

The holobiont is not a useful model for most host-microbiome interactions

Gavin M. Douglas^{1,*} and S. Andrew Inkpen^{2,*}

¹Department of Biology, University of New Brunswick, Fredericton, New Brunswick, Canada

²Department of Philosophy, Mount Allison University, Sackville, New Brunswick, Canada

*Emails for correspondence: gavin.douglas@unb.ca and ainkpen@mta.ca

Abstract

The holobiont concept refers to a host and its associated microbes. It has been criticized, primarily on the grounds that individual holobionts are not an appropriate level for analyzing multi-generation host-microbiome dynamics, as most microbes are acquired from the environment. The main response has been that, regardless of this criticism, the holobiont concept promotes a more useful, holistic, realistic, and distinctive model of host biology, since hosts are always in association with microbes and phenotypes change in response to these associations. Furthermore, it has been argued that allele frequencies shifting across host populations and microbes shifting in composition across hosts exist on the same conceptual continuum. We demonstrate how this thinking equally applies to entire communities of macro-organisms, and explain that there is no principled reason to privilege hosts and microbiota specifically. We also highlight how employing the holobiont concept creates conceptual confusion regarding host genetic variance. Finally, we discuss the social impacts of this model, particularly in terms of its implicature: what it conveys beyond how it is explicitly defined. Although biological categories have vague boundaries, and vagueness can sometimes be beneficial, we should strive for informative and unambiguous categories. An individual host represents such a category, while a holobiont does not.

Keywords: Holobiont; microbiome; hologenome; metaorganism; unit of selection; individuality

Holobiont terminology

A holobiont refers to a host and microbes living on or within this host (Theis et al. 2016). This term is increasingly used (Stencel and Wloch-Salamon 2022), in keeping with a general increase in microbiome-related publications (**Figure 1**). The closely related terms hologenome (Jefferson et al. 1997; Zilber-Rosenberg and Rosenberg 2008), all genomes within a holobiont, and metaorganism (Bell 1998; Bosch and McFall-Ngai 2011; Bang et al. 2018; Jaspers et al. 2019), a host and associated microbes that have functional impacts within a specific environment, have also become more frequent (**Figure 1**). For instance, recent initiatives and institutional titles explicitly highlight these terms, particularly hologenome (Leonard et al. 2024; Gaun et al. 2025). Here we assess the purported benefits and costs of this terminology and its use as a biological model. Previous critiques primarily addressed the issue of whether the holobiont qualifies as a unit of selection (Moran and Sloan 2015; Douglas and Werren 2016; Skillings 2016; Doolittle and Inkpen 2018). However, not all holobiont theorists used the term in this way, and some holobiont theorists have, in any case, responded to this charge (Theis et al. 2016; Lloyd and Wade 2019). Here we consider their key responses. The primary challenge they face, as we see it, is to develop language that is informative and biologically distinctive—that describes, in a fruitful and non-arbitrary way, biological entities not already covered by more common terminology—as we expand on below. We argue that framing host-microbiome interactions with the above terms is unnecessary and undesirable: though there may be benefits for cross-disciplinary or public-facing communication and interaction, it primarily creates confusion rather than promoting useful and unambiguous communication.

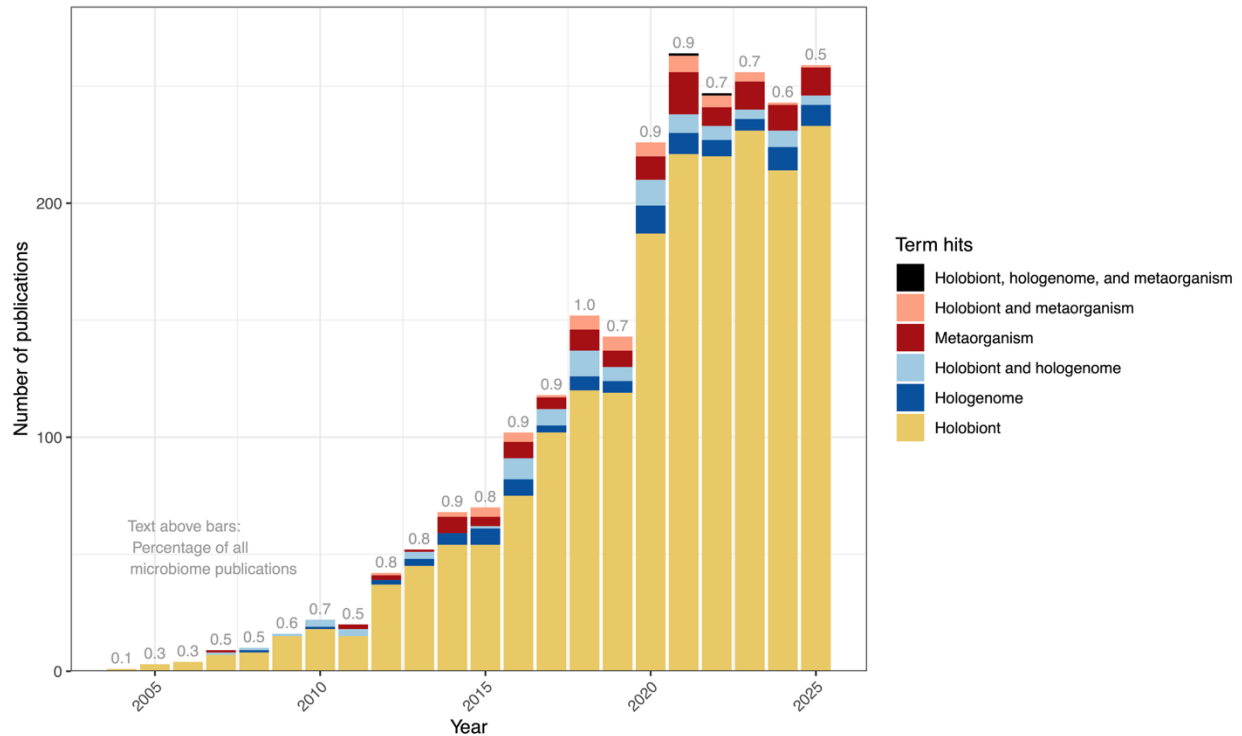


Figure 1: The number of articles and reviews that prominently contain holobiont-related terms from 2004-2025. These data were downloaded from Scopus on April 20, 2026. Matches were only considered within the title, abstract, or keywords of publications. The considered terms are indicated in the legend, and correspond to cases where only those terms were identified. The grey text indicates the percentage of microbiome publications (defined as matching “microbiome”, “microbiota”, “microbial community”, or “metagenome” in the title, abstract, or keywords, or which matched the above holobiont-related terms) that each bar represents. We show these values to give context relative to the overall field, but readers should not over-interpret changes in this percentage over time, as there are many possible driving factors. Only matches to articles and reviews were considered here, but there are additional matches to other formats.

