The Causal Homology Concept

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I propose a new account of homology, according to which homology is a correspondence of developmental mechanisms due to common ancestry, formally defined as an isomorphism of causal graphs over lineages. The semiformal definition highlights the role of homology as a higher-order principle unifying evolutionary models and also provides definite meanings to concepts like constraints, evolvability, and novelty. The novel interpretation of homology suggests a broad perspective that accommodates evolutionary developmental biology and traditional population genetics as distinct but complementary approaches to understand evolution, prompting further empirical and theoretical research.

1. Introduction. Homology refers to the correspondence of organismal features across different taxa or within the same organism, as seen in the striking similarity among vertebrate limbs or the repetitive arrangement of flower petals. While the importance of such correspondences for the study of evolution has long been recognized (Ereshefsky 2012), its conceptual nature has remained elusive and created debates and skepticism among philosophers as well as biologists. Richard Owen (1843, 379) famously defined homology as "the same organ in different animals under every variety of form and function," but this definition is perplexing rather than enlightening: what warrants the sameness of "organs," if not their form or function?

The philosophical debates over homology have centered around three issues. The first concern is about the *unit* of homology. Evolutionary theory tells us that homology is an identity due to a common origin, but an identity of what? Various features, including morphological characters, activities,

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clusters of properties, or genetic networks, have been proposed as biological units of homologs, with no consensus. The second problem is *metaphysical*. As Ghiselin (1997) points out, homology-as-identity partitions the whole tree of life into equivalence classes, but the supposition of such universal classes has been criticized as a remnant of an obsolete essentialism that is incongruous with evolutionary theory. And third, there is a *pragmatic* question: why do we care about homology at all? Some neo-Darwinians such as G. C. Williams see homologs as mere "residues," that is, relics of past common ancestry not yet washed out by natural selection (Amundson 2005, 237–38). In this view homology by itself has no explanatory role, and the quest for its definition, however well defined and metaphysically sound, becomes a mere armchair exercise with no scientific value.

All these problems, however, do not arise when the concept of homology is applied to DNA sequences. Here the sameness is well defined by matching bases that can be one of the four chemical kinds, cytosine, guanine, adenine, or thymine. Moreover, the scientific importance of orthologs and paralogs is undeniable in reconstructing evolutionary history and predicting gene functions, to name a few. Things get complicated when it comes to phenotype, in particular complex phenotypes like morphological or behavioral traits that lack clear-cut "kinds" as those of nucleotides. Most phenotypes like height and weight come in degree with no objective breakpoints or "joints" to carve them into discrete equivalence classes. The difficulty in defining phenotypic homology lies in this fact, namely, that the phenotypic space seems devoid of nonarbitrary units on which an equivalence relationship, and thus homology, can be defined.

In the face of the absence of phenotypic units, this article proposes to shift the focus from measurable features to the underlying mechanisms. The basic unit of phenotypic homology, I argue, is provided by *causal graphs* that formally represent developmental or behavioral mechanisms. Homology is thus defined as graph isomorphism over lineages, which represents conservation of a causal structure over evolutionary history (sec. 2). I argue in section 3 that the semiformal treatment of homology (i) resolves the philosophical issues and skepticism regarding the homology concept; (ii) provides clear meanings to some key but elusive concepts such as constraints, evolvability, and novelty; and (iii) suggests a theoretical perspective that accommodates evolutionary developmental biology (evo-devo) and traditional population genetics as distinct but complementary research programs. The new account is compared to other existing theories of homology in section 4, in order to highlight its relative strengths, challenges, and philosophical implications. The primary goal of this article is to open up new empirical as well as theoretical research agendas, rather than to give a definitive, monistic account of homology. The last section concludes with some of the questions and tasks prompted by the current analysis.

2. Defining Homology with Graphs. The idea of characterizing homology in terms of causal structures is not new. Various biologists have suggested, albeit in different fashions, that developmental or behavioral mechanisms serve as a unit of homology (e.g., Riedl 1978; Wagner 1989, 2014; Gilbert and Bolker 2001; Müller 2003). These proposals, however, are based mainly on concrete case studies, and the lack of a unified treatment has obscured their philosophical as well as theoretical implications. The aim of this section is to formulate the idea of developmental sameness by using causal graphs, in view of exploring the conceptual nature of homology in the later sections.

