Probabilistic Epigenetics: An informational Approach

Tiago Rama
trama.folco@gmail.com
https://orcid.org/0000-0002-1531-7233
Manuscript accepted in *Synthese*

Abstract

The career of the developmental psychobiologist Gilbert Gottlieb revolved around the construction of a probabilistic view of epigenetics. In drastic contrast to instinct and nativist theories which portray development as a determinate sequence of changes controlled by a genetic master plan, Gottlieb's experiments and theory picture (behavioral) development as a highly multicausal complex process, with bidirectional interactions across different levels of organization and profound influences from ecological causes. Notwithstanding, the rejection of deterministic epigenetics was accompanied by the neglect of the concept of information in developmental biology, which various developmental systems theorists advocated. Information, particularly its interpretation in the gene-centered framework, was seen as an obstacle to probabilistic epigenetics. In recent years, however, Paul Griffiths and colleagues have developed an informational view of development that encompasses the theoretical and experimental background of developmental systems theory. There is thus an opportunity to build a bridge between probabilistic epigenetics and information theory, and this paper explores this avenue. Here I explore probabilistic epigenetics by adopting an informational view that allows us to represent and model specific aspects related to the probabilistic nature of development: dynamic epigenetic landscapes, probabilistic phenotypic repertoires, and the multicausality, non-linearity, and bidirectionality of developmental processes. This paper intends to enrich probabilistic epigenetics with informational tools while extending the applicability and utility of Griffiths et al.'s theory to previously unexplored developmental phenomena.

Keywords: Gilbert Gottlieb, Coaction, Epigenetic Landscape, Biological Information, Developmental System Theory, Developmental Specificity

1 Introduction

Gilbert Gottlieb belongs to the outmoded trend of scientists across the twentieth century that attempted to overcome the gene-centered view of development and evolution by focusing on the complexity of developmental processes and their consequences for phenotypic evolution. He worked on behavioral embryology and provided a wealth of experimental findings and theoretical reflections on how development must be understood beyond genetic reductionism. At the heart of his conceptual endeavor was the probabilistic epigenetic view, a sharp opposition to any kind of epigenetic predeterminism. Gottlieb's legacy is honored not only in the various fields he contributed to, such as developmental psychobiology or developmental systems theory (DST), but also in the current philosophical debates on the foundations of evolutionary theory. Many of his ideas are taken up today by various theoretical approaches related to the Extended Evolutionary Synthesis (EES; Pigliucci and Müller (2010); Laland et al. (2015)), and his reflection on the importance of development in evolution (Gottlieb 2002, 1984, 1987; Johnston and Gottlieb 1990) contributed key theoretical insights to several novel fields, such as niche construction theory, molecular epigenetics, eco-devo, evo-devo, and extended inheritance theory.

Nonetheless, in the process of moving away from a gene-centered perspective, the concept of information was often sidelined in the writings of Gottlieb and other developmental systems theorists, who associated "information talk" with gene-centric views of development and the outdated nature-nurture dichotomy. The emergence of information talk in genetics took place with the advent of molecular genetics (Keller 2002). Metaphorical, heuristic, or fully explanatory expressions referring to information have surrounded explanations of development since the material (molecular) bases of genes were understood in the mid-twentieth century (Griffiths and Stotz 2013). A strong genetic reductionism has been associated with informational concepts in development, with widespread metaphors depicting development as an expression of a program, blueprint, or code (Sarkar 2005; Oyama 2000a; Moss 2003). The emerging image of the gene as a unit of information brings to the fore earlier conceptions of the role of genes in evolution and development that can be traced back to the origins of neo-Darwinism.

Nevertheless, despite its reductionist connotations, there are compelling reasons to regard information as both central and explanatorily valid in developmental explanations. The primary reason, which will be elaborated in detail later, is that information represents a specific kind of cause—not one that produces matter or energy, but one that confers specificity to a developmental process. In developmental biology, informational discourse highlights those causes responsible for determining which developmental outcomes are produced, or, as (Oyama 2000b, 3) put it, "those causes that impart order and form to matter." For this reason, information is a crucial concept in both reductionist and holistic (or systemic) approaches: Crick's sequence hypothesis is fundamentally a hypothesis about information; and also extended inheritance theory addresses information, or eco-devo investigates the influence of ecological information on development (Rama 2024b). Consequently, developmental theory cannot dispense with informational discourse. Given the explanatory significance of information, it is fruitful to integrate many of the theoretical insights from Gottlieb's probabilistic view of epigenetics into a robust, reductionism-free informational theory of development.

This article precisely aims to present, analyze, and model probabilistic epigenetics in informational terms.

This objective can be divided into two complementary directions. First, to provide an informational account of probabilistic epigenetics, which is largely absent in Gottlieb's original theory; and second, to employ Gottlieb's insights to enrich and expand the current informational perspective on development. Regarding the first aim, developing a rigorous information-theoretic framework to capture the probabilistic nature of development would elucidate key properties that characterize epigenesis as a fundamentally probabilistic process. Central theoretical concepts such as repertoire, "causation-as-coaction," canalization, constraints, plasticity, robustness, and others can gain clarity and precision when grounded within a formal framework. In this respect, the article follows a common methodology in the philosophy of science: using mathematical modeling to clarify, represent, and deepen the understanding of key theoretical concepts (e.g. Bueno and French 2018; Franklin 2014). The focus on information is deliberate, as it constitutes one of the principal explanatory notions in developmental biology. Concerning the second aim, the main informational framework to be employed was developed by Paul Griffiths and collaborators across a series of influential works. Their approach provides a foundation for defining information without reliance on gene-centric assumptions. Nonetheless, further analysis of developmental phenomena is likely to introduce new complexities into an informational account of development. In this vein, Gottlieb's theoretical framework invites extensions that model and represent core developmental processes not yet fully addressed. Consequently, the effort to model central developmental phenomena entails both an extension of Griffiths et al.'s perspective and integration with other key modeling tools in developmental biology, such as epigenetic landscapes. In this regard, it should be emphasized that the aim of this article is purely theoretical and does not intend to provide a framework for direct empirical analysis of development, although further elaboration could prove valuable for computational approaches.[1]

Once the goals are clarified, let's introduce the structure of the article. In the next section, I briefly introduce the core of probabilistic epigenetics and Gottlieb's motivation for its development. In Section 3, I present a new view of information in development recently developed by Paul Griffiths and colleagues. In Section 4, the more extensive part, I attempt to link Gottlieb's view of probabilistic epigenetics with Griffiths et. al.'s informational account.

2 Gilbert Gottlieb's and the foundations of probabilistic epigenetics

Gilbert Gottlieb belongs to a group of behavioural embryologists and psychologists who devoted their career to understanding the origins of behavior, alongside other scientists such as Zing-Yang Kuo, Theodore Schneirla, and Daniel Lehrman (see Lickliter and Logan (2007) for a special issue on Gottlieb's legacy). Their experimental and theoretical research led to developmental psychobiology (Michel and Moore 1995) as

[1] I thank the anonymous reviewer for highlighting the importance of clarifying the article's explanatory aims and scope.

an alternative to the instinct theory prevalent in twentieth-century ethology. As Gottlieb has repeatedly emphasized since the 70s, instinct theories are deeply rooted in a *predetermined view of epigenetics*, in which the genetic basis of neural maturation explains the emergence of behavior. Behavior is only an "epiphenomenon" of a master genetic plan (Gottlieb 2001a, 41). Developmental processes follow the unidirectional unfolding of function and structure from genes to behavior. As expressed more clearly in the writings of Lehrman (1953, 1970), it was Lorenz (1986) who developed and disseminated a gene-centered view of behavioral development.

An illustrative case that Gottlieb worked on throughout his life is the recognition of mother calls by ducks. Immediately after hatching, ducks (e.g. mallards) can recognize their mother's calls and clearly prefer their mother's sounds over the calls of other species (such as chickens). It has also been shown that newborns isolated from their mothers during embryonic development still recognize their mother's call. Gottlieb noted that this was explained based on a predeterministic view of epigenetics: the development of mother calls perception is explained by the genetic effect on neural development, independent of environmental and developmental conditions. The recognition of mother calls is an instinct, an innate behavior in ducks (Gottlieb 1976).

Gottlieb was averse to nativist interpretations. He had a strong intuition that development requires other sources of specificity and that behavioral development is not just about gene-driven neural maturation (Gottlieb 2001a). Like earlier developmental psychobiologists—most notably Kuo, under whom he studied—Gottlieb conducted a series of experiments manipulating variables during duck embryonic development (Gottlieb 1971). A pivotal finding, enabled by the ability to devocalize embryos, was that auditory experience during specific embryonic stages is crucial for developing species-specific preferences: without exposure to sound, ducklings do not prefer maternal calls. This revealed that self-stimulation—auditory feedback from the embryo's own vocalizations—is essential for perceptual development. In devocalized embryos isolated from both mother and (also devocalized) siblings, maternal call recognition failed, suggesting that sibling-generated sound is another key source of environmental input. Remarkably, devocalized embryos exposed to chicken sounds later preferred the chicken call over their own species', indicating sensitivity to subtle acoustic features. Though duck and chicken calls may seem alike to human ears, embryos discriminate based on abstract properties such as frequency modulation (e.g., 1200 Hz in wood ducklings) or note repetition rates (e.g., four notes per second in mallards) (Miller 2007). These findings challenge classical instinct theory: "innate" behaviors emerge through normal prenatal environmental influences. Gottlieb's (1997) search for the "prenatal roots of instinctive behavior" marked a turning point in developmental psychobiology. These findings represent only a portion of Gottlieb's contributions, and only some of the species studied by him and his collaborators (see Lickliter and Logan 2007; Gottlieb 2001a). His central message highlights the oversimplification and limitations of predeterministic models of epigenetics.

In the gestation of developmental psychobiology, Gottlieb began to construct an alternative epigenetic view, defined in *opposition*[2] to the predeterministic view: *probabilistic epigenetics*(Gottlieb 2007), a theory of development that focuses on "the bidirectionality of traffic among and within the levels" (Gottlieb and Halpern 2002, 423). As he put it:

> Probabilistic epigenesis holds that behavioral development of individuals within a given species does not follow an invariant or inevitable course, and, more specifically, that the sequence and outcome of individual behavioral development is probable (with respect to norms) rather than certain (Gottlieb 2001a, 43).

One of the usual (Gottlieb 1998, 1997, 90) ways in which Gottlieb introduced predetermined epigenetics is by restating the Central Dogma in molecular biology presented by Crick (1958) (and slightly modified in 1970 after the discovery of retroviruses). According to this view, the construction of behavior follows a unidirectional arrow: genes generate neural structures, and neural structures generate behavior. The action of genes, their transcription and translation, is insensitive to behavior, and as such there is no bidirectional interaction between the elements of development: experiences and actions do not influence development because gene expression is insensitive to environmental conditions. Underlying this framework is the Central Dogma, framed in informational terms, that ascribes the leading role of protein-coding sequences in development.

