects of genetic information through the genetic capacity to drive development by organizing material resources.

Contra the gene centric view described above, I do not think that genes and organisms should be ontologically separated, as they often are, as if genes have any more ontological status outside the context of an organism than do, say, organelles, cells, or organs. To think that they do opens up the possibility of conceiving of gene-environment interactions as the only theoretically meaningful interactions in development. Robert alludes to this error in what he calls the 'interactionist consensus', in which the dichotomy of genes vs. environment is thought to give an adequate framework in which to explain the events of

development:

> Everyone agrees that…genes and environments 'interact' in the generation (and explanation) of organismal traits[7] [and that] neither genes nor environments, neither nature nor nurture, suffices for the production of phenotypes.[8]

Given that an interpretation of development is sometimes grounded in separate, preformed genes, the interactionist consensus offers to explain how environmental factors support these genes by activating their internal, directive potential:

> A standard interpretation is that the inherited genome initiates and directs development, and that we can understand the development of organisms best by beginning with the genome and investigating the minutiae of gene activation.[9]

But why represent genes and environments as involved in such opposing roles, in which the former controls, specifies, and constructs, while the latter supports and activates? Surely, analyzing embryological formation in this way leads one to conclude that understanding how genetic information is revealed is all there really is to know about development. I do not think this is so. To repeat, I do not think that genes should be conceived as separate from or prior to the developing organisms of which they are part. Rather, it is the organism that is the starting point of any meaningful endeavour in biology. And if organisms are the starting point, it follows that the molecular interactions occurring during its development should be interpreted in light of the functional unity of its parts. Specifically, rather than using genes to explain developmental outcomes through

[7] Robert (2004), p. xiii.
[8] Ibid, p. 2.
[9] Ibid, p. xiii.

their interactions with organismal environments, the activities of parts such as DNA, proteins, cells, or tissues should be seen to be grounded in the functionally integrated organism in creating the final form. In this way, when it comes to DNA, genetic potential is created because it is grounded in the functional unity of the whole.

Interpreting molecular interactions in light of whole organisms prevents one from placing in genes or isolated mechanisms the ultimate capacity to causally explain the repeating form of the organism. Beginning with genes leads to stories about genetic programs or intentional genetic information, which are presumed to contain the potential for ontogenetic form. Take, for example, the process of skin tissue formation or the development of the vertebrate limb. On the organismic approach, the mechanisms of development should be interpreted by carefully observing how these mechanisms are related to the functions of the whole developing organism rather than accepting uncritically the idea that these mechanisms reveal a form that is specified and directed by genes. It is simply misguided to think that the outcomes of development are ultimately explained by an organic form that is inherited in the chemical structure of DNA. Thus, it is misguided to give genes primacy in developmental control and organization.

To reiterate, organisms are not epiphenomena of genes that direct development and whose effects are revealed in development. Development does have effects which are the product of a complex process. But as Robert remarks,

> hereditary potential is…a function of the developmental manifold, not merely the genome.[10]

This is not to deny the biologically important concept of heredity but, rather, to resist an interpretation of development and heredity that takes genes as prior to and separate from the organisms of which they are a part. In conceiving of development, I favour the primacy of whole organisms, which I think improves how one explains the outcomes by offering an account based on a functionally unified process rather than on a way of mechanically and conceptually relating genes in evolution to phenotypes in development.

If heredity potential is created through a process each generation, instead of preformed, and if this process is best explained by causally interrelated functions rather than by genes + environments, why are so many investigators motivated to find gene-centred explanations for developmental events? Partly, I think this relates to the benefits of heuristics, or simplifying assumptions, which are important in science when it comes to processes or entities that are otherwise difficult to explain. No one doubts that simplifying assumptions are important in biology, as in any science, but we must take care to consider the adequacy of our assumptions.

Any introduction to contemporary biology confronts students with the idea that organisms can be immediately analyzed into their parts. To understanding the development of organisms, then, one must begin with an immediate analysis of genes or with the relationship between genotypes and phenotypes or genes and

[10] Robert (2004), p. 129.

environments, all of which are abstractions from the whole organism to begin with. The goal is to simplify the process itself, which is otherwise too complex to explain. Findings are then published on the functions of genes, on the role of environmental factors x, y, or z in regulating genes to produce phenotypes, or on the way genes conserved in evolution specify programs that generate fly antennae. Because the concepts are familiar and the molecular tools sophisticated, these findings are then given primacy in explaining a much larger developmental process.

In environmentally controlled experiments on organisms like Drosophila or C. *elegans*, for example, one concludes that specific genes responsible for 'switching on', or regulating, other genes in a proximate mechanism are also primary causal directors and organizers of the development of specific parts or behaviours. In a paper describing the model system of C. *elegans*, Thomas Burglin argues for a molecular explanation of nematode behaviours, including 'pumping food with its pharynx', 'expelling digested food through the anus', retracting itself when it makes contact with an object, and responding to stimuli such as chemicals and temperature changes:

> Researchers are now using genetic and molecular tools to unravel the function of the nervous system to understand how the worm's behaviour is controlled by genes.[11]

Burglin admits that the worm 'has a large set of behaviours that allow it to survive

[11] Burglin in *Genes in Development* (2006), p. 18.

and propagate', but his explanation of the cause of such behaviours is that they are 'controlled by genes'. And so, beginning with genes as primary, preformed, and separate entities, one takes the problem of behavioural development in C. *elegans* as a problem to be explained by the controlling function of specific genes. In this case, gene function explains the developmental outcomes of phenotypes.

In other cases, it is not genes *alone* that are immediately analyzed. It is genes plus other factors, which regulate gene expression. Much of the effort of developmental biology and genetics is put towards understanding which factors and mechanisms are involved in activating genes. This effort in itself is not misplaced, provided one recognize that the real problem of development is neither a problem of specifying the function of the genome nor a problem of determining how the genome is regulated spatio-temporally throughout the course of development. To think it is is to make the presuppositions about genes I mentioned earlier.

The error in the simplifying assumption, thus, lies in the interpretation of genes in the developing organism. That genes may sometimes be linked with specific traits I take as given. That genes have a primary role in directing, driving, and organizing the processes of development I do not. The argument capturing the inaccurate assumption could be formalized here: **Given E, then G → FF,** with E as the environment, G as its genes and FF the final form. Given some set of necessary environmental factors, then if genes are activated, the form of the individual will be revealed. Therefore, given a passive mechanical environmental context, genes explain the final form. From the assumption that

the organism consists of a passive set of mechanisms, one concludes that genes have a primary formative function in the organism and that environments have no function whatever – only passive support. Given this, all that is really sufficient for development are genes, whose effects are revealed by necessary environments.

The heuristic is, therefore, inadequate to explain development because it both applies a mechanical passivity to whole organisms and a primary formative role to genes, which are one of its constituents. And yet, it is the functions of the whole organism rather than its genes that grounds the mechanical interactions of its parts. Given such presuppositions about the formative functions of genes, then rearing organisms in identical environments and altering genes leads one to draw conclusions about both the primacy of genes and the passivity of environments. But presumably, if one controls the environmental conditions in which an organism is reared, varying only its genes, there is no reason to claim that the whole organism is merely passive or supportive with respect to its genes. In fact, there is no reason to draw any conclusions about its role. If one controls the environment, then presumably it is unknown what role it plays in the process. One can draw conclusions only about the role of those genes that are varied in the experiment. Nevertheless, the fallacious conclusion is reached that the organismal environment is passively involved in regulating genes, with genes taking on the lion's share of the explanation. The fallacy relies on the premise that gene primacy, informationism, and animism are necessary to interpret correctly the status of genes.

Despite the formal problems with gene centrism, the gene-based approach is still preferred as a standard account for many biologists. Evidence for this comes from within the contemporary fields of molecular and developmental genetics, which sometimes see development as a gene-level problem. The motivation seems at least partly due to a heightened knowledge of genomic content and to an interest in explaining how genes are regulated. After all, with molecular techniques for sequencing genomes, cloning genes, and mapping genotypes, it is simpler to infer that organic form is explained by genes rather than take on the laborious task of studying those diverse functions involved in its development. It is in this way that one recasts the problem of development.

And so, these fields leave out much by way of explanation because they begin with genes and mechanisms rather than whole organisms. In this way, it must be stressed that the problem goes beyond that of invalidity. It bears on the kinds of questions biologists ask about development. Why does development only occur in the presence of particular organismal conditions? What explains variation in form despite there being no variation in genes? Why does form sometimes remain the same despite genetic differences? And why are there constraints on the kind of form that is generated? Proximate, gene-based mechanisms could be offered up to describe such phenomena, but this does little good over the long term to explain these things because these mechanisms are not grounded in the functions of the whole organism. If the organism is the unit of development and the product of evolutionary change, then it would seem prudent to take a broader view of development than is normally considered. Many gene

centrists also see the problem and elevate the status of the environmental context to explain normal patterns and variations. But they do not go far enough.

At the very least, too much effort is likely spent on questions surrounding genetic content and the regulation of gene expression and not enough is spent on specifying the interrelated roles of multiple factors. In what way, for example, do the functions of tissues, cells, or organs bear on future events in development? Or which factors are most important in developmental plasticity? Or how do the roles of multiple systems involved in gametogenesis bear on the mechanical generation of gametes?

For the sake of this thesis, I am interested neither in a theory of how gene expression is regulated nor in understanding how specific genes are linked to, or correlated with, specific traits. I am interested, instead, in the broader theory of development itself. My contention is that a theory of development grounded in gene centrism, in which the function of genes or the regulation of gene expression is the primary explanandum, does not take development seriously and, therefore, needs to be replaced. I argue against a molecular, gene-centred approach as the basis for an interpretation of development and defend the unity of organisms as central in grounding the right questions and methodology. By taking seriously the whole organism, one establishes the conditions by which to take seriously the whole set of factors involved in development rather than being preconditioned to prefer only one of them. Throughout my argument, I seek to preserve the unity of the organism as separate from its environment. Therefore, I focus on the functional interrelatedness of factors within the organism as involved in creating

heredity potential during development. Such factors include biological systems, organs, tissues, cells, organelles, biochemicals, and genes, all of which interact with each other at various spatio-temporal locations and, therefore, have some role in causing organic development. One cannot take seriously the study of development unless one first takes seriously the nature of these interactions.

This thesis will unfold as follows. In chapters one and two, I argue that there are at least two versions of gene centrism and that neither provides a basis to explain the problem of embryological development because neither takes the ontological unity of the organism as a necessary starting point. Chapter three argues that once one makes the move away from genes to consider whole organisms, one can examine the problem of development in a new way. Throughout the chapter, I argue first for the importance of the concept of 'function' in biology and then use this concept to ground a biological explanation in development. I show examples of how this concept of 'function' has been employed. Finally, I use an organismic approach to briefly examine a contemporary problem that has arisen in the field of developmental biology.

CHAPTER 1

DEVELOPMENT AS GENETIC CONTROL

Past challenges in the interpretation of development have given way to recent warnings that one ought to take development more seriously.[12] And so, the view I defend in this section is in no way new. What is intriguing is that despite these warnings, there remains a tendency to return to a gene-centred, 'bottom-up', account of developmental formation. As I will show, this attitude persists among both popular writers as well as academic biologists and philosophers, who see in development a primarily genetic basis because they take genes to be the primary directors, drivers, and material organizers of developmental outcomes. Often, the tendency to give primacy to genes is observed in those who recognize the practical and theoretical ease of doing so. Many who analyze gene function, for example, think that because there is shared genetic content among a large number of organisms across phyla, that the main function required to produce form is genetic. In other words, the development of form can be causally attributed to some commonly inherited gene or gene family.[13]

It is important to note at the outset that the study of genetics does not in itself seek to frame a theory of development. Students of genetics are often not concerned with theories of development. What concerns me is that interpreters of development often draw on current trends in genetic research. Such trends show

[12] See Oyama (2000), p. 3; Griffiths in *Genes in Development* (2006), pp. 177-82; and Robert (2004), p. xv.
[13] Carroll (2005), pp. 61-5.

little evidence that gene sequence, engineering, and cloning will diminish anytime soon. And so, I think it is important to respond to efforts to form theories of development within a research program that is largely centred around genes. Although no one can deny the immediate benefits of a research program centred around genes, there is a price to be paid when gene-centred research is carried out without at least an equal emphasis on organisms to match. This is particularly true when the problem arises of how to explain development. Current theories of development both affirm and are affirmed by experimental work in the field. Therefore, given the current gene-centred trends in the field, one concludes that most explanations will be centred around genes.

In this chapter, I intend to do two things. The first is to show that there are challenges facing one of the two versions of gene centrism I introduced above. This first version I dub 'extreme gene centrism', or 'the extreme version'. My second goal is to argue that 'extreme gene centrism' has implications for future work in development and evolution. After all, if the basis for embryological development is primarily genetic, then the basis for how variation is introduced in development is a primarily genetic problem. A molecular account presumes that genes are the primary basis for development and that genes, therefore, serve as the basis for phenotypic changes arising during development. In other words, as genes have primacy in controlling developmental outcomes, so too do genes have primacy in explaining variation. This, of course, bears on the way one explains evolution.

Extreme gene centrism places the basis for life in genes, with everything

else being either causally explained by genes or passively supporting gene function. Indeed, the whole organism might be taken as the product of genes, which construct its parts from the ground up. The problem with basing life in genes was observed as early as 1946 by E. S. Russell, who responded to the preference to interpret development purely mechanically rather than in light of the natural functions of organisms, which are development, reproduction, and the maintenance of life. For Russell, these internal functions are reached by behavioural, morphogenetic, and physiological actions:

> All three kinds of action show common characteristics, such as persistence of effort towards achieving the normal goal, cessation when this goal is reached, and that these modes of action may be functionally complementary or even substitutionary.[14]

Because Russell began with the organism and its natural functions, he saw no reason to explain it purely in terms of molecular, gene-level interactions. Rather, his explanation was based on the 'behavioural, morphogenetic, and physiological actions' of the organism in carrying out the natural functions of 'development, reproduction, and maintenance of life.' This entails that development, for Russell, was not a molecular problem so much as it was an organismal problem.