A *causal graph* $\mathcal{G}$ is a pair $(\mathbf{V}, \mathbf{E})$, where $\mathbf{V}$ is a set of phenotypic or genetic variables and $\mathbf{E}$ is a set of edges representing causal relationships between these variables. Graphical structures have been used to represent developmental phenomena or pathways (Gilbert and Bard 2014). The basic assumption of such a representation is that the target phenomena, say limb bud formation, is common to a certain group of organisms, say chickens. This sameness of developmental mechanisms can be captured by the notion of graph isomorphism. A causal graph $\mathcal{G}_1 = (\mathbf{V}_1, \mathbf{E}_1)$ is *isomorphic* to another $\mathcal{G}_2 = (\mathbf{V}_2, \mathbf{E}_2)$ if their nodes are connected in the same way, that is, if there is a bijection $f : \mathbf{V}_1 \rightarrow \mathbf{V}_2$ such that $(v, w) \in \mathbf{E}_1$ if and only if $(f(v), f(w)) \in \mathbf{E}_2$. Likewise, isomorphism can be defined for subgraphs, which are just parts of causal graphs restricted to a subset $\mathbf{V}' \subset \mathbf{V}$. We write $\mathcal{G}_1 \sim \mathcal{G}_2$ if two (sub)graphs are isomorphic. It is easy to see that '$\sim$' is symmetric, reflexive, and transitive, and thus defines an equivalence class.

Note that the intrinsic nature of the variables does not matter for two causal graphs to be isomorphic. What matters is the topological feature of the networks—what causes what—and thus developmental mechanisms of different organisms can be isomorphic even if there are considerable modifications in the nature of phenotypic or genetic components.

Let $\mathcal{G}(a)$ be a causal graph representing a particular developmental mechanism of an individual organism a. Collectively, $\mathcal{G}(A)$ is a set of the relevant causal structures for a set of organisms A. We assume usual ancestor/descendant relationships over organisms. If b is an ancestor of a, the *lineage* between b and a is the set of every individual between them. Given this setup the causal homology is defined as follows.

> For two sets of organisms A, B, let $\mathcal{G}'$ be a subgraph of all $g \in \mathcal{G}(A)$ and $\mathcal{G}''$ be a subgraph of all $g \in \mathcal{G}(B)$. Then $\mathcal{G}'$ and $\mathcal{G}''$ are homologous if and only if
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> 1. $\mathcal{G}' \sim \mathcal{G}''$;
> 2. there is a set of common ancestors C of A and B;[1] and

1. Note that C may be A or B themselves. Condition 1 is redundant if a lineage includes both of the ends, but here it is retained for clarity.

3. for every d in all the lineages from C to A and C to B, $\mathcal{G}(d)$ has a subgraph $\mathcal{G}'''$ such that $\mathcal{G}''' \sim \mathcal{G}' \sim \mathcal{G}''$.

The definition explicates the idea that homology is an identity of causal structures due to common ancestry. Two (sets of) organisms share a homologous causal structure if every individual on the lineage between and including them shares the same causal graph, capturing the idea that the developmental mechanism has been conserved through the evolutionary history.

The same treatment applies to serial homology, that is, the correspondence between parts of the same organism, such as teeth, limbs, or tree leaves. We can just set $A = B$ and compare distinct subparts $\mathcal{G}'$, $\mathcal{G}''$ of the overall structure $\mathcal{G}(A)$. Serial homology asserts that there is an organism c in which the mechanism in question was duplicated, and the lineages from c to A have conserved the duplicated structures.

