

Integrative Pluralism for Biological Function

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Abstract:

We introduce a new type of pluralism about biological function that, in contrast to existing, demonstrates a practical integration among the term's different meanings. In particular, we show how to generalize Sandra Mitchell's notion of integrative pluralism to circumstances where multiple epistemic tools of the same type are jointly necessary to solve scientific problems. We argue that the multiple definitions of biological function operate jointly in this way based on how biologists explain the evolution of protein function. To clarify how our account relates to existing views, we introduce a general typology for monist and pluralist accounts along with standardized criteria for judging which is best supported by evidence.

Keywords: conceptual analysis, explanation, monism, protein function, evolution, gene duplication

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Abstract:

We introduce a new type of pluralism about biological function that, in contrast to existing, demonstrates a practical integration among the term's different meanings. In particular, we show how to generalize Sandra Mitchell's notion of integrative pluralism to circumstances where multiple epistemic tools of the same type are jointly necessary to solve scientific problems. We argue that the multiple definitions of biological function operate jointly in this way based on how biologists explain the evolution of protein function. To clarify how our account relates to existing views, we introduce a general typology for monist and pluralist accounts along with standardized criteria for judging which is best supported by evidence.

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4 **1. Introduction**
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6 Many philosophers of science have endorsed the general ideal that conceptual analysis
7 should aim to provide necessary and sufficient conditions for a term's correct use. Philosophers
8 analyzing particular scientific terms, however, have consistently struggled to agree on one set of
9 necessary and sufficient conditions satisfying all relevant demands. Several familiar examples
10 include explanation, Newtonian force, and biological function (Wilson 2006; Garson 2016;
11 Woodward 2017). In response, philosophers have formulated a range of alternative solutions for
12 conceptual analysis, such as homeostatic property clusters (Boyd 1999) and degree of similarity
13 to an exemplar (e.g. Godfrey-Smith 2013). Some philosophers have also adopted more pragmatic
14 views of meaning that defend pluralist accounts as legitimate (Brigandt 2003; Wilson 2006;
15 Waters 2014).
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31 The debate over the meaning of biological function nicely exemplifies this growing
32 complexity. The current discussion traces back to the 1960s, and since then it has accumulated
33 an impressive number of divergent accounts (Garson 2016) and standards of evidence (c.f.
34 Wright 1973; Neander 1991; Mitchell 1995). During this time, philosophers of biology shifted
35 away from attempts to provide universal necessary and sufficient conditions and moved toward a
36 pluralist view that recognizes two major senses of function: an etiological account based on a
37 trait's history of natural selection, and a causal role account based on how parts of a system
38 contribute to a system-level capacity of interest. Nonetheless, even some pluralists about
39 function find this view unsatisfying: it recognizes each meaning as legitimate in its own sphere
40 but fails to articulate any positive relationship tying them together.
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55 We introduce a new type of pluralist account for biological function that defends a sort of
56 practical integration among function's multiple senses. In particular, we show how one can
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4 generalize Sandra Mitchell's (2003) notion of integrative pluralism to apply to philosophical
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6 accounts of scientific terms. Mitchell originally developed and defended integrative pluralism
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8 using a case where biologists needed multiple models with incompatible idealizations to produce
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10 a comprehensive explanation for the division of labor in social insects. We expand integrative
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12 pluralism to circumstances where multiple epistemic tools of the same type are jointly necessary
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14 to answer scientific questions. We then examine scientific explanations for the evolution of
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16 protein function and argue that they integrate definitions of "function" in this sense.
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21 In order to present rigorous evidence for integrative pluralism, we introduce a general
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23 typology for different monist and pluralist accounts along with standardized criteria for judging
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25 which is best supported by evidence. Our method in this paper is inspired by ideas Joyce Havstad
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27 outlined in an unpublished manuscript titled "Species Concepts: Attrition and Contrition" from
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29 2015 about the species debate. Our approach uses evidence based on how biologists use the term
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31 "function" in practice rather than on ordinary language observations or folk intuitions, and for
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33 this reason we characterize it as "practice-oriented conceptual analysis." We therefore do not
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35 take philosophical intuitions or necessary and sufficient conditions to be inherent to conceptual
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37 analysis as a method. Reviewing the relevant evidence for each type of account, we find that the
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39 closest competitors to integrative pluralism are hierarchical monism and disjunctive pluralism
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41 (see Sections 5 and 6 for definitions). We conclude that disjunctive pluralism fails to
42
43 accommodate the case of protein function evolution, while no account of hierarchical monism
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45 currently succeeds in unifying all definitions of function under one logical hierarchy.
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52 **2. Generalizing integrative pluralism**

