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PREFORMATION *VS.* EPIGENESIS: INSPIRATION AND HAUNTING WITHIN AND OUTSIDE CONTEMPORARY PHILOSOPHY OF BIOLOGY

Abstract

The 17th and 18th centuries were the theatre of the fight between two main theories concerning the development of organisms: preformationism (or preformism) and epigeneticism (or epigenesis). According to the first, the formation of new features during organisms' development can be seen as the result of a mere *unfolding* of features that were preformed in the sperm, the egg, or the zygote. According to epigeneticism, there is no pre-existing form, and development is a process where genuinely new characters *emerge* from formless matter. The debate involved naturalists, anatomists, physiologists, microscopists, medical doctors, and philosophers as well. Current developmental biology is, according to some, still inspired (or haunted) by the age-old controversy. The aim of this contribution is twofold. First, to discuss in which guise, if any, the old controversy is still shaping the contemporary debate in biology and philosophy of biology; and, second, to sketch Schelling's position on that debate, suggesting that it may contain some still valuable philosophical insight.

Introduction

Schelling's naturephilosophy is not the most popular subject for Schelling scholars. This is due in part to its obscurity (Iain Hamilton Grant 2006, p. VII) declared that it is "among the most opaque parts of an unusually motile and profligate philosophy", that "requires considerable, text-consuming reconstruction"), and in part to its alleged connection with vitalism. The very same features probably make Schelling's naturephilosophy an even more suspicious subject among contemporary philosophers of biology. Does it make sense to look at the naturephilosophy, not only against the background of the 17th-18th centuries debate on organisms' development, but also from the perspective of current philosophy of biology? I think so, but some preliminary caveats are in order.

First. In this contribution I shall buy into the characterization of philosophy of nature as a way of doing philosophy of biology – as argued by Peter

Rivista di estetica, n.s., n. 74 (2/2020), LX, pp. 119-138

Godfrey-Smith in the first chapter of his book *Darwinian Populations and Natural Selection* (2009). Here, Peter-Godfrey Smith distinguishes the project of philosophy of science from that of what can be called "philosophy of nature". While the focus of the philosophy of science is science itself, how it works and its achievements, the focus of the philosophy of nature is "the natural world as seen through the instrument of science" (p. 3). In other words, philosophy of nature takes scientific (and biological, in particular) results and insights in order to work out what that work tells, philosophically, about nature and our place in it.

It may be objected, of course, that we may take our view of the world directly from science, without the intermediation of philosophy. The twofold answer to this possible objection is, on the one hand, that the worldview provided by science is somehow constrained by science itself (e.g. its language and concepts are developed according to the demands of science and the scientific community); accordingly, when that worldview is exported to a broader discussion, it may become misleading. On the other hand, that it is rarely among the purposes of science to clarify and make explicit "the picture that science is giving to us of the natural world and our place in it" (p. 3).

Second. As said, Schelling's naturephilosophy, also because of its alleged connection with vitalism, had and has a difficult reception. However, claims such as Lenoir's on the "unscientific vitalism of the *Naturphilosophen*" (Lenoir 1982: 215) are questionable, at least in reference to Schelling. In general, it may be noticed that Schelling engaged successfully in making himself aware of the state of the art in contemporary science (for instance, he was familiar with transformational ideas coming from England and Erasmus Darwin's work – see Richards 2017) lamenting the scarcity and limitations of experimental science (Heuser-Keßler 1992). More specifically, according to some, it would be a mistake ascribing to Schelling the so-called "metaphysical vitalism", i.e. the position that postulates the existence of an immaterial entity or principle that, operating in organisms only, would explain their peculiarities compared to inorganic matter. In fact, while agreeing with vitalism in wanting to preserve the specificity of organic phenomena, Schelling "rejects principles such as vital forces or the formative drive postulated by vitalism, even for purely heuristic purposes" (Kabeshkin 2017: 1180).

Third. I shall focus on one specific topic, i.e. organisms' development. In the 17th and 18th centuries naturalists and philosophers with an interest in natural history and science were engaged in what we call today developmental biology, and in particular in the understanding of the mechanisms of morphogenesis, which remains one of the most formidable challenges of contemporary developmental biology. How do organisms, that start formless, acquire a definite form, growing and differentiating their parts according to a certain trajectory? How is it that organisms, unlike inorganic matter, are capable of regenerating their tissues, organs, parts or even whole bodies, or again, to undergo metamorphosis? This kind of questions inspired the debate in the seventeen and eighteen centuries, and this very kind of questions inspires developmental biology also today. While the *explananda* remain the same since Aristotle, the *explanantia* clearly have changed, thanks to biological findings and knowledges. However, at least according to Mahner and Bunge (1997, ch. 8), the new *explanantia* are "haunted" by the old ones. In the course of this contribution, I shall outline the nature of developmental *explananda*, (sect. 1); I shall then look at the 17th-18th century main models of explanation, i.e. at the epigeneticism *vs.* preformationism debate (sect. 2), to investigate whether they are still somehow adopted today (sect. 3 and 4). Finally (sect. 5), I shall draw some conclusion and sketch Schelling's position on the debate, making mainly reference to the *First Outline of a System of the Philosophy of Nature* (1799), suggesting that it may contain some still valuable philosophical insight.

