

Bridging the gap between developmental systems theory and evolutionary developmental biology

Jason Scott Robert,^{1*} Brian K. Hall,² and Wendy M. Olson²

Summary

Many scientists and philosophers of science are troubled by the relative isolation of developmental from evolutionary biology. Reconciling the science of development with the science of heredity preoccupied a minority of biologists for much of the twentieth century, but these efforts were not corporately successful. Mainly in the past fifteen years, however, these previously dispersed integrating programmes have been themselves synthesized and so reinvigorated. Two of these more recent synthesizing endeavours are evolutionary developmental biology (EDB, or “evo-devo”) and developmental systems theory (DST). While the former is a burgeoning and scientifically well-respected biological discipline, the same cannot be said of DST, which is virtually unknown among biologists. In this review, we provide overviews of DST and EDB, summarize their key tenets, examine how they relate to one another and to the study of epigenetics, and survey the impact that DST and EDB have had (and in future should have) on biological theory and practice. *BioEssays* 23:954–962, 2001.

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Developmental systems theory

Developmental systems theory is not so much a single theory as a set of theoretical and empirical perspectives on the development and evolution of organisms. The developmental systems approach has its roots primarily in developmental and behavioural psychology,^(1–9) expanded and amended more recently primarily by philosophers of biology and molecular biologists.^(10–15) For many, the *locus classicus* of developmental systems theory is Susan Oyama’s 1985 book, *The Ontogeny of Information*,⁽⁴⁾ wherein Oyama rejected dichot-

omous views of development relying on the division of ontogenetic causes into genetic causes and generic (everything else, but usually mainly environmental) causes. For Oyama, as for other adherents to DST, developmental information resides neither *in* the genes nor *in* the environment, but rather emerges from the *interactions* of disparate, dispersed developmental resources — hence, the *ontogeny* of information. As against the usual interpretation of evolution as the transmission of genetic information between successive generations, DST underscores the ontogenetic construction of developmental information in each generation from both genetic and generic sources. Accordingly, ontogenetic processes are responsible for both the relatively reliable reproduction of type and the introduction of potentially evolutionarily significant variation. Developmental systems theory thus offers an alternative to the gene’s-eye view of evolution and development held by many reductionists.

For DSTheorists, genes must be *deeply* contextualized. “If development is to reenter evolutionary theory, it should be development that integrates genes into organisms, and organisms into the many levels of the environment that enter into their ontogenetic construction” (p. 113).⁽⁵⁾ In this task of deep contextualization, a central construct of DST is the *developmental system*, defined as “a mobile set of interacting influences and entities” comprising “all influences on development” at all levels, including the molecular, cellular, organismal, ecological, social and biogeographical (p. 72).⁽⁵⁾ This interactive matrix of resources is contingent and may be spatiotemporally discontinuous, but the fluid components of the matrix share the evolutionary task of reliably (though not unfaillingly) reproducing the organism/niche dyad.

Central tenets of DST

DST is not a specific theory, nor do all developmental systems theorists adopt an identical framework. This duality forces the imaginative abstraction (or reconstruction) of the central themes of DST. We have identified seven interrelated theses, which appear to be accepted by most proponents of the developmental systems approach (Table 1). A conceptually similar table also appears in the Introduction to the most recent book on DST.⁽¹⁵⁾

¹Department of Philosophy and ² Department of Biology, Dalhousie University, Halifax, NS Canada B3H 4J1.

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Order of authors is random; the authors contributed equally to this paper.

*Correspondence to: Jason S. Robert, Department of Philosophy, 1355 Dalhousie University, Halifax NS Canada B3H 4H6.

E-mail: Jason.Robert@dal.ca

Table 1. The seven key tenets of developmental systems theory, reconstructed from Refs. 4, 5, 9, and 10

Contextualism	Life cycles are contingent and contextually determined
Nonpreformationism	Hard: No ontogenetic information pre-exists individual ontogenies Soft: some ontogenetic information, though not exclusively genetic information, pre-exists individual ontogenies
Causal co-interactionism	Developmental causes interact in complex, often non-additive, ways
Causal dispersion	Causes of development are diffuse and fluid
Expanded pool of interactants	Ontogeny is initiated and maintained by multiple entities and influences
Extended inheritance	A large set of heterogeneous ontogenetic resources and means are inherited
Evolutionary developmental systems	Evolution is change in the composition and distribution of developmental systems

Contextualism

Whether the required developmental resources come together in the right way at the right time is a matter of contingency. The apparently exquisitely precise phenomena of development are not evidence of a program for development located in the genes, but only, at most, evidence of the *appearance* of such a program. The reliably present, over-determined, multilevelled context of development is sufficient to explain the remarkable reliability of reproduction and development, without invoking the problematic notion of a genetic program. Moreover, the reliability of developmental contexts is in large measure a function of their being constrained, influenced, selected, and even made by organisms, conspecifics, and symbionts.

Nonpreformationism

Despite the common view that preformation and epigenesis have been reconciled—preformed genetic information is expressed epigenetically—DST rejects the claim that “genetics proposes and epigenetics disposes” (p. 114).⁽¹⁶⁾ Whatever developmental, genetic, genomic, cellular, and environmental information there is, neither exists prior to development nor is transmitted between generations. Rather, information is constructed anew in each ontogeny. DST is therefore sometimes referred to as developmental constructionism; Oyama herself has switched from “interactionism” to “constructivist interactionism”,^(4,5) reflecting the perspective that developmental interactions generate new information in ontogeny. Many developmental structures are not stable and do not exist before ontogeny, but rather emerge from causal interactions in ontogenetic space and time. Note that there are both strong and weak versions of nonpreformationism: in the strong version, no developmental information whatever is preformed; in the weak version, developmental information may be preformed in a wide range of resources (not just genes). Both the weak and the strong versions deny a unique informational role for genes.