The above definition is illustrated in figure 1, which depicts a hypothetical genealogical tree of groups of organisms A through G. Two mutations on the developmental mechanism denoted by solid bars occurred in the lineage leading to F, in which one of the causal edges was first removed and then restored. In this example, the causal structure $\mathcal{G}(D)$ of population D is

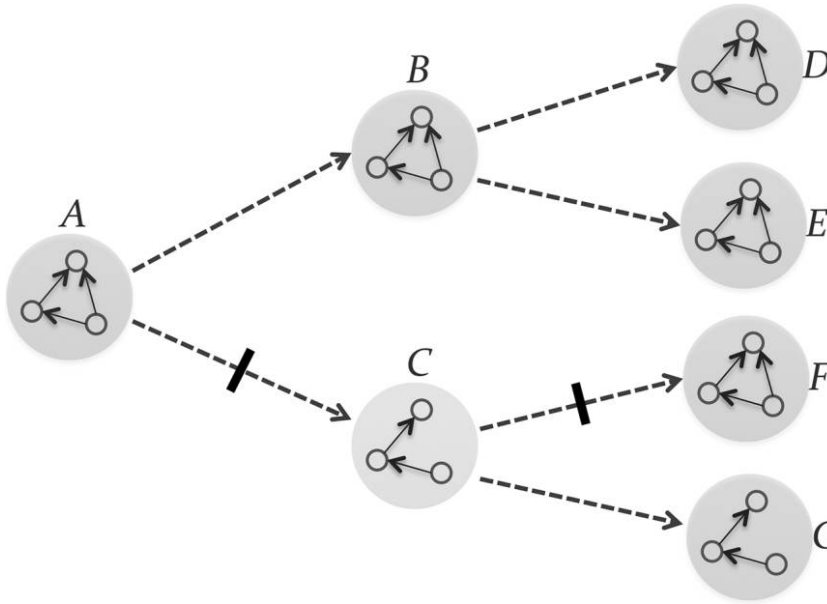

Figure 1. Causal homology. Shaded circles represent the causal structures over three developmental nodes of hypothetical populations A through G. Solid bars denote mutation events.

homologous to $\mathcal{G}(E)$, for they are both inherited from the ancestral graphs $\mathcal{G}(B)$ and $\mathcal{G}(A)$. In contrast, it is not homologous to $\mathcal{G}(F)$ even though they are graph isomorphic. This is because the lineages connecting D and F do not conserve the causal structure in question: it is not shared by C.

The example makes explicit the idea that homology is a concordance of developmental mechanisms due to common ancestry. Notice that the definition makes no reference to phenotypic outcomes that would be represented by values or distributions of the variables. It does not require that, for example, two populations E and D show similar morphological distributions. Nor does it assume that the graphs consist of variables of the same nature. If the causal graphs in figure 1 model genetic networks, the kinds of genes/variables that constitute the networks may vary across populations, as long as they serve the same causal roles within the overall structure. It is a structural, rather than material, identity that defines causal homology. This shift in the definiens brings with it various philosophical implications, as we will see in the following sections.

3. Conceptual Advantages of the View. Given the semiformal definition of casual homology, this section examines how the current approach copes with the three difficulties of homology thinking raised at the beginning, namely, the problems concerning phenotypic units, utility in scientific investigations, and the metaphysical status of homologs. I claim that the graphical approach not only solves these problems but also sheds light on the importance of homology as a conceptual bridge between macro/microevolutions and a unifying principle of biological models.

As discussed in the introduction, the major obstacle in defining homology is the absence of definite phenotypic units. Homology is an identity rather than similarity relationship (e.g., Ghiselin 1997; Müller 2003; Wagner 2014), but no two or more phenotypic characters are identical in a strict sense—there are always subtle differences in, say, shape or size. Homology thinking thus requires a natural and nonarbitrary way to factorize the phenotypic space into discrete regions within each of which phenotypes are regarded as "identical" despite their apparent differences. This is a difficult task, especially because the topological feature of the phenotypic space is largely unknown (Wagner and Stadler 2003). To circumvent this issue, the current analysis takes the generative mechanisms, rather than phenotypic features themselves, as basic units. Once these mechanisms are represented by causal graphs, which by nature are discrete mathematical entities, the desired identity relationship is given by graph isomorphism regardless of differences in developed forms or functions. The graphical representation thus provides a natural unit that is prerequisite to defining homology.

