What Is "Epi" about Epigenetics?

JAMES GRIESEMER

Department of Philosophy, University of California, Davis, Davis, California 95616-8673, USA

ABSTRACT: What counts as epigenetic depends on what counts as genetic. It is argued that Weismannism, the doctrine of genetic continuity and somatic discontinuity, is the basis for an overly inclusive concept of epigenetics as every inherited resource "beyond the genes." An alternative theoretical perspective, the "reproducer" concept, is introduced to facilitate analysis of multiple inheritance systems without labeling all nongenetic inheritance "epigenetic."

KEYWORDS: epigenetics; Weismannism; reproduction

TAKING A PERSPECTIVE ON EPIGENETICS

It is not my aim to present epigenetic or genetic models for biological phenomena, to describe new phenomena, to derive predictions from models, or to offer tests of predictions from models. Thus, I do not aim to make an empirical contribution to epigenetics. Nor do I aim to synthesize the wealth of phenomena and their model descriptions into a new or differently organized theory of epigenetics. Instead, my aim is to develop a new *theoretical perspective* on the project of epigenetics. In doing this, I also take a new perspective on genetics, since epigenetics is nearly always defined in relation to genetics (FIG. 1).

Theoretical perspectives coordinate models and phenomena through commitments researchers make to constructing models in terms of particular categories (manifest in the state variables of the models) and in judging fit between models and phenomena in particular respects and degrees.[2]

A key theoretical perspective that has dominated biology in the 20th century is Weismannism, the doctrine of the continuity of germ and discontinuity of soma. In its most abstract form, Weismannism expresses the basic causal structure used to articulate ideas not only about germinal and somatic cells, but also about genotype and phenotype, heredity and development, evolution

Address for correspondence: James Griesemer, Department of Philosophy, One Shields Avenue, Davis, CA 95616-8673. Voice: 530-752-1068; fax: 530-752-8964.
jrgriesemer@ucdavis.edu

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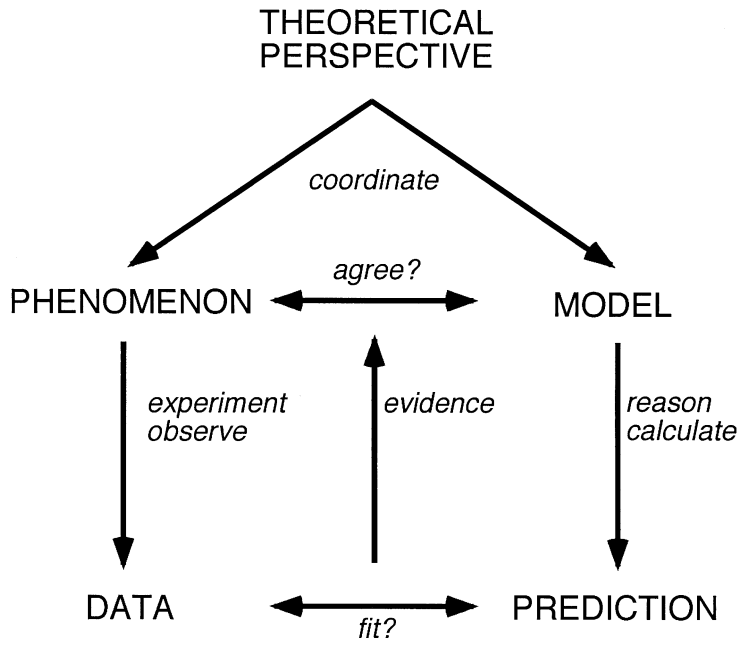

FIGURE 1. Theoretical perspectives. Theoretical perspectives coordinate models of phenomena through scientific commitments in the research process. They govern the relevant respects and acceptable degrees of fit in the evaluation of theoretical hypotheses, thus focusing scientific attention on relevant aspects of models and establishing conditions for acceptance and rejection of hypotheses. The part of the figure representing scientific evaluation in terms of relations between phenomenon, model, data, and prediction is after Giere.[1]

and selection. According to Weismannism, all causality (other than that due to environments, which is ignored at the level of the individual cell or organism) traces to germ or genes; the body or its phenotype is a causal dead end (FIG. 2).

