Developmental Synergistic Information

Tiago Rama
trama.folco@gmail.com
Institute of Philosophy, University of the Republic Montevideo, Uruguay
https://orcid.org/0000-0002-1531-7233

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Abstract: This article characterizes Oyama's concept of ontogenesis of information formally. I apply the mathematical notion of synergistic information to the framework proposed by Griffiths et al. (2015) for developmental information and specificity. This allows us to examine the specificity revealed by the interaction of variables as a result of *interventions on interactions*. I define *Developmental Synergistic Information* as the specificity of interacting variables obtained by measuring how much mutual information interventions on interactions carry about the effect variable. To formalise this concept, I use partial information decomposition, one of the most robust frameworks for analysing synergistic information. Some examples of developmental synergistic information are presented. Finally, I consider the philosophical implications of developmental synergistic information, arguing that it supports important tenets of organism-centered biology: (i) synergistic information has ontogeny—order is generated in epigenesis; (ii) such information is non-transmissible through channels of inheritance—the specificity of outcomes must be reconstructed anew in each generation; (iii) the developmental organism (or any synergistic system under consideration) is itself a cause of development—causation resides in the coaction of developmental variables; and (iv) the developmental context of information must be taken into account—that developmental causation is always embedded in and constrained by a developmental matrix of other specifiers.

Keywords: Ontogeny of Information; Biological Information; Distributed Specificity; Developmental Systems Theory; Biological Order; Organicism

Information is conceived to be a special kind of cause among
all the factors that may be necessary for a phenomenon,
the cause that imparts order and form to matter.
Susan Oyama, 2000a, 3.

1. Introduction

The astonishing image of a phylogenetic lineage connecting a unicellular ancestor with a current complex multicellular organism finds its parallel in the developmental emergence of diverse cell types, tissues, and organs from a single fertilized cell. How are 'developmental lineages' specified? How is cell commitment determined? In essence, how are traits developed? These questions bear directly on evolutionary theory: how are traits developed in ways that resemble those of parental organisms—inheritance—in non-exact ways —variation—, and thus causing differential reproductive success—fitness—?

Setting nuances aside, the main response these questions received is reflected in Schrödinger's (1944) seminal analysis of the developmental origins of order (see Nicholson (2025) for a detailed revision): the *order-from-order* principle. Accordingly, the organization observed in living systems arises from a pre-existing ordered structure that encodes all necessary information to build an organism—which specifies developmental lineages. The remarkable complexity of a sponge, with its intricate structures and functions, is thus attributed to another ordered entity responsible for its emergence. This pre-existing structure was theoretically conceived as the gene well before Schrödinger's book, and its material basis—DNA—was identified shortly thereafter. The gene-eyes view (Ågren, 2021) emerged within the framework of the Modern Evolutionary Synthesis (MS), rooted in population genetics and shaped by foundational conceptions such as the Weismann barrier and the particulate theory of inheritance. In this sense, Schrödinger's order–form–order principle predates Schrödinger's own formulation and continued to advance throughout the second half of the twentieth century. Developmental processes came to be explained through various conceptual frameworks—determinants, factors, replicators—and popularized via vivid metaphors such as 'developmental programs'. Within this context, two influential ideas emerged as the dominant views of development in the latter half of the twentieth century. First, Crick's Central Dogma asserts that genetic information unidirectionally governs the synthesis of protein products in each cell type (Crick, 1958, 1970). Second, Dawkins' (1976, 1982) replicator concept, influenced by Hamilton's and Williams' work on

gene selection, embraced an order-from-order strategy: replicators are the driving force behind developmental organisms (vehicles) and constitute the true units of evolution and development—that is, the order of vehicles is explained by the order of replicators.

Schrödinger's order-from-order principle (and its later developments) has, however, been contested from within developmental theory. An alternative perspective, rooted in epigenesis and organizational approaches, has been steadily gaining support. In this view, development is not the execution of pre-established instructions or the mere expression of replicators. Instead, it is a dynamic process orchestrated by a complex array of developmental resources that organisms regulate to achieve specific phenotypic outcomes. What emerges is not predetermined but arises from the organized interplay of multiple developmental inputs across ontogeny. Organisms, not genes, direct development; 'vehicles' govern 'replicators' and cells exert custodianship over genes, not vice versa. This strategy traces back to pre-(neo-)Darwinian thought (Amundson, 2005) and organicism (Nicholson and Rawne, 2014). Today, it is championed by proponents of an 'organism-oriented' perspective in developmental and evolutionary theory (Laland et al., 2015; Sultan et al., 2022; Walsh, 2015; Corning et al., 2023; Rama, 2024a), advocating non-reductionist, epigenetic accounts of developmental order. Within this framework, an *organismic theory of development* is pursued across various fields—niche construction (Odling-Smee et al., 2003), eco-devo (Sultan, 2015), evo-devo (Wagner, 2014), molecular epigenetics (Davidson, 2010), extended inheritance theory (Jablonka and Lamb, 2014), developmental psychobiology (Michel and Moore, 1995)—seeking to explain how traits emerge from causal interplay and how developmental analysis informs evolutionary explanations. A major philosophical impetus behind the organismic view of development is Oyama's *The Ontogeny of Information* (2000a). The core idea behind the ontology of information is that, in contrast to gene-centric and preformationist views, the order of an organism emerges through the interplay of different developmental variables across ontogeny.[1]

[1] Based on Nicholson's (2025) recent and insightful analysis, it would be misguided to link this strategy with Schrödinger's *order-from-disorder principle*. This principle concerns the spontaneous emergence of order due to stochastic fluctuations among multiple variables (as in the case of Turing's reaction–diffusion mechanism). Since the ontogeny of information is grounded in the information produced through interactions between variables, it is therefore not equivalent to this principle. While the ontogeny of information resembles important insight of this principle (such as the contingency and not-preformationism of development), it offers a distinct explanation of order. In this sense, the ontology of information occupies a middle ground between the order-from-disorder and order-from-order principles.

However, although Oyama's concept has gained traction, it has *not* been linked to a well-developed informational account of development. This article seeks to address that gap by offering a robust characterization of Oyama's ontogeny of information, drawing on information theory and recent developments in the philosophy of science that examine the interplay between information, causality, and complexity. This requires analyzing *how information arises from interacting variables during development*—how order is created during the ontogenetic interplay of developmental resources. I argue that the concept of *developmental synergistic information* provides a rigorous and coherent account of biological information that aligns with the theoretical and empirical foundations of the organismic perspective.

In this way, the aim of this article is primarily theoretical: to deploy mathematical and philosophical tools toward a rigorous and scientifically grounded elucidation of a central concept in biology. Accordingly, the principal objective is not to develop instruments for direct application by experimental or computational biologists; developmental biologists may find this analysis of limited utility for their practical work, even if it remains valuable for their theoretical frameworks. In this way, mathematics is employed primarily as an elucidatory tool for conceptual refinement and clarity, rather than for direct empirical applicability (for discussion, see Bueno and French, 2018; Morrison, 2015; van Fraassen, 2008). In Section 4, I present selected examples of developmental synergistic information in empirical biological contexts. However, this section serves chiefly to reinforce the theoretical orientation of the work and to demonstrate how the proposed framework of developmental synergistic information constitutes a suitable formal scheme for representing the emergence of information from the interplay of multiple variables. It is hoped that future advances will further refine and extend the mathematical framework developed here, thereby enabling the construction of more sophisticated computational models. Such models may, in turn, prove valuable for probing the complexity of developmental interactions across temporal and organizational scales.[2]

The structure of the paper is as follows. Section 2.1 examines the explanatory role of information in developmental biology. Section 2.2 presents the informational theory of distributed specificity (Griffiths et al., 2015), one of the most sophisticated attempts to move beyond a gene-centric account of biological information. In Section 2.3, I contend that while Griffiths et al.'s framework marks a significant advance, further theoretical development is

[2] I thank an anonymous reviewer for highlighting the importance of being explicit about the theoretical aims of this article, as well as its limitations with respect to empirical research.

required to fully capture the philosophical implications of Oyama's concept of the ontogeny of information. Section 3 introduces synergistic information through the lens of partial information decomposition, culminating in the definition of developmental synergistic information. Section 4 illustrates instances of developmental synergistic information in development. Section 5 addresses the broader philosophical implications of developmental synergistic information in developmental theory. Section 6 closes with programmatic research questions.

2. Information in Development: the path towards order

Information is a widely debated concept in biology, with diverse applications across fields such as signaling systems, animal communication, and cognitive science (Artiga, 2024; Stegmann, 2017; Dickins, 2023). It also plays a central role in developmental biology, where discussions about the nature of development and its evolutionary significance are often framed in informational terms. Let's start by presenting Oyama's concept of the ontogeny of information and then move to Griffiths et al.'s proposal on distributed specificity.

2.1 Oyama's Ontogeny of Information

Biological information has served as a key concept in explaining the gene's role in development under the order-from-order strategy. Notably, the concept of the gene predates the discovery of its molecular basis. Yet, the gene's explanatory role in development is not tied to its physical substrate. As Griffiths and Stotz (2013, 144) argue, "the material form of the gene is inessential"; regardless of its physical nature, "the gene itself is a unit of information." An informational, gene-centered version of the order-from-order strategy thus entails a form of *informational preformationism:* the information required to construct an organism is pre-specified prior to development. Or as Oyama (2000b, 21) expressed, "the idea that traits are 'transmitted' in heredity, rests on notions of genetic programming that are ultimately quite preformationist." This position is defended by Monod (1971, 7, emphasis in original):

> No preformed [in the morphological sense debated in the XVII century] and complete structure preexisted anywhere; but the architectural plan for it was present in its very constituents. It can therefore come into being spontaneously and autonomously, without outside help and without the injection of additional information. The necessary information was present, but unexpressed, in the constituents. The epigenetic building of a structure is not a *creation*; it is a *revelation*.