It is granted that a graphical representation may not be determined uniquely because the same developmental mechanism can be modeled in various levels

of abstraction and idealization, yielding causal graphs of different complexities. However, I take this to be a strength rather than a weakness of the current thesis because homology too is considered to be description dependent. The human forearms and the whale's pectoral fins are homologous as vertebrate limbs. They are also homologous to the tuna's fins, not as limbs but rather as a broader category of paired vertebrate appendages. One tempting hypothesis is that homology relationships of different degrees as in these examples correspond to isomorphisms of causal structures described at different granularities. In the above example, it is hypothesized that although the developmental processes underlying teleost fins and tetrapod limbs accord at some abstract level, tetrapod species share the causal structure in much finer detail.

Fixing the level of abstraction determines not only the equivalent classes but also the degree of similarity between these classes. Two distinct causal graphs may be closer or further away depending on the number of changes required to obtain one from the other. If $\mathcal{G}''$ is obtained by removing one edge from $\mathcal{G}'$, which in turn lacks one of the edges of $\mathcal{G}$, $\mathcal{G}''$ is one step further than $\mathcal{G}'$ is from the original $\mathcal{G}$. Each such deletion or addition of a causal connection is called a *novelty*. A novelty in this framework is a modification of a causal graph and as such creates a new equivalence class of causal graphs, namely, a homolog. Evolutionary novelty also comes in degrees. In general, a single modification in an abstract graph often corresponds to multiple edge additions or deletions in detailed graphs, and thus is weighted more. In this regard, changes in the causal graph shared by both teleosts and tetrapods may count as a more significant novelty than modifications affecting the tetrapod structure alone.

This brings us to one of the central contentions in today's evolutionary biology, namely, the alleged inability of the Modern Synthesis framework, and in particular population genetics, to incorporate macroscale evolutionary phenomena uncovered by evo-devo (e.g., Müller and Pigliucci 2010). It has been claimed that homology (macroscale conservatism) and novelty (a large phenotypic change) pose difficulties for the neo-Darwinian gradualism and constrain evolutionary dynamics studied by population genetics (e.g., Amundson 2005; Brigandt 2007). The theoretical relationship between evo-devo and population genetics, however, has remained elusive, which makes it difficult to evaluate the call for a "new synthesis."

The current approach, by expressing homology and novelty in terms of graph equivalence and modification, suggests a new perspective on this polemic connection and a way to turn these claims into empirical hypotheses. Because causal models induce evolutionary changes as studied in population and quantitative genetics (Otsuka 2015, 2016), the graphical representation allows one to analyze how developmental structures generate and constrain evolutionary dynamics. In particular, topological features of a graph (such as modularity) yield, via the so-called Markov condition, testable pat-

terns on phenotypic variations and determine possible evolutionary trajectories or *evolvability*. The causal graph approach thus substantiates the view that a homolog constitutes a unit of morphological evolvability (Brigandt 2007).

In population genetics, causal structures of target populations serve as background assumptions on which evolutionary models are built to track changes in genetic or phenotypic frequencies. Although these structures themselves are assumed to remain unchanged during short-term evolutionary dynamics, they must come from somewhere, and this evolutionary process is a primary interest of evo-devo. Studies on homology and novelty—graph stasis and change—amount to "higher order" evolutionary analyses that deal with changes in the theoretical framework used in population genetics to predict local population dynamics. The graphical conception of homology thus suggests a broad perspective that accommodates these different, sometimes seen as antagonistic, research fields as complementary approaches to understanding evolution.

Finally, let us turn to the metaphysical problem. As seen above, homologs are defined as equivalence classes over a set of causal graphs. But to what do such classes correspond, if not some ideal types or essences? Homology thinking has been criticized as antievolutionary because of its alleged commitment to essentialism. The only way to avoid essentialism, the critics have argued, is to define homology as a mereological whole that comprises individual organs as its parts—hence, human forearms and whales' fins are homologous not because they instantiate the same universal plan but rather because they constitute parts of a larger genealogical entity (Ghiselin 1997). This dichotomy between instantiation and mereology, however, is a false one. A metaphysical implication of the current approach is that a homolog stands to concrete organs not as a universal to particulars, or as a whole to parts, but rather as a model to phenomena to be modeled. A homology hypothesis is based on an observation that two or more developmental processes can be modeled by the same causal graph.[2] Hence, the proper relationship is not instantiation or mereology but representation (Suppes 2002). Just like an oscillator model characterizing various kinds of pendulum clocks, a homolog-as-model is a mathematical entity (directed graph) that may represent more than one individual but that does not commit us to any form of essentialism.