Recent criticisms

The holobiont concept was introduced to describe a few well-known symbioses (Margulis and Fester 1991; O’Malley 2017; Baedke et al. 2020). Using the concept to refer to host-microbiome associations specifically began in the context of coral biology, where it was intended to highlight multispecies dependencies, rather than evolutionary history (Rohwer et al. 2002; Rosenberg et al. 2007). From this context, the term’s reference expanded to

cover host-microbiome interactions across diverse animals and plants, including humans, and in some of these cases it was argued that the holobiont qualifies as a unit of natural selection (Zilber-Rosenberg and Rosenberg 2008; Gilbert et al. 2012), suggesting that populations of holobionts, and not just their components, showed heritable, including vertically transmitted, variation in fitness differences. This claim, which was not made by all holobiont proponents, was strongly criticized (Moran and Sloan 2015; Douglas and Werren 2016; Skillings 2016), primarily on the grounds that it requires exact organism lineages to be heritably co-transmitted across generations. This is the case for entities with obligate co-vertical transmission, such as for human egg cells and their mitochondria. However, this is not the case for most microbes, as they are not vertically transmitted with high fidelity and can be gained and lost over a single host generation (Douglas and Werren 2016).

Holobiont proponents have since responded that this criticism fails to grasp the pluralistic nature of the concept. They do not accept this strict formulation of “unit of selection,” nor the assumption that it must underwrite what is of value about the holobiont perspective. In what follows we address two recent paths of defense of the holobiont concept, and related ideas, which proponents offer as responses to the initial criticism and as better reflecting what they accept as the historical use of the concept.¹ The first has been to argue that the concept (or a related and updated concept, “metaorganism” (Bosch and McFall-Ngai 2011)) picks out an important and distinctive category of biological entities, regardless of whether those entities primarily evolve by natural selection as a unit (Theis et al. 2016; Stencel and Wloch-Salamon 2022; Hazelwood 2025). This work fits with older uses of the holobiont label to refer to physiological or ecological units, rather than evolutionary ones (Rohwer et al. 2002; see, e.g., O’Malley 2017 for the complex history of this term).

The second path has been to answer the criticism more directly, by explaining how some host-microbe communities evolve as a unit of selection despite organism turn-over

¹ In talking directly with those on both sides of this debate, we find that there is considerable disagreement about the history, and so the field could benefit from an updated and detailed historical analysis.

and lineage instability. This work overlaps with several recent developments in evolutionary theory (**Box 1**), which represent exciting new theoretical areas, but which do not require the holobiont concept. In the context of the holobiont debate and the above criticisms, Elizabeth Lloyd's work is particularly noteworthy (see summary in Lloyd (2020)). Building on work by Hull (1980), Lloyd has demonstrated that recurring debates over the proper "unit of selection" are ambiguous. There are at least four different senses in which a biological entity has qualified as a "unit of selection": as a replicator/reproducer (an entity that is faithfully copied across generations), as an interactor (an entity that interacts with its environment and is subject to direct selection), as a beneficiary of selection (an entity that benefits from a selection process), or as a manifestor of adaptation (an entity that exhibits adaptation to a local environment) (Lloyd 2020). Lloyd, and others (Roughgarden et al. 2018), have argued that some holobiont systems can act as units of selection in at least one of these four senses, and that the early criticisms of the holobiont concept merely showed that very few holobionts were lineage-forming, reproducing entities (i.e., most holobionts are not reproducers).

Lloyd's helpful framework provides much needed clarity to debates about units of selection. But we do not think it exonerates the holobiont concept. The problem is that each of the four senses of units of selection systematically cuts across holobiont boundaries. Consider the interactor concept. An interactor is the entity interacting with the environment and experiencing selection, as opposed to the replicator which is the material replicated (typically DNA), but usually does not experience selection directly. In the context of individual organisms and their genomes this dynamic can be summarized as: selection acts on phenotypes, not genotypes. Many host phenotypes arise partially from host-microbiome interactions (McFall-Ngai et al. 2013; Lynch and Hsiao 2019), such as immune system development (Belkaid and Hand 2014), nutrient metabolism (Russell et al. 2009; Rowland et al. 2018), and certain behaviours (Nguyen et al. 2024; Suzuki et al. 2025). Due to these phenotypic impacts, proponents of this view argue that the holobiont is a defensible concept under the interactor model (Theis et al. 2016; Lloyd and Wade 2019).

The problem, as we illustrate below, is that, in most cases, the causally relevant interactor is not limited to host-microbiome interactions. A grouping of entities relevant to the interactor concept would nearly always include those outside of the holobiont and would nearly always exclude some of those internal to it (e.g., microbes with negligible influence on the host). Thus, if we were to accept the interactor framework, the holobiont would be a poor proxy for the causally-relevant interactor. The “holobiont” directs attention to the wrong grouping, and thus might obscure, rather than clarify, the selection process occurring. But before addressing this point further, we will first attend a simpler point: some researchers may find the holobiont concept useful, regardless of whether it is defensible from an evolutionary perspective. This is the first path of defense mentioned above.