Causal co-interactionism

These causal interactions—sometimes referred to as *coactions*⁽³⁾—are complex and not simply additive. Moreover, causal interactions in development are not limited to gene-activation but rather involve inducing, facilitating, maintaining, and participating in time-sensitive positive and negative feedback loops at a variety of levels within and without the developing organism. DST-inspired accounts of causality do not reduce to the formula of “genes-*plus*-[other cause, stimuli, trigger]”. The nonadditivity of causal co-interactions makes it in many cases implausible either “to assign causal primacy [or] to dichotomise developmental causation into internal and external components” (p. 175).⁽⁸⁾

Causal dispersion

As causal power is neither centralized nor dichotomized, it must be dispersed. Causal power does not reside in any particular entity or class of entities, but rather in the relations between developmental interactants. Accordingly, “a gene is a resource among others rather than a directing intelligence that uses resources for its own ends” (p. 118).⁽⁵⁾ DST thus refocuses developmental inquiry on a multitude of factors, forces, and mechanisms, without insisting that genes are ontogenetically or ontologically primary.

Expanded pool of interactants

Causal cointeractions occur not just “between genes and environments”, but within and between the wide range of heterogeneous components of the developmental system. Within the organism, these include the extracellular matrix, DNA sequences, mRNA, hormones, metabolites and enzymes, for instance. Beyond the organism, the developmental interactants include habitat, behaviour,^(2,3,17) temperature, nutrition, social structure,⁽¹⁸⁾ and (depending on the system) even gravity and sunlight (the specific impact of these “environmental causes in ontogeny” is explored in Ref. 19). These interactants are often recognized as such within particular biological research programmes—their interactive

effects were, after all, identified by biologists. DST requires explicit investigation of the specific nature of the causal interactions between these and other developmental resources before any adequate account of development can be formulated.

Extended inheritance

The usual hypothesis is that the sole unit of hereditary transmission is the gene. DST suggests otherwise, holding that there is considerably more to inheritance than genes, and that the very stability of genetic inheritance depends on the nongenetic inheritance of many members of the expanded pool of interactants. Thus, DST understands “inheritance” quite broadly, to include not only DNA and the complex cellular matrix, but also reliably present elements of the “ontogenetic niche”.⁽²⁰⁾ More fundamentally, though, DST reinterprets transmission (sometimes understood as simply “passing on”) as *reliable reconstruction of resources-in-interactive-networks in the next life cycle*. Thus, “the developmental systems perspective stresses the processes that bring together the prerequisites for successive iterations of a life cycle” (p. 199).⁽⁵⁾

Evolutionary developmental systems

As “what is transmitted between generations is not traits, or blueprints or symbolic representations of traits, but developmental *means* (or *resources* or *interactants*)” (p. 29),⁽⁵⁾ evolution works on elements at all levels of developmental systems. In other words, since genes are not the only units of hereditary transmission, selection pressures act on the whole developmental manifold at all levels of complexity. Evolution is, therefore, change in the life-cycles of organisms in their co-constructed niches, reflected by differential reproduction and distribution of developmental systems. A complete understanding of evolution thus requires understanding development, while a complete understanding of development requires understanding evolution: understanding both “requires ‘unpacking’ the developmental system” (p. 180).⁽⁴⁾

Evolutionary developmental biology

The search for links between development (embryology) and evolution considerably predates DST, dating back to Aristotle if not earlier. In more modern times, connections were established by (among others) von Baer, Meckel, Serres, Haeckel, Balfour, Lankester in the 19th century, and by (among others) Garstang, Morgan, de Beer, Waddington, Schmalhausen, Goldschmidt, Osborn and Bonner in the 20th.^(21–25) The latest incarnation of links between development and evolution is evolutionary developmental biology (increasingly becoming known by the sobriquets *evo-devo* and *EDB*). *EDB* has as it aims an understanding of:

- the relationship between embryonic development and evolution;
- how developmental processes effect evolutionary change; and
- how development itself has evolved (Box 1).

The establishment of EDB

Modifications of development or of developmental processes (the evolution of development) lie at the basis of morphological change during evolution, as is especially evident in the production of evolutionary novelties. Most might not go as far as Charles Otis Whitman, the first director of the Marine Biological Laboratory at Woods Hole, MA, but they share his sentiment that “all that we call phylogeny is to-day, and ever has been, ontogeny itself. Ontogeny is, then, the primary, the secondary, the universal fact. It is ontogeny from which we depart and ontogeny to which we return. Phylogeny is but a name for the lineal sequences of ontogeny, viewed from the historical standpoint” (p. 178).⁽²⁷⁾ *Evo-devo* seeks to open the black box of development that lies between mutation and selection, and that contains processes that have been termed correlated progression,⁽²⁸⁾ ontogenetic repatterning,⁽²⁹⁾ or developmental reprogramming.⁽³⁰⁾

EDB is now an established discipline within biology. Within no more than a decade, or perhaps two, *EDB* has matured to the stage that there are two journals specifically devoted to the integration of development and evolution (*Evolution & Development*; *The Journal of Experimental Zoology (Molecular Developmental Evolution)*). Other journals—*American Zoologist*; *BioEssays*; *Genes, Development and Evolution*; *Genesis*; *International Journal of Plant Sciences*; *TREE*—give particular attention to *evo-devo*. Key early books or monographic treatments on the interface of development and evolution^(31–36) have been joined by books on *evo-devo* or aspects of *evo-devo*.^(24,37–43) More are in the works.^(44–46)