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55 Philosophers studying integrative science have examined all sorts of cases, from
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57 integration of data to explanations to disciplines (Darden and Maull 1977; Bechtel 1993; Love
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4 and Lugar 2013; Brigandt 2013; Gerson 2014; Leonelli 2016). The relationship between
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6 integration and scientific terminology, however, has gone largely unexamined, perhaps for
7
8 historical reasons.¹ Integrative research originally earned philosophers' interest as an alternative
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10 regulative ideal for science that does not aim at total unification, which typically required logical
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12 derivability among two or more theories (e.g. Schaffner 1967; Kitcher 1981). Theory reduction,
13
14 for example, requires bridge laws that define the terminology of one theory in terms of the other.
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16 The project of defining scientific terms using necessary and sufficient conditions was thus
17
18 closely allied with providing logical reconstructions and derivations of the content of scientific
19
20 theories. Since then, however, new defences of pluralism and alternative forms of monism have
21
22 expanded the possibilities for conceptual analysis. The time is therefore right to reexamine what
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24 we can learn by putting insights from integration and conceptual analysis back into dialogue.
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31 We argue in particular for the fruitfulness of generalizing Sandra Mitchell's conception
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33 of integrative pluralism beyond its original focus on models and explanation to incorporate a
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35 broader range of scientific tools and aims. Mitchell's argument for integrative pluralism
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37 illustrated how scientists can give sophisticated causal explanations for complex phenomena
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39 without relying on a unified theory (Mitchell 2003). The case study she used examined how
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41 social insect biologists explained the emergence of a division of labor within insect colonies in
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43 terms of causes acting at multiple levels of composition (genetics, single organisms, and
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45 colonies). What Mitchell noticed was that biologists had built explanatory models that focused
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47 on the effects of causes at one level while idealizing away the other potentially relevant factors.
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49 Considered as representations of actual insect colonies, then, the models were logically
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58 ¹ Sabina Leonelli's recent work on bio-ontologies does address the general importance and
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60 potential downfalls of standardized vocabulary for data packaging and integration, for example,
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62 but she doesn't draw clear implications for conceptual analysis of single terms (Leonelli 2016).
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4 incompatible and couldn't be unified into a single depiction of the causal processes at work.
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6 However, biologists did use the models to estimate the importance of each factor individually for
7
8 a species, and they were able to combine this knowledge about each factor into a more
9
10 comprehensive and integrative explanation.
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14 While Mitchell's work has focused on the epistemic utility of having multiple
15
16 representations to explain complex phenomena, we believe integrative pluralism has the potential
17
18 for far greater scope. We generalize its underlying conceptual structure in the following way:
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20 integrative pluralism requires multiple epistemic tools of the same type that each apply to a
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22 scientific problem; individually these tools are capable of providing only a partial or imperfect
23
24 solution; and their capacities cannot be unified according to our present capabilities.² Integrative
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26 pluralism is therefore not limited to logical relationships among the contents of representations
27
28 or terms but extends to incorporate practical relationships of joint use among epistemic tools for
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30 problem solving (see also Bzovy 2017). This allows integrative pluralism to apply equally well
31
32 to models, instruments, experimental protocols, and classification systems. It also expands
33
34 integrative pluralism to include types of problems such as measurement and prediction that
35
36 extend beyond explanation. Finally, it suggests a general distinction between integration based
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38 on combining epistemic tools of the same or different types (c.f. O'Malley, Elliott, and Burian
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40 2010; O'Malley and Soyer 2012).
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48 In what follows, we show how to apply this expanded conception of integrative pluralism
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50 to definitions of a scientific term. For simplicity, we keep Mitchell's focus on explanation in this
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59 ² Mitchell also gives in-principle reasons against theoretical unification for the social insect case,
60 but we use a weaker condition that is based only on present knowledge.
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4 paper, but we discuss in the conclusion how our account can be expanded to incorporate
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6 prediction.

9 **3. Practice-oriented conceptual analysis**

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11 In the initial decades of academic philosophy of science, conceptual analysis centered on
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13 the explication of scientific concepts in relation to scientific theories: philosophers aimed to
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15 define a concept through formalizing its definition in one or more logically reconstructed
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17 theories. Scientific language is of course much richer than this, but the importance of
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19 terminology and definition for the integration of diverse bodies of knowledge and methods has
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21 received limited attention in recent work motivated by the study of scientific practices (Brigandt
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23 and Love 2012; Leonelli 2013). Philosophers' views on conceptual analysis have also evolved
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25 since the mid-20th century, with increasing interest in the pragmatic goals that concepts serve
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27 (Brigandt 2009; Brigandt 2011; Brigandt and Steinle 2012; Queloz 2019; Brigandt and Rosario
28
29 Forthcoming). Since the literature on biological function spans many decades and approaches,
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31 being explicit about one's aims and standards of evidence in defending a new account is
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33 important for clarity and rigor (Kraemer 2018). This especially true in our case because the
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35 evidence we present for an integrative pluralist account of function relies on paying attention to
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37 previously overlooked features of scientific practice.

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39 In what follows, we will distinguish carefully between a term, concept, definition, and
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41 philosophical account. This vocabulary is not strictly necessary for our argument, but we believe
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43 it is helpful to make our intended usage explicit. A term is a word or phrase, while we take a
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45 concept to be a mental entity of some sort. (To the extent possible, we mean to avoid taking sides
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47 on the issue of an "individualistic" theory of meaning (Putnam 1973) or the psychological nature
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49 of concepts (Machery 2009).) A term is an appropriate subject for conceptual analysis if a group
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4 of people regularly uses it as part of carrying out one or more practices. A definition states
5 explicit conditions for a term's correct use in the context of one or more of those practices. A
6 definition could provide, for example, necessary and sufficient conditions for a term's correct
7 use (a type of intensional definition), or a list of things to which the term correctly applies (an
8 extensional definition). Definitions for a term standardize legitimate senses in which it can be
9 used in practice. A philosophical account of a concept then provides a model of correct usage for
10 the term that relates its definitions to the purposes it serves in associated practices.
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21 In particular, we will evaluate evidence for philosophical accounts from the pragmatic
22 perspective of understanding the roles that a concept plays in posing and answering scientific
23 research problems. While most philosophical discussion of goals for concepts remains at a high
24 level of abstraction — e.g. explanation, prediction, or intervention (Brigandt and Rosario
25 Forthcoming) — our focus will be on concrete research problems. For example, one form of
26 pluralism about function associates different senses of the term to different explanatory aims, e.g.
27 etiological versus causal role explanations. We might find, however, that scientists pursue these
28 aims jointly in the context of solving one research problem, raising the question of whether the
29 aims are synergistic or conflicting in practice (Brigandt and Rosario Forthcoming). For this
30 reason, it is important to consider how different senses of function are used in posing and
31 answering concrete research problems. Many philosophers of biology have taken evolutionary
32 and causal role meanings of function to be relevant for disjoint sets of explanatory problems
33 pursued by evolutionary biologists and molecular biologists: evolutionary functions are relevant
34 to problems asking for historical existence explanations, while role functions are relevant to
35 problems asking for explanations of system capacities, and the two sets of problems don't
36 overlap. Justin Garson has labeled this "between-discipline" pluralism about function (Garson
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4 2017). In contrast, Garson defends a “within-discipline” pluralism that claims both senses are
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6 used in each field, but he still takes them to be relevant to disjoint sets of problems.
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9 Our analysis of function below thus emphasizes two main features of philosophical
10 accounts. First, which definitions does an account recognize and how does it characterize their
11 semantic relationships? Most philosophers today recognizes multiple distinct and legitimate
12 definitions of function today, although there are some recent attempts at unification (Mossio,
13 Saborido, and Moreno 2009). Some views on function furthermore aim to organize these
14 multiple meanings into a semantic hierarchy with a single definition at the root from which all
15 other definitions can be uniquely specified (e.g. Walsh and Ariew 1996). Alternatively, the
16 integrative pluralist account we propose rejects the existence of any such unique and
17 comprehensive semantic hierarchy.
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31 The second key feature we consider is how an account describes the relationship (i.e.
32 mapping) between a term’s meanings, goals, and research problems in which it appears. Here we
33 draw on a long-standing view of science as a problem-solving activity (Dewey 1938; Nickles
34 1981; Kitcher 1993; Love 2008), and we emphasize the role of language in articulating research
35 problems and stating solutions (e.g. Brigandt and Love 2012). For example, biologists have
36 investigated several relevant problems about lactose gene *LCT*, which helps humans digest milk
37 (Ségurel and Bon 2017): Why was the *LCT* gene maintained in humans prior to the development
38 of agriculture, what function does the *LCT* protein play in an adult’s ability to digest lactose, and
39 why did the *LCT* gene’s function change in some pastoralist populations? Answers to the first
40 two questions would invoke evolutionary and causal role senses of “function,” respectively. The
41 third question, however, is an example a new class of explanatory problem for the functions
42 literature, and we argue in the next section that solutions to these problems invoke multiple
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4 senses of function. We present this case study first to emphasize its role as independent evidence
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6 separate from any of the monist and pluralist accounts we consider in later sections.
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9 **4. Explaining the evolution of protein functions**

