The Ingredients for a Postgenomic Synthesis of Nature and Nurture

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Abstract
This paper serves as an introduction to the special issue on "Reconciling Nature and Nurture in Behavior and Cognition Research" and sets its agenda to resolve the 'interactionist' dichotomy of nature as the genetic, and stable, factors of development, and nurture as the environmental, and plastic influences. In contrast to this received view it promotes the idea that all traits, no matter how developmentally fixed or universal they seem, contingently develop out of a single-cell state through the interaction of a multitude of developmental resources that defies any easy, dichotomous separation. It goes on to analyze the necessary ingredients for such a radical, epigenetic account of development, heredity and evolution: 1. A detailed understanding of the epigenetic nature of the regulatory mechanisms of gene expression; 2. The systematical questioning of preconceptions of 'explanatory' categories of behavior, such as 'innate' or 'programmed'; 3. Especially in psychological research the integration of the concepts of 'development' and 'learning', and a richer classification of the concept of 'environment' in the production of behavior; 4. A fuller understanding of the nature of inheritance that transcends the restriction to the genetic material as the sole hereditary unit, and the study of the process of developmental niche construction; and last 5. Taking serious the role of ecology in development and evolution. I hope that an accomplishment of the above task will then lead to a 'postgenomic' synthesis of nature and nurture that conceptualizes 'nature' as the natural phenotypic outcome 'nurtured' by the natural developmental process leading to it.

Introduction

A scientific understanding of the nature and history of living beings depends crucially on our understanding of the most basic of biological processes that brought them about: development. Since ancient times this process has captured the imagination of scholars but has eluded a satisfactory explanation or consistent framework until today. From the beginning, the main problem in the interpretation of development has been the question of whether organisms are the result of the emergence of structures and processes not entirely predictable from the undifferentiated properties of the embryo, or whether they

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merely unfold or mature out of something preformed or predetermined from the beginning. The term development with its literal meaning of ‘unfolding’ unfortunately suggests this latter interpretation. Today’s received view of development attempts to reconcile both visions: a (multicellular) organism begins as one cell packed with ‘innate’ information of how to build the phenotype, from which the final form emerges in interaction with the ‘acquired’ influences from the environment.

This ‘interactionist consensus’, however, perpetuates the nature-nurture debate by maintaining its inherent dichotomy. Despite being declared dead many times, this debate is alive and well today in the dichotomy of nature as the genetic, and stable, factors of development, and nurture as the environmental, and plastic influences (Kitcher, 2001). The term *nature* is applied to those traits that seem genetically determined, fixed in their final form and are present in all cultures, as in discussion about Human Nature; the term *nurture*, on the other hand, implies variable rearing conditions, including human culture. In contrast to this received view, I want to promote the idea that all traits, no matter how developmentally fixed or universal they seem, contingently develop out of a single-cell state through the interaction of a multitude of developmental resources that defies any easy, dichotomous separation.

One of the foremost aims of a new conception of development is therefore to challenge the widely held view that the physiological or behavioral phenotype derives from *either* nature *or* nurture, or from *both* nature *and* nature. Both the exclusive and the additive model make no biological sense whatsoever, since no genetic factor can properly be studied independent of, or just in addition to, the environment. The same is true for the environment, which in itself is a concept that includes a wide variety of very different causes and factors, from the genomic environment of a gene, over its chromatin packaging and cellular context, up to ecological, social and cultural influences upon the whole organism. The message of this paper will be that the familiar dichotomies, of which many are so fond, stand in the way when attempting to study and understand development. Those different dichotomies, such as innate-acquired, inherited-learned, gene-environment, biology-culture, and nature-nurture, are not just inappropriate labels in themselves but they do not map neatly onto each other: *genes* do not equal innate, biology, or nature, and neither does the environment stand for acquired, culture, or nurture. So-called innate traits include effects of the organism's extended inheritance of epigenetic factors, which are reliably reproduced with the help of ontogenetic niche construction. As a matter of fact, no developmental factor coincides with either nature or nurture, or so I contend. Instead I advocate new and scientifically more useful distinctions between developmental resources, and ultimately promote the understanding of 'nature' as the natural phenotypic outcome 'nurtured' by the natural developmental process leading to it.

The papers of this issue are the outcome of an international symposium on "Reconciling nature and nature in behavior and cognition research" in March 2007 at Indiana University, organized by Colin Allen and myself and funded by Indiana University. Part of its objective was to explore interdisciplinary frontiers in this controversy that may as well promise new insights into the human condition and the idea of 'human nature' (see the papers by Robert and Machery in this issue). It was *not* our intent to have the speakers, who came from different sub-disciplines of cognitive science (including philosophy and biology), merely debate why a certain behavior or cognitive competence is due to either nature or nurture, but instead to use the symposium as an opportunity to reflect on the empirical, semantic, conceptual, methodological/epistemological and metaphysical issues that may help to *resolve* this unhealthy debate. The symposium, we hoped, would provide the perfect venue to think aloud about new directions current research should take and how the proposed directions could be integrated. The current issue is the outcome of these reflections.

To resolve the nature-nurture debate with a newly emerging view of development several distinct but related sub-problems need to be addressed (Stotz, 2006a) that I shall introduce and discuss in this paper:

1) An understanding of development requires a deep knowledge not only of the sequences of the genome but of their regulated expression. A realistic view of gene activation is of pivotal importance since better than any other developmental process it

manifests in detail the intricate interaction between genetic material and other developmental factors (Stotz, 2006a, 2006b). In addition, a fully mechanistic picture guards against conflating explanations of the role of genes in development with an explanation of the complete process of development.