Box 1: Related novel developments in evolutionary theory

Several developments in evolutionary theory have challenged the field’s traditionally skeptical attitude towards the possibility or strength of natural selection acting on multi-species systems. These include contributions in the following six areas, among others: (1) Approaches to evolution by natural selection that reformulate fitness as differential persistence rather than differential reproduction (Bouchard 2011; Bourrat 2014; Doolittle and Inkpen 2018). (2) Approaches that decouple heredity from the formation of species lineages (Charbonneau 2014; Papale 2021; Veigl et al. 2022). For a criticism of this approach to holobiont evolution, see Hazelwood (2025). (3) Mathematical models that bridge vertical and horizontal transmission dynamics (Roughgarden et al. 2018; Roughgarden 2020; Week et al. 2025). Although some valuable work in this area explicitly models hologenome evolution, it is worth noting that the models treat hosts and microbes as separate entities rather than as a collective (Roughgarden 2023). In other words, these models do not require a holobiont entity to exist for the host-microbe interactions to be equivalently modelled. (4) The development and application of community genetics frameworks to show, in particular, that vertical inheritance is not required for evolution by natural selection (Whitham et al. 2006; Lloyd and Wade 2019; Lean et al. 2022). (5)

Simulations demonstrating the role of ecological scaffolding in the evolution of individuality (Black et al. 2020). (6) Multi-level selection theory and related reformulations of Price's equation (Sober and Wilson 1998; Lean and Jones 2023; Doolittle 2024; Week et al. 2025). One contribution in this last area concerns the need to model the traits of collectives that depend on varying group member configurations, not just their frequencies (Bielawski 2026 Jan 18). This is a valuable contribution that warrants further exploration as it could apply to many collectives in nature. However, this approach requires a collective to be defined: focusing on the holobiont as such a collective would often be problematic due to issues of neutral and transient members, and questions of how to set boundaries, which we expand on herein. More generally, there is now an interest in developing some of these and related frameworks in ways that lend themselves to empirical testing (Week et al. 2025). These frameworks do not require holobiont terminology or categorization to function. In addition, using the holobiont concept could oversimplify interactions in nature, as exemplified by our honeybee example presented below.

Utility of the holobiont concept

The main response from proponents of holobiont terminology to the original criticisms regarding the lack of co-transmission between host and microbiome was to argue that these critics were misunderstanding the concept, as the term is not meant to specify a unit of selection (Theis et al. 2016). Instead, they argued, a holobiont refers to a host and their associated microbiome, which can be but is not necessarily a unit of selection. These host-associated microbes can be involved in any type of symbiotic relationship (beneficial, deleterious, or neutral), and furthermore, the specific type of symbiotic relationship between host and microbe will depend on the context (Casadevall and Pirofski 2014; Inkpen 2024). Microbes can be acquired horizontally (from the environment, including other hosts) or vertically (parent to offspring, typically during reproduction). Although this addresses the concern that there are very few holobionts that qualify as units of selection in the co-reproductive sense, it presents other issues.

182 This way of defining the holobiont concept is often justified because it is helpful: it
183 highlights the previously unappreciated complexity of host-microbiome associations
184 (Bordenstein and The Holobiont Biology Network 2024). Metagenomics sequencing has
185 indeed revealed widespread microbial diversity (Handelsman 2004; Gilbert and Dupont
186 2011), and raising awareness of the complexity and nuances of host-microbiome
187 dynamics is important. For instance, understanding the potential role of host-microbe
188 interactions underlying speciation events (Brucker and Bordenstein 2012; Miller et al.
189 2021) and the myriad impacts of microbes on host fitness (Franché et al. 2009; Zheng et al.
190 2020) is valuable. However, critics have pointed out that appreciating these dynamics
191 does not require the holobiont concept: these exciting observations are entirely consistent
192 with existing eco-evolutionary frameworks for inter-species co-evolution and wider
193 interactions (Moran and Sloan 2015; Douglas and Werren 2016; Skillings 2016). For
194 instance, a recent review described frameworks for modelling and understanding host-
195 microbiome interactions (Week et al. 2025), describing complex interactions, including
196 multi-level selection, but without invoking the holobiont concept. So, the immediate
197 question is why we need this term, given that we have terminology that already covers this
198 biological ground.

199 One might argue that if some researchers find holobiont terminology useful, then
200 the holobiont is a useful concept for biological practice. On the one hand, this is
201 understandable because all biological categories are somewhat arbitrary and imprecise,
202 and as a result there will always be disagreement over the correct scope and use of key
203 terms and concepts (Dupré 1993). And although we should in general strive for terms,
204 concepts, and categories that are unambiguous and informative (Corter and Gluck 1992),
205 which will facilitate the scientific communication required for knowledge production,
206 attaining this ideal for all scientific terms and concepts is impossible. Central concepts
207 like gene and species are imprecise and interpreted ambiguously. And even if it were
208 possible, it might not always be desirable because imprecision has some virtues, including
209 facilitating integration across scientific fields. For example, Neto (2020) demonstrates how
210 the imprecision of concepts like molecular gene, biological lineage and evolutionary

novelty provides a flexibility that helps scientists from different subfields recognize the connections between their explanations and encourages interdisciplinarity. Kohl (2025) similarly argued that not tying the holobiont concept to any specific definition will offer greater flexibility, and support the integration of work across the wide spectrum of host-microbe interactions.

However, acknowledging the value of imprecision does not imply that all concepts are equally useful for describing the natural world. Two points are worth considering when we evaluate any scientific concept.

First, entrenchment matters. Highly entrenched concepts, those now nearly necessary to sensibly discuss biological units in everyday biological practice, are difficult to imagine completely abandoning and so need to be dealt with in some other way. Arguing that we should eliminate such concepts is not unprecedented, but it is contentious (Ereshefsky 1992; Brigandt 2003). In contrast to concepts like gene and species, the holobiont concept is neither entrenched nor necessary for discussing microbiome dynamics.