Ghiselin's (1997) nominalism has also cast a shadow of doubt on the epistemic role and significance of the concept of homology, leading to the view that the study of homology cannot be anything more than a historiography since there is no law for individuals. A very different picture, however,

2. This, in turn, implies that these biological systems would respond in more or less the same fashion to hypothetical interventions (Woodward 2003). Hence, homology statements eventually boil down to counterfactual claims.

emerges from the current thesis. A homology statement is a historical hypothesis regarding causal isomorphism—that two or more (sets of) organismal parts can be represented by the same causal model—and as such makes various predictions. For example, it supports extrapolations from model organisms, predicting that homologous organs will respond in the same or similar fashion to physiological, chemical, or genetic interventions. In addition, since developmental structures generate and constrain phenotypic variations (see above), homologs are expected to show similar evolutionary trajectories or responses to evolutionary forces. Establishing homology relationships, therefore, not only is of historical interest but also has predictive value in physiological and evolutionary studies.

4. Comparisons and Objections. This section compares the causal homology concept as described above with alternative accounts, with a view to examining its relative strengths and challenges. One popular account of homology among philosophers is the *homeostatic property cluster*, or HPC, theory that defines a homolog as a cluster of correlated properties underpinned by homeostatic mechanisms (e.g., Boyd 1991; Rieppel 2005; Brigandt 2009; Love 2009). Since clustering and correlations are a matter of degree, homology according to this view is a similarity rather than identity relationship. It thus faces a boundary problem—to what extent must properties be clustered to form a homolog? Some HPC theorists suggest that each property cluster be demarcated by its generative or "homeostatic" mechanism, but without a clear definition of such a mechanism the argument leads to a circularity. In particular, if it is defined as "those causal processes that determine the boundary and integrity of the kind" (Brigandt 2009, 82)—the charge of circularity cannot be avoided.

This kind of problem will not arise if the generative mechanisms are defined explicitly in terms of causal graphs. While using the graphical representation, my approach does not make any assumption or restriction on the form of a causal structure: in particular it does not require the mechanism to be homeostatic, circumventing the criticism that a homeostatic mechanism by definition cannot evolve (Kluge 2003). Moreover, the reference to clusters or even properties becomes superfluous because the variational properties of a phenotype are mere derivatives of the underlying causal graph and inessential to the definition of homology by themselves. Of course, covarying traits suggest some ontogenetic connections and thus may serve as a useful heuristic for finding homologs. They are, however, only symptoms—what defines homology are not properties, clustered or homeostatic, but generative mechanisms.

The current approach has a close affinity to the so-called *biological homology concept* that seeks the basis for morphological similarities in shared developmental pathways such as gene regulatory networks (e.g., Wagner

1989, 2014). An important empirical challenge to this idea, as well as any other attempts to identify a homolog with a certain developmental structure, is the well-known fact that morphological similarity does not necessarily entail developmental sameness. Apparently homologous characters in related species may develop from different genes, cell populations, or pathways—this phenomenon is called *developmental system drift* (True and Haag 2001).

Although further research is needed to assess the import of developmental drift on the biological homology concept, the graphical approach offers some strategies to cope with the difficulty. For example, if drift occurs in genetic or cell materials, it need not alter topological features of the causal network and does not pose a counterexample. Descriptive levels also matter, for two causal structures differing at fine-grained details may coincide at a more abstract level. Finally, my view does not require the entire developmental system to be conserved: a partial correspondence in subgraphs suffices to establish a homology relationship. Locating the commonality in this way may serve as a heuristic to identify which part of the developmental system is responsible for a morphological similarity.