The Weismannist perspective has also been extended to the molecular level, through recognition of its isomorphism to Crick's central dogma of molecular genetics. These formulations together structure our basic representations and models of what counts as genetic and, therefore, our basic representations of what counts as epigenetic.[6]

The curious power of theoretical perspectives is that they can become entrenched in scientific practice even among those who reject them. I think this is the case with epigenetics research. In order to interpret epigenetic phenomena, it is typical to make use of the Weismannist causal structure to express ideas, even if the results of epigenetic research imply that Weismannism is false. If, for example, cytosine methylation can cause sequence changes via hydrolytic deamination of 5-methylcytosine to form thymidine,[7] Weisman-

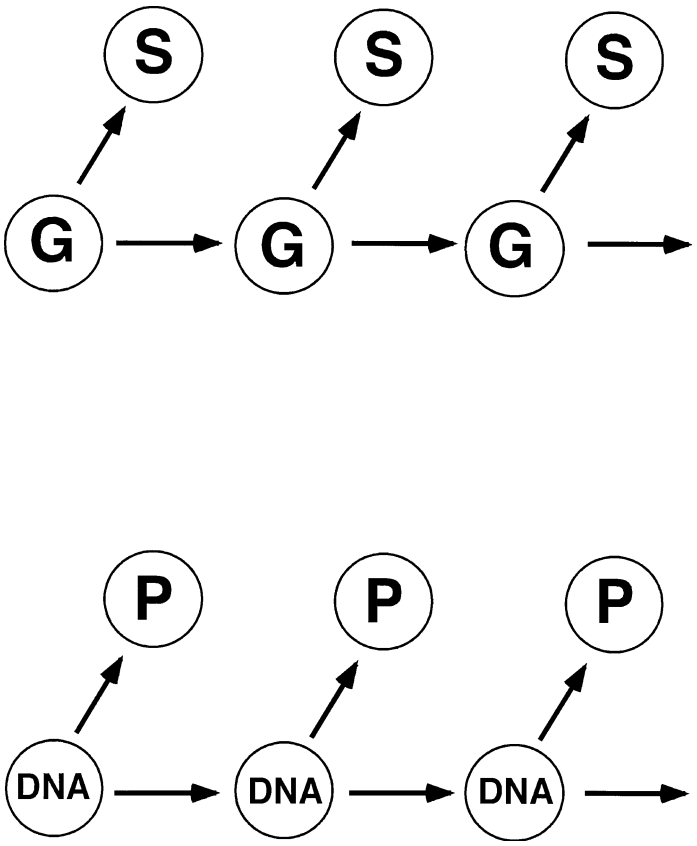

FIGURE 2. Weismannism. Weismannism is the doctrine of the separation of germ and soma in which the germ gives rise to the soma, the germ is transmitted from generation to generation, and there is no somatic input into the germ line. Thus, there is transgeneration continuity of the germ line and discontinuity of the soma. Maynard Smith[3] illustrated the isomorphism between Weismann's[4] doctrine and Crick's[5] central dogma of molecular genetics. (Figure drawn after Maynard Smith (Fig. 8, p. 67).[3]

nism and the Central Dogma are both false. That is, it is not the case that causation flows only from the genes to the proteins or from genotype to phenotype. Presumably, whether deamination occurs does not depend on any particular sequence variation in the genes coding for the methylation enzymes, so causation cannot be traced indirectly to genes (via determination of enzyme sequence) either. The entrenchment of Weismannism is manifest in this example because the same paper that describes it also defines epigenetic effects as resulting "in a heritable change in phenotype in the *absence* of any change in the nucleotide sequence of the genome."[7] In other words,

while the paper acknowledges a violation of the perspective that identifies what counts as genetic with the causal, it nevertheless labels epigenetic a process that is beyond the genes. But if the upshot is to undermine the conceptual basis for singling out genes as the heart of what is genetic, then it is surely a conceptual mistake to label methylation–deamination "epigenetic."