Development is a revelation of what was already there. Order begets order; genetically inherited information is the source of order, preceding developmental activity.

Oyama critiqued the very concept of genetic information, identifying several key shortcomings. First, it privileges genes with a (misguided) unique causal and explanatory role: development is not autonomous from the outside, since the environment also provides an "injection of additional information" (something widely accepted nowadays in ecological development biology; see Sultan (2015)). Second, it reinforces the nature–nurture divide by drawing a sharp boundary between the inside (nature, inherited information) and outside (nurture, ecological context). Most critically, she rejected informational preformationism. As a leading figure in Developmental Systems Theory (Oyama et al., 2003; Griffiths & Gray, 1994), Oyama advocated an organismic view: developmental outcomes are not pre-specified but emerge through the developmental process. The information required for phenotypic emergence is not present in advance but is generated through development itself. In contrast to Monod, Oyama urged us to see "development as creation, as in-formation" (2000a, 159). Information, she argued, *has an ontogeny*—it is epigenetically produced by the very processes that generate ordered systems. Her critique was pointed: information is a poisoned concept in biology, one that invites preformationist assumptions and misleading questions about nature and nurture—a view echoed by other developmental systems theorists (Griffiths, 2001; see also Sarkar, 1996; Godfrey-Smith, 2000).

Despite ongoing criticism, information remains a pivotal concept in developmental theory. As illustrated, we have two distinct informational interpretations of development: preformationist and ontogenetic. What, then, is the explanatory role of information in this context? Oyama's epigraph captures its epistemic and ontological significance: information is the cause that imparts order. While multiple causes contribute to trait formation, those that determine developmental outcomes are precisely the ones that provide information. Matter and energy are always involved, but it is information that figures centrally in explaining 'developmental lineages' (Rama, 2026a)—as Wiener said in his seminal work on cybernetics (1948, 155), "[i]nformation is information, not matter or energy." Therefore, due to its conceptual relevance, rather than discarding the concept of information due to its preformationist baggage, it is more productive to reframe it within an appropriate philosophical analysis of developmental causation. Accordingly, my primary aim is to offer a formal account of Oyama's ontogeny of information.

Fortunately, the relationship between causation and information has been extensively explored since Dretske's (1981) influential application of Shannon's theory. Numerous accounts of biological information have since emerged (Stegmann et al., 2006; Neander, 2013; Bogen & Machamer, 2010; Walker, 2017; Pearl, 2009; Weber, 2006; Lewis, 2000; Millikan, 2000; Shea, 2007; Cohen & Meskin, 2006; Scarantino, 2008, 2015; see also Fresco et al., 2020; Bourrat, 2019; Pocheville, 2018). Here, however, I focus on a recent and theoretically rigorous proposal by Paul Griffiths and collaborators (henceforth 'Griffiths et al.'), developed across a series of works (Calcott et al., 2020; Griffiths, 2013, 2016, 2017; Griffiths et al., 2015; Stotz, 2006, 2019; Stotz & Griffiths, 2017).

2.2 Distributed Specificity

Griffiths et al.'s proposal begins with an analysis of Crick's notion of information as articulated in his 'sequence hypothesis'. Genes, through their specific coding nucleotide sequences, are regarded as informational causes of development due to the "precise determination" (Crick, 1958, 153) they provide regarding the outcome—namely, the sequence of amino acids in a polypeptide chain. In this sense, *Crick information* refers to the *causal specificity* of one element concerning another. Causal specificity is the key term that aligns with the explanatory role of information previously discussed: the capacity of one variable to precisely determine another reduces uncertainty and imparts order to developmental outcomes. For Griffiths et al., *biological information in development is synonymous with causal (developmental) specificity*. A factor provides developmental information insofar as it exercises precise control over its effects—it provides a degree of *specificity* over a variable. Therefore, resembling Oyama's epigraph, "distinguishing 'matter and energy' from 'information' corresponds to the distinction between the efficiency and specificity of a molecular process" (Stotz, 2019, 325).

Griffiths et al.'s contribution lies in the formalization of causal specificity in development through the integration of Shannon's mathematical theory of information with Woodward's interventionist account of causality. According to Shannon (1948), mutual information between two variables quantifies the reduction in entropy (H)—uncertainty—of one variable given knowledge of the other. It measures how much knowing the value of one variable decreases uncertainty about the other. Formally, the mutual information between variables X and Y is expressed as follows:

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

Mutual information is inherently symmetrical ($I(X;Y) = I(Y;X)$) and thus does not capture the asymmetry characteristic of causal relationships (Artiga, 2024; Stotz & Griffiths, 2017; Šustar, 2007). A widely adopted framework for modeling causation in scientific explanation is Woodward's interventionist theory (2003, 2010). At its core lies a straightforward intuition: if, under a certain background condition, intervening on a variable X leads to a systematic change in variable Y, then X may be considered a cause of Y. According to Woodward's invariance model, establishing whether X causes Y involves assessing counterfactual scenarios in which X is altered or absent, and determining—*ceteris paribus*—whether Y correspondingly changes.

Griffiths et al. integrate the interventionist framework with information theory to quantify the mutual information gain about a variable Y resulting from an intervention on variable X. Here, $H(Y|\widehat{X})$ denotes the conditional entropy of Y given X under intervention—capturing the variability in Y attributable to manipulated values of X. The mutual information between X and Y, incorporating intervention (typically represented using the do. operator; see Pearl, 2009; Griffiths et al., 2015, Appendix B), is thus formalized as follows:

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

Equation (2) formalizes the simple idea that "the more specific the relationship between a cause variable and an effect variable, the more information we have about the effect after we perform an intervention on the cause" (Griffiths et al., 2015, 532). Unlike Equation (1), Equation (2) captures the asymmetry of causal relations such that $I(Y;\widehat{X}) \neq I(X;\widehat{Y})$. For example, under Crick's sequence hypothesis, changes in the nucleotide sequence (in non-synonymous regions) can alter the amino acid sequence, whereas changes in amino acids do not affect the underlying DNA. Thus, DNA sequences are said to causally specify amino acid sequences. On this basis, biological information in development—causal specificity within developmental systems—can be defined as follows:

> 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).

Two salient features of SPEC merit emphasis: first, it is a *probabilistic* notion; second, it yields *quantitative* assessments. Entropy, and consequently mutual information, are defined with respect to probability distributions, and their values vary depending on the underlying

probabilities. The analysis of invariance, therefore, captures the *degree of control* that one variable exerts over another. High developmental specificity, therefore, functions as an indicator of the level of detail with which developmental outcomes are determined. Calcott et al. (2020, 246) contrast developmental causes that provide specificity with a tuning dial, which allows one to specify what is to be heard (music, sport, news), as opposed to an on/off switch, which lacks fine-grained control. Both the dial and the switch can be regarded as causes of what one hears; however, the dial constitutes a markedly more specific cause. In developmental terms, the presence of a variable *X* may be considered a cause of a trait T if, for instance, T is produced only when X is present—thus functioning as an on/off switch. However, if the aim is to understand the more specific features of T, or to determine which of its many possible variants is expressed, additional causes may provide more fine-grained information about the variation underlying *T*. These causes operate as tuning mechanisms, determining which particular form of *T* ultimately develops.

The gradient character of developmental specificity frames development in probabilistic terms, as recently analyzed in Rama (2026b; see also Calcott, 2017; for probabilistic accounts of information, see Scarantino, 2015; Cohen & Meskin, 2006; Fresco et al., 2020; Stegman, 2015). This view is closely aligned with Susan Oyama's perspective: developmental causes do not fully specify outcomes prior to the unfolding of ontogeny; rather, they establish the *probability that certain traits will be constructed*. In other words, a single cause does not generally determine a phenotype but instead defines a range of *possible phenotypes* that may emerge—an epigenetic *landscape*, or repertoire, of possibilities, some more probable than others. It is within the developmental process itself that a particular phenotype is selected from among these possibilities.

In connection with the probabilistic nature of epigenetics, it is important to emphasize that SPEC quantifies the extent of the causal relationship between two variables (Keller, 2010; Tabery, 2014), but does not replace mechanistic explanation. It addresses how-much questions rather than how questions. Knowledge that one variable exhibits specificity with respect to another does not, in itself, reveal the underlying mechanistic pathway linking cause and effect. It provides a measure of the strength of the connection, but not an account of the qualitative nature of the process. It remains silent on the underlying mechanisms linking variables, instead offering a formalization of Gregory Bateson's idea (1972) of information as 'a difference that makes a difference'.