Rather than interpreting development in light of the organism and its natural functions, today's biologists often see the problem in terms of inherited genes, whose content is preformed, or given. In Russell's day, the division was

[14] Russell (1946), p. 178.

sometimes conceived as occurring between a mind-based teleology, explaining complex organic functions by the immaterial mind of the organism, and a gene-centred materialism, which relocated the driving force from the top to the bottom.[15] Today, the terms used are often more subtle, but the idea is not substantially different. In favouring a gene-centred approach, modern biology holds that inherited genes contain the potential for every organic trait. This is not substantially different from the idea of genes as driving forces. As I will show, many of today's biologists hold precisely this view. Ultimately, I think that biology can do without either top-down or bottom-up explanations. I prefer to begin with the organism and its natural, internal functions and build up a causal explanation from here. For now, let us proceed with the smaller goals at hand.

Let us consider Robert's account of extreme gene centrism, in which "the gene is the basis for both development and evolution"[16] and in which "genes are foundational and the only foci of developmental interest."[17] Given this primacy of genes in development, it follows that

> epigenetics…is no more than the differential regulation and expression of…genes; therefore…development is subsumed under genetics. Genes and phenotypic traits are tightly linked.[18]

This first version reflects the theses of genetic animism, informationism, and primacy in the following way. The development of organisms is controlled, driven, and organized mostly by genes, which are 'tightly linked' with

[15] see Ruyer (1952), pp. 190, 210.
[16] Robert (2004), p. 11.
[17] Ibid. p. 111.
[18] Ibid. p. 111.

phenotypes. Some environmental conditions are necessary in the process, but these act for the sake of genes by initially regulating their expression. This involves switching 'on' or 'off' specific genetic programs. Because genes are primary in their capacity to direct developmental processes, once genetic programs are activated, they unfold in a predictable sequence. Lastly, 'genes are properly about phenotypes'[19] in the sense that genetic information is intended *for* specific phenotypes. Therefore, development is the process by which the effects of intentional information are revealed through the controlling, organizing activity of genes.

Notice that on this view, in order to explain development, one must discriminate between the uniquely inherited genome driving development and the organismal environment of which genes are a part. Once these are separated, one can argue that only genes and those parts interacting directly *with* genes are important in generating the adult form. Separating genes from environments entails that genes have unique meaning and that this meaning 'is relatively independent of other conditions'.[20]

An examination of the literature reveals that this extreme version holds at least some sway in the interpretation of development and evolution today. This is the case particularly in molecular and developmental genetics, where analysis of gene function has sometimes led biologists to make strong assertions about the capacity of genes to direct the construction of parts such as eyes and limbs, or the

[19] Robert (2004), p. 46.
[20] Ibid. p. 46.

development of behaviours including ingestion, digestion, and neurochemical interaction.

I introduced the topic of gene centrism with Burglin's work on C. *elegans.*[21] Recall his view that the set of behaviours contributing to nematode survival and reproduction are 'controlled by genes'. Burglin can say this because he begins by taking inherited genes as prior to and separate from their organismal environments. From here, it follows that genes control phenotypic outcomes. Beyond the logic of genetic control, biologists make use of many available techniques, which amplify, map, sequence, and distribute DNA and genomic information. Taken together, these factors appear to confirm that the role of genes is primary.

The idea that genes actually *control* the development of a neuron, a gut, or the worm's behaviour of pumping food with its pharynx requires that inherited genetic content be ontologically separated from everything else. The structure of genes is prior to organisms, and genes function independently of organisms in producing phenotypes, whose structures and functions are epiphenomenal. Beginning with this picture of gene independence, one can speak about a 'final gene product'[22] and define a gene according to the function of its encoded proteins. One might speak, for example, about structural genes, hormonal signaling genes, or antibody producing genes. One can also define the functions of cells according to the actions of controlling genes:

[21] See my comments in the introduction.
[22] Burglin in *Genes in Development* (2006), p. 21.

> The genes activated by [some factor] could be neuronal, growth factors, neurotransmitters, or other genes which turn the cell into a neuron….Thus, complicated cascades of [factors] turn different genes on and off during the development of an organism to generate the vast diversity of cell types found in the adult animal.[23]

And so, preformed inherited genes define the functions of other organic elements by being 'turned on and off during development'.

Sean Carroll gives a good example of this structural and functional primacy in his book *Endless Forms Most Beautiful*, in which he emphasizes the importance of genetic programs in constructing organisms:

> What are some of the major rules for generating animal form [and] where do we look for these rules and instruction? In DNA. In the entire complement of DNA of a species (the genome), there exists the information for building that animal.[24]

Carroll is an extremist in his commitment to the model of genetic programs housed as instructions inside genes. Within the 'entire complement of DNA' is contained the 'rules for generating animal form' and the 'information for building that animal'. This describes the genetic basis for the control of development, the information for unique structural traits, and the organization and arrangement of material. Such gene primacy is also witnessed in his references to protein coding and regulatory genes as 'toolkit genes':

> In general, all members of the toolkit shape development by affecting how other genes are turned on or off in the course of development.[25]

[23] Burglin in *Genes in Development* (2006), p. 23.
[24] Carroll (2005), p. 35.
[25] Ibid, p. 74.

One might be able to extract some truth from this latter claim. If the 'turning on and off of genes in the course of development' is taken to describe the proximate interactions between specific genes and numerous others at various stages in the course of development, there appears to be no problem. But this claim should be taken as a mere description of the proximate influence genes have on other chemicals with which they directly interact. Such an account would not place the explanatory burden of developmental control on a pre-existing genetic potential that functions independently of other organic elements in controlling and organizing developmental outcomes.

Part of what interests Carroll is the molecular analysis of what are sometimes called homeobox, or Hox, genes. These are genes which, when mutated, lead to the replacement of one body part by another. An example is the replacement of an antenna with a leg.[26] Much has been made by gene centrists of the study of Hox genes in *Drosophila* as well as other model organisms. Perhaps, this is because these genes are highly conserved and their activation is correlated with well timed events of limb development.[27] This leads some to accept the extreme view on the grounds that often the same highly conserved genes are involved in laying down similar types of body segments, such as eyes, legs, or wings across phyla. Because these genes are shared among many kinds of organisms, the body parts they lay down are described as 'serially homologous'. In this way, it is thought that genes causally explain the formation of body

[26] Burian (2005), pp. 213-4.
[27] Ibid, pp. 214-5.

segments. This provides enough motivation for some, like Carroll, to determine which genes contain instructions for which body parts:

> The instructions for making five fingers, or two eyespots, or six legs, or black and white stripes, are somehow encoded in the genomes of the species that bear these traits.[28]

In the case of the development of body segments, he argues that a small number of 'toolkit genes', called 'master' genes, are responsible for controlling the formation of each segment:

> In Drosophila, only a small number of 'homeotic' genes give homeotic forms when they are mutated, indicating that a small number of 'master' genes govern the differentiation of serially homologous body parts in the fly.[29]

Thus, in the search for genes containing instructions for the generation of body parts, Carroll suggests he has found it in toolkit genes that take on the master function of controlling the cascade of events leading to the construction of 'serially homologous body parts.' And so executive function is applied to particular genes once it has been determined that these genes are causally involved in generating this cascade of events. The reasoning seems to be that if the phenotypic outcome is associated with the expression of a 'master' gene, then given the presuppositions of the extreme view, the 'master' gene involved is the efficient cause, or director, of that body part. And so, Carroll can argue that only a 'small number of "master" genes govern the differentiation of serially homologous body parts'. On these same grounds, the observation that these genes

[28] Carroll (2005), p. 35.
[29] Ibid, p. 51.

are shared by other organisms for the same function lends support to his conclusion.

In their 2011 entry on genes in development, Larsen and Atallah remark that genes are often interpreted as instructive executors of development if their action is correlated with the production of particular cellular phenotypes:

> It is often said that a gene is instructive for a particular cell fate or fates if it can be shown that expression of a gene in a particular group of cells is correlated with a particular cell fate and, conversely, if absence of that gene product is associated with loss of a cell fate.[30]

But if correlation between the expression of a gene and the appearance of a neuron or a muscle cell is all it takes to call a gene 'instructive', then it seems that these genes are not 'instructive' in any meaningful way. In other words, they are not sufficient to provide a full account of the cause of muscle cells or even of the tissue, limbs and musculoskeletal system of which they are part. To do this, we need more than a mere *correlation* between genes and phenotypes.

Alan Love (2020) observes this problem of using the 'instructive gene' or the 'genetic program' to explain developmental events:

> The strongest claims about genetic programs or the genetic control of development have empirical and conceptual drawbacks that include an inattention to plasticity and the role of the environment, an ambiguity about the locus of causal agency, and a reliance on metaphors drawn from computer science.[31]

Not only is correlating genes with developmental outcomes insufficient in

[30] Larsen and Atallah in *Epigenetics: Linking Genotype and Phenotype* (2011), p. 106.
[31] Love in *The Stanford Encyclopedia of Philosophy* (Spring 2020 Edition).

regarding these genes as controlling agents of development. So too is the 'ambiguity' and 'reliance on metaphors' these genes sometimes generate. In encountering the term 'program', one is led to believe that the locus of control lies within the gene or that, perhaps, like computer programs, genetic programs are placed in genes by some immaterial, vital source. But, surely, there are other sources that explain the internal form of organisms. One of these is observed in the following entry on heart development from Hove et al. (2003):

> The pattern of blood flow in the developing heart has long been proposed to play a significant role in cardiac morphogenesis. In response to flow-induced forces, cultured cardiac endothelial cells rearrange their cytoskeletal structure and change their gene expression profiles.[32]

Therefore, at the very least, one must admit that there are also physical forces at work in explaining how form is generated. Form, then, need not be interpreted as given in genes, whose functions map onto the functions of organismal parts.

Contra the account of causal determination by 'instructive genes', Richard Burian (2005) notes that much of the control of the outcome of body part development is determined *within* the cascade of regulatory events rather than by so-called 'master' genes at the front end of the cascade.[33] For this reason, he says that

[32] Hove et al. In *Nature* (2003, 421), 6919, pp. 172-7.
[33] Burian (2005), p. 215.

> genes that set off a cascade that alters the identity of a body part or a fundamental pattern or morphology are thus rather naturally characterized as switch or selector genes.[34]

In this way, Burian observes that a better interpretation of genes is, perhaps, as elements that are parts of proximate mechanisms in the standard genetic sense rather than as 'instructive' or 'toolkit' genes in the extreme sense sometimes implied by biologists. In any case, one struggles to understand how genes can be controlling or instructive in the meaningful sense of being causally primary in producing developmental outcomes.

It seems, therefore, that even concerning the relatively straightforward problem of body segment development, achieving an accurate account is more difficult than some biologists make it out to be. For this reason alone, it is clear that invoking an instructive program based on a preformed genetic potential that guides development is unhelpful because it generates an inaccurate heuristic. The lessons to be learned here are important. Presuppositions made about gene status have implications for the way the landscape of the organism is broken down. The first is that, if genes are primary, then all interactions relevant for explaining development occur at the level of the gene, where genes act and are activated to produce proteins, cells, and so on. The study of development is a study of gene regulation. Second, what is unique to the extreme version is that the genetic program grounds the functional duality of organisms. This entails that one must offer a molecular explanation for the functions of things like the liver, the

[34] Ibid. p. 225.

vertebrate limb, or the tissues of the gut. If genes that are conserved across organisms correspond to the appearance of similar body patterns, then these patterns and structures are grounded in the functions of genes to produce them.

In his book, *Master Control Genes in Development and Evolution,* Walter Gehring cites the example of brachydactylism, or 'short-fingeredness', in which the middle finger of humans is shorter than normal. Since fingers and toes are homologous structures and are thus 'specified by variations in the same genetic program', people with short middle fingers also have short middle toes. He then goes on to say that

> The genome, the sum of our genetic material, provides the framework within which we develop and sets the limits for influences from the environment.[35]

This account of the primacy of genes is recognizable in the phrases 'provides the framework' and 'sets the limits for influences', so that development is about what happens between genes and those factors that regulate them. The genome controls the influence the environment has by controlling which gene effects are observed in the phenotype. Like the account of genetic control of wings, eyes, and antennae, Gehring says about the inherited gene in short-fingeredness that

> A defect in this one gene reduces the second bone in the second finger, which means the normal gene controls the size and shape of just this one bone.[36]

If one begins with gene primacy in development, then knocking out gene N

[35] Gehring (1998), p. 2.
[36] Ibid, p. 1.

to produce a reduction in finger length leads one to infer that the normal function of N is to control the size and shape of the 'second bone in the second finger'. Despite this optimism, it is not clear that genes have this controlling function in a way that is biologically important in causing the outcome. The discovery that a defective trait is linked to a mutated gene does not entail that the gene is normally important in causing the trait. It seems Gehring's interpretation is a necessary outcome of a gene-centred view of development, in which genes are tightly linked with phenotypes and environments turn 'on' and 'off' genetic programs.

Each of the examples I have examined so far interprets development as subsumed under genetics. Because of the tight link between genes and phenotypes, the structures and functions of development are the direct outcome of genes whose functions are conserved in evolution and inherited each generation. Presupposing that genes are primary, one maintains that there must be a direct line between genotypes and phenotypes. And so, the study of development is about mapping genotypes directly onto the phenotypes they specify. This link between genes and traits is so strong as to lead one to think of genes are directly causing the traits they specify.