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11 As we've noted, philosophers now generally recognize several senses in which functions
12 can explain: evolutionary functions explain the existence of a trait, role functions explain a
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14 system-level capacity, and propensity functions explain the expected frequency of a trait in the
15
16 next generation of a population (Garson 2016). However, philosophers have devoted relatively
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18 little attention to analyzing how biologists explain *changes* in evolutionary functions over time.
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20 That evolutionary functions do change is familiar from the fact that a trait can have been selected
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22 for a beneficial effect in the past that is different from its present effect on fitness, which may in
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24 fact be neutral or even negative (Godfrey-Smith 1994). Nonetheless, philosophers have not
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26 examined the implications of how biologists explain change in evolutionary functions for our
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28 understanding of the relationship between the multiple definitions of function. In this section, we
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30 describe some causal models biologists have developed to explain changes in the evolutionary
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32 functions of proteins. Later sections will use this case as evidence for or against different
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34 accounts of function.
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43 The discovery of the mechanistic basis for protein synthesis in the 1950s and '60s
44 established a critical connection between DNA sequences and the chemical properties of proteins
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46 (Kay 2000). Random mutations in the DNA sequence of a protein-coding gene can cause cells to
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48 substitute new amino acids at particular positions in the protein sequence compared to their
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50 ancestors. The same substitution at different places in the protein may have widely divergent
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52 effects since specific positions make very different contributions to the protein's chemical
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54 properties, e.g. stabilizing its spatial shape, attracting substrates through electrostatic
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4 interactions, or serving as proton donors in catalytic reactions. Changing one negatively charged
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6 amino acid to a chemically inert one in one part of the protein, for example, may totally
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8 inactivate it chemically while the same substitution in a different location has little effect.
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11 Genetic mutations in the regulatory regions of a protein-coding gene can also alter when and
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13 where the protein is expressed in the organism. In general, changes in amino acid sequence and
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15 gene expression may have positive, negative, or neutral effects on the organism's fitness.
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19 Many proteins have been sufficiently optimized by natural selection to catalyze specific
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21 reactions that the proteins cannot evolve to catalyze a new reaction through single mutations
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23 without first losing performance in their current functions (Dittmar and Liberles 2011). As a
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25 result, biologists expect the evolution of new catalytic capacities through a series of amino acid
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27 mutations to be rare. Empirically, however, they have found ubiquitous empirical evidence for
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29 regular changes in the evolved functions of proteins.
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33 Gene duplication offers a major alternative mechanism for the evolution of new
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35 evolutionary functions. "Gene duplication is probably the most important mechanism for
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37 generating new genes and new biochemical processes that have facilitated the evolution of
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39 complex organisms from primitive ones" (Li 1983, 14). Like amino acid mutations, gene
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41 duplications introduce new random genetic variation into populations. However, duplication
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43 events are different in that they create variation in the total number of gene copies possessed by
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45 individuals in the population without altering the copies' DNA sequences.
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50 As with any genetic variation, gene duplications may initially have a negative, neutral, or
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52 positive effect on individual fitness. Even when the duplication provides no benefit at first, it can
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54 still be maintained in the population by chance through drift. If the duplicate gene persists for
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4 long enough, additional point mutations may accumulate in the ancestral or new copy, impacting
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6 its performance in any historically selected functions of the gene.
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9 Over the past century, biologists have developed a range of causal models describing how
10 gene duplications can increase the probability that a gene will acquire new or different
11 evolutionary functions (Ohno 1970; Piatigorsky 2007; Hahn 2009; Dittmar and Liberles 2011).
12
13 The classical starting point for contemporary research is Susumu Ohno's *Evolution by Gene*
14 *Duplication*, but theoretical and empirical work has especially accelerated in the last twenty
15 years. At present, biologists still disagree about which models and evolutionary processes (e.g.
16 adaptive selection versus drift) are the most important for explaining the retention of gene
17 duplications. Part of the problem is that the models often overlap in the predictions they make,
18 and existing inference methods often lack sufficient accuracy and statistical power to provide
19 definitive results (Hahn 2009).
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33 For our purposes, however, what matters is how many of the models explain the fixation
34 of gene duplications using multiple senses of biological function. Figure 1 illustrates three major
35 classes of models currently being studied by biologists. While the models all share a common
36 causal structure based on gene duplications, they differ on the evolutionary and propensity
37 functions of the gene copies at specific points in time and the relevance of the causal role
38 functions of the protein's amino acids. We give two examples that both use natural selection to
39 explain the fixation of the gene duplication: the Dykhuizen-Hartl model (Kimura 1985; Hahn
40 2009) and the gene sharing model (Piatigorsky 2007). See (Hahn 2009) and (Lynch and Katju
41 2004) for other models that do not require natural selection.
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55 The Dykhuizen-Hartl model explains the emergence of a new evolutionary function in
56 the gene based on the functional redundancy produced by having multiple gene copies. Before
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4 duplication, all copies of the gene in the population are assumed to share a single evolutionary
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6 function. When the duplication occurs, a new copy of the gene is created at some other locus.
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8 Initially, having the additional copy neither sufficiently helps nor harms the organism to be the
9
10 target of natural selection. As a result, the new copy is redundant and over time neutral random
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12 mutations arise and become fixed at the new locus. These mutations may cause a loss or change
13
14 in the catalytic activity of the protein encoded by the duplicate gene, or a change in how that
15
16 copy is expressed. At some point, the environment changes and places new selection pressures
17
18 on the organism. The mutations in the new copy that were previously neutral now provide
19
20 positive fitness benefit, causing selection for the new copy. If the duplication becomes a fixed or
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22 common trait in the population, then the gene has acquired a new evolutionary function: all
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24 copies at the ancestral locus still have their original evolutionary function, but all copies at the
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26 new locus have acquired a different evolutionary function.
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34 On the gene-sharing model, in contrast, gene duplication explains functional change by
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36 releasing the gene from “adaptive conflict” between multiple evolutionary functions. Before the
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38 duplication event, all copies of the gene share two evolutionary functions.³ However, the
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40 protein’s biochemistry prevents natural selection from optimizing these two functions at the
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42 same time. In other words, the protein has reached a point where mutations improving its
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44 performance in one function also lower its performance in the other. Gene duplication addresses
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46 this situation of “adaptive conflict” by creating redundancy and enabling each copy to specialize
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48 in one of the functions. After duplication, mutations that were previously neutral or deleterious
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50 due to trade-offs can now be subject to positive selection so long as the copies maintain
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58 ³ Note that at the time of the duplication the gene is assumed to still be fulfilling the propensity
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60 functions for which it underwent selection in the past. Technically the gene therefore has two or
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62 more paired sets of evolutionary and propensity functions.
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4 complementary functionality. This complementarity generates the necessary fitness benefit for
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6 selection to drive the duplication to fixation in the population. At the end, each locus specializes
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8 in only one of the two ancestral functions.
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11 Both models integrate evolutionary, propensity, and causal role senses of “function” to
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13 provide explanations for how gene duplications become fixed in a population. The models
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15 describe different ways that duplications can acquire positive fitness effects, e.g. through a
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17 change in environment or by releasing biochemical constraints. In the case of environmental
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19 change, the duplication initially lacks a propensity function but then acquires one when the
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21 organism’s environment applies new selective pressures. Moreover, acquiring the propensity
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23 function depended on previous (selectively neutral) changes in the causal roles played by amino
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25 acid positions encoded by the duplicate gene. In the case of released constraints, the same amino
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27 acid positions in the protein are implicated in different and conflicting roles for the gene’s two
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29 evolutionary functions. The duplication thus acquires a propensity function once a mutation
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31 occurs that leverages the new redundancy among copies.
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38 The two models illustrate the point that “ultimately, the interplay between population
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40 genetic dynamics and biochemistry dictates the fate of duplicate genes.” (Dittmar and Liberles
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42 2011, 16). In answering a why-question about the fixation of a particular gene duplication, these
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44 models make use of multiple senses of function in the same explanation. It doesn’t work, then, to
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46 argue that evolutionary, causal role, and propensity definitions of function are relevant to disjoint
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48 sets of explanatory questions. This is also not merely a case of evolutionary biologists taking a
49
50 side-interest in the study of causal role functions: facts about role functions are necessary for the
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52 explanation both models provide for changes in a protein’s evolutionary function. Knowing what
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54 each model implies about changes at the amino-acid level is also essential for testing which
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4 model is correct for any particular gene duplication; see (Lynch and Katju 2004; Hahn 2009;
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6
7 Dittmar and Liberles 2011).