Bateson's idea of a difference maker was used by Waters (2007) to support the distinctiveness of genes in development—and thus a further argument in favor of the order-from-order

principle. Under Watson's approach, following the characterization of SPEC, Crick's sequence hypothesis states that specificity is exclusively reduced to DNA. So if we know the sequence, we get all the information (entropy is reduced to 0) about the phenotype to be produced—we might 'compute the embryo', as Wolpert (1994) conjectures (see also Rosenberg (1997)). Definitely, genes, or specifically some coding sequences of DNA, can be understood as causal specifiers that provide information about development insofar as interventions on the genes can cause modifications to their effects (as different analyses might show, such as quantitative genetics searching for SNPs, or interventionist analysis in gene knockout experiments). However, Griffiths et al.'s definition of specificity allows them to show up "additional specificity of a kind not captured by the original 'sequence hypothesis'" (Griffiths, 2016, 83). This is tantamount to showing that there are non-genetic causal specifiers of phenotypic outcomes, and part of their work is to show several cases in which specificity is found beyond DNA. Griffiths et al.'s proposal is, therefore, a direct (and explicit) response to Waters' claim (Griffiths and Stotz, 2013, chapter 7): difference makers extend beyond genes; the distinction between information on the one hand, and matter and energy on the other does not correspond to the distinction between genetics and epigenetics. The net conclusion is the *Distributed Specificity Thesis*: specificity is distributed beyond the gene to different factors across different levels of organization.[3]

2.3 Beyond Distributed Specificity

Griffiths et al.'s account of information is apt to avoid many of Oyama's worries. First and foremost, distributed specificity ascribes no special role to genes in development among other causes of development. Moreover, the explanatory logic behind the separation of nature and nurture seems problematic if the information is distributed throughout the developmental system and present at different stages of development. A catalog of traits based on the separation of nature and nurture finds no empirical or theoretical support within the thesis of distributed specificity: environmentally induced traits need not be learned traits, robust traits may depend on relevant environmental information, inherited

[3] Within Developmental Systems Theory, the original formulation of the Parity Thesis (Griffiths and Gray, 1994) states that many developmental variables beyond genes are also explanatory relevant for development. In this sense, the Distributed Specificity Thesis can be seen as a form of the Parity Thesis. However, the original formulation of the Parity Thesis has been challenged because it does not provide a way to identify developmental causes or distinguish the contribution of each variable to the developmental process. In this regard, the Distributed Specificity Thesis represents a more advanced and refined version of the original Parity Thesis.

traits may not be strongly genetically specified, culturally specific traits may be genetically robust, to name but a few examples (Keller, 2010; Bateson and Gluckman, 2011).

Yet, can distributed specificity be regarded as conceptually equivalent to Oyama's ontogeny of information? In my opinion, such correspondence remains incomplete. Bridging the conceptual distance between the two requires further theoretical elaboration. I propose that two critical explanatory aims remain insufficiently addressed within Griffiths et al.'s framework:

1. *The analysis of interacting variables:* The analysis of interacting variables within developmental systems remains an underexplored dimension of SPEC's account of information. Importantly, the analysis of causal interplay need not conflict with the foundational tenets of SPEC. Nevertheless, as I shall argue, Oyama's dictum calls for a more thorough examination of how information emerges through the interplay of multiple developmental variables. The reasons are twofold. First, from a philosophical perspective, Oyama's central argument is that, to understand the origins of developmental order, we must examine the interplay between variables—an aspect that is not made explicit in the distributed specificity thesis. Second, from a modelling point of view, in the absence of a detailed analysis of interactions, significant sources of developmental specificity may remain obscured. Several illustrative cases will be examined in Section 4; however, a preliminary example may help clarify the point. Consider two variables, x_1 and x_2, each analyzed concerning a phenotypic outcome Y, and, when they are manipulated in isolation, no strong correlation with Y is observed, thus neither variable appears to exhibit a fine-grained or specific relationship with the phenotype, and neither is attributed developmental specificity. However, when x_1 and x_2 are *jointly manipulated*, the interaction may prove highly informative regarding the developmental trajectory of Y. In short, the analysis of causal interaction has the potential to reveal forms of specificity that remain undetectable when variables are examined in isolation. (Although Pocheville et al. (2017) address interactions, their focus lies primarily on issues such as proportionality and stability, rather than on the generative role of interaction in developmental processes.)

2. *The limits of (extended) replicators:* Oyama's critique of informational preformationism targeted the assumption that the specification of developmental outcomes is independent of developmental processes. Her principal interlocutor was not Crick and his central dogma *per se*, but rather Dawkins' replicator model of evolution (and

its footprint in the construction of the MS, from Wiesmann to Fisher). The key issue is that distributed specificity—despite its shift away from gene-centric views—can still be interpreted through a preformationalist lens. Replication is not necessarily confined to genes (for extended replicator views, see Dawkins (1982), Sterelny et al. (1996), and Shea (2007, 2013)). The common strategy in such accounts is to argue that inherited information is not exclusively genetic, and that distributed specificity, too, can be understood as heritable. However, this move preserves the structure of *informational preformationism*, wherein *extended replicators*—rather than genes alone—determine phenotypic outcomes. The distinction between genetic specificity and distributed specificity lies in the kinds of variables considered to be causal specifiers. Yet the deeper philosophical issue is that the ontogeny of information is not merely a matter of 'adding to the replicator' or supplementing it with additional sources of biological information. In this respect, the formalism developed by Griffiths et al. leaves the door open to extended replication models (even though they provide philosophical critiques of extended views (Griffiths, 2013; Griffiths & Stotz, 2013)). However, following Oyama, many biologists and philosophers contend that this door ought to be decisively closed.

The subsequent section advances the concept of *developmental synergistic information* as a theoretical construct designed to compensate for these unresolved dimensions.

3. Synergies: the cause that makes the difference

The term synergy derives from the Attic Greek *synergia*, meaning 'working together'; according to Haken, who introduced the concept in 1969, synergy is "the science of cooperation" (Haken, 2009, 8926). Suppose my friend and I can each paint a wall in one hour. If we merely combine our efforts, we might finish in thirty minutes. However, through genuine synergistic cooperation, we might complete the task in just twenty minutes. This captures the basic idea about 'working together': the joint effort that surpasses the sum of each part.

In this section, I introduce the notion of synergy to analyze the information gained in the interaction between variables in development. To do so, I first introduce in Section 3.1 the approach on partial information decomposition and PI-diagrams, as probably the most acceptable representation of synergistic relationships. Section 3.2 overviews the principal measurements of synergistic information. Finally, in Section 3.3, I introduce the notion of

Developmental Synergistic Information (DSI). Biological examples are in Section 4, and the philosophical significance of DSI is analyzed in Section 5.

3.1 Interacting variables: Partial Information Decomposition

Although originating in physics, the concept of synergy has been widely adopted across disciplines—from chemistry and biology to the social sciences and humanities (see Haken (2004) for a classic textbook). Informational approaches to synergy are not novel, and various models have been proposed to capture it. However, in recent decades, significant progress has been made, and ongoing debates persist over appropriate measures, formal conditions, axioms, and principles (Griffith, 2014; Griffith and Koch, 2014; Griffith et al., 2014; Williams and Beer, 2010; Bertschinger et al., 2013; Quax et al., 2015; Chicharro and Panzeri, 2017; Chicharro et al., 2018; Vyatkin, 2019; Gomes and Figueiredo, 2023, 2024; Harder et al., 2013; Kolchinsky, 2022; James et al., 2018).

A pioneering contribution to the field was Williams and Beer's (2010) analysis of *Partial Information Decomposition* (PID), which laid the groundwork for subsequent research—even though there have been alternative frameworks (Quax et al., 2017)—and surpasses previous multivariate analysis, such as 'interaction information' (McGill, 1954) or 'co-information' (Bell, 2003). Notably, they begin their study by highlighting a goal closely aligned with mine in developmental biology: the need to analyze interacting variables to better understand informational dynamics.

> "[c]onditional mutual information considers interactions between multiple variables in only the most rudimentary sense: it seeks to eliminate the influence of other variables in order to isolate the dependency between two variables of interest. In contrast, many of the most interesting and challenging scientific questions [...] involve understanding the structure of interactions between three or more variables" (Williams and Beer, 2010, 1).

PID is introduced for the aim of understanding the 'structure of interactions' between variables by decomposing the information provided by each variable (understood as *sources*) about another variable (taken as the *target*). In a system with source $X = \{x_1, x_2, \ldots, x_n\}$ and Y as the target, information is decomposed into three categories, taken as "the basic atoms of multivariate information" (Williams and Beer, 2014, 2):

1. *Unique information (Uni)* concerns the information about Y that is only provided by each variable x_J.
2. *Redundant information (Rdn)* is the information about Y that is present in one variable x_J and is repeated in the other variable x_K.
3. S*ynergistic information (Syn)* is that information produced by the coalition of all n variables, or some subset of n.

The total (mutual) information that source X has about target Y is measured by the sum of mutual information of each atom of a PID (Gomes and Figueiredo, 2024):

$$(3)\ I(Y;X) = Rdn + Uni + Syn$$

A valuable representative tool for understanding PID and synergistic relationships is *Partial Information Diagrams* (PI-diagram, Figure 1) (lattices have also been systematically employed as modelling tools of PID (Chicharro and Panzeri, 2017)). A PI-diagram is composed of *nonnegative partial information regions* (PI-regions), and the sum of all regions in the PI-diagram is the mutual information of the coalition variables of set X, such that I(X; Y). As can be noted in Figure 1a, three kinds of coloured regions are depicted, which represent that information is unique (blue), redundant (yellow), or synergistic (red). The total mutual information in a PI-diagram with n=2 is thus defined by the sum of the mutual information of each PI-region (Griffht and Koch, 2014):

$$(4)\ Uni = \{x_1\}, \{x_2\}$$
$$(5)\ Rnd = \{x_1, x_2\}$$
$$(6)\ Syn = \{x_1 x_2\}$$

The same three properties are observed for PI-diagrams with n = 3 (Figure 1.b).

