**A New Role for Roles in Biomedical Ontologies**

**Abstract**

**Introduction**

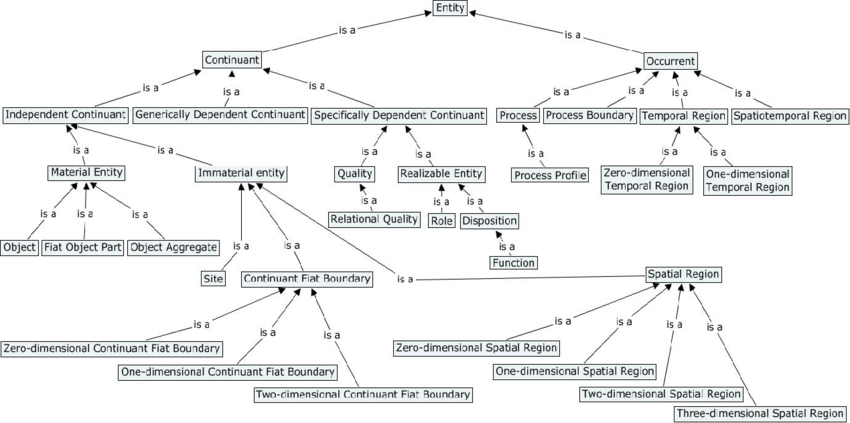
The prevalence of functions and roles in contemporary life science literature is hard to overstate. Chemists refer to functional groups, enzymes are said to play roles in metabolism, pacemakers play a role in regulating heart rhythm malfunctioning. Given the prevalence of these terms, proper ontological characterization is important. These are, however, disputed waters. Debates persist among life science researchers as to how these terms should be understood (Brunett & Doolittle, 2014). Some treat “role” as something a function can play “role of mitochondria function” (Murphy, et. al. 2016), while others treat “role” as a type of function, e.g. “causal role function” (Thomas, 2017). Some argue “function” should only be used at the level of organism while (causal) role should be used everywhere else (Doolite, et. al. 2014), while others argue “function” picks out why an entity exists while “role” is an ahistorical description of how an entity contributes to a complex system (Keeting, et. al. 2019). Debates similarly persist among ontologists as to how these terms should be understood (Buller, 1998; Wouter, 2005; Krohs & Krohs, 2000; Rohl & Jansen, 2014; Artiga, 2016; Spear, Ceusters, & Smith, 2016). What unifies these disputes is the difficulty associated with characterizing normative and future-directed features of “function” and “role” as they are used in life sciences and in natural language more broadly.

A powerful, unifying, ontological treatment of functions and roles has been developed and defended in Basic Formal Ontology (Arp, et. al. 2015; Smith, et. al. 2015). Functions are treated as a type of disposition while roles are distinguished from dispositions. While BFO’s characterization is widely used, it is nevertheless incomplete, which may result in misuse, confusion, or rejection of its characterization of functions and roles. We develop BFO’s treatment of these terms in what follows, in the interest of clarifying use for the broader ontology and life science community.

**Methods**

*Overview of BFO*

Ontologies are widely used in bioinformatics and biomedical data standardization, supporting data integration, sharing, reproducibility, and automated reasoning (Gene Ontology, 2019). The Open Biomedical and Biological Ontologies (OBO) Foundry was created to provide guidance for ontology developers and promote alignment and interoperability while structuring data. Among the OBO Foundry design principles is the requirement that Foundry ontologies conform to a top-level architecture. Basic Formal Ontology (BFO) is the OBO top-level ontology covering general classes such as *material entity*, *quality*, *process*, *function*,and *role*, and provides the architecture adverted. Consequently, BFO is used by over 350 ontologies conforming to OBO principles.