Second, acknowledging that imprecision can sometimes be a virtue means only that we must carefully weigh the benefits of imprecision, such as for interdisciplinarity or science communication, against the costs of using the concept to determine its overall utility. The holobiont and related terms are commonly misunderstood and applied in diverse ways (Douglas and Werren 2016; Morris 2018; Madhusoodanan 2019), and so can be interpreted ambiguously, which has an obvious cost. But even if we solve the concerns about ambiguity (that is, stick to one and only one definition), there are further issues about informativeness: we should strive for concepts that (i) track causally important structures in nature and (ii) support novel explanation and prediction. We do not think the holobiont is informative in these ways.

Host and microbial genetic variation

One novelty of the holobiont view is the hologenome theory of genome variation. A holobiont possesses a hologenome consisting of the host genome and all microbial

genomes present, regardless of how labile or stable (Theis et al. 2016). The traditional view of a (mainly) static genome over an individual's lifetime is said to be supplanted by a dynamically changing hologenome in typical mammals, for instance. Changes in microbial membership can have profound effects as microbial genes can drive phenotypic shifts within a single host generation. This dynamic is sometimes said to resemble Lamarckian evolution (Rosenberg et al. 2009; Bordenstein and Theis 2015; O'Malley 2017), and can include both changes in the presence and absence of microbes, as well as shifts in microbe relative abundances. Proponents of the hologenome perspective frame this as genetic variation that selection can act upon to drive adaptations (Bang et al. 2018). And more generally, evolutionary changes resulting from microbial composition and those resulting from host genetic variation have been argued to be conceptually equivalent (Bordenstein and Theis 2015) (**Figure 2**). Under this view, microbiota (and/or their composite genes) with beneficial, deleterious, or neutral fitness impacts on the overall holobiont fitness should be thought of as a broader extension of nuclear genetic alleles, which also have varied fitness impacts. Although microbes are more frequently lost from hosts than host genetic alleles are from a population, the argument is that these processes are similar on a conceptual continuum, and that microbes can be likened to alleles, albeit often with extremely high (and within-generation) rates of recombination (Bordenstein and Theis 2015).

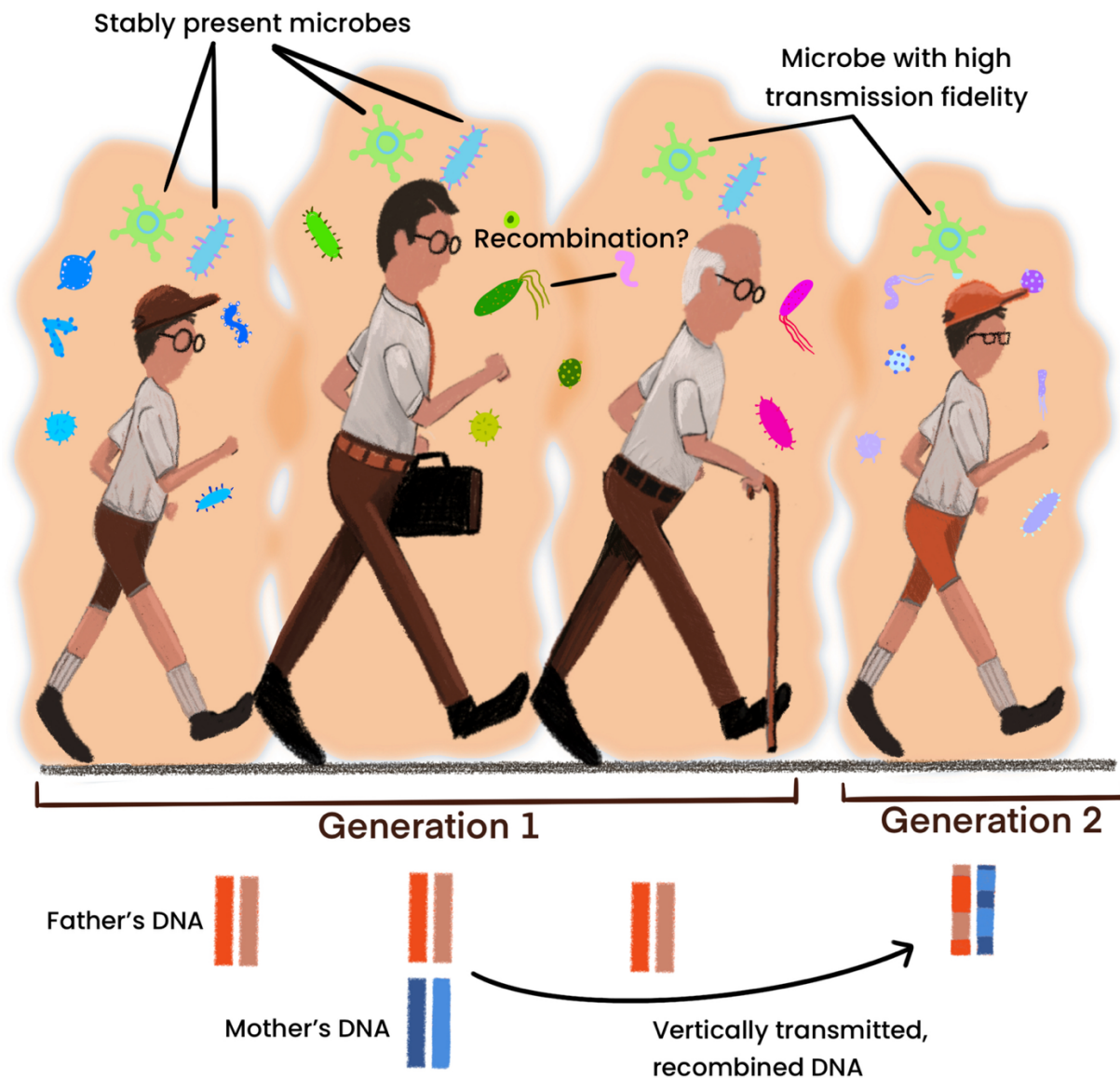


Figure 2: The key analogy linking variation between host genes across generations and microbial strains within generations, and that is closely related to the hologenome model of evolution. These types of variation have been argued to be part of the same continuum of genetic variation, albeit with differing rates of recombination, that contribute to an overall hologenome. Artwork: Morgan MacPherson.