1. Developmental explananda

If we look at a contemporary textbook of developmental biology (Gilbert 2018: 2-3), the two fundamental questions of developmental biology are: (1) how does the fertilized egg give rise to the adult body? and (2) how does that adult body produce another body? These questions clearly echo the lines according to which Kant, at the end of 18th century, framed the modern conception of organism. For Kant, organisms pose a challenge to purely mechanical explanations because they are, unlike artifacts, natural ends, i.e., they are the cause and effect of themselves,[1] in at least three senses (Kant 1790 § 64; 2000: 243 ff). First, "a tree generates another tree in accordance with a known natural law" and "the tree that it generates is of the same species; and so it generates itself as far as the species is concerned", and this is the root of the second of Gilbert's questions. Second: "a tree also generates itself as an individual. This sort of effect we call, of course, growth", and from here it comes the first of Gilbert's question, which is, in Kant's view, that an organism does not grow through a mere addition of matter "in accordance with mechanical laws", but through the assimilation and transformation of matter from the outside. The third sense, which is part and parcel of the previous question, is functional integration: "one part of this creature also generates itself in such a way that the preservation of the one is reciprocally dependent on the preservation of the other". As Schelling will write, organic matter is "*forced* to assume a *determinate form and figure*, which precisely for this reason appear to human judgment as a *purpose* of nature" (Schelling 1798, cit. in Gambarotto 2017: 79).

[1] On Kant's internal and external purposiveness, see Illetterati 2014.

In the first question we may include today, using a "cell-language" that Kant could of course not have used, the explanation of phenomena such as differentiation (how is it that a single cell, the fertilized egg, gives rise to hundreds of different cell types?); morphogenesis (how is it that the cells are not randomly distributed, but rather form ordered structures such as tissues and organs?); regeneration (some organisms can regenerate every part of their bodies,[2] how can they do that, and while not all of them can?). The reproduction question may instead be formulated as follows: only sperm and egg can transmit the "instructions" for making an organism from one generation to the next; how they do so?

All these *explananda* were, even though under a different guise, the focus of the debate on the development of organisms in Schelling's time among embryologists, medical doctors, chemists, naturalists, and philosophers.

2. Developmental explanantia*: Preformationism vs. epigenetiscim*

The 17th and 18th centuries were the battlefield of two opposing theories concerning the development of organisms: preformism and epigenesis. Basically, preformationists thought that organisms' development consisted in the *unfolding* of characters that were already preformed in the sperm, the egg, or the zygote and that the novelties emerging during development were only apparent. Epigenesists, on the contrary, thought that there was no pre-existing form, and that development implied the emergence of truly new features from an unstructured original germ.

The first authors to formulate a preformationist hypothesis were Hippocrates, who proposed that all the structure of the adult was present in the zygote, and Anaxagoras, who believed instead that all parts of the child were preformed in the paternal semen. The roots of epigenesis theory go back instead to Aristotle[3]. In the *Generatione animalium*, he described how the four causes (i.e., material, final, formal, and efficient) worked in producing and organizing the development of individual organisms. In particular, he conducted his observation on chicken eggs, explaining that there was no form there, but rather the form was gradually acquired over time.

The 17th and 18th centuries witnessed the alternating fortunes of the two theories. The conventional birthdate of modern epigenesis is 1651, the year of the publication of *On the Generation of Animals* by the English physician William Harvey. The theory was in contrast to other leading scientists of that time, such

[2] At least not in this form, but see Richards 2017.

[3] That Aristotle might be considered a forerunner of epigenesis is the "standard view" (see for instance Maienschein 2017). However, not all authors agree with it. Delbrück (1971), for instance, considers Aristotle a preformationist.

as the pioneers of microscopy Jan Swammerdam, who is considered the father of modern preformationism, and Marcello Malpighi. The most iconic proponent of 17th century preformationism was undoubtedly the Dutch mathematician and physicist Nicolaas Hartsoeker, who, in observing human sperm cells for the first time in history, claimed to have observed a tiny person, a "*petit enfant*", curled up within them, of which he drew a sketch in his *Essai de dioptrique* (1695).[4]

Figure 1 - *Preformation*, drawn by N. Hartsoecker 1695

The reputation of scientists such as Swammerdam, Malphighi, and Hartsoeker made preformationism prevail in the first middle of the 17th century, and by the beginning of the 18th century, preformationism was widely accepted. However, the fight did not end. The middle of the century was the arena of the dispute between the Swiss anatomist and physiologist Albrecht von Haller and the German physiologist Caspar Friedrich Wolff. The former, after performing experiments on chicken embryos, defended preformationism; the latter, also thanks to the use of more advanced microscopy techniques, disproved Haller's results and endorsed the theory of epigenesis. According to Wolff, plants and animals develop from an amorphous and undifferentiated substance in which, progressively, vesicles or corpuscles, and vessels emerge in the form of small spherical cavities filled with a nutritive fluid. This fluid gradually loses its volatility, creating vesicles and vessels that then become organs. In Wolff's view, this was sufficient to explain the development of plants and animals without any need for preexisting structures (Gambarotto 2018: ch. 1). Wolff's view was not well received at the time, mainly because it postulated a *vis essentialis* that caused the tendency of fluid to coagulate. After all,

[4] How it happened that the early microscopists saw what was not there? More generally, two factors seem to have played a role: the imperfection of the early microscopes that caused optical aberrations (mainly arising from the interaction of light with glass lenses); and imagination (cf. Mahner, Bunge 1997: 277).

it was the time of the Scientific Revolution, and, as Gould (1977: 21) noticed, "the preformationists were the mechanists of their time" so that the postulation of vital forces was incompatible with the mechanistic Zeitgeist. By the middle of 19th century, the conflict was put aside, mainly in consequence of the dismissal of preformism due to the development of cell theory by 1839.