We now know that this is not the case, that as Gottlieb argued, there are plenty of different cases of "activity-dependent gene expression" (Gottlieb 1991, 33). Gene expression is highly regulated by multiple sources of developmental specificity and a systems view is definitely warranted in developmental science (see Sultan 2015; Gilbert and Epel 2015; Keller 2014; Thorner et al. 2014). As a result, probabilistic epigenetics is closely intertwined with a bidirectional and complex view of developmental causation. What makes development a contingent process is the fact that multiple factors interact in the emergence of phenotypes, and these complex coactions cannot be captured by a predeterministic view. As he said: "The probable nature of epigenetic development is rooted in the reciprocal coactions that take place in complex systems" (Gottlieb 1997, 140). Like many other currents in the contemporary philosophy of biology that take an organismic and agential view of development and evolution, Gottlieb strongly opposed the idea that developmental processes can be explained in terms of gene-based evolutionary causes and that developmental complexity must be regarded as the central *explanans* and *explanandum* (Robert 2004) in developmental theory:

> Rather than the passive translation of phylogenetic causes into ontogenetic happenings, ontogeny in each generation is a consequence of the coaction of hereditary or genetic factors and many different local environing circumstances that determine the expression of the phenotype during the course of development (Gottlieb 1987, 264).

[2]The informational framework developed throughout this article to model probabilistic epigenetics is therefore opposed to any form of epistemological physical reductionism. Developmental explanations are not exhausted by knowledge of the physical world, since many processes and patterns require a distinctly biological level of description in which certain concepts—paradigmatically, 'organism'—are not reducible. I do not intend to engage in a detailed ontological inquiry here. Nonetheless, some form of emergence is clearly indispensable in organism-oriented biology, even if it may range between weak and strong emergentist positions. I thank an anonymous reviewer for raising this point.

3 Biological Information as Causal Specificity

The concept of information has long been linked to predeterministic assumptions and, as a result, has been marginalized in probabilistic epigenetics. Its use risks reinforcing binary oppositions such as nature versus nurture. This critique is most forcefully expressed by Oyama (2000b,a) and other developmental systems theorists, including Griffiths (2001), Sarkar (1996), and also Godfrey-Smith (2000), who view informational language as conceptually problematic—liable to invoke outdated deterministic models.

Nonetheless, as discussed in the introduction, information discourse is still widespread, particularly in fields influenced by Gottlieb's work and aligned with the EES. Here, information is understood as residing across multiple substrates: genomic sequences, epigenetic marks, environmental inputs, and symbiotic interactions. The central explanatory role of information in developmental biology implies that its dispensability would incur an unacceptably high cost. Therefore, it is valuable to attempt a reformulation of this concept that disentangles it from the preformationist and gene-centric assumptions (for a critical and historical appraisal, see Capurro (2009)).

Fortunately, recent work by Griffiths and colleagues (now on: Griffiths et al.) offers a mathematically rigorous and philosophically refined account of information in development, advancing beyond reductionist models. Their framework is notable for addressing the diversity of developmental causes and clarifying the explanatory role of information (Griffiths et al. 2015; Griffiths 2017; Griffiths and Stotz 2013; Stotz and Griffiths 2016, 2017; Stotz 2019).[3]

Griffiths et al. analyze Crick's concept of information as articulated in his sequence hypothesis. Protein-coding genes are seen as informational drivers of development because their nucleotide sequences *precisely determine* amino acid sequences. Crick's notion of information denotes causal specificity—how a DNA sequence reliably specifies a particular protein. Griffiths et al. argue that such specificity underpins informational discourse in developmental biology: "causal relationships in biological systems can be regarded as informational when they are highly causally specific" (Stotz and Griffiths 2017, 371, 374). Thus, biological information refers to causes that confer specificity to developmental outcomes. Their key contribution lies in formalizing this concept by integrating the mathematical theory of information with an interventionist model of causality.

Based on the theory of Shannon (1948), the mutual information between two variables is quantified as the change in entropy (H) of one variable due to the presence of the other. It measures how much uncertainty is reduced in one variable by knowing the value of another variable. The mutual information between the variables X and Y is expressed by the following equation.

$$I(Y;X) = H(Y) - H(Y|X) \tag{1}$$

[3] Their work has been motivated by other causal approaches to specificity (Waters 2007; Pearl 2009; Weber 2006; Lewis 2000; Woodward 2010) as well as other probabilistic approaches to information (Dretske 1981; Stegmann 2015; Cohen and Meskin 2006; Scarantino and Piccinini 2010; Scarantino 2015); see Fresco et al. (2020); Bourrat (2019); Pocheville et al. (2017); Rama (Under Revisionb) for recent extensions and analysis.

It is important to note that mutual information is a symmetric concept ($I(X;Y) = I(Y;X)$) and does not serve as a measure of causal relationships, since causal relationships are asymmetric (Potochnik 2017; Rama 2022). A widely used framework for modeling causal relationships in scientific explanations is Woodward's interventionist approach (Woodward 2003). The central idea is that if, *ceteris paribus*, changing the value of one variable leads to changes in another, this indicates some degree of causal link between them. To determine whether X is a cause of Y when a correspondence between the two is observed, one should, according to Woodward's model of invariance, consider a counterfactual scenario in which, under certain background conditions, X is changed or absent and examine whether Y changes as a result.

Griffiths et al. extend the interventionist approach to mutual information and use it to quantify how much information about one variable is gained by intervening in another. $H(Y|\hat{X})$ stands for the conditional entropy, which captures the changes in Y as a result of different values of X. The mutual information between Y and $\hat{X}$, which incorporates the concept of intervention (usually modeled with the do. operator (Pearl 2009; Griffiths et al. 2015, appendix B) and denoted here by the *hat*), is defined by the following expression:

$$I(Y;\hat{X}) = H(Y) - H(Y|\hat{X}) \tag{2}$$

This approach provides an asymmetric characterization of the relationships between variables that is suitable for identifying causal relationships (Stotz and Griffiths 2017; Šustar 2007; Artiga 2024). Building on this informational perspective, biological information—defined technically as causal specificity within biological systems—can be characterized as:

> SPEC: the specificity of a causal variable is obtained by measuring how much mutual information interventions on that variable carry about the effect variable (Griffiths et al. 2015, 538).

Genes can indeed be regarded as causal specifiers that provide information about development since interventions in these genes can lead to fine-grained changes in their effects. However, Griffiths et al.'s definition of specificity expands this understanding by revealing "additional specificity of a kind not captured by the original 'sequence hypothesis'" (Griffiths 2016b, 83). This expanded view emphasizes the existence of non-genetic causal specifiers that influence phenotypic outcomes. Their work demonstrates numerous cases where specificity goes beyond DNA. The overarching conclusion is the thesis of *distributed specificity*: specificity is not restricted to genes but is distributed across different levels of biological organization.

This proposal possesses several notable strengths. Chief among them is its ability to elucidate the concept of causal specificity without reducing it to any particular variable (such as genes). Subsequent elaborations have applied this approach to the analysis of related phenomena, including biological signals (Calcott et al. 2020), teleology (Griffiths 2016b), the proportionality and stability of causal variables (Pocheville et al. 2017), and the interactions among developmental variables (Rama Under Revisiona), among others. This article aims to explore the model proposed by Griffiths et

al. to examine various aspects of development that contribute to its characterization as a probabilistic process.

4 Deploying Biological Information in Probabilistic Epigenetics

The aim now is to underpin the central elements of Gottlieb's view, which led him to adopt a probabilistic view, with an informational approach; i.e. to describe the probabilistic nature of developmental processes in informational terms. This section rests on three landmarks of probabilistic epigenetics: *repertoires* (Subsection 4.1), a *dynamic epigenetic landscape* (Subsection 4.2), and the *coaction of developmental causes* (Subsection 4.3).

4.1 Probability and repertoires

A first indication of probability is based on the fact that no phenotype (P) depends on a single source of causal specificity (x). We can describe this by noting that

$$I(P, x) < 1 \tag{3}$$

The multicausal underpinning of all traits must recognize that development requires different causes to produce an outcome (Vecchi and Santos 2023). Despite his emphasis on environmental causes, Gottlieb (1998) rejected two mistaken conclusions: i) that genes are not involved in behavioral development, and ii) that consequently an environmentalist view of development should be advocated. Rather, his emphasis on an ecological view of development implies that an individual's genetic material is not solely responsible for determining phenotypic outcomes, but that, as Griffiths et al. attempted to model, ecological causes also provide causal specificity. We can represent the information that each gene x_j provides for the development of a particular phenotype P by considering the set $X = \{x_1, x_2, ..., x_n\}$ such that

$$I(P; X) = \sum_{i=1}^{n} I(P; x_i) \tag{4}$$

Here, set X as the sum of the information provided by each gene $x_j$that provides causal specificity in the development of a phenotype P. This additive measure does not account for non-linear genetic interactions, which will be explored in Subsection 4.3. However, it is sufficient to represent the idea that the information provided by the individual genes is not sufficient to determine the phenotypic outcome; i.e.,

$$I(P, X) < 1 \tag{5}$$

The fact that a particular set of causal specifiers does not determine an outcome means that there is a *repertoire* of possibilities. This idea has been repeatedly

emphasized by several authors (see McGhee 2006, for an in-depth analysis), be it Waddington's epigenetic landscape (Waddington 1957), Alberch's morphospace (Alberch 1989), or the recent view of developmental repertoires presented by Walsh (2013, 2015). In all these approaches, development outcomes or paths are not fixed but are located within a limited but diverse repertoire of possibilities. Repertoires play an important role in defining morphological variability (as in Alberch), the canalization of development (as in Waddington), or the agent-driven regulatory capacities of developmental systems (as in Walsh). The point here, however, is that recognizing repertoires is a hallmark of probabilistic epigenetics in Gottlieb's view, expressed by the fact that "the range of *possibilities* of behavioral development always *exceeds* the range of behavior that is *actualized* during the course of individual development" (Gottlieb 1976, 80, emphasis added). In contrast to the *one-to-one* model implied by Crick's sequence hypothesis—where a single source is presumed to determine a single outcome—the existence of a repertoire of possible outcomes suggests that each developmental variable can give rise to multiple effects, reflecting a *one-to-many* mapping. Each option within a repertoire of phenotypes defined by the set X has a certain probability of being produced, given the amount of information provided by X. While I defined X based on a set of genes involved in phenotypic development, the idea can be expanded by including other non-genetic causes. Epigenetics is a probabilistic process concerning any set X of causal specifiers with a range of possible phenotypic outcomes; it is a *many-to-many* mapping: multiple sources can lead to many possible outcomes within the repertoire. When a particular outcome 'is actualized', the relationship eventually becomes a *many-to-one* relationship, as many interacting variables jointly determine the developmental result.