2) We need to systematically question preconceptions of 'explanatory' categories of behavior, such as innate, acquired, genetically determined or programmed, or even just ascriptions such as 'genetic' trait or disease, all of which obscure the necessity of investigating developmental processes in order to gain insight into the actual mechanisms of behavior (see Moore this issue). In addition such preconceptions are prone to commit the 'phylogenetic fallacy', which conflates evolutionary and developmental explanations. The classical research technique to divide the 'innate' from the 'acquired' are so-called 'deprivation experiments', in which the exposure of the developing organism to certain – mostly 'obvious' – environmental parameters are controlled. However, it does not provide evidence for some general property of 'independence of the environment. Restricted housing of cowbirds, for instance, reveals innate artifacts without illuminating actual developmental pathways (see West and King, this issue; Griffiths and Machery, this issue; but also Weinberg and Mallon, this issue).

3) Especially in psychological research the concepts of 'development' and 'learning' need to be integrated instead of being studied in isolation and by distinct research traditions (see for instance Jones, this issue; Moore, this issue). This involves a richer classification of the influence of the environment starting with basic environmental influences, e.g. of gene expression or cellular behavior, over low-level sensory processes and real individual experience, to full-fledged individual and social learning (Stotz & Allen, Forthcoming). Careful investigations of the origin of behavior demonstrate the need to distinguish between bioavailability as opposed to simple exposure to stimulation. The distinction is between what an animal has the capacity to do as opposed to how social/ perceptual systems function to gate what is available to be learned (see for instance West and King, this issue).

4) We require further a fuller understanding of the nature of inheritance that transcends the restriction to the genetic material as the sole hereditary unit. Instead, heredity must be more widely understood as the processes providing transgenerational stability through the

reliable availability of developmental resources in the next generation either through its transmission or reproduction. This includes maternal and paternal (parental) effects, epigenetic factors in a narrow and wide sense, behavioral, cultural and symbolic inheritance systems. Many of these processes come together to form the ontogenetic niche for the offspring (see West and King, this issue; Jablonka and Lamb, this issue; Alberts, this issue).

5) Ideas such as (developmental) niche construction and adaptive phenotypic plasticity, and the discussion of the difference between mere exposure to stimulation versus bioavailability suggest that ecological validity will be an indispensable factor for studying development and evolution, and how both processes interact with each other. The long history of reliance on restricted investigative methods in combination with highly insensitive model organisms has given genetic explanation unwarranted dominance by masking the prevalence of nonlinear interactive effects between a multitude of developmental resources (see West and King, this issue; Robert, this issue). Also, a wider understanding of inheritance that often relies on the provisioning by organisms underscores the importance of development for answering evolutionary questions (Jablonka and Lamb, this issue).

6) A new epigenetic understanding of development encompassing the organism in its developmental niche takes seriously the idea that all traits, even those conceived as 'innate', have to develop out of a single-cell state through the interaction between genetic and other resources of development. Such a view should ultimately resolve the dichotomy between preformationism and epigenesis, and instead provide us with a real postgenomic[2] synthesis of development, evolution and heredity.

1. Molecular Epigenesis

> "A true appreciation of development will never emerge without a focus on the genome and its regulation by the environment, and it is precisely this field of biology that most forcefully demonstrates that the mere presence of a genetic variant, in all but the

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[2] The term Postgenomic is simply referring to the era of biological research after the availability of mass-sequencing datas through large-scale genome projects.

> extreme cases, is not sufficient to explain variation at the level of the phenotype. ... It is not the mere presence of a gene that is of functional importance, but rather its expression. […] The structure of the genome highlights the importance of gene-environment interaction." (Meaney, 2004: 5)

Genuine understanding of development depends on a knowledge not merely of the sequence of the genome, but of the regulated differential expression of these sequences. Genetic activity is involved in most biological processes, but so are non-genetic activities. Explanations that list only interacting genes are vacuous, or at the very least one-sided and incomplete. Postgenomic biology has brought with it a new conception of the 'reactive genome' – rather than the active gene – which is activated and regulated by cellular processes that include signals from the internal and external environment (Stotz, 2006a, 2006b). This is not the place to report in detail results that have only very recently come to light concerning the mind-numbing complexities of the expression of genes during development; instead a few examples should suffice. The last decade of whole-genome sequencing led to the formulation of the so-called N-value paradox that the number of genes does not increase to match increases in organismal complexity. Instead, the ratio of non-coding DNA rises, and so does the number of functional, regulatory roles played by non-coding DNA and RNA that help to translate, with the active help of instructive environmental signals, sequential information encoded in the genome into developmental complexity (Mattick, 2004). In other words, the more complex an organism, the more complex the expression of its limited number of coding sequences. This lends support to Michael Meaney's conclusion that what is of particular importance during development is not the *existence* of some genes but their differential time- and tissue-dependent *expression*. In the last two decades development has become equated with *differential gene expression*, but what is hidden behind this equation is the complex network of molecules other than DNA (such as proteins and metabolites), cellular structures, 3-dimensional cellular assemblages and other higher-level structures that control or are otherwise involved not only in the differential expression of genes but in a wide range of other developmental processes decoupled from the direct influence of DNA sequences.

