Article

A Shot in the Arm for Philosophy of Biology: How to Treat Infectious Diseases

SAGE Open
January-March 2014: 1–14

DOI: 10.1177/2158244014529134
sgo.sagepub.com
SAGE

Constance Bradley[1]

Abstract

This article analyzes infectious diseases (IDs) within a philosophy of biology framework to locate factors that play a role in the development of a successful account of IDs. One way to handle the analysis of kinds in biology is through a traditional essentialist approach whereby biological entities are construed as natural kinds with essences. Approaching IDs in this way is unworkable, however, because it is difficult to find essences that occur in all and only IDs. Rather than engaging IDs from this perspective, my analysis of the nature of IDs more appropriately falls under the rubric of philosophy of biology whereby I treat particular IDs as products of evolution with a unique relationship to the biological hierarchy. This approach is what I refer to as an *evolutionary perspective* of IDs because it emphasizes that the constituent mechanisms and processes of ID are sensitive to evolutionary pressures. Such an approach is useful because it allows us to sidestep difficulties pervasive traditional kind essentialist accounts of ID. To begin, I analyze two contemporary methods for analyzing kinds in biology—Richard Boyd's Homeostatic Property Cluster (HPC) kind approach and Paul Griffiths' treatment of kinds with historical essences. I discuss both approaches and identify the limitations of each that prevent a successful account of IDs. I then analyze how elements of each account can be revised into a successful philosophy of biology approach to IDs. The article is concluded with a brief discussion of the benefit of incorporating an evolutionary perspective into the analysis of IDs and outlines future projects that result from approaching IDs from an evolutionary perspective.

Keywords

infectious disease, epidemiology, evolutionary biology, natural kinds, philosophy of science

A frequent starting point for investigating the nature of infectious disease (ID) is contemporary philosophy of disease literature. In this tradition, analysis of disease typically turns on whether or not a value-free account of disease is possible. Most authors who discuss the nature of disease contend that the success of a value-free account of disease leaves room for the possibility that disease is a natural kind; that is, divorcing the nature of disease from any values or judgments we have about disease is necessary to conceive of disease as a natural kind. Those arguing in favor of viewing disease as a value-free theoretical notion (such as Boorse, 1977) offer a naturalistic interpretation of disease. Boorse suggests that because a value-free account of disease is possible, diseases may form natural kinds. Boorse (1977) contends that there are natural classes of organisms with uniform functional design and one way we can understand disease is a kind that deviates from this natural design. Proponents of a value-laden account of disease (such as Reznek, 1987, 1995) argue that diseases do not form a distinct natural kind because diseases have neither real nor nominal essences. Reznek (1987) suggests that diseases may have nominal essences but do not form a natural kind because the explanatory nature of a pathological condition is such that it depends on our values and interests. Because it is not possible to divorce a concept of disease from the values we hold about disease, Reznek maintains that diseases are best thought of as an artificial kind existing only because we have an interest in avoiding them.

Although the analyses of disease prevalent in this tradition are interesting in their own right, I suggest a different approach to the identification and analysis of the conceptual issues of ID. The questions and problems at stake in contemporary philosophy of disease literature are much different than the analysis I have in mind; for example, a central problem in philosophy of disease is the role *normalcy* plays in the treatment of what qualifies as a disease. Rather than engaging ID from this perspective, my goal here is to consider ID as a philosopher of biology. Specifically, I treat particular IDs as products of evolution with a unique relationship to the biological hierarchy and, as a result, we can investigate IDs by applying the principles and problems associated with microbes in the evolution of the biological hierarchy and assess related problems. This approach is useful because it allows us to sidestep problems encountered in philosophy of

[1]Phoenix, AZ, USA

Corresponding Author:
Constance Bradley, PhD, Phoenix, AZ 85023, USA.
Email: constance23@me.com

disease literature. A challenge I face is that philosophers of biology have not dedicated much time to examining disease. O'Malley and Dupré (2006) consider microbes in general (i.e., both pathogenic and nonpathogenic microbes) and show how recent advances in microbiology bear on issues such as levels of selection, the nature of multicellularity, and understanding of evolutionary mechanisms. As a result of such advances, they urge philosophers to pay closer attention to microbes and incorporate microbial insights into philosophy of biology investigations. Framing my discussion of IDs in the context of philosophy of biology highlights that the mechanisms and systems involved in delimiting entities such as pathogens and the capacity for immune response are products of evolution and tightly tied to the biological hierarchy, thereby yielding a robust account of IDs.

One way to handle the analysis of kinds in biology is through a traditional essentialist approach whereby biological entities are construed as natural kinds with essences. Approaching IDs in this way is unworkable because it is difficult to find essences that occur in all and only IDs. Contemporary methods for analyzing kinds in biology are offered by Richard Boyd's Homeostatic Property Cluster (HPC) kinds approach and Paul Griffiths' treatment of kinds with historical essences.[1] In this article, I introduce novel criticisms of both HPC kinds and historical essence approaches via IDs and then evaluate portions of each approach that can be salvaged for a successful philosophy of biology analysis of IDs. Instead of sketching out a variant account of HPC kinds or kinds with historical essences, my goal in this article is to demonstrate that we can sidestep concern over essentialism altogether and give attention to articulating the components necessary for a successful account of IDs. To begin, I discuss HPC kinds and identify the limitations of this approach that prevent a successful account of IDs as HPC kinds. Next, IDs are evaluated according to both broad and narrow understandings of Griffith's treatment of kinds with historical essences. I evaluate why accounting for IDs according to a narrow understanding of Griffiths' approach results in what I call the one-factor problem. I propose revisions to the broad sense of Griffiths' approach and argue that such modifications provide a richer account of extrinsic relational properties, which can therefore successfully account for IDs. I then revisit both Boyd's and Griffith's accounts and examine how components of each approach could be part of a successful philosophy of biology approach to IDs. The article is concluded with a brief discussion of the benefit of incorporating an evolutionary perspective into the analysis of IDs.

HPC Kinds and the Homeostatic Problem

Traditionally, natural kind theory rests on strict kind essentialism, as can be seen in the works of Plato (1997; *Phaedo* 76d, 102b; *Phaedrus* 265d) and Aristotle (1999; *Metaphysics* 1030a3, 1034a6) and more recently in Kripke (1972) and Putnam (1975). Ereshefsky (2001) explains four main tenets of such a view. First, all and only the members of a kind share an essence; second, that essence is a property (or a set of properties) that has an explanatory value about the features and characteristics of members of that kind; third, a kind's essence causes the necessary properties shared among members of a kind; fourth, a kind's essence explains the presence of all other contingent properties that entities of a kind may possess. Richard Boyd (1999) rejects natural kind essentialism and instead argues in favor of the view that kinds are defined by HPCs, which allow for a degree of indeterminacy in their extensions. Boyd discusses at length what he considers to be features of HPCs; I will highlight three of the most important here. First, HPC kinds are groups of entities that share contingently clustered properties such that the properties co-occur in an "important number" of cases. Second, such clustering is "homeostatic" in that an underlying mechanism maintains the presence of the cluster of properties. Third, the causal significance of HPCs, taken with the underlying homeostatic mechanism, allows the entities to which the HPCs apply to serve as a natural kind. HPC kinds theory has been applied to many things, including Boyd's forceful argument that species are HPC kinds.

Applying Boyd's view to IDs means that, for any given particular ID to qualify as a HPC kind, the ID must be characterized by a group of contingently clustered properties that are caused by an underlying homeostatic mechanism. Robert A. Wilson (1999) endorses and expands upon Boyd's idea. He begins with an acceptance of Boyd's view and further elaborates on the "homeostatic" mechanism that maintains clustering of properties. An entity's possession of any one of the properties from the cluster increases the likelihood that the entity will also possess other properties from the same cluster. This fact, R. A. Wilson states, is a causal feature of the world and provides a predictive value. "The instantiation of certain properties," R. A. Wilson writes, "increases the chance that other particular properties will be coninstantiated because of underlying causal mechanisms and processes" (p. 197). Thus, we are able to make predictions of an entity's properties by knowing that it is a member of a HPC kind. R. A. Wilson also points out how clustering plays two roles in the HPC theory. First, an entity need instantiate *enough* of a cluster of defining properties for it to belong to a kind (as opposed to traditional kind essentialism under which an entity must instantiate all and only the defining properties to belong to the kind). Second, the defining properties themselves tend to cluster or *hang together* and are coninstantiated in the world (R. A. Wilson, 1999).

