Bodily Parts in the Structure-Function Dialectic

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Abstract

Understanding the organization of an organism by individuating meaningful parts and accounting for organismal properties by studying the interaction of bodily parts is a central practice in many areas of biology. While structures are obvious bodily parts and structure and function have often been seen as antagonistic principles in the study of organismal organization, my tenet is that structures and functions are on a par. I articulate a notion of function (functions as activities), according to which functions are bodily parts just as structures are. Recognizing part-whole relations among an organism's various structures and functions permits fruitful investigation and multilevel explanation of organismal properties and functioning, across both developmental and evolutionary time. I show how my perspective clarifies debates surrounding homology and evolutionary novelty that stem from an alleged structure-function dichotomy. My approach favors a pluralism about individuation, where the criteria of what counts as a meaningful bodily part depend on the particular epistemic aims pursued in a scientific context.

Keywords: structure, function, activities, part-whole relations, hierarchy, individuation, biological systems, homology, evolutionary novelty

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<A> Introduction

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This essay discusses bodily parts and their epistemological role in biological theorizing. Many contributions to this volume discuss what constitutes an individual, also addressing the relation between unicellular individuals and colonies of cells (Herron this volume) or between cells and a multicellular individual (Reynolds this volume). But cells are not he only relevant parts of individuals (Love and Brigandt this volume), and other kinds of bodily parts also persist as particular parts across developmental time and as homologues across evolutionary time, so that they have some integrity and biological identity. The various parts of an organism stand in part-whole relations, raising the theoretical issue of hierarchical organization, which can also be found in discussions of biological individuality (Nyhart and Lidgard this volume; Rieppel this volume). Moreover, epistemic issues about how to draw boundaries arise not only in the case of complicated cases of individuality (e.g., symbioses and evolutionary transitions in individuality), but also in the delineation of the parts that come to form and sustain the individual. Practice in many biological disciplines concerns the identification and individuation of bodily parts and how their relations and interactions explain complex organismal phenomena, where what qualifies as a meaningful part depends on the epistemic aims that biologists pursue in a particular context.

Throughout history, *structure and function* have been major organizing principles for the study of organisms and their organization, with implications for the individuation of bodily parts and the characterization of their nature. However, often structure and function have been seen as antagonistic (Russell 1982[1916]; Gould 2002; Amundson 2005; Love 2013a).[1] In the first half of the 19th century, the Geoffroy-Cuvier debate in France was driven by the divergent viewpoints

that structure determines function or that function determines structure (Appel 1987; Hall 1998). Structural considerations were closer to those who like Geoffroy favored an individuation of bodily parts in terms of homology; and in Great Britain Owen (2007[1849]) terminologically contrasted homology with analogy and used homologies as a phenomenon that the functionalist natural theologians of the Bridgewater Treatises could not explain. While Darwin introduced with the idea of natural selection a convincing functionalist component to biological theorizing, in the remainder of the 19th century many practitioners of the tradition of evolutionary morphology focused on homology and the phylogenetic transformation of structures regardless of functional considerations (Coleman 1971, 1967; Nyhart 1995). With the rise of the Modern Synthesis, natural selection and function became central pillars of evolutionary theorizing, leading to morphology gaining relevance again in the form of functional morphology (Wake 1982; Gans 1985). Yet the notion of developmental constraint (sometimes termed architectural constraint) introduced a structural component often seen in opposition to natural selection (Brigandt 2015b). And recent approaches such as phylogenetic systematics and evolutionary developmental biology have reinvigorated the notion of homology, and made the explanation of the evolutionary origin of novel structure —often regardless of considerations about adaptation—a focal concern.

My aim is to lay out a perspective on bodily parts that does not view structure and function as antagonistic notions. The starting point is that while there are different kinds of function (and different legitimate notions of function), many of the uses of "function" in the generation of biological knowledge can be encapsulated in the idea of a function as an activity taking place internal to an organism, so that such a function is a bodily part. After pointing out that in some cases even structures are individuated using functional considerations, I argue that

functions (as activities) are bodily parts just like structures are. While functions are usually seen as a mere attributes of structures, from my perspective structures and functions are on a par, so that function is an indispensable and fundamental ingredient of any biological ontology.[2] I detail how this perspective clarifies some current debates and in several contexts permits fruitful biological investigation beyond the structure-function dichotomy. One reason is that function in my sense is compatible with but conceptually independent of natural selection. Another reason is that a body composed of functions is at the same time composed of structures, where the structures and functions can stand in hierarchical part-whole relations among each other, enabling the multilevel explanation of organismal organization and its developmental formation and evolutionary modification. I conclude with a pluralistic approach to individuation, which assumes that different individuation schemes for bodily parts are to be used in different biological contexts, relative to the epistemic aims in operation (see also Lidgard and Nyhart this volume; Love and Brigandt this volume; Sterner 2015).

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<A> Individuating a Structure Can Take Us to Its Functional Context

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Apart from traditional accounts of biological individuality that address physiological functioning and autonomy, nowadays evolutionary approaches are prominent that focus on individuals as units that are subject to selection and figure in transgenerational evolutionary change (Godfrey-Smith 2013; Love and Brigandt this volume). Especially on the latter approach, an important characteristic of biological individuality is the ability to reproduce. A bodily part—a part of an organism—usually does not have this ability (with the exception of the cells of a multicellular individual, which retain a significant degree of individuality). Bodily parts may still be said to

form cross-generational lineages, as in cases of homology the same kind of part reappears across generations (the bodily part is replicated), though the bodily part alone does not have the causal means of replicating itself.[3] But despite their lack of full biological individuality, it is of central epistemic importance to *individuate* bodily parts, by recognizing parts and deciding on their boundaries. In taxonomic and evolutionary contexts, comparison among different species requires the use of meaningful traits, and a properly identified homologue's transformation in evolution can be tracked and explained. In many different areas of biology, from molecular biology to physiology and functional anatomy, a whole is understood in terms of its parts, often by explaining the properties or functioning of the whole in terms of the organization and interaction among its parts, an issue that in the last decade has become the subject of extensive philosophical investigation under the label of "mechanistic explanation" (Bechtel and Richardson 1993; Bechtel and Abrahamsen 2005). Generating such biological understandings presupposes that a whole is first decomposed into meaningful parts (Craver 2007; Winther 2011). Rasmus Winther (2006) distinguished between compositional biology (which offers part-whole explanations) and formal biology (which explains using mathematical models) as distinct styles of biological reasoning. But even in contexts where formal-mathematical models are prevalent, finding the right units matters (as Winther also recognizes in his 2011 piece). Systems biologists, for instance, have to break down an overall system's complex functioning into components, and they have to decide which among the plethora of cellular entities and molecular pathways to include in their mathematical models (Brigandt 2013b).

