Mechanisms and Principles: Two Approaches to Scientific Generalization

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Abstract

Many philosophers have explored the extensive use of non-universal generalizations in different sciences for inductive and explanatory purposes, analyzing properties such as how widely a generalization holds in space and time. In the present paper, we concentrate on developmental biology to distinguish and characterize two common approaches to scientific generalization—mechanism generalization and principle generalization. The former approach seeks detailed descriptions of causal relationships among specific types of biological entities that produce a characteristic phenomenon across some range of different biological entities; the latter approach abstractly describes relations or interactions that occur during ontogeny and are exemplified in a wide variety of different biological entities. These two approaches to generalization correspond to different investigative aims. Our analysis shows why each approach is sought in a research context, thereby accounting for how practices of inquiry are structured. It also diagnoses problematic assumptions in prior discussions, such as abstraction always being correlated positively with generalizations of wide scope.

Keywords: Scientific generalization; mechanisms; principles; developmental biology

1. Introduction

Confirmed empirical generalizations are central to the epistemology of science. Through most of the 20th century, philosophers focused their attention on the special case of universal, exceptionless generalizations—laws of nature—and took these as essential to both scientific theory structure and explanation (e.g., Hempel 1965, Lange 2000). However, over the past two decades, many philosophers of science, and especially those interested in biology, have sought to characterize a broader range of generalizations. For example, Waters (1998) divided biological generalizations into two categories: descriptive generalizations concerning the distribution of certain biological entities, and explanatory generalizations concerning causal regularities. Mitchell (2000) proposed a conceptual framework for characterizing and categorizing scientific generalizations in terms of three distinct properties: stability (how widely a generalization holds), strength (how probable a conditional relation is), and degree of abstraction (how many details are ignored). Mitchell argued that scientific generalizations in different areas exhibit these properties to different extents and thereby rejected the traditional dichotomy between universal laws and accidental generalizations. More recently, Green (2015) provided a taxonomy of biological generalizations that consists of two broad categories: generalizations concerning material homogeneity or causal regularities, and generalizations derived from constraints imposed on possible behaviors of systems. These (and other) analyses have yielded a diverse toolkit that facilitates more illuminating comparisons and a better understanding of generalizations in different areas of scientific inquiry.

Here we concentrate on a particular area of science—developmental biology—to comprehend two different forms of (or approaches to) scientific generalization: *mechanisms* and *principles*. Mechanism generalizations in developmental biology are narrative and pictorial representations of constituents (such as biomolecules, cells, or tissues) organized into causal relationships that operate in specific times and places during ontogeny to produce a characteristic phenomenon, which are claimed to be shared across some range of different biological entities (e.g., taxa, component systems, or temporal stages). Principle generalizations in developmental biology are abstract and typically symbolic representations of relations or interactions that occur during ontogeny and are claimed to be exemplified in a wide variety of different biological entities.

Our discussion of mechanisms and principles is motivated not solely by philosophical attempts to characterize scientific generalizations. Developmental biologists themselves sometimes seek to contrast the details of mechanisms and abstract nature of principles. "The details of embryonic development have turned out to be complicated, particularly at the molecular level, and this has encouraged researchers to integrate results and formulate abstract principles … principles stand above the level of the specific details of any particular developmental system" (Davies 2017, 1146). This has been especially poignant in situations where models based on different abstract principles can yield the same developmental pattern.[1] For some developmental biologists, the question of which molecules are actually involved is

[1] "If different models of pattern formation capturing qualitatively different biological phenomena can generate the same patterns, how can the models inform our understanding of the patterning process?" (Economou and Green 2014, 58)

required above and beyond a principle generalization: “the diffusible molecules that implement the Turing network have not yet been identified” (Raspopovic et al. 2014, 566). For others, a welter of mechanistic detail is relatively uninformative until there is a principle generalization (Pezzulo and Levin 2016). One of our goals is to delineate the implicit distinction between mechanisms and principles operating in developmental biology discourse.

We begin by discussing investigative aims in the context of developmental biology, which provides a necessary template for identifying the distinct inferential and explanatory roles that mechanism generalizations and principle generalizations play in scientific investigations. We then characterize each approach to generalization. As a result of our characterization, we can comprehend why one approach to generalization with a particular combination of properties is (or is not) sought in a research context and thereby understand why practices of inquiry are structured in a certain way. More generally, our analysis isolates key issues in prior philosophical discussions of the properties of generalizations, such as ambiguities regarding “scope” (how widely a generalization holds) and a presumption that abstraction is always correlated positively with generalizations of wide scope.

2. Generalizations in Developmental Biology

The field of developmental biology attempts to explain how the development of an organism, in particular embryogenesis, occurs through intertwined processes of cell differentiation, pattern formation, growth, and morphogenesis (Love 2022). As a consequence, developmental biologists seek to account for a wide range of phenomena, including but not limited to cell movement, the emergence of different cell types, the origin of body axes, and

organ formation. A generalization consists of a description or explanation of a feature or process of ontogeny and the range of biological systems where the description or explanation holds ("scope"). Scope can be represented in terms of four distinct but non-exclusive dimensions: across taxa, across component systems, across developmental stages, and across spatial scales.[2]

First, and perhaps most familiar, developmental biologists seek to identify generalizations that hold across different taxa, which undergirds the rationale for using a small set of model organisms in experimental practice. "The motivation for their study is not simply to understand how that particular animal develops, but to use it as an example of how all animals develop" (Slack 2006, 61). Second, developmental biologists seek to generalize across component systems of organism(s), such as organs or tissues. For example, blood vessels share patterns of organization with the nervous system because their development involves responsiveness to localized molecular cues that initiate reticulation and guide them to destinations on similar spatial scales throughout the organism (Carmeliet and Tessier-Lavigne 2005). Third, developmental biologists seek generalizations across time in development, such as whether adult blood vessels are made through the same developmental processes as those built earlier in development. This is because a generalization might not hold for all developmental stages, even for the same component system of the same species. Although the initial formation of vasculature (vasculogenesis) and adult formation of vasculature (angiogenesis) share many

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[2] Robert (2004) offers a similar classification relevant to generalizations in stem cell biology: developmental stage, system type, species, genetic and epigenetic background, and experimental setting. Waters (1998) also points out that distributions of biological properties generalize over various domains, such as taxa, cell lineage, or spatial regions of organisms of a taxon.

molecular features, the two processes are not identical, which is relevant for treating cardiovascular pathologies (Fancher et al. 2008). Fourth, developmental biologists seek generalizations that hold across spatial scales. For example, the relative role of general optimization principles can differ across spatial scales and thereby account for patterns of asymmetry in vascular networks (Tekin et al. 2016).