A central question is whether this novel perspective on genomic variation yields informative groupings about nature. Does it, in other words, track causally important

structures? We do not think so because once we start down the path of expanding genomic analysis in this way there is no reason to limit holobionts, nor hologenomes, to hosts and their microbiome. Holobiont proponents often argue that a holistic approach to studying biological complexity is needed, and that the holobiont and hologenome concepts encourage this. But if this is true, these concepts are too limiting. If one is interested in phenotypic outcomes, or if one is similarly interested in identifying evolutionary “interactors,” then the boundary should not be limited to the host and microbiota. A complete understanding of the biotic interactions that can (or that potentially can) impact phenotypes clearly requires a broader view of community interactions (**Figure 3**). A host interacts with and is often interdependent with many other organisms beyond members of its microbiome. Simply stating that, for example, interactions between a pollinator and a flower represent separate holobionts interacting, because a holobiont is defined solely as a host and microbiota (Bordenstein and Theis 2015), deals with the issue by assertion, rather than providing reasons why the holobiont should be so limited. A causal, “interactor” perspective offers no basis for drawing these boundaries. In other words, although the holobiont concept is often presented as an expansive view, from the perspective of remaining open-minded about the potential factors and interactions causing host phenotypes, it is restrictive.

Holobiont and hologenome boundaries can be seen to be especially arbitrary when neutral microbes are considered. The holobiont includes the host and all their associated microbes, including those with a neutral relationship. But this means that we include as parts of the holobiont, and hologenome, entities that have no effect on the host simply because they are microbes, and exclude biological entities that do interact with the host simply because they are either not microbes or not co-located. In other words, causally unrelated elements are grouped by arbitrary boundaries. The severity of this issue depends in part on how frequently persistent contact encourages coevolution, and eventually, vertical transmission. While it is true that neutral genes are present in host genomes, those are still part of a shared inheritance system, whereas many neutral microbes will not be vertically transmitted with high fidelity, but instead horizontally acquired (Douglas and

Werren 2016; Roughgarden 2023). We do not think persistent contact justifies the inclusion of large fractions of likely neutral resident microbes as a holobiont unit.

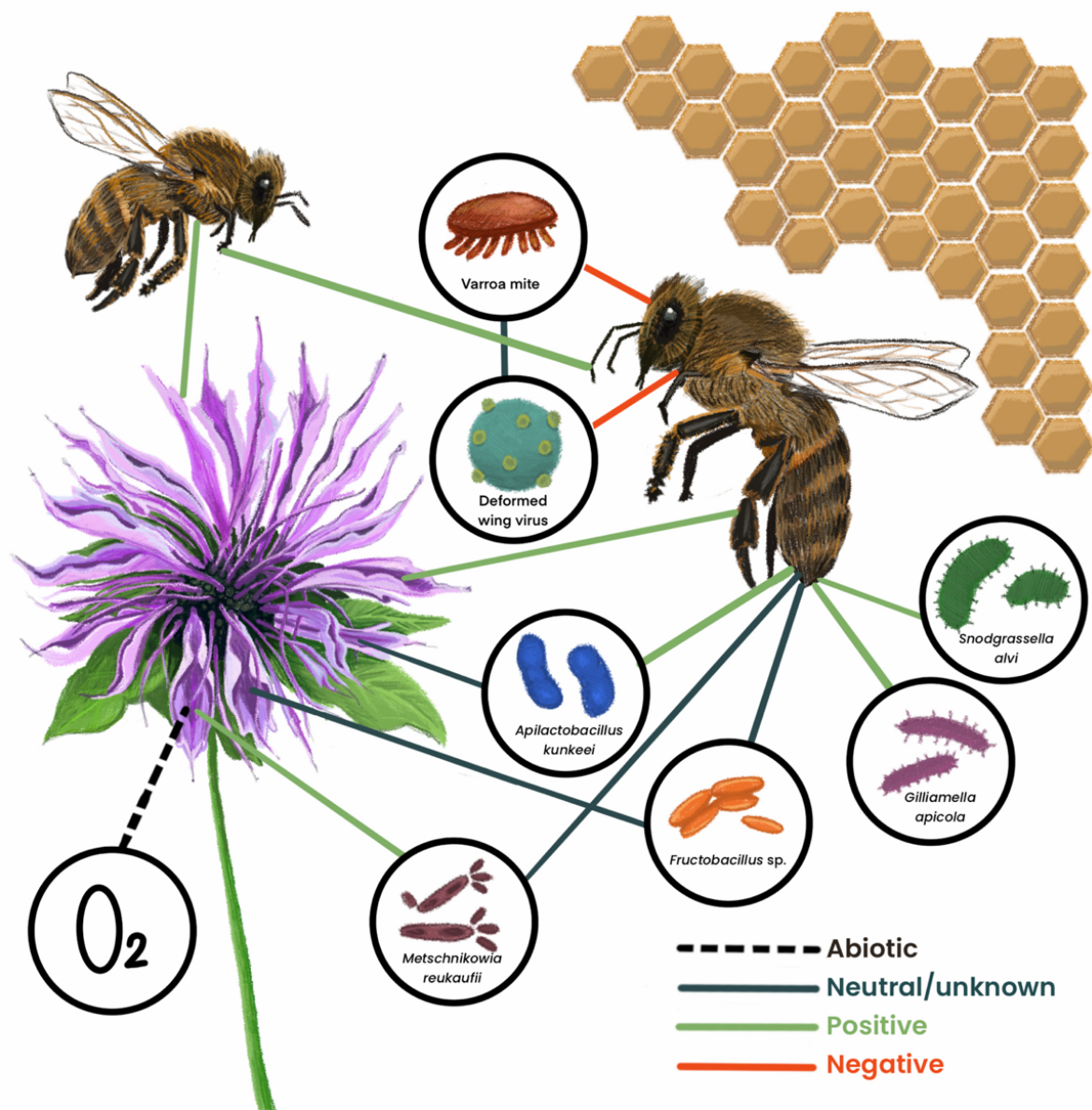


Figure 3: Interactions between honeybees, a flower, and interconnected microbes. This example is meant to highlight that there is no principled reason why these entities should not all be part of the same holobiont, particularly under the interactor model. In the most extreme case, an interactor would include interactions of all magnitudes, including indirect interactions through environmental

modulation (as through oxygen production). We are not arguing that this should be the case, but instead simply that the holobiont concept lacks clear causal justification for the boundaries it draws. Importantly, if the response to this critique is that the holobiont requires physiological integration, then this conflicts with how the holobiont concept has been repeatedly defined to include transiently present and neutral microbes. Simplistic interactions are shown here for illustrative purposes, but these can be contextual and temporally shifting. Artwork: Morgan MacPherson.