In eukaryotes, DNA is part of a densely packed chromatin structure, which allows it to fit neatly into the nucleus, but which is also a major mechanism to control gene expression. The DNA's weak chemical bond to the histone proteins, around which it is tightly wrapped to form nucleosomes like beads on a string, needs to be broken down in order to free the DNA molecule to undergo new bonds with transcription factors. Hence the default position of DNA in eukaryotes is no expression unless expression is activated. Several large complexes of transcription factors and several other accessory proteins such as chromatin remodeling factors are needed in order to proceed with the transcription of a stretch of DNA. Beyond the activation of DNA an ever-expanding array of processing and targeting mechanisms are coming into play that not only determine the final gene product but which amplify the repertoire of protein products specified through the eukaryotic genome. We have to understand that genes are not straightforward, structurally- or functionally-defined entities, or even mixed functional-structural entities. Instead, genes are ''things an organism can do with its genome'' (Stotz, 2006b: 905): they are ways in which cells utilize available template resources to create biomolecules that are needed in a specific place at a specific time. The same DNA sequence potentially leads to a large number of different gene products and the need for a rare product calls for the assembly of novel mRNA sequences. Hence the information for a product is not simply encoded in the DNA sequence but has to be read into that sequence by mechanisms that go beyond the sequence itself. Certain coding sequences, plus regulatory and intronic sequences, are targeted by transcription, splicing, and editing factors (proteins and functional RNAs), which in turn are cued by specific environmental signals. Regulatory mechanisms determine not only whether a sequence is transcribed, but where transcription starts and ends, how much of the sequence will be transcribed, which coding and noncoding regions will be spliced out, how and in which order the remaining coding sequences will be reassembled, which nucleotides will be substituted, deleted, or inserted, and whether and how the remaining sequence will be translated. Many of these mechanisms do not simply produce alternative protein-coding transcripts. A sequence may be transcribed into several parallel, coding, and noncoding transcripts. The factors that interactively regulate genomic expression are far from mere background conditions or supportive environment; rather they are on a par with genetic information since they co-specify the linear sequence of the gene product together with the target DNA sequence. Networks of genome regulation, including several different kinds of gene products and instructional environmental resources, specify a range of products from a gene through the *selective use* of nucleotide sequence information and, more radically, the *creation* of nucleotide sequence information. This thesis of "molecular epigenesis" argues that even at the molecular level no strict preformationism is warranted since gene products are not specified through DNA sequences alone (Stotz, 2006a).

I again would like to stress the importance of environmental factors in most mechanisms of gene expression. Even though one might argue that most work is done by proteins and other gene products, it generally holds for all eukaryotes that

> "in the absence of their respective inducing signal, transcriptional regulators tend not to be found in the nucleus with (in the case of activators) their activating regions free to work. Rather, activating regions are masked … or … the regulators are maintained outside of the nucleus, until the inducing signal is detected". (Ptashne & Gann, 2002: 67).

Many genes require for their differential activation and selection the integration of a proper combination of several environmental signals, and this combination of signals, together with the presence of a particular combinations of activational factors, controls which exact sequence will be transcribed, and how much. It will also affect cotranscriptional processes such as alternative splicing and RNA editing. The 'same' genes can therefore be expressed in many distinctive ways by different set of signals and activators.

These complicating factors of gene expression are not the only reason why it is important not to regard development as *nothing but* gene action and activation. Genes have an important role in development, but their role can be properly understood only within the larger system that holds controlling influence over them. Jason Scott Robert summarizes this attitude:

> "To take development seriously is to take development as our primary explanandum, to resist the substitution of genetic metaphors for developmental mechanisms … The translation of embryology's hard problem (how a specific organism arises from a single, relatively homogenous cell) into a problem about gene action and activation generates explanations at the level of genes; but these explanations solve (or, rather, begin to solve) the subsidiary problem of the role of genes in development, not the problem of development as such. … There is indeed good reason to believe that genetics reduces to development, and not the other way around." (Robert, 2004: 22)

2. The Reconceptualization of 'Explanatory' Concepts and Categories of Behavior

This section attempts to analyze a few overused concepts, dichotomies, metaphors, and shorthand formulations that are commonly used in the explanation of behavior. It claims that these, instead of being useful characterizations of behavior or shorthand classificatory schemes they sidestep deep explanatory analyses of developmental processes and therefore prevent useful and necessary further research into the nature and origin of characteristics or traits that we want to explain. To name just a few of such explanatory concepts: Nature-nurture; innateness; interaction; information; program; inheritance; gene action; maturation; genes-and-environment. I advocate here the replacement of these placeholders by real explanations with specified mechanisms of developmental interaction.

The main problem with all allegedly explanatory categories and concept of behavior, such as instinctive, learned, or genetically programmed, is that they block further investigations into the real ontogenetic and evolutionary causes of a behavior just by their very nature of purporting to explain while really doing nothing but labeling it. After careful and often arduous empirical investigation, all apparently 'innate' processes operating to regulate behavior have turned out to involve epigenetic or experiential factors (Blumberg, 2005). As Paul Griffiths has argued, the vernacular concept of innateness can imply three different and unrelated things, namely the developmental fixity (non-involvement of experience), species-typicality or universality, and adaptedness or normativity of a trait (Griffiths, 2002; see also Griffiths & Machery, this issue; Weinberg & Mallon, this issue). All three of these are sometimes equated with genetic determination. Beside the fact that I want to argue against the existence of any genetically determined trait; a deeper investigation of these three characteristics is able to show their relative independence of each other (Griffiths, Machery, & Linquist, Submitted). Evolutionary adaptations need not be developmentally fixed, independent of life experience, and hard to change but can instead be phenotypically plastic, as is the case with many highly environmentally sensitive polyphenisms, distinct phenotypes that are elicited by different environmental conditions (see below section 4). Nor do adaptations need to be species-typical or universal, since they can result from frequency-dependent selection, where a trait is only adaptive if a certain percentage of the population carries it. Species-typical or universal traits are not necessarily the result of natural selection but can be dictated by strong physical or developmental constraints that render them hard or even impossible to change, as for instance been shown by many examples uncovered by the new "physicoevolutionary" approach, or by research into the homologies of organisms (Gilbert, 2003; Newman, 2003). Last but not least, universality need not be and often is not due to the developmental fixity or experience-independence of a trait. It may be, and often is due to the reliability of certain experiences, which the organism needs to have to develop a trait. Song learning in many bird species is a case in point. In some species of birds, such as the brown-headed cowbird, all birds of a population sing the same song (while in many others the songs of individuals may differ substantially, such as in the Australian Lyre bird, or the Indian Common Mynah). While such instances have formerly been taken as support for the genetic determination of song 'learning', we now know that all individuals have to be exposed to other members of their species in order to acquire their population-specific song. The story in cowbirds, which are nest parasites and are therefore not even raised by their own parents or even a member of their own species, is even more complicated and intriguing than with birds which acquire the song from their parents, but the details of how they acquire their song need not interest us here. Suffice it to say that cowbirds nevertheless always learn to sing the particular dialect of the population they belong to because of the reliability with which they meet, recognize, and flock with members of their own species and are therefore exposed to the right stimulating experience when maturing (Freeberg, West, King, Duncan, & Sengelaub, 2002; West, King, & Duff, 1990).