For these four dimensions, generalizations can be descriptive or explanatory. Descriptive generalizations involve a detailed characterization of a developmental phenomenon that is observed in a range of biological systems, while explanatory generalizations provide an account of causes that make a difference to or produce a phenomenon in a range of biological systems. In developmental biology, what distinguishes a description and explanation is whether an account includes information about causation. More specifically, we can characterize the concept of explanation in developmental biology in terms of an interventionist account of causal explanation (Woodward 2003).[3] Explaining a developmental phenomenon then consists in elucidating causes that make a difference to the phenomenon, and this requires controlled experimental interventions on the system of interest. For instance, a microscopic observation of a movement of a particular type of tissue at a specific stage of development is a description. But if causal interactions leading to such a movement (e.g., how a molecular signal changes the migratory behavior of the cells constituting the tissue) are identified through experimental

[3] We do not deny that other views of explanation are potentially applicable in developmental biology or more appropriate in other fields or contexts in science. Our claim here is only that an interventionist account of causal explanation captures explanatory practices in developmental biology and accords well with how most developmental biologists view explanation.

interventions, such as via gene knockout, gene knockin, ablation, transplantation, or other means, then the tissue movement is regarded as (at least partially) explained. *Not* all interventions produce explanations; interventions that are sometimes labeled "perturbations" are also conducted for the purpose of characterizing the nature of the phenomenon. To explain a phenomenon, developmental biologists often must conduct elaborate experiments that systematically combine various interventions with specific controls to identify a difference maker. It is also important to note that generalization is not constitutive of explanation in developmental biology. Explanatory generalizations are claims of the range of applicability of a causal explanation. Unlike what is suggested by the covering-law model of scientific explanation, according to which law-like generalization is the source of explanatoriness, we claim that explanatoriness is *not* derived from the fact that an account applies to a wide range of biological systems in the explanatory practice of developmental biology. Instead, explanatoriness is derived from an established relationship of invariance between certain causal factors and an effect (Woodward, 2001). This means that one can provide a legitimate causal explanation for a developmental phenomenon in a specific type of biological system, even when it is not known whether the explanation can be generalized to other biological systems.

Descriptive generalizations are critical for characterizing features of developing embryos and identifying what needs explanation. The claim that lungs, kidneys, and blood vessels of mammals and salivary glands, trachea, hindgut, and dorsal appendages of fruit flies are formed through budding is an across-taxa and across-component systems descriptive generalization

(Iruela-Arispe and Beitel 2013).[4] It describes a type of morphogenetic process (budding) that is manifested in different component systems (e.g., lung, kidney, or vasculature) and across different taxa (mammals and insects). In contrast, an explanatory generalization for the growth of blood vessels in vertebrates involves the causal claim that vascular endothelial growth factor (VEGF) secreted by a nearby tissue binds to its receptor (VEGFR) on a vascular cell, which causes the cell to migrate toward the source of secreted VEGF and directs a growing blood vessel. This mechanism is common across different vertebrate taxa (e.g., zebrafish, chicken, and mouse) (Ochoa-Espinosa and Affolter 2012).

Since detailed descriptions are a prerequisite for a successful explanation of any developmental phenomena, explanatory generalizations involve descriptive generalizations. Explanatory generalizations usually do not provide every detail of the relationships they represent; the above claim about vertebrate vascular growth does not include how VEGF binding to VEGFR triggers changes in a vascular cell's mobility. Many details are intentionally abstracted away or idealized for the sake of convenience or because they are held fixed in experiments that establish the causal relationship (see, e.g., Woodward 2003; Strevens 2009; Love and Nathan 2015).

Another issue related to characterizing generalizations is the *conditions* under which a descriptive or explanatory generalization holds. At least two conditions are relevant: *material* and *conceptual*. The former refers to experimental settings (e.g., *in vivo* or *in vitro*), and the latter is concerned with research contexts and the framing of inquiry, such as what research questions a

[4] Budding is a process through which a new tube structure is formed from a sheet of cells or preexisting tube.

generalization pertains to (e.g., research questions about morphogenesis vs. research questions about differentiation). Conceptual conditions are especially relevant for explanatory generalizations because they make explicit why a generalization is explanatory (i.e., because it answers a research question from one domain rather than another).

Both conditions are critical for understanding descriptive and explanatory generalizations in developmental biology. For example, a generalization in one experimental setting, such as the pattern of gene expression detected via *in situ* hybridization in arthropod segments, may not hold in a different experimental setting where patterns of protein accumulation are detected via antibody staining in the same segments (Abzhanov and Kaufman 1999). Similarly, an explanatory generalization that answers a research question in one conceptual context, such as the mechanism of anterior-posterior axis formation in animals (Kimelman and Martin 2012), often does not export to another context where different research questions are in view, such as the mechanisms of neuron formation (Reichert 2009). This might seem trivial—different questions require different answers. However, some explanatory generalizations do export from one context of research questions to another in developmental biology, such as the developmental genetic mechanisms of arthropod limb patterning (one MG) also explaining horn development in multiple species of beetles (another MG) (Moczek and Nagy 2005). It is an empirical matter that requires explicit investigation. Thus, in characterizing and analyzing generalizations in this domain, it is meaningful and useful to have this variable available. Overall, the values for different material and conceptual conditions can be independent of each other and represented differently in generalizations. Often, aspects of these dimensions and conditions are only implicit in scientific discourse.