Although a familiar application of HPC kinds theory is to species, Boyd argues that many other philosophical categories and relations might also be usefully thought of as HPC kinds. It should be mentioned, however, that neither Boyd nor R. A. Wilson discusses IDs. My contribution, therefore,

is to test the HPC kinds approach and determine if IDs can be successfully individuated as HPC kinds. A good way to begin such an investigation is to employ the ID cholera as a test case. This will demonstrate why, in practice, conceptualizing IDs as HPC kinds does not render a successful account of IDs.

When applying the HPC kinds approach to a particular ID, the main question at stake is whether or not the ID exhibits clustering of properties produced by an underlying causal mechanism. Using cholera as an example of a particular ID, we can begin to map out an answer to that question. Particular cases of cholera share a cluster of properties such as presence of *Vibrio cholerae* bacteria; physical symptoms such as diarrhea, extreme thirst, poor skin turgor, sunken eyes, weak pulse, vomiting, wrinkled hands/feet, and abdominal cramps; transmission via a fecal–oral route from drinking-contaminated water; eating shellfish that originate from certain parts of the ocean; ingesting food cooked in contaminated water; and expression of the virulence factors of *V. cholerae* bacteria (Sack, Sack, Nair, & Siddique, 2004).

To explain why a case of cholera instantiates these properties, we can appeal to the homeostatic mechanisms that operate to ensure the stasis of the ID cholera. The underlying homeostatic mechanisms for cholera are the pathogenesis[2] of *V. cholerae* and the virulence factors expressed by *V. cholerae* that affect its interaction with the host and the environment. On a HPC kind view, this information can be used to make predictions about properties of the ID cholera. That is, knowing the homeostatic mechanisms underlying the ID, we can speculate about the likelihood that a patient presenting diarrhea and wrinkled hands/feet is instantiating a case of the ID cholera.

One of the main benefits of the HPC view of natural kinds is that it allows for indeterminacy and vagueness in its extensions. This attribute is well suited for analyzing particular IDs, because different cases of an ID will instantiate properties of the disease imperfectly. Consider the variety of ways the properties of cholera are instantiated among cases of cholera. Some cases progress quickly, whereas others progress slowly; some cases display every physical symptom, whereas other cases display only a few or none at all; some cases are transmitted through a fecal–oral route and others by ingesting shellfish. Unlike a traditional essentialist view, imperfect instantiation of shared properties does not preclude specific cases of an ID from being members of that ID construed as a HPC kind. Cases need to only instantiate enough of a cluster of properties that are homeostatically sustained by underlying mechanisms to be considered members of the kind cholera. Viewing particular ID in this way is therefore useful because it eliminates concern over how to classify cases of a particular ID that do not appear to possess every known property associated with the ID. Nonetheless, despite the benefit of viewing particular ID as a HPC kind, a significant problem—what I call the *homeostatic problem*—results from this construal.

The Homeostatic Problem

Due to the evolution of virulence factors and pathogenicity, we might wonder if such homeostatic mechanisms are really homeostatic at all. I suggest that, because homeostatic mechanisms of an ID can change without resulting in a change in the properties of the ID, property clusters of a particular ID are not tightly linked to an underlying mechanism. I contend that putative homeostatic mechanisms of an ID are not appropriately connected to properties instantiated by that ID and, as a result, relying on such mechanisms to individuate IDs results in a homeostatic problem. The consequence of the homeostatic problem is that any predictive value associated with individuating IDs as HPC kinds is lost because properties of an ID do not predict the kind of entity that ID is. Moreover, conceptualizing IDs as HPC kinds leads to a proliferation of groupings that produce uninteresting inferences. I conclude this section with a brief discussion of why the homeostatic problem reveals difficulties with HPC kinds theory in general.

HPC kinds theory depends on the underlying homeostatic mechanism to cause the clustering of properties shared by members of the kind. However, homeostatic mechanisms of IDs are not reliably connected to property clusters of IDs in the way HPC kinds theory requires because underlying homeostatic mechanisms do not maintain the presence of clusters of properties instantiated by IDs. Homeostatic mechanisms of IDs, such as virulence factors and pathogenicity, are not static entities; they are dynamic biological processes constantly undergoing change. Properties instantiated by cases of ID *may or may not* be sensitive to changes in underlying virulence or pathogenicity mechanisms. For example, differences in virulence genes between *V. cholerae* serotypes may or may not result in changes in properties of cholera (see Table 1). The O1 and O139 serotypes of *V. cholerae* are dissimilar in terms of serology and virulence; however, O1 and O139 are phenotypically identical and the clinical symptoms displayed are nearly identical between cases of each strain. As such, changes in underlying mechanism may not affect properties of an ID. Conversely, the cholera toxin (CT) gene sequences of O1 and O139 are the same and the same transcriptional activator (ToxR) controls production of virulence factors in both strains. O139, however, produces larger amounts of CT and is considered more virulent due to its ability to survive aquatic conditions of spreading more rapidly among hosts than O1. Properties of ID can therefore change in ways that do not correspond to changes in underlying mechanisms.

The previous example serves to highlight unreliable connections between *V. cholerae* virulence mechanisms and properties of cholera. This concept bears on whether construing IDs as HPC kinds retains the predictive value required by the HPC kinds approach. Advocates of a HPC approach may respond to this point by stating that unreliable connections between *V. cholerae* virulence mechanisms and properties of

Table 1. Properties of Cholera May or May Not be Different Across Different *V. cholerae* Serotypes.

***V. cholerae* serotypes and cholera outbreaks**
• *V. cholerae* reservoirs include rivers, coastal waters, and estuaries (Krauss et al., 2003).
• Seven recorded cholera pandemics; the first began in 1817 (Hays, 2005).
• More than 155 serotypes of *V cholerae*; only a few serotypes are toxigenic and serve as the etiologic agent of cholera (Faruque & Mekalanos, 2003; M. Wilson, McNab, & Henderson, 2002).
• Toxigenic serotypes evolved from environmental nonpathogenic (i.e., do not cause disease) serotypes through acquisition of virulence genes (Faruque & Mekalanos, 2003).
• OI serotype responsible for most cholera epidemics and can be divided into "El Tor" and "Classical" biotypes (M. Wilson et al., 2002).
• El Tor is responsible for the ongoing cholera pandemic; strains isolated from 1881 and 1899 pandemics were of Classical serotype (M. Wilson et al., 2002).
• In 1992, non-OI serotype (0139 Bengal) isolated as a sole causative agent of cholera outbreak in India (McClane & Meitzner, 1999).
• OI and 0139 cases of cholera demonstrate nearly identical clinical symptoms and modes of transmission (Hoge, Bodhidatta, Echerverria, Deesuwan, & Kitporka, 1996).
• OI and 0139 strains are phenotypically identical in that both belong to group I of Heiberg's classification (i.e., both strains ferment sucrose and mannose but not arabinose) and the nucleotide sequence of the cholera toxin (CT) gene is identical in both strains (Nair et al., 1994).
• Transcriptional activator ToxR regulates production of virulence factors (CT and toxin-coregulated pili) in both OI and O139 (Waldor, Colwell, & Mekalanos, 1994).
• Despite nucleotide sequences of OI and 0139 CT genes being identical, 0139 produces larger amounts of CT than OI (Nair et al., 1994).
• It is also suggested that 0139 is more virulent and ecologically robust with significant pandemic potential because 0139 spreads more rapidly in populations and has a sustained ability to survive in aquatic environments (Dalsgaard & Larsen, 1995).

cholera are not ruinous to understanding IDs as HPC kinds. In situations where genes controlling the virulence factors and pathogenicity of the O1 and O139 serotypes evolve such that cases of O1 and O139 no longer share common properties, the result is two new HPC kinds (and, consequently, two new IDs)—O1 cholera and O139 cholera. This response may momentarily deflect concerns about unreliable connections among homeostatic mechanisms and properties. However, it exposes another difficulty for the HPC kinds approach, namely, that we are able to individuate O1 and O139 cholera as different kinds only once we have an account of why any given homeostatic mechanisms are the relevant homeostatic mechanisms underlying an ID. The HPC kinds approach posits a homeostatic mechanism as a means of providing a causal account of why members of a HPC kind instantiate certain traits and features; the approach does not explain what it means for a homeostatic mechanism to be bound to the properties and features instantiated by a HPC kind. Determining which homeostatic mechanisms are relevant to individuating an entity is not a result of any predictive value associated with a HPC kind; instead, to individuate something as a HPC kind, we must have prior knowledge of what counts as the relevant underlying causal mechanisms of that kind. The difficulty for the HPC kinds approach is that establishing what it means for any given homeostatic mechanism to count as the homeostatic mechanism relevant to a HPC kind collapses into the homeostatic problem.