Bodily parts can be individuated by different kinds of criteria, which can be used in combination. A part can be delineated by spatial boundaries, and in the case of developmental traits, temporal boundaries such as a particular developmental stage often bears on the trait's

identity (see also Nyhart and Lidgard this volume). Alternatively, the part's internal structure or internal interactions can be deemed to be more relevant than its boundaries. Molecular systems as studied by systems biologists have blurry boundaries at best (something similar holds for developmental processes), and entities are considered to be parts of a system not because they are within some visible spatial boundaries, but because they have such properties or engage in such interactions that these entities contribute to the system property of interest. In fact, many of the molecular entities within a cellular region do not contribute to the system function under consideration and for this reason are not considered parts of the system studied. Sometimes a bodily part is individuated as being an entity of a certain *type*, i.e., belonging to the same kind as other such entities. For instance, a gene is not spatially disjoint but part of a continuous DNA molecule. A particular gene such as *fushi tarazu* may indeed be spatially delineated by a start and a stop codon (where the start codon is preceded by a promoter), but what makes such structural features significant is that they make *fushi tarazu* a gene, and are features shared by any other gene. Something similar applies to homologues as bodily parts, as in this context a spatial part of one particular individual is a meaningful biological part only if it is of the same type as parts of other organisms.

Biologists generally emphasize that organismal parts cannot be studied in isolation, as they interact with other parts in an organized fashion. Moreover, one part is often transformed by the impact of others.[4] But in addition to being *causally* affected by its context, I want to take this issue further as there are cases where the ontological *identity* conditions of a bodily part include biological factors outside of this part. Consider a stem cell, which has two basic characteristics. It can divide and self-renew for an extended period of time (by dividing such that at least one of the two daughter cells is a stem cell), and it can give rise to various differentiated cell types. When

the latter happens and what type of differentiated cell is produced is influenced by the stem cell's niche, i.e., its molecular and cellular microenvironment, which includes other cells, their surface structures, factors secreted by them, and the extracellular matrix. A stem cell maintaining its capacity to self-renew (and thus remaining a stem cell) is likewise influenced by its microenvironment (Li and Xie 2005; Moore and Lemischka 2006; Morrison and Spradling 2008). If so, a cell being a stem cell is partially determined by factors external to this cell. Even a gene as a specific DNA segment is a gene in virtue of its larger context. It is well-known that due to such processes as alternative splicing, the particular product resulting from a gene strongly depends on the cellular context (Griffiths and Stotz 2013), but this carries over to some DNA segment qualifying as a gene at all. Being a gene is to be able produce a molecular product—a protein or at least an RNA—and a DNA segment may lose this ability in a different regulatory context or when it is part of a different genome that renders the DNA segment non-functional because of modified enhancers or changes to other genes that used to regulate it. A gene is not a cellular *process* (that would include many non-DNA entities and their activities), it just is a particular DNA segment as a *structure*. But its identity as a gene is still constituted by conditions and entities outside of this DNA segment. The relevance of such an ontological situation is that even when the focus is on a structural part alone, it is *epistemically* necessary to take the relevant outside factors into account.

Thus, ontological identity conditions can take us beyond a bodily part. Moreover, this context to be epistemically taken into account often includes *functional* aspects; some biological entities are defined in terms of having certain causal and functional capacities, which are context-dependent (Brigandt 2009, 2011b). The above example of individuating genes foreshadowed this. Consider pseudogenes, DNA sequences similar to genes, but no longer

coding for proteins or other material products or processes in a cell. A pseudogene may have many structural hallmarks of a gene, but it is not a gene precisely because it is non-functional. A structure is a gene by virtue of a function—the ability to produce a molecular product. Whether a DNA segment is involved in the formation of gene products and what the products are depends on various transcriptional and post-transcriptional processes, all of which implicate molecular and cellular functions (Griffiths and Stotz 2013). From the perspective of functional genomics, Finta and Zaphiropoulos (2001) suggest that genes are "statistical peaks within a genome-wide pattern of expression of the genetic information" (160). On this approach, the extent to which a genomic region (a segment of DNA) qualifies as a gene depends on how the degree of its activity *compares to the activity* of other genes, so that a larger functional context matters, in fact, genome-wide expression due to a cell's activities.

Another example is homologues as seen from the perspective of evolutionary developmental biologists, who are interested in the developmental basis of homology (Brigandt 2003). A homologue has a certain type of individuality as a morphological unit of evolutionary transformation, given that it is able to change across generations while still being the same character. The homologue is also quasi-autonomous from other homologues (Laubichler 2000) in the sense that across generations it can vary relatively independently from the organism's other bodily parts, making it a part that is meaningfully individuated from an evolutionary perspective (Wagner and Stadler 2003; Brigandt 2007; Wagner 2014). These variational abilities—in particular how one homologue can be modified independently of others—are due to the complex mechanisms that underlie the development of these homologues, which are addressed by evo-devo in line with its agenda of accounting for the developmental basis of morphological evolvability (homology is explicitly tied to evolvability in Brigandt 2007).[5] Thus, even if the

focus is on an anatomical structure, this structure is a bodily part in the sense of being a homologue (capable of undergoing morphological change) in virtue of *function* features, to wit, the causal, functional, and dynamical aspects of an organism's development, which can generate morphological variation across generations. Contrary to the temptation to assume that a structure is defined by structural-spatial features alone, an organism's structural organization into different homologues and their boundaries are ontologically constituted by the organism's functional-developmental dynamics, which bolsters epistemic agendas that pay attention to organismal context and developmental processes.