Conferences are being organized around *EDB* themes. The Society for Integrative and Comparative Biology (SICB) launched an *EDB* division with an inaugural symposium in January, 2000.⁽⁴⁷⁾ The Dibner Institute for the History of Science and Technology at MIT sponsored a symposium “From Embryology to *Evo-devo*” at Woods Hole in the summer of 2001. Evolutionary developmental biology permeated the 6th International Congress of Vertebrate Morphology in Jena, Germany in summer 2001, as indeed it had the last two congresses in Bristol and Chicago. Advertisements for academic positions now target *EDB*ists. Granting agencies such as NSF (US) are funding programmes in *evo-devo* (NSF published an overview of their approach to *EDB* in *J. Exp. Zool. (Mol Dev Evol)* 2000;288:285–286, in *Genesis* 2000;28:45–46 and in *Evol Dev* 2001;3:1–2). *Science* devoted a six-page special news report to *EDB* (4, July, 1997 277, 34–39), while the 1996 McGraw-Hill Yearbook of Science and Technology

Box 1. The Aims of EDB, According to Three Practitioners of EDB

Lists of the aims of evo-devo are not carved in stone, even when emanating from the same individual. Thus, evo-devo seeks to understand, as a minimum:

- The origin and evolution of embryonic development;
- How modification of development processes lead to the production of novel features;
- The adaptive plasticity of development in life-history evolution;
- How ecology impacts on development to modulate evolutionary change; and
- The developmental basis of homoplasy and homology (p. 177)⁽⁶⁰⁾

or

- ... The principal and inter-related problems are how development has evolved, and how developmental evolution has resulted in changes in particular structures or features of body organization (p. 75)⁽²⁶⁾

or

- Evolution of development
- Homology assessment
- Genotype-phenotype map
- Patterns of phenotypic evolution
- Evolutionary innovations (p. 829)⁽⁵⁷⁾

included an entry on the topic.⁽⁴⁸⁾ An encyclopaedia of evolution with considerable coverage of EDB is in production⁽⁴⁹⁾ as is a volume of keywords and concepts in EDB.⁽⁴⁴⁾

Evolutionary developmental biology has arrived. What are its goals and how do they intersect, complement or parallel those of DST?

EDB meets DST

Evolutionary developmental biology is not merely a fusion of the fields of developmental and evolutionary biology, the grafting of a developmental perspective onto evolutionary biology, or the incorporation of an evolutionary perspective into developmental biology. EDB informs genetics, epigenetics, hierarchy, constraint (historical, structural, developmental, genetic), unity of type, *Baupläne* (body plans), varieties of types of animals and plants (archetypes), homology and homoplasy, morphology, the relative roles of external (selectionist) and internal (developmental) factors, levels of evolutionary change, and patterns versus processes. In short, EDB seeks a synthesis of proximate and ultimate explanations of biology.

Recent approaches/advances that illustrate the synergy that is EDB include:

- comparative approaches to embryonic development, with studies interpreted in the contexts of well-founded phylogenies so that the direction of evolutionary change may be inferred;
- analysis of genes that are both conserved across the animal kingdom and orchestrate the shared develop-

mental processes involved in establishing antero-posterior polarity, bilateral symmetry, body plans, and organ formation;

- a glimmer of light on such major transitions in evolution as the origin of the chordates, flowering plants and tetrapods;
- understanding how modification of development has led to loss of organs (loss of limbs in snakes, loss of hind limbs in whales) while retaining the ability to form the self same organ rudiments (limb buds in snakes and in whales); and
- recognizing that life history stages (embryos, larvae, adults) are modular and evolve independently, perhaps best seen in extreme modification of larvae, and in loss of larval stages (direct development) in amphibians, echinoderms and ascidians that normally have a larval stage in the life cycle, in both cases with no recognizable changes in the adults.

Both EDB and DST strive to forge a unification of genomic, developmental, organismal, population and natural selection approaches to evolutionary change. Evolutionary developmental biology views development as hierarchical. Emergent properties, whose characteristics cannot be explained or even predicted from properties at a lower level in the hierarchy, emerge as ontogeny progresses.⁽²⁴⁾ As two examples:

- the coming together of the optic lobes from the vertebrate forebrain with head ectoderm induces the ectoderm to transform into a lens, while at the same time the optic lobes transform into the optic cup from which the retina of the eye will develop; while

- the juxtaposition of the epithelial cap of a developing limb bud with the underlying mesenchyme sets in motion a cascade of interactions (epigenetic interactions; see the next section) that initiate outgrowth of the limb bud and patterning of the limb skeleton along the proximodistal limb axis.

Evolutionary developmental biology thus champions a hierarchical approach to biological organization from the molecular/genetic to population levels. Findings relate to life-history evolution, adaptation and responses to, and integration with, environmental factors. Many aspects of biology inform EDB, including an historical perspective.^(21,22,24,25,50–52) Evolutionary developmental biology draws from a wide range of biological disciplines, but has its own set of questions, approaches and methods. But EDB has yet to draw extensively from behaviour/ psychology (with some notable exceptions such as Refs. 2 and 53), is only beginning to re-engage with ecology and to a limited degree with population-level biology, and has yet to fully embrace community, ecosystem biogeographical or global approaches (but see Refs. 24, 30, 54–58 for exceptions). As nicely summarized and argued by Gilbert,⁽⁵⁸⁾ EDBists have to rediscover the close interest that early (i.e., 19th and early 20th century) workers in embryology (Spemann, Weismann, von Siebold, Weiss) had in embryonic development in the twin contexts of ecology and life history.