The use of metaphors can be understood as another form of stand-in for a full-fledged explanation in causal terms. A metaphor is a rhetorical trope that enhances a description of a subject through the application of implicit and explicit attributes from a well-known subject taken from a different domain. The use of a metaphor tacitly involves and assumes as valid all the familiar logical implications, consequences and interrelations between the concepts used and metaphors" and the described concept (Kurakin, 2005: 46). A famous example is the ascription of properties of a 'program' to genes, the genome or the genotype. Since the beginning of molecular genetics coincided with the beginning of the informational and computational era this seemed to be a natural move. The postgenomic era, however, brought with it an insight in the structural complexity of the genome and the heterogeneity of the genetic material to which a computational and also a classico-mechanistic interpretation seem illfitted. More appropriate seems

> "an alternative conceptualization of cell differentiation and development (…) where the developing organism is viewed as a dynamic self-organizing system of adaptive interacting agents. This alternative interpretation appears to be more consistent with a probabilistic nature of gene expression and the phenomena of cell plasticity, and is coterminus with the novel emerging image of the cell as a self-organizing molecular system" (Kurakin, 2005: 46).

The program metaphor, however, has stuck. This metaphor inspired generations of biologist to describe whole cellular or organismic behavior in terms of gene networks and programs (Luscombe et al., 2004; Weber, Polen, Heuveling, Wendisch, & Hengge, 2005; Wilkins, 2008). In his philosophical gloss on this kind of biological work Alexander Rosenberg claims that the development of *Drosophila* can be exhaustedly described in a '*Drosophila* developmental program' following "Boolean switching rules in a small number of relatively simple linear programs". Rosenberg writes: "It bears emphasis that I do not mean this claim to be metaphorical. As I shall illustrate and then argue, the genes literally program the construction of the *Drosophila* embryo in the way the software in a robot program the welding of the chassis of an automobile" (Rosenberg, 2006: 61-2).

Rosenberg disregards the fact that models of gene networks such as the ones reproduced in his book are in reality only a convenient shorthand for the elucidation of functional co-dependencies of genes, and an intentional simplification of the reality of these dependencies. There is no mention that this shortcut collapses a multi-molecular network, which includes genes, regulatory DNA sequences, a large variety of gene products, intra- and extra-environmental signals, and the contingent history of the cell, onto a single dimension of structural and regulatory (protein-coding) genes. This is deliberate, because it makes the genome *appear* to constitute a program (with the exception that genetic 'programs' rarely ever crash like computer programs!). It also has to be acknowledged that Boolean models offer only a rather crude representation of real world gene networks in that they can only describe discrete, instead of continuous changes in the cell (Schlitt & Brazma, 2006).

The time- and tissue-dependent activation, selection and even creation of the relevant nucleic acid sequences from the 'same gene' requires, among other necessary factors, instructional environmental resources. The regulatory network integrates many different aspects of cell activity (transport, cytoplasmic enzyme activities, and energy metabolism) into the transcriptional and posttranscriptional decision. This makes it literally impossible to separate physiology from genomic regulation in any living cells (Shapiro, 1999). The common assumption of predetermination inherent in many such descriptions of gene action begs the question of what determines changes in a sequence of activities; it is always the model rather than the reality which seems to suggest a dictatorial rather than a democratic vision of cell action. I want to argue that what appears as a 'program' is constituted *a posteriori* by a network of interactions within the whole cell.

There are of course no hard-core genetic determinists around who would seriously dispute the necessity of any 'environment' for the production of a trait. A more common version defends genetic determinism against a background of a 'normal' or 'standard' environment in which a gene is tightly correlated with a behavioral trait. In many such cases elucidating the details about a 'normal' environment – instead of just taking it for granted – would have shown how much the organism or its parents must invest in order to reliably provide the stable environmental resources that allow for a predictable pattern of gene expression (i.e. a tight correlation between gene and trait). I will turn to the importance of developmental niche construction in section 4. Here I only use the notion to provide further support for the idea that similar to a self-organized ant colony, agency is located neither in the genome nor the environment but in the organization of all factors in an intricate network.

3. Understanding and Integrating Development, Learning, Experience and Environment

In the last decade it has become fashionable for cognitive comparative psychologists to study animal behavior in an 'integrated' fashion to account for both the 'innate' and the 'acquired'. I argue that these studies of the animal learning against an evolutionary background, instead of really integrating the concepts of 'nature' and 'nurture', rather cement this old dichotomy. They combine empty nativist interpretations of behavior systems with blatantly environmentalist explanations of behavior acquisition. While in some areas of biology interest in the relationship between behavior and development has surged through topics such as parental effects, extragenetic inheritance, and phenotypic plasticity, this has gone almost completely unnoticed in the study of animal behavior in comparative psychology, and is frequently ignored in (cognitive) ethology too. Reasons for this may include the traditional focus on the function of behavior in its *species-specific* form in *adult* animals, which can favor a preformationist or deterministic conception of development, or generally the separation of psychology from biology. In psychology the process of learning is often set against the maturational unfolding of the young to the adult instead of being understood as part and parcel of behavioral development, either as a process that drives or explains certain developments, or a process influenced by other developmental processes. One of the necessary prerequisites to the integration of nature with nurture is to clarify the relationship between the concepts of learning and development, and to investigate whether and how both concepts can be usefully deployed in the study of animal behavior. This will require the full integration of the concept of learning into a much wider concept of individual experience, or if this term is itself already understood as a higher-order sensory process only applicable to higher organisms, then another more basic concept such as sensation or sensing (Ginsburg & Jablonka, 2007).