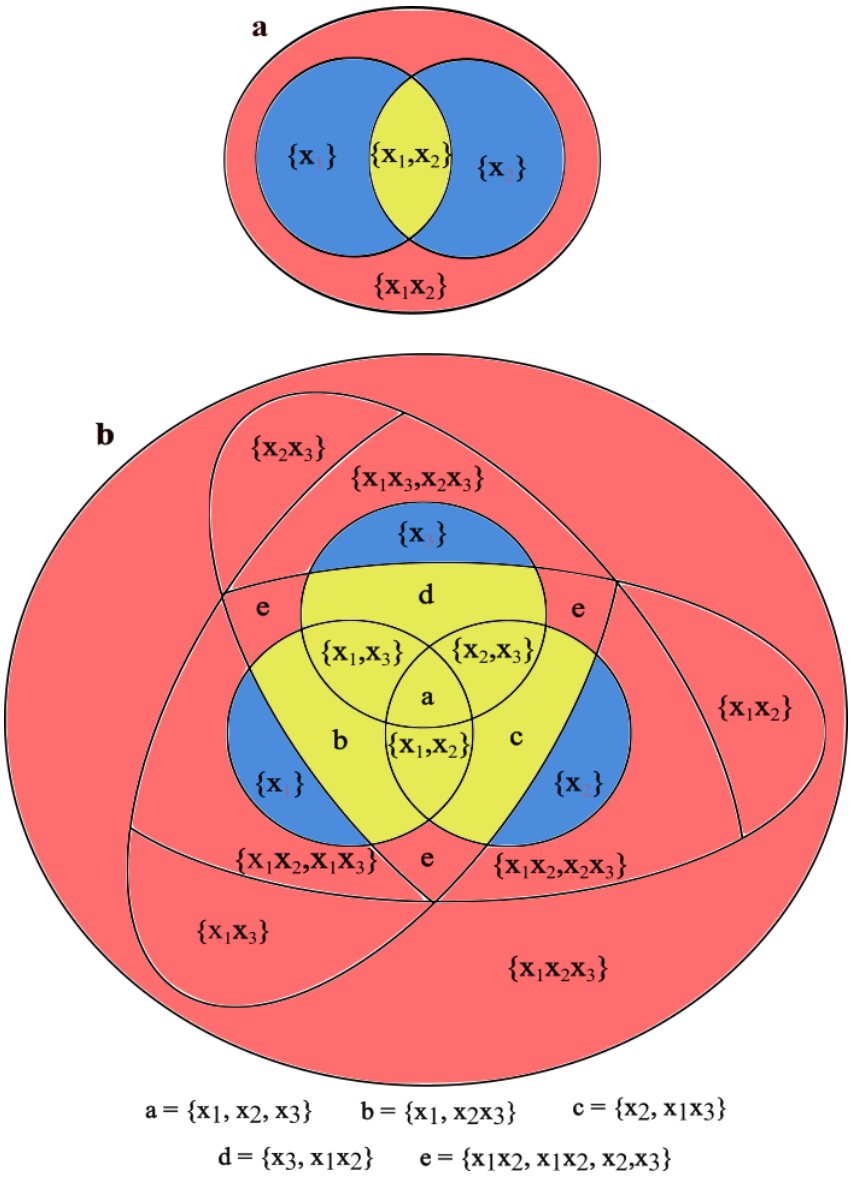
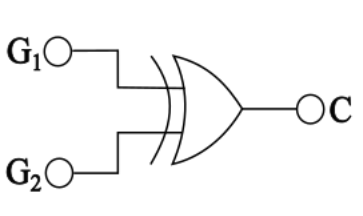


Figure 1. *PI-diagrams for n = 2 (**1.a**) and n =3 (**1.b**) Description in text.*

A classic and widely used example of synergy is the XOR (exclusive disjunction) gate. In this case, determining the output requires knowledge of both input variables simultaneously. This exemplifies the principle that 'the whole is greater than the sum of its parts': neither variable alone suffices to predict the outcome, but their joint state fully determines it. Anastassiou (2007) applies this concept to quantitative genetics, demonstrating how conditional mutual information changes when multiple variables are considered together—a challenge also identified in Griffiths et al.'s proposal (Section 2.3). In his example, two genes, G1 and G2, are analyzed for cancer (C). Each gene appears to be expressed with equal probability (50%) in both healthy and diseased individuals, seemingly indicating no correlation between G1 or G2 and the presence of cancer—no fine-grained control of these genes over C. As Anastassiou (2007, 5) notes, "these genes would never be found high up in

any typical individual 'gene ranking' computational method!" However, when second-order statistics are considered—the joint behavior of G1 and G2—a synergistic pattern might emerge: cancer develops only when one gene is expressed but not the other, exactly mirroring an XOR gate (see Figure 2). While the individual information contribution of each gene is zero, their combined state yields full information (mutual information = 1 bit).



G_1	G_2	C	
1	1	0	1/4
1	0	1	1/4
0	1	1	1/4
0	0	0	1/4

Figure 2: *Xor example in quantitative genetics. Description in text (the PI-Diagram here is an equivalent representation to the PI-diagram in Figure 1.a).*

This is a very simple synergetic system. However, it is enough to introduce the core ideas around synergistic information and the usefulness of PI diagrams. More details will be added as we proceed. Let's now see how synergistic information was measured.

3.2 Measurements of Synergistic Information

Measurements of synergistic information aim to formalize "synergy as a special case of irreducibility—specifically, synergy is irreducibility to atomic elements" (Griffith, 2014, 5). How, then, is synergistic information modeled? As Quax et al. (2017) suggest, there are two general approaches. The first is heuristic, offering an intuitive definition while forgoing formal rigor, detailed properties, or complex cases. The second, theoretical approach seeks a precise definition of each element involved in multivariate information analysis.

Among heuristic approaches, one of the earliest and most intuitive definitions of synergy—proposed by Gawne and Richmond (1993) in neural dynamics—is known as WholeMinusSum (WMS). In this framework, the synergistic information of a set X over a target Y (denoted *Syn (X;Y)*) is defined by the following equation:

$$(7)\ Syn\ (Y;X)\ =\ S^{WMS}(Y;X)\ =\ I(Y;X)\ -\ \sum_{i=0}^{n} I(Y;x_i)$$

In the XOR gate case seen before, being X={G1, G2} the source and C the target, we can appreciate that

$$(8)\ S^{WMS}(C;X) \ = \ I(C;X) \ - \ (I(C,\ G_1) \ + \ I(C,G_2)) \ = \ 1 \ - \ (0 \ + \ 0) \ = 1$$

This approach offers an intuitive and accessible way to capture synergy and may suffice for the philosophical aims of this article. However, Griffith and Koch (2014) critically assess WMS and related definitions (see also Griffiths, 2014). WMS faces measurement issues and formal limitations—for instance, it may double-count atomic elements or yield negative or ambiguous values under source correlation (see Griffiths and Koch, 2010, 8–9; Griffiths, 2014, 16–17; Quax et al., 2017, 3).

The limitations of heuristic approaches like WMS or 'interaction information' (McGill, 1954), along with advances in the PID framework, have prompted the development of theoretical models of synergistic information that satisfy key formal properties (identity, non-negativity, monotonicity). Several proposals for measuring redundancy (Chicharro et al., 2018; Harder et al., 2013; Gomes & Figueiredo, 2023) and synergy (Griffith & Koch, 2014; Quax et al., 2014; Gomes & Figueiredo, 2024; Vyatkin, 2019) have emerged. Yet, the formalization of synergistic information remains contested. Griffith and Koch (2014), responding to WMS's limitations, suggest defining synergy as the *whole minus the union of its parts* (WMU), where union information concerns the amount of information provided by at least one of the sources, hence defined by (Kolchinsky, 2022):

$$(9)\ I_{\cup} = \ Uni \ + \ Rdn$$

Thus,

$$(10)\ Syn\ (Y;X) \ = \ Syn^{WMU} \ = I(Y;X) \ - \ I_{\cup}$$

How is union information measured? Griffiths and Koch (2014) acknowledge that no computable method was available, but Gomes and Figueiredo (2024) have recently provided such an analytical tool. Kolchinsky (2022) also employs set-theoretic tools to render measurements of union information more intuitive and precise. Beyond WMU, other options include the analysis of 'information loss lattices' (Chicharro & Panzeri, 2017) and 'synergistic random variables' (Quax et al., 2017). For my philosophical purposes, however, the mathematical details of this ongoing debate need not be addressed. While WMU differs from WMS, it is enough as a general introduction to distinguish between heuristic and theoretical approaches to measuring synergy. Further inquiry may gain explanatory traction

by applying specific measures of synergistic information in developmental contexts, where particular formal frameworks may serve distinct scientific objectives.

3.3 Developmental Synergistic Information: intervention on interactions

Synergistic information arises when the mutual information generated by a coalition of developmental variables exceeds that provided by the union of the individual variables. The DSI defined here aims to serve my main goal: to provide a framework for capturing the intended philosophical meaning of the "ontogeny of information"—that is, that information is produced through the interplay between variables, so that the determination of phenotypic outcomes cannot be reduced to individual developmental variables.

However, to define DSI, an additional and essential condition must be introduced: the analysis of the *specificity* of synergistic relationships—to treat synergy as a *difference-maker*. As Griffiths et al. argue, mutual information alone is inadequate for capturing causal relations in developmental biology: mutual information is symmetrical. Syn, therefore, is not intrinsically informative about causation (Kolchinsky, 2022; James et al., 2018): it shows mutual information between the interacting variables and the target variable. While Syn is grounded in mutual information, SPEC relies on information derived from interventions. In short, what we seek are robust counterfactual relationships—understood through Woodward's analysis of invariance—between specific interactions (the sources) and developmental outcomes (the effects). This would make DSI *a causal notion* in developmental biology.