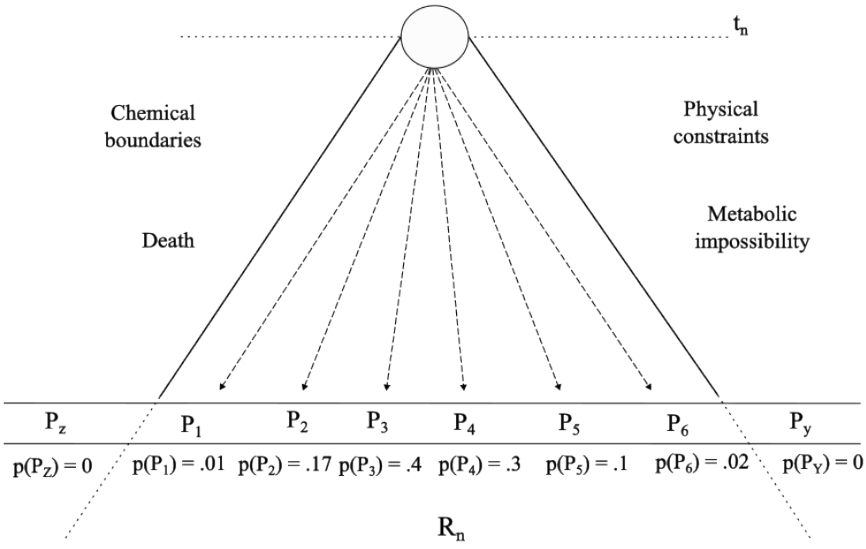

Fig. 1
Probabilistic Epigenetic Landscape. Description in text

A Probabilistic Epigenetic Landscape (Figure 1) represents the different possible outcomes (i.e. a repertoire R_n) that a developing system (white circle) can achieve based on the available information at a given time n (t_n) of ontogeny.[4] In Figure 1, R_n consists of six phenotypes ($R_n = \{P_1, P_2, P_3, P_4, P_5, P_6\}$). None of these phenotypes is fully determined ($p(P_x) < 1$ for $1 \leq x \leq 6$)) and all phenotypes are possible ($p(P_x) > 0$ for $1 \leq x \leq 6$). Beyond the limits of the repertoire, however, no possible forms and functions can be produced (thus representing a limit in the (artificial or natural) malleability of development (Gottlieb 1997, chapter 7)). This is usually understood as the limits imposed by developmental (physical, chemical, or biological) constraints (Maynard Smith et al. 1985; Amundson 1994) that define the domain of possibility, i.e. which phenotypes can and cannot be constructed (see Solé et al. 2024, for a recent review).

4.2 The ontogeny of a landscape

There are other ways to illustrate the probabilistic nature of epigenetic processes. Why is it that, given a set of causes, the phenotypic produced is only one of a repertoire of possibilities? In other words, how is one possibility selected from many? This question has many facets, including stochastic processes, feedback regulatory mechanisms, and non-linear interactions, as we shall see. However, an important point that is closely related to Gottlieb's work is that at different stages of ontogeny further information emerges: some developmental causes are not present at a particular ontogenetic stage, but emerge at later ontogenetic stages. These new sources of specificity are central to the determination of a particular phenotype. With the emergence of new specificities, uncertainty changes, and also the repertoire of possibilities—we have more information: $I(P; X_{n+1}) > I(P; X_n)$.

One might think that some developmental causes are independent of developing organisms and preexist the developmental system (e.g., temperature in reptile sex determination). In this sense, such factors might be said to become available (and not emergent) during ontogeny. This, however, is not entirely correct. It is important to note that, although some variables may exist independently of developing systems, their qualification as developmental causes—namely, as sources of information—is organism-dependent. A factor becomes information only if it is used by a system for trait specification, and only during specific developmental stages (as in the case of reptiles, which use temperature for sex determination only within a particular embryonic window). Prior to this stage, the factor cannot be considered a developmental cause: interventions on temperature before the relevant developmental window would produce no phenotypic effect. This reflects a clearly constructive view of information, or an 'ontogeny of information' sensu Oyama (2000b), according to which the status of information depends on how organisms use it to construct their phenotypes—and is

[4] Shannon's concept of mutual information is typically grounded in a frequentist interpretation of probability, and many modeling and sampling techniques in developmental biology similarly adopt a frequentist framework. While this may represent the dominant approach to information—one that also appears to underpin the interventionist methodology employed by Griffiths et al.—the potential value of Bayesian or subjective interpretations of probability in developmental modeling remains an open and important question. I am grateful to an anonymous reviewer for drawing attention to this point.

closely related to Sultan's notion of "experienced (developmental) niche construction" (Sultan 2015).[5]

The ecological causes that Gottielb investigated occur at certain ontogenetic stages. Part of his experiments were devoted to analyzing the heterochrony of behavioral development: the importance of acoustic perception at certain moments of embryological development and how changes in the timeliness of this cause lead to phenotypic changes. The acoustic information received at one embryonic stage may not necessarily be present at earlier ontogenetic stages. Maternal sounds may be present since conception, but they can only be understood as information when the embryo can perceive them, which happens at a certain stage and not before (i.e. intervention on maternal sounds before this stage would not lead to different phenotypic outcomes, so there is no causal specificity). The same applies to the sounds of siblings or acoustic self-stimulation by the embryo. In all these cases, the cause occurs at a certain point at which the sound arises and the embryo is able to perceive it. This cause is not present beforehand, and as Gottlieb has shown, changes to this cause (e.g. the imprinting of the chicken call) would lead to alternative phenotypic outcomes. The "experiential canalization" of development is thus based on the emergence of specific environmental input at particular ontogenetic stages (see Rama 2024a; Gottlieb 1997, chapter 6).

Generalizing, there are (at least) two ways in which new specificity arises in development: either it is epigenetically[6] transmitted or constructed by the developing organism itself. The first option includes various phenomena: environmental causes (such as temperature in sex determination in reptiles[7]), the interaction between mother and offspring (such as embryo nutrition), parental care (such as differential licking in rats), symbiotic interactions (such as the influence of gut microbiota in mammalian neurodevelopment), or horizontal transmission of information (as in Gottlieb's analysis of sibling relationships). As far as the second option is concerned, various sources of specificity are created by the organism itself: information that is not present in the previous phase but is produced by the developing system during ontogenesis. As Gottlieb examined in his analysis of devocalized embryos, self-stimulation is a central source of behavioral specificity produced by the very organisms as soon as they can emit sounds. Certainly, the spectrum of self-constructed information includes different types of causes: hormones that regulate cell specification, morphogens that determine axial gradients, signaling pathways that regulate layer formation, and many others.

[5] I thank an anonymous reviewer for raising this issue.

[6] Epigenetics has been subject to diverse interpretations and definitions, rendering it a contested concept within the literature. In this paper, the term is employed in its broad, Waddingtonian sense to denote the processes that mediate the relationship between genotype and phenotype, thereby encompassing a wide array of causes and mechanisms. This usage contrasts with the narrower conception of epigenetics—derived from Nanney's work—which is primarily concerned with the molecular regulation of gene expression. Gottlieb's notion of probabilistic epigenetics aligns predominantly with the broad definition, although he has also engaged with epigenetic processes in the narrower sense (e.g. Gottlieb 1998). For a comprehensive discussion of the distinctions between broad and narrow definitions of epigenetics, see Baedke (2018); Stotz and Griffiths (2016). I acknowledge an anonymous reviewer for emphasizing the importance of this clarification.

[7] Although temperature itself is not transmitted from parents to offspring in a literal sense, the terminology of transmission can nevertheless be justified. The concept does not necessarily require an active sender, as both scientific and ordinary language routinely describe causal influences as transmitted by a medium. Moreover, parental structures such as nests often exhibit features shaped by selection to generate specific thermal conditions, and can therefore be understood as systems that reliably transmit particular environmental causes to offspring. I acknowledge an anonymous reviewer for noting this point.

However, the relevant point for our analysis is that the information available to developing systems is not the same at all ontogenetic stages. If the set of causal specifiers X change from time n to time m ($X_n \neq X_m$), then $I_n \neq I_m$.

Changing information states entail that the probability of each phenotype also changes and that, consequently, the repertoire is modified. The question that therefore arises is how the probability changes in the course of ontogenesis due to the changing information states. Before addressing this issue, however, I should note an important idea that Gottlieb repeatedly emphasized. Although Gottlieb was a supporter of Waddington's view, he argued that Waddington's epigenetic landscape represented a narrow and limited version of the possibilities in development (Gottlieb 1997, chapter 6). Specifically, Gottlieb complained about the gene-based view of the landscape and that "developmental canalization does not emanate merely or solely from the genetic level" (Gottlieb 2002, 1294). Instead, he suggested that the definition of the epigenetic landscape should take into account other, non-genetic causes, i.e. "to extend the normally occurring influences on genetic activity to the external environment, thereby further demonstrating that a genome is not encapsulated" (Gottlieb 1998, 794). The point here is that even though each ontogenetic stage defines a repertoire of possibilities, *the landscape is not fully constructed, but has its ontogeny*: new sources of causal specificity can alter the landscape and modify the repertoire towards particular outcomes. The landscape is also constructed as ontogeny moves forward—it is not a given and fixed repertoire of possibilities. This shifting picture is difficult to draw. Usually, the landscape is drawn as an already-formed valley with multiple possible paths (Squier 2017). However, the emergence of new information in the course of ontogeny has the effect of changing the valley while ontogeny moves on. This is a *dynamic* rather than a static picture of an epigenetic landscape (Baedke 2013).[8] As new information is incorporated into ontogeny, the repertoire of possibilities may change, and with it the probability distribution of phenotypic outcomes.[9]

In a Dynamical Probabilistic Epigenetic Landscape, new information changes the probability distribution and composition of the repertoire over time.[10] In Figure 2, new biological information is represented by black dots, which appear only at the times indicated in the figure. The emergence of new information leads to "geological" changes

[8] Calcott (2017) develops a conception and representation of the epigenetic landscape ("Waddington boxes") that aligns with several aspects of my own perspective. Although his primary aim—to distinguish between permissive and instructive causes—differs from mine, future research could fruitfully integrate these approaches and representations of epigenetic landscapes.

[9] The information-theoretic model employed in this work is closely aligned with developmental dynamics approaches grounded in attractor theory, which has been extensively applied in epigenetic landscape modeling (e.g., Kauffman (1993); see Subsection 4.3 for a specific application). However, from a philosophical perspective, our focus on information introduces important distinctions from attractor-based frameworks. First, our aim is to position information as a central conceptual construct in developmental biology, as elaborated in Section 1. Second, adopting an informational approach to probabilistic epigenetics facilitates a more direct engagement with its contrasting perspective—namely, the predeterministic view exemplified by Crick's sequence hypothesis, which advocates a unidirectional flow of information within developmental genetics. Moreover, the use of probability measures grounded in Shannon entropy provides a conceptually rigorous tool to capture the inherent contingency of developmental processes—an idea fundamental to developmental systems theory. Finally, information-theoretic approaches enable the tracking of the functional contributions of specific causal factors (e.g., prenatal auditory stimulation), whereas attractor models primarily focus on characterizing global behavioral patterns. I thank an anonymous reviewer for highlighting the importance of this distinction.