What has all this talk about biological development to do with cognitive or behavioral phenomena? The symbolic approach of ‘good old-fashioned artificial intelligence’ (GOFAI) (Haugeland, 1985) that sees a principled distinction between the cognitive and the non-cognitive, or the mind and the body, investigates cognitive processes as if they were disembodied and decoupled from the world and consisting of symbolic manipulation of abstract and enduring mental representations of events in the world. This representational stance can’t or won’t deal with the emergence of such symbolic representation out of biological processes, and therefore usually goes hand in hand with a *nativist* understanding of development. In contrast, the embodiment and dynamical systems paradigm understands cognition as emergent, embodied, embedded, situated, and softly assembled action, and attempts to break down the distinction between sensorimotor activity and cognition. In other words, this view is much more conducive to the epigenetic understanding of life and history proposed by the developmental systems perspective that refuses to partition the phenotype into genetic, morphological, psychological and social levels. These two related perspectives, both of which focus on explanations of how novel properties can emerge, complement each other: they investigate ‘behavior’ as the *product* of development but also as the *process* through which development takes place. On the one hand, the developmental systems theory grounds cognition in developmental processes. On the other hand, dynamical systems theory attempts to ground development in cognitive processes.

Questions about which species are capable of which forms of learning are typically treated as if organisms come to the task as fully-formed representatives of their species. Thus questions about, for example, the imitative capacities of primates rarely take individual development into account (Jones, 2005, see also Jones, this issue). In fact, it is widely believed on the basis of non-developmental studies that monkeys aren't capable of genuine imitation. But the importance of development is underscored by experiential findings with human-reared or enculturated apes that show the differential effects of enculturation in human socio-cultural environments on the development of a whole range of capacities in great apes. Among those are many that are theoretically consigned to humans alone, such as mental representational capacities and a whole range of social cognitive capacities like intentional understanding, empathy, and ‘true imitation’ (see also Bering, 2004; Call & Tomasello, 1996; Furlong, Boose, & Boyson, 2007; Tomasello & Call, 2004). In a recent paper Povinelli and collaborators strongly urge taking the discontinuities between humans and apes more seriously, especially those regarding higher-order, systematic, relational capabilities of a physical symbol system. However, just as with most of traditional cognitive science, they confound cultural symbolic achievements with individual cognitive competencies. By not allowing any explicit role for learning and development their core rationale for claiming a discontinuity between human and on-human primates rests on a hybrid symbolic-connectionist, formal model of cognition, LISA. Such models are criticized by an embodied stance as a quite unrealistic model of cognitive growth (McGonigle & Chalmers, In Press; Penn, Holyoak, & Povinelli, In Press).

In most work within comparative psychology, the basic classificatory scheme is methodological and not tied to recognizing the shortcomings of the operationalism underlying the traditional classification scheme. For instance, Grau & Joynes argue for a ‘neurofunctionalist’ approach, which seeks to classify learning in terms of both neural mechanisms and adaptive function. Their results with rat spinal cords suggest that even in the spinal cord, “experience” has lasting effects on the capacity of neurons to respond adaptively to future environmental conditions. The basic cellular mechanisms for learning and memory are highly conserved between invertebrates and vertebrates (Burrell & Sahley, 2001) and may even go further back in evolutionary history. Furthermore, the NMDA receptors involved in the synaptic plasticity of neurons use proteins for binding amino acids that are highly conserved from bacteria (Kuryatov, Laube, Betz, & Kuhse, 1994). Even the simplest organisms, bacteria, respond differently to similar configurations of cues in their surroundings on the basis of their specific life experiences. But the concept of bacterial learning may be no more than a philosophical abstraction; do bacteria *really* learn? The answer you give, of course, depends very much on your definitions of learning and experience. Not if learning is restricted to organisms with nervous systems that connect sensory to motor systems, and that extract from the environment information for action (behavior narrowly defined). Possibly yes, if 'environment' is understood as the source of a "quite heterogeneous mix of resources called experience" extracted by a wide variety of means, only one of which is sensory, and if knowledge and means for behavior derive from more than what is known to the senses (Moore, 2003: 350).

Central to the project of synthesizing development and learning is to identify types or token of epigenetic interaction, the role of experience and learning in the development of particular traits and in development in general, and the role of development in the phenomenon of learning. We need to ground the process of learning in development, and development in cognitive processes. As Samuelson and Smith have noted, "coupling the dynamics of perceiving and remembering with the dynamics of development will lead us to a more complete theory of knowledge and its development" (Samuelson & Smith, 2000: 98). From a psychobiological perspective, learning appears as a category within an overall framework of development as the lifelong, adaptive construction of the organism-environment system. Taking the idea of phenotypic plasticity seriously may lead to a conception of development as a lifelong process of 'learning' or 'acquiring' an adaptive mode of living in a partially constructed environment. And learning as the acquisition of novel behavior and gain of knowledge about the environment becomes synonymous with developing. In a systems view of development learning is certainly just one among many processes in which experience influences behavior. This new synthesis should help to overcome the age-old dualism between the innate and the learned. Something may not be learned in the strict sense but it is still acquired in the sense that some environmental factors will have played a pivotal role in its origin. A trait may be learned and is still reliably reproduced generation after generation. This is not to say that there aren't differences between developmental trajectories. It is to call for the development of scientifically more fruitful distinctions.

4. From Extended Inheritance to Ontogenetic Niche Construction

> "The triumph of the reductionist path, from the instrumental particularization of heredity, through the hardening of the particles as material genes, to the resolution of the heredity material in molecular terms, could not, in the final analysis, provide the answer to the plight of inheritance. Heredity is a property immanent to living systems and needs the perspective of the life sciences." (Falk, 2000: 339)

Transgenerational stability need not rely on the faithful transmission of DNA alone. Natural selection selects for adaptive traits or phenotypes, which are always derived from the non-linear interaction among a range of diverse developmental resources. Their organization frequently exhibits phenotypic plasticity, a capacity that allows the organism to react adaptively to different environmental conditions (Pigliucci, 2001; West-Eberhard, 2003). The stable inheritance of this adaptive phenotype depends on the reliable transmission of all the necessary developmental factors across generations. In other words, phenotypic plasticity relies on a stable 'developmental niche' which is faithfully reconstructed by the species, the parent and the organism itself (West & King, 1987). The subject of selection is the whole developmental system (Oyama, Griffiths, & Gray, 2001b).