Claims about the distinctiveness of the holobiont as a host and its microbes sometimes rely on arguments about co-localization and the strength of interactions. Determining which interactions are proximate enough to be considered part of the holobiont rather than the external environment is non-trivial, as previously raised (Morris 2018). Regardless, we agree that co-localization is denoted by the term holobiont, however this is already redundant with the simpler and less ambiguous terms of host and microbiota.

Some have argued that the holobiont boundary is defined by the immune system, which itself results from the interactions of hosts and microbiota (Gilbert and Tauber 2016; Gilbert 2024). We appreciate the importance of microbes in immune system development, although the exact fraction of immune functioning and relative importance of microbes compared to other environmental interactions remains to be determined (Liston et al. 2021). Regardless, even under a scenario where immune system functioning results entirely from host-microbiome interactions, this would not resolve the boundary concern. It is true that the immune system is a major mechanism explaining why microbes are co-localized with a host: the immune system tolerates them, or they escape immune system selection. This provides a causal explanation for which microbes are present, but it does not follow that this set should be considered an individual unit. These microbes can still represent diverse levels of transiency, symbiotic interactions, and importance to the host. It remains unconvincing that defining a single holobiont unit representing this diverse grouping due to the immune boundary, rather than simply referring to a “host and microbiota”, is helpful.

Similarly, defenses of the concept based on the strength of interaction or metabolic integration face two challenges. First, many symbiotic interactions between macro-organisms share this feature (Boucher et al. 1982): this is not unique to host-microbe interactions. Secondly, the holobiont concept has been defined to include neutral symbionts, who need not be metabolically integrated with any other entities, or at least do not impact host fitness. In other words, stating that a host and microbiota are a holobiont does not imply that they are metabolically integrated, only that they are co-localized. This discussion highlights the mix of concepts under the umbrella of “holobiont.” Referring to either a host and microbiome, including neutral microbes, or to an interactor entity could each be useful, but using the term holobiont to represent both creates unnecessary ambiguity.

One way to avoid the above criticisms is to be more specific about what is included in the holobiont, and the “metaorganism” concept is sometimes used to accomplish this. Jaspers et al. (2019: 82) define the metaorganism as, “the sum of a eukaryotic host and its associated species in a narrower context as compared to the holobiont, with the focus on those associates for which function, i.e. any form of contribution (beneficial or detrimental) to the metaorganism, is known or implied [and ...] whether a specific function/microbe is functionally relevant can depend on host developmental stage, age, reproductive state, or physiological condition.” So, unlike the holobiont concept which includes a host and all of its microbes, the metaorganism concept does not include microbes without functional effects.

Although the metaorganism concept deals with some of the above concerns, it suffers from a different issue that is related to the fact that it is interest-relative in a fine-grained way, meaning it explicitly depends on a researcher’s specific interests and goals rather than only intrinsic properties of a host-microbiome system. Consider that, often, hosts harbour many microbes that contribute in many different ways to many different physiological processes. Say we are researching the role of microbes in pollen digestion in the honeybee gut (Motta and Moran 2024). If our interest is in studying how waste nitrogen is recycled in the pylorus section of the gut, then the metaorganism we are studying will be

constituted by the host bee and a specific set of microbial species that give rise to a particular phenotype. But if on the other hand our interest is in digestion of pollen wall components in the ileum section of the gut, then our metaorganism will be constituted by the host bee plus a different set of microbial species. But which is *the* metaorganism we are studying? There are nearly as many metaorganisms as we have different interests. We do not think it is worth articulating diverse metaorganisms rather than simply stating the phenotype of interest and the interacting organisms that are involved. So, the specificity of the metaorganism concept solves some of the issues of the holobiont concept, but at the cost of generality. We should drop this language and instead use the common language of host-microbiome interactions that does not risk reifying what we do not intend to reify. In other words, and similar to at least two previous critics (Douglas and Werren 2016), we are worried that host-microbiome systems will be seen as entities, rather than as sets of interactions, even though the latter seems more apt given the diversity of such systems and the context dependency of the interactions.

Epistemic complications of the hologenomic view

Beyond the above concerns, there are clear examples of conceptual confusion that arise from using the framework. If one accepts the hologenome view, many aspects of how host genetics are conventionally studied can seem simplistic. After all, for example, human microbiota encode more unique protein-coding genes than the human genome (Qin et al. 2010; Rosenberg and Zilber-Rosenberg 2018). If microbial genes are excluded, then, from the hologenomic perspective, any studies of human genetic variation are missing a large proportion of meaningful data. This insight has been the basis for some to argue that heritability estimates of human traits are systematically biased downwards due to this problem (Sandoval-Motta et al. 2017; Marques 2018; Huitzil et al. 2020). These points have been raised in the context of genome-wide association studies finding lower heritability estimates compared to pedigree-based studies across many organisms, which is referred to as the “missing heritability” problem (Maher 2008). There are many possible

explanations for this observation, including that larger sample sizes and including rare genomic variants are needed to capture trait heritability (Wainschtein et al. 2025).