9 **5. Evidence for monism or pluralism?**

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11 What evidence do these explanations of protein function evolution provide for or against
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13 accounts of function? The answer isn't straightforward because there are multiple types of
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15 accounts philosophers have introduced and defended. In order to give a rigorous argument for
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17 integrative pluralism, we need to clarify relevant similarities and differences among the
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19 alternatives. We also need to identify which pieces of evidence for and against each type of
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21 account are decisive.
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26 In the remaining sections, we present and evaluate five schematic types of philosophical
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28 account that are commonly used in conceptual analysis.⁴ Our names for the account types,
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30 especially their monist and pluralist labels, aim to reflect their important distinguishing features,
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32 but our argument for integrative pluralism does not depend on a general, principled distinction
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34 between monist and pluralist views.
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38 **6. Monist Accounts**

39 **6.1. *Hard Monism***

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43 The hard monist schema asserts that term's correct usage can be represented using a
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45 single, universal definition that provides necessary and sufficient conditions. The account
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47 therefore excludes any borderline, vague, or partial cases for the term's use. For example, a hard
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49 monist account of "electron" would rule out any borderline or partial cases in favor of a precise
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51 definition by the particle's characteristic invariant mass and electrical charge. In other words,
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59 ⁴ Havstad originally proposed the first four of these schemas in her manuscript, though we have
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61 revised their definitions in our presentation.
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4 any usage of a hard monist term that does not fulfill the necessary and sufficient conditions must
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6 be treated as incorrect. Since hard monist accounts only recognize a single definition as
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8 legitimate, the term trivially can only have one sense when it appears in the solutions to scientific
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10 problems. The question of whether its senses appear in overlapping or disjoint sets of solutions is
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12 therefore moot.
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16 Philosophers have proposed various hard monist accounts of function (e.g. Ruse 1971,
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18 Bigelow and Pargetter 1987), but we will focus on a recent, innovative approach introduced by
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20 Mossio, Saborido, and Moreno (2009), who seek to unify the etiological and causal role
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22 traditions rather than reject one in favor of the other. The novelty of their approach comes in part
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24 from taking a metabolic view of life as a self-maintaining, organized system.
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28 According to (Moreno and Mossio 2015), a trait T has a function if, and only if:

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30 C1. T exerts a constraint that contributes to the maintenance of the organisation O;
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33 C2. T is maintained under some constraints of O;
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36 C3. O realises closure.
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38 Briefly, a constraint is a causal process or physical structure that has the effect of channeling
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40 energy into thermodynamic work rather than heat. Protein enzymes, for example, are physical
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42 structures that are constraints on chemical reactions they catalyze because they increase the rate
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44 at which the available free energy do thermodynamic work without themselves being altered by
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46 the reaction. A living system contains many parts that are produced by reactions that occur in
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48 nature only because other parts act as constraints to drive the reaction forward. This captures the
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50 sense of a trait being maintained under a constraint in the system. The system is closed when it
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52 depends on a set of constraints that are mutually dependent — each constraint in the set
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54 maintains at least one other and is also maintained by a constraint in the set.
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4 The organizational account unifies the etiological and systems-based traditions in the
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6 sense that it explains the existence of the trait at some time based on its ongoing contribution to
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8 the system's capacity for self-maintenance. In other words, the core features of both traditions
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10 appear within the same definition. However, the organizational account does not unify the
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12 traditions in the sense of presenting a single definition that works equally well for all the research
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14 problems in which biologists regularly use etiological or causal role senses of function. In
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16 practical terms, the organizational function definition is even more difficult to apply empirically
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18 than evolutionary function, which requires evidence for past natural selection acting on a trait.
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20 Empirically demonstrating that condition C3 is true, for example, requires comprehensive
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22 knowledge of a system's causal structure in order to rule out any gaps in the interdependence
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24 among constraints. As a result, the organizational account is inconsistent with practices of
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26 functional morphologists, for example, who apply functional analysis in species often known
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28 only by fossils without to explain evolutionary constraints and exaptations without presupposing
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30 positive contributions to self-maintenance (Amundson and Lauder 1994).
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38 Pending a new unification of evolutionary, propensity, and causal role functions under a
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40 single set of necessary and sufficient conditions, hard monism is also incompatible with the
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42 models of protein function evolution we described above. Evolutionary biologists explaining
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44 protein function evolution do not provide evidence for the existence of closure of constraints at
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46 either the lineage or organismal level or about the detailed organization of constraints millions of
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48 years ago. Indeed, knowledge of the past fitness effects is sufficient epistemically for biologists
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50 to state the relevant effects of the gene duplication on organismal survival and reproduction
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52 without need for invoking closure or constraints.
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58 *6.2 Hierarchical Monism*

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4 In contrast to hard monism, hierarchical monism recognizes multiple legitimate
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6 definitions for a term. However, it requires them to fall into a strict semantic hierarchy with a
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8 unique “root” or “core” definition at the top. As a simple illustration, one could give a
9
10 hierarchical account of the chemical element “oxygen” in the following way. As the core
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12 definition, let “oxygen” refer to atoms that contain eight protons. We can then differentiate more
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14 specific senses of “oxygen” based on the number of neutrons in the atom, i.e. atoms that contain
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16 eight protons and 15 neutrons, or atoms that contain eight protons and 16 neutrons. We could
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18 even continue to consider further subtypes of oxygen based on the number of electrons. The core
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20 definition of “oxygen” is thus progressively differentiated into more refined senses based on the
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22 number of neutrons and electrons.
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29 The progressive differentiation of definitions in hierarchical monism is intensional rather
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31 than extensional in nature: the hierarchy is characterized using nested sets of conditions, not
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33 members. The primary definition at the top of the hierarchy states a minimal set of properties
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35 that are shared by all definitions in the account. Each descending level in the hierarchy
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37 progressively splits the definitions at the higher level by adding a new criterion (e.g. number of
38
39 neutrons) that differentiates each branch. Moreover, any condition applied one level in the
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41 hierarchy should not be reused at a lower level or used for only one branch along the hierarchy.
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43 The extension of the core definition is thus partitioned into smaller and smaller subsets as we
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45 descend in the hierarchy, and at each level these subsets add up to the same collection.
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51 A further requirement on hierarchical monism is that there must be only one way to
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53 organize the definitions in this way around a core. We cannot reconstruct the hierarchy for
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55 oxygen, for example, by starting the definition of an atom possessing a certain number of
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57 electrons or neutrons. Hierarchical monism may superficially look like pluralism because it
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4 permits multiple definitions for a single term, but we treat it as a form of monism because all the
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6 definitions are related as finer-grained divisions of a single, unique root or core.
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9 Although hierarchical monism makes strong claims about the semantic relationships among
10 definitions, we take it to be agnostic about whether those definitions get used in solutions to
11 disjoint or overlapping sets of problems. In other words, hierarchical monism is consistent with
12 senses of function figuring in the answers to different or the same types of explanatory problems.
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14 In the latter case of overlapping usage, we'll see that hierarchical monism differs from
15 integrative pluralism solely in virtue of demanding that definitions fit a unique semantic
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17 hierarchy.
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26 There are a few hierarchical accounts in the literature (Walsh and Ariew 1996; Perlman
27 2009; Saborido 2014). Walsh and Ariew's account nicely fits the schema since it locates both
28 causal role and evolutionary functions under causal dispositions as the primary definition (Figure
29 2a). At the root of the hierarchy is a simplified version of Cummin's definition: "the function of
30 a part of a system is just its causal contribution to some specified activity of the system" (Walsh
31 and Ariew 1996, 493). Within this, Walsh and Ariew distinguish a subset of definitions that
32 restrict the nature of the system activity to biological fitness, i.e. the system's capacity for
33 survival and reproduction. They label these definitions as evolutionary functions and further
34 differentiate among them based on the time at which the contribution to fitness occurs, i.e. past
35 or present.
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50 Walsh and Ariew's account is consistent with the co-occurrence of causal role,
51 propensity, and evolutionary senses of function in explanations of protein function evolution. On
52 their view, causal role functions explain minimally how a token part of a particular system
53 contributes causally to any system capacity of interest to the investigator. Only evolutionary
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4 functions, through their reliance on fitness, are able to explain the existence or maintenance of a
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6 trait *type* over time, and whether an evolutionary function provides an historical or forward-
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8 looking explanation depends on the time when the trait tokens made or make their contributions
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10 to fitness. Their account thus recognizes all three senses as legitimate and having distinctive
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12 explanatory uses as required by the Dykhuizen-Hartl and gene-sharing models we considered
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14 above. While Walsh and Ariew don't explicitly address the possibility of their joint necessity for
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16 answering some explanatory problems, they don't rule this out either. For this reason, we treat
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18 their version of hierarchical monism as consistent with the protein function evolution case.
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24 However, we argue that the semantic relationships asserted by existing hierarchical
25
26 monist accounts are not well supported. One criticism of existing hierarchical accounts is that
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28 they fail to encompass all definitions relevant to the life sciences (e.g. Krohs 2007; Boorse 1976;
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30 Moreno and Mossio 2015). The way that organizational function combines etiological and
31
32 system-level properties, for example, poses a major challenge for Perlman's (2009) hierarchy,
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34 which differentiates naturalistic definitions of function primarily by their use of time. More
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36 recently, Saborido (2014) revised Walsh and Ariew's hierarchy by expanding their causal role
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38 branch to incorporate goal-directed and organizational senses of function (Figure 2b). This
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40 update is problematic in a couple ways.⁵ It places goal-directed and organizational functions with
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42 role functions rather than evolutionary definitions, even though fitness is the most common
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44 biological goal used for goal-directed functions, and any contribution to system maintenance in
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46 the organizational account will also be a contribution to survival or persistence. Goal-directed
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48 and organizational functions could therefore be plausibly located under the evolutionary branch
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59 ⁵ It is not clear what distinctions Saborido means to draw between approaches, theories, views,
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61 and definitions in the figure. We will interpret the hierarchy as relating definitions.
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4 instead, which weakens the hierarchy's value as a unification. There is also an ongoing dispute
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6 about whether the organizational account covers all etiological functions, e.g. functions with
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8 purely reproductive benefits for an individual, or vice versa (Artiga 2011, Saborido et al. 2011,
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10 Artiga and Manolo 2016, Mossio and Saborido 2017).