The ease with which many presuppose these things is remarkable. In *Forms of Becoming,* Alessandro Minelli claims that

> Generally, we cannot predict how [a new individual] will develop or its probabilities for success in the daily struggle for survival with the same precision with which we can formulate a similar prediction concerning genetically identical individuals. And this helps reinforce the widespread conviction of genes' quasi omnipotence. Each animal, each plant, each organism is what it is because it has precise

> inherited genetic information that determines its functional and structural characteristics, the way in which it develops, and also its behaviour, the manner in which it responds to environmental stimuli.[37]

By placing in genes the potential for the final organic form, the burden of explaining *the process* development is completely removed. However, if one sets out to explain development *as a process* occurring between a single-celled zygote organism and a fully-formed adult, then it is misguided to think that the inherited genome contains the answer.

Genetic programs and master genes seem to project the mystery of development to the gene rather than to the mind (as in Russell's day), because the way the genetic program gets decoded in development is largely ignored. It seems that applying a function to a gene makes irrelevant the causes involved in the process, and so the question of how the program is decoded is irrelevant. So is the question of what causal role the genome has in the process at all. That one can make clear 'predictions concerning genetically identical individuals' does not convince me that genes are 'quasi omnipotent' or that 'genetic information' determines the 'functional and structural characteristics' or 'behaviours' that develop in plants and animals. What actually occurs in generating complex organisms seems much more complex than many biologists are prepared to admit or consider.

Recall the feature of the extreme version which insists that environmental

[37] Minelli (2009), p. 59.

factors are necessary supports in a process which is otherwise genetically controlled. If one insists that environmental support is necessary for development, then one is led to believe that all bases have been covered because every possible factor responsible for development (genetic or environmental) has been considered. In this way, difficulties with gene-centrism sometimes go unnoticed:

> Even though we may be able to conceptualize a direct mapping of genotype to phenotype, in reality a phenotype cannot be produced outside the context of the environment. DNA may contain the information necessary to initiate construction of an organism, but every bit of that information is environment-dependent.[38]

But does the biochemistry of genes really allow them to 'initiate' the course upon which all subsequent construction is set? No doubt genes initiate some cascades of events but only by their direct interaction with other genes and proteins. What seems implied here is that to 'initiate construction' is for a gene to also *control* development, since what genes initiate is a constructive process whose phenotypic result genes can be 'mapped onto.' Therefore, one is led to believe that there is no problem in thinking that genes initiate development or map directly onto the phenotype because of the reminder that 'every bit of genetic information is environment-dependent'. The error here is not in thinking that environments interact with genes, when in fact they do not. It is to presuppose that genes have the capacity to initiate and control a process. Because these claims are hidden among claims about the necessary environment, they often go

[38] Schlichting in *Keywords and Concepts* (2003), p. 109.

unnoticed. Gehring also insists that the environment is necessary:

> Once fertilization has occurred, we are genetically programmed, and even though there are strong environmental influences, they are limited by the genetic framework.[39]

Oddly enough, with regard to the differential regulation of gene expression among E. coli, he then goes on to claim that

> this theory of differential gene activity controlling development proved to be essentially correct.[40]

By beginning with the primacy of genes to control development, one admits that environments are necessary and then proceeds to map the genes that initiate to the phenotypes that are outcomes. Given this common view that what is inherited are 'genetic programs' along with the admission that there are 'environmental influences', then it follows that 'gene activity controls development'. All along, however, I have wondered whether genes themselves really have the capacity to control and direct as some think they do. I have already suggested in various ways that they do not. But if not, then why insist that genes control within a set of necessary environmental conditions? Why insist on the dichotomy between genes vs. environments? For the problem of development, it seems the dichotomy is misleading, as it removes the emphasis on development as the process by which form is created and places it, instead, on the problem of how independent, preformed genetic material functions to direct developmental ends. In this way, the problem of development is ignored.

[39] Gehring (1998), p. 7.
[40] Ibid, p. 18.

Thus far, I have presented a series of examples to support the claim that extreme gene centrism holds at least some sway among contemporary biologists and that its presuppositions often lead to inaccurate interpretations of development. I will now proceed to consider in greater depth the logical fallacy with which I began and consider some of the implications of this gene-centred approach for the study of development and evolution. Recall that proponents of this fallacy assert that 'Given E, then if G → FF.' As the following examples illustrate, interpreting genes as primary determines which conclusions one is willing to draw from observing genes and environments at work in development. Larsen and Atallah notice that for many biologists, the doctrine of gene centrism rests

> on solid evidence of genes, whose molecular biology and regulation materialistically underpin morphological development. Not only does the morphology of an embryo unfold in a predictable sequence but so too, it is envisioned, does an underlying genetic program. Although it is now recognized that genes are highly conserved among metazoan, and hence cannot be solely responsible for variation, the regulatory networks controlling gene expression are thought to be the 'essence of animal development'.[41]

The way one views genes, surely, has serious implications for the study of development. Here are some presuppositions: genes 'materialistically underpin morphological development', genetic programs 'unfold in a predictable sequence', and the regulation of gene expression is 'the essence of animal development.' Adherents rightly admit that environmental factors must have

[41] Larsen and Atallah in *Epigenetics: Linking Genotype and Phenotype* (2011), p. 104.

some role to play, since highly conserved genes 'cannot be solely responsible for variation.' Nevertheless, they are not prepared to go into any depth to describe the exact role of anything in the environment. Neither are they prepared to experimentally describe the exact role of regulated genes.

Despite the acknowledgement that an indeterminate set of environmental factors are responsible for interpreting development, one is told to base one's interpretation primarily on genes. The claims made about the roles of genes and environments are thus based on presuppositions made about the status of genes rather than upon careful observations of these things. It seems a better heuristic is one that leads strictly to conclusions about the role of genes across diverse metazoan phenotypes or, perhaps, about the roles of separate environmental factors. The gene centrist can do neither, because on *his* heuristic, specific presuppositions are made about the status of genes and environments. And from here, one can only draw vague or even false conclusions.

Take another example. In a discussion on the modulation of phenotypic patterns by genetic variation, one sees how the author leaves himself open to the same kind of fallacy:

> Mutations of both insufficiency and excess of function…control the activity of other genes which implement their systemic signals in developmental terms. Their activity is in turn controlled by other regulatory genes which define their spatial specificity of action. We do not know how general is this complex hierarchical dependence between genes, nor whether we can extrapolate these conditions to other genes involved in morphogenesis. It is important, nevertheless,

> to recognize that patterns can be modulated by the activity of a few, functionally related genes.[42]

From here, one sees that activated genes 'implement their systemic signals'. Other genes 'define the spatial specificity of action' of still other genes. Surely, the ability to specify which effects are revealed cannot be attributed to any one part of the organism. And yet, because one initially accepts that patterns can be modulated, directed, or organized by *genes*, then one concludes that it is *genes* define the spatial specificity of action or implement systemic signals and that *environmental* influence is supportive only.

But what capacity do genes, in fact, have in these kinds of activities? Surely, the activity of genes is always constrained by their proximate biochemical conditions. In this sense, there is simply no capacity in genes to 'implement systemic signals' or organize the material arrangement of parts. Rather, their role seems limited to the biochemistry of their immediate surroundings – to the transcription of DNA to RNA, for example, through its interactions with enzymes and transcription factors. There is simply no reason to see in genes themselves the capacity to execute, direct, or organize any of the complex events of development.

One last note on evolution is in order. I have just discussed the implications the extreme version has for development. If development is a matter of the functional capacity of genes to control the outcomes of development, then nothing else has any great role to play in causally producing these outcomes. All

[42] Garcia-Bellido in *Development and Evolution* (1983), pp. 230-1.

research efforts should be set upon comparing genomes and determining gene functions, which makes development a task for molecular biology. The implications for evolution may be slightly different. Recall Larsen and Atallah's claim that because genes are 'highly conserved among metazoan', they 'cannot be solely responsible for variation'. This entails that it is the 'regulatory networks controlling gene expression' that are necessary in the study of how variation is generated. Nevertheless, it is clear than any approach to development and evolution requires that attention be focused either exclusively on genes or else on the way genes are regulated within a network. In the last chapter, I speak more of this gene-based approach of explaining how variation is generated.

On the basis of the foregoing analysis of what I have called the extreme version of gene centrism, it seems one must reject the view that genes have a capacity to causally direct or control developmental outcomes. Genes do have roles in development, but these as well as the roles of numerous environmental factors are frequently left out when considering the problem of development. I will now return to consider a second version of gene centrism, which is probably more influential today than the one just considered.

CHAPTER 2

DEVELOPMENT AS GENETIC REVELATION

I have argued, thus far, that an extreme interpretation of development is misleading because it sees in genes the functional capacity to control the outcomes of development. The account is based on the idea that genes have ontological primacy in the organism. Therefore, one interprets the inherited genome as housing the capacity to specify adult phenotypes and to organize and control, through bottom-up causation, the process by which these phenotypes develop. I showed that presupposing gene primacy justifies methodologically separating genes from their environments, which leads to false conclusions about the supportive role of the environment.

Ultimately, I have argued that of the three theses of genetic animism, information, and primacy, one is justified in rejecting animism, since there is no reason to think that there are genetic programs functioning to causally direct developmental outcomes or that genotypes map directly onto phenotypes. On Gehring's interpretation of the study of development:

> The enormous power of the genetic approach is to identify the genes that regulate development by mutation, to isolate the key genes by recombinant DNA technology, and to study the structure and function of the respective gene products, which eventually leads to an understanding of the molecular basis of development.[43]

I have demonstrated that one may be easily convinced of the 'molecular basis of development' if one uncritically accepts particular views about genes and, thus,

[43] Gehring (1998), p. 61.

about the power of DNA technology to reveal something about developmental causes. A more critical approach prevents this from happening. Making the move to reject the directive capacity of genes frees the investigator to consider the roles of other organismal elements that might be involved in producing adult form.

I now intend to argue that the theses of genetic informationism and primacy must also be rejected if one is to make development about more than the environmental revelation of a phenotype that is still more-or-less encoded in genes. Many investigators have resisted the tendency to accept uncritically specific claims about genes. Therefore, they are not taken in by the idea that the directive function is contained somehow in preformed genes, which are conserved in evolution and uniquely inherited prior to the organisms containing them. For them, the remedy seems to involve taking seriously the details of the environment in revealing the content of genes. Multiple factors including physical and geometric constraints, stochastic processes, morphogenetic fields, and external environments all contribute to the *context* in which the effects of genes are revealed.

Larsen and Atallah reflect this position, when they argue that emphasis in development should be placed on the *context* of genes rather than on genes themselves:

> …any system depending on a code…must be decoded; and thus, the system's 'meaning' is dependent on the context of the decoding

> process….Context is…necessary to convert DNA base pair sequences into 'meaning' in organisms.[44]

In their rejection of the earlier theories of preformation and epigenesis, Hall and Hallgrimsson argue that epigenetics is the new framework in which development should be studied. In doing so, they emphasize that there are multiple factors involved in the control of gene expression:

> Epigenetics is the sum of the genetic and non-genetic factors acting upon cells to control selectively the gene expression that produces [development] and evolution.[45]

And so, development is about the control of 'gene expression' that is shared between 'genetic and non-genetic factors' rather than about a control found solely in genes. Therefore, the expression of genes, which is the basis for development and evolution, is dependent on more than just genes. These authors later emphasize the dominant role played by the environment:

> Epigenetics…[encompasses] increasing hierarchical complexity and the influences of the environment on phenotypic expression through control of gene expression.[46]

Richard Francis (2011) captures the importance of environments in his popular book on development:

> You couldn't cook up a single cell, much less a human being, given the instructions in the genetic recipe. Much of what you need to know lies elsewhere….Our genes are as much a part of our hardware as any other biochemicals, and as much instructed as instructors.[47]

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[44] Larsen and Atallah in *Epigenetics: Linking Genotype and Phenotype* (2011), p. 106.
[45] Hall in *Epigenetics: Linking Genotype and Phenotype* (2011), p. 10.
[46] Ibid, p. 11.
[47] Francis (2011), p. 126.

Francis recognizes that there is no genetic program directing outcomes from the outset. Nonetheless, he implies that, while there is a 'genetic recipe', much of what is needed to instruct genes lies outside of genes themselves. It is the environmental context that is necessary to reveal particular gene effects.

Each author recognizes that programs or 'master' genes are insufficient to explain the normal generation of traits. Instead, multiple contextual factors reveal in development the effects of genes. This version seems more reasonable then the last one, since emphasis is placed on the need to carefully attend to the way *context* generates outcome. Because genes do not control phenotypic outcomes, one must consider more seriously which factors are responsible for revealing genetic information.

One wonders, however, if the 'conversion of DNA base pair sequences into meaning' or the 'control of gene expression that produces development' are the most important observations of development itself. If one maintains that genes are ontologically separate and the phenotype is the end stage of development, then development is the study of the factors that fill the gap between genes and phenotypes. The mechanical interactions occurring between environments and genes explain how information is revealed to produce the phenotype. But surely, these mechanisms are not all that one considers in thinking about the *cause* or *explanation* of development. There are, indeed, mechanical interactions between a multitude of genetic and non-genetic factors, which are involved in the material production of parts. Over the course of development, these parts constitute parts of the structures of cells, tissues, and

organs. But I think that interpreting these interactions as the only important ones is to hold too simple a view of the development process.

Here, we return to the problem of heuristics in science. One might think that a heuristic that analyzes the organism into genes and environments is better than one that does not. However, as I will argue in the next section, an alternative to gene centrism does not require that one abandon heuristics. It only requires that one apply a different heuristic. For now, before moving to specific examples from biology, let us consider precisely what presuppositions are made by adherents to this more moderate version of development.