Similar concerns have been raised regarding the sufficiency of homeostatic properties. Slater (2014), for example, worries that the existence of an underlying homeostatic mechanism responsible for clustering of some properties is not, by itself, enough ground claims about the sort of thing an entity is. This is because the underlying homeostatic mechanism(s) that maintain the stable instantiation of an entity's properties depend on enabling mechanisms that keep the homeostatic mechanisms active (Slater, 2014). A HPC kinds approach is only made possible by a series of mechanisms that support underlying homeostatic mechanisms. At worst, this line of thought ends in regression; at best, it takes us far afield from a mere homeostatic causal mechanism as we must search for a mechanism that guarantees stability, so as to provide a basis for making epistemic claims (Slater, 2014).

The HPC kinds approach allows for homeostatic mechanisms and property clusters of a HPC kind to evolve over time. In the case of species, Boyd (1999) claims that factors such as gene exchange, reproductive isolation, common selective pressures, co-adapted gene complexes, and so on serve as homeostatic mechanisms within a biological species. Boyd (1999) also maintains that multiple and varied types of homeostatic mechanisms can be found among members of a HPC kind and, furthermore, the property clusters and underlying homeostatic mechanisms may change over time such that conditions for what counts as members of a particular HPC kind may vary over time. In the case of species, the aforementioned homeostatic mechanisms acting to maintain the integrity of any given species are susceptible to evolutionary pressures and, as a result, evolve and change over time. Analogously, underlying mechanisms of IDs evolve over time, thereby producing multiple and varied homeostatic mechanisms among any particular ID. Boyd could therefore reply that it does not matter *which* mechanism acts to maintain the integrity of an ID, as long as enough of them are acting at any given time. HPC kinds are not therefore wedded to any particular mechanism. Indeed, advocates of the HPC kinds approach laud this feature as one of its primary advantages. As a result, individuating an entity as a HPC kind and the ability to make inferences about that kind requires only the existence of *some* underlying causal mechanism that maintains a cluster of properties.

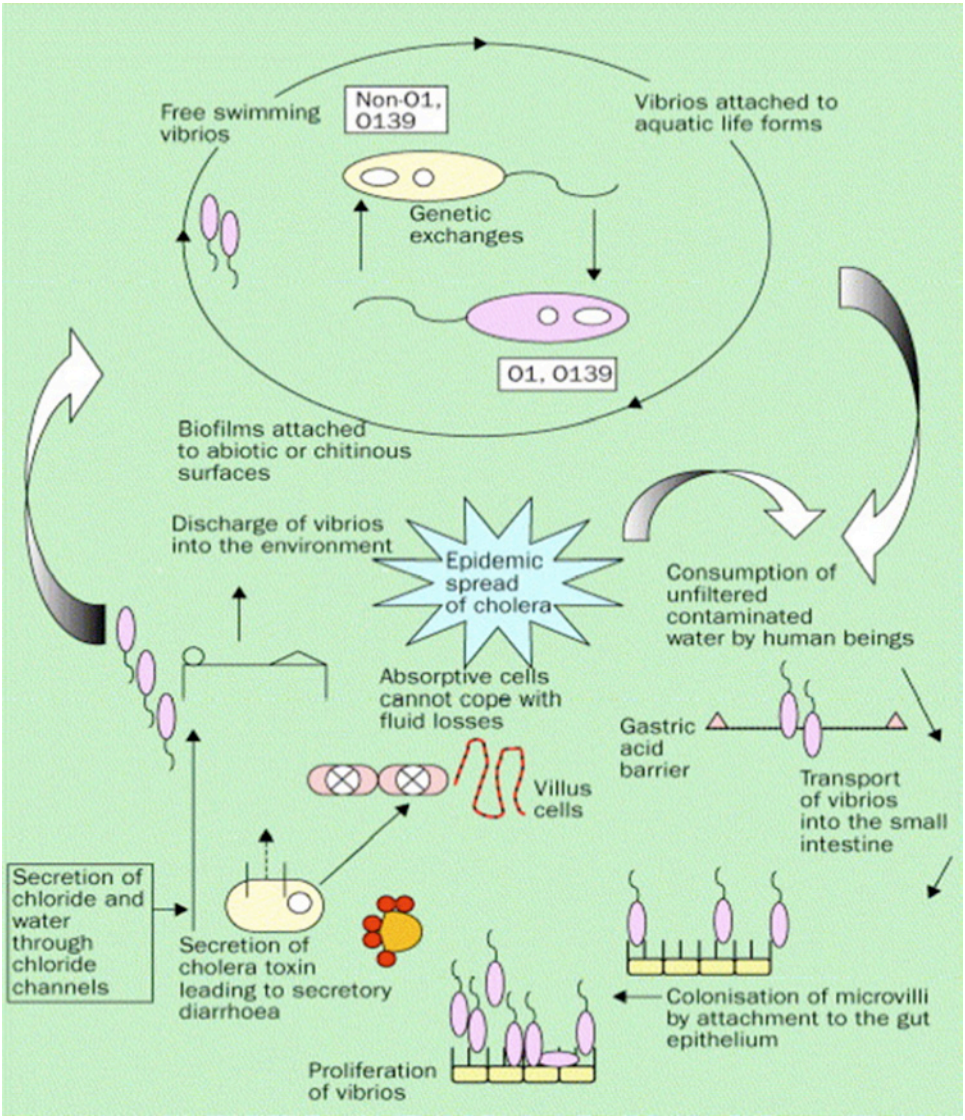

Figure 1. Life cycle of *V. cholerae* involves both environmental and human segments, which sometimes intersect.
Source. Figure from Sack, Sack, Nair, and Siddique (2004). Reprinted with permission from Elsevier, copyright (2004).

Such a response is ultimately unsatisfactory because it does not address the crux of the homeostatic problem. In terms of IDs, properties instantiated by cases of an ID may or may not be sensitive to changes in underlying virulence or pathogenicity mechanisms because IDs and their underlying mechanisms (such as virulence factors) are each evolved entities. Because homeostatic mechanisms of IDs such as virulence factors can evolve and fluctuate over time, then property clusters of a particular ID are not tightly linked to an underlying mechanism, and what counts as a virulence factor of an ID varies. Boyd can defend HPC kinds theory on this point; what cannot be accounted for, however, is that a multiplicity of homeostatic mechanisms within any given ID obscures the ability to make predictions about the sort of entity that ID is. Because the cluster of homeostatic mechanisms of an ID arises from a varied assortment of possible mechanisms, we must determine what homeostatic mechanisms are relevant to individuating an ID at a given time.

For any given ID, there are several different underlying mechanisms that generate properties we care about. Consider, for example, the varieties of underlying mechanisms *V. cholerae* are exposed to during its life cycle that affects virulence and pathogenicity, none of which are necessary for conferring its virulence or pathogenicity. Figure 1 shows the life cycle of *V. cholerae* and such mechanisms include attachment to aquatic life forms, formation of biofilms, colonization of intestinal milieu, secretion of CT, and environmental

interactions when immediately discharged from host. Which of these mechanisms are the ones at work to generate the virulence and pathogenicity of *V. cholerae* changes gradually over evolutionary time (which Boyd can account for) and also change between generations. As a result, the factors affecting the underlying mechanisms of *V. cholerae* evolve so frequently and rapidly that it is unclear what mechanisms are at work in maintaining the properties of cholera at any given time.