Similar to many other sciences, developmental biologists seek both descriptive and explanatory generalizations. These are structured in four different dimensions—across taxa, across component systems, across developmental stages, and across spatial scales—and in terms of two conditions: material and conceptual. These generalizations often appear in complex combinations within scientific reasoning where different dimensions or conditions are foregrounded (e.g., distributions of developmental phenomena and causal interactions that underlie them in a specific component system at a particular stage under specified experimental conditions to answer some subset of research questions). This reconstruction of the geography of generalizations in developmental biology positions us to see a crucial distinction between two approaches to explanatory generalization.

3. Mechanisms versus Principles

Explanatory generalizations in developmental biology account for why developmental processes operate in a particular fashion and yield specific phenotypic outcomes across taxa, across component systems, across developmental stages, or across spatial scales for specified material and conceptual conditions. Two different kinds of explanatory generalizations can be distinguished: mechanism generalizations (MGs) and principle generalizations (PGs). Whereas both MGs and PGs explicate causation behind developmental phenomena and hence are explanatory, they generalize in virtue of different aspects of causal interactions. MGs generalize about specific types of biomolecules or cells that interact to produce a characteristic phenomenon in different biological systems, whereas PGs generalize about relations or interactions that can be instantiated by heterogeneous entities. For a PG, the properties of particular entities, such as a

transcription factor, a signaling molecule, or a cell type are abstracted away and only the relation or interaction among them is represented. Although a MG can and often does involve abstraction (Levy and Bechtel 2013), the specific molecule or cell types and particular interactions among them are *not* abstracted away and play the primary explanatory role. MGs depend on the identification of concrete details (e.g., specific proteins and their interactions), whereas PGs depend on abstracting away from concrete details to invoke a generic description. Thus, a key difference between mechanisms and principles is whether entities or relationships are or are not abstracted, which generates different kinds of possible generalizations.

[Insert Fig 1 near here.]

Consider a common molecular mechanism in developmental biology: bone morphogenetic protein (BMP) signaling (Fig 1). BMP signaling generally involves secreted BMPs binding to BMP receptors (BMPRs) on the cell surface, which triggers phosphorylation of Smad1/5/8 protein in the cytoplasm. The phosphorylated Smad1/5/8 forms a complex with Smad4, which in turn translocates to the nucleus and regulates expression of specific genes (Wang et al. 2014). This change in gene expression makes a difference in the formation of diverse phenotypic features and manifestation of various developmental processes. Thus, BMP signaling is a mechanism involving cell-cell interactions that functions to regulate expression of particular genes through a chain of specific molecular interactions. It is considered a MG when BMP signaling can be shown to operate across taxa, across component systems, or across developmental stages to produce particular features of development under specified conditions.

> Many processes in early development are dependent on BMP signaling for cell growth, apoptosis, and differentiation. BMPs also play important roles in maintaining adult tissue homeostasis, such as the maintenance of joint integrity, the initiation of fracture repair, and vascular remodeling (Wang et al. 2014, 88).

This quotation emphasizes the generality of BMP signaling across component systems (joints and vasculature) and developmental stages (early development and adult tissue), as well as highlighting several different conceptual conditions (e.g., research questions about growth and differentiation).

Some MGs concern cellular mechanisms, which may or may not include reference to molecular components. A good example is a MG about neural crest cell generation. Neural crest cells are highly migratory, transient cells that appear in vertebrate embryonic development. They originate from the dorsal (back) side of the embryo and migrate long distances to reach their destinations to form various types of tissues, such as skull bones, peripheral nervous system, and pigment cells. Cellular mechanisms underlying the formation of neural crest cells are evolutionarily conserved across vertebrate species. They originate through delamination from the neuroepithelium (i.e., a sheet-like embryonic tissue that will form the central nervous system). Among those cells that constitute the neuroepithelium, some reduce the strength of cell-cell adhesions, lose the polarity characteristic of epithelial cells, move away from the tissue, and start migrating. When explaining how neural crest cells are generated, developmental biologists often construct a detailed mechanistic explanation that includes both cellular and molecular components. However, they also sometimes generalize just about cellular specifics: “Cells

weaken their adhesion, lose their apical–basal polarity, and acquire polarized motility. Although these phenotypic changes are shared across species, their genetic control varies" (Szabó and Mayor, 2018, 45). This is an example of a MG concerning a cellular mechanism rather than a molecular one; it focuses on how specific types of cells (neuroepithelial cells) engage in specific types of activities (e.g., weaken cell-cell adhesion; lose apical-basal polarity; migrate away from the neuroepithelium) to generate neural crest cells in a manner that is conserved across different vertebrate species.

[Insert Fig 2 near here.]

Let us turn to PGs. A significant PG in developmental biology involves processes of reaction and diffusion that produce distinctive outcomes (Fig 2). Models of reaction-diffusion processes show how biological patterns (e.g., pigment stripes or dots) can emerge from an initially homogeneous state through the interaction of entities (typically molecules) that change in concentration and diffuse at different rates in a spatially contained area (Turing 1952). In a simple case, an activator molecule promotes the production of an inhibitor molecule and of the activator itself, whereas the inhibitor retards the activator's production (Fig 2a). If the inhibitor diffuses faster than the activator, then initially homogeneous distributions of the activator and inhibitor can change into periodic patterns based on their concentrations (Green and Sharpe 2015). This is a PG when the relevant type of reaction-diffusion process can be shown to operate across taxa, across component systems, across developmental stages, or across spatial scales to produce periodicity under specified conditions.

> [Reaction-diffusion processes] are thought to underlie many different examples of developmental patterning, including mesendodermal and left-right organization, mammalian palatal rugal ridge formation, hair follicle spacing, finger formation and nano-features of insect cornea (Davies 2017, 1148).

