

Two “EvoDevos”

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There are two ways of conceptualizing evolution, the externalist and the internalist perspectives, also called functionalism and structuralism respectively (Webster and Goodwin 1982; Hughes and Lambert 1984; Lambert and Hughes 1988; Smith 1992; Resnik 1994).¹ The nature of matter, on which these two systems of thought have been constructed, is their crucial difference. Darwinism, and consequently, the standard theory of evolution, derives from the externalist perspective. From this point of view, living matter is a passive and non-intrinsically ordered entity, requiring organic form to have been forged by an *external agency*. This framework is the result of importing Newtonian mechanics into the study of living organisms by both preformationists and Darwin during the 18th and 19th centuries respectively (Lenoir 1987; Rádl 1988).

If matter is inert, how is biological form generated? The idea is that form is somehow preformed. During the pre-evolutionary era, the existence of a *homunculus* was proposed, a miniature of the progenitor contained in either the spermatozoid—as defended by spermists—or in the ovum—as defended by ovists. Here form was already completely present in the embryo. The development from a parcel of homogeneous and transparent matter to a heterogeneous and complex organism was only apparent in this view; there was no qualitative change during ontogeny, only growth: the “evolution” (unfolding) of the *homunculus*.

During the evolutionary era it was suggested that hereditary traits were transmitted by particles. The idea was not new;

it was already proposed by some Greek philosophers (Terrall 2007). These particles, called “gemmules” in Darwin’s version, specified the different types of cells that constitute the organism. Later, Weismann called them “hereditary particles,” and de Vries called them “pangenes.” This last name was shortened to “genes” by Johannsen (Gayon 2000; Gould 2002). In their early versions, these particles defined an organism’s cells; however, how the different cell types were directed to form tissues and organs during ontogeny (i.e., morphogenesis) remained to be explained (Amundson 2007). In their later version, initiated by Morgan (Allen 1986; Robert 2004; Amundson 2007), these particles were supposed to specify both an organism’s cellular differentiation and morphogenesis. This led to the idea of a genetic program for development, viz., that “DNA provides the programme which controls the development of the embryo and brings about epigenesis” (Wolpert 1991). It seems that “in modern incarnation of preformationism, miniature encapsulated adults or their parts have been replaced by coded information or instructions contained within a genetic programme, executed epigenetically” (Robert 2004: 40).

The metaphor of a genetic program for development (i.e., that form is coded in DNA) has been the explanation for the problem of form within the mechanistic paradigm.

The external organizing principle proposed by Darwin was natural selection. Thus, organization in living beings is the result of repeated episodes of natural selection of random phenotypic variants produced by random alteration of this genetic program: “since Darwin, we turn to a single singular force, natural selection, which we might as well capitalize as though it were the new deity. Random variation, selection-sifting. Without it, we reason, there would be nothing but incoherent disorder” (Kauffman 1995: 8).

From the internalist perspective, living matter is an active agent—an excitable medium (Goodwin 1994; Newman 2003) capable of self-organization, i.e., capable of exhibiting “order for free” (Kauffman 1993) by the interaction between different subcomponents, without requiring an external

organizing factor (Halley and Winkler 2008). While genes and their products also have an important role in this framework, they are considered insufficient to explain biological organization. Genes encode some of the system's components, including those participating in self-organizing dynamics, and also specify molecules that, via natural selection, *stabilize* the self-organized forms, but do not *generate* them (Goodwin 1982, 1994; Newman and Müller 2000; Forgacs and Newman 2005).

The internalist perspective antedates Darwinism. Its roots can be traced back to morphologists of the beginning of the 19th century who, influenced by Kant, were principally involved in the search for the natural laws governing the organization of living beings. Contrary to the conception of an organism as a machine, where the whole is constructed from separate parts and the relationships between them are external or nonconstitutive, Kant interpreted organisms as self-organizing wholes, whose parts are both cause and effect of each other. From this perspective, organisms present internal (constitutive) relationships between their parts (a real structure), which are a result of the organizing principles leading the generation of form.