While homology pertains to a bodily part's identity across evolutionary time, an issue germane to a part's development and its identity across developmental time is robustness. Robustness is the ability of an organismal system to produce or maintain a certain trait despite modifications internal and external to the system (Kitano 2004; Masel and Siegal 2009). Often robustness is an evolved ability where the organismal system actively responds to disturbances, so as during embryonic development to permit the reliable generation of the adult phenotype in the face of perturbations to development, and subsequently to maintain functioning and an adaptive phenotype in a changing environment. There is also robustness to genetic modifications. While this is most commonly known from experimental knockout studies, where the deactivation of a gene implicated in a molecular pathway surprisingly does not yield a changed phenotype, robustness to genetic change is also of evolutionary significance (discussed in Brigandt 2015a). Traits on various levels of organization can exhibit robustness, from the structure of RNAs and proteins, up to metabolic networks and organismal traits (Wagner 2005b). Different aspects of the early segment formation in *Drosophila* exhibit robustness (Umulis et al. 2008), including the formation of the expression patterns of gap genes (Manu et al. 2009) and segment polarity genes

(von Dassow and Odell 2002). In the nematode *Caenorhabditis elegans*, the vulva of hermaphrodites develops such that the final pattern is reached in spite of cellular disturbances (Braendle and Félix 2008; Milloz et al. 2008). In such a complex anatomical structure as the tetrapod limb, muscles are reliably innervated and supplied with blood because in development a surplus of nerves and blood vessels grow from the body core toward their target, guided by chemical signals (with those nerves degenerating that do not find a target), so that the target muscle becomes innervated and connected to blood vessels even if this process is disturbed (Kirschner and Gerhart 2005).

Occasionally robustness can be due to structural redundancy (the situation where an additional copy of a structure is present so that the loss of one does not have any negative impact), but often robustness is a *distributed process* in that the overall system undergoes various functional changes to compensate for the loss of one component (Wagner 2005a, 2005b; Ihmels et al. 2007). In the case of a gene regulatory network, the experimental deactivation of a gene may leads to compensatory changes in the activities of the other genes of the network. The above example of the development of a functioning limb is an instance of exploratory behavior, which is likewise a distributed process. As a result, while it is a particular structure (e.g., a spatial pattern of gene expression or an anatomical structure) that is robust to certain perturbations, its robustness lies in the underlying developmental and physiological processes, including how their functioning adapts to disturbances, implicating again a bodily part's functional context.

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<A> Functions as Bodily Parts

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So far I have pointed out that even if a structure is at stake, in many cases its individuation as a

structure makes reference to functions involving the structure's surrounding context. Now I want to make a more thought-provoking point about function by arguing that functions are bodily parts just like structures are. There are different legitimate notions of function, and the type of function relevant for my purposes is already implicitly used in different biological fields, but the task is to articulate this notion and to show how function on this construal is on par with structure in scientifically important respects. The latter involves first that structures and functions are bodily parts and stand in part-whole relations, so as to enable the study of organismal organization (discussed in this section). It also includes that structures as well as functions can be homologized across species and their change in the course of evolution can be studied (addressed in the next section).

The term "function" can mean different things in different biological contexts (Wouters 2003). Sometimes it refers to what a structure has been selected for—a structure is an evolutionary adaptation for a certain function. Another notion of function, which like the sense of function of concern to me does not invoke selection history, pertains to how a structure currently contributes to the bodily system of which it is a part or to the whole organism's survival and reproduction. Sometimes called a causal-role function, an example would be to say that the heart's function is the circulation of blood, in that given how it is situated within the circulatory system, the heart contributes to blood circulation. On this use of "function," a function is an attribute of a structure, yet the notion of function I am after is to make structures and functions bodily parts with equal standing. This is the notion of *function as activity*, by which I mean the activity performed by a structure or an organized collection of structures. The heart muscle's activity is its rhythmic contraction in a specific pattern across time; and the heart's activity may include blood being pushed out of it. An organismal part's activity is what

takes place internally to this part (contracting) or includes its most proximal effects on adjacent parts (pushing blood into the aorta), but its activity-function does not involve how this part contributes to the surrounding organismal system, on which other notions of function focus. The heart contributes to the circulation of blood, but only because of how this part is related to other organismal parts; and a structure contributes to an organism's survival and fitness in a certain fashion, given the organism's relation to its environment. Causal-role functions (and other notions of function not of concern to me) capture such relations by addressing what a bodily part is *for*, but an activity-function focuses on what a bodily part *does* (Love 2007, 2013a).

A structure (e.g., the heart) as well as an activity-function (e.g., the contracting of the heart) is a physical part of an organism. Consisting in quite specific changes across time, an activity always takes place during a certain period of time, but given that I conceive of an organism as a living being across time, an activity is still a physical part of the organism. (And a structure such as a mature bone likewise exists during a longer period of time, even when not undergoing any particular change.) The fact that both structures and activity-functions are *bodily parts* (being present or taking place within an organism) is a crucial reason for why on my approach structure and function are on a par. A bodily part, regardless of whether it is a structure or an activity-function, is characterized by features *internal* to it, even though it does contribute to the surrounding system (which is captured by the notion of function as causal role). Indeed, although in standard examples causal-role functions are attributed to a structure, also an activity-function has causal-role functions, e.g., the contracting of the heart contributes to the circulation of the blood. This reinforces the equal standing of structure and function as activity. Unlike a causal-role function, an activity-function is not a mere attribute of some bodily part, it is a bodily part.

Functions in my sense are studied in a variety of biological disciplines. (This is the same sense of "function" that was used in the previous section on the relevance of functional context.) Anatomical functions—as this term is often used—are functions as bodily activities. Examples are limb movement and mastication in tetrapods, both of which consist in the coordinated activities of skeletal elements, among other components. Functional anatomists study how such functions contribute to survival and have been shaped by natural selection, but important research questions pertain to a particular anatomical function as such (regardless of fitness contribution), in particular the analysis of its internal biomechanical operation. One obvious example concerns how articulated bones, given the contraction of attached muscles, result in the bones' coordinated movement so as to enable the mastication of food, which is the anatomical function investigated. Behavioral patterns are likewise activity-functions, as they involve the movement of some parts of the body or the whole body (Ereshefsky 2007).