Both theories had pros and cons. Preformationists could not explain why two gametes are necessary for reproduction, but they were free from the burden of explaining in virtue of what the developmental process takes place, what triggers it and what force drives it. In fact, since no new characters emerge, the development just consists in the unfolding of entirely pre-existing forms created by God (forms that, however, we cannot observe, *pace* Hartsoeker). We might say that God is the ultimate preformationist *explanans*. On the contrary, epigenesists had the advantage of making no reference to invisible things as *Homunculi* and the like, but had problems in explaining why all development in a species, in many distinct conditions, leads to similar offspring (Huneman 2013); and, in general, they had to face the burden of answering the above questions that preformationists were exempted from. In fact, for epigenesists, nothing organized exists at the beginning of the development of the embryo; development takes place by means of the continuous action of forces that, step after step, build the organism, one layer after the other. In this process, many structures present at one stage disappear at the next stage, and new structures emerge. But in virtue of what? If the egg is formless, then some force must impose form upon matter, guiding formation from egg to adult organism. Epigenesists then had to buy into one or another form of vitalism. Vital forces are thus the ultimate *explanantia* of epigenesists: Wolff postulated a *vis essentialis*, Buffon a *force pénétrante*, Blumenbach a *nisus formativus* or *Bildungstrieb*. Making these forces compatible with the Newtonian paradigm was a challenge that some epigenesists, Blumembach for instance, took up (see section 4).

Gould (1977: 17-18) summarized effectively this tension:

> What greater mystery can there be than the growth of something so complex as a human baby from humble beginnings in an essentially formless egg or, as Aristotle would have it, the menstrual blood? The two extreme solutions have their strengths and problems. One can believe what one sees and argue that parts are formed sequentially by external forces acting upon matter only potentially capable of normal development (epigenesis). But what epigenesists could then regulate ontogeny? Indeed, the eighteen-century epigeneticists often took refuge in vitalism or outright mysticism. Or one can label what one observes as mere appearance and contend that the complexity of the final product is present from the first, though the germ and young embryo may be too tiny or too transparent to show it (preformationism). Ontogeny, then, is the evolution – literally, the unrolling – of this preformed complexity. This position avoids the dilemma of mystical forces, but it compels us to postulate what we do not perceive.

Neither traditional preformationism nor epigenesis are sustainable in the light of contemporary biology's knowledge. And yet, 20th century developmental biology "was still inspired (or haunted) by the age-old, though somewhat updated, controversy over preformationism versus epigeneticism" (Mahner and Bunge 1997: 271). A reason why it is so has been suggested by Vecchi and Hernandez (2014). Preformationism and epigenesis should be conceived as metaphysical research programs, *sensu* Popper, rather than genuine scientific hypotheses. This would explain both their resilience and their fruitfulness, accounting for the fact that epigenesis and preformationism continue to come back under new guises, somehow permeating and shaping the debate. In fact, insofar as they are metaphysical programs, they are not testable, accordingly they cannot be really disproven and dismissed. What can be disproven (or accepted) are the scientific hypotheses that are generated within their frameworks such as, for instance, the existence of the *Homunculus* (disproven) or the existence of "instructions" for development (accepted). In this sense, metaphysical research programs are scientifically useful, providing a framework for testable scientific hypotheses and contributing to the production of new hypotheses.

In the next two section, I shall show in which guise preformationism and epigeneticism may be said to still shape (in their respective weak versions) the 20th century debate in developmental biology and philosophy of biology. To make this point, I shall offer a quick overview of two models of morphogenesis theorized in the second half of the nineties, i.e. Wolpert's and Turing's models. I shall then have a look at today's debate, suggesting that possibly the haunting has come to an end.

3. From the Homunculus *to informational preformationism (*ex DNA omnia*)*

Already from the middle of the 18th century on, most embryologists abandoned the *Homunculus* and, with it, naïve preformationism. An important part in this was played both by Wolff' polemical attacks to Haller's and Bonnet's preformationism (Gambarotto 2018: ch. 2), and Trembley's experiments on the green hydra, a fresh-water animal of the phylum Cnidaria. When cut in half, a green hydra regenerates recreating the whole organism, showing no difference with the original; this remarkable regenerative power was seen as a prove of the presence of an inherent power of living matter.

The *Homunculus* epitomises naïve preformationism, according to which in the original egg/sperm were somehow contained entire miniature adults. We should distinguish this naïve position from a critical or weak form of preformationism that arose thanks to the experimental and theoretical contributions of Malpighi, Haller, and Bonnet (cf. Gould 1977: 19 ff). Critical preformationists, rather than believing that an entire, miniaturized, adult organism was present in the egg or the sperm, typically thought that something invisible proper to the species type – some "disposition", as Haller and Bonnet called it – was already effective and active within the first stages of the embryo, somehow "coding" (we would say today) the adult organism, or its parts. Bonnet, for instance, in his *Palingénésie philosophique* of 1769 claimed that God created a mass of germs. Each germ encapsulates (*emboîtes*) an embryonic organism, which in turn encapsulates another, smaller, embryonic organism with its own germs and so on, like Russian dolls, until the original germs. The offspring, for him, existed preformed in the female gametes, accordingly the ovary of the ancestress would contain all the descendants. As a proof of his theory, he brought the fact that generation of offspring without copulation was possible: aphids – he discovered – can reproduce by parthenogenesis (he kept one aphid in isolation for its entire life, proving that it reproduced anyway). But, while at first Bonnet probably thought that the germ represented a preformed individual, he soon came to the conclusion that the germ characterized only the species, while the individual variation was produced by external factors: "It is not necessary to believe that the germ has in miniature all the traits which characterize the mother as an individual. The germ carries the original imprint of the species, and not that of the individual" (*Considérations*, sect. LXV, *Oeuvres*, 5: 134; quoted in Bowler 1973: 262-263).

The metaphysical framework of preformationism, i.e. the idea that the adult organism is *somehow* preformed in the female egg, male sperm, or fertilised egg, is still alive in informational preformationism (Müller and Olsson 2003): "modern-day biology often has a very similar use of the concept of information: as a set of 'instructions', the genome preforms the adult organisms'" (Huneman 2013: 1734). With the advent of molecular biology and the discovery of DNA's structure, preformationism was back in a new guise: the encapsulated germs have become coded instructions. The genetic program, in a way that reminds Bonnet's germs, is conceived to include, as a recipe, all the information to produce precisely and entirely the adult organism, determining when and how cells, tissues, and organs will be build. Morphogenesis, growth, and differentiation are then, once again, pre-formed.