This passage focuses on across-taxa (e.g., mammals and insects) and across-component system (different anatomical features and tissue organization) dimensions of generalization under different conceptual conditions where the reaction-diffusion model is applicable (i.e., research questions regarding different aspects of pattern formation, such as left-right asymmetry and epithelial periodicity).

Although both MGs and PGs provide general explanations of developmental phenomena, they require distinct research strategies and are justified differently. The account of BMP signaling includes many particular details (BMPs, BMPRs, Smads, phosphorylation, etc.). These details are critical for understanding how the signaling mechanism operates (e.g., BMPs bind to BMPRs, not something else). In contrast, the reaction-diffusion model involves more abstract descriptions of its constituents ("activator" or "inhibitor") and their interactions ("promote" or "retard"). Different types of entities instantiate the same reaction-diffusion processes in different developmental contexts (Green and Sharpe 2015; Kondo and Miura 2010). The specific details do not matter as much as the overarching "principle": periodicity emerges from types of interactions among entities that only depend on their concentration and diffusion rate in a bounded region. "These principles stand above the level of the specific details of any particular

developmental system" (Davies 2017, 1146). This is in sharp contrast with MGs that hold precisely because of specific details in particular developmental systems.

This difference in the relevance of abstraction between MGs and PGs is related to the difference in what underwrites or justifies their scope, which is characterized in terms of the four dimensions. The scope of a MG is a consequence of evolutionary conservation; the same type of mechanism with particular molecular or cellular components can be common across different biological entities because it has been conserved through evolutionary history and operates in the same context of development or has been co-opted into different developmental contexts (spatially or temporally). The scope of a PG does not have the same basis. Wide applicability of a PG is based on mathematical relations that can hold in heterogeneous entities (molecular and otherwise), which express abstract relationships.

One might wonder whether the distinction between MGs and PGs maps onto the distinction between homologies and analogies (i.e., the distinction between traits shared across lineages due to evolutionary conservation and traits across diverse lineages that are similar due to evolutionary convergence). It is true that MGs are closely associated with homologies because both categories are based on evolutionary conservation. However, PGs and analogies are not so closely associated. Although analogy is defined by the specific type of evolutionary scenario that produces it (i.e., convergent evolution), PGs may or may not be correlated with patterns of evolutionary history. PGs are *indifferent* to phylogenetic relations. Additionally, a characterization of an analogy refers to similar environments or ecological niches that shape similar characters (e.g., the claim that the fusiform body shape is an adaptation to aquatic environments), but a characterization of a PG typically does not refer to such environments (e.g.,

the generalization concerning reaction-diffusion processes is not characterized as a response to similar environments, but as a consequence of activities and interactions between substances that satisfy certain criteria concerning activation, inhibition, and diffusion). PGs are frequently understood as *intrinsic* to a system. Thus, although there is a complex relationship between these two distinctions, they clearly track different features.

Richmond and Oates (2012) provide an example of how the distinction between mechanisms and principles matters to working developmental biologists. In their article "The Segmentation Clock: Inherited Trait or Universal Design Principle?," they discuss whether the segmentation clock (i.e., oscillatory expression of certain genes that produce periodic patterns of body segments) is an evolutionarily conserved mechanism or a general patterning principle. Specificity of molecules involved in the segmentation clock and evolutionary relations are the key elements in their discussion. They introduce a "three-tiered model" of segment formation, which consists of: (i) oscillatory expression of certain genes within individual cells; (ii) local synchronization of oscillators between neighboring cells; and (iii) a tissue-level signaling gradient that produces repeated segments. Richmond and Oates emphasize that "these basic organizing principles do not rely on the particular molecules involved, allowing the genetic program to differ across species" (Richmond and Oates 2012, 602). Furthermore, they point out that this three-tiered model can account for segmentation in bilaterians as well as lateral root formation in *Arabidopsis thaliana* (a plant model organism). They argue that "since the last common ancestor of plants and animals was unicellular, any similarities in body segmentation that span this divide cannot be owing to common ancestry and may therefore reflect the existence of general patterning principles" (600). Thus, developmental biologists themselves are

sometimes concerned with whether a general developmental process is a conserved mechanism or widely applicable principle, where they refer to specificity and evolutionary conservation as crucial elements for distinguishing the two forms of generalizations.

4. Consequences for the Structure of Inquiry

An important result of our analysis is that we can better account for why scientific practices are structured in different ways to isolate different kinds of generalizations. An illuminating example is the coincidence between the identification of MGs and the use of model organisms. We can understand this coincidence by considering the distinction between conserved mechanisms and widely applicable principles. Recall a major motivation for studying a model organism: "to use it as an example of how all animals develop" (Slack 2006). Developmental biologists study a relatively small number of species as exemplars and extrapolate the results to related taxonomic groups (Ankeny and Leonelli 2011, 2020). This extrapolation is justified empirically by identifying conserved mechanisms (i.e., MGs) across model organisms (i.e., across taxa) where phylogenetic relationships among species have been established (Love 2018). If researchers have found that a mechanism is shared by several vertebrate model organisms, then this supports an inference that the mechanism is conserved throughout most vertebrates (i.e., a non-universal generalization). Thus, evolutionary relationships undergird the conservation that is the basis for MGs across taxa and this is discoverable in the concrete practices of model organism research.

In contrast, the applicability of PGs is not based on evolutionary conservation and instead is dependent on whether formal principles are instantiated in one or more of the four dimensions.

This illuminates why PGs are often applicable across spatial scales; in these cases, specific constituents and their interactions differ. MGs do not often generalize across spatial scales because specific types of activities of specific types of biological entities, such as biomolecules, are confined to one spatial scale. The dependence of PGs on whether formal principles are instantiated also informs why computer simulations are often pursued to identify PGs. Abstract logical and mathematical properties can be modeled *in silico*. Therefore, recognizing the distinct bases for MGs and PGs illuminates why developmental biologists use particular strategies of inquiry, such as model organisms to elucidate MGs and computer simulations to identify PGs (Economou and Green 2014).