EDB and DST both see different kinds of information in genes and in other units, all equally valid, and all equally necessary to effect ontogenetic and phylogenetic change. The continued discussion in the EDB literature of external versus internal causes may be one of the major differences between EDB and DST. When EDBists speak of external versus internal, they are using the phrase as shorthand for the desire to apportion responsibility to internal and external factors.⁽²⁴⁾

To take an example. A nucleus in a tadpole intestinal cell is engaged in interactions that maintain that cell as a differentiated intestinal cell with a characteristic morphology and function. Leave that nucleus in the intestinal cytoplasmic environment and it will continue to play a role maintaining intestinal differentiation. Transplant that nucleus into an enucleated frog's egg, however, and it will cease "intestinal activity", interact with components in the egg, and participate in the development of that egg into a mature individual,⁽⁵⁹⁾ the nucleus is used to begin another ontogeny. What was the nature of the information for producing a new individual that lay latent within the nucleus in the intestinal cell? It was potential: potential to reside and survive in a different cellular environment; potential to interact with elements in a new cytoplasmic environment (the ovum) that fails to maintain intestinal activity but initiates activity related to synthesis of DNA, cleavage and the initiation of a new ontogeny.

Evo-devo, in contrast to DST, sees the gene as the unit of inheritance, and sees gene regulation and cells and cellular processes (eggs, zygotes, cell movement, cell specification and differentiation, cell condensations) as the means by which ontogeny is generated and features modified over evolutionary time. The gene is given a privileged position as the unit of inheritance, but not a unique position as the repository of a genetic program; in EDB as in DST, the gene is not an "homuncloid gene" or "an encoded homunculus"⁽⁴⁾ but rather genes in development act "as suppliers of the material needs of development and, in some instances, as context-dependent catalysts of cellular changes, rather than as 'controllers' of developmental progress and direction" (p. 441).⁽⁶¹⁾ A typical position is that expressed by Dover in observing development through evolutionary eyes: "nothing in evolution makes sense except in the light of processes, starting within genomes, that affect developmental operations and ultimately spread through a population" (p. 283).⁽⁶²⁾

If primacy were to be assigned in EDB, it might be to the cell as the fundamental unit of life,⁽²⁴⁾ the gene being the fundamental unit of inheritance. A distinction could perhaps be made (and would be made by many EDBists) between units of inheritance (genes) and units of transmission of information (genes, cells, cytoplasm, organelles, extracellular environment). DST does not assign such hereditary primacy to the gene and would include even more components under units of transmission of information (extra-genomic inheritance, including parental behaviour, culture, environment and ecology), regarding all as units of inheritance.

EDBists realize that organisms inherit more than their genes. They inherit an ovum, cellular machinery for metabolism, mitochondria and mitochondrial genes, and so forth. EDBists—who mostly reside in biological research laboratories—see these entities that pass from generation to generation as the products of maternal gene action, i.e., each generation inherits a zygotic genome and the material products of the maternal genome, as well as maternally derived mitochondrial (or chloroplast) genes. Devotees of DST—many of whom speak from armchairs of philosophy—see these inherited entities as somehow separate from gene-based inheritance, as an extra-genomic inheritance; in reality, epigenetic inheritance. EDB sees the situation as one of two generations of inheritance in each new offspring, one zygotic and the other maternal, where maternal covers maternal gene products expressed early in development of the next generation (often called maternal cytoplasmic control of early development) and the physical manifestation of maternal gene action as eggs, mitochondria, polar granules and so forth.

Most in EDB are motivated by the desire to bring an evolutionary approach to developmental/molecular studies on the one hand, and a developmental approach to evolution on the other. We suspect that most evo-devoists are not concerned with enhancing, completing, modifying or overturning

the modern synthesis of evolution which was forged by Dobzhansky, Huxley, Mayr, Simpson and Stebbins.⁽⁶⁰⁾ While increasing numbers of workers seek to forge evo-devo with paleontology,^(63–67) only few are seeking to forge EDB with population genetics. With rare exceptions,^(68,69) and perhaps not surprisingly, those seeking such a synthesis came into (“converted to”) EDB from backgrounds in population genetics or in theoretical biology.^(30,42,57,70–76) Those trained in the developmental biology tradition, with exceptions such as Scott Gilbert^(58,77) and Duboule and Wilkins⁽⁷⁸⁾ among few others, are less troubled by the inability to reconcile variation as the stuff of evolution with the apparent lack of variation in development or developmental processes, seeing stages and processes as conserved, and individual variation as minimal and seemingly constrained. As with the relation of development to ecology, which was important for early embryologists but now has to be rediscovered, so the importance of variation was known, and has to be rediscovered. As Whitman noted, “...if organization and the laws of development exclude some lines of variation and favor others, there is certainly nothing supernatural in this, and nothing which is incompatible with natural selection” (p. 11);⁽²⁷⁾ even earlier Balfour had asserted “I see no reason for doubting that the embryo in the earliest periods of development is as subject to the laws of natural selection as is the animal at any other period. Indeed, there appear to me grounds for the thinking that it is more so” (p. 343).⁽⁷⁹⁾

Evolutionary developmental biology is a thriving scientific discipline. Both EDB and DST provide appropriate worldviews to combat extreme reductionism. While DST may be too global to be translated into a research programme, it provides a framework, or a way of thinking, that is operationalized (in part) by EDB in the context of epigenetics. What is epigenetics, and how does it bridge the gap between theory and practice?