Informational preformationism is well fitted to the Modern Synthesis, which interprets evolution as a change of gene frequencies in populations, and which typically sees the relation between genes and phenotypic traits as one-one rather than many-many (a view that also permeates some of our scientific practices, think for instance of genetic engineering). Yet, as Vecchi and Hernandez put it, "accepting the strategy of molecularization does not solve in one stroke all the fundamentally metaphysical issues at the core of developmental biology" (2014: 80). In particular, it does not solve the differentiation question (recall Gilbert's questions listed at the beginning of sect. 1), and specifically the "differentiation paradox"[5], i.e. the fact that all cells of the embryo have the same

[5] Also called "Lillie's paradox". As Lillie (1927: 365) puts it: "It is apparently not only sound, but apparently almost universally accepted genetic doctrine to-day that each cell receives the

genes, accordingly differentiation cannot be explained on a genetic basis only, and additional information seems to be required. It is to handle this paradox that Lewis Wolpert proposed the hypothesis of *positional information* (Wolpert 1969; 1971).

In a nutshell, according to Wolpert (1969; 1971), the additional information required to the genetic information (contained in the fertilised egg) would be provided by the position of the cell in the developing systems. Cells would "interpret" their positional value and they would differentiate accordingly. The thesis was still too simplistic, and substantiating it biologically was problematic; nothing was known about the capability – if any – of cells to "evaluate" their position and to develop accordingly. Between 1971 and 1975, positional information was then reinterpreted in terms of genes, with cells eventually considered as automata computing instead of interpreting, following automatically the rules dictated by the master plan.

In such a view, unlike traditional preformationism, the fertilized egg neither contains a miniaturized adult nor a complete description of it. But it contains a genetic program for making it, with gene networks controlling the behaviour of cells (Wolpert, Lewis 1975). Each cell would contain the specification of the behaviour of every cell in every position, and a sort of complete list of the cells that will differentiate as a type or another. All this information would be localized in the Dna. The nuclear Dna is then thought to contain "the program" that will trigger (through genetic switching) and unroll the normal developmental process; as a consequence, all other variables (e.g. the cytoplasmic and embryonic environments) end up being irrelevant. Thus, according to Wolpert's computational embryology, the embryological output can be computed on the basis of the macromolecular input of the components only (specifically proteins and nucleic acids), without taking into account the nature of cells' responses (Rosenberg 1997).

In sum, for informational preformationism (of which Wolpert's model may be seen as an exemplification), all information needed to build an organism is genetic and it controls cells' behaviour. As a consequence, cells become causally redundant, and the process of spatial regulation is reduced to that of differential genes expressions (Vecchi, Hernandez 2014).

The theory of positional information was initially introduced to complement genetic information with another kind of developmentally-relevant information in order to explain differentiation (genes provide a program, but such a program is *interpreted* step by step by cells, which behave accordingly). In doing so, it may be seen as an attempt to reconcile the old debate integrating (critical) preformationism with epigenesis, with genes partially "preforming" organism's

entire complex of genes. It would, therefore, appear to be self-contradictory to attempt to explain embryonic segregation by behavior of the genes which are ex hyp. the same in every cell".

development, and cell's interpretation allowing the emergence of new features, in an epigenesist spirit. But too little was known of cells' behaviour, and the attempt did not succeed.[6] Informational preformationism has not been proven to be outright wrong but rather to simplistic as a model of development: things have turned out to be much more complicated.

4. From vitalism to emergence

17th and 18th century epigenesists, unlike preformationists, had a formidable difficulty to face, namely to account for what drives development. Historically, epigenesis committed itself with one kind or another of vitalism.

Traditional epigenesists embraced two different kinds of vitalism. On the one hand, we find the animistic version, mainly associated to the name of Georg Ernst Stahl, which echoes Aristotle in conceiving the force driving development as some kind of soul-like principle. On the other hand, we find the materialistic version, which conceives the force driving development as a physical force, in analogy to Newtonian gravitation, as is the case with Blumenbach.

Blumembach's *Bildungstrieb* was taken up by Kant in his *Critique of Judgment*, and that inspired Schelling (see below, sect. 5). The occasion for Blumembach to elaborate the idea of *Bildungstrieb* was again the observation of a hydra in a mill pond. He cut away parts of the hydra and over some days he observed their regeneration, coming to the conclusion that "there exist in all living creatures … a particular inborn, life-long active drive. This drive initially bestows on creatures their form, then preserves it, and, if they become injured, where possible restores their form" (Blumenbach, *Über den Bildungstrieb und das Zeugungsgeschäfte*, 1781: 12-13, quoted in Richards 2000). This force, he claimed, is different from the other natural forces, and he named it *Bildungstrieb* (*Nisus formativus*). It was, according to him, one and the same force that was at play in reproduction, nourishment and parts' restoration. Such a force, in analogy with Newtonian's attraction, originates from unknown causes, knowable and characterizable only through its multiple and pervasive effects.

According to Lenoir (1981: 155) – *contra* Richards 2000, who argued against this interpretation – even though Blumembach view was a kind of vitalism, *Bildungstrieb* has not to be conceived as a force separated from the matter and somehow pervading it, but rather as a result of a certain precise organization of

[6] However, it should be noticed that Wolpert's framework – as he recognizes today – was meant to be more a formal model of the morphogenetic process than a genuine, experimental, explanation of morphogenesis. In such model, the logical nature of the developmental program was postulated, and the details of molecular mechanisms (i.e. the causal role of cellular responses) methodologically ignored.

matter. The emergence due to *Bildungstrieb* then might be seen as a kind of biological emergence not so different from the one typically accepted by partisans of emergence in contemporary biology: "New properties emerge at each level in the biological hierarchy … These emergent properties are due to the arrangement and interaction of parts as complexity increases" (Campbell *et al.* 2008: 3) – more on this in sect. 5.