A related issue is the distinctive kinds of advantages and difficulties that are involved in confirming MGs and PGs. A PG involves very few entities and a limited set of interactions, all modeled with a high degree of abstraction. This makes PGs amenable to formal representation; mathematical tools (such as differential equations) are available for demonstrating with precision that a principle can account for the phenomenon of interest in appropriate circumstances. The highly abstract nature also facilitates establishing a *how-possibly* explanation (Bokulich 2014). A PG can initially be proposed in a highly speculative manner, even when there is no evidence that the principle is instantiated by any actual biological systems. Indeed, this is how the reaction-diffusion model was originally proposed. When Turing published his pioneering article in 1952, the model was just a speculative hypothesis that could *possibly* explain certain patterns of biological systems. Turing indicated mathematically, without empirical evidence, that substances which satisfy certain criteria concerning activation, inhibition, and diffusion could produce periodic patterns. Note that MGs cannot be proposed in such a highly speculative manner.

Because of both complexity and concreteness, a mechanism needs to be discovered in a specific biological system and then its conservation must be confirmed in other systems by similar experimental means.

In contrast, empirically confirming a PG is often challenging. To establish the full empirical relevance of a principle, researchers must demonstrate that the principle is actually instantiated in a biological system, which requires identifying entities and their interactions that instantiate the principle—a demanding task (see, e.g., Raspopovic et al. 2014). Furthermore, even if entities that implement the principle are identified in a system, this does not guarantee that the principle is confirmed in other systems because the principle can be instantiated by different entities across taxa, across component systems, across developmental stages, and across spatial scales. Full empirical confirmation of a PG depends on the confirmation of a number of corresponding causal relationships, some of which may be organized into mechanisms, in different biological systems.

A good example of this difficulty can be observed in studies using reaction-diffusion models to explain the formation of periodic patterns in developing systems. In research on hydra regeneration, the involvement of a reaction-diffusion process was suggested by mathematical modeling in the 1970s (Gierer and Meinhardt 1972). Subsequent studies identified WNT3 as a candidate activator in this process, but what serves as the inhibitor remains unclear even today. While several candidate factors have been suggested as an inhibitor, definitive results have not yet been obtained (Wang et al. 2023). The case of reaction-diffusion models also illustrates that mechanistic knowledge about how a principle is instantiated in a specific biological system cannot be extrapolated easily, because the pertinent physico-chemical process

can be realized by different entities and activities in different taxa and different component systems. It has been shown that reaction-diffusion processes are instantiated heterogeneously: FGF and SHH (activators) and BMP (inhibitor) in feather patterning in chickens (Jung et al. 1998); FGF (activator) and SHH (inhibitor) in palatal rugae formation in mice (Economou et al. 2012); WNT (activator) and DKK (inhibitor) in hair follicle spacing in mice (Sick et al. 2006); and Nodal (activator) and Lefty (inhibitor) in the generation of left-right asymmetry in mice (Nakamura et al. 2006). Even interactions between certain types of cells, instead of diffusible molecules, might realize the reaction-diffusion process. This has been suggested for pigment patterning in zebrafish skin, where pigment cells, such as melanophores and xanthophores, interact in a manner that is mathematically equivalent to reaction-diffusion processes based on diffusible molecules (Watanabe and Kondo 2015). Although the discovery of a mechanism that instantiates a principle in a specific system might provide some guidance to similar mechanistic inquiries in other systems, extrapolations relevant for confirming a PG can be unreliable and often fail.

Unlike a PG, a single MG—such as the involvement of BMP signaling in cell growth and differentiation across taxa—often involves many entities and their activities organized into a complex set of causal interactions. Developmental biologists are equipped with various experimental techniques to detect whether specific molecular types and their activities are present. These facilitate the empirical confirmation of the complex set of causal interactions that compose the mechanism in a studied system. Furthermore, it can be empirically established that molecular mechanisms are widely conserved through evolution, which supports extrapolation of a mechanism from one system to another. However, the initial characterization of a mechanism is

often laborious because of its complexity. Dissecting the various elements of the relevant causal pathways is experimentally demanding. And, even after a MG is established, the causal dynamics of an entire mechanism are often understood only qualitatively. Although mechanisms can be represented formally like PGs typically are, their mathematical formalization is not related to their status as generalizations because a MG depends on the specificity of the mechanism's components and activities. However, mathematical formalization can contribute significantly to quantitative predictions about a mechanism. Investigations of vertebrate somitogenesis illustrate this nicely. Blocks of cells called "somites" are formed regularly in a sequence along the anterior-posterior axis of vertebrate embryos before differentiating into a variety of organismal structures. A mechanism for this phenomenon conserved across vertebrates is called the Clock and Wavefront model, which involves a segmentation clock mechanism of oscillating gene expression combined with a FGF8 signaling wavefront that moves posteriorly. Mathematical modeling of this mechanism (e.g., Baker et al. 2008) does not increase or augment its status as a MG because the generality of a MG does not depend on abstraction; rather, it provides quantitative predictions for how this mechanism behaves in different taxa, such as the speed of somite formation or their number based on the size of the organism.[5]

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[5] At the end of section 3, we introduced Richmond and Oates' (2012) discussion of the segmentation clock. Their "three-tiered model" abstractly characterizes segment formation and hence counts as a PG, whose scope includes segmentation in vertebrates and arthropods as well as lateral root formation in plants. This is a distinct generalization from the MG mentioned in this paragraph, which focuses on specific molecular components (e.g., FGF8 signaling) and applies to segment formation in vertebrates.

5. Consequences for Analyses of Scientific Generalizations

Although our analysis has focused on MGs and PGs in the context of developmental biology, it has consequences for more general discussions of scientific generalizations. First, the distinction between MGs and PGs is relevant beyond developmental biology. For example, some generalizations in physiology describe specific metabolic pathways common across a wide range of taxa. The citric acid cycle is a series of reactions through which acetyl-CoA is oxidized and releases chemical energy (Pratt and Cornely 2015). This cycle is widely conserved across taxa, although there are variations in which enzymes are involved. It is a MG because its generality depends crucially on evolutionarily conserved reactions that occur among specific substances. Other generalizations in physiology are PGs, which concern abstract relations between properties of an organism. For instance, during the life history of pelagic (i.e., living in open water) animals, metabolic rates often increase in a 1:1 proportion to body mass. This PG applies to diverse, unrelated pelagic animals across five different phyla (Glazier 2006).