Based on this analysis, to establish DSI, we must incorporate the SPEC framework into measurements of Syn. Following SPEC, we need to make interventions to search for developmental causes. Intervention on what? DSI definition requires applying an interventionist framework to *interactions themselves*. In brief, DSI entails analyzing mutual information derived from *interventions on interactions*. DSI quantifies *synergistic specificity*, understood as the effect generated by interventions on interactions that remain undetectable if interventions are applied only to the individual components of the system. The guiding question becomes: how do developmental outcomes change when the interactions themselves are modified? By adapting SPEC to interacting variables, I arrive at a verbal definition of DSI:

> *DSI: The specificity of interacting variables (source) is obtained by measuring how much mutual information interventions on interactions carry about the effect (target) variable.*

PID analysis and the modeling debate suffice to frame the concept of DSI. The first step is to define the core notion of information arising from *interactions* between variables. To this end, I adopt an intuitive notation, drawn from PI-diagrams: for a set X = {x_1, x_2,…,x_n}, INT_X denotes a metavariable such that $I(Y; INT_X)$ represents the mutual information generated by any synergistic interaction between variables in X (the source) and the target variable (Y). Equation (11) models mutual information between INT_X and Y:

$$(11)\ I(Y; INT_X) = H(Y) - H(Y|INT_X)$$

Under this formulation, to define DSI, *intervention on interaction* entails applying SPEC to INT_X:

$$(12)\ DSI(Y; \widehat{INT_X}) = H(Y) - H(Y|\widehat{INT_X})$$

$\widehat{INT_X}$ denotes any intervention applied to the interaction among variables; Equation (12) examines the entropy changes resulting from varying interaction values within X. Thus, DSI implies that intervention targets not individual components, but the metavariable INT_X.

Once $\widehat{INT_X}$ has been introduced to elucidate the idea of intervention on interaction, a more refined formal analysis should quantify DSI using WMU, yielding the following expression:

$$(13)\ DSI^{WMU}(Y; \widehat{X}) = I(Y; X) - I_u(Y; \widehat{X})$$

Equation (13) provides an approximation to a more rigorous definition of DSI. Further analysis could extend Equation (13) by adopting one of the various existing approaches to measuring union information. Equation (13) captures changes in informational states resulting from variations in union information in relation to the information of the whole system. DSI^{WMU}, in turn, identifies the information produced by specific interventions, namely, those that go beyond union information.

The definition of DSI presented here aims to capture Oyama's idea that the order produced in development arises from the interplay of developmental causes. This, in turn, requires identifying the source of mutual information (Syn) and demonstrating that the correlation

between target and source variables reflects a causal relationship (SPEC). DSI is the result of linking Syn with SPEC. The key notion that emerges is that of intervention on interaction. Importantly, it must be noted that it is not possible to intervene in an interaction without also intervening in the individual variables. This, however, does not undermine the analysis, since the point is that DSI emerges when interventions on individual variables are less informative than interventions on the joint state of the variables. Specifically, when the variables of a system are manipulated jointly, the information gained can exceed the union of the information obtained from manipulating each variable in isolation.

Returning to the case of genetic interaction in cancer development from Section 3.1, we observe that information emerges from the specific interaction between two sources (G1 and G2). This is revealed through alternative analyses of INT_X for $X = \{G_1, G_2\}$. As illustrated in Figure 3, an XOR interaction conveys specific information if interventions on the interaction alter the outcome—when, for instance, NOR, AND, or NAND gates yield different results. To define synergy in causal terms, we need to show that interventions on individual variables don't have mutual information with the downstream effect, but interventions on the interaction do; if this is the case, the interaction itself qualifies as a cause—the metavariable INT_X is causally implicated in cancer development. Figure 3 illustrates changes in outcome values (Y–Y‴) under varying interaction configurations (different gates). Intervening on individual variables in isolation does not provide information about the outcome; however, joint manipulation of the variables specifies the target variable. Since cancer consistently arises from a specific configuration of variable values—and changes under alternative configurations—the synergistic effect is expected to exhibit outcome-specificity. A particular value of INT_X exerts a fine-grained causal influence not reducible to its components. It is a case of *synergistic specificity*.

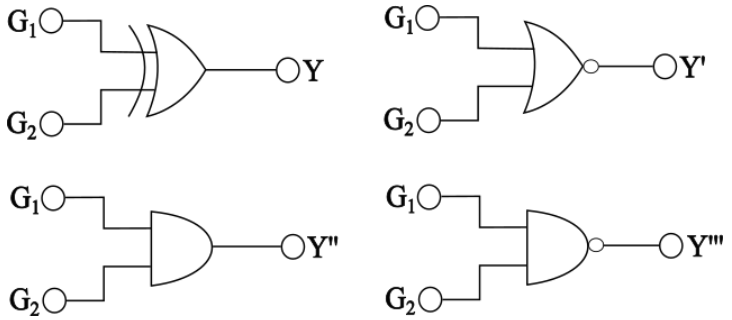


Figure 3. *Intervention on interactions: Distinct configurations of the relationship between G1 and G2 yield different outcomes: XOR → Y; NOR → Y'; AND → Y"; NAND → Y‴.*

This analysis would be enriched by emphasizing the probabilistic character of DSI. Probability lies at the very core of the definition of information: entropy measures changes in probabilistic states when two correlated variables are analyzed. Accordingly, the analysis of causation (SPEC) is inherently grounded in probabilistic reasoning, as it examines how the probabilistic states of one variable change under the intervention of another. As a consequence, DSI likewise incorporates probabilistic elements in both its verbal and formal definitions. As noted above, the key theoretical insight is that probabilities are closely tied to epigenetic landscapes. Developmental causes delineate the space of what is possible in development; in other words, not all forms and functions are attainable, as development is subject to various constraints. Moreover, developmental causes not only define what is possible but also shape the probabilities by which possible outcomes become actual. Put differently, given certain developmental conditions—such as the presence of a specific gene, epigenetic mark, or environmental influence—a phenotype Y may be more probable than phenotype Z, even if both remain within the space of possibility. The crucial point is that, among many possible outcomes, one is ultimately realized: although it is not predetermined which outcome will occur, a single phenotype emerges from a range of alternatives. As emphasized, this is because information has its own ontology. The information required for trait determination does not preexist development (although the landscapes themselves do!); rather, it is generated through the developmental process, during which probabilities dynamically shift toward the production of a particular trait within the landscape. This process is inherently probabilistic and necessitates a multicausal and interactive analysis of epigenesis; to elucidate it, DSI is proposed as a suitable framework.

4. Synergy in Development: Examples

Synergy is a concept widely employed across biological disciplines, appearing in quantitative genetics (Anastassiou, 2007), genetic regulatory networks (Chan et al., 2017), biochemistry (Ganner et al., 2012), symbiosis (Chandra and Bhatt, 2022), ecology (Palmer et al., 2010), computational biology (Balduzzi and Tononi, 2008), neuroscience (Gawne and Richmond, 1993), genetic medicine (Watkinson et al., 2008), pharmacology (Chen et al., 2015), or even the analysis of consciousness (Oizumi et al., 2014), among many others (see Sucher, 2014 for a comprehensive review). Theoretically, biological synergy is often linked to Peter Corning's *Holistic Darwinism* (2003, 2010), which highlights the explanatory potency of synergistic processes across multiple scales (see Gontier (2015), Martínez (2020), and de Llanza Varona (2022) for further exploration of synergy in philosophical debates). While my organismic perspective aligns with Corning's evolutionary emphasis on synergy, my work concentrates specifically on the role of synergy within developmental biology, without extending into

evolutionary theory. Future research may fruitfully integrate these insights with Corning's framework.

I will now present three illustrative cases of synergy in developmental biology, selected to demonstrate synergistic interactions across distinct sources: between genes (4.1), regulatory networks (4.2), and gene–environment interplay (4.3). These examples are intentionally simplified, omitting extensive empirical detail to concentrate specifically on the application of PID in each context. In each example, the coloured PID regions indicate sources of specificity, with particular attention given to *synergistic specificity*—that is, the information uniquely generated through the interaction of developmental variables. These examples, in turn, illustrate cases where developmental outcomes are altered in the absence of such synergy; specifically, they demonstrate counterfactual scenarios in which the interactions between variables are disrupted, leading to changes in the outcome variable.

Once again, it should be emphasized at the outset that this model has a primarily theoretical aim: to represent emergent (synergistic) information in developmental interactions. For this reason, and to keep the cases illustrative, both mathematical and empirical complexities are deliberately set aside. First, the analysis of these examples abstracts away from probabilities—an admittedly unrealistic assumption, even if useful for present purposes (see Rama, 2026b). Second, multiple layers of developmental causality are omitted, and only a limited set of variables is considered; more faithful biological representations would necessarily take into account a far broader range of interacting factors. Given these simplifying assumptions, the analysis may appear of limited utility to experimental and computational biologists. However, when viewed in light of its theoretical objectives, the following examples serve as clear illustrations of DSI.

4.1 Synergistic Gene Interaction: the ABC Model

Perhaps the earliest and most thoroughly systematized observations of synergy emerged in quantitative genetics, particularly in the study of genetic interactions (Pérez-Pérez et al., 2009). This tradition can be traced back to classical accounts of epistasis, where non-additive genetic interactions were first identified (Phillips, 2008; Mackay, 2014; Watkinson et al., 2008). Notably, Anastassiou's (2007) analysis represents one of the pioneering and most influential applications of the concept of synergistic information. His central aim was "to analyze genes in terms of the purely cooperative, as opposed to independent, nature of their contributions towards a phenotype" (Anastassiou, 2007, 1).