[10] The probability distribution of each phenotype in Figure 2 (as in the subsequent dynamical landscapes) is represented in a separate table (see below for different cases).

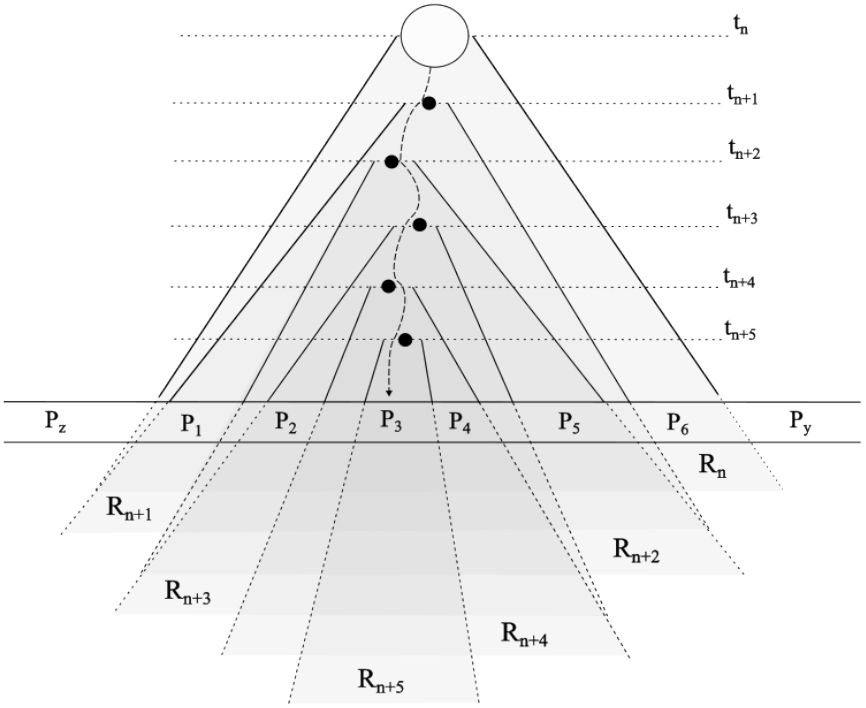

Fig. 2
Dynamical Probabilistic Epigenetic Landscape (description in text)

in the landscape that alter the possible developmental pathways. The probable state of each phenotype at each time point is stipulated in Table 1.[11] This can have different consequences. First, as shown in Table 1, the probability of each phenotype changes as ontogeny progresses (e.g., $p(P_2) = 0,17$ at t_n and $p(P_2) = 0,195$ at t_{n+1}). In addition, the repertoire also changes at different times during development. For example, in Figure 2, $R_{n+1} = \{P_1, P_2, P_3, P_4, P_5\}$, while $R_{n+4} = \{P_3, P_4\}$. This means that some of the possible outcomes that can be achieved at a given time will be removed from the repertoire at future ontogenetic stages. Development becomes more constrained when the repertoire is reduced. For example, in Figure 2, P_1 and P_6 are no longer possible at time t_{n+2}. Thus, while some traits are possible at some stages, they can no longer be achieved at future stages. Finally, the developing system reaches the "final"[12] state

[11] In this case, probabilities are stipulated solely to illustrate a particular property of development. In actual scientific contexts, however, probabilities can be derived from various sources and methodologies. Traditionally, interventionist approaches involving individuals within a population yield probability measures indicating the extent to which specific interventions influence developmental outcomes. Likewise, quantitative population-level techniques—such as analyzing norms of reaction (NoR) or heritability scores—can offer probabilistic insights into the contribution of specific variables to developmental processes. The analysis presented here is agnostic with respect to the methods used to estimate probabilities; its focus lies instead on how those probabilities evolve as development unfolds. I am grateful to an anonymous reviewer for pointing this out.

[12] The idea that an end product is constructed during development is in tension with the open-ended nature of development and the rejection of adultocentric views. As noted by many (Griesemer 2016a; Minelli 2011; Camazine et al. 2003; Balari and Lorenzo 2014; Bich and Skillings 2023; Rama 2026), developmental changes continue throughout the life cycle of an individual, so that the idea of a final phenotypic outcome at

of a particular phenotype at t_{n+5} ($p(P_3) = 1$), and the repertoire R_{n+5} is formed only by P_3.

Table 1 Probability distribution across ontogenic times Represented in Figure 2. See description in text.

$t_x \vert p(P_x)$	P_1	P_2	P_3	P_4	P_5	P_6	P_z	P_y
t_n	.01	.17	.4	.3	.1	.02	0	0
t_{n+1}	.005	.195	.44	.35	.01	0	0	0
t_{n+2}	0	.145	.5	.354	.001	0	0	0
t_{n+3}	0	.08	.6	.32	0	0	0	0
t_{n+4}	0	0	.7	.3	0	0	0	0
t_{n+5}	0	0	1	0	0	0	0	0

If we present the epigenetic landscape as something that also has an ontongey—the landscape as something that is constructed—we can now shed some light on the probabilistic character of epigenetics in more detail.

4.2.1 Changing uncertainties and potency reduction

In general, we can say that (local) uncertainty decreases at different stages of development: the emergence of new information causes the probability of some traits to decrease, while the probability of others increases. In the course of development, some traits lose the possibility of being developed until they have disappeared from the repertoire. Other traits become more probable as development progresses because the presence of certain causes influences their production.

The transition to the reduction of uncertainty can be observed in cell potentiality. Potentiality decreases as developmental processes unfold, from totipotent cells at the morula stage to pluripotent blastomeres to multipotent somatic stem cells. Certainly, many developmental processes preserve cell potency, but potency tends to decrease (for a critical discussion, see Minelli 2021).[13] In the process of cell specification, cell commitment means that the lineage of the cell cannot become a cell type outside the lineage. As potency decreases, so does uncertainty: for all cells of the morula, the

a certain point in time is an idealization. Thus, the emergence of a phenotype at a particular point in time does not mean that further causes will not lead to new changes in phenotypic states at future stages. Various factors are at play, from species-specific trajectories (such as complex life cycles, aging, regeneration) to relevant changes in the landscape (genetic mutation, invasions, drastic environmental changes (see Section 4.2.2). This perspective has interesting consequences, such as the fact that the landscape should represent the entire life cycle, that there is always a repertoire of possibilities despite the robustness of a trait, and that the specification of one trait (e.g. morphology) occurs at a different time than that of another trait (e.g. cognition). These ideas deserve special consideration and will not be dealt with in detail here, even though it is worth making clear the idealizations I am assuming.

[13] The existence of reprogrammable cell potency in adults is not inconsistent with this point. If some adult cells can increase their potency, they theoretically already have this potency (it must be considered as part of the repertoire). In other words, an epigenetic landscape of cell lineage that considers reprogrammable cells must take into account the possibility of cell reprogramming: the appearance of new causes (usually artificially induced) that bring about changes in the landscape so that one of the possibilities increases its probability and might be realised (or in other words, there are constraints, not all adult cells can be reprogrammable). In turn, the probability of artificially induced phenotypes is not strictly zero at previous ontongetic stages.

decrease in cell potency at future stages means that we know in which cell types a particular lineage can be specified and, importantly, in which it cannot. In this sense, the number of possible phenotypes in a repertoire may be maintained or reduced across time, but not increased.

For example, if we look at Table 1, we can see that $p(P_3)$ increases over time. The decrease in uncertainty over time simply means that the formation of a particular organization in development becomes more likely, i.e. the chaos in development decreases as phenotypic specification progresses.

While the reduction in (local) uncertainty may serve as a guiding rule (maybe not so distant from von Baer's second law), it may also be that the presence of a particular cause alters the probability distributions in a repertoire without reducing uncertainty. The phenotypic outcome to be produced may become less specific as new information changes the landscape. In terms of development, this means that new information makes some phenotypes more likely that were less likely at earlier stages. Although the applicability of these scenarios to real cases is beyond the scope of this paper, this helps to model the various changing states in the dynamics of the epigenetic landscape across ontogeny. Table 2 illustrates this situation by reinterpreting the changing probability distribution in Figure 2. If we focus only the columns P_3 and P_4, we can see that (local) uncertainty does not necessarily decrease at each time.[14] We can observe this at different transitions. For example, at the transition from t_n to t_{n+1}, $p(P_3)$ remains the same. At the transition between t_{n+1}, and t_{n+2}, $p(P_3)$ decreases and $p(P_4)$ increases, but reaches the same probability of $p(P_3)$ at t_{n+1}. At the transition between t_{n+2} and t_{n+3}, $p(P_3)$ and $p(P_4)$ are reduced and equated to $p(P_2)$. Finally, the uncertainty is reduced at t_{n+4}, where $p(P_3) = 0.7$. Thus, even though the reduction of uncertainty throughout ontogeny appears to be the general rule, there may be exceptions: although the probability distribution changes in all the cases reported in Table 2, we cannot claim that uncertainty is always reduced.

Table 2 Changing uncertainty over time Changes in the probability distribution of phenotypes in Figure 2, where some transitions decrease (local) uncertainty over time, while others increase it. When a trait is fully specified and uncertainty is reduced to zero, its probability reaches 1 and its entropy is also reduced to zero (further description in text).

$t_x \vert p(P_x)$	P_1	P_2	P_3	P_4	P_5	P_6	P_z	P_y
t_n	.01	.17	.4	.3	.1	.02	0	0
t_{n+1}	.005	.195	.4	.39	.01	0	0	0
t_{n+2}	0	.209	.39	.4	.001	0	0	0
t_{n+3}	0	.333	.333	.333	0	0	0	0
t_{n+4}	0	0	.7	.3	0	0	0	0
t_{n+5}	0	0	1	0	0	0	0	0

[14] Global uncertainty remains constant at 1, reflecting the sum of the probabilities of all possible outcomes within the repertoire.

4.2.2 Developmental earthquakes

I have followed Waddington's picture of a landscape of possible developmental paths in development. I extended this idea by introducing Gottlieb's insight that the landscape is also defined by the inclusion of other, non-genetic causes. This invited us to analyze how new information that emerges during ontogeny alters the probability distribution between many pathways to different phenotypic outcomes. However, one important case remains unanalyzed: some cases in which drastic changes in developmental causes produce drastic changes in the probability distribution of phenotypes in a repertoire. These cases can be labeled as *developmental earthquakes*, as they represent a drastic geological reorganization of the landscape.