There are of course other kinds of biological activities than relative movement and contraction. In neurobiology, while the structure of individual neurons and the connectivity structure of many neurons is investigated, so is neuron function (the electrophysiological activity at the membrane of an individual neuron) and neural network function (the electrophysiological activity within the network). At the molecular level, a gene's function is its transcriptional activity, which may include the cell types and spatial regions of the organism in which the gene is expressed. A developmental process is a complex activity-function in that a developmental process consists in the activities and interactions of several entities across time, though when speaking about "developmental process" one naturally focuses on the process's many ingredients rather than the overall activity taking place. A similar situation holds for "system" as used by systems biologists, as this term foregrounds the system's various active components rather than

the resulting system functioning. Many such molecular-cellular activities have neither clear spatial nor clear temporal boundaries to other activities. But this underscores the need to pay attention to the particular epistemic considerations underlying a contextual individuation decision (and even in the case of structures I have pointed to different possible individuation criteria).

Overall, there is quite a variety of activities within an organism, but the notion of an activity-function highlights common themes across different domains and disciplines. One issue already illustrated by the above examples is that an activity-function is a part of an organism and thus is just as much a bodily part as a structure is. A living organism (extended through time) is composed of many activity-functions from gene functions to complex anatomical functions; however, this is not to deny that an organism is also composed of structures. Structure and function are not notions that are in competition, nor does the biological study of one exhaust the other.[6] In fact, there are important connections between structures and functions, to wit, *part-whole relations*. I have mentioned that structures and activity-functions contribute to the larger system (of which they are a part). This is more precisely contributing to the system's *activity*, which shows that this activity-function has as its components structures and lower-level activities (e.g., activities performed by these individual component structures). Just like one chimpanzee's hand as a concrete structure does not exist without its lower-level component structures (e.g., bones, muscles, nerves), so does this chimpanzee's grasping movement as a concrete activity not exist without its component structures performing characteristic activities, e.g., the contraction of the opponens pollicis muscle muscle—which as a *component part* of the hand grasping activity is an activity-function on a lower level (Fig. 10.1). Importantly, part-whole relations also obtain *across* structures and functions. A function such as a grasping-activity performed by the hand

has not only other functions, but also structures (e.g., the opponens polis muscle) among its component parts. And the contraction of the opponens pollicis is an activity-function that is a physical part of the chimpanzee's hand, persisting as a structure across time. Even though it can be epistemically legitimate to consider an organism's structure in abstraction from function, in reality a concrete structure (existing across time) performs activities or in any case is maintained by (component) activities.

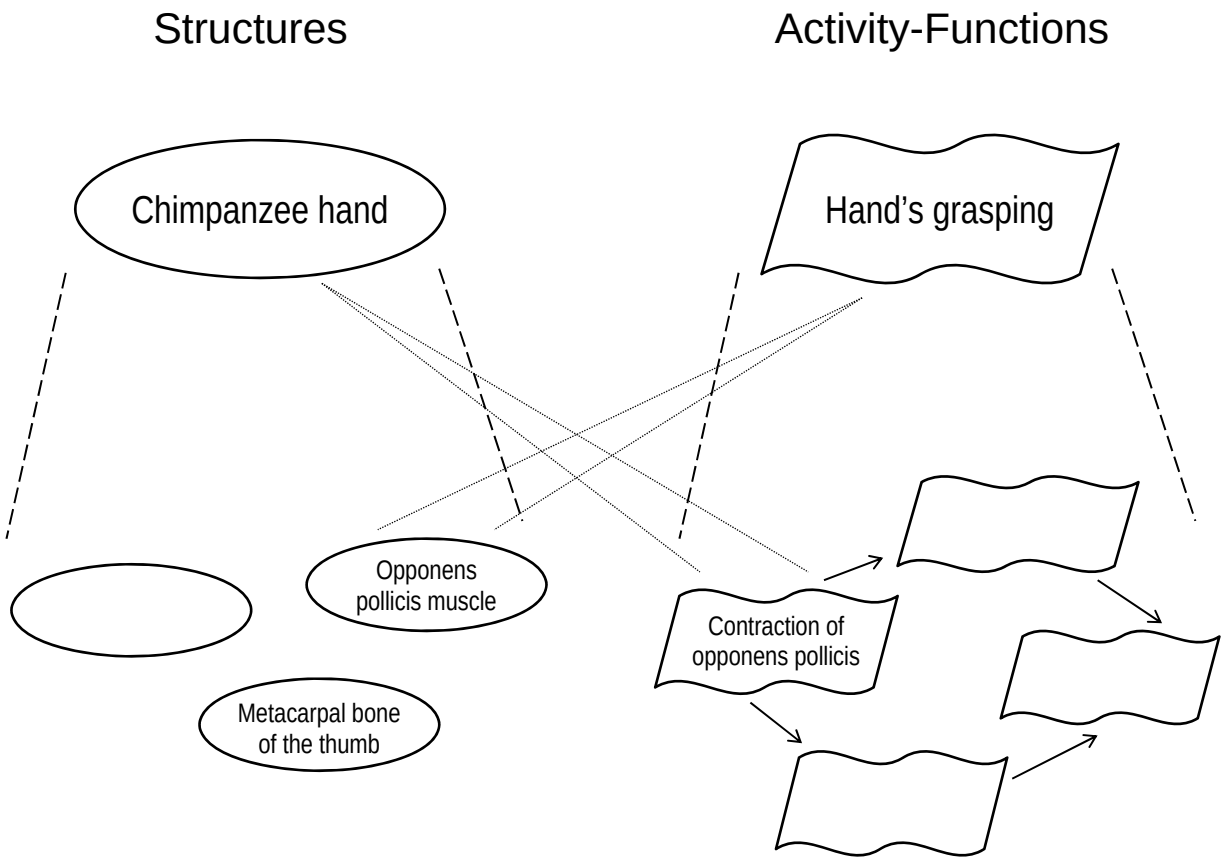

Figure 10.1: Part-whole relations among structures and activity-functions. Just like a structure consists of several lower-level structures (left side), so can a function be decomposed into lower-level functions (right side, the arrows indicate temporal-procedural relations in addition to the spatial relations of structures). Moreover, a

structure (e.g., the opponens pollicis muscle) can be a component part of a function (e.g., a grasping activity of the hand), and an activity can be a physical part of a structure.