Some prominent advocates of the alternative view were Goethe, Cuvier, St. Hilaire, Owen, and, later, the embryologist Hans Driesch² (Webster and Goodwin 1982; Lenoir 1987; Smith 1992; Goodwin 1994). The idea was proposed in general terms by the epigeneticists of the 18th century, like Caspar Friedrich Wolff, who asserted, contrary to the preformationists, that the appearance over time of structures during ontogeny was not an illusion, but a real phenomenon. They postulated that it was a law-like process and, consequently, scientists should be able to explain the final forms resulting from development by investigating the laws governing this process (Rádl 1988).

Internalist theories were definitively abandoned at the beginning of the 20th century due to the difficulty to empirically characterize the "inner force" that guided organization in living beings. However, when both mathematics and computing had been sufficiently developed to study the behavior of complex systems, it was possible to visualize that that matter might be capable of self-organization:

This was a real lesson concerning the nature of matter: complex systems tended to spontaneously simplify, giving rise to levels of organization and phenomena unanticipated by examination of the systems' fundamental units. But these emergent modes of behavior and organization were only evident when the systems were viewed at appropriated scales—they were not generated by the units acting like clockwork machines or programmed computers. (Newman 2010)

No modern physical scientist adheres to the old conception that all matter is passive, like a billiard ball, pulled and pushed by external forces (the crucial Newtonian–Darwinian

assumption) (Davies 1989; Goodwin 1994; Depew and Weber 1996; Solé and Goodwin 2000). The recognition that matter is capable of self-organizing has given strong support to the alternative view of evolution (Davies 1989; Depew and Weber 1996; Kirschner et al. 2000; Solé and Goodwin 2000; Newman 2003; Belousov and Grabovsky 2007; Batten et al. 2008; Salthe 2008). This trend has been reinforced by a general turning away from the idea of a genetic program for development encoded in the DNA sequence (King and Wilson 1975; Hahn and Wray 2002; Waterston et al. 2002), and specific criticism of this metaphor (Goodwin 1985; Nijhout 1990; Newman 2002). At present, the internalist perspective represents a robust alternative to the dominant evolutionary paradigm.

The need for an appropriate theory of morphogenesis has practical implications. Researchers working in regenerative medicine, who attempt to build organs from stem cells, have pointed out the conceptual lag between the processes of cell differentiation and how they are arranged into organs, some stressing the importance of self-organization in organogenesis (Chuong et al. 2006).

Two Versions of EvoDevo

In the early 20th century, embryology was excluded from the Modern Synthesis (Hamburger 1980), from which the most widely accepted theory of evolution derives. Before the profusion of projects devoted to the study of genes and genomes, the existence of regulatory genes (those which produce transcription factors, which bind to DNA and regulate the expression of other genes) was just a hypothesis (Goldschmidt 1940). The identification of the first transcription factors corresponding to the homeotic genes described by transmission genetics involved in the formation of body plans, the *Hox* genes (for a review, see Gehring and Hiromi 1986), led to calls to incorporate developmental biology into the evolutionary framework (Sterelny 2000; Robert 2001, 2002; Gould 2002; Amundson 2007; Pigliucci 2007). Further work, leading to the characterization of the hierarchical organization of the genome, implied that a mutation in an upstream gene could have more pervasive phenotypic consequences than a mutation in a downstream gene. Prior to these discoveries, it was thought that the genome was composed of a series of "adaptive gene complexes" composed of structural genes, i.e., coding sequences for proteins other than regulatory factors, for the different body parts, and it was thus assumed that phenotypic effects of different mutations were of similar magnitude (Depew and Weber 1996).