The interests behind developmental earthquakes are manifold and their connection to Gottlieb's work is notorious. First, why might earthquakes occur? One obvious possibility is a genetic mutation during cell division that cannot be repaired and therefore leads to severe phenotypic changes. In this case, the change in genetic composition could lead to drastic consequences as it contains a large amount of information about phenotypic outcomes. However, a new specificity that reshapes the landscape could come from the environment. Species invasion, environmental changes, or ecological accidents could have profound consequences on phenotypic outcomes that were not previously part of the landscape. However, it is not necessary to assume these cases of subtle and drastic changes. As Gottlieb himself has analyzed, a specific change in hearing could be enough to produce an unanticipated variant (e.g. different frequencies of repetition rates). Certainly, the probability of recognizing chicken calls in ducks under normal (species-specific) circumstances is low. However, Gottlieb has shown that altering some causes increases the probability of recognition of the chicken call by newborn ducks to the point where they prefer it over their mother's call. In this scenario, conspecific or acoustic self-stimulation was deprived, and a different auditory input was introduced (recordings of chicken calls). All these elements provide causal specificity to development and their presence can lead to drastic changes in the outcome, repertoire, and probability of each phenotype at different stages. In this way, a change in the information a system has leads to a different landscape in which the system moves. The tectonic plates are never fixed. They are always in motion. The epigenetic landscape is not fixed either. Similar to earthquakes, which have a certain magnitude depending on their geological effects, there is a gradient in the dynamics of a probabilistic epigenetic landscape that leads from more stable epigenetic landscapes to more unstable ones in the course of ontogenesis.

Figure 3 shows a developmental earthquake at t_{n+2}, in which the changing probability states of the phenotypes are stipulated in Table 3. As we can see, the situation at t_n and t_{n+1} is identical to Figure 2, Table 1. However, at t_{n+2}, a new causal specifier (black dot) appears in the landscape that triggers a developmental earthquake: a drastic reorganization of the probabilistic distribution occurs and the repertoire is greatly altered. While $R_{n+1} = \{P_1, P_2, P_3, P_4, P_5\}$, $R_{n+2} = \{P_4, P_5\}$. Furthermore, the most probable result at t_{n+1} was $p(P_3) = 0,44$, however (P_3) is no longer possible in the next phase t_{n+2}. Finally, while P_5 was almost impossible at t_{n+1}, it becomes pretty much the most probable in t_{n+2}.

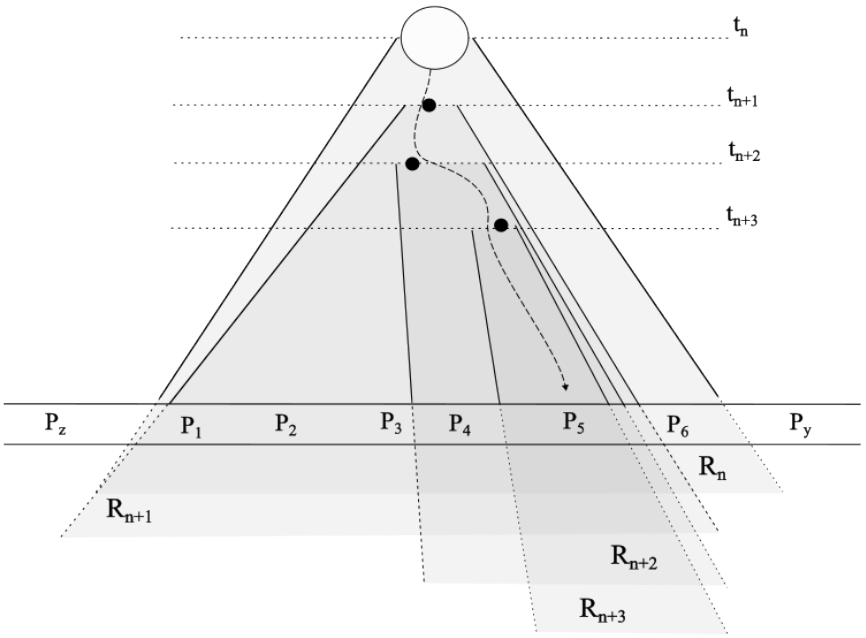

Fig. 3
Developmental earthquakes (description in text)

Table 3 Probability distribution changes across ontogenic times. Represented in Figure 3. Description in text.

$t_x \vert p(P_x)$	P_1	P_2	P_3	P_4	P_5	P_6	P_z	P_y
t_n	.01	.17	.4	.3	.1	.02	0	0
t_{n+1}	.005	.195	.44	.35	.01	0	0	0
t_{n+2}	0	0	0	.18	.82	0	0	0
t_{n+3}	0	0	0	0	1	0	0	0

The possibility of earthquakes is closely linked to a central tenet of current evolutionary theory and Gottlieb's work, namely the developmental origin of variation and novelty. Both Gottlieb and today's eco-evo-devoists (see Brigandt and Love 2010; Gilbert and Epel 2015) have focused intensively on the developmental origin of new forms and functions. Developmental earthquakes are a suitable model to illustrate how specific information changes can lead to non-species-specific phenotypes. As an idea that goes back at least to the origins of teratologies (Amundson 2005) and Goldschmidt's hopeful monsters (Goldschmidt 1982; Gottlieb 2001b; Cao et al. 2024) and has been revisited in Alberch's morphospace (Alberch 1989; Balari and Lorenzo 2008; Nuño de la Rosa and Müller 2024), the rapid rather than gradual emergence of new phenotypes becomes central to the eco-evo-devo agenda. The analysis of how certain

developmental changes can introduce variation into nature includes several developmental aspects, from the specific changes in regulatory genes to modifications of ecological causes.

Developmental earthquakes therefore represent one way in which developmental systems can control the phenotypic repertoire in novel ways, and how this can be linked to the emergence of new information across ontogeny. This idea was at the center of Gottlieb's evolutionary-oriented work and led to his own proposal: *neophenogenesis* (Gottlieb 1984, 1976, 1987, 2002; Gottlieb and Halpern 2002; Kuo 1976). Gottlieb insisted on how new phenotypes could emerge from developmental processes as a result of the interplay of different developmental causes in a new ecological context, thereby advancing the "genes-as-followers" perspective popularized by West-Eberhard (2003) and advocating a "plasticity-first" view of evolution that is widely discussed today (Levis and Pfennig 2016).

4.2.3 Robust outcomes from plastic means

Developmental outcomes do not need to be variable within a species to underscore the probabilistic nature of epigenesis. Probabilistic elements are inherent not only in the outcomes but also in the developmental trajectories themselves—that is, in the paths followed within the developmental landscape. Notably, developmental plasticity plays a central role in explaining a seemingly contradictory property: robustness. The perceived dichotomy between robustness and plasticity is, as several scholars have argued (e.g., Bateson and Gluckman 2011), largely superficial. Robust trajectories in the development of certain traits are often essential to permit plastic modifications in others; that is, specific components of the system must remain stable to allow adaptive variation elsewhere (Wagner and Cheverud 2007). Conversely, plastic mechanisms are also fundamental to the achievement of robust outcomes, as robustness frequently entails the capacity of a system to reach a consistent endpoint via multiple developmental pathways (i.e., equifinality).

In this context, even when the variability of an outcome is limited within a population, this does not imply that the outcome is predetermined. Rather, it indicates that multiple developmental pathways can converge toward the same phenotypic endpoint. This key idea challenges many nativist interpretations by emphasizing that the robustness of developmental outcomes does not imply context-insensitivity during development (in Gottlieb's terms, deprivation from the mother call during development does not imply context-insensitivity).

A dynamic interpretation of the epigenetic landscape remains valid, as alterations in sources of developmental information—for example, a mutation on a specific gene, or a changing environmental context—may initially divert the system toward a non-species-typical phenotype. However, compensatory mechanisms involving other variables can redirect development back toward a species-typical outcome. Figure 4 and Table 4 illustrate this process, showing three distinct developmental trajectories that ultimately converge on the same phenotypic outcome (P_3) within the repertoire. As exemplified in Figure 4, at time point t_{n+2}, each trajectory appears to be progressing toward a different potential outcome—specific informational sources have displaced them along distinct paths in the developmental landscape. Nevertheless, subsequent

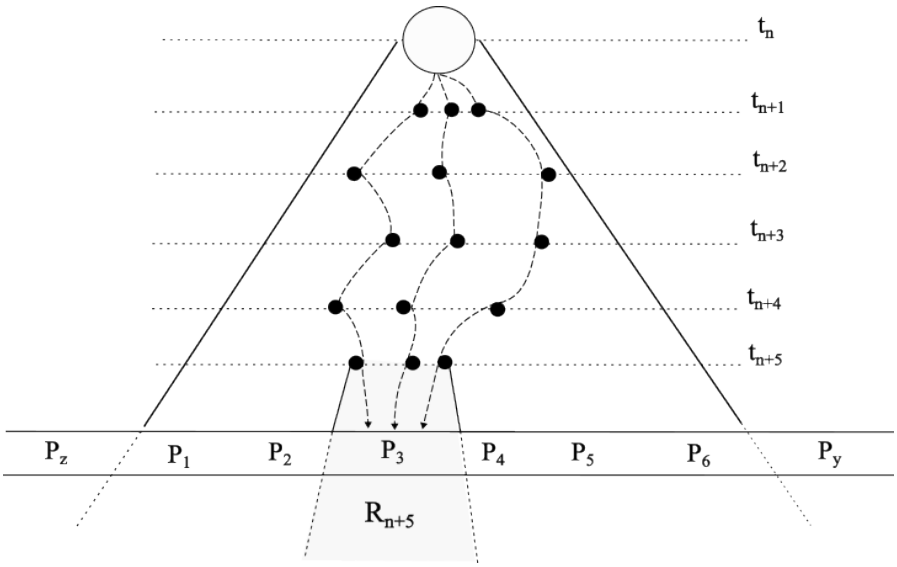

Fig. 4
Plastic means for robust outcomes. (Description in text.)

developmental inputs at t_{n+3} and t_{n+4} alter these trajectories, ultimately canalizing them toward a common endpoint at t_{n+5}. Thus, even if developmental pathways seem to diverge within the repertoire at a particular ontogenetic stage—as shown in Table 4, where $p(P_3)$ differs across paths at t_{n+2}—they can be reoriented and compensated for over the course of development, converging on a species-specific phenotypic outcome.

Table 4 Changing probability of P_3 along each ontogenetic path over time. All paths converge on the same outcome despite different trajectories and probability states.