One way Boyd could respond to this point would be to claim that the factors underlying homeostatic mechanisms of an ID could be treated as HPC kinds themselves. Consequently, something like the *V. cholerae* attachment to chitin or colonization of intestinal milieu could be construed as both underlying homeostatic mechanisms of cholera as well as properties of cholera that are themselves maintained by underlying mechanisms. This response effectively pushes HPC kinds down a level whereby the underlying mechanisms *of* underlying mechanisms are understood as HPC kinds. In this way, it would not matter which mechanisms act to maintain the integrity of *V. cholerae* virulence, only that there are enough mechanisms acting at any given time and such mechanisms could change rapidly between generations. The difficulty with this answer is that when we start treating the factors underlying mechanisms as HPC kinds, the HPC kinds approach becomes attenuated in a way that challenges its explanatory force. To individuate something as an ID, we must determine which homeostatic mechanisms are at work on different levels; this includes ascertaining both the homeostatic mechanisms, which maintain the properties of the ID, as well as the homeostatic mechanisms that underlie this first level of homeostatic mechanism. There need not be infinite regress of levels of homeostatic mechanisms for the original motivation of approaching entities as HPC kinds to be sorely tried. HPC kinds approach is lauded by its proponents for its flexibility; it allows for a great deal of leeway in the properties instantiated by a kind while providing a method by which we can make robust inferences about that kind. Nonetheless, if we were to understand the factors affecting underlying homeostatic mechanisms of a kind as HPC kinds themselves, the HPC kinds approach becomes a less efficient method for making inferences. At each level, we construe homeostatic mechanisms as HPC kinds, it becomes more difficult to maintain the explanatory value of the entity about which we were originally interested in making inferences. For IDs to be a kind with the robust sort of explanatory value claimed by proponents of the HPC approach, we must be able to ascertain a great deal of information about the various levels of homeostatic mechanisms at work within that kind. This sort of information relies, in part, on our ability to have a complete and detailed scientific and epidemiologic profile of an ID; it is incredibly difficult (and, in some situations, nearly impossible) to gather this information.

Kinds With Historical Essences

Although the aforementioned homeostatic problem is an issue for the HPC kinds approach, it may be possible to apply an associated perspective in hopes of gaining a better account of ID. Paul Griffiths (1999), whose view is derived from Boyd's, argues in favor of recognizing the role played by extrinsic relations in generating instances of a kind. Griffiths' account seeks to modify what it means for something to serve as an essence of a kind to avoid the entanglements of traditional essentialist views. Griffiths' concept of natural kinds revolves around three main points. First, natural kinds are necessary for induction and explanation, and they represent theoretical categories "that we judge to be projectable, which requires them to enter into lawlike, counterfactual supporting generalizations" (p. 219). Second, kinds are "defined by the processes that generate their instances, and for many domains of objects, these processes are extrinsic rather than intrinsic to the instances of the kind" (p. 219). Third, the "causal homeostatic mechanism that guarantees the projectability of a kind plays the traditional role of an essence, but it need not be a traditional, microstructural essence" (p. 219).

The main focus of Griffiths' project is the application of his line of thinking about natural kinds to species taxa. Species (what he calls cladistic taxa) have historical essences and no other essential properties. Species taxa are a kind defined by a shared history, which is an extrinsic relation among members of the kind. Furthermore, shared history serves as the causal homeostatic property of a species taxa because it guarantees projectability of the kind. According to Griffiths, there is a Darwinian basis for thinking that shared history contributes to shared morphological and physiological characters among members of species taxa. The phylogenetic inertia of the principle of heredity is what allows the induction and explanation of a host of properties (e.g., morphological, physiological, behavioral) using kinds that are defined solely in terms of common descent (Griffiths, 1999). As such, properties occurring in one organism are more likely to occur in related than unrelated organisms. The predictive value of the historicity of species collects "more correlations between characters, from molecular to behavioral, than any other taxonomy we know how to construct" (p. 219). This predictive force allows organisms to be grouped into natural kinds. Furthermore, Griffiths claims that causal mechanisms such as gene exchange or niche selection reinforce phylogenetic inertia "in keeping the members of a species clustered together in the space of biological possibility" (p. 219). Griffiths' historical approach to classification differs from Boyd's HPC kinds theory; HPC kinds theory emphasizes the causal mechanisms within members of a kind whereas Griffiths' historical view emphasizes the causal relations among the entities being individuated (Ereshefsky, 2001).

It is possible to understand Griffiths' view in two senses—both broadly and narrowly. A broad construal considers

extrinsic relational properties in general whereas a narrow understanding concerns historical essences, which are a specific type of extrinsic relational property. In what follows, I conduct a dual investigation of how IDs might be accounted for under both narrow and broad senses of Griffiths' account. Under a narrow construal, the issue is whether IDs have historical essences in the same way Griffiths takes species taxa to have historical essences. A broad application explores extrinsic relations of IDs more generally. Each will be considered in turn.

In the narrow sense, individuating IDs as kinds with historical essences prioritizes shared history and therefore circumvents the homeostatic problem encountered when individuating IDs as HPC kinds. Recall the cholera example mentioned previously where I argued that, because properties of cholera are not reliably and appropriately linked to underlying causal mechanisms, there is no predictive value associated with individuating cholera as a HPC kind. Such a problem does not exist if we view particular IDs, such as cholera, as natural kinds with a historical essence. Analogous to Griffiths' view of species, we can posit the historical essence of a particular ID as the profile of its underlying infectious agent. This is because infectious agents involved in IDs belong to an evolutionary lineage much in the same way that species belong to an evolutionary lineage in Griffiths' view. On this account, so long as the infectious agents involved in cases of a particular ID share a historical origin, then cases of that ID will be members of the same kind regardless of any other properties instantiated. With this in mind, it is possible to reexamine what it might mean if the O1 and O139 serotypes of *V. cholerae* evolved divergently whereby each serotype expressed completely different virulence factors and pathogenesis and, consequently, the only property shared by cases of O1 and O139 cholera is the presence of *V. cholerae.* On this construal of Griffiths' account, provided that O1 and O139 serotypes of *V. cholerae* share a historical origin, cases of O139 cholera and O1 cholera will be members of the same kind because O1 and O139 serotypes belong to the same genealogical nexus.

The One-Factor Problem

Classifying ID based on historical essence certainly disengages the homeostatic problem resulting from Boyd's HPC kinds approach. However, because individuating IDs as kinds with a historical essence ultimately classifies ID based solely on the historical origin of an infectious agent, it results in what I call the *one-factor problem.* Griffiths' analysis of species treats historical essences as both necessary and sufficient for individuation. For IDs, a historical component is necessary but not sufficient for individuation. Because a variety of biological processes are involved in IDs, individuating IDs according to only one factor (such as a historical essence) does not take into account the complex nature of such processes.

An example of such complexity is a particular ID with multiple infectious agent etiologies, such as conjunctivitis where simultaneous polymicrobial infection occurs (Tuft, 2006). If the various microbes involved in conjunctivitis each have a different historical origin, then one may wonder how the ID known as conjunctivitis would be differentiated. Griffiths might respond that *conjunctivitis* is mistakenly thought of as a single kind, when it actually is a term that picks out a constellation of various IDs (much like the term *common cold*) and subsequently, many kinds of conjunctivitis can exist, each with its own microbial etiology and corresponding historical origin. Such a response allows conjunctivitis to be individuated in a way consistent with Griffiths' view, and therefore results in several kinds of conjunctivitis (e.g., *conjunctivitis X, conjunctivitis Y, conjunctivitis Z*, etc.) based on the different kinds of microbial etiologies involved. Such a response is not entirely satisfactory because individuating the different types of conjunctivitis in this way still relies on one factor, namely, the historical lineage, which constitutes the essence of each type of conjunctivitis. A more fundamental issue, however, is that polymicrobial IDs are not disjunctions, such that only one microbe is present; a single case of conjunctivitis involves several different microbes (and therefore, multiple historical lineages and multiple essences) simultaneously. The difficulty is that this issue leaves open the question of how one ought to determine which of the various involved historical essences have priority in individuating conjunctivitis.[3]

To address this issue, we could consider the possibility of individuating polymicrobial IDs based on an amalgamation of various historical essences. This might be analogous to what occurs in the case of lichen, where a particular fungus (a mycobiont) and an algae (a photobiont) conjoin to create a symbiosis known as lichen. Lichens incorporate at least two distinct organisms, each with its own evolutionary history (Bungartz, 2001). Lichen individuation is based on the history of the lichenized fungi; that is, the way a fungus is associated with a photobiont[4] (Bungartz, 2001; Tehler, 1996*)*. Correspondingly, polymicrobial IDs could be individuated based on the associations among the involved microbes. Suppose, for example, a bacterium and a virus (each with their own historical essences) interact such that a case of conjunctivitis is generated. Analogous to the lichenized fungi, individuation of the conjunctivitis could be based on the historical essence of the *conjunctivitized virus* (i.e., the way the virus relates to the bacteria such that conjunctivitis occurs).[5] Although this possibility is worth mentioning, it still does not go all the way in successfully individuating conjunctivitis. Conjunctivitis may in fact have its own historical essence that is derived from the conjunctivized virus. However, the relation among the microbes involved is just one of many relations at work in producing a case of conjunctivitis. Factors such as the vulnerability of a host, the means by which the infectious microbes are transmitted, or conditions of the external environment may all be relevant in

determining whether a case of conjunctivitis develops. The conjunctivized virus may be necessary to individuate conjunctivitis, but it is not sufficient.