The problem of articulating a new theoretical perspective is extremely difficult because of this fact of entrenchment. It is typical in science to treat distinct models as competitors to the truth about nature. If two models differ in fundamental respects, it is assumed they cannot both be true and a central goal of science is to devise empirical tests that can decide between them. I view models differently and in important respects noncompetitively. I take the view championed by William Wimsatt that truth discovered through models depends on finding empirical results that are robust to a variety of independent idealizations and falsifying abstractions.[8] In the same way, I think a variety of perspectives is needed to guide the *evaluation* of models to produce robust theories. Thus, in offering a new perspective, it should be clear that my goal is not to replace Weismannism, but rather to complement it so as to improve the chances that our empirical theories are robust.

In this paper, I will consider issues raised by epigenetics phenomena and models that facilitate the ways in which Weismannism is inadequate as a theoretical perspective and suggestive of ways to formulate a new one. I begin by considering briefly some details of the logic of Weismannism, which opposes heredity to development as distinct and separable kinds of biological processes. Then I will go on to consider epigenetic phenomena suggesting that, instead of this opposition, development can be viewed as heredity and heredity can be viewed as development. I then develop a new perspective that expresses the way in which heredity and development are intertwined. This new perspective can then be used to pinpoint successes and failures of Weismannism,[6] which I will not discuss here. I close with the observation that from the point of view of Weismannism, everything in and about biological entities other than DNA sequences is epigenetic. This, I argue, is what makes Weismannism rather unhelpful for organizing theories of epigenetics. I will then draw some possibly hasty conclusions about what, in light of the new perspective, counts as "epi" about epigenetics. Because this will turn out not to be nearly as extensive as what counts as epigenetics under Weismannism, I conclude that it may be fruitfully different and thus potentially of empirical value to use it in talking about epigenetics.

HEREDITY *VERSUS* DEVELOPMENT

I have already introduced Weismannism with a simple diagram and comparison to the central dogma, so I will continue using it to make the further point that this theoretical perspective draws a strong distinction between pro-

cesses of inheritance and processes of development. Elsewhere, I have discussed the history of this abstract representation and how it emerged from 19th century cyto-embryology.[9] In my view, the opposition of heredity and development emerged from the modeling practices and was not imposed at their origin to distinguish between the two disciplines of genetics and developmental biology.

The diagram can be read as expressing several claims about causal structure. In the central dogma, the paths represent the flow of genetic information. As Crick said, "once genetic information gets into proteins, it cannot get out again."[5] In its classical form, Weismannism expresses the doctrine of continuity of germ-cell lineage from generation to generation and discontinuity of somatic-cell lineage. But we can also look at it as expressing the causal autonomy of processes of heredity (germ to germ or genotype to genotype) and development (germ to soma or genotype to phenotype). As the early transmission geneticists argued, the processes of genetic transmission could be studied in isolation from the much more difficult problems of gene expression, and Weismannism shows how this assumption is structured.[6]

A hallmark of late 20th century biology has been the emergence of various synthetic projects, in particular the synthesis of genetics with development, evolution with development, and several other permutations involving cell biology, biochemistry, and even ecology. I think it is likely that the synthesis of genetics and development appears the most "reductionistic" of these attempts because of its strong dependence on Weismannism to guide models, experiments, and descriptions of results. If genes are the only possible causes, then genes will turn out to be the primary explanations of development. It is no surprise that syntheses less dependent on Weismannism sometimes disagree with developmental genetic interpretations. A classic case of conflict between genetic and developmental insights is disagreement over how to interpret knock-out experiments. Failures of gene knock-out to yield expected phenotypic deficits requires looking for *gene* interaction to explain the results only if Weismannism is assumed. Otherwise, a wide range of processes beyond the gene might be implicated.