The problem that has been the basis for discussion so far is how a single-celled organism develops into a fully formed adult. The informationist reformulates the problem by asking how information in genes is mechanically expressed. The basis for the reformulation is summarized in the two commonly-held beliefs about genetic information. The first is that

> the immaterial information, coded in the medium of DNA, *specifies* the adult structure of the organism.[48] [emphasis added]

The second is that

> genetic information undergirds…a strong and irreducibly important distinction between nature and nurture – though nurture is required to trigger nature, nature is primary and necessarily so, given that nature is *inherited* and nurture is not.[49] [emphasis added]

The central motive for separating genes from organismal environments and

[48] Robert (2004), p. 44.
[49] Ibid, p. 44.

holding that genetic information specifies adult structure is that the information coded in genes is unique because genes are inherited.

These beliefs are still held to some degree by those who accept this second version of gene centrism. Adherents avoid a front-loaded account of genetic control, often because they do not see in development a direct mapping on of genotypes to phenotypes. Neither do they see in evolution the selection of genes for specific adaptive ends.[50] They resist the view of the functionally independent genome in development and evolution. Nevertheless, the basic account of informationism described above is still accepted. This means that while development is not *directed* by genes, it is still *about* genes, since it seeks an account of how the environment reveals the meaning of unique genetic information, which species the adult organism.

Consider again the following quotation from Francis:

> You couldn't cook up a single cell, much less a human being, given the instructions in the genetic recipe. Much of what you need to know lies elsewhere….Our genes are as much a part of our hardware as any other biochemicals, and as much instructed as instructors.[51]

The term 'instruction' is misleading. Despite attempts to reduce the importance of the 'genetic recipe', genes still have primacy. This is captured in the comment that genes are 'as much instructed as instructors', given that 'our genes are as much a part of our hardware as any other biochemicals.' Were it really the case that our genes are simple biochemicals like all others, it seems there is no reason

[50] Robert (2004), pp. 46-8.
[51] Francis (2011), p. 126.

to refer at all to genes as 'instructing' or 'being instructed'. The idea that genetic instructions require environmental instructions presumes to give genes a primary role, presumably one in which genes contain a potential to instruct but whose revelation requires environmental input.

What is clear from this is that even on the moderate interpretation, coded genetic information specifies adult form. Even if one studies carefully the specific roles of the multitude of environmental factors involved in gene expression, one still presupposes that genes have a primary status in development because development is still about the study of what happens at the level of genes. What seems to be missing is more careful attention to the exact *role* that genes play in the details of development. Consider again our flawed heuristic: 'Given E, then if G → FF'. If the problem in the extreme version is attributing primacy to genes by failing to consider the exact roles played by genes *and* environments, the problem in the moderate version is attributing primacy to genes by failing to consider the exact roles played by *genes*. My suspicion is that a careful analysis of the roles of environments *and* genes leads one away from gene primacy of any kind because it leads one away from the gene-environment dichotomy.

Many research efforts along the moderate line are convincing because of their practical application in predicting the outcome of environmental influences on gene expression. Elsewhere in his book, Francis speaks of how maternal licking of mice during early development influences the amount of DNA that is

methylated.[52] Methylation can be described as adding a methyl group (a chemical) to specific locations along the DNA sequence.[53] In this process, while the DNA sequence itself is left unchanged, methylated DNA is less able to bind to proteins that assist in producing RNA, making it less able to build proteins needed in the construction of tissues, organs, etc. In this case, the presence of maternal licking is a factor in the organismal environment that leads to the phenotype of 'non-fearfulness' by influencing which genes are expressed. When specific genes are not expressed, or 'mis-expressed', the altered phenotype of fearfulness is more frequently observed in maturing mice:

> Good mothering [maternal licking] promotes the demethylation pathway, while bad mothering leads to methylation. When [the GR (glucocorticoid receptor) gene] is methylated, the transcription factor NGF does not bind well; as a result, fewer GR proteins are produced in the hippocampus and the stress axis becomes hyperactive, predisposing the mouse to fearfulness and anxiety.[54]

Similar conclusions are drawn for the long-term explanation of differences among identical twins.[55]

Notice that emphasis here is placed on environment-induced phenotypic changes rather than on genetic control of such changes. It is not enough to analyze the ways genes are regulated to organize and direct the outcome. The environment is necessary to influence the activation of genes, which do nothing on their own to direct development. In this environment-induced activation, the

[52] Francis (2011), p. 47.
[53] Hall in *Epigenetics: Linking Genotype and Phenotype* (2011), pp. 11-12.
[54] Francis (2011), p. 47.
[55] Ibid, p. 47.

phenotype of 'fearfulness and anxiety' is interpreted in terms of the GR gene whose mis-expression produces the behaviour. In this case, the mis-expression is the result of several environmental factors. 'Maternal licking' promotes 'de-methylation of genes', which causes the protein 'NGF not to bind well' to the GR gene. This, in turn, predisposes the 'mouse to fearfulness and anxiety.' Given the presence of multiple environmental factors (E), specific genes (G) are activated to produce phenotype of fearfulness (P).

In this example, given the prior commitment to the thesis that genes specifying adult form are abstracted from their organismal environments, one can maintain that there is a 'GR gene', or even a 'gene for fearfulness and anxiety in mice'. Such a gene is defined by the effects it brings about rather than by the causal role that gene has in a larger process. And so, what occurs during development is the decoding process whereby context converts DNA sequences into meaning. The context of the GR gene reveals its meaning in development. The argument here is not that the GR gene has no role to play in the phenotype of fearfulness but, rather, that presupposing that the GR gene specifies some trait leads one to draw faulty conclusions about the primacy of that gene in producing the phenotype in an environmental context. Once genes are activated, the potential in genes *for* specific effects is somehow revealed. Therefore, the really important question in development is to explain how environments link genotypes with phenotypes.

One possible solution to the problem is to carefully observe the role that a so-called 'GR gene' *actually has* in the complex process of generating the long-

term trait of fearfulness or the role of other genes in generating long-term differences among identical twins. It is not clear that by identifying a gene as being *for* some effect that we have come very close to analyzing or explaining the cause. Separating genes from environments implies that there is intentional information contained in genes, which makes development about gene-environment interactions. Furthermore, because of its emphasis on gene-environment interactions, this version makes development mostly about discovering the material cause, which is the way the material of the organism is built from the bottom up. Surely, genes are involved in the material cause, but as I mentioned earlier, this gene-environment interaction is much more proximate than many theorists are prepared to admit. Other factors are required in the explanation.

By taking seriously the actual role of specific genes in the generative process, one gains a realistic view of the material cause and need not insist that the only causes of adult form are elucidated by considering interactions at the level of genes. Even if one were able to generate a full account of the role of every gene at work in materially generating form, one would lack an adequate account of development, since one would presuppose throughout that form is already specified by genes. What a thorough understanding of the roles of genes and environments reveals is that development is not caused by genes. Neither is it caused by genes that are activated by environments. In the next section, I argue that presupposing the primacy of organisms, instead of genes, allows one to take seriously this broader interpretation of causes.

Another example that ascribes primacy to genes is that which involves the revealing of genes by morphogenetic fields. Robert notes that historically, morphogenetic fields were defined by collections of cells required for the development of particular structures, such as eyes, limbs, or hearts. These fields were never understood as possessing the potential to cause developmental events. Nowadays, however, they are sometimes defined in terms of the genes they contain.[56] Larsen and Atallah argue that the boundaries of morphogenetic fields are changing constantly during development and that this change is important in explaining future development.[57] Therefore, while these fields might be defined in terms of genes, they argue,

> it is unlikely…that particular molecules will be of universal significance in understanding field phenomena.[58]

In his account of fields, Gilbert notes that

> the general fate of a morphogenetic field is determined; thus, a particular field of cells will give rise to its particular organ (forelimb, eye, heart, etc) even when transplanted to a different part of the embryo.[59]

Gilbert also gives an example of the importance of genes in defining such fields. He describes the development of the early zebrafish embryo, which is composed of cells called blastomeres. Throughout the process, the expression of genes in adjacent cells is triggered by a protein called *Nodal*:

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[56] Robert (2004), p. 112.
[57] Larsen and Atallah in *Epigenetics: Linking Genotype and Phenotype* (2011), pp. 110-1.
[58] Ibid, p. 111.
[59] Gilbert (2006), p. 66.

> *Nodal…*accumulates in the blastomeres that will form the dorsal margin of the zebrafish embryo. These cells will activate the *goosecoid* gene, whose product commits these blastomeres to become the cells that instruct the anterior portion of the head to form. Cells slightly further away from the dorsal margin activate the *floating head* gene, which commits the cells to become notochord.[60]

One can consider the 'dorsal margin' and 'notochord' simply as different phenotypes that are produced through environmental activation of particular genes at specific times and spaces in the embryo.

This passage indicates that, for Gilbert, the morphogenetic field is an environmental factor involved in the activation of genes within the field. Therefore, while there is no suggestion here that the genes involved in zebrafish development also control its development, by defining these fields in terms of genes, the development of the early zebrafish is *about* the way the environment activates genes to produce the phenotypes of the 'dorsal margin' and the 'notochord'. The field is the region of the embryo in which these genes are activated, making the field necessary to reveal the cell and tissue types specified by genes. Perhaps Gilbert would agree with Larsen and Atallah that because field boundaries are constantly changing, 'it is unlikely that particular molecules will be of universal significance in understanding field phenomena'. Nevertheless, by defining fields in terms of genes, he presupposes explanatory primacy in genes. As I have argued, this interpretation is misguided because it does not fully recognize the functionally integrated organismal conditions on which

[60] Gilbert (2006), p. 64.

development is based. If it is true that fields are constantly shifting, then this movement itself must be explained. And there seems no reason *not* to proceed by beginning with other organic elements not yet considered, such as organs, tissues, or biological systems rather than with either genes themselves or genes that are environmentally-regulated.

One might object that my intention to this point has been to dismiss the importance of gene-environment interactions. The error, however, lies in the interpretation of these interactions rather than in their importance. Rather than taking environments as 'acting upon cells to selectively control gene expression', I emphasize that the interactions between genes and environments are much more proximate than many suppose them to be. The protein *Nodal,* for example, is not involved in the selective control of the expression of *goosecoid,* as if the latter specifies the anterior portion of the zebrafish head. Given the complex, dynamic process involved in the generation of the zebrafish head, why place such primacy on *goosecoid* to specify that structure?

I argue, in the next section, that at least part of this reason is based in the hierarchical interpretation of the organism, in which structures emerge at different levels but are always specified by the elements they contain at lower levels. In this case, because genes are contained within cells and cells within tissues, genes specify particular cell types, which, by virtue of their location in the embryo, specify which tissue will be generated. But, surely, it is possible that other factors, such as an organism's metabolism, its hormones, or the relation of the anterior head to relevant systems might also be included in the explanation. Yet,

these are seldom examined because of the primacy of genes and the gene-environment dichotomy. The heuristic that separates *goosecoid* from the *Nodal* protein and the morphogenetic field of this protein makes the gene primary in the organization and specification of the phenotype.

One should not suppose that the examples above are isolated cases. All throughout the literature on developmental genetics and epigenetics, it is taken for granted that development is the study of how genetic content is revealed by environmental activation. In their paper on nervous system development, Chris Kovach, et al. (2011) claim that

> A fundamental question is how cells acquire their specific identities and functional properties during embryogenesis. The intricate molecular controls that guide progression from pluripotent stem cells, which make up the early embryo, to a differentiated cell with a unique identity have begun to be elucidated.[61]

Here one observes the problem of how 'cells acquire their specific identities' to be 'a fundamental question' and that this question can be answered by considering 'the intricate molecular controls' (mechanically) guiding this process. In her entry on the regulation of genomes, Lynn Helena Caporale (2006) observes that

> The strings of nucleotides that we proudly translate into proteins amount to less than 2% of the human genome. We know well that additional DNA sequences are involved in the regulation of expression. However, fully understanding the information content of genomes will involve expanding our imagination with respect to both what types of information may be there and how information might be represented.[62]

[61] Kovach et al. in *Epigenetics: Linking Genotype and Phenotype* (2011), p. 138.
[62] Caporale in *The Implicit Genome* (2006), p. 4.

The 'regulation of expression' is the problem of development because one must discover how the informational content in genes is linked to the content of the phenotype. Lastly, in their account of the mechanical processes involved in generating behavioural traits, J. D. Sweatt, et al. (2014) claim that

> A major component of the processes by which the environment and experience alter individual behavior includes epigenetic molecular mechanisms such as regulation of chromatin structure and DNA methylation. The historical dichotomy between "nature" (genes) and "nurture" (environment and experience) is a false one – genes and experience are mechanistically intertwined. The emerging discovery is that epigenetic molecular mechanisms contribute importantly to this intertwining.[63]

Here, one is led to believe that generating form is solely about understanding how nurture mechanically interacts with nature. An interpretation of epigenetic mechanisms as 'regulating chromatic structure and DNA methylation' makes epigenetics about the study of how the environment mechanically reveals genetic information.

To this point, I have argued that there are logical and empirical motives for rejecting the moderate version of genetic primacy and informationism described above. To conclude this section, I suggest an area of current investigation that might benefit by shifting its focus away from genes and towards the importance of the whole unified organism in development. Biologists have recognized for some time that there is a problem with the interpretation of what are sometimes called 'constraints'. In their entry on the subject, Schwenk and Wagner observe that the

[63] Sweatt et al. in *Epigenetic Regulation in the Nervous System* (2014), p. 7.

only thing anyone seems to agree on when it comes to constraints is that they are

> mechanisms or processes that limit the ability of the phenotype to evolve or bias it along certain paths.