Individuating IDs according to historical essence runs into a related difficulty when we consider that several different ID etiologies cite the same microbe as the infectious agent. *Staphylococcus aureus*, for example, is the etiologic agent in IDs such as septicemia, pneumonia, urinary tract infections, infective endocarditis, toxic shock syndrome, and scalded skin syndrome (Todar, 2007). If it is the case that the *S. aureus* involved in each of these IDs shares a historical origin then, on Griffiths' view, all of these aforementioned IDs must be classified as one kind based on a shared microbial history. However, by relying on only one factor, such a classification fails to properly individuate IDs with *S. aureus* as the infectious agent because other factors are necessary for the proper individuation of each ID. For example, the pathogenesis and virulence factors of *S. aureus* in toxic shock syndrome are different than the pathogenesis and virulence factors exhibited in scalded skin syndrome whereas *S. aureus* involved in impetigo and infective endocarditis are acquired through different modes of transmission (Keys, 2008; Todar, 2007). Microbial etiology is therefore one of several factors necessary for appropriate individuation of IDs.

Despite historical essences of microbes not being sufficient for the individuation of IDs, this example illustrates the possibility that higher level individuation might be accomplished with this method. That is, *S. aureus*, as the only factor under consideration, does not adequately individuate particular IDs, but does individuate a class of IDs with *S. aureus* as microbial etiology. Other factors, such as modes of transmission and virulence, can be used to further individuate IDs belonging to the class. Thus, pneumonia would not be individuated as the same kind of ID as scalded skin syndrome. However, pneumonia and scalded skin syndrome could belong to the same class of IDs because they are closely related due to the shared history of their microbial etiology. The upshot of individuating IDs as kinds with historical essences is that a historical component is necessary but not sufficient for individuation. Polymicrobial IDs and IDs with shared microbial etiology demonstrate why more than one factor is necessary to portray the complex biological processes comprising IDs.

This same reasoning is exactly why intrinsic properties do not individuate species well. Identifying species according to an intrinsic essence such as morphology or similar genes fails to individuate species in a way that is consistent with modern evolutionary theory. Analogously, identifying IDs according to historical components only is unsuccessful because it fails to capture other relevant nonhistorical factors that are necessary for individuation. As such, Griffiths' view is useful in bringing to light the necessity of a historical factor in ID individuation, but further analysis shows why historical essences are not sufficient for individuating IDs.

While individuating IDs as kinds with historical essences may not produce a satisfactory account of ID, examining how a broader scope of extrinsic relations applies to individuation of IDs provides a framework from which we can build a workable version of Griffiths' account. Griffiths claims that processes generating instances of a kind are, for most entities, extrinsic to instances of that kind. For IDs, there are two types of extrinsic relationships that stand in need of analysis: the relationships existing among instances of a kind and the relationships existing between instances of a kind and entities external to the kind. It is important to point out that instances of an ID are considered cases of the ID. In the first analysis, extrinsic relations considered to be underlying homeostatic causal mechanisms of an ID must obtain among instances (i.e., cases) of an ID. That is to say, the relation between cases X, Y, and Z of Hepatitis is considered an underlying causal mechanism of Hepatitis. The extrinsic relationship among cases of a particular ID, which play a causal role in linking together properties of a particular ID, is the transmission of the microbial infectious agent. However, individuating ID simply based on extrinsic relations among cases of ID also results in the one-factor problem. Transmission of a microbe is not the only factor that generates instances of an ID. Other factors, such as host vulnerability, which is a process that does not depend on extrinsic relations between cases of ID, and environmental conditions, which is a process that depends on relations external to cases of ID, must also be considered to give a complete account. Extrinsic relations among members of a particular ID cannot therefore be the only factor under consideration when determining what processes generate instances of a kind.

This leads to the second type of extrinsic relationships that generate instances of ID: those relations completely external to a particular ID (i.e., the relationship does not occur among members of the kind but instead holds between a particular case of an ID and external factors). Griffiths (1999) argues that relationships external to a kind can generate instances of a kind and, as an example of this, he claims that "characteristic ecological successions represent natural kinds in ecology, the causal homeostatic mechanism for the kind 'Fiordland rainforest succession' will include the available range of seeds and other propagules, the climate of the region, and so forth" (p. 218). On Griffiths' account, all that is necessary for a natural kind to exist is a causal process (what he calls homeostatic mechanisms) in nature connecting several different properties of the objects influenced by that process. The ID parallel to this example is that if we consider IDs kinds defined by extrinsic relations, the causal homeostatic mechanisms generating instances of the kind consist of pathogen(s), host(s), any possible vector(s), and environmental conditions of a particular ID. These mechanisms are extrinsic relations in that they occur between cases (i.e., instances) of an ID and factors external to those cases. In this way, cases of an ID share a constellation of similar

properties based on how the cases stand in relation to extrinsic factors. For example, bacterial gastritis in cheetahs is associated with the presence of *Helicobacter pylori.* Environmental and host conditions such as captivity, diet, and stress levels are extrinsic relations that play large and varied roles in whether or not the presence of *H. pylori* in a cheetah's stomach results in the development of bacterial gastritis (Munson et al., 2005). Relations external to the kind, therefore, serve to generate instances of bacterial gastritis.

Griffiths argues that extrinsic relations can be viewed as homeostatic mechanisms of a kind, but this view is problematic because what serves as homeostatic mechanisms of an ID kind can be shared among supposedly different ID kinds. For IDs, the same pathogen(s), host(s), any possible vector(s), and environmental conditions can be associated with more than one ID. In such situations, there must be an account of how ID kinds that share homeostatic mechanisms are individuated by which other extrinsic factors play a role in the individuation.[6] If this is lacking, then supposedly different kinds of ID could be conflated as the same kind. Consequently, extrinsic relations alone (conceptualized as homeostatic mechanisms of a kind) do not do the work of individuating; to avoid a one-factor problem, other extrinsic factors are necessary to individuate ID.

To understand this completely, consider the example of sinusitis and otitis media, which are typically individuated as two different IDs. The homeostatic mechanisms of bacteria-mediated sinusitis are relationships between *Streptococcus pneumoniae* bacteria; transmission through inhalation; environmental factors such as time of year, geographic location, and population size; virulence factors such as pneumococcal surface protein A (PspA) and a polysaccharide capsule; pathogenesis including nasopharyngeal colonization and subsequent spread to sinuses; and host vulnerability factors such as immunodeficiency, alcoholism, and malnutrition (Todar, 2007). The homeostatic mechanisms of bacteria-mediated otitis media (middle ear infection) are exactly the same as sinusitis, except *S. pneumoniae* bacteria are spread to the ear rather than the sinuses. Because each ID shares the same homeostatic mechanism, what is used to individuate these IDs from one another? One possibility would be to conclude that sinusitis and otitis media are different ID kinds because the physical symptoms and location of bacteria in each ID manifest in different locations of the host's body.

If IDs are individuated based on the location of physical symptoms/microbes, then we must be careful to understand the nuances of this approach. If we think that location is *the* single criterion that can be used to individuate ID, then tuberculosis, strep throat, the common cold, and pneumonia could be classified as the same kind because each of these diseases manifest in one location. As a result, we would be relying on a single factor to distinguish between different types of IDs. This is also a one-factor problem, although it is of a different ilk than the one-factor problem previously mentioned. The one-factor problem I discussed above concerned individuating an entity based on only one factor, such as historical essence (i.e., using one factor to identify an entity). The one-factor problem at stake here concerns situations where multiple factors are shared among different entities, yet there is only a single difference between factors and that difference is what is doing the individuating (i.e., using one factor to distinguish between entities). Of the multiple factors that are shared among different entities, it is not the case that all factors are necessary and sufficient conditions for distinguishing that entity; sometimes a single difference is *the* relevant one. Therefore, what is up for grabs in this one-factor problem is determining what makes this single difference significant such that it can be successfully used to distinguish among different kinds. The salient difference maker in this example just so happens to be location—the physical location of bacteria and physical symptoms *are* a relevant difference that can be used to distinguish between sinusitis and otitis media. The upshot is that we must be careful not to fall into the trap of thinking that location will always be a relevant difference maker—it is not the case that we will always know the relevant distinguishing factor.