The strong nature of the causal reductionism implied by Weismannism is a problem, as I indicated in the introduction, because it treats virtually everything other than sequence variation as epigenetic and, at the same time, asserts that only genetic (sequence) variation can be explanatory. I don't think any serious biologist accepts this strong view, and yet Weismannism structures biological explanation along these lines even for anti-reductionists.

DEVELOPMENT *AS* HEREDITY

Here I consider phenomena that are typically classified as epigenetic in the molecular literature on the subject. Methylation, which modifies nucleotides

covalently, is perhaps the paradigm case of this class of phenomena, though DNA-binding proteins such as transcription factors, chromosomal proteins such as histones, and more complex structures such as polycomb machines are also cases of "chromatin-marking systems."[7,10] Many of these depend directly on the behavior of DNA in replication for their particular epigenetic effects and for their qualification as systems of *inheritance*.

I want to note two features of chromatin-marking systems. First, they are causally dependent on DNA for their effects. Second, their investigation is primarily aimed at understanding processes of the establishment, regulation, maintenance, and propagation of differentiated cellular states of *cells* in multicellular bodies. That is to say, the problem of epigenetics concerns the ways in which the differentiating and differentiated states of cells are established in development, as a function of the cellular *heredity* of epigenetic control. Development and, more broadly, cellular difference is to be understood in terms of processes that bring about cellular heredity.

In an overview of epigenetics, Holliday offered a definition of epigenetics that makes explicit the interpretation of development (differentiation) in terms of cellular heredity, operating under the Weismannist perspective defining development as a function of genetic causes: "The study of the changes in gene expression which occur in organisms with differentiated cells, and the mitotic inheritance of given patterns of gene expression."[11]

Holliday's limitation of epigenetics to *mitotic* inheritance perhaps expresses only a fact about the relatively frequent role of chromatin-marking in somatic development as opposed to meiotic inheritance, though that is really an empirical question of relative frequency that ought not to be settled by a definition. At the level of theoretical perspectives, the important aspects of the definition are (1) that development is to be understood in terms of the origin, maintenance, and spread of epigenetic variation within and among *cell* lines and (2) that the interpretation of development in terms of cellular heredity depends on the way Weismannism frames the relation between genetic and epigenetic. In this perspective, any causal process that does not trace directly to nucleotide sequences and sequence variations counts as epigenetic. But by the same token, the epigenetic is of relative insignificance *because* it is not genetic. It is typical among epigenetics researchers to note the heterogeneity of molecular mechanisms involved in cellular heredity, but this heterogeneity is at least as much a consequence of defining the epigenetic as *any* inheritance, indeed any causation, beyond the genes as it is an empirical discovery about the role of genes relative to other developmental resources in inheritance.

HEREDITY *AS* DEVELOPMENT

A very different tradition of epigenetics work, which nevertheless is also framed in terms of Weismannism, concerns epigenetic or "nongenetic" inter-

actions in development above the molecular level. Classical work by embryologists on problems of morphogenesis—the developmental process of emergence of tissue and organ form and structure—as well as phenomena described by Waddington as canalization and genetic assimilation fall into this tradition.

Newman and Müller exemplify one recent strand of this tradition. They describe epigenetic mechanisms as "generative agents of morphological character origination," which is a much broader view than that encompassed by molecular Weismannism, since generative agents need not be genes.[12]

Nevertheless, Weismannism dominates this tradition in the same curious way as it does molecular epigenetics because of its tight hold on DNA sequence and sequence variation as what counts as genetic, relegating everything else as epigenetic. I say "dominates" advisedly, because many of the workers here are about as far from the ideology of Weismannism as can be found among practicing biologists. This tradition includes scientists such as paleontologists, many of whom do not work with genes.