No biologist today would endorse vitalism, but the question is still to be answered: what is it that drives development? How is it that organisms' development *has a certain direction* and not another one? Why certain cells become kidney cells and others heart cells? Why cells at a certain point stop replicating? This is the reason why epigenesis was still shaping the debate in the 20th century, in a new form. This form, I would like to suggest, is the heir of a certain interpretation of materialistic vitalism.

Let us return to the 20th century debate. As seen in the previous section, Wolpert tried to solve the paradox of cellular differentiation introducing the theory of positional information, i.e. the theory that cells somehow *interpret* their position, and differentiate accordingly. The limit of Wolpert's theory was that he gave no clue about how to understand how this "interpretation" worked, ending with an entirely geneticist approach whereby cells are treated as black boxes.

Two decades before Wolpert proposed his model, Alan Turing had provided, with his reaction-diffusion model, a possible conceptual solution to this question, a solution that Wolpert explicitly considered the antithesis of his own view (Wolpert 1971).

According to Turing, it is not needed to postulate an agent causing the beginning of the morphogenetic process. Rather,

> … it is a random disturbance that causes the instability of the homogenous equilibrium in the embryonic environment which, as a consequence, causes the emergence of the pattern or morphological structure. This process is spontaneous and lacks the central control through agency (Vecchi, Hernandez 2014: 88).

The random disturbance is neither spatially nor temporally programmed, and then it is not predictable. Yet, it is the cause that activates a self-organizing process which does not presuppose any prior pattern (form) out of which the self-organizing form emerges, thus offering "a mechanism of self-organization in which structure could emerge spontaneously from homogeneity" (Fox Keller 1983: 516). It is hard not to see that this kind of emergence echoes Blumembach's *Buildungstrieb* or (Kantian) internal purposiveness.

At the end of this section I shall highlight two main points in order to draw a first preliminary conclusion. The first point is that, even though the two models that we have shortly sketched (Wolpert's and Turing's models) have been traditionally considered to be incompatible, not only both of them survived the test of time, remaining preeminent today, but also have been recently proposed to be fully complementary rather than incompatible alternatives, "two big ideas in developmental biology" that, "despite being conceptually distinct, are in fact wonderfully complementary and often collaborate to establish the complexity of developmental forms that we see" (Green and Sharpe 2015). The same, and this is my second point, holds for epigenetic emergence and informational preformism and. Their compatibility characterizes 21st century preeminent views on the development of organisms: today, epigenesis and preformationism are considered as complementing each other, and no more in opposition (Bodart 2015, ch. 1), and the concept of preformation remains a minimal condition, under the guise of the genetic information needed for the building of the structures of a certain adult organism (for instance, in the form of so-called homeotic genes).

On the basis of the above, Mahner's and Bunge's claim that the old controversy between epigenesis over preformationism is still inspiring or haunting the contemporary debate was probably true when they made it, back in the nineties, but it is disputable today, when the complementarity between the two views is widely recognized. As Lawrence and Levine (2006: R236) notice, "Embryology courses and text books still feel it necessary to give students a sense of these debates, and we can understand this – we too grew up with them. However, there has been a revolution brought about by genetics and molecular biology and it is time to bury some of the old arguments". Their example can clarify this point. In the nineties, a sharp distinction was introduced between mosaic and regulative embryos. Mosaic embryos, considered typical of the invertebrates, were thought to derive from eggs that are a patchwork of determined "territories". They were supposed to develop according to a program and each cell to have a predetermined fate, in a preformist fashion. On the contrary, regulative eggs, considered to be characteristic of vertebrates, are "formless" (i.e. in the specific sense that they are not divided in "territories") and the determination of the particular organs and parts of the embryo occurs during later stages of development, determining "their own fate", in an epigenesist fashion. However, experimental evidence (Lawrence, Levin 2006), has clearly showed that a purely regulative egg and a purely mosaic egg are ideal extremes, nowhere realized in nature (Bodart 2015, ch. 1).

In the final section I am going to suggest, in a sketchy, hypothetical way, that Schelling's view on organisms' and nature's development may be not so at odds with some contemporary positions in evolutionary and developmental biology.

5. Schelling's view on organisms' development

Schelling's theory of organisms cannot be ascribed – if Kabeshkin (2017) is right – neither to vitalism standardly understood (be it metaphysical or heuristic) nor, of course, to reductive mechanism or materialism, that Schelling calls, in the *First Outline of a System of the Philosophy of Nature*, "physiological materialism" (p. 62)[7], i.e. the idea that organisms are entirely explicable in terms of the same (mechanistic) laws and principles that work for inorganic matter. On the background of his general view of nature as infinite productivity, Schelling thought that "The essence of every organism consists in the fact that it is not absolute activity … but an *activity mediated* by *receptivity*; for the existence of the organism is not a *being*, but a perpetual *being-reproduced*" (p. 160). It shall be noticed that "reproduction" here must not be understood as replication only; the term was indeed initially introduced to refer to regeneration of damaged bodily parts (Kabeshkin 2017: 1183). And this brings us to the core of the debate on organisms' development.

Recall the two main questions of developmental biology as framed by Gilbert (sect. 1), but "translated" in a cells-free language (cell theory, as already said, was not yet been proposed when Schelling elaborated his naturephilosophy). One concerns the development from the fertilized egg to the adult body, including the phenomena of differentiation, morphogenesis, and regeneration; the other one concerns reproduction, i.e. how does that adult body produce another body? The answer of Schelling's naturephilosophie to both of them provides insights for conceptualizing these biological phenomena that are quite original.