The new and fast growing discipline arising in part from this work has been called evolutionary developmental biology or EvoDevo (Gilbert et al. 1996; Arthur 2002). Several authors have noted the presence of different research programs under this designation and the need to distinguish them; but there

is no consensus on the conceptual structure of the field (Hall 2000; Gilbert 2003).

I distinguish two “EvoDevos” and suggest that these two versions reflect the externalist–internalist dichotomy. As Hall (2000) has proposed, the need to distinguish them could be of great importance to evolutionary theory. While one version can be considered a subdiscipline of an *extended evolutionary synthesis* (EES) (Pigliucci and Müller 2010), the second one is a different interpretation of evolution.

These two perspectives are quite clear in their distinct interpretation of the Cambrian explosion: the radiation of animal body plans, “compressed in time” (Rokas et al. 2005) that occurred around 530 million years ago. Under the expectation that different body plans were constructed by different regulatory programs, distantly related species should have more divergent homeotic sequences than closely related ones. However, homeotic genes are astonishingly well conserved across phyla (Lemons and McGinnis 2006), and so are their functions. The conservation is such that they can be interchanged between divergent and different taxa: “Only a jaded biologist could not be astonished at the ability of the Pax-6 Hox gene from mice (which triggers eye formation) to induce in the fruitfly *Drosophila* the formation of fly eyes all over the body, even on the wings” (Coyne 2005: 1029).

This leads to a paradox: If different body plans are constructed by similar homeotic genes, how can we explain this morphological diversification?

One answer is that this diversity is explained by changes in the switches that regulate genes (Carroll 2005, 2008). That is, the coding sequence of transcription factor–specifying genes has been conserved, but the promoters where their products bind have changed their affinity or their location relative to downstream genes. Changes in the switches mean changes in the wiring of the genetic network, which could mediate the corresponding changes in body plans.

This interpretation is rooted in the externalist perspective. It assumes that a hierarchical organization of regulatory genes, as has been observed in several organisms, is a *sine qua non* of body plan organization. Thus, a process of random genetic variation followed by selection gave rise to the different genetic networks, which organized multicellular organisms into the different body plans. On this view, organization is an epiphenomenon of genetic programs.

An alternative explanation is rooted in the internalist perspective. It holds that the first body plans were “generic” (i.e., also present in nonliving systems), self-organizing forms produced by the intrinsic physical and chemical characteristics of ancient cell aggregates (Newman 1994, 2002; Newman et al. 2006). To cite one example, differences in quantities and distribution of cell adhesively in an aggregate of cells can produce the most characteristic forms of early animal embryos: hollow balls, tissue layers, and tubes. The importance of differential

cell adhesion has been demonstrated in the formation of the neural tube in the frog *Xenopus* (Detrick et al. 1990).

On this view, the genetic programs observed in organisms are considered to be products of evolution, in which forms already organized by inherent properties were stabilized by post-hoc genetic circuitry. These programs are not considered a precondition for living systems to organize, but a highly derived condition. During the early stages of multicellular evolution, the most prolific cell–cell interactions for the generation of morphological novelty by self-organization were mediated by “emergent” genetic networks, with numerous positive and negative feedback loops. Only later would the hierarchical networks seen in present-day organisms have become dominant (Salazar-Ciudad et al. 2001). Here, genetic programs are an epiphenomenon of self-organization.

One implication of this distinction for the philosophy of biology is the following: From the externalist perspective, where organization is a product of chance and sorting, the existence of organizational principles is denied and evolution is considered a historical narrative. From the internalist perspective, organic form is the result of the laws of organization, implying that evolution has a law-like component.

Stephen Jay Gould saw evolution as a process with much contingency. He suggested that if we could rerun “the tape of life,” then “any replay . . . would lead evolution down a pathway radically different from the road actually taken” (Gould 1989: 51). Things are rather different from the internalist perspective: “If the ‘tape of life’ were to be replayed things would probably turn out not too different at the level of bauplan” (Newman and Bhat 2009: 10).