I lump together Newman and Müller's work with the heritage from Waddington for the following reason. In both cases, epigenetic phenomena arise from "phenotypic" interactions above the molecular level, although there are clearly molecular mechanisms involved in these epigenetic mechanisms of character origination. In genetic assimilation, phenotypic change arises directly as a phenotypic response to environmental perturbation, as in Waddington's famous ostrich callous example. The phenotype is *then* genetically assimilated by mutation of modifiers of the genetic determinants of the characters that interacted phenotypically to produce the initial change. In a similar vein, Newman and Müller talk about "pre-mendelian" phenomena in which a variety of interactions of cells or tissues with their physiochemical environments could result in new morphologies. Although there would have been a genetic basis for the *components* of these interactions, selection need not have favored genes to play a role in the epigenetically emergent characters. Genes play a role *after* character origination to integrate and stabilize characters produced epigenetically. Thus, Newman and Müller argue for a different time order in the role of genes in the epigenetic origination of characters in evolution than occurs in the molecular epigenetic processes discussed above that play a role in producing these characters in development. In their work, as in Waddington's genetic assimilation, the character comes first and the genetic integration and stabilization comes after.

Newman and Müller argue for the view that "different epigenetic processes have prevailed at different stages of morphological evolution, and that the forms and characters assumed by metazoan organisms originated in large part by the action of [conditional, nonprogrammed physico-chemical and tissue interactions in] such processes."[12]

In this kind of view, heredity is interpreted through the lens of development rather than the other way around, as a stage of evolutionary history that is

driven fundamentally by epigenetic character origination, not by genetic sequence change and molecular epigenetic control of sequence expression. Genes do play a role before the epigenetic interactions leading to character emergence, but not as determinants of the emergent characters.

Newman and Müller's perspective is explicitly anti-Weismannist. They complain that "in all the contending views [of character evolution] the notion that an organism's morphological phenotype is determined by its genotype is taken for granted. This tenet is also essentially undisputed in developmental biology, which today is commonly characterized as the study of 'genetic programs' for the generation of body plan and organ form."[12] So, the trick in pursuing their project is to avoid the logical attractor of molecular Weismannism: if epigenetic tissue interactions lead to new characters, the fact that those tissues had genetic (and molecular epigenetic) determinants before character origination shows that, ultimately, Newman and Müller's brand of epigenetics may be reduced to a molecular interpretation consistent with Weismannism. That is, there is a kind of regress argument against Newman-Müller epigenetics: for any epigenetic character origination, there must have been prior genetic determination of the component characters involved in the phenotypic interactions leading to the emergent character. A defense of Newman and Müller against the Weismannist regress argument involves pointing out that their work concerns the *evolution* of morphological characters, so the Weismannist regress can be traced all the way back to the origin of *all* "characters" at the origin of life. At the origin of life, however, Weismannism can be defended only by making the most extreme RNA world assumption that life began with a naked and complete ribozymic gene. Otherwise, there must have been some character origination that did not depend on genes in either the Mendelian sense of factors that follow Mendel's rules or the classical molecular sense of coding sequences. Put differently, regress arguments employing the Weismannist idea that genes are the ultimate, if indirect, causes of all phenotypes must fail if the regress leads to an origin of life without genes.

I do not pretend to know how the story of the origin of life will turn out. My point is simply that the different notions of epigenetics in play, whether at the molecular level or above, all turn out to depend on the fundamental Weismannist dichotomy of heredity and development. Whether the theoretical and empirical strategy for overcoming Weismannism is to think of development as a kind of heredity or heredity as a kind of development, the logic of Weismannism still frames the issues. I turn now to a different way of formulating a conception of heredity that does not assume Weismannism.[13,14]

HEREDITY *INTERTWINED WITH* DEVELOPMENT

Despite the dominance of the Weismannist perspective, it is clear that epigenetic phenomena do not easily fit. Some of them indicate flows of biolog-

ical information to the DNA as well as away from it. Some indicate pathways of "somatic" inheritance autonomous from the genetic pathway leading from DNA sequence to DNA sequence. There is a further point, beyond the uneasy fit to Weismannism that gives a clue to a new perspective, which is the fact that the variety of epigenetic mechanisms permits treating heredity from the point of view of development and development from the point of view of heredity. This is not licensed by Weismannism, which takes these simply as distinct processes with no relation other than their sharing a common cause in the genes.