The microbiome will not help solve the “missing heritability” problem, at least not as a source of missing host genetic information (Douglas et al. 2020). For example, in humans the “missing heritability” problem is based on the observation of high heritability of traits inferred (primarily) through twin studies. In this study design, identical (monozygotic) and fraternal (dizygotic) twins are compared and heritability is defined as the extent of increased phenotypic similarity between identical twins specifically. Identical twins have more similar microbiomes on average (Goodrich et al. 2016), which, among other potential factors (Felson 2014), is likely due to shared genetic variation modulating exposure or colonization success of microbes. However, for this signal to be relevant to the “missing heritability” problem, a mechanism for why the same microbes are more likely to be directly transmitted to identical twins, compared to fraternal twins, is needed. Importantly, this mechanism cannot simply be that identical twins’ higher genetic similarity increases their predisposition to acquire certain strains from the environment: this would be just standard genetic-by-environment interactions. Nor can it simply be that human genetics cause the presence of a microbe, regardless of the environment, as this would already be captured by host genetic variation, and thus including the resultant microbe would be double counting of this effect. Framing such interactions as (human) gene-by-(microbe) gene interactions that represent a component of missing human genetic variation is misleading to those seeking to understand trait heritability, as it conflates genetic and environmental variance.

Researchers who have recently argued in favour of the hologenome model (Bordenstein and The Holobiont Biology Network 2024) will likely disagree with our above characterization. They have rightly highlighted that more variance in host traits can be explained when both host genetic and microbial information is incorporated, compared to host genetic information alone. Similarly, host genetic variants associated with traits can depend on the host microbiome’s composition. For instance, some quantitative trait loci associated with functional traits in bunch grass interact with the soil microbiome

composition (Khasanova et al. 2023). In other words, the host genomic regions identified that likely contain causative variants driving functional traits can vary depending on the microbial context. These and related findings have been used to argue in favour of “a hologenomic view of life that does not prescribe prominence to either host or microbial genomic contributions to a given trait” (Bordenstein and The Holobiont Biology Network 2024).

The role of microbiomes in modulating host traits has indeed been unappreciated historically. However, to capture the complexity of biotic interactions, the interaction between hosts and microbes to produce traits can be explicitly modelled with different trait optima and selective consequences for each species (O’Brien et al. 2021). Species-specific dynamics can be obscured if instead the focus is on the overall collective. More generally, this broader view is consistent with standard quantitative genetics modelling: some traits are driven primarily by host genetics, while some are environmentally driven, and any inferences about the relative contribution of each, and their interaction or covariance, are always environment-specific (Falconer and Mackay 1996). In addition, environmental variance can be split into more specific components, such as maternal effects (Kruuk and Hadfield 2007). Many environmental components could be relevant, including the shared social environment by which microbes are transferred between hosts (Sarkar et al. 2024).

When host genetic and microbial variation are uncorrelated, the microbiome can similarly be modelled as a separate component of variance (Difford et al. 2018). In some cases, such as when studying levels of methanogenesis in cow rumens, there is good reason to think microbes are causally connected to the host traits of interest, with a clear direct mechanism. However, applying this framework more generally, to any host trait, is much harder to interpret. Many environmental factors (e.g., diet) can impact both the microbiome and host traits. This means that microbial variation that statistically explains a high proportion of variation in a host trait can be, and likely often will be, due to independent impacts from an unmeasured environmental cause on both the microbiome and host trait. For example, it would be unsurprising to find that the nutritional content of

an organism's diet affects both the host's growth rate and its microbiome. Uncritically assessing how microbial variation is associated with variation in growth rate would not provide insight into the causal factors involved, except as a proxy for a separate, unmeasured, environmental factor.

More generally, it will often be unclear what information is provided by knowing the degree to which microbial variation is associated with a host trait, compared to estimating the overall environmental variance. The ultimate causal factors driving the association are often unclear in both cases. Of course, this does not mean that identifying associations between host traits and microbiota is not helpful: this can generate useful hypotheses. However, the same is true for any high-throughput profiling data that could be applied to hosts, such as gene expression and metabolic profiles. Leveraging these data would also result in a higher proportion of variation in host traits being explained, but would similarly not distinguish between cases where these data are causally important and where they are simply correlated with unmeasured environmental factors.

Social aspects of the hologenomic view

Recent work on the hologenome view (e.g., Bordenstein and The Holobiont Biology Network 2024) emphasizes the social benefits of the concept as well as the epistemic, which are important to consider but were often overlooked in earlier criticisms. If we are reviewing how to address contested terminology, we must consider these potential benefits as well. One benefit, as mentioned above, is in terms of interdisciplinarity. Using holobiont terminology means that host organisms are defined as containing microorganisms and their genomes, so there is no question of separating host biology from microbiology. This rejects the siloing of microbiology from, e.g., evolutionary biology, development, anatomy, and ecology, and might justify disciplinary transgressions as necessary for a full understanding of host-microbiome systems. A related benefit has to do with the historical context: before the 2000s, and despite the interest and arguments of Lynn Margulis and others (O'Malley 2017), macro-organisms were often studied without much thought to microorganisms. Part of the change was driven by technical

advancements in sequencing, but concepts can also help, and the holobiont is an example.

Proponents also draw attention to potential benefits for public outreach and for developing ethical relationships with the rest of nature. There is some supporting social science evidence, e.g., that people with some exposure to the holobiont concept report a higher connection to nature (Robinson et al. 2026). More empirical work would be needed to determine the strength of the benefit of the holobiont concept specifically. In particular, it remains unclear whether existing “holistic” terminology (i.e., community, ecosystem, host-microbiome, etc.) has a similar effect.

Moving to social costs, a point of confusion introduced by the holobiont framing concerns health. Because of the now recognized role that microorganisms play in human physiological and psychological processes central to our health and well-being (Bäckhed et al. 2012; The Human Microbiome Project Consortium 2012; Lloyd-Price et al. 2016; Morar and Skörmann 2018), it has been suggested that the appropriate locus for assessing or treating health is the holobiont, rather than the individual human (Catania et al. 2021; Bosch et al. 2024). But this is problematic for two reasons (Inkpen 2024). First, if it is really the health of the whole holobiont that matters, then it is unclear why the human member of the holobiont cannot be replaced by another human, given that microbial members consistently turnover. This renders the idea unhelpful for most human medical contexts. Second, if instead the health of the holobiont is indexed to the health of the human host, then it is unclear why the holobiont concept is necessary. Studying interactions between hosts and their microbes that are relevant to the health of each member is more clearly tackled without the holobiont concept, and by instead employing well-developed “ecosystem health” and “ecosystem services” frameworks from ecology (Inkpen 2019).