Epigenetics

Wishing to avoid the implication of a mechanical program, Waddington⁽⁸⁰⁾ initially offered the term “epigenetics” as a replacement for the more cumbersome “*Entwicklungsmechanik*” (developmental mechanics). For Waddington, epigenetics was the study of the causal interactions of development, with an emphasis on genes as the primary determinants of development. Modern EDB definitions of epigenetics vary considerably, but many maintain Waddington’s emphasis on genes, allowing for both genetic and non-genetic influences during development, although in its most narrow sense, epigenetics refers only to inherited structures of the gene, such as patterns of methylation and imprinting.⁽⁸¹⁾ Ultimately, epigenetics is the selective control of gene expression.^(24,81) More DST-oriented definitions do not mention genes specifically, but rather emphasize the “conditional, non-programmed determinants of individual development” (p. 305).⁽⁸²⁾ Most broadly defined, epigenetics is simply the study of ontogenetic

interactions, or “the mechanisms which, at all levels of organization, are responsible for the transformation of (a single cell to an adult)” (p. 140).⁽⁸³⁾

Epigenetics embraces the view that there is more to both development and evolution than genes and gene action. As such, it is the perfect meeting ground for DST and EDB. If DST has anything to offer the realm of science, it is in the study of epigenetics; epigenetics is the practice of what DST proposes. Yet despite this potential agreement, DST and EDB remain divided over two key issues: causation and inheritance. The main tenets of DST argue strongly against reductionism and the primacy of the gene in assessing both causation and inheritance. Thus, for DST, epigenetics should include the active study of all causal interactants, and inheritance is both extended and epigenetic. EDB, in contrast, continues to show a tendency toward reductionism and gene-centrism; developmental mechanisms are ultimately genetic (as reflected in the EDB definition of epigenetics), and there is no such thing as epigenetic inheritance.

Epigenetics and causation

DSTheorists see no *a priori* causal asymmetry in development or evolution, and no class of biological units (genes, cells, organisms, and so forth) as privileged or possessing causal primacy. Rather, DST advocates causal democracy, positing that, because of their interdependencies and interrelations, causation cannot be assigned to genes or to environment, to nature or to nurture, perhaps not even to organism or to environment. Each developmental interactant has an equally valid and necessary role in the production of the (expanded) phenotype; a complete understanding of development thus requires an understanding of factors, forces, and mechanisms operating at all levels of the structural and causal hierarchy.

One persistent complaint against developmental systems theory is that, while the DST perspective may be theoretically useful, it is experimentally unwieldy.⁽⁸⁴⁾ That is, DST may effectively guard against extreme reductionism and promote broader, more integrative analyses of development, but it proposes no novel research programme. Adherents to DST have responded to this challenge; Gray,⁽⁹⁾ for instance, has recently offered a diverse list of DST-inspired research programmes (Box 2). This list consists entirely of existing research programmes in genetics, development, and EDB. All pre-date DST, were not inspired by DST, and do not depend on DST for their execution.

Evolutionary developmental biologists agree with developmental systems theorists, insofar that it is clearly insufficient to ‘explain’ development solely in terms of genes and gene action. Epigenetic causation incorporates genetic and environmental factors; both are necessary for the production of the phenotype. And whereas the gene is often viewed as evolutionarily privileged, environmental factors clearly affect, effect,

Box 2. DST-inspired Research Programmes, as Suggested by Gray (pp. 202–203)⁽⁹⁾

- Developmental analysis of “black boxes”: how do traits develop, what resources are required, and to what extent (and under what conditions) are developmental outcomes stable?
- Extragenetic inheritance: investigate the longevity, fidelity, and impact of extragenetic inheritance, and its coevolution and genetic change. “Extragenetic” factors include methylation patterns, cytoplasmic constituents, and habitat.
- Adaptive mechanisms of inheritance: test the potential adaptive value, evolvability of different forms of inheritance (genetic and extragenetic).
- Niche construction: what are the evolutionary consequences of active selection and modification of the environment?
- Contextual analysis of development: study the interdependencies and causal dynamics of developmental factors.
- Developmental organization and integration: to what extent is development and inheritance (both genetic and extragenetic) coupled vs. modular? And what are the functional, developmental, and evolutionary consequences of coupling vs. decoupling?

and reinforce divergence and differentiation of cell (and species) lineages. Thus, EDB recognizes many causes in development, and there is no *a priori* assumption of causal primacy, at least in theory. In practice, however, many EDBists continue to give implicit priority to genes, largely because of their role in inheritance (see below), but also because of their current epistemological dominance over other developmental factors. Given the ever-growing diversity of molecular tools and techniques, as well as the veritable explosion of information they produce, it is small wonder that EDB focuses so heavily on gene regulation and changes in gene expression; it is within this context that the role of the environment must be explored.

Genetic and epigenetic explanations differ only in proximity of cause. Thus, biologists “tend to be either genetic or epigenetic in orientation” (p. 156),⁽⁸⁵⁾ and apportion causal responsibility according to their particular research programme. Indeed, there is growing interest in the field of ecological developmental biology (or “eco-devo”), which is dedicated to analyses of biotic and abiotic environmental inductions and the environmental control of development.^(19,24,58) Perhaps here, DST will find its most sympathetic audience.

Epigenetics and inheritance

Inheritance is the largest point of contention between DST and EDB. In its most basic sense, a gamete consists of genetic material (nucleic acids) plus the intracellular and extracellular environment in which (and with which) to begin development. Both genes and environment are necessary but not sufficient; remove either, and development will fail. So what, then, is the unit(s) of inheritance? Although there are hard and soft views on both sides, inheritance can be generalized as either gene-based (EDB) or extended (DST). The main differences, summarized in Table 2, are discussed below.