Organic individuals are, in Schelling's view, the only things capable of struggling, at least temporarily, against external nature's perpetual productivity. The phenomenon of metamorphosis plays a peculiar role in Schelling's naturephilosophy, because it illustrates how both a single organism – be it a plant or an insect ("What the blossom is in relation to the tree, the butterfly is in relation to the caterpillar", p. 38) – or Nature as a whole, develop; we shall then focus, at least for the first *explanandum*, on Schelling's analysis of this phenomenon.

The hypothesis that I am going to explore is that Schelling proposes an explanation of the developmental questions that cannot be categorised as neither preformationist nor epigenesist, but rather as a middle-way position, not at odds with the 21st century view on organisms' development.

First question. Development

In the fourth part (*Inhibition and Stages of Development*) of the *First Outline*, Schelling devotes a two-pages long footnote to metamorphosis (pp. 37-38). Firstly, he explains that "in earlier times the metamorphosis of the insects was taken to be a kind of miraculous event", while the contemporary study of nature, in order to explain it, has transferred "the 'involution' or 'preformation system' to this phenomenon of organic nature … Already in the worm every part of the butterfly is supposed to be there, imperceptibly small, and yet individually

[7] Since from now on I will make mainly reference to the English edition of the *First Outline*, I will cite it simply by page numbers.

preformed". He then passes to refute the preformationism of Swammerdam, allegedly proved by Swammerdam by showing a specimen in which the parts of the future butterfly were already in the pupa. But he dissected the pupa on the verge of the spinning of its cocoon, as Schelling remarks:

> But it is quite conceivable that when one opens the cocoon immediately before the final metamorphosis, after everything is already prepared for it, one can find everything that would shortly come to light on its own … Therefore, that specimen proves absolutely nothing about the preexistence of parts *before* the metamorphosis.

Not only, then, we do not have proofs in favour of preformationism but, on the contrary, we have proofs against it. In particular, according to Schelling, (i) preformationism is not able to explain the disappearance of parts that were there before (since in the butterfly one cannot find the organs that were in the pupa, and yet nothing is lost from the pupa); (ii) the digestion apparatus of the butterfly is entirely different from that of the caterpillar, as required by the fact that the first one "sucks in ethereal nourishment", i.e. nectar, while the second "nourishes itself through crude nourishment", i.e. hard leaves; (iii) the organ of respiration are entirely different as well.

Schelling then proposes his own explanation. And even though, rhetorically, he claims that he does "not yet want to invoke here the general principle that no individual preformation, but only *dynamic* preformation exists in organic nature", he actually does it. What is meant by *dynamic preformation*? Clearly it is not any kind of individual preformism, namely the idea that the individual organism is preformed in the egg, the sperm, or the zygote. It is generic preformation instead, namely development within, and according to, a species (recall the Kantian view on organisms sketched in the first section; see also Zammito 2018, ch. 10). According to Schelling, while there are no forms in miniature ("*preformed seed*, for whose existence there is not a shadow of proof" (p. 47), there is, instead, at the origin of each species, a multiplicity of tendencies, i.e. different possible directions that the formative drive may take. To the "stem organism" – the first individual of each species – all directions are equally possible, since the formative drive is still "free", its direction not yet determined. For one or another direction to be taken, an additional triggering factor is needed:

> The formative drive was *free* with respect to those directions because they were *all equally possible*; not, however, as if which of these directions it would take in any one individual were dependent on chance. There must, therefore, be an external influence on the organism in order to determine the organism toward one of these directions (p. 44).

Schelling's explanation is clearly epigenesist ("organic formation is … the epigenesis of individual parts", p. 37), yet a certain degree of generic preformation, or predetermination is allowed: "various organs, parts, etc., signify nothing but *different directions* of the formative drive; these directions are predetermined, but the individual parts are not" (*ibidem*). It seems then that Schelling is here buying into a middle-way between *epigenesis*, able to explain growth and differentiation by means of the possible different directions of the formative drive, and *dynamic preformationism*, to be understood as predetermination of those directions (once that a direction is taken – and which one is not "dependent on chance" – the others are no more available alternatives: "the prior development of the one makes the development of the other impossible", p. 44).

Notice that this view is is not in the least at odds with the renowned epigenetic landscape metaphor for how gene regulation modulates development suggested by Conrad H. Waddingon firstly in 1940 and then in a refined form in 1957 (Waddington 1940; 1957). Imagine a number of marbles rolling down a hill towards a wall. The marbles will compete for the grooves on the slope, and the ridges between the grooves represent the increasing irreversibility of cell type differentiation. Each marble will come to rest at the lowest possible point, representing eventual cell fates, or tissue types. According to the metaphor, the genome sets the contours of the landscape (predetermining possible directions) but the ball can roll in whichever direction (epigenesis), always generating a functional but slightly different phenotype. Now, on the one hand the metaphor may be criticized as a too genocentric view of development; on the other hand, of course, Schelling knew nothing about genes or gene regulation. However, my point here is that, with his *dynamic preformationism* in which "the directions are predetermined but the individual parts are not", Schelling prefigured, in that imaginative way proper of naturephilosophy, the complementarity between preformism and epigenesis – in the form of a continuous, dynamic, interaction between possible ways that development can take and environmental triggering – that characterizes, as seen at the end of the previous section, the contemporary view in developmental biology.

Second question. Reproduction

Recall the reproduction *explanandum*: Only sperm and egg can transmit the instructions for making an organism from one generation to the next: how they do so? As for the first question seen above, Schelling's answer shall be read in the light of his view of Nature as perpetual productivity. If the phenomenon of metamorphosis plays a peculiar role in Schelling's naturephilosophy, because it illustrates how both a single organism and Nature as a whole, develop ("We know Nature first of all simply as organic or as productive. All of productive Nature is originally nothing other than infinite *metamorphosis*. It can never achieve determined and fixed shapes, i.e. fixed products, if the productive drive is not split into individual stages of development, or if the product does not separate into opposed directions just when it has reached a certain stage of formation" (1799; 2004: 36, italics added)); sexual difference illustrates instead how nature, which is pure productive force, inhibiting itself, generates organisms as its own temporary products.