$p(P_{x,t_x})$	Path 1	Path 2	Path 3
$p(P_{3,t_n})$	.32	.3	.29
$p(P_{3,t_n+1})$	.43	.4	.38
$p(P_{3,t_n+2})$	.1	.5	.009
$p(P_{3,t_n+3})$	.52	.65	.49
$p(P_{3,t_n+4})$	.7	.74	.7
$p(P_{3,t_n+5})$	1	1	1

4.3 Causation as Coaction

Beyond the issues discussed earlier, the probabilistic nature of epigenesis also stems from a fundamental phenomenon: the complex coaction of developmental causes. In

this context, probabilistic epigenetics is closely linked to the complexity of developmental systems and how the interactions among causes within these systems give rise to emergent developmental patterns. This complexity makes the relationship between source and effect variables in development more intricate. I will describe central aspects of probabilistic development from the point of view of complex science, which Gottlieb did not formalize, but which he did explicitly address. Moreover, all of these phenomena can be abstracted from the common diagram (Figure 5) that Gottlieb uses to illustrate the "bidirectional and coactional nature of genetic, neural, behavioral, and environmental influences throughout individual development" (Gottlieb 2001a, 50). Figure 5 shows the relationships among different levels of organization during individual (behavioral) development (similar diagrams could also be drawn for non-animal organisms (e.g., plants) with their own interacting levels of organization).

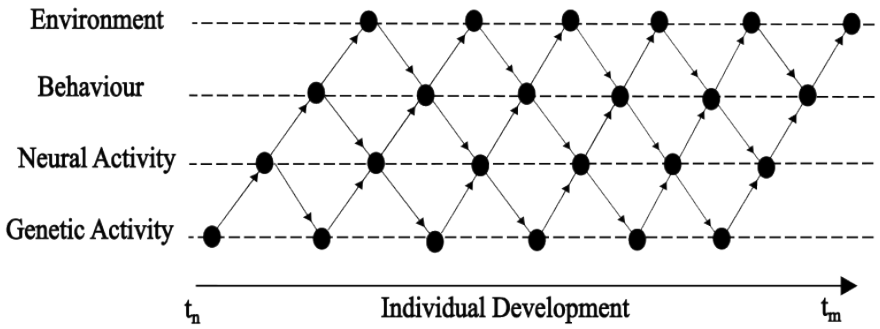

Fig. 5
Coaction in development. Adapted from (Gottlieb 2001b, 184).

A central point in Gottlieb's coactional and relational view concerns the non-linearity of developmental processes, a theme that Gottlieb repeatedly emphasizes. However, he has two different interpretations of non-linearity. The first, and most common in his writings, concerns the idea of non-linearity as the presence of non-obvious developmental causes: "Because of the emergent nature of epigenetic development, another important feature of developmental systems is that causality is often not 'linear' [...] to say that developmental causality is often not obvious" (Gottlieb 1997, 98). This is an interesting phenomenon that provides important insights, especially for experimentalists, since developmental causes might be hidden in non-obvious places.

However, another interpretation of non-linearity is tied to its importance in complex systems theory (Mitchell 2009), namely the non-linear dynamics of a system that produces emergent behavior due to the complex interaction between its parts. This idea has been present in developmental biology for several decades, with Turing (1952) being one of the pioneers in this field, and further explored by Kauffman (1993) and Goodwin (1994), among others (Müller and Newman 2003; Camazine et al. 2003). Nowadays, there are various models and biological phenomena that deal with this property of developmental systems. Modeling developmental systems with the tools of

complex systems has also brought to the fore the self-organizing properties of development (Edelmann and Denton 2006; Newman 2022) that give rise to emergent organic structures such as tissue (e.g., patterns in an animal's skin), morphology (e.g., the formation of toes in the limbs of vertebrates), and to behaviour itself (e.g., Thelen 2008; Barandiaran and Rama Under Revision, 2025).

Although the literature on this topic is vast, it is worth noting here that the interaction between the system parts in Gottlieb's Figure 5 can be approached using the tools of information systems, an area closely associated with complex systems theory (Mitchell 2009, chapter 3). Figure 6 shows a simple boolean network in which five different causal specifiers X_j interact. Networking approaches and transition space modeling are widely used in biology, especially in "omics" sciences such as genomics, transcriptomics or proteomics. This type of approach has proven to be particularly useful in the representation of genetic regulatory networks (GRNs). However, this abstract view can also be extended to other causes involving different levels of organization. Gottlieb's schematic representation in Figure 5 is a general picture of developmental relationships, but he repeatedly recognized that the levels of organization should be peeled at a fine-grained level to include other levels of causation, such as nuclear, intracellular, intercellular, endogenous, and exogenous causes. Thus, Figure 6 can represent different types of relationships: gene-gene, gene-protein, gene-cytoplasm, cell-cell, environment-cell, and so on.

Figure 6 is therefore suitable for illustrating certain characteristics of developmental coaction in terms of information. The same interactions are represented in three different ways (boolean networks, logical rules, and the periodic attractor of seven states that the system reaches from any initial state). In this dynamical system, we can observe three interesting properties regarding non-linearity: regulatory feedback, periodic attractor, and non-linear, *more-than-additive* interactions.

First, there are regulatory feedbacks in the relationships between X_1 and X_4, and X_3 and X_5. X_1 has indirect control over X_4 through X_2 and X_3, while $X_{4,t}$ inhibits $X_{1,t+1}$. Moreover, there is oscillatory behaviour in the relationships between X_3 and X_5, since $X_{3,t}$ affects $X_{5,t+1}$, and $X_{5,t+1}$ affects $X_{3,t+2}$. This type of regulatory behaviour is ubiquitous in the development process, and the interdependence between parts is a hallmark of the organizational properties of development (Montévil and Mossio 2015). To represent regulatory feedback in informational terms, we need to account for the transfer of information between variables, so that it can be modeled with the transfer entropy ($T_{X_j \to X_i}$) over time between variables X_j and X_i, such that:

$$T_{X_j \to X_i} = \sum p(X_{j,t}, X_{i,t}, X_{i,t+1}) log \frac{p(X_{i,t+1}|X_{j,t}, X_{i,t})}{p(X_{i,t+1}|X_{i,t})} \tag{6}$$

Finally, we obtain the feedback (f) between two variables X_i and X_j:

$$f(X_i; X_j) = (T_{X_j \to X_i} + T_{X_i \to X_j}) \tag{7}$$

Second, although this is not a chaotic system (which would make a probabilistic view of the development even richer, but for reason of space it is not developed

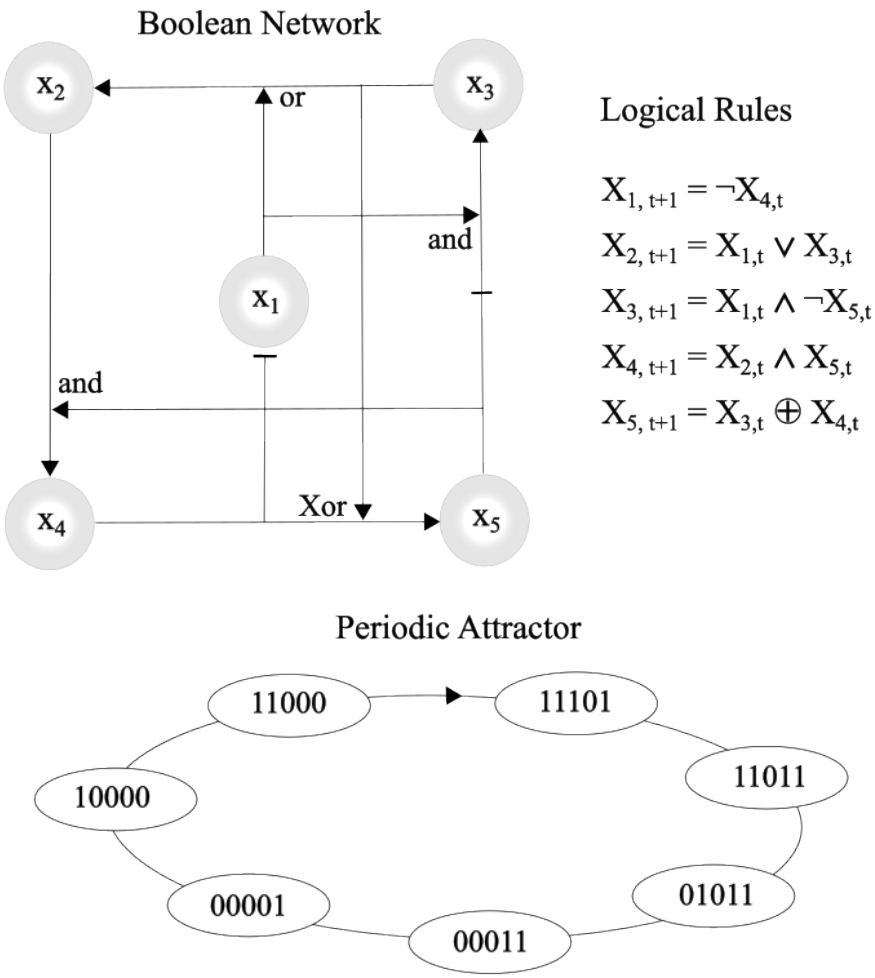

Fig. 6
Simplified example of non-linear coactions in development.

here), there is no final state that the system has, but a periodic attractor of seven states. Therefore, given any initial configuration X_0, we cannot predict the state of the network at a distant time n. We just know that there is a repertoire $R_0 = \{11000, 11101, 11011, 01011, 00011, 00001, 10000\}$ of seven equiprobable options, such that

$$I(X_n, X_o) = 0,143 \tag{8}$$

Finally, the most notorious aspect of this diagram from an informational point of view concerns the synergetic relationship between its parts. This is a direct consequence of the Xor gate (Griffith and Koch 2014). As I explained in Subsection 4.1, we

have defined the information of a set X in an additive way. However, when synergistic interactions come into play, additive measures do not capture the entire information of the system—i.e. the information of the whole is greater than the sum of the information of its parts (Griffith and Koch 2014; Martínez 2020): In development, being $X = \{x_1, x_2, ..., x_n\}$ a set of developmental causes and P a particular phenotypic outcome, X is synergetic set if

$$I(P; X) \neq \sum_{i=1}^{n} I(P; x_i) \tag{9}$$

In the Boolean diagram in Figure 6, this is represented by the following equation, where $X = \{x_1, x_2, ..., x_5\}$, X_t is the state of the network at time t and $X_{i,t}$ is the information of a particular variable i at time t:

$$I(X_{t+1}; X_t) \neq \sum_{i=1}^{5} I(X_{t+1}; x_{i,t}) \tag{10}$$

In particular, considering the fifth logical rule,

$$I(X_{5,t+1}; X_t) \neq I(X_{5,t+1}; X_{3,t}) + I(X_{5,t+1}; X_{4,t}) \tag{11}$$

since

$$I(X_{5,t+1}; X_{3,t}) = 0 \tag{12}$$

$$I(X_{5,t+1}; X_{4,t}) = 0 \tag{13}$$

$$I(X_{5,t+1}; X_t) = 1 \tag{14}$$

In sum, these types of relationships are well-known in development: epistatic gene interaction, cellular communication in cell differentiation, or synergistic information in regulatory GxE interactions, to name a few (see Rama (Under Revisiona)). The key aspect is that this brings a central insight to developmental theory present in Gottlieb's thinking: "The cause of development—what makes development happen—is the relationship of the two components, not the components themselves" (Gottlieb 1997, 91). In informational terms, this means that new information arises from the interaction of causal specifiers.