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14 A further criticism of (Walsh and Ariew 1996; Perlman 2009; Mahner and Bunge 2001)
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16 is that their accounts have the problematic consequence of limiting function attributions to parts
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18 of systems, thereby overlooking functions of properties of whole systems.⁶ Cummins (1975)
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20 noted that causal role explanations are neither necessary nor useful for system dispositions that
21
22 can be subsumed under physical laws. He gives the bouyancy of objects in water as a paradigm
23
24 example, since the phenomenon is better explained by more general physical laws relating net
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26 force to motion than an analysis of the causal relationships between the object's material parts.
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28 Nonetheless, the trait of bouyancy can be selected for over time in a way that produces an
29
30 etiological function. Moreover, a variety of other important biological traits, such as body mass,
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32 body size, and territory size, can have histories of positive selection and hence etiological
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34 functions without requiring any analytical decomposition of the system into parts. It is not the
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36 case, then, that every etiological function implies the existence of a causal role function at some
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38 point in time. As a result, the logical hierarchies asserted by their accounts fail to provide the
39
40 necessary progressive differentiation of all definitions from a single unique root.
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48 *6.3 Fuzzy Monism*

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50 A fuzzy monist account ascribes gradual, vague, or fuzzy boundaries to a term. As these
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52 adjectives suggest, one can identify a range of more specific versions of fuzzy monism, including
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58 ⁶ Walsh and Ariew in particular move ambiguously between attributing functions to parts and
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60 traits without clarifying whether their concept of trait also includes properties of whole systems
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62 (e.g. Walsh and Ariew 1996, p. 493, 501–2, 506).
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4 cluster concepts such as Richard Boyd’s homeostatic property clusters (Boyd 1999),
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6 mathematical fuzzy sets, and similarity to an exemplary case. Peter Godfrey-Smith’s (2009)
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8 account of Darwinian individuality is an excellent illustration of the last type. What these
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10 versions of fuzzy monism share in common is that the correct usage of term is defined according
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12 to a potential instance’s relation to a single reference standard, which then can be measured in
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14 various ways.
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19 Interestingly, there is no standing fuzzy monist account of biological function. In her later
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21 work, Millikan explicitly treats etiological and causal role functions as lacking clear-cut
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23 boundaries, but only in the context of defending a pluralist account (Millikan 2002). Since her
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25 use of fuzzy boundaries does not prove central to our arguments in this paper, we will not treat
26
27 the issue in more depth but have included for the sake of completeness.
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30 31 **7. Pluralist Accounts**

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33 In turning to consider pluralist accounts, we carry forward two main conclusions from the
34
35 previous section. First, biologists and philosophers recognize multiple distinct senses of function
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37 as appropriate to different explanatory goals. Second, the currently recognized definitions of
38
39 function are not consistent with the semantic structure posited by hierarchical monism. Function
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41 therefore doesn’t satisfy the requirements of any existing monist account.
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46 It is important, then, to clarify what distinguishes disjunctive and integrative pluralism.
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48 We take both pluralist accounts to reject the semantic structure hierarchical monism describes (as
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50 well as the semantic structures described by fuzzy monist accounts, although these is not relevant
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52 here). For example, a pluralist view might describe the definitions for a term as exhibiting a
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54 family resemblance with no single condition shared universally in common. Massimo Pigliucci
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56 has proposed such an account of species (Pigliucci 2003). Family resemblance rules out
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4 hierarchical monism by eliminating the possibility of a unique, core set of necessary conditions
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6 from which all other meanings can be differentiated. Among the two pluralist accounts, the key
7
8 discriminator will be whether the account treats each meaning of function as relevant for distinct,
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10 non-overlapping sets of problem solutions (disjunctive pluralism) or as co-occurring together in
11
12 some cases (integrative pluralism).
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15 16 *7.1. Disjunctive Pluralism* 17