The above conceptual issues point to an additional concern about the holobiont concept: its implicature, what the concept conveys beyond how it may be explicitly defined. For example, the phrases “Lee stopped the car” and “Lee got the car to stop” convey the same explicit information, but the latter conveys a more complex or uncommon causative chain compared to the simpler phrasing (Horn 1984). Similarly,

choosing to use the term holobiont rather than simply stating “host and microbiota” signals that this is a single entity rather than interacting separate entities. Readers will likely always be tempted to interpret a holobiont as something well-defined and “real” in nature. Perhaps even to “elevate the host plus its microbiome to the status of an organism,” as Angela Douglas and John Werren (2016) worry. These implicatures are more than this vaguely-bounded and interest-relative concept should imply, and more than the evidence can support for the great majority of holobionts. This problem is exacerbated by the varying definitions for the holobiont, hologenome, and metaorganism that have been presented in the literature. If, as we have argued, these concepts are either too general or too interest-relative to support this implicature, then this will always be a problem. It is thus also what the concepts convey, and not only how they are defined, that is costly.

Moving forward

We recommend researchers avoid the term holobiont, as well as the related terminology hologenome and metaorganism in most circumstances. All microbes on and in a host are not of equal impact or interest, and categorizing them all as the same unit is unhelpful. There is no principled biological reason to privilege the assortment of microbes on a host and the host itself as a single entity, without arbitrarily excluding more distant organisms. It is sufficiently clear to state “host and microbiota” if a researcher’s focus is on these co-localized organisms, which does not risk misinterpretation. More generally, we agree with previous critics that the holobiont framework is an oversimplification of biotic interactions in nature (Douglas and Werren 2016; Skillings 2016).

Importantly, our commentary is not meant to deter or criticize research into host-microbiome interactions, including research that has been presented under a holobiont framework. For instance, the pattern of compositional differences across microbial communities that tracks with host phylogeny, referred to as “phylosymbiosis”, has been used as evidence for the holobiont concept (Bordenstein and Theis 2015), although this interpretation has been criticized (Moran and Sloan 2015; Douglas and Werren 2016). In terms of the potential for co-diversification of particular microbes, phylogenetic

congruence can occur between non-microbial lineages through known co-evolutionary mechanisms that do not require the holobiont concept (Farrell and Mitter 1990; Farrell and Mitter 1998; Cruaud et al. 2012). In addition, host filtering, such as differences in gut anatomy that track the host phylogeny, could be a simple explanation for some observations (Mallott and Amato 2021). Regardless of the cause, continued investigations of this topic and host-microbiome interactions in general will undoubtedly uncover useful insights. More generally, there is great value in appreciating, and further investigating, the interconnectedness of nature highlighted in the microbiome field. Our point is simply that the holobiont concept is not needed to do so.

Collectively, we have argued that: (i) the holobiont is often a poor proxy for the causally-relevant interactor; (ii) its boundaries are interest-relative; (iii) it includes too many causally irrelevant elements (i.e., neutral microbes); (iv) it does not make clear predictions beyond what existing frameworks provide; (v) the term might encourage reification (treating a pragmatic grouping as a “real” cohesive unit); (vi) though there may be some social benefits, there are also social costs.

Many concepts in biology are imprecise and ambiguous, even central ones like “individual” and “gene.” There is nothing inherently wrong with imprecision or ambiguity: we are not arguing that the alternatives to holobiont terminology will be perfectly unambiguous. However, we are in favour of assessing the pragmatic value of competing concepts. It is when ambiguous terms become epistemically or socially costly, and this outweighs the benefits, that we should rethink our adherence to them. In the face of a critique like ours, there are many options. We favour an eliminativist thesis in terms of how the holobiont is loosely used in the microbiome literature: that we abandon (or eliminate) the holobiont concept in favour of unambiguous language. We believe this is the appropriate position given our above points, at least until evidence is provided that the holobiont concept provides value beyond existing categories. However, we welcome further theoretical work and counter-arguments to our points on the holobiont concept: it is not such work, but the uncritical usage of a vaguely defined holobiont entity in microbiome research that we specifically favour avoiding.

There are also other options. Authors could more strictly define the holobiont concept (and related terms) upon using them, for instance authors could define the label as applying only for obligate symbioses in well-known contexts, such as certain corals and lichens, or those with very high transmission fidelity, such as certain symbionts of lower termites (Brune 2014), which has some historical precedence (O'Malley 2017). It is cases like these that guided our title choice: "The holobiont is not a useful model for *most* host-microbiome interactions." In this case there will be fewer holobionts, as others have previously argued. This option, however, fails to address all issues raised above, such as its implicature, particularly because the less strict version of this term is already widely used. A similar option would be to divide the holobiont concept into subtypes, akin to other contemporary examples: developmental gene versus molecular gene, or biological species versus ecological species. We do not think this would be a worthwhile approach. There is a risk of confusing readers; one could simply explain the intended meaning in plain terms without the use of a specialized term that could be interpreted ambiguously. In addition, this pluralistic strategy is more appropriate for terms that are practically indispensable (or highly entrenched) in biological thinking, such as species and gene. Ultimately, it is up to the biological community to decide what concepts and frameworks they employ.

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Data accessibility statement

The raw data and a description of our methods and R code for creating Figure 1 are available on Zenodo (<https://doi.org/10.5281/zenodo.19682360>).

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Both GMD and SAI: Conceptualization, Investigation, Writing – original draft, and Writing – review & edit. GMD: Formal analysis and Visualization for Figure 1.

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