Schelling's understanding of Nature in terms of a duality of fundamental forces – which he took, as an alternative model to Newtonian mechanics, as many at his times, from chemistry and the doctrine of latent heat (Rueger 2012: 181) – brought him to consider sexual difference as the culminating form of this polarity (Stone 2014). Nature by itself is original and unlimited productive force. In order to explain how products of nature may exist, it is necessary to postulate the existence of a second kind of force, that inhibits – at least provisionally – nature's productivity. To use the well-known Schelling's analogy, organisms are like eddies in a river, "resting points within nature's unending productivity" (Stone 2014: 263). Like a river "produces" its own eddies through the resistance of the liquid to itself, in the same way nature's products keep their (temporary) shape by means of the resistance of the productive force of nature to itself. The same thing happens with sexes throughout the entire organic realm. In the very same way polarization into two forces makes possible nature's productivity and nature's products, organic individuals may reproduce on the condition of undergoing the same polar opposition: "the separation into different sexes is just the separation which we have furnished as the ground of inhibition in the productions of Nature" (Schelling 1799; 2004: 39). The reason why sexes arise, Schelling infers, must be because sexual difference is necessary for reproduction. And organisms' seeking of reproducing "manifests the productive force within them, which drives them to try to pass beyond their finite boundaries in a creative way" and "to realize the unity of their entire species" (Stone 2014). Schelling's answer to the reproduction question, as said, inserts itself in the general Schellingian view of the nature of dynamic development sketched above.

A consideration on this general view is now in order. Concerning nature as infinite productivity, Schelling took up Herder's view (who postulated a continuity between inorganic and organic matter), extending the notion of self-organization coming from Blumembach and Kant to the inorganic and cognitive sphere, so to explain the evolution of the entire universe, from the primordial inorganic matter through the origin of life until the emergence of human mind (Heuser-Keßler 1992).[8] "Nature is self-organizing and, accordingly, self-creating: it develops allowing different levels of organizations to emerge: "The *whole* of Nature, not just a *part* of it, should be equivalent to an ever-*becoming* product. Nature as a whole must be conceived in constant formation, and everything must engage in that universal process of formation" (Schelling 1799; 2004: 28).

Now consider the kind of ontological, naturalistic emergence embraced for instance by one of the fathers of the Modern Synthesis, Ernst Mayr.[9] According to

[8] See also Ferraris 2016.

[9] Tons of pages have been written on emergence in general, few less on emergence in biology. I will not enter in the debate; I will just make reference to Mayr's view as a paradigmatic example of the possibility of conceiving biological emergence in a contemporary "scientifically respectable" way.

him, a false claim against emergentism must be rejected, namely that emergentists are vitalists: "This claim, indeed, was valid for some of the nineteenth-century and early twentieth-century emergentists, but it is not valid for modern emergentists" (1982: 63 ff). According to Mayr (1959), when entities are combined at higher levels of integration, not every property of the new entity is a predictable consequence of the property of the components, new properties can emerge as the result of the integration of existing parts into new, high levels' structures, rather than as the result of old structures acquiring new functions. And emergence, for Mayr, is not an exclusive property of organic matter. Even though it is "vastly more important in living than in inanimate systems" (1982: 131) – and this contributes to the difference between the physical and biological sciences–, "emergence is equally characteristic of inorganic systems" (1982: 63).

Conclusive remarks

As Beiser writes, "*Naturphilosophie* has been ignored or spurned for decades, by historians of philosophy and science alike. Its reputation suffered greatly under the shadow of neo-Kantianism and positivism, which had dismissed it as a form of pseudoscience… For many philosophers and scientists, *Naturphilosophie* became the very model of how *not* to do science" (Beiser 2002: 507). However, a new tendency is emerging – shared by authors like Robert Richards (2002), Frederich Beiser himself (2002), and John Zammito (2018) – that asks for a revision of the role of *Naturephilosophie* in the gestation of biology in Germany and, more generally, for a different reading of the relation between *Naturephilosophie* and the sciences at that time.

In this contribution, I have briefly reconstructed the debate on a specific field – the development of organisms – that took place mainly over 17th and 18th century. This was the background, so to speak, that Schelling inherited. Then I have tried, on the one hand, to outline Schelling's position in that debate, reconstructing his view on organisms' development; on the other hand, to discuss what, if anything, is left of that debate in today's developmental biology. In doing so, I have suggested that Schelling's view is an original one, that cannot be simply ascribed to one or the other of the two positions at stake (preformism or epigenesis) and that, being not at odds with recent results in biology, might contain philosophical insights worth being considered.[10]

[10] I thank Emilio Corriero and Davide Vecchi for their useful comments to a previous version of this contribution, which is part of the project "Emergence in the natural sciences: towards a new paradigm" (R&D Project. Ref. PTDC/FER-HFC/30665/2017) funded by the FCT - Fundação para a Ciência e a Tecnologia.