Inheritance is the reliable availability of developmental resources for and in successive generations either through transmission or reconstruction. The rise of classical genetics produced the theory of the genetic material in the germ line as the only factors faithfully transmitted from parent to offspring; inheritance became synonymous with genetic inheritance. In section one I have argued for the thesis of molecular epigenesis: "Even for the clearest examples of molecular genes such as those traditionally thought to specify polypeptide sequence, epigenetic change ensures that nucleotide sequence alone is not sufficient to predict whether a polypeptide product will be produced or, if it is, what the resulting sequence of amino acids will be" (Burian, 2004: 60). Regulatory mechanisms of genome expression amplify the literal coding sequence of the 'reactive genome' by providing additional sequence specificity to the literal DNA sequence; this extends the range of constitutive epigenesis all the way down to the molecular level of sequence determination. Inheritance systems have evolved to make the transmission of crucial information from parents to offspring more reliable and enhance the offspring's fitness. However, it is not so much the particular gene you inherit that counts, but when, where and how a particular sequence is transcribed or translated by the higher order network of gene regulation that controls the time- and tissue dependent expression of genes. As Matt Ridley has remarked, "the more we lift the lid on the human genome, the more vulnerable to experience genes appear to be" (Ridley, 2003: 3). Evolution's answer to this plight of inheritance, or the parents' answer to assert a more reliable influence on the fitness of their offspring, was to provide more than just genetic resources to the next generation, to construct a stable 'niche for the genome'. West and King were one of the first to urge: "Ask not what's inside the genes you inherited, but what the genes you inherited are inside of" (West & King, 1987: 552). Looking at the enormous complexity of gene expression of eukaryotes that reveals a very flexible and reactive genome open to many intra-and extra-organismal environmental influences, "it was simply a matter of time before some systems found ways to manage aspects of their own developmental environment" (Lucas, 2006 (ms)). In other words, many aspects of experience have evolutionary explanations, an insight shared by some of the most recent and some of the oldest contributors to evolutionary thought:

> "To the extent that there exists heritable variation among mothers in their ability to discern high-quality mates, pick an appropriate host to place seeds or eggs, or provide protection from predators, and so on, such traits are expected to evolve in much the same way as any other trait subject to the inevitable consequences of Darwinian natural selection". (Mousseau & Fox, 1998: Preface v)

> "We live from birth to death in a world of persons and things which is in large measure what it is because of what has been done and transmitted from previous human activities. When this fact is ignored, experience is treated as if it were something which goes on exclusively inside an individual's body and mind. It ought

> not to be necessary to say that experience does not occur in a vacuum. There are sources outside an individual which give rise to experience." (Dewey, 1938/1963: 39)

The ontogenetic niche comprises all molecular, cellular, ecological and social circumstances inherited by the organism and includes all developmental factors that are reliably and dependably provided from one generation to the next. All these resources are indispensable for the successful reproduction of a developmental system. The construction of a developmental niche relies heavily on the extragenetic or extended inheritance of developmental resources. The great variety of inherited resources are made reliably available through epigenetic, behavioral, cultural and symbolic inheritance 'channels' (Jablonka & Lamb, 2005). These channels include maternal and paternal (parental) effects, which are defined as the causal influence of the parental phenotype, or the environment the parents' experience, on offspring phenotype. Such effects are completely independent of the genes contributed to the offspring, and can also not be reduced to the influence of parental genes or RNAs, even though they can and do play a role in many instances. Parental effects are comprised of differential resource allocation either through egg size and composition, placental nutrition, or nursing; preference induction (oviposition, imprinting on food, habitat, and mates); mate choice; the non-facultative and facultative imprinting of genes and reprogramming of gene expression through chromatin remodeling and DNA methylation (Jablonka & Lamb, 2005; Mousseau & Fox, 2003). The cytoplasmic chemical gradients plus the messenger RNA and transcription factors, all of which are inherited with the mother's egg, give the influence of the offspring's gene expression a head start, but as the examples above show, the mother's control over the fetus' environment does not stop there. Even after birth rearing practices, such as the licking of pups by rat mothers; the facilitation of offspring experience through the creation of opportunities; and various forms of social learning continue to influence gene expression levels and other developmental processes. Parental activity can facilitate, guide and entrench social learning, which in the case of humans and higher animals falls under the rubric of the cultural and even symbolic 'transmission of information'.

There have been repeated attempts to reduce all of these mechanisms to the action of inherited or parent-of-origin genes, so that ultimately the real causes are all genetic. This special pleading fails in the light of the discovery that development relies less on the existence of genes in an organism than on the regulated expression of these genes, which ultimately depends on a host of environmental factors. Wherever there are genes there are extragenetic factors necessary for their regulated expression.

I have called the design-like control of the next generation's developmental environment extended inheritance or ontogenetic niche construction. What all of the above cases of inheritance through environment construction have in common is making the transmission of crucial information more reliable. And while some of the above mechanisms have at first sight not much in common with the construction of epistemic structures by an extended mind, in the latter cases of behavioral, ecological and cultural inheritance the biological shades smoothly into the cognitive.

As Jablonka and Lamb have pointed out, epigenetic inheritance, just like genetic inheritance, is not just about reliability, stability and fixity, it can also lead to "transgenerationally extended plasticity, and developmentally-induced heritable epigenetic variations provide additional foci for selection" beyond genetically-induced heritable variations (Jablonka and Lamb, this issue).