Based on my arguments above, it seems this account of constraints is perfectly consistent with the account of development that is predominant at the moment. As I mentioned earlier, if development is about the way genes either control development or are activated to generate form, then it follows that 'mechanisms limiting the ability of the phenotype to evolve' are explained by how gene expression is constrained in development. Generating variation is necessary if phenotypes and populations are to evolve, and constraining the generation of variation is accomplished by the environment constraining the expression of genes in development. In some cases, careful study of constraints on anything other than genes is discouraged.[64] On the consensus interpretation, phenotypic variation is limited, or biased,by the failure of environments to reveal variations on genes. While it is recognized that most of the variation that is generated is generated during development, the basis for this variation is attributed to genes rather than anything else in the organism.

In his paper on development and evolution, James Griesemer observes that many accounts of development are accounts of transformation, which set out to explain how elements in the genotypic space are changed into elements in the phenotypic space.[65] On this interpretation, generating variation in development

[64] Personal Communication with Rama Singh, May, 2017.
[65] Griesemer in *Genes in Development* (2006), p. 202.

involves explaining how altering genes leads to altered phenotypes. Accounts like this are distinctly non-processual because they concern themselves either with logically linking genotypes with phenotypes or else with explaining how adaptive traits in the juvenile organism are selected.[66] It seems to me that this developmental framework may be involved in conceptually limiting how phenotypic variation is generated to the way genes are constrained. I discuss the problem of constraints in more detail in the next section. For now, it is important to recognize that because of the difficulties I have already identified with conceptualizing development, this tends to ground the limitations one applies to the study of constraints.

In this section, I have argued that many accounts of development emphasize the primacy of genetic information in specifying form during development. This limits the ability of the investigator to take seriously the interpretation of development as a unified process involving a variety of causes. Development is about more than genes and their expression. And it seems that a full investigation into the causal roles of multiple organic parts is a necessary shift in focus. In the next section, I consider how the problems I have identified might be addressed by reinterpreting development as a process involving the whole organism.

[66] Griesemer in *Genes in Development* (2006), p. 202.

CHAPTER 3

AN ORGANISM-CENTRED APPROACH

Up to now, the focus of my argument has been on the role of *genes* in development. Specifically, I have resisted interpretations that give genes a primary role because I take such interpretations to be both logically and empirically problematic. In this chapter, I argue for a *positive* theory of development, which begins by considering the whole organism instead of its genes. Because I interpret individuals, rather than genes, as the units of development, I take them to contain structures and systems whose interactions during development are explanatorily irreducible to the molecular parts they contain. It is the life cycle functions of development, survival, reproduction, and maintenance of life which can be explained only by taking seriously the mechanical roles of these interrelated systems. Therefore, explaining development requires that one understand the varied interactions that occur throughout the organism and between the organism and its environment.

This organism-centred approach to development entails that one will resist explanations that give primacy to gene control or gene activation. As I have already addressed the problems with gene centrism, I now turn to address the problem of organismal primacy. To do this, I consider first the interpretation of function in biology and the role of function in explanation. I then explore diverse examples of functionally interrelated structures in development and consider why such cases exemplify an organism-centred approach. Lastly, I pick up the problem of biological constraints and explore at least one way the organismic

approach might help to respond to certain difficulties and limitations arising from its study.

3.1 Function and Explanation in Biology

Because this section is intended to emphasize the role of the *organism* in development, it is important to begin by examining how the whole organism might be re-interpreted as ontologically primary. To do this, I consider the problem of function. In contemporary biology, complex organic elements are often used to explain the adaptive functions and behaviours of adult individuals, in the way that the structure of a beak is used to explain the eating habits of birds or the chemistry of the nervous system is used to explain reward-driven behaviours. Other examples include eyespots in butterflies or camouflage among fish. One might say, for example, that a wide beak functions to break open large seeds or that the sandy colour of fish living on the ocean floor functions to protect them from predators.

However, contemporary biology often fails to account for the functional role of organic elements in explaining the *normal development* of the same created form each generation. In this way, functions are interpreted in terms of the phenotypes of the *fully formed* adult organism, and the functions of the whole organism *during development* are ignored. I have already argued that genes do not have primacy in directing, specifying, or organizing the generation of form. I now argue that if this is the case, then the most important questions of development relate to how complex organic parts function to generate the form of the organism. For reasons that will become apparent, it is the functionality of the

whole organism that grounds its phenotypic functions. To put it differently, a phenotypic function is proximately explained by the phenotypic structure, but this structure depends on the fact that it is a product of the whole functioning organism.

3.1.1 Objections to the Problem of Form

Let me provide more detail about the modern interpretation of function in biology. For many biologists, structures are functionally important in the sense that they carry out processes for the sake of the fully formed adult individual. Functions in this sense are thought to have purpose in biology. A leaf functions to carry out the process of photosynthesis by which carbon dioxide is converted into glucose. This is done for the sake of the survival and reproduction of the plant. Therefore, the systems of the leaf function for the survival and reproduction of the plant.

While the leaf, on this view, has behavioural or physiological function, its systems are not seen as functionally important in generating the form of the leaf. Behaviours and physiological processes are proximately explained by the purposes they serve in the organism, while development (as I have shown) is generally explained by mechanical interactions involving genes. Thus, while phenotypic functions have important roles in the processes of the adult organism, organismic functions are generally neglected in explaining development. Interpretations of organismic functions are often the same when it comes to evolution. For example, a genetic explanation is usually preferred for how

variation is constrained during development.[67] Therefore, on the received interpretation of function, the whole organism causally explains neither the generation of form nor the presence of phenotypic variation. Because the function of a leaf is carried out only in the content of its final form, organismic functions are not considered in development. Organismic functions are phenotypic functions, which on a gene centred view, are products of genetic activation and control and genetically- constrained variation.

The tendency to ignore organismic function in evolution and development is grounded in the modern objection to the problem of form. Webster and Goodwin argue that with the evolutionary paradigm, organisms were conceived and interpreted in terms of their genes, which produced a 'conceptual impoverishment vis-à-vis the problem of form.'[68] While organic systems functionally exist *for* each other and *for* the organisms they constitute, they do not exist *by means of* each other, since it is genes that are the means by which these systems are produced.[69] Focusing attention on the functions of organic content, it became possible to ignore the way the organism functions during its development. In my discussion on reductionism, I argue that while there is often a preference for a molecular explanation because of its practical benefit, there is no reason why the functions of organic systems should not be considered in the study of development and evolution. Before I come to this, it is helpful to show how the

[67] See Austin (1999), pp. vii-ix and Loeschcke (1987), pp.1-2 as examples of accounts of genetic constraints on adaptive evolution.
[68] Webster and Goodwin in *Genes in Development* (2006), p. 108.
[69] Ibid, p. 106.

focus on phenotypes has generated a teleological, or goal-directed, interpretation of function. Later, I will argue that for a thorough investigation into the organism in development and evolution, one must consider an *integrativ*e interpretation of function.

In *Toward a New Philosophy of Biology* (1988), Ernst Mayr argues that to a degree, the use of teleological language is permissible in biology. What is important is to be clear on how such language ought to be used and the degree to which it should be taken seriously in biological explanation.[70] If one observes that there is function in phenotypic content, one must then ask about the cause of this content. Of course, in any biological explanation, one wants to eliminate a divine creator seeing absolute purpose in the parts of nature, a Lamarckian mind that generates new phenotypes on the basis of needs, or an immaterial organic nature that guides the outcome of development. These uses of purpose or goal-directedness should be rejected because they ground the cause of organic content in an external or immaterial source, thereby failing to offer a biological explanation.

One might argue that explaining this content by genes or genetic programs eliminates the risk of invoking such a purposive, immaterial organizing power. In his discussion on finality and evolutionary biology, Raymond Ruyer quotes Julian Huxley as noting that

> the teleology of adaptation is a pseudo-teleology, capable of being accounted for on good mechanistic principles, without the

[70] Mayr (1988), p. 38.

> intervention of purpose, conscious or subconscious, either on the part of the organism or of any outside power.[71]

In order to avoid the charge of interpreting teleology in terms of vital or cosmic forces, one is sometimes led to prefer the alternative interpretation of phenotypic functions explained 'on good mechanistic principles'. What Ruyer was referring to were mechanisms involving genes, which seems to match the current biological trend of what counts as a good mechanism. But it seems that on such competing interpretations, the whole concept of function is at risk of being trivialized. I take it for granted that no biologist considers an organism to consciously guide its own outcomes or that these outcomes are externally guided, which would ground biological function in an external source. And I have already argued that the structures and systems created during development are not explained solely by gene function or gene activation, which ground biological function in a molecular source.

But it is precisely this latter view of function that is often emphasized. In arguing that the study of biology should involve explanations autonomous to those of chemistry and physics, Mayr recognizes the importance of referring to biological systems:

> Attempts to 'reduce' biological systems to the level of simple physico-chemical processes have failed because during the reduction the systems lost their specifically biological properties. Living systems…have numerous properties that are simply not found in the inanimate world.[72]

[71] Ruyer (1952), p. 165.
[72] Mayr (1988), p. 1.

Such unique 'properties' are observed in the functional content of the organism. Nevertheless, the explanation is decidedly molecular, since Mayr proceeds to explain this content by genetic control and gene specification. The use of teleological language, he thinks, is necessary if one is to avoid explaining biological systems by inanimate matter.[73] In order to explain bird behaviour, it is important to describe the functions of a bird's beak or its patterns of flight and nest building. Otherwise such behaviour is explained by physico-chemical interactions, which are not biologically unique.

For all his concern to separate the study of life from that of inanimate matter, however, he holds some things in common between them. For example, he draws an analogy between organisms and machines, in which both machines and phenotypes have functions that are foreseen from the outset. What is biologically unique is that goal-directed functions are specified by an *internal* genetic program instead of being intentionally or automatically achieved by *external* forces.[74] Rather than a product of the whole organism whose parts constrain and causally explain structural and functional outcomes in development and evolution, function for Mayr is the product of genetic programs that explain at least the initial outcomes of development from the outset.

It is the importance of both teleological language in biology and the mechanical explanation of functions by genetic programs that combine to form his interpretation of function. Functions are the 'seemingly goal-directed behaviour

[73] Mayr (1988), p. 1.
[74] Ibid, pp. 44-5.

in organisms', which he calls 'teleonomic'.[75] The function of a bird's beak is to consume the kinds of foods or exhibit the kinds of behaviours necessary for its survival and reproduction. However, these apparent goals of the bird cannot serve as a real explanation for its beak. When seeking this explanation, one must refer to the genetic program that causally explains beak development:

> [Teleonomic behaviour] is guided by a 'program', and it depends on the existence of some endpoint, goal, or terminus which is foreseen in the program that regulates the behaviour. This endpoint might be a structure, a physiological function, the attainment of a new geographical position, or a 'consummatory' act in behaviour.[76]

And so, systems and their functions are relevant only in phenotypic content, which is causally explained by genetic programs. Mayr later interprets these programs as 'material' parts that exist 'prior to the initiation of the teleonomic process'[77], which means natural development is explained by material genes that are passed down in evolution and activated in development.

T. L. Short notes that contemporary uses of teleology often take the consequences a trait has had in the past to explain the existence of that trait in the present.[78] If a bird's beak was adaptive in the past, this explains why it exists in the present. Although explanations like these do not make explicit genes as the cause, they are consistent with the received view that current functions are explained mechanically by something in the past that is inherited and activated in

[75] Mayr (1988), pp. 44-5.
[76] Ibid, p. 45.
[77] Ibid, p. 48.
[78] Short in *Biology and Philosophy* (2002), 17, p. 324.

the present. This inference, I think, is possible by the model that separates phenotypes from genotypes and then links a past trait with the gene or genes that explain it. By contrast, an organismic approach, which grounds function in the whole organism, explains the present existence of beaks and wings by the integrative functions of the parts in evolution.

Philip Kitcher extends Mayr's position on the biological importance of function and teleological language by observing that many processes require its use, despite there being a genetic code that explains them all. He argues that in every branch of biology, there are unique entities used to explain different phenomena. In explaining the 'distribution of genes to gametes', for example, one must use the terms 'chromosomal alignment' and 'cell division', which are preferred over terms like 'molecular reshuffling'.[79] In this way, it is cellular functions rather than genes that explain *at the cellular level* the pattern of gene distribution in reproduction. The careful biologist should say, for example, that the function of the cell is to ensure the distribution of genes in reproduction, even though this function is ultimately explained by the genome that specifies and controls the outcome.

In biology today, it is common to emphasize the importance of cell function in development. For example, Freeman et al. (2008) observe that

> Cells 'know' where they are in time and space because they are constantly interacting via cell-cell signals. In effect, much of development is organized by signals that cells send and receive. These signals activate transcription factors that turn specific genes on

[79] Kitcher in *Philosophy of Science* (1998), pp. 993-4.

> or off. As development proceeds, the distinctive suite of genes that are activated at successive stages determines the fate of each cell.[80]

Here one sees that cells interact through signal transmission to explain how specific genes are expressed. And so, referring to the signalling functions of cells is necessary to explain development. However, the authors lay out this account of cell function within a broader interpretation of gene primacy, in which the functions of cells are defined in terms of the genetic mechanisms involved[81], which are ultimately grounded in the master function of specific genes.[82] Webster and Goodwin hold that explanatory models like this one are additions to Jacques Monod's hierarchical interpretation of the organism, in which the 'structure generated at each level of the hierarchy [is] uniquely specified by the properties of the constituents at the lower level.'[83]

The above text seems to be a good example of this revised model in which spatio-temporal information is transmitted between cells which, together with activated genes, are intended to specify and explain the developmental process.[84] The point here is that while cells clearly have functional significance in development, the genes they contain can be interpreted as the primary determiners of cell type. By extension, the type of tissue or organ that forms in the embryo might be interpreted as specified by the kinds of interactions that occur among cells, etc. Ultimately, all organic functions are specified from the bottom by

[80] Freeman et al. (Volume 1) (2008), p. 460.
[81] Ibid, pp. 454, 457-467.
[82] Ibid, p. 460.
[83] Webster and Goodwin in *Genes in Development* (2006), p. 119.
[84] Ibid, p. 121.

genes.