If Weismannism indicates the relationship between germ and soma, as well as genotype and phenotype, as links in a chain of causes, perhaps a different perspective can be motivated with the metaphor of a rope of causation.[15] Instead of links between distinct entities, the rope metaphor suggests intertwined processes. Heredity and development are strands of this rope and each runs the whole length of the rope. We can regard the rope—that is, trace its path—from the point of view of either of the entwined strands, but either will take us the entire distance along the path. In addition, the spiraling path we trace as we travel the one strand that our experimental procedures have allowed us to study will cause us to neglect the path of the other strand. Genetic experiments will thus tend to ignore how developmental consequences arise, while developmental experiments will tend to ignore how genetic variation originates and is sorted (FIG. 3).

If heredity and development are the strands of a rope, what process does the rope represent? My answer is reproduction. A reproduction process involves the entwined processes of hereditary propagation and developmental emergence. The chain metaphor might suggest that reproduction is an event, a single connection between parent and offspring links, but the rope metaphor suggests an extended process. How can we think about reproduction as something occurring over the life cycle of a biological entity rather than as an event such as gametic or nuclear fusion or cellular fission? I suggest the following abstract picture:

Reproduction at its most abstract is the multiplication of entities with a material overlap of parts between parents and offspring.[13] Material overlap means that parts of the parents (at some time) become parts of the offspring (at some other time). Thus, reproduction is no mere transmission or copying of form—it is a flow of matter. At least some of the parts that flow from parents to offspring must have a special character: they must be mechanisms of development. A mechanism of development, at its most abstract, is a part with the capacity to acquire the capacity to reproduce. Thus, reproduction is the multiplication of entities in such a way that the parts transferred to the offspring confer on them the capacity to develop. And the capacity to develop is the capacity to acquire the capacity to reproduce.

This is a recursive structure, and its recursiveness captures what I mean by saying that heredity and development are intertwined in reproduction pro-

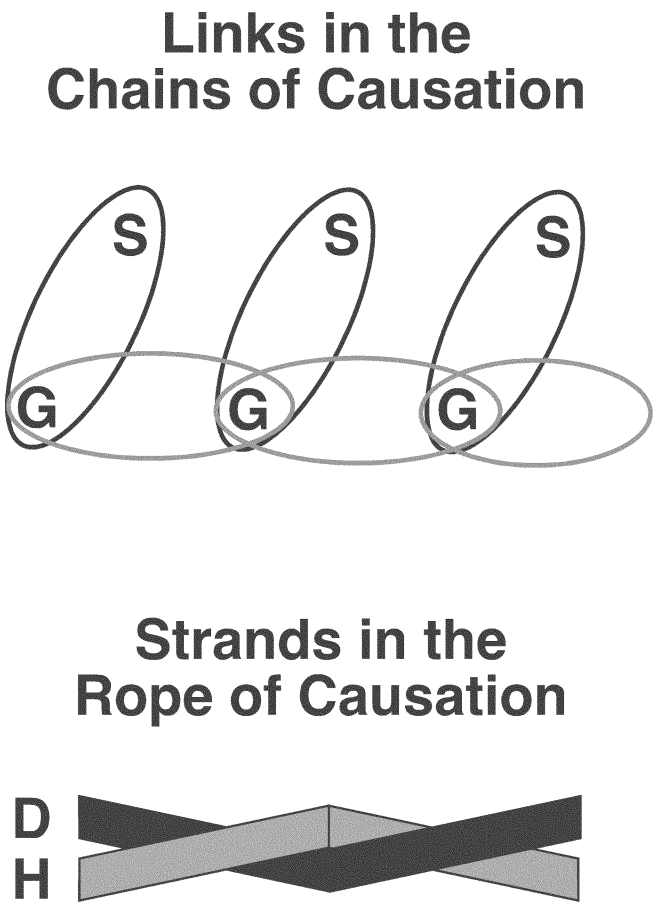

FIGURE 3. Chain versus rope models of biological causation. The typical chain of causation viewpoint (*top*) represents causes and effects as events linked in a chain. In the figure, there is a chain of genetic continuity and "idle" causal links extending from the germ in each generation to the soma that it causes. The discontinuity across generations between somata reflects the causal picture of Weismannism. The alternative rope of causation viewpoint considers heredity and development to be extended processes extending throughout life cycles and across generations. The distinction between them concerns the type of continuity traced rather than any fundamental distinction between continuous and discontinuous processes. Development, like heredity, must be continuous throughout the life cycle and so is represented as intertwined with heredity.