A paradigmatic case of specificity through genetic interaction is provided by the ABC model of floral development, originally proposed by Bowman et al. (1991) and Coen and Meyerowitz (1991). This model has become a canonical example in developmental biology, elucidating how specific gene combinations contribute to the formation of floral organs (see Bowman et al., 2012; Bowman & Moyroud, 2024, for updated analyses). Moreover, the phenotypic consequences of gene knockouts within the model are well-documented, offering insight into the effects of interventions. In *Arabidopsis thaliana*, the ABC model explains the sequential development of four concentric floral whorls—sepals, petals, stamens, and carpels—each corresponding to distinct genetic interactions and expressed in a defined temporal and spatial pattern (Figure 4). Three gene families govern flower development: A genes—APETALA1 and APETALA2; B genes—APETALA3 and PISTILLATA; and the C gene—AGAMOUS. The ABC model links floral phenotypes to the combinatorial action of these genes (Irish, 2017). Typically, A specifies sepals; A and B jointly specify petals; B and C specify stamens; and C specifies carpels (Figure 4.a). The phenotypic consequences of gene knockouts are well documented (see Figure 4.b-d). This schematic suffices to analyze partial information decomposition (PID) in flower (F) development:

$$(14)\ I(F;X) = Uni_a + Uni_c + Syn_{ab} + Syn_{bc},\ for\ X = \{A, B, C\}$$

$$(15)\ I(F;X) = Uni_a + Syn_{ab},\ for\ X = \{A, B\}$$

$$(16)\ I(F;X) = Uni_c + Syn_{bc},\ for\ X = \{C, B\}$$

$$(17)\ I(F;X) = Uni_a + Uni_c,\ for\ X = \{A, C\}$$

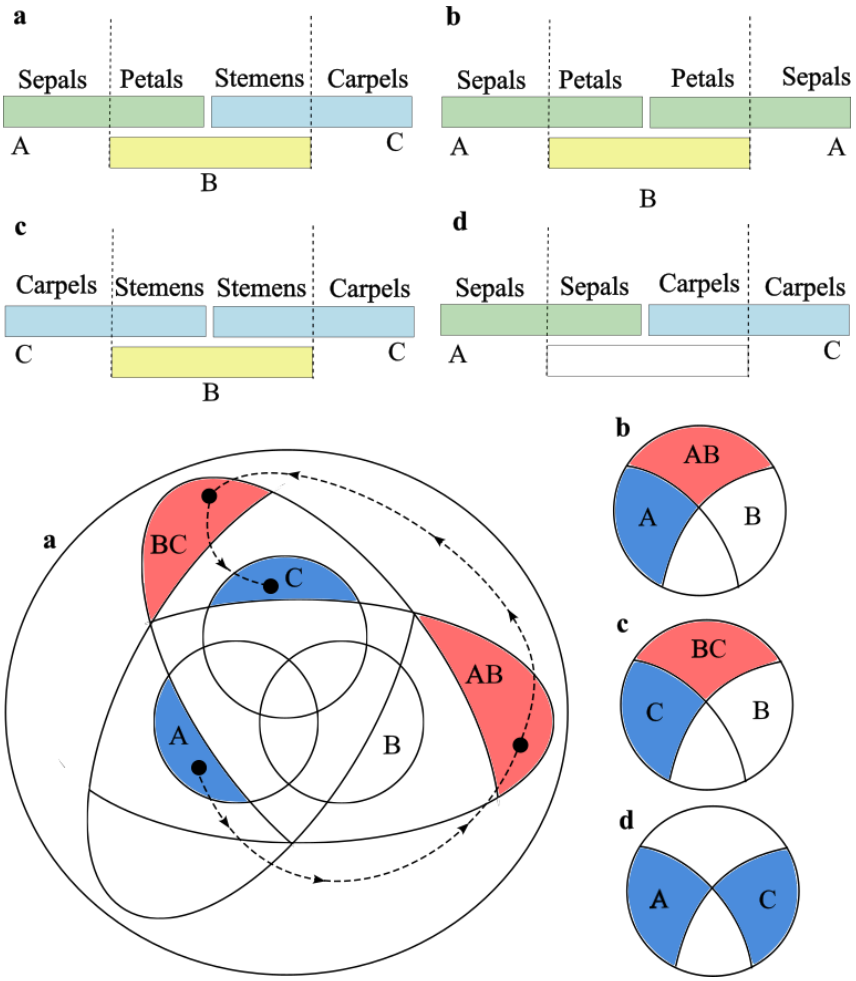


Figure 4. ABC model and PI-diagrams. ***(4a)*** *Normal development with genes A, B, and C (n = 3). The dashed line indicates temporal progression, and black dots represent floral morphological structures: A-unique region specifies sepals; the AB-synergy segment specifies petals; the BC-synergy segment specifies stamens; and the C-unique region specifies carpels.* ***(4b-d)*** *Flower development for n = 2, showing (top) phenotypic outcomes in the absence of one gene and (bottom right) PI diagrams for each case.*

4.2 Synergistic genetic regulatory networks: primary sex determination

Beyond gene interaction and regulatory complexes, we can find synergistic interactions in genetic regulatory networks (GRNs), a topic explored and advanced by Davidson (2010). Even in this context, we find one of the main works (maybe the only one) analyzing synergy in development by deploying PID (Chan et al., 2017).

A well-known case of synergy in genetic regulatory networks concerns primary sex determination (Sekido and Lovell-Badge, 2008; Gilbert and Barresi, 2016, 187-194). In the formation of the testis, we can observe different synergistic interactions in three phases, in

which the absence of some of these interactions could signify a different developmental outcome (Figure 5).

1. The *initiation phase* consists of the production of *Sfi*—a protein produced by the sex-independent regulatory gene Sfi.

2. In the *upregulation phase*, *Sfi* binds *Sry* proteins produced by Sry, one of the principal determinants of sex in mammals and Sox9 autosomal gene is expressed by the synergistic binding of *Sfi* and Sri to the enhancer Sox9 (Sekido and Lovell-Badge, 2008). In the few hours in which SRI has been expressed (Hiramatsu et al., 2009), SRI participates in Sox9 activation, and also, cooperatively with Sox9, they block β -catenin pathway (Bernard et al., 2008), which induces ovary formation.

3. In the *maintenance phase*, three actors are central: Sfi, Sox9, and Fgf9. Once SRI is turned off, feedback loops between Sfi and Sox9 enable self-maintenance of their own active state (Sekido and Lovell-Badge, 2008). Sox9 furthermore directly contributes to its own activation, and also activates Fgf9. Positive feedback loops between Sox9 and Fgf9 also contribute to the maintenance of Sox9 and Fgf9 (Kim et al., 2007). Fgf9 also represses the Wnt4 pathway involved in ovary formation (Maatouk et al. 2008). Finally, Sox9 and Fgf9 collaboratively affect Sertoli cell precursors (SCP in Figure 6) for testis formation (Kim et al., 2007).

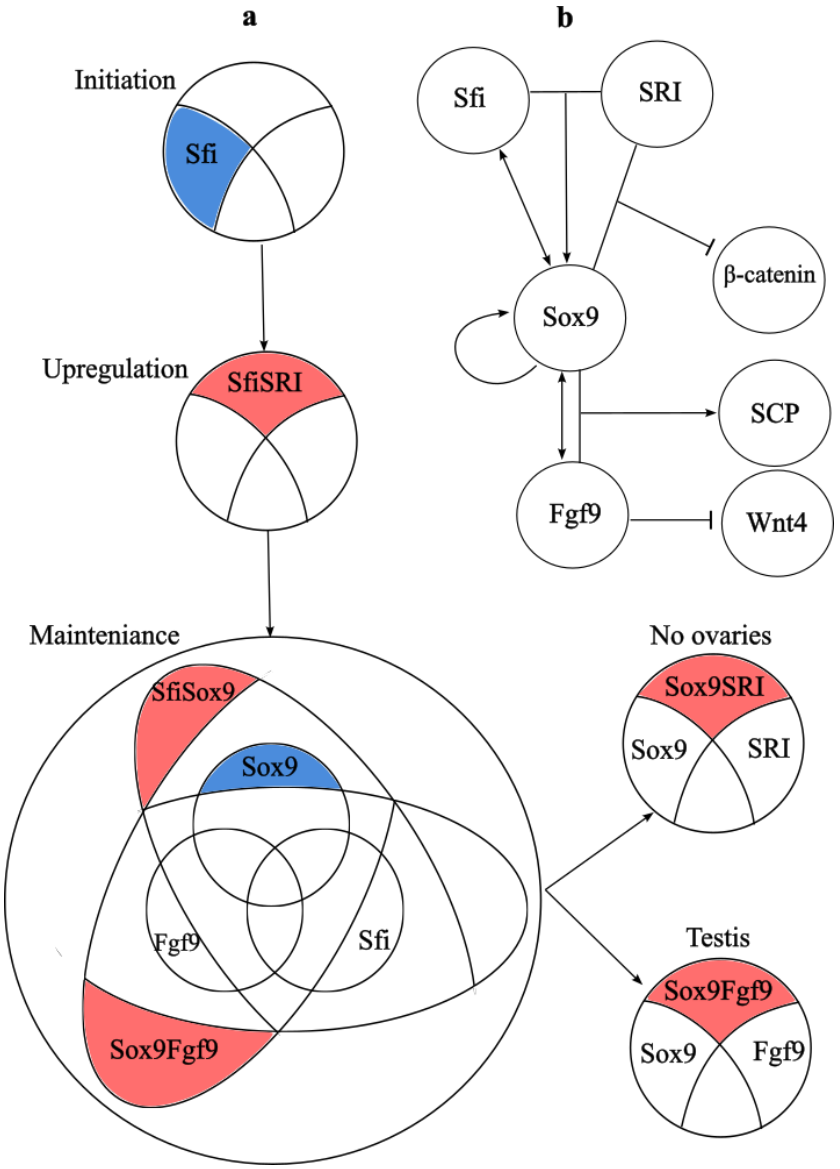


Figure 5. *Schematic representations of interactions in different stages of primary sex determination.* ***(5a)*** *PI-diagrams for each stage.* ***(5b)*** *Network of relationships. Description of the case in text.*