Of the five categories listed in Table 2, EDB and DST agree that the first three are heritable. EDB, especially the hard version, identifies the gene (defined as actual genetic material) as the sole unit of inheritance; DST recognizes multiple units of inheritance, of which the gene (so defined) is only one. Similarly, gene states, which include phenotypic aspects of genetic material, such as genomic imprinting, methylation patterns, and chromatin structure, are also heritable. Gene states, once acquired, may be replicated and transmitted into the next generation, and thus influence gene expression patterns in the zygote.

Evo-devoists argue that only genes are inherited, and with them, the potential to realize the phenotype. Epigenetic *potential* is heritable, epigenetic *processes* are not. There is an important difference between the ability to respond to environmental and genetic cues (epigenetic potential), and the actual responses to those cues (epigenetic processes). Epigenetics, as a process, is not trans-generational, but rather is constrained to the regulation of an individual ontogeny; it is not self-replicating.⁽⁸⁶⁾ “Epigenetic inheritance” is thus non-

Table 2. Different interpretations of inheritance

What is inherited?	DST		EDB	
	Hard	Soft	Soft	Hard
Genes (genetic material)	Yes	Yes	Yes	Yes
“Gene states” ¹	Yes	Yes	Yes	Yes
Epigenetic potential	Yes	Yes	Yes	Yes
Epigenetic processes	Yes	Yes	No	No
Environment	Yes	(Some)	(Some)	No

¹“Gene states” = the phenotype of the gene, including genetic imprinting, methylation patterns, and chromatin structure.

sensical within the framework of EDB. Similarly, the inheritance of the end product of epigenetics does not equal epigenetic inheritance. Developmental systems theorists, on the contrary, define inheritance as the reliable reconstruction of interactive causal networks. Epigenetic processes are heritable and are, in effect (with heritable genetic and environmental components), actively and faithfully replicating themselves into the next generation.

The final category is that of the environment. Environmental factors present at all levels do carry over to the next generation; i.e., they are to a large extent reliably present from one generation to the next. But to what extent are they actively transmitted? Setting the two extremes, the hard EDB position rejects inheritance of environmental factors, whereas the hard DST position argues that all aspects of the environment, from intracellular to ecological to social, are heritable, including in inheritance “any resource that is reliably present in successive generations” (p. 196).⁽⁸⁷⁾ The soft views, which agree that some aspects of the environment clearly are inherited, differ fundamentally in the nature of that inheritance. Evolutionary developmental biologists claim that the heritable components of the gametic environment (both intracellular and extracellular) are products of maternal gene action; thus each offspring is the product of two generations of gene-based inheritance, one maternal and one zygotic. In the eyes of DST, defining the environment as gene-based is gene-centrism at its worst. Does knowing the maternal genome predict the future environment of the gamete? If not, and if maternal effects involve emergent properties (extending so far as to the environment into which the gametes are placed), then to describe environmental inheritance as gene-based is at most a second-order explanation, or gene reductionism once-removed.

Conclusion

On the one hand, developmental systems theory provides useful counter-arguments to gene-centrism and encourages integrative analyses of development and evolution. On the other hand, DST is not a science and has yet to provide a new research programme. Evolutionary developmental biology is now an established science which already provides the integrative research programme advocated by DST. Both DST and EDB would benefit from increased communication. Given such fundamental differences however, bridging the gap will not be easy.