cesses. Heredity is the correlation between parents and offspring due to reproduction. Reproduction transfers the capacity to develop. Development is the acquisition of the capacity to reproduce. As long as there is a null condition somewhere in the system, that is, there is something that can be born *with*

the capacity to reproduce without needing to *acquire* that capacity through development, then reproduction can be recursively analyzed.

Now, what is the scientific value of such an abstract analysis of reproduction, heredity, and development? I want to make two points. The first point concerns material overlap. Any reproduction process, as I have defined it, involves so-called "epigenetic" inheritance because no reproduction process can result merely from a flow of genes: other material flows from parent to offspring are required to make a new entity with the capacity to develop. Jablonka and Lamb described three categories of epigenetic inheritance system: the chromatin-marking systems mentioned above and also steady-state "metabolic" inheritance systems and structural inheritance systems.[10] The best known case of structural inheritance that does not involve chromatin marking is Sonneborn's structural inheritance in paramecia. Sonneborn showed that cutting out and reinserting, in a rotated orientation, a piece of the surface cortex of the organism resulted in the inheritance of the "epimutated" ciliary organization. That is, paramecia with a rotated patch having cilia pointing the "wrong" way passed the trait on to their offspring. Steady-state systems involve the perpetuation of metabolic patterns due to the chemical equilbria that these systems produce. The propagation of the system results from the way metabolisms are multiplied by cell division. Because metabolisms are autocatalytic and fluid,[16] their bulk division into two spatially separated parts causes the metabolic steady-state to be transmitted to both offspring. "Mutation" of the state through environmental perturbation can result in a new, heritable steady-state.

Both these kinds of epigenetic inheritance depend on the fact that reproduction always involves material overlap of parts, in this case of the epigenetic parts as well as of genetic parts. If a steady-state or structural system plays a developmental role in the sense of (helping to) cause the acquisition of the capacity to reproduce, then they are mechanisms of development as specified above and the system containing them is a "reproducer."[13,14] In other words, if every cause that is not genetic is epigenetic (as implied by Weismannism), and if some epigenetic causes form inheritance systems because they involve the transfer of material parts that confer developmental capacities, then the fact that all reproduction processes require transmission of such epigenetic causes together with Weismannism entails epigenetic inheritance. That conclusion sounds too strong, but it is only because Weismannism is too strong. It makes every developmental entity beyond the genes that is transmitted in reproduction a candidate inheritance system.

The second point about the scientific relevance of the reproducer perspective is that it is entirely independent of genes and nucleic acids. It was, in fact, designed to be independent of genes in order to describe the problem of evolutionary transition—the evolutionary origin of new levels of biological organization—without reference to "replicators."[17] From this perspective, we can describe evolutionary transition in a way that does not assume that genes

existed before the existence of systems having heritable variation, that is, prior to the existence of units of evolution, which is desirable if one wants a noncircular evolutionary theory of the origin of genes.

The relevant implication here is for how we can think about the relationship between this abstract reproducer perspective and genetic inheritance. This will allow us to adjust the picture of epigenetic inheritance in relation to both reproduction and conventional genetic processes without falling back on the logic of Weismannism.

If biological reproduction is multiplication with material overlap of mechanisms of development, we can define inheritance as reproduction with material overlap of *evolved* mechanisms of development. In other words, to count as an inheritance system, the component parts of developmental mechanisms must have evolved to play that developmental role. In this definition, there is still no reference to genes. Evolution can occur without any inheritance system at all because evolution can operate on reproducers in virtue of the heritability that results from material overlap simpliciter. A more fine-tuned sort of adaptive evolution is possible once the mechanisms of development have evolved, since their evolution brings specialization, division of developmental labor, ecological diversification, and stabilization of the new level of organization to disruption from uncooperative components below whose reproductive success is now dependent on the new, higher level.