Griffiths' argument is friendly to this point and it is possible to amend his approach in such a way that it gives a robust account of how extrinsic relational properties can successfully individuate IDs. When discussing extrinsic relations, Griffiths does not claim that only one extrinsic relation can generate instances of a kind. In applying his account to species, Griffiths claims that species have only historical essences and no other essential properties. This does not mean that Griffiths' account excludes the idea of multiple extrinsic relations; in the case of species, Griffiths is making the claim that there is only one extrinsic relation (historical essences) that generates instances of the kind. Species, however, do not translate directly to IDs—whereas Griffiths approached species as being individuated by a single factor, IDs are more complex and there are many relations that obtain between cases such that they cohere as an ID. As a result, we can bootstrap Griffiths' account to accommodate the possibility of multiple extrinsic relationships generating instances of a kind. So long as it is the case that a single extrinsic relationship is not always the most relevant criterion for individuating a kind, then a one-factor problem does not result from this analysis. Individuating IDs based on physical location in a host's body is therefore not as disreputable as it initially appears so long as it is not claimed that location is the universal individuating criterion of IDs. Furthermore, we must also bear in mind that relevant differences can exist between IDs based on the location of a microbe/physical symptoms within a hosts' body, and such differences might be relevant enough to draw a distinction between ID. The location of an ID's physical manifestation in conditions such as otitis media and bacterial sinusitis is a relevant difference between the two IDs because this difference allows a distinction to be drawn between two IDs that share many common underlying mechanisms. Conversely, the location of the physical manifestation of strep throat and

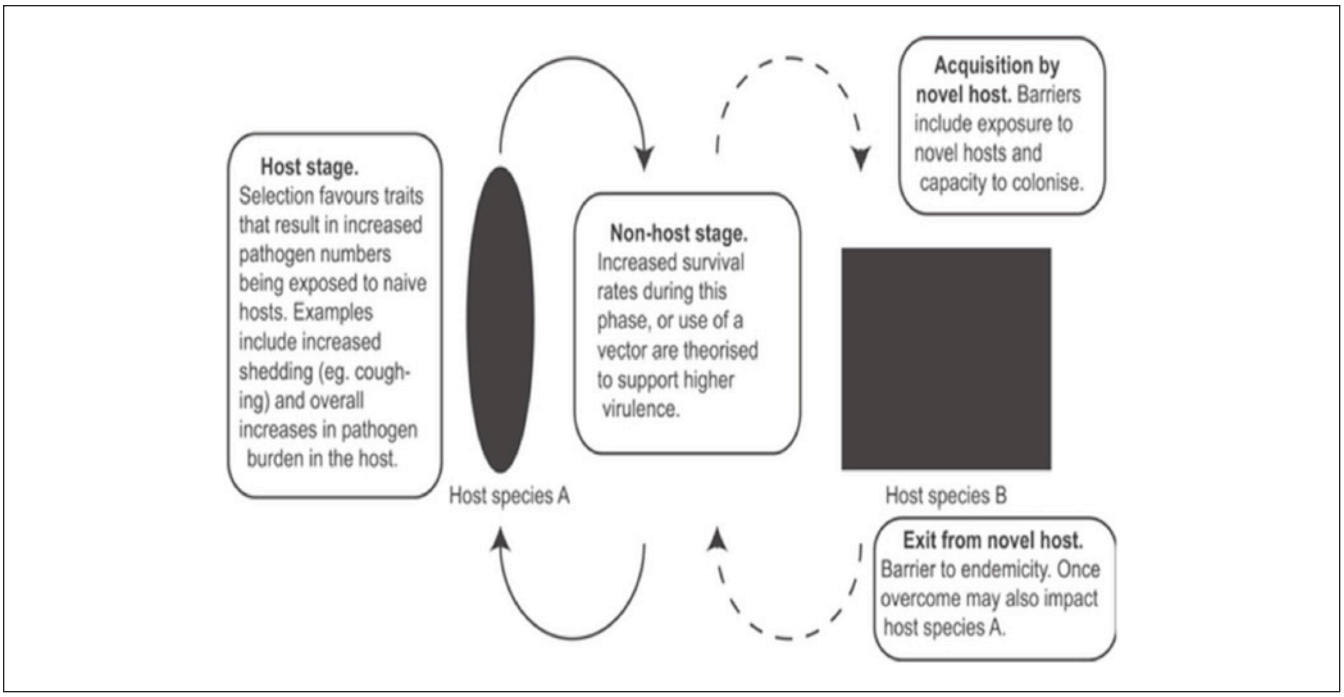

Figure 2. Flow diagram of a generic pathogen life cycle indicating the selective pressures that have been suggested or shown to be important in shaping pathogen virulence.
Source. Figure from Brown, Wickham, Coombes, and Finlay (2006). Reprinted with permission in accordance with the Creative Commons Attribution License (CCAL).
Note. Although Brown et al. differentiate "Host species A" from "Host species B," it is also possible to interpret this figure as the microbial transmission between A and B to be intraspecific.

tuberculosis may not be a relevant similarity because each ID presents a different microbial and epidemiological profile. The upshot of this analysis is that it draws attention to the importance of how multiple factors play a role in the individuation of IDs. When the individuating criterion of an ID is a single extrinsic relationship, such as shared history or microbial etiology, we are then committed to distinguishing the ID by one factor and therefore fail to account for multiple factors that play a role in generating instances of the ID. Griffiths' apparatus of thinking about extrinsic relationships as defining biological entities can therefore be applied to IDs with the recognition that multiple extrinsic relationships serve as criteria that are relevant to individuating IDs. Under this revision, Griffiths' theory is able to give a richer account of extrinsic relational properties and therefore individuate IDs successfully.

A Successful Philosophy of Biology Account of IDs

In the previous sections, approaching IDs as either HPC kinds, kinds with historical essences, or kinds individuated according to extrinsic relations brought to light the importance of avoiding the homeostatic and one-factor problems. My goal in this section is to stake out the basic elements of what a successful account of ID must include to circumvent each of these problems. Recall the homeostatic problem came to light when attempting to individuate IDs as HPC kinds. The homeostatic problem underscores that properties of IDs are not reliably connected to underlying mechanisms and, as a result, the HPC kind does not have a predictive value in the way required by HPC kinds theory. To avoid this problem, a successful account of IDs must take into consideration the dynamic nature of ID processes and constitutive elements.

This notion is especially evident if we consider that both pathogens and hosts are involved in complex evolutionary processes. Consequently, pathogen and host evolution occur both independently and as a result of interaction with one another (Lederberg, 1997). As an example of this idea, we can consider selection pressures affecting virulence traits of a pathogenic microbe. The life cycle of a microbe is itself a varied entity as some microbial life cycles (e.g., helminths) require interaction among multiple hosts, other microbes have direct host-to-host life cycles (e.g., HIV), and still other microbes (e.g., *V. cholerae*) can successfully live outside of a host for its entire life cycle (Brown, Wickham, Coombes, & Finlay, 2006). A variety of selective pressures act on a microbe during each phase of its life cycle in ways that affect its overall virulence. Figure 2 graphically demonstrates this idea. In the host stage, selection favors microbial traits that serve to expose the microbe to naive hosts (i.e., exposure

traits). When a novel host acquires a microbe, selection pressure shifts favoring exposure traits to those traits that increase capacity to invade and colonize. When exiting a novel host, selective pressure exists for the microbe to overcome barriers to endimicity, such as drug treatments. In the nonhost stage, it is posited that selective pressures act to increase survival rates and possibly integrate use of a vector as a way to increase overall microbial virulence.

Examining selective pressures of pathogenic microbial virulence factors only describes one side of the virulence factor equation, however, because selective pressures are also simultaneously acting on host immune capacity and response mechanisms, which in turn affect a pathogen's virulence factors. Furthermore, dynamic processes affecting virulence factors are just one contributor to the dynamic nature of IDs. The same story can be told regarding the dynamics of microbial pathogenicity, host immunology, environmental factors, and the interactions among them. For instance, a variety of environmental factors—such as weather, water and air temperature, and host population size—are all dynamic processes in their own right, as well as the dynamic interaction occurring between these factors and a microbe. We must therefore recognize that IDs are themselves dynamic entities that result from the interaction among a variety of factors, where many of these factors are dynamic processes in and of themselves.