Let us return to Kitcher's account of development. In one passage describing the explanatory importance of not reducing biological systems to their molecular constituents, he makes this claim:

> Anti-reductionists are not only able to contend that there are autonomous levels of biological explanation. They can also resist the weaker reductionist view that explanation always flows from the molecular level up….Understanding the phenotypic manifestation of a gene, they will maintain, requires constant shifting back and forth across levels.[85]

He then goes on to describe that contra a molecular explanation, which gives to organic structures no functional role whatever in the determination of outcomes, focusing on organic complexity allows one to interpret structures such as tissues as activating genes necessary for limb development.[86]

While focusing on the functions of complex structures such as cells and tissues suggests that these functions are being taken seriously, it may be that these functions are trivialized. Like Mayr, who permits teleological language because he recognizes that phenotypes are grounded in inherited genetic programs, Kitcher grounds ontogenetic functions in genes that specify traits. Both accounts hold that functions are ultimately explained by genes. But if, as I have shown, genes are not primary in explaining developmental outcomes, then phenotypic or developmental functions should not be explained ultimately by genes. Kitcher's approach serves to preserve the functional content of biological entities without

[85] Kitcher in *Philosophy of Science* (1998), p. 994.
[86] Ibid, p. 994.

taking seriously the integrative functions of the whole organism. An integrative interpretation of function gives roles to the whole of the developing organism, so that function is not trivialized, while the teleological, content-based interpretations I have considered give apparent function to parts, which are explained by genes.

Using the whole organism to explain function, rather than its genes, has implications for the study of development. Even if one recognizes wings or nest-building patterns as functions contributing to species survival and reproduction, one is not constrained to explain their existence by genes passed down in evolution. Of course, the whole organism in evolution is involved in the explanation of traits. But one cannot assume that 'a trait's past adaptiveness is the explanation for its existence now', since the trait is produced as part of a functionally integrated whole. Only this whole is sufficient to ground the functional content one observes.

This idea of the primacy of whole organisms was first realized by Aristotle in his account of final causes, which Darwin himself sometimes used.[87] In a discussion on the teleological views of Aristotle and Darwin, Short observes in Aristotle's doctrine of final causes something of importance for the current discussion:

> A final cause is a general type of possible outcome. A type of outcome need not be achieved. But if it is achieved at all, it can be achieved in different ways, by different means (i.e., by different mechanical causes), with results that differ in detail.[88]

[87] Short in *Biology and Philosophy* (2002), 17, p. 326.
[88] Ibid, p. 327.

Short then goes on to suggest that conceived this way, final causes are neither present, past, nor future particulars. They are not events at one time that causally explain outcomes at some other moment in time. Therefore, a final cause is not a cause in the ordinary sense. It is not a past or present event that causes other events in the future, in the way that mechanical ventilation brings oxygen into the lungs, which leads to its circulation in the blood, and its transportation to the tissues. Neither is it a goal that the organism foresees, directing its parts to generate beaks or build nests.

This use of teleology has more in common with the usage I prefer than does the common interpretation of teleology as 'goal-directed'. In my own usage, function is grounded in the whole organism – in all of its constituent parts – which, because they are functionally interrelated, can in turn be mechanically combined in multiple ways to produce the organic functions of survival, reproduction, and maintenance of life. The way in which these parts functionally interact explains how the organic functions are achieved in development and evolution.

In similar fashion, others have suggested that one should begin with something comparable to this notion of a whole organism as the way to explain the kinds of mechanical interactions one observes. Russell argues that one should always begin by looking at the structures and functions of the whole organism because the organism is functionally integrated:

> No part of any living unity and no single process of any complex organic activity can be fully understood in isolation from the structure and activities of the organism as a whole.[89]

Applying this method allows one to interpret molecular activities and interactions in light of functionally integrated systems of parts. For example, interactions between the articulating parts of the skeletal system are important in causing or constraining developmental outcomes:

> Not only do systems of organs, by being adjusted to special modifications of function, influence one another, but so also do parts of the same organ. This is noticeably the case with the skeleton, where hardly a facet can vary without the others varying proportionately….[90]

Let us return then to Mayr's concern about material vs. immaterial explanations. The real issue in all this is not whether material explanations are better than immaterial ones. It is whether beginning with the organism and its integrated parts is a better approach to determining the causes of development than considering the organizing capacity of genes to specify and control outcomes. Beginning with the whole organism focuses one's attention on the elucidation of those functions involved in *every* natural process. Rather than limiting one's attention to the functions of the observed phenotype, focusing on the whole organism leads one to ask whether and how a part is involved in a form-generating process.

At this point, one might accept that organic systems are functionally

[89] Russell (1930), pp. 146-7.
[90] Russell (1916), p. 36.

important in biasing, or constraining, development because of obvious examples like that of the skeletal system, in which parts clearly bias the organism by preventing particular kinds of variation over limited evolutionary periods. Another example is the function of teeth in mammals, where it may be observed that a dental modification in development causes the adult to starve for inability to chew and swallow its food. Examples like these are widely accepted as constraints based on functional integration, where altering one element of an integrated system leads either to death or decreased fitness.[91]

Nevertheless, one can argue that the Darwinian interest in the problem of phenotypic function and variation makes irrelevant the problem of how form is normally generated. After all, it is the observed phenotypic content that varies across organisms and in evolution, and this can be explained by addressing this problem of variation. In other words, explaining how form is generated in development is irrelevant, since these concerns have been replaced by the problem of the phenotype and its variations. Because the Darwinian already sets out to explain the phenotypic content of all of life, all previous concerns about form should be set aside.

However, if one denies the importance of the generation of form, he takes for granted that form is 'preformed' in the sense I describe it above. All that is important is how preformed genes are expressed and how this expression is constrained by various external factors. I have already argued that this account is

[91] Schwenk and Wagner in *Keywords and Concepts* (2003), p. 60.

logically and empirically problematic. Furthermore, the problem of form has never really been 'explained away', despite this Darwinian focus on phenotypic function and variation. The perspectives I offered from earlier biologists on the ongoing importance of beginning with whole organisms is supported by Webster and Goodwin, who observe, in their discussion on the history of studies in animal morphology, that from the early stages,

> the individual organism and the biological domain as a whole were to be considered as systematic wholes or structures, that is, in terms of sets of internal relations. From this perspective the problem of biological organization, and therefore of form, was the primary problem and questions of material composition were secondary.[92]

By varying genes and observing phenotypic changes, which is common practice in molecular biology[93], one sets out to find the genetic basis for development by discovering the material conditions of gene expression. In doing this, one ignores the question of how these systems are caused and organized by supposing that these things are given in genes. Therefore, the order that was maintained throughout the history of biology is reversed and the problem of form remains. Observing this requires that one take a broader view of function than what is often given.

3.1.2 Objections to anti-Reductionism

Even if the arguments I have laid out make the problem of form a legitimate area for investigation, one could argue that it does not follow that these

[92] Webster and Goodwin in *Genes in Development* (2006), p. 101.
[93] See my discussion about Hox genes in chapter 1

very structures and systems cannot be analyzed into their parts. And once the analysis is complete, it seems that what was once explained in terms of the vertebral column or the smooth muscle tissue might now be explained in terms of the interactions among the molecular parts of that system. This leads one to wonder what, if anything, is it about complex biological structures that makes them explanatorily irreducible despite the obvious fact that they contain nothing beyond their molecular constituents? If function, as I have argued, ought to be reinterpreted in light of the whole organism rather than its mere phenotypic content, then there no reason why biological structures themselves should not sometimes be interpreted as causal elements of the organism. The complex interrelated cells and tissues of the early embryo might be equally important functionally in causing the wing to form as are the hormones, proteins, and genes at work at the molecular level. And the interrelated structures of a dragonfly wing might be just as important in constraining the course of development as its interacting molecular parts.

If it is the whole organism with its peculiar arrangement and ordering of parts that grounds the functions of these parts, then there is no reason why the cause of development should not be explained at different levels of the organism. One can imagine such a view meeting with considerable skepticism, especially given that modern empiricism prefers to reduce the organism to a molecular aggregate. Let us consider again Kitcher's claim about the nature of biological explanation:

> Understanding the phenotypic manifestation of a gene…requires constant shifting back and forth across levels.[94]

I noted above that this kind of antireductionism has the flavour of a pseudo-antireductionism because one interprets function as phenotypic content and finds in genes the ultimate explanation for such content observed. Presumably, this so-called antireductionism is more plausible because it promises to yield more exact hypotheses and predictions. In truth, any approach that analyzes an organism into its parts is bound to meet with more approval among scientists than that which relates these parts to the whole organism. But if it is true that no part or single process of any complex organic activity 'can be fully understood in isolation from the structure and activities of the organism as a whole', then it seems it is at least sometimes important to understand the ways by which organic structures and systems causally influence the development process.

The pseudo-antireductionism described above seems common among many biologists. Mayr suggests as much here:

> [The modern biologist] does not question that all organic processes can ultimately be reduced to or explained by physico-chemical processes. None of the events and processes encountered in the world of living organisms is in any conflict with a physico-chemical explanation at the level of atoms and molecules.[95]

He then goes on to say that

[94] Kitcher in *Philosophy of Science* (1998), p. 994.
[95] Mayr (1988), p. 11.

> New properties and capacities *emerge* at higher hierarchical levels and can be explained only in terms of the constituents at those levels.[96]

That developmental processes, for example, are not 'in any conflict with a physico-chemical explanation at the level of atoms and molecules' (A) no one would deny. But, surely, it does not follow that these processes can ultimately be explained by 'physico-chemical processes' (B). Mayr is careful to observe that 'explanations must occur in terms of the constituents at those levels' (C), but he objects to the problem of form by regarding B as the metaphysical basis for C.

Examples of this interpretation of anti-reductionism, or emergentism (as it is sometimes called), might be found in cell biology, which uses explanatory concepts different from those in genetics, since cells exist at a higher level of complexity. Explanations employed in cytology differ from those of histology, and so on. However, while explanations differ at different levels of complexity, ultimately, because organisms themselves possess nothing beyond their physico-chemical parts, they can be explained *in toto* at the physico-chemical level.

Related to this idea that organisms can ultimately be explained *in toto* at the bottom is the often implicitly accepted idea that the only real entities of a complex organism are its physico-chemical ones. Ruyer describes this acceptance as grounded in 'a poorly defined primacy of the molecular and the elementary.'[97] In the following passage, he sheds light on why he thinks the molecular primacy that was residual in emergentism should be rejected:

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[96] Mayr (1988), p. 11.
[97] Ruyer (1952), p. 155.

> Composition is at least always subordinate to development, as in the passage from the egg to the adult multicellular organism. The idea of reduction and of analysis was meaningful so long as one believed in the primary character of the phenomena of classical physics. This will no longer be the case when we realize that every individual organism is, as such, as primary (i.e., unanalyzable into aggregate phenomena) as any other individual.[98]

Surely, the only way one can properly speak of organic primacy is in terms of the spatio-temporal manifold of the whole organism, which is nothing beyond its material parts. And yet, it is precisely because of such organic primacy that one should reject the explanatory primacy of molecular parts. Organic primacy does not entail that organisms cannot be analyzed. They *can* in a sense possess nothing beyond their molecular constituents. What it entails is that understanding the nature of molecular interactions between genes and their environments does not bring one closer to understanding what it is that drives the process of development, since it is the whole organism that grounds the nature of these molecular interactions.

It is for the reasons mentioned here that I resist the pseudo-emergentism which seems to be grounded in explanatory reductionism rather in the whole organism. The idea is unwarranted in history, and there is no reason to think that modern biology demands its acceptance. Genes *are* activated and expressed during development and a multitude of molecular interactions *do* occur in the material construction of organisms, but the form that is produced is not somehow 'ultimately explained' by either genes or physico-chemical parts. In fact, given an

[98] Ruyer (1952), pp. 155-6.

organismic interpretation, it seems likely that at least some *biologically* relevant explanations do not involve genes or molecules at all. And, as I will show, the more one recognizes the functions and interrelatedness of organic structures during development, the more one sees their explanatory relevance.

In his discussion on the role of good empiricism in science, Paul Feyerabend observed the tendency among investigators in quantum mechanics to prefer the accepted theory and make dogmatic assertions about its legitimacy simply because it is the accepted theory. He argues that there is a better approach:

> Alternatives must rather be developed in such detail that problems already 'solved' by the accepted theory can again be treated in a new and perhaps also more detailed manner. Such development will of course take time….Still, it would be very unwise to bring the process to a standstill in the very beginning by the remark that some suggested new ideas are undeveloped, general, metaphysical.[99]

One criticism often laid against an organismic approach is that it fails because it is 'undeveloped' and 'too general' in its methods and in the kinds of predictions it can draw. For example, one might reason that the project of beginning with whole organisms to develop a better picture of how form is generated should be abandoned on the grounds that the organism is always better explained when it is analyzed into its smallest constituents. Presumably, this is why investigators often emphasize the hierarchical structure of the organism. Beginning with the assertion that important functional events occur at multiple levels, one can proceed to explain them primarily in terms of that which occurs at the lowest

[99] Feyerabend in *Philosophy of Science, The Delaware Seminar*, Volume 2, (1963), pp. 3-39.

level.