A further innovation is for evolved mechanisms of development to be articulated into a very specialized kind of structure, that of a *coding* mechanism of development. I cannot here go into a full account of what constitutes a coding mechanism, but a core property of all such systems is the evolution of autonomy from constraints imposed at the lower level. In general, biologically autonomous mechanisms are ones that are released in some respect, to some degree, from chemical constraint—a property I will call "stoichiometric freedom." Stoichiometric freedom is part of the basis upon which sequences constitute biological rather than merely chemical properties of macromolecular polymers. For present purposes, we can simply take the modern, DNA-based system of genetic coding as an exemplar. Call those inheritance systems in which the mechanisms of development transferred in reproduction are coding mechanisms *genetic* inheritance systems.

From these definitions, a picture begins to emerge. Reproduction is the most general sort of process in which heredity and development are entwined. Its basic structure results from material overlap of parts that have autocatalytic or "autopoietic" (self-organizing and self-maintaining) organization.[16,18] Inheritance is a special case of reproduction processes in which the developmental mechanisms have evolved to serve developmental functions. Genetic inheritance is a special case of inheritance in which the developmental mechanisms have evolved to the "coding" grade of organization.

From this point of view, epigenetics describes a variety of inheritance systems that are not genetic. But it does not require defining "epigenetic" in

terms of what counts as genetic. Indeed, genetic inheritance need not have evolved in order to have epigenetic inheritance. The relations between reproduction, epigenetic, and genetic inheritance is in terms of the relation between the general and the special, not in terms of causal relations between the kinds of systems (other than their evolutionary causal relations). By the same token, the reproducer perspective can interpret molecular and physicochemical ideas of epigenetics, provided that these are taken to describe both hereditary and developmental aspects of a process and not as states of a given hierarchical level biological organization.

Finally, I come to the topic identified in the title of this paper.

WHAT IS "EPI" ABOUT EPIGENETICS?

From the Weismannist point of view, everything besides DNA sequences and sequence variation is "epigenetic." Weismannism renders the category so broad as to make it virtually impossible to comprehend any kind of general theoretical order in the phenomena, much less to search for simple rules of order, such as the early geneticists found in Mendelism. On the strict Weismannist interpretation, genes are monarchs in the kingdom of development since they don't even change their own clothes—even genetic mutation turns out to be epigenetic. The irony is that by making genes the causal basis of everything, genes alone can explain nothing.

We have seen that the various kinds of epigenetic projects can be sorted into those that treat heredity as development and those that treat development as heredity. They are thus attempts to find middle-range theories that try to explain some salient phenomena, but not by means of a single kind of developmental resource—the genes—nor by reference to an unworkable holism. However, these efforts are still hampered by Weismannism in conceptualizing what counts as epigenetic.

I have adopted a different strategy by developing an alternative perspective. On the reproducer perspective, we can take the prefix "epi" almost literally, meaning "upon, at, on the ground of, in addition," because we are taking a material process perspective rather than a formal, structural one. What is epi in epigenetics is what is literally "upon" the genes. Chromatin-marking systems are good examples of epigenetic systems. In so far as the methyl groups or the transcription factors or the histones are "upon" the genes, they are epigenetic. Of course, the *inheritance* of these systems cannot rest solely upon the genes, since they cannot be inherited except in the context of structural and steady-state inheritance of the molecular apparatus necessary to methylate and demethylate DNA in the offspring. But we need not call all these forms of inheritance *epi*genetic. From the reproducer perspective, this is simply inheritance.

So, while the Weismannist perspective labels nearly everything epigenetic and urges explanation of nearly everything in terms of nearly nothing, the re-

producer perspective labels much less epigenetic, leaving room for a cooperative relationship among geneticists, epigeneticists, and those of us interested in the origin and evolution of reproduction and development.

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