In some fields, the application of our distinction between MGs and PGs might be less straightforward. Consider ecology. Consumer-resource oscillation, which is represented typically by the Lotka-Volterra equations, is a PG in ecology that can be implemented by a variety of organisms (Turchin 2001). On the other hand, some generalizations in ecology exhibit MG-like features. A meta-analytic study (Liao et al. 2008) suggests that plant invasion increases carbon and nitrogen stocks in an ecosystem across different types of ecosystems (forests, grasslands, and wetlands). This generalization describes the behavior of specific entities (carbon and nitrogen) across different situations of ecosystem composition and hence might be characterized as a MG.

However, unlike MGs in developmental biology, we do not attribute this generality to the evolutionary conservation of the ecological interaction itself. (The ecological interaction might involve evolutionarily conserved organisms, but the interaction itself does not have to be evolutionarily conserved; rather, similar ecological interactions arise in different ecosystems independently.)

Is our distinction between MGs and PGs applicable to fields outside of biology, such as the social sciences? Ylikoski (2019) argues that social scientists generalize from case studies by developing "social mechanisms," which might sound like MGs in our sense. However, social mechanisms that play this role in generalization are not detailed stories that include specific entities and their activities, but mechanism schemes consisting of more abstract representations of agents and their interactions (Ylikoski 2019). Whereas we characterize MGs in terms of specific types of entities and their activities, this notion of a social mechanism is not necessarily associated with such specificity. Ylikoski calls mechanisms with such specificity "causal scenarios" and claims that, unlike mechanism schemes, they are typically not generalized. This brief consideration suggests a potential disanalogy between generalization practices in developmental biology and social sciences, although more comparative analysis would be needed to clarify the potential applicability of our account to social sciences. More broadly, the examples from ecology and social sciences suggest questions for further inquiry: How straightforwardly and broadly do our characterizations of MGs and PGs apply to other fields? How strong is the association between types of generalization (MG/PG) and the bases of scope (evolutionary conservation/formal rules) across sciences? What additional types of approaches to

generalization are pursued in other fields of science? How are they associated with different investigative practices in different fields?

A second general consequence of our analysis is that it isolates ambiguities in discussions of scope (i.e., how widely a generalization holds). The scope of scientific generalizations has often been represented in terms of the range of application in space and time (e.g., Mitchell 2000; Smart 1963). Philosophers of biology also have discussed generalizations distributed across biological entities (e.g., Robert 2004; Waters 1998). We isolated four distinct dimensions related to the scope of generalizations for both MGs and PGs in developmental biology: across taxa, across component systems, across developmental stages, and across spatial scales. We also identified both material and conceptual conditions that calibrate MGs and PGs. Dimensions of scope and different conditions correlate with different explanatory and inferential roles that distinct types of generalizations play. In developmental biology, MGs provide explanations based on mechanisms conserved across taxa that are identified through the investigation of concrete model organisms, whereas PGs provide explanations applicable across spatial scales due to the irrelevance of specific constituents and are often modeled *in silico*. All of this implies that there is no such thing as the scope of a generalization *simpliciter*. Instead, one must delineate what kind of generalization (MG or PG), what dimension(s), and what condition(s) to ascertain the scope of a generalization.

A related consideration is that different fields investigate different domains and hence seek generalizations that hold in different sets of dimensions. For example, Linquist et al. (2016) point out that there are three major dimensions for ecological generalizations: taxonomic distance, habitat type, and spatial scale. While the dimensions of across-taxa and across-scales

are shared with developmental biology,[6] the dimension of habitat type (commonality "across a broader set of distinct regions or biotic contexts"; Linquist et al. 2016, 7) is not usually relevant to generalizations in developmental biology. Conversely, the dimension of across-component systems, which interests developmental biologists in studies of many mechanisms and principles, is not relevant to ecology because ecology studies relations between (and not within) organisms. Identifying a relevant set of dimensions is an initial step to characterize generalization practices of a given field.

A final consequence of our analysis has to do with the relationship between abstraction and generality. It might appear natural to assume that abstraction is crucial for generalizations of wide scope, but our analysis of MGs shows otherwise. Unlike PGs, the wide scope of MGs depends on particular details being conserved widely in different biological systems through evolutionary time. This does not mean that wide scope is never positively correlated with abstraction in MGs. For example, BMP falls under a larger category of proteins called the transforming growth factor β (TGF-β) superfamily, which includes other signaling proteins (Wu and Hill 2009). Consequently, the TGF-β superfamily signaling mechanism is more abstract than BMP signaling mechanism, and, in some circumstances, the former has wider scope than the latter (for specified dimensions and conditions). However, a crucial point of our analysis is that

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[6] However, note that the taxonomic distance for ecological generalizations (*sensu* Linquist et al. 2016) and across-taxa dimension for developmental biological generalizations are not identical. The former refers to the range of taxa that can instantiate or participate in a certain ecological relation or interaction, whereas the latter refers to the range of taxa whose ontogenetic development involves a certain relation or interaction.

MGs in developmental biology—unlike PGs—can have wide scope (for specified dimensions and conditions) even without such abstraction because of the evolutionary conservation of specific constituent molecules and their specific activities.