While so far I have emphasized part-whole relations among structures and activity-function to underscore the parity of structure and function, in the next section part-whole relations will play a much more important role by showing what benefits my framework has for scientific theorizing. But beforehand, I have to address the related topic of hierarchical organization.[7] Organismal organization is a well-known principle, however, my focus on function introduces a special issue. Structures are hierarchically organized in that one structure can be a spatial part of another one. But a purely spatial containment cannot hold for functions, which are intrinsically temporal, and sometimes quite short-lived. Hierarchy and part-whole relations still obtain, provided that *procedural organization* is taken into account in biological theorizing. Procedural organization involves the temporal order and causal relations among different activities (Fig. 10.1, right side; see also Love 2007). In a developmental process there are various structures that exhibit specific activities (e.g., the binding of a transcription factor to a DNA segment), where the temporal organization of these activities—together with the spatial locations of structures being present and activities occurring at certain points of time—yields the overall operation of the developmental process. The binding of a certain transcription factor at specific genomic region as a particular step of the developmental process is one molecular function that is a lower-level part of the overall functional process. One component of such a complex anatomical function as the closing movement of the mammalian jaw is the contraction of the medial pterygoid, which itself is an activity-function, so that one function can indeed be a part of another function (even though it is not a purely spatial part, but includes containment among regions of time), yielding a hierarchical, spatial-procedural organization.

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<A> Fruitful Investigation Beyond the Structure-Function Dichotomy

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I now show how the notion of a function as an activity and a body having activity-functions (as well as structures) as its parts alleviates some long-standing tensions between structure and function in biology. These nowadays arise in different contexts related to evolutionary issues, often because some epistemic principles or explanatory agendas rightly distinguish between structure and natural selection, but turn this into an opposition of structure and any kind of function.

One issue is the important practice of homologizing bodily parts, which recognizes that such parts have some identity across evolutionary time. Homology has traditionally been distinguished from analogy, i.e., structures that are similar because they have the same function. Even if nowadays homology is contrasted with homoplasy (similar traits not derived from common ancestry), it is still not to be conflated with analogy. Well before the advent of Darwin's evolutionary theory, the contrast between homology and shared function was clearly made, and it was structures but not functions that were seen as homologous across species (Brigandt 2011a). The historical origin of the homology concept was tied to disputes about whether form or function was prior (Russell 1982[1916]; Appel 1987; Nyhart 1995). But one can fruitfully *homologize functions* in different species, provided that these are activity-functions and thus bodily parts. For in this case, the "function" pertains to the things that are homologized, but not to the reason why the relation of homology obtains (which still is common descent of bodily parts), so that there is no illicit conflation with analogy.[8]

Alan Love (2007) has made this point in the context of comparative developmental

genetics, where talk about functional homology is quite common. He argues that the phrase "functional homology"—which sounds like a contradiction in terms—can be made coherent if it is understood as "homology of function." In such cases, gene activities are the traits homologized, solely because of their common descent and regardless of their fitness-contribution. Both a gene as a structure and a gene's expression activity as a function can be present within a taxon and thus be homologous. In case of an evolutionary transformation in gene activity, it may well be that homology of the gene obtains but not of the gene's function. For instance, while *distal-less* is a highly conserved gene, found in one copy in nearly all invertebrates and in multiple copies in vertebrates, its expression patterns differ substantially across these taxa, sometimes being expressed in different tissue types or in a structure not possessed in some taxa. Within echinoderms alone, Lowe et al. (2002) point to autapomorphic *distal-less* expression regions (where they associate this novel gene activity with the origin of a new anatomical structure or a change in the species' life history). Even when *distal-less* is expressed in similar bodily regions—consider vertebrate and arthropod appendages—this expression pattern did not exist in the appendage-less common ancestor, entailing non-homology of gene expression activity. While such examples have been used to argue that similarity of gene expression does not entail homology of the developed structures (Nielsen and Martinez 2003), the point I make here is that a particular gene (a structure) and the gene activity (an activity-function) are non-identical bodily parts and thus can operate as different evolutionary characters.

I have stated that a gene's function is its (changing) expression pattern across developmental time, in line with my above articulation of the notion of an activity-function, which includes the internal activity of a bodily part or at most its most proximal effect on adjacent parts. To be sure, some uses of "gene function" refer to which other genes are regulated

by the gene, and thus more distal effects of the gene. But this can be captured by my approach as well, and highlights again the relevance of hierarchy and part-whole relations. Uses of "gene function" that include regulatory relations among different genes are best seen as the activity of a gene regulatory network, and thus as an activity-function on a higher level than the activity of a single gene (which is a *part* of and thus on a lower level than the regulatory network's activity).

Other domains where functions are homologized include functional anatomy. Anatomical functions are features that are conceived to be shared across taxa in a cladistic context (Amundson and Lauder 1994; Lauder 1994). As mentioned, anatomical functions are functions in the sense of activity-functions, and so can stand in relations of homology without running afoul of the homology-analogy distinction. The same holds for behavioral homology, which more precisely means homology of behavioral patterns (Ereshefsky 2007). Under the label of "process homology," a few have suggested that developmental processes can be homologized across species (Gilbert et al. 1996; Gilbert and Bolker 2001; Minelli 2003). While many shy away from this idea on the grounds that it conflates homology and function,[9] in my view it is a perfectly coherent notion provided one views a developmental process as a complex activity-function. In this case the focus is on the *internal* operation of a developmental process (and how the internal operation compares to other species), regardless of the fitness-impact and adaptive purpose of this developmental process.