5 Conclusion

Probabilistic epigenetics is one of a series of theoretical reconstructions in twentieth-century biology that have had a major impact on current biological theory and practice. This article explored the connections of probabilistic epigenetics with an

informational view of development, a field of research to which Gottlieb himself contributes indirectly. As argued here, an informational view can be integrated into probabilistic epigenetics without contradicting its own principles, so that it can illuminate, represent, and explain the theoretical insights of Gottlieb's work using the tools of informational theory.

The connection between probability and information is based on three points, which do not claim to be exhaustive, but represent the core of Gottlieb's view. First, I have established the existence of a repertoire as a marker of probability in development, based on the fact that probabilistic repertoires represent possible outcomes at any ontogenetic time. Second, I have examined Gottlieb's analysis of landscape and his call for the inclusion of non-genetic sources in the definition of a landscape. This allows us to consider the possibility that new information emerges in development that changes the probability distribution and composition of the repertoire over time. In turn, the epigenetic landscape is not fixed but dynamically contingent upon the developmental processes themselves—the landscape has an ontogeny. Finally, a central idea in both the current literature and Gottlieb's work concerns the complexity of causal interaction in development and how this affects the construction of phenotypes. I approach this topic by considering various processes associated with relational causality in development. The result in all cases is that information tools help us to model the probabilistic nature of developmental processes due to the complexity of causal relationships. The aim here was primarily to provide a theoretical and philosophical approach without going into the complexity of the models or the richness of the experimental data on developmental processes. Further elaborations of the ideas developed here could develop into richer mathematical models of probabilistic epigenetics as well as integration with experimental analyses in more complex ways beyond the cases treated by Gottlieb.

Acknowledgments: I am grateful to three anonymous reviewers for their helpful and detailed comments on my manuscript. I am also grateful for the ideas exchanged with Sergio Balari on the topics of this paper. I thank the participants at the conference "Probabilistic Reasoning in the Sciences," held at the end of August 2024 at the Marche Polytechnic University in Ancona, Italy, for their insightful comments and discussions. Special thanks to Michał Sikorski for his contribution to and help with the publication process. This work was supported by the National Agency of Investigation and Innovation (Uruguay) through grant $PDNAC20231176930$.

References

Alberch, P.: The logic of monsters: Evidence for internal constraint in development and evolution. Geobios **22**(Supplement 2), 21–57 (1989) https://doi.org/10.1016/S0016-6995(89)80006-3

Amundson, R.: Two concepts of constraint: Adaptationism and the challenge from developmental biology. Philosophy of Science **61**(4), 556–578 (1994) https://doi.org/10.1086/289822

Amundson, R.: The Changing Role of the Embryo in Evolutionary Thought: Roots of Evo-Devo. Cambridge University Press, Cambridge (2005)

Artiga, M.: Biological Information. In: Zalta, E.N., Nodelman, U. (eds.) The Stanford Encyclopedia of Philosophy, Fall 2024 edn. Metaphysics Research Lab, Stanford University, California (2024)

Baedke, J.: The epigenetic landscape in the course of time: Conrad Hal Waddington's methodological impact on the life sciences. Studies in History and Philosophy of Science Part C: Studies in History and Philosophy of Biological and Biomedical Sciences **44**(4), 756–773 (2013) https://doi.org/10.1016/j.shpsc.2013.06.001

Baedke, J.: Above the Gene, Beyond Biology: Toward a Philosophy of Epigenetics. University of Pittsburgh Press, Pittsburgh, PA (2018)

Bueno, O., French, S.: Applying Mathematics: Immersion, Inference, Interpretation. Oxford University Press, Oxford (2018)

Bateson, P., Gluckman, P.: Plasticity, Robustness, Development and Evolution. Cambridge University Press, Cambridge (2011)

Balari, S., Lorenzo, G.: Pere Alberch's developmental morphospaces and the evolution of cognition. Biological Theory **3**(4), 297–304 (2008) https://doi.org/10.1162/biot.2008.3.4.297

Brigandt, I., Love, A.C.: Evolutionary novelty and the evo-devo synthesis: field notes. Evolutionary Biology **37**(2), 93–99 (2010)

Balari, S., Lorenzo, G.: The end of development. Biological Theory **10**(1), 60–72 (2014) https://doi.org/10.1007/s13752-014-0180-0

Bourrat, P.: Variation of information as a measure of one-to-one causal specificity. European Journal for Philosophy of Science **9**(1), 11 (2019)

Barandiaran, X.E., Rama, T.: The organismic turn. teleosemantics after 4e. In: Heras-Escribano, M. (ed.) Analytic Philosophy and 4E Cognition, pp. 143–159. Routledge, New York (2025)

Barandiaran, X., Rama, T.: Sensorimotor teleology and goal-directedness. an organismic framework for normative behaviour. Phenomenology and Cognitive Science. (Under Revision)

Bich, L., Skillings, D.: There are no intermediate stages: An organizational view on development. In: Organization in Biology, pp. 241–262. Springer, Switzerland (2023)

Calcott, B.: Causal specificity and the instructive–permissive distinction. Biology & Philosophy **32**(4), 481–505 (2017)

Capurro, R.: Past, present, and future of the concept of information. TripleC: communication, capitalism & critique. open access journal for a global sustainable information society **7**(2), 125–141 (2009)

Camazine, S., Deneubourg, J.-L., Franks, N.R., Sneyd, J., Bonabeau, E., Theraula, G.: Self-Organization in Biological Systems. Princeton University Press, Princeton, NJ (2003)

Cao, D., Garai, S., DiFrisco, J., Veenvliet, J.V.: The logic of monsters: development and morphological diversity in stem-cell-based embryo models. Interface focus **14**(5), 20240023 (2024)

Cohen, J., Meskin, A.: An objective counterfactual theory of information. Australasian Journal of Philosophy **84**(3), 333–352 (2006)

Calcott, B., Pocheville, A., Griffiths, P.E.: Signals that make a difference. The British Journal for the Philosophy of Science **71**(1), 233–258 (2020) https://doi.org/10.1093/bjps/axx022

Crick, F.H.: On protein synthesis. In: Symp Soc Exp Biol, vol. 12, p. 8 (1958)

Dretske, F.: Knowledge and the Flow of Information. The MIT Press, Cambridge, MA (1981)

Edelmann, J.B., Denton, M.J.: The uniqueness of biological self-organization: Challenging the Darwinian paradigm. Biology & Philosophy **22**(4), 579–601 (2006) https://doi.org/10.1007/s10539-006-9055-5

Fresco, N., Ginsburg, S., Jablonka, E.: Functional information: A graded taxonomy of difference makers. Review of Philosophy and Psychology **11**(3), 547–567 (2020)

Franklin, J.: An Aristotelian Realist Philosophy of Mathematics: Mathematics as the Science of Quantity and Structure. Springer, London (2014)

Gilbert, S.F., Epel, D.: Ecological Developmental Biology: The Environmental Regulation of Development, Health, and Evolution. Sinauer, Sunderland, MA (2015)

Gottlieb, G., Halpern, C.T.: A relational view of causality in normal and abnormal development. Development and psychopathology **14**(3), 421–435 (2002)

Griffith, V., Koch, C.: Quantifying synergistic mutual information. In: Prokopenko, M. (ed.) Guided Self-Organization: Inception, pp. 159–190. Springer, Berlin (2014)

Goldschmidt, R.: The Material Basis of Evolution. Yale University Press, New Haven, CT (1982). Reprinted 1940 edition with an introduction by S. J. Gould.

Goodwin, B.: How the Leopard Changed Its Spots: The Evolution of Complexity. Weidenfeld & Nicholson, London (1994)

Gottlieb, G.: Development of Species Identification in Birds: An Inquiry Into the Prenatal Determinants of Perception. University of Chicago Press, Chicago (1971)

Gottlieb, G.: Conceptions of prenatal development: behavioral embryology. Psychological review **83**(3), 215 (1976)

Gottlieb, G.: Evolutionary trends and evolutionary origins: Relevance to theory in comparative psychology. Psychological Review **91**(4), 448 (1984)

Gottlieb, G.: The developmental basis of evolutionary change. Journal of Comparative Psychology **101**(3), 262 (1987)

Gottlieb, G.: Epigenetic systems view of human development. Developmental Psychology **27**(1), 33–34 (1991) https://doi.org/10.1037/0012-1649.27.1.33

Gottlieb, G.: Synthesizing Nature-Nurture: Prenatal Roots of Instinctive Behavior. Lawrence Erlbaum, Mahwah, NJ (1997)

Gottlieb, G.: Normally occurring environmental and behavioral influences on gene activity: From Central Dogma to Probabilistic Epigenesis. Psychological Review **105**(4), 792–802 (1998) https://doi.org/10.1037/0033-295X.105.4.792-802

Gottlieb, G.: A developmental psychobiological systems view: Early formulation and current status. In: S. Oyama, R.G., Griffiths, P. (eds.) Cycles of Contingency: Developmental Systems and Evolution, pp. 41–54. The MIT Press, Cambridge, MA (2001)

Gottlieb, G.: Individual Development and Evolution: The Genesis of Novel Behavior. Oxford University Press, New York (2001)

Gottlieb, G.: On the epigenetic evolution of species-specific perception: The developmental manifold concept. Cognitive Development **17**(3-4), 1287–1300 (2002) https://doi.org/10.1016/s0885-2014(02)00120-x

Gottlieb, G.: Probabilistic epigenesis. Developmental Science **10**(1), 1–11 (2007) https://doi.org/10.1111/j.1467-7687.2007.00556.x

Griffiths, P.E., Pocheville, A., Calcott, B., Stotz, K., Kim, H., Knight, R.: Measuring causal specificity. Philosophy of Science **82**(4), 529–555 (2015) https://doi.org/10.1086/682914

Griffiths, P.E.: Genetic information: A metaphor in search of a theory. Philosophy of Science **68**(3), 394–412 (2001) https://doi.org/10.1086/392891

Griesemer, J.R.: Reproduction in complex life cycles: Toward a developmental reaction

norms perspective. Philosophy of Science **83**(5), 803–815 (2016) https://doi.org/10.1086/687865

Griffiths, P.E.: Proximate and ultimate information in biology. In: Couch, M., Pfeifer, J. (eds.) The Philosophy of Philip Kitcher, pp. 74–97. Oxford University Press, Oxford (2016)