6. Conclusion

Generalizations play central roles in scientific research. In this paper, we focused on developmental biology to distinguish two approaches to explanatory generalizations: mechanisms and principles. MGs describe specific entities organized into causal relationships that operate in particular times and places during ontogeny to produce a characteristic phenomenon and are shared across different biological entities in virtue of evolutionary conservation. PGs are abstract descriptions of relations or interactions that are exemplified in a wide variety of different entities. This distinction, along with the characterization of associated dimensions and conditions for generalizations, accounts for how particular research practices are structured, clarifies ambiguities in prior discussions of scope, and demonstrates that increased abstraction does not always facilitate generalizations of wide scope. Additionally, our analysis is germane to generalizations across a broad range of scientific fields. Similar studies within and across diverse areas of science are needed to provide further insights about the nature and role of scientific generalizations.

Fig 1 caption: The bone morphogenetic protein (BMP) signaling mechanism (Wang et al, 2014, Fig. 1). In the canonical pathway (the right-hand side), binding of BMPs to BMP receptors

triggers phosphorylation of Smad1/5/8 proteins. The phosphorylated Smad 1/5/8 forms a complex with Smad 4, which translocates to the nucleus and regulates gene expression.

Fig 2 caption: The principle of reaction-diffusion (Torii, 2012, Fig. 1). (a) The simplest version of the reaction-diffusion model involves two factors, an activator (*A*) and inhibitor (*I*) that satisfy the following conditions: *A* activates its own production as well as the production of the *I*; *I* inhibits the production of *A*; and *I* diffuses at a faster rate than *A*. (b) Reaction-diffusion processes can produce different periodic patterns depending on different values for their parameters. (c) Differential equations that represent the relations and interactions between *A* and *I*.

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References

Abzhanov, A., & Kaufman, T. C. (1999). Homeotic genes and the arthropod head: Expression patterns of the *labial, proboscipedia,* and *Deformed* genes in crustaceans and insects. *Proceedings of the National Academy of Sciences*, *96*(18), 10224–10229. https://doi.org/10.1073/pnas.96.18.10224

Ankeny, R. A., & Leonelli, S. (2020). *Model organisms*. Cambridge University Press. https://doi.org/10.1017/9781108593014

Ankeny, R. A., & Leonelli, S. (2011). What's so special about model organisms? *Studies in History and Philosophy of Science Part A*, *42*(2), 313–323. https://doi.org/10.1016/j.shpsa.2010.11.039

Baker, R. E., Schnell, S., & Maini, P. K. (2008). Mathematical models for somite formation. In *Current Topics in Developmental Biology* (Vol. 81, pp. 183–203). Elsevier. https://doi.org/10.1016/S0070-2153(07)81006-4

Bokulich, A. (2014). How the tiger bush got its stripes: "How possibly" vs. "how actually" model explanations. *The Monist*, *97*(3), 321–338. https://doi.org/10.5840/monist201497321

Carmeliet, P., & Tessier-Lavigne, M. (2005). Common mechanisms of nerve and blood vessel wiring. *Nature*, *436*(7048), 193–200. https://doi.org/10.1038/nature03875

Davies, J. A. (2017). Using synthetic biology to explore principles of development. *Development*, *144*(7), 1146–1158. https://doi.org/10.1242/dev.144196

Economou, A. D., & Green, J. B. A. (2014). Modelling from the experimental developmental biologists viewpoint. *Seminars in Cell & Developmental Biology*, *35*, 58–65. https://doi.org/10.1016/j.semcdb.2014.07.006

Economou, A. D., Ohazama, A., Porntaveetus, T., Sharpe, P. T., Kondo, S., Basson, M. A., Gritli-Linde, A., Cobourne, M. T., & Green, J. B. A. (2012). Periodic stripe formation by a Turing mechanism operating at growth zones in the mammalian palate. *Nature Genetics*, *44*(3), 348–351. https://doi.org/10.1038/ng.1090

Fancher, T. T., Muto, A., Fitzgerald, T. N., Magri, D., Gortler, D., Nishibe, T., & Dardik, A. (2008). Control of blood vessel identity: From embryo to adult. *Annals of Vascular Diseases*, *1*(1), 28–34. https://doi.org/10.3400/avd.AVDrev07011

Glazier, D. S. (2006). The 3/4-power law is not universal: Evolution of isometric, ontogenetic metabolic scaling in pelagic animals. *BioScience*, *56*(4), 325. https://doi.org/10.1641/0006-3568(2006)56[325:TPLINU]2.0.CO;2

Green, J. B. A., & Sharpe, J. (2015). Positional information and reaction-diffusion: Two big ideas in developmental biology combine. *Development*, *142*(7), 1203–1211. https://doi.org/10.1242/dev.114991

Green, S. (2015). Revisiting generality in biology: Systems biology and the quest for design principles. *Biology & Philosophy*, *30*(5), 629–652. https://doi.org/10.1007/s10539-015-9496-9

Hempel, C. G. (1965). *Aspects of scientific explanation and other essays in the philosophy of science*. Free Press.

Iruela-Arispe, M. L., & Beitel, G. J. (2013). Tubulogenesis. *Development*, *140*(14), 2851–2855. https://doi.org/10.1242/dev.070680

Jung, H.-S., Francis-West, P. H., Widelitz, R. B., Jiang, T.-X., Ting-Berreth, S., Tickle, C., Wolpert, L., & Chuong, C.-M. (1998). Local inhibitory action of BMPs and their

relationships with activators in feather formation: Implications for periodic patterning. *Developmental Biology*, *196*(1), 11–23. https://doi.org/10.1006/dbio.1998.8850

Kimelman, D., & Martin, B. L. (2012). Anterior-posterior patterning in early development: Three strategies. *Wiley Interdisciplinary Reviews: Developmental Biology*, *1*(2), 253–266. https://doi.org/10.1002/wdev.25

Kondo, S., & Miura, T. (2010). Reaction-diffusion model as a framework for understanding biological pattern formation. *Science*, *329*(5999), 1616–1620. https://doi.org/10.1126/science.1179047

Lange, M. (2000). *Natural laws in scientific practice*. Oxford University Press.