5. Ecological Evolutionary Developmental Biology

The nature-nurture dichotomy is not reduced to the field of developmental biology and psychology but plays an important role in our conception of the process of evolution. One might even say that it was the very separation of nurture (germ line, genes) from nature (soma, environment, individual development) that cemented the exclusion of developmental biology from the Modern Synthesis of Evolution. The last two decades saw a growing interest in questions that the received view was not able to address, such as questions about patterns and processes of phenotypic evolution, and the origin of evolutionary novelty and innovation. A new synthesis of evolutionary developmental biology (evo-devo) began to form. From the Developmental Systems perspective, the elucidation of extended processes of inheritance made it clear that the reason to exclude so-called processes of nurture or individual development – for not producing heritable variation – no longer holds. Increasingly now, one hears that in order to situate a synthesis of development and evolution 'in the real world' the role of ecology needs to be fully integrated as well (Gilbert, 2001).

The rise of the new science of *Entwicklungsmechanik* (developmental mechanics) in the late 19th and beginning of the 20th century regarded the anatomical tradition, with its evolutionary context and its methods of observation of developing organisms in their natural context, old-fashioned and unscientific, and completely rejected any (at that time regarded as) mystical ideas of epigenesis. The new mantra of experimentation with its new methodology of manipulating the animal in controlled laboratory settings brought the discipline of embryology, now called developmental biology, from the sea shore to the laboratory. Against this background we have to understand the emerging 'model organism' approach. To make animals constantly available and as uniform as possible, and the scientist independent from the dictate of seasonal availability and natural variability, laboratories started to breed their own animals. This constrained the choice of organism, which "must be selected for the inability of their development to be influenced by specific environmental cues". In other words, "the influence of … environmental sources of phenotypic diversity were progressively eliminated under the physiological context of embryology" (Gilbert, 2003, 88f).

While the physiological tradition favored the whole organism at the expense of the environment, the newly emerging genetics, especially molecular genetics, focused on genes at the expense of the organism. Also, the paradigm model organism of genetic research, *Drosophila*, showed such a remarkable robustness against the limited scale of environmental variables in the lab that the original conceptualization of genes in the Norm-of-Reaction approach shifted soon to genes as the only marker of phenotypic variation (Collins, Gilbert, Laubichler, & Müller, 2007). Both research traditions discounted and dispensed with the environment, the former the external niche of the organism and the latter the internal cellular niche of the genes and their expression. This shows an unexpected parallelism to the so-called ‘environmentalist’ movement in psychology that emerged at the same time. By moving the study of animal behavior and learning from the field and mere observational approaches into a laboratory that allowed for rigorous testing and experimentation, the behaviorist tradition dispensed with both the variety of organisms – after all, it presupposed the generality of learning mechanisms – and their natural habitat in favor of uniform organisms and controlled (environmental) test conditions.

Recently this exclusion of the natural environment from experimental studies in evolutionary, developmental and also behavioral studies has been criticised, most notably by calls for an ‘ecological developmental biology’ or ‘Eco-Devo’ (Gilbert, 2001) and West and King’s call for a ‘Developmental Ecology’ (West, 2003; West and King, this issue). These criticisms included concerns about the use of model organisms and their limited generalizability for the interpretation of research results (see Robert, this issue). Together with growing research into parental effects these approaches have inspired a flood of new observations and experiments cementing the influential role of ecology on development and evolution. West and King’s surprising results in their extended research of the development of cowbirds warn us how a neglect of the natural, social conditions of flock living can mislead us in our interpretation of the developmental causes of behavior. Maternal effect research has produced many examples of how environmental conditions can exert an influence on the development of many successive generations (Gilbert, 2001; Mousseau & Fox, 1998; West et al., 1990; see references in West & King, this issue).

In summary, we can identify three reasons for the exclusion of development from the Modern Synthesis: a) The misconstruction of development as the mere unfolding or maturation of the organism out of its genetic ‘blueprint’ or’ program; b) The reduction of inheritance and transgenerational stability of traits to the transmission of genetic ‘information’; and c) The neglect of the problem of evolutionary novelty, the so-called ‘arrival of the fittest’. Taken together, these attitudes have not paid serious enough attention to the necessary and sufficient conditions for the process of adaptation by natural selection to take place: the origin of reliably reproducing developmental systems. In other words, evolutionary biology has hitherto failed to address the very possibility of evolution through the variability, adaptability and evolvability of phenotypes.

The last decade has seen the emergence of multiple approaches that focus on the active role of organisms and their development in evolution. These accounts are Developmental Systems Theory (Oyama et al., 2001b), Extended Inheritance (Jablonka & Lamb, 2005), evolutionary developmental biology (Evo-Devo) (Hall, 2000) and developmental evolution (Wagner, Chiu, & Laubichler, 2000), ecological developmental biology or Eco-Devo (Gilbert, 2001), phenotypic and developmental plasticity (Pigliucci, 2001; West-Eberhard, 2003), and Niche Construction (Odling-Smee, Laland, & Feldman, 2003). I believe that the concept of *developmental* niche construction has the power to integrate many if not most of the ideas laid down in the other approaches. The central idea behind developmental niche construction, and developmental systems theory, is the developmental system. It unifies many of the pressing questions and ideas mentioned above: the developmental system as the subject of evolution and their forces; the developmental system as the producer of evolutionary innovations; the interdependency and codetermination of the organism and its niche; the developmental system as the provider of many different interdependent channels of inheritance that reliably make available the necessary developmental resources for the reproduction of successive generations of developmental systems. Research in the process of developmental niche construction can elucidate three main evolutionary questions:

a) The *origin of a trait* by introducing new epigenetic resources for variation and innovation beyond mutation and recombination and describing how developmental processes situated in their ecological niche can produce novel phenotypes; b) the *spread of a trait* by showing in detail how organisms or their parental generation co-construct a selective environment; and c) the *maintenance of a trait* through processes of transgenerational stability of variation that extend the inheritance through the transmission of genetic material with the reliable availability of necessary developmental resources through multiple mechanisms of reproduction or transmission.