Another domain that is fundamentally concerned with function is neuroscience and cognitive science. While comparative accounts in these areas have for the most part homologized the brain structures of different species, which is conceptually uncontroversial, there is an emerging literature on cognitive homology that addresses brain activities and cognitive activities (Platt and Spelke 2009; García 2010; Murphy 2012). Here again, clarity is served by determining

what kind of biological traits are individuated (as activity-functions, cognitive activities belong to the same basic category as many other bodily functions), how they are related to other traits (e.g., to cognitive structures of the same organism), and why they can be meaningfully homologized. Moreover, the need to relate different cognitive functions of an individual raises the issue of *serial homology* in the context of functions. A single performance of a neuronal or cognitive activity is a concrete bodily activity, and several such performances within an individual are different particular bodily activities of the same type, which are thereby serially homologous in a trivial fashion. More interesting is the situation where one cognitive activity is a real modification of another activity within the same individual, e.g., when an activity is redeployed for a quite different purpose, as in the common phenomenon of neural reuse (Anderson 2007, 2010). If one is a modification derived from the other they are serially homologous, in spite of differing somewhat in their internal operation and fulfilling substantially different cognitive tasks—the latter as the activity's impact on the larger organismal system is irrelevant to activity-function and homology. For instance, Jason Clark (2010a, 2010b) argues that some higher cognitive emotions are serially homologous to basic emotions, and Taylor Murphy (2012) suggests that mentalization (our ascribing mental states to ourselves and others) is serially homologous to the activity of the default network (a network of brain regions active even when the brain is at wakeful rest).

Apart from merely homologizing bodily parts across species, their evolutionary transformation has to be tracked and explained. Here the presence of part-whole relations is important as they are the precondition for structures and functions to be able to evolve. A structure can reappear in different generations as the "same structure" while undergoing "structural change." If this sounds paradoxical, it can be clarified by distinguishing between

characters and character states (Brigandt 2007; Wagner 2007, 2014). Bodily parts in different organisms that are homologous are the same character, so that a character can form an historical lineage, while the character undergoes evolutionary modification in the sense that its character state changes. In the case of a structure, this means that across generations some of its parts (component structures) or their spatial relations change. An activity-function can likewise undergo evolutionary modification because it has both structures and lower-level activity-functions as its parts, some of which can change or the spatial-procedural organization of which can be subject to modification.

Another reason for recognizing functions as an important type of bodily part is the origin of *evolutionary novelty*. An issue more general than transitions in evolutionary individuality, accounting for the evolution of novelty is one of the major challenges for contemporary evolutionary biology, with scientific efforts being devoted to many individual cases (Brigandt and Love 2010, 2012). But whereas this research often has a bias towards novelties that are structures, functions on different levels of organization can likewise be interesting evolutionary novelties in need of explanation. Rather than appealing to structural features (e.g., complex cell-cell junctions as seen in derived taxa), Sally Leys and Ana Riesgo (2012) consider an aggregate of cells a true epithelium if it has the *capacity* to seal and control the ionic composition of the internal milieu, so that an epithelium is considered a function feature. Based on this they argue that the epithelium is also present in sponges and thus a novelty of metazoans. On a higher level of morphological organization, the fin movement underlying locomotion in fish is a novel anatomical function of vertebrates.

There are at least two reasons why so many studies of evolutionary novelty focus on the origin of novel structures. One is pragmatic: it is easier to explain the development and

evolutionary origination of a few structures (e.g., the skeletal elements of a fin; Hall 2007), compared to an anatomical function that consists in different types of structures interacting and changing in time so as to perform a complex activity (e.g., how muscles attach to skeletal elements of the fin, how they are supplied with blood, innervated and contract so as to create characteristic fin movements; Brigandt 2010). However, the difficulty of explaining the evolutionary origin of complex anatomical functions should not make us overlook their biological importance (Love 2003, 2006, 2013a). In fact, since individual structures usually do not originate in isolation but together with the evolutionary advent or modification of other structures as part of a structure-function-complex performing new bodily activities, developmental and evolutionary studies scrutinizing a structure in isolation may in fact offer a false account of its origination. Recognizing this entails the need for interdisciplinary research and integrative explanations that capture complex, multilevel characters (Love 2013a, 2013b).

My account of part-whole relations and functions as activities is helpful in this context, as it clarifies that a complex bodily part is composed of both structures and functions as its parts (arranged in a spatial-procedural organization), which themselves have components parts on yet a lower level. There is notorious disagreement about how to define evolutionary novelty and which traits count as novelties, given the difficulty of distinguishing between a mere quantitative variant (which does not qualify as a novelty) and a qualitatively different trait (Brigandt and Love 2010, 2012; Palmer 2012). No matter how novel a structure may look, there are always some evolutionary precursors, at least on lower levels. For example, in the transition from fins in fish to limbs in tetrapods, the tetrapod autopodium (including the digits) as the most distal element has traditionally been deemed a novelty (Hall 2007). But more recent evidence has shown that fin rays and limb digits share gene expression patterns—a precursor on a lower

level—which together with paleontological evidence has led some to conclude that the tetrapod autopodium and not even the digits are novel (Johanson et al. 2007; Boisvert et al. 2008; Hall and Kerney 2012). Yet from the perspective of my hierarchical framework, the important task is not to decide whether or not an evolutionary change counts as "novel," but to empirically investigate which of a derived trait's component parts on several levels (structures as well as functions) were already present in the ancestor and which were not. Subsequently, an evolutionary origin explanation can fruitfully be put forward by detailing how precursor structures and activity-functions on different levels change during developmental time, and how such developmental processes and their spatial-procedural organization were modified across evolutionary time so as to result in the novelty (Love 2006; Brigandt and Love 2012).