The internalist perspective does not cease to be relevant after body plans have evolved. Although the first developmental stages are strongly canalized by hierarchical genetic networks (Dassow et al. 2000), generic physical mechanisms are still fundamental in the morphogenesis of body parts and organs (Newman and Bhat 2008, 2009).

This second version of “EvoDevo” represents what Hall (2000) called developmental evolutionary biology (DevoEvo), an evolutionary theory that is not centered on genes but on the organizing principles governing the generation of form. The development of this theory has just begun, but as pointed out by Hall, it would represent a revolution in evolutionary biology.

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Notes

1. It is important to stress that the same terms have been used within the Darwinian paradigm (Gould 2002; Amundson 2007; Sansom 2008) in a rather

different sense to discuss form and function from the way I (following some other writers) use them here. In the Darwinian framework, structure is directly (adaptations) or indirectly (spandrels) the result of natural selection, which is taken to be the only cause of biological order; thus, structure is contingent. Structure does not obey the spatiotemporal invariance of organizing principles as proposed by structuralism sensu Webster and Goodwin (1982). Contrasting these two kinds of structuralism, Gould (2002) wrote: "Most evolutionists (including the author of this book) are historians at heart, and must view such derisory dismissal of phylogeny as anathema . . . Spandrelists, in strong contrast, generally share the evolutionary biologist's traditional fascination for contingent details of history" (Gould 2002: 1055).

2. In common with one another, these biologists interpreted organisms as a structural unity governed by natural laws. However, they also held strong differences. For example, Cuvier argued that internal structure was the result of internal functional relationships, with specific necessary combinations of organs establishing the functional harmony of the whole, while St. Hilaire argued that this structure represented a pure morphological plan whereby functional considerations were secondary. Notice that Cuvier's functionalism is completely different from Darwinian functionalism. Russell stressed this difference in his book *Form and Function*: "By 'conditions of existence' he [Cuvier] means something quite different from what is now commonly understood. The idea of the external conditions of existence, the environment, enters very little into his thought. He is intent on the adaptations of function and organ within the living creature" (Russell 1916: 34).