We now have all necessary ingredients for a real postmodern or postgenomic synthesis of development, heredity and evolution.

6. A Postgenomic Synthesis: an Epigenetic Understanding of Development

The ‘century of the gene’ (Keller, 2000) spawned a new and more sophisticated preformationism, with the homunculus as the preformed ‘form’ of the organism replaced by the ‘information’ to make an organism encoded in the genome. This modern consensus accepts the emergence of qualitative change in development, which it explains with the preformed inherited genetic program as a materialized vital force directing the epigenesis of the organism out of a seemingly homogenous mass. Hence the new conception is rather a kind of ‘animistic’ predeterminism, where genes ‘program’ outcomes. True to the spirit of today’s interactionism the mainstream ‘modern consensus’ can be “standardly construed as the epigenesis of something preformed in the DNA” (Robert, 2004: 34). Instead of avoiding the unscientific dangers of both preformation and vitalist epigenesis, however, it combines, the shortcomings of these age-old ideas and rests ultimately on an unrealistic conception of genes and gene action.

In its place I want to promote what others have called ‘probabilistic, contingent, or constitutive epigenesis’, a systems view that understands development as an epigenetic process of qualitative change based on the orderly emergence of novel behavioral traits during development without recourse to either an internal or external, preexisting plan. Taking development seriously is demanded by its contingent nature due to the immense importance of experiential factors at all stages of development, via the environmental regulation of gene expression. This ranges from the chemically facilitated emergence of new behavior (like sucking in rats, see Alberts’ paper, this issue), to individual learning of new behaviors through various processes including trial and error and social learning (such as the emulation or real imitation of new solutions to problems, as shown by the tool use in chimp and crows), and includes “ultra-social” learning through cultural participation, instruction, and formal schooling (as in the acquisition of language) (Gottlieb, 2001; Herrmann, Call, Hernandez-Lloreda, Hare, & Tomasello, 2007; Michel & Moore, 1995; Oyama et al., 2001b; Robert, 2004).

What a new account of development really has to accomplish is not just to go beyond these vexed dichotomies such as innate and learned, but to provide a framework that integrates a complex set of heterogeneous factors into a system of developmental resources all of which are reliably reproduced in succeeding generations of a developmental system but none of which really belong alone to either 'gene', 'organism' or 'environment' (the famous "Triple Helix" of Richard Lewontin, 2000). Its contextualization of genes should obviate "even naïve temptations toward gene/environment dichotomies, and … will open up a very rich area of empirical investigations to examination and conceptualization in developmental-system terms. … Ultimately, such a view should work towards "overcoming inner/outer dichotomies in favor of self-organizing, causally reciprocal systems of interaction" (Moss, 2001: 85). Developmental Systems Theory (DST), an alternative approach to the integration of evolution, development and inheritance, provides just such a framework and its conception of development is basically the one promoted in this paper (for a short introduction in its central tenets see Oyama, Griffiths, & Gray, 2001a).

The important systems features of such a view are the rejection of dichotomous description of behavior in favor of a full analysis in terms of continuing interaction between, and the joint determination by, heterogeneous developmental resources. Learning may be involved but only as part of an overall concept of experience which includes less obvious contributions, such as self-stimulation. An important part of such an analysis implies seeing behavior as belonging to the organism's overall anatomical and physiological make-up. A dynamical systems view of locomotor development exemplifies such an approach very well by including the growth of muscles and the infant's strength in an account of behavioral coordination of movement (e.g., Thelen, 1995). Other important features are the context sensitivity and developmental contingency of any factor, including genetic factors; the distributed control of development upon its heterogeneous resources, and the acknowledgement of the role played by the developmental system to control its further development; extending the idea of inheritance to include factors other than DNA, including factors formerly thought of as ‘environmental’ or ‘experiential’ if they are reliably reproduced or ‘passed on’ for succeeding generations; and last but not least the reconceptualization of development (and evolution) as the interactive construction in a thoroughly epigenetic account of development that “never sidesteps the task of explaining how a developmental outcome is produced” (Oyama et al., 2001a: 4).

Alleged explanatory categories of behavior such as ‘innate’, ‘acquired’, ‘programmed’, ‘hard-wired’, or ‘instinctive’ don’t really explain the origin of the behavior. Worse, by their presumptuous nature they preclude further investigation into the real causes of the trait, which are never just genetic or environmental but are necessarily ‘epigenetic’ by nature. This broad conception of epigenesis is expressed succinctly by Eva Jablonka:

> “Epigenetics … focuses on the general organizational principles of developmental systems, on the phenotypic accommodation processes underlying plasticity and canalization, on differentiation and cellular heredity, on learning and memory mechanisms. Epigenetics includes the study of the transmission of subsequent generations of developmentally-derived differences between individuals, thereby acknowledging the developmental aspect of heredity.” (Jablonka, pers. comm., cited in Gottlieb, 2001)

The last decade has witnessed enormous scientific advances in genomics, systems biology, social neuroscience, evolutionary, and ecological and developmental biology (‘evo-devo’, ‘eco-devo’, phenotypic plasticity, niche construction, extragenetic inheritance, developmental systems theory). They challenge overly gene-centered/predeterministic and environmentalist explanations of behavior. Nature and nurture don’t interact as if they were separated entities, with nature as the *a priori* plan being separated from concrete living and nurture being the means for modifying nature’s plan through experience. Every trait develops out of the nonlinear interactions among a range of very diverse developmental resources that cannot be usefully divided into genetic and non-genetic resources. It starts with the environmental regulation of gene expression, continues over a range of experiences beneath the skin and above the gene, through stages of sensory and social learning in vertebrates, to the exquisitely sensitive learning capacities of the human brain. ‘Nurture’ is this ongoing process of development, while ‘nature’ is the natural outcome of the organism-environment-system (Oyama, 1999).

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