Therefore, the issue at stake in avoiding the homeostatic problem is that these processes are not merely dynamic over long stretches of evolutionary time, but dynamic over such a short time scale that it is unclear what the underlying homeostatic mechanisms are at any given time. We could attempt to push a HPC kinds approach over this obstacle by construing these dynamic processes as HPC kinds; that is, understanding IDs as HPC kinds maintained by underlying dynamic processes, which are also HPC kinds maintained by their own underlying dynamic processes. Such an idea, however, waters down our ability to make inferences about IDs; for there to be any explanatory advantage to IDs, we must be able to ascertain *which* dynamic processes are the homeostatic mechanisms of the ID and, furthermore, which dynamic processes are the homeostatic mechanisms of these dynamic processes. However, because these processes evolve and change very rapidly, it is extremely difficult (if not impossible) to pinpoint the dynamic processes at work in any given slice of time. We expend a great deal of effort to ascertain which dynamic processes are homeostatic mechanisms and do not gain a lot of predictive value about the kinds of entities IDs are in return. In this way, analyzing IDs according to the HPC kinds approach is similar to owning a super-size sports utility vehicle—costly to operate with inefficient fuel economy.

Examining the dynamic nature of IDs leads to a discussion of how to avoid the one-factor problem. Recall the central issue of this problem is that classifying IDs based on only one factor generates an incomplete account of ID. This is because grouping IDs according to only one factor (such as organ system affected or microbial etiology) not only combines several IDs usually considered distinct entities but also fails to account for multiple factors that contribute to generating instances of IDs. In order to not miss out on important aspects of ID, a successful account of ID cannot rely solely on one criterion to individuate ID. Moreover, we must also bear in mind that these factors are not necessarily perfectly instantiated in every case of a particular ID. Imperfect instantiation of properties was one of the main benefits of viewing ID as HPC kinds or as extrinsic relational property kinds. As such, the notion of imperfect instantiation need not be jettisoned. If a successful classification of ID takes into consideration multiple factors that generate instances of ID, then accounting for imperfect instantiation of those factors in cases of ID must also occur.

So far, we see that successful account of ID must take into consideration the dynamic nature of ID, the multiple factors involved in generating instances of IDs, and imperfect instantiation of these factors in cases of IDs. I suggest that these points can be addressed by incorporating an evolutionary perspective into the analysis of IDs. Such a perspective emphasizes that the constituent mechanisms and processes of IDs are sensitive to evolutionary pressures. Moreover, the constituent mechanisms and processes of IDs are themselves products of evolutionary processes. A successful account of IDs must therefore embrace that ID mechanisms and ID processes are simultaneously sensitive to current evolutionary pressures and the result of an evolutionary process.

Consider, for example, virulence factors of bacteria, which result from interactions among bacteria, hosts, and environmental conditions. For pathogenic bacteria to evolve relationships with eukaryotic hosts, it is necessary for bacteria to possess the capacity to develop coordinated gene expression in response to the host environment (S. I. Miller, Hoffman, & Sanowar, 2007). This is because bacteria must be able to "regulate the production and secretion of toxins and other virulence factors temporally and spatially during infection to evade host immune functions, and to enable colonization and sometimes invasion of host tissues" (S. I. Miller et al., 2007, p. 85). To coordinate gene expression in response to a host environment, bacteria must be able to sense and respond to molecular clues present in the host. It is thought that mechanisms bacteria use for sensing molecular cues of the host environment (and consequently regulating virulence toxins) evolved from systems used to recognize environmental cues present in prokaryotic microbial communities, before the presence of eukaryotes (S. I. Miller et al., 2007; Torres et al., 2007). Thus, bacterial capacity for environmental sensing mechanisms evolved, in part, due to selective pressure produced by the evolutionary transition from prokaryotic to eukaryotic organisms.

Similar investigations of the evolutionary origin of mechanisms that contribute to an entity's capacity to function in a particular way relevant to an ID can be accomplished for any

number of capacities, such as immune response. Such investigations are beyond the scope of this project. Rather than to provide a complete account of the evolutionary origin of these capacities, the purpose of the present analysis is to demonstrate that a successful account of what sort of entity IDs are informs the study of the evolution of new levels of biological organization. A generalized account of ID evolution, which formulates ID evolution diachronically, emphasizes the evolved nature of an entity's capacity to participate in ID processes and draws out how the investigation of the evolution of IDs can be conducted in a fine-grained manner. The evolutionary origin of capacities that may be *the* relevant participating processes of IDs can be studied in further detail, such as examining the origin of those mechanisms leading to the capacity for pathogenesis or immune response. This research informs the study of evolutionary transitions because we can evaluate whether the origin of these mechanisms is coincident with evolutionary transition and, if so, whether their origin bears on the emergence of new levels of organization

Understanding IDs through the lens of an evolutionary perspective makes it apparent why, to give a complete account of IDs, we cannot neglect that ID mechanisms and processes are evolved features. This is why, as discussed in the example above, an infectious agent must evolve capacity for pathogenicity and virulence and why a host must evolve an immune system in such a way that it is able to respond appropriately to infectious agents[7] for ID to be present. Bringing an evolutionary perspective to bear on ID analysis accounts for the dynamic nature of IDs, the multiple factors involved in generating instances of IDs, and imperfect instantiation of these factors in cases of IDs. Conducting this type of analysis highlights that the existence of IDs depends on three factors: a host with an appropriately evolved immune system, an infectious agent with an appropriately evolved capacity for pathogenicity, and a coevolved relation between the two. Such assessment is a value additive because it lays groundwork for future investigation of IDs as well as the study of evolution of the levels of biological organization.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research and/or authorship of this article.

Notes

1. Other variants of the Homeostatic Property Cluster (HPC) approach exist, namely, the Stable Property Cluster (SPC) kind approach put forth by Slater (2014). SPC kinds prioritize the stability a cluster of properties possesses, thus providing the cluster with explanatory and inductive values. What sets Slater's account apart from the HPC kinds approach is that Slater's SPC kinds approach focuses on the sort of stability in which epistemic claims could be grounded rather than the underlying mechanism that is causing that stability. Although Slater's position is worthwhile to consider, a review of HPC kind variants is not in the scope of this article. Instead, I have narrowed the focus and consider only Boyd's and Griffiths' approaches. Although neither is recent, per se, both approaches have been widely and enthusiastically received as tenable methods to account for biological entities (namely, species). I therefore focus attention to assessing whether either of these fundamental approaches are widely applicable to biological entities beyond species, namley infectious diseases (IDs).
2. Pathogenesis is the "capacity of a microbe to cause damage in a host" and a virulence factor is "a component of a pathogen that damages the host; can include components essential for viability including modulins" (Casadevall & Pirofski, 1999, p. 3704). It is recognized that the term *damage* is a contentious notion and stands in need of further philosophical analysis. For purposes of this study, however, the concept of "damage" is left unanalyzed as such analysis is beyond the scope of the current project.
3. It is noteworthy that, given the above analysis of the homeostatic problem, a HPC kinds approach would also fail to account for IDs with multiple microbial etiologies such as conjunctivitis. Because the cluster of homeostatic mechanisms of an ID arises from a varied assortment of possible mechanisms, we are left to determine what homeostatic mechanisms are relevant to individuating an ID at any given time. This is information gained from previous understanding of the properties and homeostatic mechanisms of an ID rather than from the HPC kind itself. As such, we must have prior knowledge of what cases are considered conjunctivitis and their associated homeostatic mechanisms at any given time to definitively individuate conjunctivitis as a HPC kind and subsequently describe the properties and homeostatic mechanisms of conjunctivitis.
4. Bungartz (2001) explains, "This concept may be difficult to understand but there are several reasons why the taxonomy of lichens is largely the taxonomy of lichenized fungi. The mycobiont is an obligate symbiont. Under natural conditions lichen fungi have not been found free-living. The photobiont cells are facultative symbionts which an frequently be found independent of the lichen symbiosis. A huge diversity of lichen fungi can be distinguished whereas only very few species of photobionts have been found in a lichen symbiosis."
5. I recognize that not all cases of conjunctivitis involve both a bacterium and a virus; some conjunctivitis involves only bacteria, some involve only viruses, and some involve only fungi, and other cases involve a variety of combinations among different types of bacteria, virus, and fungi. By calling this relationship a "conjunctivized virus," I am following Bungartz's lead in discussing "lichenized fungi." Bungartz refers to the algae/fungus symbiosis as "lichenized fungi" because the fungi are rarely found independent (i.e., free-living) from the symbiosis. Similarly, I call the bacteria–virus relation that results in conjunctivitis a "conjunctivitized virus" because viruses are not free-living in a way that bacteria are. Regardless, I employ this term solely for the sake of example and as such one should not read too much into it.
6. A similar criticism has been directed against Developmental Systems Theory (DST). DST broadens the notion of what can

be included as a causal agent of an organism's developmental system to include more than just genes. Under this view, however, a problem persists regarding how developmental systems are delimited and how organisms sharing developmental systems are individuated (see Griesemer, Haber, Yamashita, & Gannett, 2005; Griffiths & Gray, 1994).