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19 In a disjunctive account, definitions are not competitors in the sense that we expect one of
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21 them will turn out best but we're uncertain about which one (see Mitchell 2002). In other words,
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23 it isn't an early stage of hard monism where analysis has yet to uncover the one right definition.
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25 Furthermore, a disjunctive account asserts that each sense of the term is useful for answering
26
27 different, non-overlapping sets of research questions. Most of the functions literature, for
28
29 example, is devoted to analyzing how functions are explanatory in distinctive ways, each
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31 scientifically legitimate in its own right (Mitchell 1995; Wouters 2007; Perlman 2009). There is
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33 also an ongoing debate over whether any non-historical definition of function is capable of
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35 supporting normative judgments about malfunction (Kingma 2010; Boorse 2014; Saborido et al.
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37 2016).
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44 As we've noted, some philosophers take the further step of claiming that each discipline
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46 within biology is only interested in one sense of function (Godfrey-Smith 1993; also see Garson
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48 2017). So only evolutionary biologists are concerned with evolutionary functions, for instance,
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50 while molecular biologists only address causal role functions. Justin Garson (2017) critiqued this
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52 between-discipline pluralism using a more generalized definition of selected effects function that
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54 encompasses other selection processes besides natural selection. Garson instead argues for
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56 within-discipline pluralism, which recognizes that disciplines outside evolutionary biology are
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4 sometimes interested in using function attributions to explain the etiological existence of a trait.
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6 However, he still treats problems whose solutions reference etiological functions as disjoint from
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8 those referencing role functions.
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11 Neither between- or within-discipline pluralism is consistent with the explanations
12
13 provided by the protein function evolution models we described. The use of evolutionary,
14
15 propensity, and causal role functions in explaining the same phenomenon (the fixation of a gene
16
17 duplication) shows that there's at least one group of biological research problems where these
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19 meanings co-occur in the solutions. Moreover, the different senses of function involved are
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21 attributed to different entities: evolutionary function is attributed to copies of the duplicated
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23 gene, propensity function to the trait of having the duplication, and causal role function to amino
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25 acids in the genes' protein products. The multiple senses of function are therefore not co-
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27 occurrent simply by implication, e.g. because attributing evolutionary function to a part implies
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29 the part must also have had a causal role function in the past. The epistemic goal of explaining
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31 *change* in evolutionary functions thus integrates meanings of function in a way not recognized
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33 by either between or within-discipline pluralism as Garson describes them. Other philosophers
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35 have made a related point about how scientists use function to explaining design constraints and
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37 exaptation (Amundson and Lauder 1994, Wouters 2003).
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45 *7.2. Integrative Pluralism*

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48 Integrative pluralism, like disjunctive pluralism, rejects the patterns of semantic
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50 relationships among definitions asserted by any of the monist accounts. The key difference
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52 between disjunctive and integrative pluralism therefore lies in how they describe the patterns of
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54 use for different senses of function.
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4 We briefly summarize the two separate lines of evidence we've presented that provide
5 support for integrative pluralism against its main competitors, hierarchical monism and
6 disjunctive pluralism. The primary evidence against hierarchical monism comes from our
7 arguments in Section 6.3 against the hierarchical semantic structure it requires based on the
8 difficulty of placing organizational functions in any hierarchical account and the fact that
9 evolutionary functions do not always apply to parts of systems. If a new account addressed these
10 points, then hierarchical monism and integrative pluralism would be equally supported by
11 current evidence.
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23 The evidence against disjunctive pluralism comes from Section 7.1, where we showed
24 how models explaining protein function evolution show that different senses of function serve
25 disjoint epistemic goals and hence figure in the solutions to disjoint sets of research problems.
26 While it is certainly true that biologists use evolutionary, propensity, and causal role functions in
27 isolation to explain distinct phenomena, the Dykhuizen-Hartl and gene-sharing models show that
28 sometimes multiple senses are needed to explain the same biological phenomenon. The type of
29 pluralism that best fits how biologists use function in practice therefore goes beyond whether any
30 single biological discipline pursues both etiological and systems explanations as goals.
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43 Given our conclusion that integrative pluralism is at present the best-supported account,
44 we turn to discuss broader implications. Mitchell's original argument for integrative pluralism
45 made central use of incompatible idealizations between multiple models for the division of labor
46 in social insect colonies (Mitchell 2002; Mitchell 2003). Our argument for integrative pluralism
47 about function, however, does not depend on incompatible idealizations. Rather, we take
48 integrative pluralism to require only the unavailability of any logical unity appropriate to a
49 monist schema. Mitchell also used the models' incompatibility to give an in-principle argument
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4 against future theoretical unification, but we are not making a similar claim against the in-
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6 principle possibility of unifying function definitions.
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9 Another difference is the role that compositional levels play in the protein folding
10 evolution case. Mitchell was concerned to show that conflict across levels is possible for
11 explaining insect division of labor, but that the models captured different causal factors (e.g.
12 genetics versus social interaction), each of which mattered for the complete explanation. In our
13 case, all the evolutionary models involve processes operating on multiple levels, from the
14 biochemistry of the protein to drift and selection acting on the whole population. But the
15 integration we sought to show was not in fact between the *models* of protein function evolution.
16 Instead, what mattered was that the models explained evolutionary change by integrating
17 different *senses* of function.
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30 31 **8. Conclusion**