Sometimes, one resists the organismic approach on the grounds that systems are too general in terms of what they explain. The functional indeterminacy of complex systems is noted by Hallgrimsson and Hall (2011) as preventing investigators from 'predicting phenotypic outcomes directly from DNA sequences or sequence variation'.[100] Of course it is desirable to predict the exact role of one part in producing phenotypes, but the primary explanandum is not how genes are activated. Taking as primary the explanation of gene activation does away with the causal role of the system itself in that explanation. If the thing to be understood is gene activation, then one could easily analyze the whole organism in terms of its molecular constituents and then determine the causal role of each part in regulating the way genes are expressed. Structures and systems as entities need have no role whatever in the explanation. This first reductionist critique, therefore, argues that biological structures are unimportant in explaining development because of the pseudo-antireductionism that ultimately explains these structures from the bottom by the genes they contain.

Robert opposes this hidden reductionism by opposing the structural hierarchy by which development is often conceived:

> The interactions comprising organism development are complex, and their effects are not simply additive. Some aspects of development, such as cell-cell signalling, cannot be represented as simple causal

[100] Hallgrimsson and Hall in *Epigenetics: Linking genotype and phenotype* (2011), p. 2.

> pathways, but rather should be construed as networks of causal interactions.[101]

The signals transmitted between cells during development are not simply parts of a bottom-up 'causal pathway' in which genes ultimately specify cell function or cells carry out genetic programs. As I have already argued, were this the case, one could explain how form is generated simply by explaining how genes are activated in different cellular or spatio-temporal contexts.

The importance of invoking these 'networks of causal interactions' is noted by Brian Ingalls (2013), who recognizes the importance of using the whole organism in the explanation. He claims, for example, that the study life is about 'understanding…the mechanisms by which living things operate.' Beginning in the last century, claims Ingalls, 'molecular biology began to reveal the networks of interacting molecules that drive all cellular behaviour (and hence all life).'[102] And so, one observes in this account a shift away from the linear, bottom-up account of causation towards an account of interacting molecules that materially construct and bring about the processes and events that occur during the cycle of life.

While this revised account invokes the whole organism in explaining what is elsewhere explained ultimately by genes, one could argue that the revised account is reductionist because it explains development purely at the molecular level. The objection is not with a theory that seeks to analyze the organism at its

[101] Robert (2003), p. 96.
[102] Ingalls (2013), p. 1.

molecular level. Rather, it is with the reductionist underpinnings, which argue that because the organism has nothing beyond its physico-chemical properties, it should be explained at the level of its physico-chemical constituents. Surely, if the whole organism is to be considered in carrying out the functions of reproduction, development, and the maintenance of life, then there are grounds for considering the different levels at which the whole organism carries out these processes. Therefore, while one must remove the emphasis from genes, one must also take care to remove an undue emphasis from molecules, particularly if this downplays the importance of research conducted at other levels.

Recall Webster and Goodwin's observation that the primary problem of biology was always 'the problem of biological organization, and therefore of form'. It, therefore, follows that 'questions of material composition are secondary.' This is emphasized by Russell, who notes that in history, the 'combinations of matter' were recognized as varying little among organisms. Thus, it was form that grounded the differences between species. Specifically, it was in form, rather than in material, that the primary variants among organisms were to be found.[103] The problem of form today is often conceived in terms of genes, which explains the contemporary interest in the molecular basis for form. However, while a certain level of exactness is bound to emerge as biology progresses, one must be continually reminded that because molecular interactions are dependent on functionally interrelated parts, the are dependent on the unity of

[103] Russell (1916), p. 38.

the whole organism. For this reason, I simply see no basis for insisting either that every investigation at a higher level is ultimately explained by genes at the lowest level or that the molecular level is always to be preferred in explanation. These are the two objections that have been raised against the organismic approach.

3.2 The Whole Organism in Development

To this point, I have argued for an interpretation of function based on the whole organism rather than on the structural dualism of phenotypic content specified and directed by genes. I now consider examples of how an organismic approach takes seriously the whole organism in the development process. Early examples capturing the importance of the whole spatio-temporal manifold of the organism are offered by Russell, who in a long list documenting several experiments conducted on multiple organisms, reveals (among other things) that organic structures are causally involved in organizing form by altering the arrangement of molecular and cellular interactions. Commenting on a study conducted on the hemipteran *Rhodnius prolixus*, for example, Russell observes that damage to epidermal tissue effects changes in cellular and molecular interactions:

> Products of the partial autolysis of proteins in the damaged cells activate the surrounding cells and provide the chemotactic stimulus to migration….Growth ceases when the products of autolysis have been removed and the epidermal cells have recovered their

> equilibrium by spreading over the wound, by mitosis in the sparse zones, by degeneration in the dense.[104]

In other words, variation in the normal structure of epidermal tissue effects a string of events, in which the cells in the damaged tissue release proteins, which in turn lead to the migration and division of other cells. This process continues until the function of the epidermal tissue is restored.

Rather than presupposing a structural hierarchy in the organism, the study leads one to conclude that the most reasonable way to interpret function is in light of the whole organism whose parts are functionally integrated. Damage to the structure of epidermal tissue triggers a series of cellular and molecular interactions. If epidermal function is apparent only, its function would be ultimately explained by the cells it contains, and these by its genes. In contemporary terms, the function of epidermal cells would be specified by genes in a spatio-temporal context. Activated genes would specify epithelial cells, which would in turn become organized into epithelial tissue. But the function of epidermal tissue seems to be grounded in the way it is arranged among the parts of the whole organism. By upsetting the natural function, the epidermis is restored through a series of mechanical interactions that are neither guided or specified by genes at all.

How then does one interpret the function of the epidermis if it is not specified by genes in development? By grounding its function in the whole organism, it is more reasonable to argue that the organic functions of *Rhodnius*

[104] Russell (1946), p. 15.

are laid down by the whole organism during its development. Likely, the development process is also affected by pathways and constraints across the organism that are laid down in evolution. Working together, these factors explain the function of the epidermis. Because its function is grounded in the organism, one explains why in the presence of damage, mechanical interactions occur to restore its original function.

It is important to note that even if genes were expressed during the wound healing process, it does not follow that the function of the epidermis is ultimately grounded in its genes. Presumably, genes are expressed in many processes. What the organismic approach demonstrates is that mechanical interactions of any kind are essentially grounded in the whole organism, which is the only way to keep from trivializing the functional interactions among its parts. Kitcher, in his defense of antireductionism, wonders what is required to explain the 'distribution of genes to gametes.' One must, he thinks, refer to the function of chromosomes to align and of cells to divide. The final phenotype, in this sense, is the 'manifestation of a gene', even though one does not need to explain the phenotype 'from the molecular level up'. Phenotypic functions like that of epidermal tissue are, in Kitcher's sense, already specified by genes, which makes them functionally important only in carrying out genetic instructions rather than in causally interacting to generate form.

Consider next the account Robert gives of the appearance of alternate head structures that sometimes occurs in the water flea *Daphnia cucullata*:

> The morphology of *Daphnia*, the water flea, will be altered if the fleas develop in water in which their predators have been reared. If juvenile *Daphnia* are made to develop in water in which the predatory larvae of *Chaoborus* (a dipteran) have been cultured, the presence of chemicals released into the water by the *Chaoborus* may induce development of a helmet during *Daphnia* development.[105]

While Russell demonstrates the organismal basis for structural restoration, Robert bases the structural variation of water fleas in the whole organism. Specifically, he considers the relevant interaction to be between the environment and the whole organism that interacts with it. The example considers that the basis for the variation is not in genes specifying alternative phenotypes but in the whole organism, whose interactions with the environment in evolution lead to the selection of alternate pathways of development, which in its own life cycle lead to mechanical interactions along a particular pathway. The point is that it is the functionally interrelated systems of *Daphnia* that ultimately explain why one phenotype is generated over another.

> The case is an example of developmental plasticity, which is defined as
>
> the simple fact that there is no one-to-one relationship between a particular genome and a particular phenotype.[106]

Specifically, one genome might be associated with many phenotypes, or one phenotype may be produced from different genomes. Cases of plasticity might be used to demonstrate the primacy of the whole organism over any one of its parts. Robert describes the development of a plastic trait as involving ‘a system of

[105] Robert (2004), p. 81.
[106] Ibid, p. 79.

epigenetic interactants coming together over a life cycle.'[107] These interactants might occur at multiple levels of the organism, and they reflect its functional interrelatedness. In developmental plasticity, nothing is different about the genomes of the two variants. Neither is this difference accounted for solely by the expression of different genes. Rather, chemicals called kairomones interact with 'helmet' *Daphnia*, whose integrated systems interact with kairomones in a way that mechanically generates the variant.

Other contemporary studies on *Daphnia magna* confirm the important role of ecologies, which interact with organic systems to produce variations. Stoks, R. et al (2016) observe that increased spine length, a tendency to avoid sunlit areas, and increased alertness are three morphological and behavioural changes occurring in the presence of fish.[108] And so, one sees examples of how integrated systems are causally significant both in maintaining normal function and in permitting the generation of variation within a life cycle.

Let us recall Robert's discussion on how functionally adaptive traits are sometimes associated with highly conserved (nonvarying) genomes. In evolution, he notes, antennae were adaptive to many organisms, yet antennae are also now associated with highly conserved genes. So, it would seem one could infer that genes control or specify this function. There is, however, another explanation. Recall how, as Russell observed, the function of the epidermis is maintained in the insect *Rhodnius* through a series of mechanical interactions. Robert notes, in

[107] Robert (2004), p. 79.
[108] Stoks et al. in *Ecology Letters*, (2016), 19, p. 181.

like manner, that if the function of antennae is adaptive for the organism, then environmental changes might require that a functionally integrated organism maintain this function by a series of gradual *molecular* changes.[109] Genes which, at one point, were used to produce phenotype A are later used for producing phenotype B. In this case, the B phenotype are functionally adaptive antennae. Therefore, in maintaining an organismic interpretation of function, one observes that it is the whole organism in evolution that explains the generation of new molecular interactions producing antennae. In other words, while specific genomes are highly conserved in specific phenotypes, it is the whole organism that explains this association.

Let us consider one last example to illustrate the need for an organismic interpretation of development. Consider the generational event of gametogenesis in the leopard frog *Rana pipiens.* This is a carefully timed process in which the seasonal effects of temperature and humidity interact with those cells, tissues, and organs involved in reproduction:

> The frog's life depends on the plants and insects in the pond where it lives and on the temperature of the air and water. A combination of photoperiod (hours of daylight) and temperature tells the pituitary gland of the female frog that it is spring. If the female is mature, her pituitary gland secretes hormones that stimulate her ovary to make the hormone estrogen. Estrogen then instructs the liver to make and secrete yolk proteins sum as vitellogenin, which are then transported through the blood into the enlarging eggs in the ovary. The yolk is transported into the bottom portion of the egg.[110]

[109] Robert (2004), p. 30.
[110] Gilbert (2006), p. 26.

Contrast this example with Kitcher's interpretation of chromosomal alignment and cell division in reproduction as carrying out a genetic program. The functional interrelatedness of parts in gametogenesis reveals how much more seriously one should take the problem. The ecosystem of the pond as well as environmental factors such as 'the temperature of the air and water' interact with the organs of its endocrine and reproductive systems. Multiple parts interact to organize form in the creation of gametes.

If these functions are teleonomic in their interpretation, then they could be viewed as merely carrying out a genetic program or as specified by the genes they contain. Were this the case, it would place the explanation ultimately in the genes, with the stipulation that one must use teleological language to refer to endocrine glands and the liver because these are functionally important *for the organism*. If genes ultimately specify these outcomes because they are contained within the cells, tissues, and organs at higher levels, then there is really no reason to take these parts as functionally primary and causally determinative of the phenotypic outcome, which in this case is egg development. This process of gametogenesis directly precedes the next stages in the frog life cycle, which are fertilization and development. If the functional integration of the whole organism is clearly emphasized in this passage on gametogenesis, one wonders why it is often not equally emphasized in descriptions of development.

In each of these examples, processes involving the generation of form, the maintenance of function, and the generation of variation are contingent on the integrated nature of the organism. This is consistent with a comment by Robert

(2003) that

> potential emerges during development, as current contexts condition possible next steps.[111]

If organic form depends on 'current contexts', which create the potential for further development, then this form is not contingent on genes that specify and control. Rather, it is the integrated parts of the whole organism that generate conditions necessary for subsequent development.

The primacy of the whole organism in development means that its parts have a causal role in producing form or in constraining developmental outcomes over time. One might wonder then, in practice, how each element or group of elements causally interacts to explain the outcome. Such elements would include parts at multiple levels or sets of parts whose functions are determined to be interconnected. Given the arguments I have advanced against gene centrism, explanatory reductionism, and the phenotypic interpretation of function, there is reason to think that this might characterize an organism-centred approach to the study of development. Of course, none of what I have argued resists a molecular approach to development. It merely resists the way things like molecules, genes, organisms, and functions have been interpreted.

3.3 The Whole Organism and the Problem of Constraints

In many cases, the issues involved in interpreting development apply also to the interpretation of evolution. One such issue is the problem of constraints. Thus far, I have demonstrated that in order to take an organismic approach to

[111] Robert in *Keywords and Concepts* (2003), p. 95.

development, one must take seriously the interacting functions of organic parts at all levels of the organism. I then gave several examples that demonstrate ways in which the whole organism is functionally interrelated. I now conclude by briefly considering how an organismic approach might be applied to the problem of constraints.