References

- Lehrman DS. Semantic and conceptual issues in the nature-nurture problem. In Aronson LR, Lehrman DS, Tobach E, Rosenblatt JS, ed; *Development and Evolution of Behavior*. San Francisco: Freeman. 1970. p 17–52.
- Gottlieb G. *Individual Development and Evolution: The Genesis of Novel Behavior*. New York: Oxford University Press. 1992.
- Gottlieb G. *Synthesizing Nature-Nurture: Prenatal Roots of Instinctive Behavior*. Mahwah, New Jersey: Lawrence Erlbaum Associates. 1997.
- Oyama S. *The Ontogeny of Information: Developmental Systems and Evolution*. Rev. ed. Durham: Duke University Press. 2000. 1st ed. 1985; Cambridge: Cambridge University Press.
- Oyama S. *Evolution's Eye: A Systems View of the Biology-Culture Divide*. Durham: Duke University Press. 2000.
- Oyama S. Causal democracy and causal contributions in developmental systems theory. *Phil Sci Assoc (Proc)* 2000;67:S332–S347.
- Johnston TD. The persistence of dichotomies in the study of behavioral development. *Devel Rev* 1987;7:149–182.
- Gray R. Death of the gene: developmental systems strikes back. In Griffiths PE, ed; *Trees of Life: Essays in the Philosophy of Biology*. Boston: Kluwer Academic Publishers. 1992. p 165–209.
- Gray R. Selfish genes or developmental systems? In Singh R, Krimbas C, Paul D, Beatty J, ed; *Thinking About Evolution: Historical, Philosophical, and Political Perspectives*. Cambridge: Cambridge University Press. 2001. p 184–207.
- Griffiths PE, Gray R. Developmental systems and evolutionary explanation. *J Phil* 1994;91:277–304.
- Griffiths PE, Gray R. Replicator II: judgement day. *Biol Phil* 1997;12:471–492.
- Griffiths PE, Neumann-Held EM. The many faces of the gene. *BioScience* 1999;49:656–674.
- Neumann-Held EM. The gene is dead—long live the gene! Conceptualizing genes the constructionist way. In Koslowski P, ed; *Sociobiology and Bioeconomics: The Theory of Evolution in Biological and Economic Theory*. Berlin: Springer-Verlag. 1999. p 105–137.
- Robert JS. *Taking Development Seriously: Toward a Genuinely Synthetic Biology*. Ph.D. thesis. Hamilton: McMaster University. 2000.
- Oyama S, Griffiths PE, Gray R (editors). *Cycles of Contingency: Developmental Systems and Evolution*. Cambridge: MIT Press. 2001.
- Medawar PB, Medawar JS. *Aristotle to Zoos: A Philosophical Dictionary of Biology*. Cambridge: Harvard University Press. 1983.
- Johnston, TD, Gottlieb G. Neophenogenesis: a developmental theory of phenotypic evolution. *J Theor Biol* 1990;147:471–495.
- Keller L, Ross KG. Phenotypic plasticity and cultural transmission in the Fire Ant *Solenopsis invicta*. *Behav Ecol Sociobiol* 1993;33:121–129.
- van der Weele C. *Images of Development: Environmental Causes in Ontogeny*. Albany: State University of New York Press. 1999.
- West MJ, King AP. Settling nature and nurture into an ontogenetic niche. *Dev Psychobiol* 1987;20:549–562.
- Horder TJ, Witkowski JA, Wylie CC (editors). *A History of Embryology. The Eighth Symposium of the British Society for Developmental Biology*. Cambridge: Cambridge University Press. 1986.
- Gilbert SF (editor). *Developmental Biology: A Comprehensive Synthesis. Volume 7. A Conceptual History of Modern Embryology*. New York: Plenum Press. 1991.
- Hall BK. Waddington's legacy in development and evolution. *Amer Zool* 1992;32:113–122.
- Hall BK. *Evolutionary Developmental Biology*. 2nd ed. Dordrecht: Kluwer Academic Publishers. 1998. 1st ed. 1992; London: Chapman and Hall.
- Hall BK, Balfour, Garstang and de Beer: The first century of evolutionary embryology. *Amer Zool* 2000;40:718–728.
- Raff RA. Evo-devo: the evolution of a new discipline. *Nature Rev Gen* 2000;1:74–79.
- Whitman CO. *Posthumous works of Charles Otis Whitman* (ed. H. A. Carr). I. Orthogenetic evolution in Pigeons. Washington DC: Carnegie Institute. 1919.
- Thomson KS. The evolution of the tetrapod middle ear in the rhipidistian-tetrapod transition. *Amer Zool* 1966;6:379–397.
- Roth G, Wake DB. Trends in the functional morphology and sensorimotor control of feeding behavior in salamanders: an example of the role of internal dynamics in evolution. *Acta Biotheoretica* 1985;34:175–192.
- Arthur W. The concept of developmental reprogramming and the quest for an inclusive theory of evolutionary mechanisms. *Evol Devel* 2000a;2:49–57.
- Goldschmidt RB. *The Material Basis of Evolution*. New Haven: Yale University Press. 1940.
- de Beer GR. *Embryology and Evolution*. Oxford: Clarendon Press. 1930.
- de Beer GR. *Embryos and Ancestors*. Oxford: Clarendon Press. 1940.
- Gould SJ. *Ontogeny and Phylogeny*. Cambridge: The Belknap Press of Harvard University Press. 1977.