References

- Allen GE (1986) T. H. Morgan and the split between embryology and genetics, 1910–35. In: *A History of Embryology* (Horder TJ, Witkowski JA, Wylie CC, eds), 1910–1935. Cambridge, UK: Cambridge University Press.
- Amundson R (2007) *The Changing Role of the Embryo in Evolutionary Thought*. New York: Cambridge University Press.
- Arthur W (2002) The emerging conceptual framework of evolutionary developmental biology. *Nature* 415: 757–764.
- Batten D, Salthe NS, Boschetti F (2008) Visions of evolution: Self-organization proposes what natural selection disposes. *Biological Theory* 3: 17–29.
- Belousov LV, Grabovsky VI (2007) Information about a form (on the dynamic laws of morphogenesis). *Biosystems* 87: 204–214.
- Carroll SB (2005) *Endless Forms Most Beautiful: The New Science of Evo Devo and the Making of the Animal Kingdom*. New York: Norton.
- Carroll SB (2008) Evo-Devo and an expanding evolutionary synthesis: A genetic theory of morphological evolution. *Cell* 134: 25–36.
- Chuong C, Wu P, Plikus M, Jiang TX (2006) Engineering stem cells into organs: Topobiological transformations demonstrated by beak, feather, and other ectodermal organ morphogenesis. *Current Topics in Developmental Biology* 72: 237–274.
- Coyne JA (2005) Switching on evolution. *Nature* 435: 1029–1030.
- Dassow G, Meir E, Munro EM, Odell GM (2000) The segment polarity network is a robust developmental module. *Nature* 406: 188–192.
- Davies PCW (1989) *The Physics of Complex Organisation*. Edinburgh, UK: Edinburgh University Press.
- Depew DJ, Weber BH (1996) *Darwinism Evolving: Systems Dynamics and the Genealogy of Natural Selection*. Cambridge, MA: MIT Press.
- Detrick RJ, Dickey D, Kintner CR (1990) The effects of N-cadherin misexpression on morphogenesis in *Xenopus* embryos. *Neuron* 4: 493–506.
- Forgacs G, Newman SA (2005) *Biological Physics of the Developing Embryo*. Cambridge, UK: Cambridge University Press.
- Gayon J (2000) From measurement to organization: A philosophical scheme for the history of the concept of heredity. In: *The Concept of the Gene in Development and Evolution* (Beurton PJ, Falk R, Rheinberger HJ, eds), 69–90. Cambridge, UK: Cambridge University Press.
- Gehring WJ, Hiromi Y (1986) Homeotic genes and the homeobox. *Annual Review of Genetics* 20: 147–173.
- Gilbert S (2003) Evo-devo, devo-evo, and devgen-popgen. *Biology and Philosophy* 18: 347–352.
- Gilbert S, Opitz JM, Raff RA (1996) Resynthesizing evolutionary and developmental biology. *Developmental Biology* 173: 357–372.
- Goldschmidt R (1940) *The Material Basis of Evolution*. New Haven, CT: Yale University Press.
- Goodwin BC (1982) Development and evolution. *Journal of Theoretical Biology* 97: 43–55.
- Goodwin BC (1985) What are the causes of morphogenesis? *BioEssays* 3: 32–36.
- Goodwin BC (1994) *How the Leopard Changed Its Spots: The Evolution of Complexity*. New York: Scribners.
- Gould SJ (1989) *Wonderful Life: The Burgess Shale and the Nature of History*. New York: Norton.
- Gould SJ (2002) *The Structure of Evolutionary Theory*. Cambridge, MA: Harvard University Press.
- Hahn M, Wray G (2002) The g-value paradox. *Evolution and Development* 4: 73–75.
- Hall BK (2000) Evo-devo or devo-evo: Does it matter? *Evolution and Development* 2: 177–178.
- Halley JD, Winkler DA (2008) Consistent concepts of self-organization and self-assembly. *Complexity* 14: 10–17.
- Hamburger V (1980) Embryology and the modern synthesis in evolutionary theory. In: *The Evolutionary Synthesis* (Mayr E, Provine W, eds), 97–112. Cambridge, MA: Harvard University Press.
- Hughes AJ, Lambert DM (1984) Functionalism, structuralism, and "ways of seeing." *Journal of Theoretical Biology* 111: 787–800.
- Kauffman S (1993) *The Origins of Order: Self-Organization and Selection in Evolution*. Oxford, UK: Oxford University Press.
- Kauffman S (1995) *At Home in the Universe: The Search for Laws of Self-Organization and Complexity*. London: Viking.
- King MC, Wilson AC (1975) Evolution at two levels in humans and chimpanzees. *Science* 188: 107–116.
- Kirschner M, Gerhart J, Modliszewski JL (2000) Molecular "vitalism." *Cell* 100: 79–88.
- Lambert DM, Hughes AJ (1988) Keywords and concepts in structuralist and functionalist biology. *Journal of Theoretical Biology* 133: 133–145.
- Lemons D, McGinnis W (2006) Genomic evolution of Hox gene clusters. *Science* 313: 1918–1922.
- Lenoir T (1987) The eternal laws of form: Morphotypes and the conditions of existence in Goethe's biological thought. In: *Goethe and the Sciences: A Re-appraisal* (Amrine F, Zucker F, Wheeler H, eds), 17–28. Dordrecht, Netherlands: Reidel.
- Newman SA (1994) Generic physical mechanisms of tissue morphogenesis: A common basis for development and evolution. *Journal of Evolutionary Biology* 7: 467–488.
- Newman SA (2002) Developmental mechanisms: Putting genes in their place. *Journal of Biosciences* 27: 97–104.
- Newman SA (2003) From physics to development: The evolution of morphogenetic mechanisms. In: *Origination of Organismal Form* (Müller GB, Newman SA, eds), 221–239. Cambridge, MA: MIT Press.
- Newman SA (2010) Stuart A. Newman [interview]. In: *Evolutionary Theory: 5 Questions* (Ofstedal G, Friis JKBO, Roussel P, Norup MS, eds). Copenhagen: Automatic Press.
- Newman SA, Bhat R (2008) Dynamical patterning modules: Physico-genetic determinants of morphological development and evolution. *Physical Biology* 5: 1–14.