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33 In his well-known article arguing for consensus without unity, Peter Godfrey-Smith
34 asked, “What reason is there to use the word ‘function’ for both Wright and Cummins functions?
35 What do the concepts have in common that justifies this usage? My reply is: there is no strong
36 reason for using the same word” (Godfrey-Smith 1993, 206). In contrast, we have argued for a
37 pluralist account of function that recognizes an epistemically virtuous coherence among
38 definitions in their joint use for explanation. Even in the absence of a logical unity, then,
39 integrative pluralism can still provide a basis for considering the set of definitions as a whole
40 worth more than the sum of its parts.
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53 Still, why include only some meanings under a term, given that solving any scientific
54 problem will require the use of many concepts? Technical terms like “function” are still words in
55 natural language that humans use as tools to reason and communicate, and this should matter for
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4 any practice-oriented conceptual analysis. While philosophers have traditionally prized the
5 clarity that comes with assigning a distinct name to each meaning, biologists are not axiom
6 systems and must pay a price in cognitive load, training, and social enforcement to master new
7 technical terms. Recent experiences with standardizing terminology in big data biology provide
8 excellent examples of these difficulties (Millerand et al. 2013; Leonelli 2016; Franz and Sterner
9 2018). When we find an established scientific term that fits integrative pluralism, we should
10 consider whether keeping one ambiguous label for all the senses in use may actually facilitate
11 their emergent value in solving problems (Currie 2014). Of course, we can always have more
12 precise names for each sense, such as “evolutionary function” and “role function,” but there are
13 good reasons why we don’t simply relabel them with unrelated strings of letters.
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28 Adding integrative pluralism to our repertoire for conceptual analysis highlights the
29 importance of carefully enumerating the problems in which a term is used. Too often monism
30 about a term has appeared reasonable only because philosophers have surveyed a small or
31 idiosyncratic sample of its usage and then generalized to all other cases. Similarly, we may find
32 more examples of scientific terms whose definitions have only been analyzed in isolated contexts
33 of use but which in fact work together jointly for some problems. Justin Bzovy (2017) has
34 independently proposed a related “toolbox” view of species concepts, for example.
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45 Indeed, biologists use function for purposes beyond explanation, and these purposes
46 deserve greater attention now that we have established practical integration among definitions as
47 an important point for conceptual analysis. In particular, we believe there are considerable
48 insights to be found in studying how biologists use function in generalization and inference
49 (Amundson and Lauder 1994; Walsh and Ariew 1996; Autumn, Ryan, and Wake 2002; Cuthill
50 2005; Brandon 2013; Wimsatt 2013; Currie 2014). Denis Walsh and Andre Ariew, for example,
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4 have claimed that “evolutionary functions are discovered by conducting [role]-function analysis”
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6 (Walsh and Ariew 1996, 508). This is incorrect if read as a universal generalization: methods
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8 exist for discovering a history of positive selection using protein sequence alignments that do not
9
10 require any knowledge of the causal role functions of the amino acids (Dittmar and Liberles
11
12 2011). In fact, the inferential path can also run the other direction: biologists regularly use
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14 estimates of amino acid substitution rates based on protein families that share a history of natural
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16 selection to make predictions about causal role functions across evolutionarily unrelated genes
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18 (Arenas 2015). Biologists also invoke different meanings of function in developing a
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20 methodological error repertoire (Mayo 1996) for making inferences about evolutionary history
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22 (Autumn, Ryan, and Wake 2002).
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29 Further study of protein function evolution may also provide new insights into other
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31 aspects of the function debate, including how rate and context figure into individuating functions
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33 and making normative judgments about malfunction (Binney 2018a; Binney 2018b; Hausman
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35 2014; Kraemer 2013; Garson and Piccinini 2014; Kingma 2015). It is suggestive in this regard
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37 that the authors of two major reviews on gene duplication both explicitly raise metaphysical
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39 questions. In trying to classify existing models of protein function evolution, for example,
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41 Matthew Hahn is led to raise
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46 “the ontological question of what makes up a function. For instance, should we
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48 consider paralogous hemoglobin genes to all have the same function or different
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50 functions, as the oxygen-binding affinities differ between fetal and adult
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52 duplicates? If we consider them all to have the same hemoglobin function, then
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54 they are clearly subfunctionalized relative to the single-copy ancestor. But if we
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4 think that they have taken on new and different functions, then the duplicates are
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7 neofunctionalized” (Hahn 2009, 611).
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9 Similarly, Joram Piatigorsky (2007) was driven to devote a whole chapter of his book on the
10 gene sharing model to analyzing the question, “What is a gene?” One reason is that which model
11 best explains the fixation of a gene duplication critically depends on correctly determining the
12 number of functions the gene possesses over time. These are interesting metaphysical issues with
13
14 a clear basis and significance in biological practice and deserve further philosophical attention.
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Fig. 1 Three categories of models explaining the fixation of duplicated genes. Circles represent gene expression regulatory regions and rectangles represent protein-coding genes. Neofunctionalization involves the creation of a new evolutionary function. Subfunctionalization splits two or more preexisting evolutionary functions among the gene copies. Gene conservation maintains the original evolutionary functions in all copies. The Dykhuizen-Hartl and gene-sharing models are examples of neo- and subfunctionalization, respectively. Functions may change through sequence evolution in regulatory regions (a) or protein-coding regions (b). From (Hahn 2009).

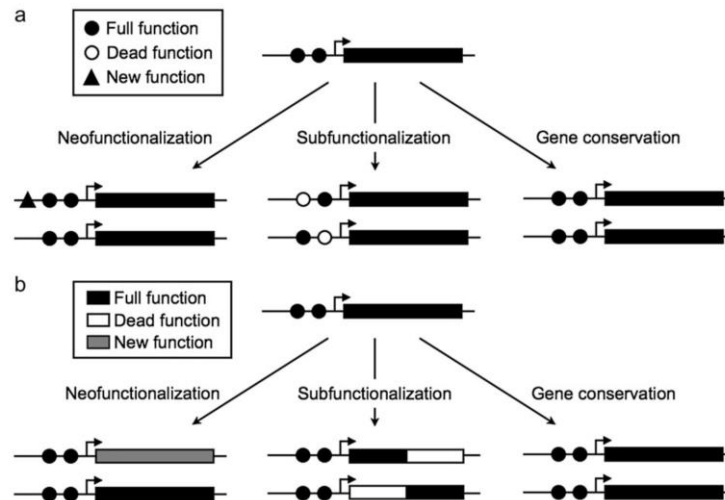


Fig. 2 Two hierarchical accounts of function. (a) Denis Walsh and Andre Ariew's (1996) account. (b) Saborido's (2014) revision of Walsh and Ariew adding the organizational and goal-contribution accounts.