One may resist the requirement of historical continuity in the definition of causal homology as too strict since it appears to preclude atavism, a reversion of an ancestral trait, from being homologous.[3] Indeed, atavism would pose a difficulty if homology is defined as a genealogical continuity of actual phenotype or mechanisms. What causal graphs encode, however, is an array of *counterfactual possibilities*, that is, relationships among variables that would be realized if certain causal conditions are met (Woodward 2003; see also n. 2). A model of digit formation is not actualized in an individual that lacks forelimbs altogether because of, say, an accidental truncation of the early limb development. The model nevertheless applies to that individual because it would still be the case that had the limbs formed normally the causal pathway as described by the model would have been actualized. In this way causal graphs can stay inactivated despite morphological discontinuity, and a study suggests the atavistic teeth formation in birds is triggered by such a dormant—but not lost—developmental pathway (Chen et al. 2000).

This brings our attention to a distinguishing philosophical feature of my account, namely, its focus on *models*. Homology has traditionally been considered to be a relationship among concrete biological entities or properties thereof: it is organs or phenotypic features that are said to be homologous. This fits with the logical positivist ideology that the ultimate reference of any theoretical concept must be the observable or, in the current case of homology, visible or directly verifiable features of organisms. In contrast, homology in my view is a relationship among (causal) models, which are by

3. I thank Yoshinari Yoshida and an anonymous reviewer for raising this point.

themselves mathematical entities and relate to actual developmental phenomena only through idealization and abstraction.

How and why does such an abstract relationship reveal anything interesting about the concrete evolutionary history? The post-positivist philosophy of science has emphasized, I think correctly, the role of "fictional" models in scientific explanations (e.g., Cartwright 1983). Causal models ignore individual peculiarities and irrelevant factors, and in this respect are unfaithful representations of reality, but such abstraction and idealization afford them generality in predicting evolutionary dynamics or consequences of hypothetical interventions. Most of these models, however, are still idiosyncratic to particular populations (e.g., population geneticists usually build or parameterize a model for each target population). Homology thinking aims at even higher generality: its core idea is that distinct species or organs allow for the same treatment/model in analyses of their evolutionary trajectory or physiological response. A homology statement is a historical hypothesis as to why such a unified explanation is possible at all. That is, it justifies the use of the same causal model across different taxa as descended from common ancestry.[4] Hence, homology from this perspective is far from "residual" but has a significant explanatory value—it allows for extrapolations of an evolutionary or physiological model to other contexts, providing the highest-level generality in biological sciences.

5. Conclusion. The concept of homology presupposes phenotypic units on which the identity relationship can be defined. This article proposed as such units causal graphs representing developmental or behavioral mechanisms and defined homology as graph isomorphism over lineage. The causal homology concept highlights the distinctive role of the study of homology while suggesting its connection to the traditional population genetics framework. That is, it not only provides definite meanings to concepts like constraints, evolvability, and novelty but also submits homology as a historical account of the generalizability of evolutionary or physiological models. This is paralleled with a shift in the ontological nature of what is said to be homologous. Homologs such as "vertebrate limbs" or "compound eyes" do not refer to fixed essences or even particular organs: they are theoretical models that represent target biological systems. Homology, therefore, is a relationship between abstract models, rather than concrete biological entities or features.

It must be granted that the current analysis is only a sketch that requires further elaboration. In particular, graph isomorphism is at the same time too

4. Analogy, in contrast, extrapolates evolutionary models across the same or similar environmental conditions. In this regard, analogy and homology represent two ways of generalizing evolutionary models.

weak and too strong. Too weak, because the definition as it stands now declares any inherited trait modeled in isolation and represented by just a single variable to be homologous to any other, for the simple reason that all singleton graphs are isomorphic. At the same time, the requirement of strict isomorphism is too strong in that it does not allow minor modifications or deletions of causal connections within homologs.

In addition to the formal refinement, the new account of homology prompts empirical as well as theoretical investigations on the concepts of novelty and evolvability, the interplay between evo-devo and population genetics, implications of developmental flexibility, and the generalizability of biological models, to name a few. Needless to say, the scope of the concept must be evaluated vis-à-vis empirical findings. A closer analysis on the formulation, implication, and application of the causal homology concept is a task for a future study.