35. Bonner JT. *The Evolution of Development. Three Special Lectures Given at University College, London.* Cambridge: Cambridge University Press. 1958.
36. Bonner JT. *On Development. The Biology of Form.* Cambridge: Harvard University Press. 1974.
37. Bonner JT (editor). *Evolution and Development. Report of the Dahlem Workshop on Evolution and Development Berlin 1981, May 10–15.* Life Sciences Research Report 22. Berlin: Springer-Verlag. 1982.
38. Raff RA, Kaufman TC. *Embryos, Genes, and Evolution.* New York: Macmillan Publishing Co. 1983.
39. Thomson KS. *Morphogenesis and Evolution.* Oxford: Oxford University Press. 1988.
40. Raff RA. *The Shape of Life: Genes, Development, and the Evolution of Animal Form.* Chicago: The University of Chicago Press. 1996.
41. Gerhart J, Kirschner M. *Cells, Embryos, and Evolution. Toward a Cellular and Developmental Understanding of Phenotypic Variation and Evolutionary Adaptability.* Malden: Blackwell Science. 1997.
42. Arthur W. *The Origin of Animal Body Plans. A Study in Evolutionary Developmental Biology.* Cambridge: Cambridge University Press. 1997.
43. Carroll S, Grenier JK, Weatherbee SD. *From DNA to Diversity. Molecular Genetics and the Evolution of Animal Design.* Malden: Blackwell Science. 2001.
44. Hall BK, Olson WM (editors). *Keywords and Concepts in Evolutionary Developmental Biology.* Cambridge: Harvard University Press. 2001; in preparation.
45. Wilkins AS. *The Evolution of Developmental Pathways.* Sunderland: Sinauer Associates Inc. 2001; forthcoming.
46. West-Eberhard M.J. *Innovative Phenotypes: Developmental Plasticity and Evolution.* New York: Oxford University Press. 2001; forthcoming.
47. Burian RM, Gilbert SF, Mabee PM, Swalla BJ (editors). *Evolutionary Developmental Biology: Paradigms, Problems, and Prospects.* *Amer Zool* 2000;40:711–831.
48. Hall BK. *Evolutionary Developmental Biology.* In 1996 McGraw-Hill Yearbook of Science and Technology. New York: McGraw-Hill Inc. 1996. p 110–112.
49. Pagel M (editor in chief). *Encyclopaedia of Evolution.* New York: Oxford University Press. 2001.
50. Richards RJ. *The Meaning of Evolution. The Morphological Construction and Ideological Reconstruction of Darwin's Theory.* Chicago: University of Chicago Press. 1992.
51. Nyhart LK. *Biology Takes Form. Animal Morphology and the German Universities, 1900–1900.* Chicago: University of Chicago Press. 1995.
52. Burian RM. General introduction to the symposium on evolutionary developmental biology: Paradigms, problems, and prospects. *Amer Zool* 2000;40:711–717.
53. Greene HW. Homology and behavioural repertoires. In Hall BK, ed; *Homology: The Hierarchical Basis of Comparative Biology.* San Diego: Academic Press. 1994. p 370–391.
54. Callahan HS, Pigliucci M, Schlichting CD. Developmental phenotypic plasticity: where ecology and evolution meet molecular biology. *Bioessays* 1997;19:519–525.
55. Schlichting CD, Pigliucci M. *Phenotypic Plasticity. A Reaction Norm Perspective.* Sunderland: Sinauer Associates, Inc. 1998.
56. Rutherford SL. From genotype to phenotype: buffering mechanisms and the storage of genetic information. *Bioessays* 2000;22:1095–1105.
57. Wagner GP, Chiu C-H, Laubichler M. Developmental evolution as a mechanistic science: The inference from developmental mechanisms to evolutionary processes. *Amer Zool* 2000;40:819–831.
58. Gilbert SF. Ecological developmental biology: developmental biology meets the real world. *Devel Biol* 2001;233:1–12.
59. Gurdon JB, Uehlinger V. "Fertile" intestinal nuclei. *Nature* 1966;210:1240–1241.
60. Hall BK. Evo-devo or devo-evo — does it matter? *Evol Devel* 2000;2:177–178.
61. Nijhout HF. Metaphors and the role of genes in development. *Bioessays* 1990;12:441–446.
62. Dover GA. Observing development through evolutionary eyes: A practical approach. *BioEssays* 1992;14:281–287.
63. Smith MM, Hall BK. Developmental and evolutionary origins of vertebrate skeletogenic and odontogenic tissues. *Biol Rev Camb Philos Soc* 1990;65:277–374.
64. Smith MM, Hall BK. A developmental model for evolution of the vertebrate exoskeleton and teeth: the role of cranial and trunk neural crest. *Evol Biol* 1993;27:387–448.
65. Conway Morris S. Why molecular biology needs palaeontology. *Development* 1994;Suppl:1–13.
66. Shubin NH. The evolution of paired fins and the origin of tetrapod limbs: Phylogenetic and transformational approaches. *Evol Biol* 1995;28:39–86.
67. Carroll RL. *Patterns and Processes of Vertebrate Evolution.* Cambridge: Cambridge University Press. 1997.
68. Palopoli MF, Patel NH. Neo-Darwinian developmental evolution: can we bridge the gap between pattern and process? *Curr Opin Genet Devel* 1996;6:502–508.
69. Wilkins AS. Evolutionary developmental biology: where is it going? *BioEssays* 1998;20:783–784.
70. Cheverud JM. Quantitative genetics and developmental constraints on evolution by selection. *J Theor Biol* 1984;110:155–171.
71. Wagner GP. The systems approach: An interface between development and population genetic aspects of evolution. In Raup DM, Jablonski D, ed; *Patterns and Processes in the History of Life Dahlem Conference.* Berlin: Springer-Verlag. 1986. p 149–165.
72. Wagner GP. What is the promise of developmental evolution? Part I: Why is developmental biology necessary to explain evolutionary innovations? *J Exp Zool (Mol Devel Evol)* 2000;288:95–98.
73. Cheverud JM, Hartman SE, Richtsmeier JT, Atchley WR. A quantitative genetic analysis of localized morphology in mandibles of inbred mice using finite element scaling analysis. *J Craniofac Genet Devel Biol* 1991;11:122–137.
74. Wagner GP, Altenberg L. Complex adaptations and the evolution of evolvability. *Evolution* 1996;50:967–976.
75. Arthur W. Intraspecific variation in developmental characters: The origin of evolutionary novelties. *Amer Zool* 2000;40:811–818.
76. Wagner GP, Booth G, Bagheri-Chaichian H. A population genetic theory of canalization. *Evolution* 1997;51:329–347.
77. Gilbert SF. *Developmental Biology.* Sixth Edition. Sunderland: Sinauer Associates, Inc. 2000.
78. Duboule D, Wilkins AS. The evolution of "bricolage." *TIG* 1998;14:54–59.
79. Balfour FM. A preliminary account of the development of the elasmobranch fishes. *Quart J Microsc Sci* 1874;14:323–364.
80. Waddington CH. *Principles of Embryology.* London: George Allen and Unwin, Ltd. 1956.
81. Holliday R. Epigenetics: an overview. *Dev Genetics* 1994;15:453–457.
82. Newman SA, Müller GB. Epigenetic mechanisms of character origination. *J Exp Zool (Mol Dev Evol)* 2000;288:304–317.
83. Løvtrup S. Introduction to evolutionary epigenetics. In Scudder GGE, Reveal JL, ed; *Evolution Today: Proceedings of the Second International Congress of Systematic and Evolutionary Biology.* Pittsburgh: Carnegie Mellon University. 1981. p 139–144.
84. Schaffner KF. Genes, behavior, and developmental emergentism: One process, indivisible? *Phil Sci* 1998;65:209–252.
85. Herring SW. Epigenetic and functional influences on skull growth. In Hanken J, Hall BK, ed; *The Skull, vol. 1: Development.* Chicago: University of Chicago Press. 1983. p 153–206.
86. Hall BK. Epigenetics: regulation not replication. *J Evol Biol* 1998;11:201–205.
87. Griffiths PE, Gray RD. Darwinism and developmental systems. In Oyama S, Griffiths PE, Gray RD, ed; *Cycles of Contingency: Developmental Systems and Evolution.* Cambridge: MIT Press. 2001. p 195–218.