Levy, A., & Bechtel, W. (2013). Abstraction and the organization of mechanisms. *Philosophy of Science*, *80*, 241–61. https://doi.org/10.1086/670300

Linquist, S., Gregory, T. R., Elliott, T. A., Saylor, B., Kremer, S. C., & Cottenie, K. (2016). Yes! There are resilient generalizations (or "laws") in ecology. *The Quarterly Review of Biology*, *91*(2), 119–131. https://doi.org/10.1086/686809

Love, A. C. (2018). Developmental mechanisms. In S. S. Glennan & P. Illari (Eds.), *The Routledge handbook of mechanisms and mechanistic philosophy* (pp. 332–347). Routledge.

Love, A. C. (2022). Developmental biology. In E. N. Zalta (Ed.), *The Stanford Encyclopedia of Philosophy* (Summer 2022). Metaphysics Research Lab, Stanford University. https://plato.stanford.edu/archives/sum2022/entries/biology-developmental/

Love, A. C., & Nathan, M. J. (2015). The idealization of causation in mechanistic explanation. *Philosophy of Science*, *82*(5), 761–774. https://doi.org/10.1086/683263

Mitchell, S. D. (2000). Dimensions of scientific law. *Philosophy of Science*, *67*(2), 242–265. https://doi.org/10.1086/392774

Moczek, A. P., & Nagy, L. M. (2005). Diverse developmental mechanisms contribute to different levels of diversity in horned beetles. *Evolution & Development*, *7*(3), 175–185. https://doi.org/10.1111/j.1525-142X.2005.05020.x

Ochoa-Espinosa, A., & Affolter, M. (2012). Branching morphogenesis: From cells to organs and back. *Cold Spring Harbor Perspectives in Biology*, *4*(10), a008243. https://doi.org/10.1101/cshperspect.a008243

Pezzulo, G., & Levin, M. (2016). Top-down models in biology: Explanation and control of complex living systems above the molecular level. *Journal of The Royal Society Interface*, *13*(124), 20160555. https://doi.org/10.1098/rsif.2016.0555

Pratt, C. W., & Cornely, K. (2014). *Essential biochemistry* (3rd ed). Wiley.

Raspopovic, J., Marcon, L., Russo, L., & Sharpe, J. (2014). Digit patterning is controlled by a Bmp-Sox9-Wnt Turing network modulated by morphogen gradients. *Science*, *345*(6196), 566–570. https://doi.org/10.1126/science.1252960

Reichert, H. (2009). Evolutionary conservation of mechanisms for neural regionalization, proliferation and interconnection in brain development. *Biology Letters*, *5*(1), 112–116. https://doi.org/10.1098/rsbl.2008.0337

Richmond, D. L., & Oates, A. C. (2012). The segmentation clock: Inherited trait or universal design principle? *Current Opinion in Genetics & Development*, *22*(6), 600–606. https://doi.org/10.1016/j.gde.2012.10.003

Robert, J. S. (2004). Model systems in stem cell biology. *BioEssays*, *26*(9), 1005–1012. https://doi.org/10.1002/bies.20100

Sick, S., Reinker, S., Timmer, J., & Schlake, T. (2006). WNT and DKK determine hair follicle spacing through a reaction-diffusion mechanism. *Science*, *314*(5804), 1447–1450. https://doi.org/10.1126/science.1130088

Slack, J. M. W. (2006). *Essential developmental biology* (2nd ed). Wiley.

Strevens, M. (2011). *Depth: An account of scientific explanation*. Harvard University Press.

Tekin, E., Hunt, D., Newberry, M. G., & Savage, V. M. (2016). Do vascular networks branch optimally or randomly across spatial scales? *PLOS Computational Biology*, *12*(11), e1005223. https://doi.org/10.1371/journal.pcbi.1005223

Torii, K. U. (2012). Two-dimensional spatial patterning in developmental systems. *Trends in Cell Biology*, *22*(8), 438–446. https://doi.org/10.1016/j.tcb.2012.06.002

Turchin, P. (2001). Does population ecology have general laws? *Oikos*, *94*(1), 17–26. https://doi.org/10.1034/j.1600-0706.2001.11310.x

Turing, A. (1952). The chemical basis of morphogenesis. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *237*(641), 37–72.

Wang, R., Bialas, A. L., Goel, T., & Collins, E.-M. S. (2023). Mechano-chemical coupling in *Hydra* regeneration and patterning. *Integrative And Comparative Biology*, *63*(6), 1422–1441. https://doi.org/10.1093/icb/icad070

Wang, R. N., Green, J., Wang, Z., Deng, Y., Qiao, M., Peabody, M., Zhang, Q., Ye, J., Yan, Z., Denduluri, S., Idowu, O., Li, M., Shen, C., Hu, A., Haydon, R. C., Kang, R., Mok, J., Lee, M. J., Luu, H. L., & Shi, L. L. (2014). Bone Morphogenetic Protein (BMP) signaling in

development and human diseases. *Genes & Diseases*, *1*(1), 87–105. https://doi.org/10.1016/j.gendis.2014.07.005

Watanabe, M., & Kondo, S. (2015). Is pigment patterning in fish skin determined by the Turing mechanism? *Trends in Genetics*, *31*(2), 88–96. https://doi.org/10.1016/j.tig.2014.11.005

Waters, C. K. (1998). Causal regularities in the biological world of contingent distributions. *Biology & Philosophy*, *13*(1), 5–36. https://doi.org/10.1023/A:1006572017907

Woodward, J. (2001). Law and explanation in biology: Invariance is the kind of stability that matters. *Philosophy of Science*, *68*(1), 1–20. https://doi.org/10.1086/392863

Woodward, J. (2003). *Making things happen: A theory of causal explanation*. Oxford University Press.

Wu, M. Y., & Hill, C. S. (2009). TGF-β superfamily signaling in embryonic development and homeostasis. *Developmental Cell*, *16*(3), 329–343. https://doi.org/10.1016/j.devcel.2009.02.012

Ylikoski, P. (2019). Mechanism-based theorizing and generalization from case studies. *Studies in History and Philosophy of Science Part A*, *78*, 14–22. https://doi.org/10.1016/j.shpsa.2018.11.009