4.3 Synergistic GxE: metamorphic acceleration in tadpoles

A final example concerns the developmental interaction between environmental and genetic specificity—a phenomenon central to eco-devo and the study of developmental plasticity (Sultan, 2015). A paradigmatic case is the heterochrony of metamorphic changes in tadpoles, where metamorphosis is environmentally accelerated through cues that modulate genetic activity. Several environmental factors have been shown to influence this process, including predators (P), food availability (F), and water levels (W). For instance, in a well-documented case of predator-induced polyphenism, wood frog larvae reared in the presence of predatory dragonfly larvae exhibit reduced body size and altered morphology, including deeper tail

fins and more robust tail musculature (Gilbert & Barresi, 2017, 769; Buskirk & Relyea, 1998). Similarly, analysis of the pond drying environment has been shown to modify body size and limb proportions (Denver, 1997; Gomez-Mestre et al., 2013). While different morphological effects have been observed in distinct tadpoles as a response to environmental conditions, my focus here is more generally on the heterochronic changes due to environmentally induced metamorphic acceleration.

Few studies or meta-analyses have addressed the interaction between environmental variables in driving metamorphic acceleration. However, as illustrated in Figure 6, we can imagine certain scenarios in which PID can model the heterochronic effects of interacting environmental conditions. Considering three variables—food availability (F), water density (W), and presence of predators (P)—each independently induces a specific morphological change (M) and, as expressed in Equation (18), each source provides *unique* information when analyzed separately.

$$(18)\ I(M;\ X)\ =\ Uni_{f},\ Uni_{p},\ Uni_{w},\ for\ X\ =\ \{f,\ p,\ w\}$$

While a variety of morphological and physiological changes have been reported across species in response to environmental inputs, let's turn our emphasis to the heterochronic shifts resulting from environmentally induced metamorphic acceleration (A), regardless of specific morphological outcomes. For example, low F and low W may jointly accelerate metamorphosis more than either alone (Equation (19)), indicating a synergistic effect. Conversely, redundancy can occur when two variables, such as F and P, convey similar information about the timing of metamorphosis (Equation (20)). Ultimately, when all three variables are considered, the redundancy between F and P and the synergy between F and W together define the total mutual information conveyed by the environment (Equation (21)).

$$(19)\ I(A;X)\ =\ Syn_{fw},\ for\ X\ =\ \{f,\ w\}$$

$$(20)\ I(A,X)\ =\ Rdn_{f,p},\ for\ X\ =\ \{f,\ p\}$$

$$(21)\ I(A;X)\ =\ Syn_{fw}\ +\ Rdn_{f,p},\ for\ X\ =\ \{f,\ p,\ w\}$$

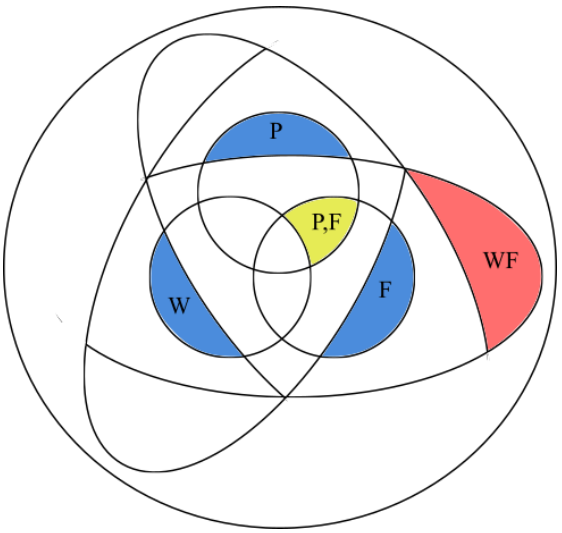


Figure 6: *PI-diagrams of environmental specificities in tadpoles' metamorphic acceleration (description in text).*

5. Discussion: The Philosophical Implications of *DSI*

The primary motivation for introducing DSI lies in its theoretical significance for developmental biology, particularly in addressing conceptual limitations left unresolved by Griffiths et al.'s account. Within this framework, four core properties of DSI emerge as especially salient and, hopefully, fruitful:

The ontogeny of information

The analysis of interacting variables reveals that phenotypic outcomes depend on information generated through interaction itself. Such information—both ontologically and epistemically—resists preformationist interpretation. DSI demands an ontogenetic perspective, aligning with Oyama's insight: developmental specificity emerges not in isolation but through entangled networks of interaction. In this respect, DSI moves beyond information preformationism: contra Monod, epigenetics does not uncover pre-existing (synergistic) information since DSI cannot be "present, but unexpressed, in the constituents." DSI is not in the constituents of a developmental process. The specificity uncovered by interventions on the metavariable INT_X is different from the specificity provided by each variable.

Alternatively, DSI is itself *created* by ontogeny, as Oyama emphasized; synergy is *in-formation* specificity. When a trait is the result of a synergistic interaction, we need to locate the specificity in the interaction between developmental variables. This is the meaning of the developmental determination of phenotypes: among the many potential phenotypes to be

constructed, the one that is actualized is defined by the interplay of causes in ontogeny, in such a way that the information needed for such actualization—reduction entropy—is not fully localizable on the system's components.

The analysis of DSI also sheds light on a classical philosophical question: when does a story begin? It is often difficult to establish the first cause (C) that produces the chain of events leading to an outcome (Z). Why not posit an even earlier cause (X) that produced C? This issue is particularly relevant in development, as Oyama extensively discusses. Indeed, it is quite difficult to determine the beginning of a developmental narrative. DNA has often been regarded as a primordial cause—that is, as the primary driver of development. However, it is well known that factors operating within the cellular context act as important causal determinants prior to the expression of DNA. For example, the first cellular divisions in *Drosophila melanogaster* occur so rapidly that DNA cannot yet be expressed; instead, these divisions are driven by maternal RNA present in the cytoplasm. What the analysis of synergy adds is the following: even if one attempts to identify the "first cause" of development, the presence of synergy prevents the attribution of a phenotype to any single originating cause. When synergy is involved, causation cannot be reduced to a linear chain producing a phenotype; the first link in a causal sequence need not be the factor that determines the phenotype. The multicausal, interactive, and probabilistic nature of development therefore resists reduction to pre-established "programs."

This analysis underscores the critical role of experimental and mathematical research focused on *intervention on interaction*. The nature–nurture debate has long centered on how interactions are conceptualized and whether they constitute meaningful difference-makers. My definition of DSI not only affirms that interactions convey developmental information but also insists on the necessity of experimental and quantitative methods to assess the effects of intervening on these interactions. Traditionally, interaction is defined as the information beyond the additive effects of isolated components (e.g., genotype and environment), a framework rooted in Fisher's (1918) population genetics. Isolation is typically tested via *interventions targeting individual factors*—such as identifying single-nucleotide polymorphisms or manipulating environmental conditions. When phenotypic variation cannot be explained by genetic or environmental differences alone, it is attributed to non-additive nature–nurture interactions. However, this indirect approach, famously critiqued by Lewontin (1974), has limitations. A more direct and methodologically demanding approach to quantifying DSI involves *intervening specifically on interactions* themselves to measure their causal impact on phenotypic outcomes.

Non-transmissible synergistic information: beyond extended replicators

A central philosophical issue in contemporary biology concerns the nature of inheritance, a topic extensively examined by Oyama (2000a, 2000b). It is now widely recognized that inheritance extends beyond genetics to multiple systems (Jablonka and Lamb, 2014; Bonduriansky and Day, 2020). The discovery of non-genetic inheritance challenges traditional views that excluded so-called soft inheritance, although some 'accretionists' (*sensu* Lewens (2019)) downplay its significance. Beyond debates about the material basis of inheritance, scholars highlight a more fundamental issue: inheritance is better understood as a process of trait (re)construction rather than mere transmission (Griesemer, 2014; Jablonka, 2007; Rama, 2024b). This entails a (long-standing) debate between transmissionist and constructivist views of heredity (Amundson, 2005). The key point is that the debate is indifferent on the material substrate of inheritance. A parallel can be drawn with the extended replicator concept (Section 2.3): broadening the modes of inheritance (towards extended replicators) does not necessarily revise our conceptualization of inheritance itself. Transmission views of inheritance hold independently of the specific material substrates involved. Historically, transmission-based inheritance has invoked different physical substrates, from Weismann's determinants to Morgan's chromosomes and DNA. Each perspective can be seen as an extension/reduction of the others (Weismann's gemmules are 'extended' from the eye of DNA inheritance); yet all assume that transmitted specificity via inheritance mechanisms underpins developmental outcomes. Crucially, such views have contributed to the blackboxing of development in evolutionary explanations.