Tetrapod limbs and digits are structures, in line with the bias of studies of novelty toward structure, but even here (lower-level) functions are implicated in the overall explanation, e.g., conserved and modified gene expression activities. A case where the very explanatory target—the evolutionary novelty—can be seen to be a function is neural crest cells. Neural crest cells have various features, including the capacity for long-range migration and for forming various cell types (so as to ultimately give rise to diverse cranial and other anatomical structures). Such capacities and in particular the performance thereof (i.e., migrating, differentiating) are not structures, but activity-functions, so that I would argue that to be a neural crest cell is best defined functionally. Neural crest cells have long been known to be a novelty of vertebrates, but also in this case ancestral precursors have been discovered, in the form of neural crest-like cells in tunicates (which most likely are the sister-group of vertebrates). Neural crest-like cells have some of the function features of neural crest cells, most notably the capacity to migrate, yet they lack other capacities, e.g., for long-term migration and for forming ectomesenchyme derivatives

(Jeffery 2007; Abitua et al. 2012). Here again, my approach is not to ponder the applicability of the label "novelty," but to track and explain evolutionary change in terms of the modification and acquisition of activity-functions and structures relative to the ancestral condition (as seen in neural crest-like cells), from higher levels (e.g., change in cell migration activity) to the molecular level (e.g., changes in gene expression activities).

A second reason for some approaches to evolutionary novelty to be centered on structure is that they stem from an agenda that focuses on the developmental generation of novelty while setting aside consideration about the fitness contribution of structures. Though research on so-called key innovations centers on how the fitness contribution and ecological impact of a new trait furthers subsequent adaptive radiation, more structuralist approaches focus on the very origination of the structure by means of development regardless of the influence of natural selection (Müller 1990; Müller and Newman 2005). The latter approach may even motivate researchers to endorse a definition of novelty that stipulates a novelty to be a new structure, thereby excluding new functions (Müller and Wagner 1991; see also Peterson and Müller 2013). However, developmental-morphological origination explanation vs. adaptation explanation (the kind of explanation sought) is an issue orthogonal to whether the focus is on bodily structures as opposed to bodily functions (the kind of bodily part subject to explanation). The two issues are (loosely speaking) "structure vs. function" pairs that should not and—using my perspective—cannot be conflated.

Even in the case of a novel *function* such as fin movement we need to ask how such a complex bodily part could have been brought about by changes in ancestral *developmental* mechanisms, or what changes in cellular-developmental mechanisms led to the evolution of the epithelium as the functional ability of tissues to seal. Thus, also those with a more structuralist

outlook on evolution should recognize functions as genuine bodily parts that can be homologous across species or be evolutionary novelties (not restricting definitions of novelty to structure) and view novel functions as in need of explanation.

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<A> A Pluralistic Coda

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I have addressed considerations about function, not to prioritize it over structure, but to stress the need to conceptualize both structure and function, by pointing to instances where considerations about structure implicate function as well, and by arguing that both structures and functions are genuine bodily parts. My account of structures and activity-functions as bodily parts has articulated their part-whole relations within an organism's spatial-procedural organization, so as to highlight multilevel investigation and explanation. While most of my discussion has centered on two generic types of bodily parts—structures and functions—this is not to say that bodily parts are individuated in a rather uniform fashion. Quite on the contrary, as mentioned earlier, there are many types of individuation considerations, which can be used in combination. A bodily part can be delineated by spatial or temporal boundaries. Alternatively, the part's internal structure can determine its identity, or some of its internal activity can be decisive. Some bodily parts are individuated in a relational fashion, where its intrinsic features alone are insufficient, but its impact on other bodily parts are crucial, or its difference from other parts (e.g., one cell ceasing to exist upon dividing into two cells). Sometimes what matters is that a particular bodily part belongs to the same class (is of the same type) as many other such parts, including parts of other organisms, for instance, a particular segment of DNA is considered as a relevant part because it is a gene. Given the variety of distinct individuation considerations, there are different

kinds of bodily parts, which differ in the nature of their identity and integrity.

Overall, this yields a *pluralism*, which is ontologically due to the complexity of nature that cannot be captured by a single individuation scheme and epistemologically made salient by there being different legitimate scientific aims. Different classificatory or explanatory aims (pursued in different research contexts) often require different individuation considerations and representation schemes. Breaking a model organism's development into normal stages is fruitful for the purposes of developmental biology, yet explaining the evolution of development and morphology requires a different individuation, as normal stages obscure natural variation in development, phenotypic plasticity, and how developmental stages are created and transformed in evolution (Love 2009, 2010, 2013a). There are different ways of abstracting an organismal system into parts (called partitioning frames by Winther 2011), and such partitioning frames are often cross-cutting and have different advantages and disadvantages. Scientific representations are tools used for particular epistemic purposes. Taking such epistemic aspects as methodological, classificatory, and explanatory aims into consideration enables one to reflect on why a certain individuation scheme is used in a certain context, what makes it appropriate given its purpose, and what its limitations are relative to the intended purpose or relative to other possible epistemic aims (Brigandt 2013a; Love and Brigandt this volume). Paying attention to epistemic aims matters beyond the individuation of bodily parts.[10] In the context of biological individuality, a pluralism based on the presence of multiple epistemic aims has recently been advocated by Beckett Sterner (2015) and by Lidgard and Nyhart (this volume) as well as Love and Brigandt (this volume).

In many instances, bodily parts have blurry boundaries. This is especially the case for activity-functions, including biological processes and molecular systems as studied by systems

biology. It is notoriously difficult to break a larger system's activity down into functional components (Krohs and Callebaut 2007). While some approaches in systems biology attempt to understand the functioning of some smaller networks (such as network motifs; Alon 2007) in isolation from their connections to the larger system, other systems biologists argue that a more global investigation of larger systems is required to understand their actual functioning (Huang 2004). The phenomenon of distributed robustness mentioned above, where for instance a gene—ostensibly a functionally relevant part—is not really functionally important in that its deactivation does not change the activity of the overall gene regulatory network (because the activities of other genes in the network are adjusted), likewise shows that some systems do not have clearly delineated components (Brigandt 2013b). Biological mechanisms, despite the connotation of being analogous to a machine, do not ontologically have clear-cut spatial or temporal boundaries; instead, biologists epistemically choose the boundaries of the mechanism of interest and individuate its components, based on pragmatic considerations and idealizations (Bechtel 2015).