Griffiths, P.E.: Genetic, epigenetic and exogenetic information in development and evolution. Interface Focus **7**(5), 20160152 (2017) https://doi.org/10.1098/rsfs.2016.0152

Godfrey-Smith, P.: On the theoretical role of "genetic coding". Philosophy of Science **67**(1), 26–44 (2000) https://doi.org/10.1086/392760

Griffiths, P.E., Stotz, K.: Genetics and Philosophy. An Introduction. Cambridge University Press, Cambridge (2013)

Johnston, T.D., Gottlieb, G.: Neophenogenesis: A developmental theory of phenotypic evolution. Journal of theoretical biology **147**(4), 471–495 (1990)

Kauffman, S.: The Origins of Order: Self-Organization and Selection in Evolution. Oxford University Press, New York (1993)

Keller, E.F.: The Century of the Gene. Harvard University Press, Cambridge, MA (2002)

Keller, E.F.: From gene action to reactive genomes. The Journal of Physiology **592**(11), 2423–2429 (2014) https://doi.org/10.1113/jphysiol.2014.270991

Kuo, Z.Y.: The Dynamics of Behavior Development: An Epigenetic View, 2nd edn. Plenum Press, New York (1976)

Lehrman, D.S.: A critique of Konrad Lorenz's theory of instinctive behavior. The Quarterly Review of Biology **28**(4), 337–363 (1953) https://doi.org/10.1086/399858

Lehrman, D.S.: Semantic and conceptual issues in the nature-nurture problem. In: Aronson, L.R., Tobach, E., Lehrman, D.S., Rosenblatt, J. (eds.) Development and Evolution of Behavior. Essays in Memory of T. C. Schneirla, pp. 17–52. W. H. Freeman and Company, San Francisco (1970)

Lewis, D.: Causation as influence. The Journal of Philosophy **97**(4), 182–197 (2000)

Lickliter, R., Logan, C.: Developmental psychobiology special issue:"Gilbert gottlieb's legacy: Probabilistic epigenesis and the development of individuals and species". Wiley Online Library (2007)

Lorenz, K.: Evolution and Modification of Behavior. University of Chicago Press, Chicago (1986)

Levis, N.A., Pfennig, D.W.: Evaluating 'Plasticity-First' Evolution in Nature: Key Criteria and Empirical Approaches. Trends in Ecology & Evolution **31**(7), 563–574 (2016) https://doi.org/10.1016/j.tree.2016.03.012

Laland, K.N., Uller, T., Feldman, M.W., Sterelny, K., Müller, G.B., Moczek, A., Jablonka, E., Odling-Smee, J.: The extended evolutionary synthesis: its structure, assumptions and predictions. Proceedings of the royal society B: biological sciences **282**(1813), 20151019 (2015)

Martínez, M.: Synergic kinds. Synthese **197**(5), 1931–1946 (2020)

McGhee, G.R.: The Geometry of Evolution: Adaptive Landscapes and Theoretical Morphospaces. Cambridge University Press, Cambridge (2006)

Miller, D.B.: From nature to nurture, and back again. Developmental Psychobiology: The Journal of the International Society for Developmental Psychobiology **49**(8), 770–779 (2007)

Minelli, A.: Animal Development, an Open-Ended Segment of Life. Biological Theory **6**(1), 4–15 (2011) https://doi.org/10.1007/s13752-011-0002-6

Minelli, A.: Understanding Development. Cambridge University Press, Cambridge (2021)

Mitchell, M.: Complexity: A Guided Tour. Oxford University Press, Oxford (2009)

Michel, G.F., Moore, C.L.: Developmental Psychobiology: An Interdisciplinary Science. MIT Press, Cambridge, MA (1995)

Montévil, M., Mossio, M.: Biological organisation as closure of constraints. Journal of theoretical biology **372**, 179–191 (2015)

Müller, G.B., Newman, S.A. (eds.): Origination of Organismal Form: Beyond the Gene in Developmental and Evolutionary Biology. The MIT Press, Cambridge, MA (2003)

Moss, L.: What Genes *Can't* Do. The MIT Press, Cambridge, MA (2003)

Maynard Smith, J., Burian, R., Kauffman, S., Alberch, P., Campbell, J.H., Goodwin, B., Lande, R., Raup, D., Wolpert, L.: Developmental constraints and evolution: A perspective from the Mountain Lake Conference on Development and Evolution. The Quarterly Review of Biology **60**(3), 265–287 (1985) https://doi.org/10.1086/414425

Rosa, L., Müller, G.B.: The legacy and evolvability of pere alberch's ideas. Interface Focus **14**(5), 20240011 (2024)

Newman, S.A.: Self-organization in embryonic development: myth and reality. In: Self-organization as a New Paradigm in Evolutionary Biology: from Theory to Applied Cases in the Tree of Life, pp. 195–222. Springer, Switzerland (2022)

Oyama, S.: Evolution's Eye. A Systems View of the Biology-Culture Divide. Duke University Press, Durham, NC (2000)

Oyama, S.: The Ontogeny of Information. Developmental Systems and Evolution, 2nd edn. Duke University Press, Durham, NC (2000)

Pearl, J.: Causality. Cambridge University Press, Cambridge (2009)

Pocheville, A., Griffiths, P.E., Stotz, K., Leitgeb, H.: Comparing causes—an information-theoretic approach to specificity, proportionality and stability. In: Proceedings of the 15th Congress of Logic, Methodology and Philosophy of Science. College Publications, London, pp. 261–286 (2017)

Pigliucci, M., Müller, G.B. (eds.): Evolution—The Extended Synthesis. The MIT Press, Cambridge, MA (2010)

Potochnik, A.: Idealization and the Aims of Science. The University of Chicago Press, Chicago, IL (2017)

Rama, T.: Agential Teleosemantics. PhD Thesis, Autonomous University of Barcelona, Spain (2022)

Rama, T.: The explanatory role of umwelt in evolutionary theory: Introducing von baer's reflections on teleological development. Biosemiotics **17**(2), 361–386 (2024)

Rama, T.: Is a cognitive revolution in theoretical biology underway? Foundations of Science, 1–22 (2024)

Rama, T.: Autonomy and Development: Distinguishing teleological development from teleological physiology. Biology and Philosophy **41**(6) (2026)

Rama, T.: Developmental Synergistic Information. Theory in Bioscience (Under Revision)

Rama, T.: The process is the cause: A processual ontology for synergistic emergent causation. Synthese (Under Revision)

Robert, J.S.: Embryology, Epigenesis and Evolution: Taking Development Seriously. Cambridge University Press, Cambridge (2004)

Sarkar, S.: Biological information: A skeptical look at some central dogmas of molecular biology. Boston Studies in the Philosophy of Science **183**, 187–232 (1996)

Sarkar, S.: Molecular Models of Life: Philosophical Papers on Molecular Biology. The

MIT Press, Cambridge, MA (2005)

Scarantino, A.: Information as a probabilistic difference maker. Australasian Journal of Philosophy **93**(3), 419–443 (2015) https://doi.org/10.1080/00048402.2014.993665

Stotz, K., Griffiths, P.: Epigenetics: Ambiguities and implications. History and Philosophy of the Life Sciences **38**(4), 1–20 (2016) https://doi.org/10.1007/s40656-016-0121-2

Stotz, K., Griffiths, P.E.: Biological information, causality and specificity: An intimate relationship. In: Walker, S.I., Davies, P.C.W., Ellis, G.F.R. (eds.) From Matter to Life. Information and Causality, pp. 366–390. Cambridge University Press, Cambridge (2017)

Shannon, C.E.: A mathematical theory of communication. The Bell system technical journal **27**(3), 379–423 (1948)

Solé, R., Kempes, C.P., Corominas-Murtra, B., De Domenico, M., Kolchinsky, A., Lachmann, M., Libby, E., Saavedra, S., Smith, E., Wolpert, D.: Fundamental constraints to the logic of living systems. Interface Focus **14**(5), 20240010 (2024)

Scarantino, A., Piccinini, G.: Information without truth. Metaphilosophy **41**(3), 313–330 (2010)

Squier, S.M.: Epigenetic Landscapes: Drawings as Metaphor. Duke University Press, Durham, North Carolina (2017)

Stegmann, U.E.: Prospects for probabilistic theories of natural information. Erkenntnis **80**(4), 869–893 (2015)

Stotz, K.: Biological information in developmental and evolutionary systems. In: Uller, T., Laland, K.L. (eds.) Evolutionary Causation: Biological and Philosophical Reflections, pp. 323–344. The MIT Press, Cambridge, MA (2019)

Sultan, S.E.: Organism & Environment: Ecological Development, Niche Construction, and Adaption. Oxford University Press, Oxford (2015)

Šustar, P.: Crick's notion of genetic information and the 'central dogma'of molecular biology. The British journal for the philosophy of science (2007)

Thorner, J., Hunter, T., Cantley, L.C., Sever, R.: Signal transduction: From the atomic age to the post-genomic era. Cold Spring Harbor perspectives in biology **6**(12), 022913 (2014)

Thelen, E.: Self-organization in developmental processes: Can systems approaches work? In: Johnson, M.H., Munakata, Y., Gilmore, R.O. (eds.) Brain Dovelopement and Cognition: A Reader, Second Edition, pp. 77–117. Wiley-Blackwell, Canada (2008)

Turing, A.M.: The chemical basis of morphogenesis. Bulletin of mathematical biology **52**(1), 153–197 (1952)

Vecchi, D., Santos, G.: The multi-causal basis of developmental potential construction. Acta Biotheoretica **71**(1), 6 (2023)

Waddington, C.H.: The Strategy of Genes. Allen & Unwin, London (1957)

Walsh, D.M.: The affordance landscape: The spatial metaphors of evolution. In: Barker, G., Desjardins, E., Pearce, T. (eds.) Entangled Life. Organism and Environment in the Biological and Social Sciences, pp. 213–236. Springer, Dordrecht (2013)

Walsh, D.M.: Organisms, Agency, and Evolution. Cambridge University Press, Cambridge (2015)

Waters, C.K.: Causes that make a difference. The Journal of Philosophy **104**(11), 551–579 (2007)

Wagner, M.P. Günter P., Cheverud, J.M.: The road to modularity. Nature Reviews Genetics **8**(12), 921–931 (2007) https://doi.org/10.1038/nrg2267

West-Eberhard, M.J.: Developmental Plasticity and Evolution. Oxford University Press, Oxford (2003)

Weber, M.: The Central Dogma as a Thesis of Causal Specificity. History and Philosophy of the Life Sciences **28**(4), 595–609 (2006)

Woodward, J.: Making Things Happen: A Theory of Causal Explanation. Oxford University Press, Oxford (2003)

Woodward, J.: Causation in biology: stability, specificity, and the choice of levels of explanation. Biology & Philosophy **25**(3), 287–318 (2010)