The key insight is that, just as distributed specificity alone cannot fully account for the ontogeny of information, extended modes of inheritance do not suffice to justify a constructivist understanding of heredity. A constructivist view of heredity states that "theories of inheritance must be articulated with a theory of development", as Griesemer (2014, 184) stated.

While this issue warrants detailed analysis, a central point of the present framework is the *non-transmissible nature of DSI*. Because DSI ontologically depends on the specific ontogenetic interactions that generate it, no inheritance system can transmit the information produced through development. Oyama (2000b) offers a critical analysis of constructivist and transmissionist views. To illustrate my point: "what is transmitted between generations is not traits, or blueprints or symbolic representations of traits, but developmental *means* (or *resources*, or *interactants*)" (Oyama, 2000b, 29, emphasis in original). Interactants—DNA sequences, epigenetic marks, maternal RNA, nutrients—are transmitted, *not the interactions themselves*. Since specificity arises from interactions, DSI is inherently non-transmissible; it

must be reconstituted in each generation through ontogeny. As shown, this challenges the transmission-based model of inheritance: traits cannot be transmitted because the specificity needed to construct them is not fully encoded in transmissible elements. From the transmissionist view, inheritance is a 'donation'; as Mameli (2005, 365) puts it: "the transfer of some developmentally privileged material from parents to offspring." In such a view, as donations, developmental explanations are 'for free'—we don't need to look at development to understand inheritance. Nonetheless, when inheritance becomes entangled with development—when specificity emerges from developmental interactions—developmental explanations are no longer gratuitous; they have a cost and a benefit in the biological market.

Crucially, nonetheless, DSI represents a kind of specificity that may remain robust across populations, even if not directly inherited through any particular mechanism of transmission. A trait that scores high in heritability need not be the consequence of genetic transmission or of reliable extended modes of inheritance. High heritability might also result from persistent developmental processes operating across generations (Rama, 2025). The intergenerational stability required for evolution that concerned Schrödinger might not arise from an order-from-order principle, a code-script, but rather from developmental processes.

Causation as coaction: the organisms as a cause

The notion of the 'organism as a cause' is widely deployed within contemporary philosophy of biology and forms a central tenet of organismic perspectives such as the Extended Evolutionary Synthesis (Laland et al., 2015). Rooted in the anti-reductionist tradition of organicism (Nicholson and Rawne, 2014), this view positions organisms as fundamental *explanans* in biology (Baedke, 2018; Bateson, 2005; Huneman, 2010). Considerable debate persists over how to interpret the idea that the "organism is a cause"—whether through top-down causation, emergent causation, or part-whole relations, among others.

The mathematical framework presented here supports a significant philosophical insight into this debate. While I do not propose an alternative here (noting that the examples in Section 4 do not operate solely at the level of the 'whole organism'), the counterfactual framework of synergistic information illuminates how interactions among parts give rise to novel causes at the systemic level—i.e., how emergent causation arises through part interplay. Developmental psychobiologist Gilbert Gottlieb's notion of 'causation as coaction' closely aligns with this perspective. If developmental information is understood as causal

specificity, and this information resides in synergistic interactions, then coaction itself constitutes a source of causal specificity. *Synergy is thus causation-in-coaction*. DSI is an emergent cause in the developmental process, not reducible to the system's components. Consequently, DSI offers a formal framework to model and identify causes embedded in developmental coaction that cannot be reduced to isolated components, embodying what Griffith (2014, 5) terms "irreducibility to atomic elements"—the cause of the whole. Ultimately, this synergistic approach may underpin the view that developing organisms are agents of their own development (Sultan et al., 2022), providing causal specificity beyond that of their constituent parts.

Further inquiry necessitates engaging with the metaphysics of synergistic causation, which shifts from an object-centric to a processual account of causation (Nicholson and Dupré, 2018; for a detailed analysis, see Rama, 2026c). For example, in a regulatory network where two genes function as an XOR gate, the causal agent is not either gene alone but the interaction process itself (the very gate). If we search in the objects that interact, some causes might remain hidden. Although unnameable as an object, there is *something* in the coaction of objects; there are causes located in the very *process* of development.

Specificity in the developmental context

A final point concerns the importance of developmental context in determining the explanatory value of a variable. This idea has been repeatedly emphasized, most notably in discussions of genes' explanatory power. For instance:

> What we think of as its [DNA's] *causal powers* are in fact provided by the cellular complex in which it finds itself. It is *this complex* that is responsible for both the code that enables a sequence of nucleotides to be translated into a sequence of amino acids, for the replication of DNA, and for the intergenerational fidelity of replication (Keller, 2010, 6, emphasis added).

This quote underscores that the information attributable to any developmental variable—genetic or non-genetic—depends on the context in which it exerts its specificity. What is at stake, as emphasized by systemic and dynamic perspectives on epigenetic processes, is the need for an integrative analysis of developmental causation. The informational value of a given variable—e.g., a string of nucleotides—depends on its context of action. The same string can serve different functions, producing proteins or microRNAs that regulate transcription processes (Griffiths and Stotz, 2013). What ultimately determines

the information provided by a particular cause of development is its place in dynamic networks of highly regulated interactions, regardless of whether these interactions are synergistic.

The synergistic framework offered here emphasizes the developmental context of information in two ways. First, it shows how the effect of a process can depend on the interaction between variables. Second, it is motivated by the recognition that information exerts its causal influence within a network of entangled specifiers. While the context-dependent nature of information has long been appreciated, the proponents of PID (Section 3.1) introduced the theory as an adequate framework that surpasses classical approaches based on conditional mutual information. PID is a general approach whose promising theoretical impact resides in the interconnection between information and complexity: it aims to identify causal interactions in complex systems and to model how developmental context both constrains and enables causal specificity.

The four ideas outlined in this section are by no means novel; rather, they reflect enduring philosophical and theoretical insights within the history and ongoing discourse of biological thought. Here, however, I delineate a precise conceptual niche—DSI—motivated by gaps identified in Griffiths et al.'s framework (Section 3.2). Hopefully, this analysis aims to address those gaps and foreground synergy as a pivotal concept in developmental theory.

6. Conclusions

Information is the cause that imparts order, Oyama emphasized. It is the cause by which a fertilized cell transforms into a complex system with distinct parts performing specialized functions. Yet, she insisted that the specification of the system to be built does not precede its construction. The ontogeny of information thesis asserts that order emerges through the building process itself. While various philosophical and empirical approaches have sought to elucidate the epigenetic origins of order, this work aims to provide a formal framework defining the ontogeny of information. Building on prior contributions—particularly Griffiths et al.'s notion of distributed SPEC—DSI encapsulates the idea that interactions among variables generate developmental specificity.

Much remains to be explored regarding the ideas outlined here. Regarding Section 3, further formal development of DSI should proceed in tandem with ongoing work on synergistic information in mathematics, as well as with deeper engagement with the probabilistic nature of ontology and the dynamics of epigenetic landscapes. Section 4 offered only a

preliminary glimpse into the various levels of biological interaction where synergy may arise. As for Section 5, its philosophical implications warrant deeper elaboration and engagement with both contemporary and historical perspectives in biology. That said, let us conclude by outlining three programmatic research directions that emerge from and are closely interwoven with the preceding analysis:

a) *The tree of synergy*: Anastassiou (2007) introduced the concept of the *tree of synergy* to illustrate how synergistic interactions unfold across hierarchical levels of biological organization. In the context of trait formation, this tree maps all contributing variables, their interactions, and the resultant synergistic values. For example, two genes may exhibit synergy, while their product may not synergize with other components. Charting the tree of synergy is thus crucial for analyzing PID throughout ontogeny. The interpretation of DSI is inherently level-dependent: an informational source—such as a protein—may provide unique information, yet its generation could rely on underlying synergistic processes. Tracing these trees may illuminate the precise levels at which synergistic interactions exert developmental influence.

b) *Channel analysis of synergy*: The formalization and computability of synergy remain subjects of ongoing debate. Nonetheless, several approaches employ channel-based analyses, such as Gomes and Figueiredo's (2024) measurement of union information. This framework may offer valuable insights into heredity and development—a topic further explored in Section 5. Given the variety of formal and theoretical models of heredity grounded in inheritance channels, a channel analysis of synergy could provide a robust foundation for understanding its non-transmissible nature. Moreover, mathematical analysis of the cross-generational reconstruction of synergy from transmitted interactants is also crucial for elucidating the evolutionary dynamics of synergistic information.

c) Synergy in quantitative genetics: The question of developmental causation among interacting variables has long been contested in biological thought, suggesting that a "third class of variability" (Hogben, 1932, 98) is to be found in the interplay of variables (Lewontin, 1974; Gilbert, 1997; Keller, 2010). Population-based approaches typically rely on partitioning variance to isolate causal factors. Yet, these methods—originating with Fisher's (1918) framework—have been criticized for their limited explanatory power, especially in relation to complex traits and diseases (Zuk et al., 2012; Tam et al., 2019). Echoing earlier critiques by Hogben and Lewontin,

Tabery (2014, 36, emphasis added) reframes the issue: "how do differences in heredity and how do differences in environment interact during development to create variation separate from hereditary and environmental variation *alone*?" As synergistic interactions intensify, the causal contribution of individual variables diminishes, and the information yielded by additive partitioning declines. This raises a conceptual challenge: in attempting to isolate causes, do we risk obscuring those that are intrinsically relational? In the quantitative analysis of causal partitioning, how can one divide the indivisible? In some cases, causes may become hidden precisely because of efforts to isolate them.

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