- Newman SA, Bhat R (2009) Dynamical patterning modules: A “pattern language” for development and evolution of multicellular form. *International Journal of Developmental Biology* 53: 693–705.
- Newman SA, Forgacs G, Müller GB (2006) Before programs: The physical origination of multicellular forms. *International Journal of Developmental Biology* 50: 289–299.
- Newman SA, Müller GB (2000) Epigenetic mechanisms of character origination. *Journal of Experimental Zoology B (Molecular Development and Evolution)* 288: 304–317.
- Nijhout HF (1990) Metaphors and the role of genes in development. *BioEssays* 12: 441–446.
- Pigliucci M (2007) Do we need an extended evolutionary synthesis? *Evolution* 61: 2743–2749.
- Pigliucci M, Müller GB, eds (2010) *Evolution: The Extended Synthesis*. Cambridge, MA: MIT Press.
- Rádl E (1988) *Historia de las teorías biológicas*. Madrid, Spain: Alianza Editorial.
- Resnik D (1994) The rebirth of rational morphology: Process structuralism’s philosophy of biology. *Acta Biotheoretica* 42: 1–14.
- Robert JS (2001) Interpreting the homeobox: Metaphors of gene action and activation in development and evolution. *Evolution and Development* 3: 287–295.
- Robert JS (2002) How developmental is evolutionary developmental biology? *Biology and Philosophy* 17: 591–611.
- Robert JS (2004) *Embryology, Epigenesis and Evolution: Taking Development Seriously*. Cambridge, UK: Cambridge University Press.
- Rokas A, Kruger D, Carroll SB (2005) Animal evolution and the molecular signature of radiations compressed in time. *Science* 310: 1933–1938.
- Russell E (1916) *Form and Function*. London: John Murray.
- Salazar-Ciudad I, Solé R, Newman SA (2001) Phenotypic and dynamical transitions in model genetic networks. II. Application to the evolution of segmentation mechanisms. *Evolution and Development* 3: 95–103.
- Salthe NS (2008) Natural selection in relation with complexity. *Artificial Life* 14: 363–374.
- Sansom R (2008) The nature of developmental constraints and the difference-maker argument for externalism. *Biology and Philosophy* 24: 441–459.
- Smith KC (1992) Neo-rationalism versus neo-Darwinism: Integrating development and evolution. *Biology and Philosophy* 7: 431–451.
- Solé R, Goodwin B (2000) *Signs of Life: How Complexity Pervades Biology*. New York: Basic Books.
- Sterelny K (2000) Development, evolution, and adaptation. *Philosophy of Science* 67: 369–387.
- Terrall M (2007) Speculation and experiment in Enlightenment life sciences. In: *Heredity Produced: At the Crossroads of Biology, Politics, and Culture* (Mueller-Wille S, Rheinberger H-J, eds), 253–275. Cambridge, MA: MIT Press.
- Waterston R, Lindblad-Toh K, Birney E, Rogers J, Abril J, Agarwal P (2002) Initial sequencing and comparative analysis of the mouse genome. *Nature* 420: 520–562.
- Webster G, Goodwin B (1982) The origin of species: A structuralist approach. *Journal of Social and Biological Structures* 5: 15–47.
- Wolpert L (1991) *The Triumph of the Embryo*. Oxford, UK: Oxford University Press.