REFERENCES

Amundson, Ron. 2005. *The Changing Role of the Embryo in Evolutionary Thought: Roots of Evo-Devo*. New York: Cambridge University Press.

Boyd, Richard. 1991. "Realism, Anti-foundationalism and the Enthusiasm for Natural Kinds." *Philosophical Studies* 61:127–48.

Brigandt, Ingo. 2007. "Typology Now: Homology and Developmental Constraints Explain Evolvability." *Biology and Philosophy* 22:709–25.

———. 2009. "Natural Kinds in Evolution and Systematics: Metaphysical and Epistemological Considerations." *Acta Biotheoretica* 57:77–97.

Cartwright, Nancy. 1983. *How the Laws of Physics Lie*. Oxford: Oxford University Press.

Chen, YiPing, Yanding Zhang, Ting-Xing Jiang, Amanda J. Barlow, Tera R. St. Amand, Yueping Hu, Shaun Heaney, Philippa Francis-West, Cheng-Ming Chuong, and Richard Maas. 2000. "Conservation of Early Odontogenic Signaling Pathways in Aves." *Proceedings of the National Academy of Sciences* 97:10044–49.

Ereshefsky, Marc. 2012. "Homology Thinking." *Biology and Philosophy* 27:381–400.

Ghiselin, Michael T. 1997. *Metaphysics and the Origin of Species*. Albany, NY: SUNY Press.

Gilbert, Scott F., and Jonathan Bard. 2014. "Formalizing Theories of Development: A Fugue on the Orderliness of Change." In *Towards a Theory of Development*, ed. Alessandro Minelli and Thomas Pradeu, 129–43. Oxford: Oxford University Press.

Gilbert, Scott F., and Jessica A. Bolker. 2001. "Homologies of Process and Modular Elements of Embryonic Construction." *Journal of Experimental Zoology* B 291:1–12.

Kluge, Arnold G. 2003. "On the Deduction of Species Relationships: A Précis." *Cladistics* 19:233–39.

Love, Alan C. 2009. "Typology Reconfigured: From the Metaphysics of Essentialism to the Epistemology of Representation." *Acta Biotheoretica* 57:51–75.

Müller, Gerd B. 2003. "Homology: The Evolution of Morphological Organization." In *Origination of Organismal Form*, ed. Gerd B. Müller and Stuart A. Newman, 51–69. Cambridge, MA: MIT Press.

Müller, Gerd B., and Massimo Pigliucci. 2010. *Evolution: The Extended Synthesis*. Cambridge, MA: MIT Press.

Otsuka, Jun. 2015. "Using Causal Models to Integrate Proximate and Ultimate Causation." *Biology and Philosophy* 30:19–37.

———. 2016. "Causal Foundations of Evolutionary Genetics." *British Journal for the Philosophy of Science* 67:247–69.

Owen, Richard. 1843. *Lectures on the Comparative Anatomy and Physiology of the Invertebrate Animals: Delivered at the Royal College of Surgeons in 1843*. London: Longman.
Riedl, Rupert. 1978. *Order in Living Organisms: A Systems Analysis of Evolution*. New York: Wiley.
Rieppel, Olivier. 2005. "Modules, Kinds, and Homology." *Journal of Experimental Zoology* B 304:18–27.
Suppes, Patrick. 2002. *Representation and Invariance of Scientific Structures*. Stanford, CA: CSLI.
True, John R., and Eric S. Haag. 2001. "Developmental System Drift and Flexibility in Evolutionary Trajectories." *Evolution and Development* 3:109–19.
Wagner, Günter P. 1989. "The Biological Homology Concept." *Annual Review of Ecology and Systematics* 20:51–69.
———. 2014. *Homology, Genes, and Evolutionary Innovation*. Princeton, NJ: Princeton University Press.
Wagner, Günter P., and Peter F. Stadler. 2003. "Quasi-Independence, Homology and the Unity of Type: A Topological Theory of Characters." *Journal of Theoretical Biology* 220:505–27.
Woodward, James. 2003. *Making Things Happen: A Theory of Causal Explanation*. New York: Oxford University Press.