In biology, many examples can be found of genes that constrain, or bias, the outcome of an organism in development and evolution. For example, in studying the appearance of phenotypic differences in the beaks of chickens and finches, an important part of the explanation is that the gene *Bmp*4 is differentially expressed in individuals with narrow and deep beaks.[112] However, because some genes are correlated, so that multiple genes are passed on together, variation in beak size and shape is constrained. This explains why wider beaks are sometimes selected in arid habitats, even though narrow beaks are more functionally optimal.[113] In both cases, explaining how phenotypes differ and which factors bias development involves explaining how genes are expressed differently and how genetic interactions bias development.

While it is clear the role genes play in biasing an organism, it seems genetic constraints are often taken as the primary explanation for the biasing of the phenotype along certain paths. Consider the following passages from Enny et al. (2020) on constraints on fin morphology:

[112] Freeman et al. (Volume 2) (2008), p. 520.
[113] Ibid, p. 524.

> Developmental constraints which could restrict the morphospace of body patterning during the ontogeny, have been proposed as a key factor shaping the character of fin form.[114]

The author goes on to say that

> Rapid advancements of genomics and molecular biology make these questions within our reach, even deploying non-model organisms into lab experiments….With the background of these dramatic changes in experimental biology, an analysis of the underlying regulation of fin morphology, serves as one of the prominent models to reveal underlying mechanisms of developmental constraints.[115]

As with talk that emphasizes genes as organizers and directors of development, much of the interpretation of constraint is offered in terms of 'the underlying mechanisms of development'. There is logical consistency in this approach. If genes either specify phenotypes or direct and organize the normal outcomes of development, then the question of how form and phenotypes are constrained will be answered by investigating those factors that limit, or constrain, mechanisms involving genes. In the example above, because the authors take a gene-centred approach, they set out to reveal the way the phenotype is constrained by revealing the 'underlying mechanisms' that regulate fin morphology. Because of 'rapid advancements of genomics and molecular biology', the only relevant mechanisms are genetic ones. And so, phenotypic constraints, in this case, are constraints on the underlying molecular mechanisms of development.

The idea that genes constrain function, however, is grounded in the idea

[114] Enny et al. (2020), p. 312.
[115] Ibid, p. 312.

that they specify and control function. I have already argued that function is not grounded in genes but, rather, in the whole spatio-temporal manifold of the organism. Therefore, constraints on genes need not be the only form of constraint one considers. James Griesemer notes that all functions that causally contribute to the generation of form might be analyzed in terms of the whole organism acquiring the capacity to reproduce.[116] If the whole organism achieves in the process of development the capacity to reproduce, then the whole organism is also involved in development and evolution in constraining any variation that works counter to this primary function.

Therefore, in addition to genes, constraints might be placed on epigenetic, physiological, or behavioural factors occurring during development. For example, Susan Herring observes two such cases in neurons and muscular systems:

> [In] developmental matching of neurons to their end organs, neurons are overproduced and survive only if they receive appropriate signals from their targets; thus, innervation ratios remain stable. Similarly, the differentiation, growth, and maturation of the muscular system are entwined with those of the skeletal system by mechanical interactions, ensuring that the levers and struts of the body are suited to the forces imposed on them.[117]

Nerves develop in appropriate relation to organs and muscles in appropriate relation to bones. This is because nerves, organs, bones, and muscles interact with each other, as each develops in relation to each other. Genes are, of course,

[116] Griesemer in *Genes in Development* (2006), p. 216.
[117] Herring in *Keywords and Concepts* (2003), p. 276.

being expressed during these processes, but in order to adequately explain the cause of the constraint, one must consider the organismic level at which constraints occur. In this case, relevant constraints should be interpreted as placed on the organs and tissues interacting in functionally significant ways during the process.

Another example shows how to take seriously the functional level at which a constraint occurs. In a recent paper by Genevcius et al. (2020), the authors consider the respective roles of genital function and genital development among stink bugs in influencing the evolution of genitals:

> If there is a mismatch between function and development, that is, groups of structures that work together are different from groups that share a unique developmental origin, it becomes possible to test which of these two factors is more determinant to trait covariation.[118]

The authors then go on to ask

> May these differences be explained by contrasting roles of development and function acting differently on males and females?[119]

In this study, it is constraints on regulated genes that is compared to constraints on the structural features of genitalia in terms of their role in biasing the organism along a certain pathway. Although the authors seem to hold a gene-centred interpretation of development, they at least allow for a careful analysis of constraints at the functional level at which they occur.

As I have shown briefly here, constraints exist at all levels of biological

[118] Genevcius et al. (2020), p. 1049.
[119] Ibid, p. 1049.

development, from genes to adult organisms. Within an organismic approach, there is no reason to give primacy to one element over any other. Neither is there reason to ground the functional basis for development in anything other than the whole organism. Because the whole organism is functionally integrated, its parts might interact at any level in causally determining form or biasing it along particular paths. Developing organisms are functioning entities taking part in a causally complex process rather than epiphenomena of genes, and it is this observation that critically influences their interpretation.

CONCLUSION

The problem of development is essentially the problem of explaining the way form is generated, and this is the problem I have argued has been ignored in much of the current work in developmental biology. The preference for genes as explanatory agents of development has a long history. The details of this history I have left out of my account, which is focused instead on the contemporary usage of genes in development. One can argue that inherited genes have been interpreted as ontologically separate from their organismal environments and prior to the processual outcomes they specify. Genes and their regulation have, in this way, been made the primary explanans of the complex process of development.

The separation of genes from environments is, perhaps, acceptable only insofar as abstracting away genes leads to a careful investigation of the causal roles of both genes and their environments at the level at which these interactions occur. By contrast, creating a dichotomy that interprets the gene as an existent 'other' minimizes the importance of explaining how the mechanical interactions at work throughout the whole organism are involved in causing the development of the final form. The problem of form, as I have presented it, is a problem that involves the whole functioning organism. To think otherwise is to encourage explanations about the bottom-up material construction of parts, which surely explain only what occurs at the level of genes and not what occurs throughout the whole. One must deny that terms like 'genetic programs', 'recipes', or 'instructions' have any bearing on a functional interpretation of development, which challenges one to rely on careful experimentation rather than metaphors.

Such metaphors may lead some to find analogies between these programs and Lamarckian minds or vital forces, which were once used to ground the processes of development and evolution from the top down.

Interpreting genes as prior to their organismal environments makes only certain improvements. For one thing, it keeps one from relying on 'programs' as the explanans. One takes the role of environments more seriously in explaining how genes are regulated at various stages in the developmental process. On this account, genes cannot run the show, as it were, because it is the environment with which genes continually interact and which determines when particular effects will be revealed. However, these effects are strictly gene effects because the inherited genome is taken as prior to the organism it specifies. During development, different cells, organs, or systems (all of which contain genes) are said to be either expressed or mis-expressed because these functions are interpreted in terms of the genes that specify such functions. Genes, in this sense, have primacy not as controlling, or guiding agents but as material parts containing information that specifies outcomes. In this case, one need not rely on a 'program' to control developmental outcomes from the bottom. Instead, one relies on genetic information which the mechanisms of development reveal over the course of the process. While one takes the role of environment more seriously, one continues to dismiss the causal role of genes, thereby removing the 'program' metaphor and retaining the 'information' metaphor.

I mentioned earlier that I thought this interpretation is more common than those interpretations relying on programs, or master genes, which tend to become

explicit in research on Hox genes, in which linear mechanisms are often sought that connect conserved genes with phenotypes such as wings and eyes. Possibly the popularity of the terms 'genetic program' or 'control genes' relies on the number of people engaged in fields like developmental and molecular genetics. However, there do seem to be a growing number interested in fields like epigenetics and evolutionary developmental biology. These people sometimes prefer to use genetic information to explain development by emphasizing the role of a rich contextual environment in activating genes at key times and places. How, when, and where genes are activated is necessary to explain development because the way genetic information is revealed is necessary to explain how phenotypes are generated. To my mind, this still does not take the role of genes seriously enough, since is presupposes that there are traits like muscle cells that are specified by genes. The contextualization of genes does not entail that genes are causally primary in specifying phenotypes, even though these genes are often part of a cause that leads to their production.

Therefore, the gene vs. environment heuristic sets out to explain how the genotype is transformed into a phenotype. In this sense, it misses the point because it does not explain what is the real explanandum, which is the creation of the whole organism from a single cell. The standard heuristic is helpful in population genetics, in which one needs to explain how genotypes are transformed into phenotypes. But it is not helpful in development, given my denial that development is about this transformation. If development were about explaining the transformation, then inherited genes must be preformed and

independent of whole organisms. I have argued that this is not so. Were this the case, then genes could naturally be taken to control and specify every organismic outcome, since organisms would be conceived as dualistic by nature. But this dualism is purely artificial and cannot, therefore, be used to ground an explanation. The process does not obviously start with genes (G) and end with phenotypes (P). Rather than a transformative process, it seems development is better conceived as a process that begins with a minimally complex organism (O_0) and ends with an organism that is more complex (O_n). Such a relationship seems to capture better the idea that development is processual rather than transformative.

Contra the gene vs. environment dichotomy of gene centrism, the whole organism seems to ground a more appropriate interpretation of things like gene activation, genetic constraints, biological systems, and biological function. Gene-based approaches subsume these ideas under genes, with phenotypes, functions, and constraints explained *by genes* alone. An organismic approach subsumes them under the whole organism in development and evolution. Phenotypes and functions are not merely relatively adaptive to organisms in environments. Neither the normal appearance nor the variations of form are explained or \ constrained by genes alone. They are also constrained and explained by the whole organism of which genes are part. For this reason, one can argue that in at least some cases, activated genes causally explain things like RNA or the proximate interactions occurring at the molecular level. In other cases, constraints on genes explain why adaptive phenotypes are not always generated. But this

only serves as part of the explanation.

The structures of the genitalia of stink bugs functionally interact in development and evolution to bias reproducing males and females along certain lines. In this way, variation in genitalia is restricted. Other examples abound. The origins of turtle shells, for example, is permitted only by the presence of interactions between its ribs and its carapacial ridge (CR), which is a region located on its back. In turn, at the cellular level, the formation of the CR requires interactions between epithelial and mesenchymal cells.[120] Therefore, the generation of normal form and its variations involves the whole organism, which entails that it is not solely a matter of genes.

Thus, the two implications of the organismic approach for the interpretation of development are concerned with the normal development of form and the development of variation. Concerning the second, constraints need not be merely genetic, since genetic constraints seem only to explain how the organism is biased against particular adaptive phenotypes. Within an organismic approach, other factors besides genes constrain, or bias, an organism along certain paths. While genes can only be exposed to adaptive constraints, whole organisms might also be exposed to constraints on form. This second type of constraint involves functionally integrated parts that bias development along a particular path.

The example above involving stink bugs is an example of how the organismic approach might be applied to interpreting constraints. If multiple

[120] See Robert (2004), pp. 102-3.

parts of genitalia are functionally integrated during reproduction, then the possibility of generating variations among these parts is reduced because these are functionally necessary for the survival and reproduction of the organism. This is significant because, in theory, even if there were no constraints on genes, it does not follow that relatively adaptive phenotypes would always be produced. The developing organism constrains itself by virtue of its parts, which functionally constrain *them*selves. One can take seriously constraints on form, however, only if one holds that organic form is not epiphenomenal of genes but is, instead, the result of the whole functionally interrelated organism.

Concerning the implications of an organismic approach for the interpretation of normal development, consider the following example from medicine. The etiology of disease is an account of the cause, or causes, involved in explaining the disease process. When one considers the various diseases afflicting humans, one would expect that on a gene-centred approach, the disease phenotype would be causally attributed to the genes that explain it. For example, Crohn's disease (CD) is characterized by the presence of altered functions of the small and large intestines leading to the presence of inflammation.[121] A perusal of the literature reveals that investigators refer to the inflammatory process of the intestines as the phenotype.[122] While the etiology of CD is unknown, current explanations involve combinations of organismal and environmental factors contributing to the generation of the disease phenotype whose function is

[121] Connelly and Kulton in *Crohn's Disease* (2015), pp. 25-6.
[122] Ibid, pp. 25, 29.

ultimately specified by regulated genes. In other words, the phenotype is explained by a set of genes whose activation is correlated with the disease process.

This complex process, which would on the organismic approach be given a distinctly functional basis, is, instead, interpreted as specified by genes that are ultimately at the root of its cause. One wonders, however, whether there is unexplored functional interrelatedness among various constituents of gut tissue, cells, or biochemicals, during the process of early or late development. Perhaps, knowing more about such a process would be useful in explaining how the disease is able to accelerate under certain conditions in the juvenile or adult. However, it seems the contemporary consensus among biologists might prevent this kind of investigation from making much headway. Perhaps it is for this reason that the etiology of diseases like Crohn's remains mysterious.

I have mentioned at least two applications of an organismic approach. The first relates to biological practice, and the second relates to medical practice. Presumably, there are others, which I will not take time to discuss here. The thing to notice is that the interpretation of the organism and its role in development involves philosophical analysis, which has implications for the way development is studied in practice. And this, in turn, has applications for specific problems in biology and medicine. I have conducted the analysis to show both the logical grounds and practical reasons for preferring an organism-centred approach over a gene-centred one.

Throughout the course of this discussion, I have indicated that study of

development is a complex field of interest which might be studied from several perspectives at many different levels of the organism. The challenge for investigators is to continually remind themselves that the organism is a functioning whole. And it seems best that any relation observed among any number of its elements should be perceived in light of the inter-related functions within the spatio-temporal manifold that is the whole organism. Investigations that are grounded in the life cycle of the real functioning organism are more likely, in the long run, to reveal important results concerning the causes of development, while investigations that ignore this seem less likely to meet with the same success.

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