7. This is why, for example, even though bacteriophages can induce minor host response when present in bacteria (Karlsson, Malmborg-Hager, Albrekt, & Borrebaeck, 2005; Osterhout, Figueroa, Keasling, & Arkin, 2007), bacteriophages would not be considered ID under this analysis because the host bacteria do not have an appropriately evolved immune system to respond to the bacteriophage in a relevant way.

References

Aristotle. (1999). *Metaphysics* (A. Madigan, Trans.). Oxford, UK: Oxford University Press.

Boorse, C. (1977). Health as a theoretical concept. *Philosophy of Science*, *44*, 542-573.

Boyd, R. (1999). Homeostasis, species, and higher Taxa. In R. A. Wilson (Ed.), *Species: New interdisciplinary essays* (pp. 141-186). Cambridge, MA: MIT Press.

Brown, N. F., Wickham, M. E., Coombes, B. K., & Finlay, B. B. (2006). Crossing the line: Selection and evolution of virulence traits. *Public Library of Science Pathogens*, *2*, 346-353.

Bungartz, F. (2001). *What is a lichen? An overview on the biology of lichens* (ASU Lichen Herbarium). Retrieved from http://nhc.asu.edu/lichens/lichen_info/lichen_info.jsp

Casadevall, A., & Pirofski, L. A. (1999). Host-pathogen interactions: Redefining the basic concepts of virulence and pathogenicity. *Infection and Immunity*, *67*, 3703-3713.

Dalsgaard, D. A., & Larsen, J. L. (1995). Is *Vibrio cholerae* serotype O139 a potential cause of a new pandemic? *Ugeskr Laeger*, *157*(3), 280-283.

Ereshefsky, M. (2001). *The poverty of the Linnaean hierarchy: A philosophical study of biological taxonomy*. Cambridge, UK: Cambridge University Press.

Faruque, S. M., & Mekalanos, J. J. (2003). Pathogenicity islands and phages in *Vibrio cholerae* evolution. *Trends in Microbiology*, *11*, 505-510.

Griesemer, J., Haber, M. H., Yamashita, G., & Gannett, L. (2005). Critical notice: Cycles of contingency—Developmental systems and evolution. *Biology & Philosophy*, *20*, 517-544.

Griffiths, P. E. (1999). Squaring the circle. In R. A. Wilson (Ed.), *Species: New interdisciplinary essays* (pp. 141-186). Cambridge, MA: MIT Press.

Griffiths, P. E., & Gray, R. D. (1994). Developmental systems and evolutionary explanation. *The Journal of Philosophy*, *91*, 277-304.

Hays, J. (2005). *Epidemics and pandemics: Their impacts on human history*. Santa Barbara, CA: ABC-CLIO.

Hoge, C. W., Bodhidatta, L., Echerverria, P., Deesuwan, M., & Kitporka, P. (1996). Epidemiologic study of *Vibrio cholerae* O1 and O139 in Thailand: At the advancing edge of the eighth pandemic. *American Journal of Epidemiology*, *143*, 263-268.

Karlsson, F., Malmborg-Hager, A. C., Albrekt, A. S., & Borrebaeck, C. A. (2005). Genome-wide comparison of phage M13-infected vs. uninfected Escherichia coli. *Canadian Journal of Microbiology*, *51*, 29-35.

Keys, T. F. (2008). *Infective endocarditis*. Cleveland Clinic Disease Management Project. Retrieved from http://www.clevelandclinicmeded.com/medicalpubs/diseasemanagement/infectious-disease/infectendo/infectendo.htm

Krauss, H., Weber, A., Appel, M., Enders, B., Isenberg, H. D., Schiefer, H. G., . . . Zahner, H. (2003). *Zoonoses: Infectious diseases transmissible from animals to humans*. Washington, DC: American Society for Microbiology Press.

Kripke, S. (1972). Naming and necessity. In D. Davidson & G. Harman (Eds.), *Semantics of natural language* (pp. 253-355). Dordrecht, The Netherlands: Riedel.

Lederberg, J. (1997). Infectious disease as an evolutionary paradigm. *Emerging Infectious Diseases*, *3*, 417-423.

McClane, B., & Meitzner, T. (1999). *Microbial pathogenesis*. Madison, WI: Fence Creek.

Miller, S. I., Hoffman, L. R., & Sanowar, S. (2007). Did bacterial sensing of host environments evolve from sensing within microbial communities? *Cell Host & Microbe*, *1*, 85-87.

Munson, L., Terio, K. A., Worley, M., Jago, M., Bagot-Smith, A., & Marker, L. (2005). Extrinsic factors significantly affect patterns of disease in free-ranging and captive cheetah (Acinonyx jubatus) populations. *Journal of Wildlife Diseases*, *41*, 542-548.

Nair, G. B., Shimada, T., Kurazono, H., Okuda, J., Pal, A., Karasawa, T., . . .Garg, S. (1994). Characterization of phenotypic, serological, and toxigenic traits of *Vibrio cholerae* O139 Bengal. *Journal of Clinical Microbiology*, *32*, 2775-2779.

O'Malley, M., & Dupré, J. (2006). Size doesn't matter: Towards a more inclusive philosophy of biology. *Biology & Philosophy*, *22*, 155-191.

Osterhout, R. E., Figueroa, I. A., Keasling, J. D., & Arkin, A. P. (2007). Global analysis of host response to induction of a latent bacteriophage. *BMC Microbiology*, *7*, 82.

Plato. (1997). *Complete works* (J. M. Cooper & D. S. Hutchinson, Eds.). Indianapolis, IN: Hackett.

Putnam, H. (1975). *Mind, language and reality* (Philosophical Papers, Vol. 2). Cambridge, UK: Cambridge University Press.

Reznek, L. (1987). *The nature of disease*. London, England: Routledge and Kegan Paul.

Reznek, L. (1995). Dis-ease about kinds: Reply to D'Amico. *Journal of Medical Philosophy*, *20*, 571-584.

Sack, D. A., Sack, R. B., Nair, G. B., & Siddique, A. K. (2004). Cholera. *Lancet*, *363*, 223-233.

Slater, M. H. (2014). Natural kindness. *British Journal for the Philosophy of Science*.

Tehler, A. (1996). Systematics, phylogeny and classification. In T. H. Nash (Ed.), *Lichen biology* (pp. 217-239). Cambridge, UK: Cambridge University Press.

Todar, K. (2007). *The nature of host parasite interactions* (Todar's Online Textbook of Bacteriology). Retrieved from http://www.textbookofbacteriology.net/NHPR.html

Torres, V. J., Stauff, D. L., Pishchany, G., Bezbradica, J. S., Gordy, L. E., Iturregui, J., . . .Skaar, E. P. (2007). A Staphylococcus aureus regulatory system that responds to host heme and modulates virulence. *Cell Host & Microbe*, *1*, 109-119.

Tuft, S. (2006). Polymicrobial infection and the eye. *British Journal of Ophthalmology*, *90*, 257-258.

Waldor, M., Colwell, R., & Mekalanos, J. (1994). The *Vibrio cholerae* O139 serogroup antigen includes an O-antigen

capsule and lipopolysaccharide virulence determinants. *Proceedings of the National Academy of Sciences, USA*, *91*, 11388-11392.

Wilson, M., McNab, R., & Henderson, B. (2002). *Bacterial disease mechanisms: An introduction to cellular microbiology*. Cambridge, UK: Cambridge University Press.

Wilson, R. A. (1999). Realism, essence, and kind. In R. A. Wilson (Ed.), *Species: New interdisciplinary essays* (pp. 188-207). Cambridge, MA: MIT Press.

Author Biography

Constance Bradley has a PhD in Philosophy from the University of Utah. She is currently studying Oriental Medicine at the Phoenix Institue for Oriental Medicine and Acupuncture. Her research interests center around the philosophical and conceptual issues of disease theory and the ontology of biologoical objects. Other topics of interest are Oriental Medcine research, including a project on the systematic application and study of acupuncture.