Something similar holds for *levels of organismal organization*. My discussion has emphasized part-whole relations and hierarchical organization. However, I do not think that there is a global set of ontological levels (e.g., molecular, developmental, anatomical, behavioral), where all the different entities on a level would share important properties. This is analogous to Linnaean ranks in taxonomy, where two taxa of the same nominal rank may differ dramatically in their phylogenetic age and their species diversity, so that some prefer the use of a rankless taxonomy. In the case of organismal organization, talk about levels is only *locally* meaningful and relative to prior *epistemic* choices. If one entity has been deemed to be a bodily part (based on epistemic considerations), then any entity that is a proper part of it is on a lower level, but this

does not commit us to a set of global levels into which all characters of an organism or even all characters across taxa could be so arranged that for any two bodily parts one could unambiguously say whether they are on the same level or on different levels.[11] In the case of a complex system of molecular pathways, one may not be able to assign the various system components to an informative set of levels, especially given feedback and circular causal interactions among the components, so that it is a better strategy to represent the system as a network than as a nested hierarchy.

Recent philosophical discussions of mechanism have emphasized part-whole explanations, in that a mechanism is to be decomposed into components and the mechanism's operation is to be explained in terms of the organization and interaction of the components (Bechtel and Abrahamsen 2005; Bechtel 2010). At the same time, such accounts have shown a problematic bias towards molecular detail, and only recently has the widespread use of abstraction and idealization in the modeling of complex mechanism come to be philosophically addressed (Brigandt 2013b, 2015a; Levy and Bechtel 2013). We yet need a serious philosophical understanding of the various epistemic considerations involved in mathematical modeling as a representational and explanatory practice (O'Malley et al. 2014). Philosophers have also tended to focus on mechanisms' structural components and their qualitative interactions (e.g., binding, activating), while often neglecting quantitative and dynamic aspects. Many parts of a molecular system are *transient*, with biochemical reactions rapidly transforming one molecule into a different kind of molecule and breaking down entities into smaller molecular components. A system's characteristic functioning is not so much due to the stable presence of entities, but to short-lived molecules that are replaced by molecules of the same type (Baetu 2015). Beyond philosopher's focus on the *actual* organization and regular operation of a mechanism, my

discussion has mentioned robustness as an important scientific issue, which as the way a system would respond upon perturbation pertains to the system's *modified* organization and operation (Brigandt 2013b, 2015a). Generally, many research questions in systems biology, developmental biology, and other fields studying organismal parts are about transformation and the emergence of novel features, so that while bodily parts have to be contextually individuated, we should not expect the represented parts, their boundaries, and their gathering into organismal subsystems to be stable and unchanging.

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[1] A similar dichotomy that has shown up in different controversies is microscopic structures vs. interacting molecules in solution (Gilbert 1987).

[2] The philosophical account of molecular mechanisms by Machamer et al. (2000) uses a dual

ontology of entities and activities. My account of structures and functions aligns with this, but extends it to higher levels of organismal organization and emphasizes hierarchical part-whole relations among structures and functions.

[3] It is common to view a species as an individual, which has organisms as its parts (Love and Brigandt this volume). A homologue as a lineage across organisms can similarly be considered an individual, which has the particular homologues of organisms as its parts (Wagner 2014), though this is not the only way to conceptualize this situation (Brigandt 2009).

[4] Reynolds (this volume) discusses cells being transformed by their context and emergent interactions among cells that motivate the label "cell sociology." Rieppel (this volume) lays out Martin Heidenhain's hierarchical view of organismal organization, which emphasized downward causation, i.e., how higher-level traits organize lower-level traits. Herron (this volume) argues that the degree of evolutionary individuality can be subject to short-term changes due to modifications in population structure; and Sterner (this volume) points out that inheritance (as a precondition for individuality) can be due not only to material overlap across generations but also to scaffolding, which involves physical features outside of individuals.

[5] While my present focus is on the relevance of function, this also shows that a bodily part as a homologue is individuated in a relational fashion. Whether a particular part can vary independently of others depends not just on the properties of this part, but on some of the other parts, and their relation, including the underlying developmental processes. This ties into discussions of modularity (Schlosser and Wagner 2004), which is often characterized by the causal interactions within a module being of a higher amount or stronger *than* the interactions

between modules, which implicates the relation among modules.

[6] Activity-functions are in fact processes, which raises the question of whether I endorse a process philosophy. Featuring processes as a category rather than the substances of more traditional metaphysics, so as to highlight becoming and occurring rather than what is, the process philosophy of Alfred North Whitehead also influenced Conrad Hal Waddington's (1975) biological thought. However, I do not endorse the view of some process philosophers that substance (or structure) is less fundamental than or even can be reduced to process (or function).

[7] Though my focus is on bodily parts, hierarchy is also an issue above the level of organisms, where even extended hierarchies of biological individuals have been proposed and their evolutionary origin studied (Bouchard and Huneman 2013; Nyhart and Lidgard this volume; Rieppel this volume). In my context, while structures and function have structures and functions as their parts, which on yet a lower level are composed of structures and functions, there will be a point where physical parts cannot any longer be deemed to be *biological* structures or functions.

[8] Owen defined a homologue as "the same organ in different animals under every variety of form and function" (1843, 379). Alan Love argues that the "function" in Owen's definition is to be understood as use-function, i.e., how it contributes to the surrounding system (causal role) or to the organism's fitness. This paves the way for a corresponding account for the homology of functions: "the same *activity-function* in different animals under every variety of form and *use-function*" (Love 2007, 679, my emphasis). Use-function is the kind of function germane to relations of analogy, so this underscores how homology of activity-function is independent from

analogy (see also Love 2013a).

[9] While Rudolf Raff once endorsed the notion of process homology (as a co-author of Gilbert et al. 1996), he does not favor this idea any longer, among other things because of the alleged homology-function incompatibility (pers. comm., May 2001).

[10] While natural kinds are typically seen an ontological issue, in Brigandt (2009) I argue that we should include epistemological considerations, such as the epistemic purposes for which natural kind concepts are used in science.

[11] In the course of phylogeny the relation among characters on different levels and the very levels themselves can be subject to evolutionary modification, as witnessed by the fact that homologous anatomical structures can be due to non-homologous developmental processes or the activity of non-homologous genes (Brigandt 2007, 2011a).