References

Beiser, F.
– 2002, *German Idealism: The Struggle against Subjectivism, 1781-1801*, Cambridge (MA), Harvard University Press.
Bodart, J.-F.
– 2015, *Embryologie expérimentale*, Louvaine-la-Neuve, De Boeck.
Bouwler, P.J.
– 1971, *Bonnet and Buffon: Theories of generation and the problem of species*, “Journal of the History of Biology”, 6, 2: 259-281.
Campbell, N.A. *et al.*
– 2008, *Biology*, 8th ed., San Francisco, Pearson Benjamin Cummings.
Delbrück, M.
– 1971, *Aristotle-totle-totle*. In J. Monod, E. Borek (eds), *Of Microbes and Life*, New York, Columbia University Press: 50-55.
Ferraris, M.
– 2016, *Emergenza*, Torino, Einaudi.
Gambarotto, A.
– 2018, *Vital Forces, Teleology and Organization*, Springer International.
Godfrey-Smith, P.
– 2009, *Darwinian Populations and Natural Selection*, Oxford, Oxford University Press.
Gould, S.J.
– 1977, *Ontologeny and Phylogeny*, Harvard, Harvard University Press.
Grant, I.H.
– 2006, *Philosophy of Nature after Schelling*, London - New Work, Continuum.
Green, J.B.A., Sharpe, J.
– 2015, *Positional information and reaction-diffusion: Two big ideas in developmental biology combine*, “Development”, 142: 1203-1211, doi:10.1242/dev.114991.
Heuser-Kessler, M.-L.
– 1992, *Schelling’s Concept of Self-Organization*, in R. Friedrich, A. Wunderlin (eds), *Evolution of Dynamical Structures in Complex Systems. Springer Proceedings in Physics, vol 69*, Berlin-Heidelberg, Springer: 395-416.
Huneman, P.
– 2013, *Preformation and Epigenesis*, in W. Dubitzky *et al.* (eds), *Encyclopedia of Systems Biology*, Springer International: 1734-1735.
Kabeshkin, A.
– 2017, *Schelling on Understanding Organisms*, “British Journal for the History of Philosophy”, 25, 6: 1180-1201, doi: 10.1080/09608788.2017.1298989.
Kant, I.
– 1790, *Kritik der Urteilskraft*, ed. by P. Guyer, tr. by P. Guyer, E. Matthews, *Critique of the Power of Judgment*, Cambridge, Cambridge University Press, 2000.
Illetterati, L.
– 2014, *Teleological Judgment: Between Technique and Nature*, in I. Goy, E. Watkins (eds), *Kant’s Theory of Biology*, Berlin-Boston, de Gruyter: 81-98.

Lawrence, P.A., Levine, M.
– 2006, *Mosaic and regulative development: Two faces of the one coin*, "Current Biology", 16, 7: R236-R238.
Lenoir, T.
– 1981, *The Göttingen School and the development of transcendental Naturphilosophie in the Romantic era*, "Studies in History of Biology", 5: 111-205.
– 1982, *The Strategy of Life: Teleology and Mechanics in Nineteenth Century German Biology*, Dordrecht, Reidel.
Lillie, F.R.
– 1927, *The Gene and the Ontogenetic Process*, "Science", 64: 361-368.
Mahner, M., Bunge, M.
– 1997, *Foundations of Biophilosophy*, Berlin-Heidelberg, Springer.
Maienschein, J.
– 2017, *Epigenesis and Preformationism*, in E.N. Zalta (ed.), *The Stanford Encyclopedia of Philosophy* (Spring 2017 Edition), https://plato.stanford.edu/archives/spr2017/entries/epigenesis/.
Mayr, E.
– 1959, *Cause and Effect in Biology*, "Science", New Series, 134, 3489: 1501-1506.
– 1982, *The Growth of Biological Thought*, Cambridge (MA), Harvard University Press.
Müller, G., Olsson, L.
– 2003, *Epigenesis and epigenetics*, in B.K. Hall, W.M. Olson (eds), *Keywords and Concepts in Evolutionary Developmental Biology*, Cambridge (MA), Harvard University Press: 114-123.
Richards, R.J.
– 2000, *Kant and Blumenbach on the Bildungstrieb: A Historical Misunderstanding*, "Studies in History and Philosophy of Biological and Biomedical Sciences", 31, 1: 11-32.
– 2002, *The Romantic Conception of Life: Science and Philosophy in the Age of Goethe*, Chicago, University of Chicago Press.
– 2017, *Did Goethe and Schelling endorse species evolution?*, in J. Lambier, J. Faflak (eds), *Marking Time: Romanticism and Evolution*, Toronto, University of Toronto Press.
Rosenberg, A.
– 1997, *Reductionism redux: Computing the embryo*, "Biology and Philosophy", 12: 445-470.
Rueger, A.
– 2012, *Conceptions of the natural world, 1790–1870*, in A.W. Wood, S.S. Hahn, *The Cambridge History of Philosophy in the Nineteenth Century (1790-1870)*, Cambridge - New York, Cambridge University Press.
Schelling, F.W.J.
– 1798, *Von der Weltseele. Eine Hypothese der höhern Physik zur Erklärung des allgemeinen Organismus*, *hrgb. von J. Jantzen unter mitwirkung von T. Kisser*, Stuttgart - Bad Canstatt, Frommann-Holzboog.
– 1799, *Erster Entwurf eines Systems der Naturphilosophie*; tr. by K.R. Peterson, *First Outline of a System of the Philosophy of Nature*, Albany, Suny Press, 2004.
Stone, A.
– 2014, *Sexual polarity in Schelling and Hegel*, in S. Lettow (ed.), *Reproduction, Race and Gender in the Early Life Sciences*, New York, Suny Press: 259-282.

Vecchi, D., Hernandez, I.
– 2014, *The epistemological resilience of the concept of morphogenetic field*, in A. Minelli, T. Pradeu (eds), *Towards a Theory of Development*, Oxford, Oxford University Press: 79-94.
Waddington, C.H.
– 1940, *Organisers and Genes*, Cambridge, Cambridge University Press.
– 1957, *The Strategy of the Genes*, London, Geo Allen & Unwin.
Wolpert, L.
– 1969, *Positional information and the spatial pattern of cellular differentiation*, "Journal of Theoretical Biology", 25: 1-47.
– 1971, *Positional information and pattern formation*, "Current Topics in Developmental Biology", 6: 183-224.
Wolpert, L., Lewis, L.J.
– 1975, *Towards a theory of development*, "Federation Proceedings", 34: 14-20.
Zammito, J.H.
– 2018, *The Gestation of German Biology. Philosophy and Physiology from Stahl to Schelling*, Chicago-London, The University of Chicago Press.