*Figure 1: Basic Formal Ontology Hierarchy*

BFO is designed to characterize the most general universals, relevant to scientific investigation. More specific ontologies are created by downward population from BFO, with more specific terms introduced to cover given domains (Babcock, et. al. 2020). BFO divides reality into disjoint categories of continuant and occurrent (Arp, et. al. 2015; Smith, et. al. 2015). Continuants exist entirely at any time at which they exist at all and lack temporal parts. Occurrents, in contrast, have temporal parts and so are often stretched along a temporal axis. BFO adopts several further subclasses of Continuant and Occurrent. *Figure 1* displays the complete BFO hierarchy where “is\_a” indicates sub-type relations, where “A is\_a B” means “instances of the universal A are instances of the universal B”. This paraphrase, moreover, reflects BFO’s emphasis on instances of universals, e.g. red on *this* apple, rather than universals themselves, e.g. the class of red things in general.

We focus on only those entities relevant to the discussion of functions and roles to follow.

*Realizable Entity Commitments*

Instances of Realizable Entity are themselves instances of Specifically Dependent Continuant, a subclass of Continuant. Specifically Dependent Continuant entities are dependent in the existential sense, that is, they depend for their existence on other entities. This feature of Specifically Dependent Continuant entities transfers to its subclasses, resulting in instances of Realizable Entity being in every case existentially dependent on other entities. This feature similarly apples to instances of Quality, another subclass of Specifically Dependent Continuant. Instances of Quality are distinguished from those of Realizable Entity in that while the former are fully manifested whenever they exist, the latter are not. For example, a red apple is plausibly described as bearing a quality, an instance of the color red. This color will manifest in its entirety whenever it manifests at all. In contrast, the apple plausibly also bears a tendency to decay if left in the heat, but this feature of the apple need not manifest for the apple to bear it. BFO draws this distinction by treating the latter as an instance of Realizable Entity.

Instances of Realizable Entity are – when compared to instances of Quality – somewhat mysterious. When investigating the natural world, identifying whether an apple *might* decay requires attention to what similar types of entity *have done* in the past under similar environmental conditions, and prediction about what similar types of entity *will do* in the future. In this respect, instances of Realizable Entity track the *mechanism* linking what has happened to what will; they are explanations unifying observable phenomena. Identifying instances of Realizable Entity thus requires attention to empirical evidence and inference to the best candidate explanatory mechanism. In contrast, identifying fully manifesting qualities like color or mass does not often require inference to the best candidate explanation. The redness of an apple is observable in its full manifestation at any time it exists; no part of the redness is hidden. This is, of course, not to say the color of an apple does not itself require an explanatory mechanism revealed by inference. But what differentiates the redness of an apple from its disposition to decay is the former is fully manifested whenever it exists, while the latter need not be.

In BFO, the class Realizable Entity is defined as a subclass of Specifically Dependent Continuant, having some Independent Continuant instance bearer which may participate in processes associated with this Specifically Dependent Continuant, themselves realized in those processes. According to this definition, instances of Realizable Entity may remain in a sense dormant. For example, a piece of sodium chloride need not ever realize its disposition to dissolve if placed in unsaturated water. Instances of Realizable Entity are, in this respect, how BFO characterizes apparent modal and probabilistic features of reality.

There are further divisions to be drawn within the class. A student, for example, appears to bear a realizable entity insofar as they may or may not participate in processes associated with being a student. The sense in which a student bears a realizable entity is intuitively distinct, however, from the sense in which salt is soluble. In the interest of capturing this distinction, BFO divides Realizable Entity into subclasses of Disposition and Role. More carefully, the former is captured as:

d is a disposition =def

d is a realizable entity &

d’s bearer is some material entity &

d is such that, if it ceases to exist, then its bearer is physically changed &

d’s realization occurs because this bearer is in some special physical circumstances &

this realization occurs in virtue of the bearer’s physical make-up

Instances of Disposition are said to be “internally grounded”, a metaphor meant to track the fact that were the instance to cease to exist, then its bearer would be materially changed in some manner. For example, if a piece of sodium chloride is soluble at some time, then not soluble at another, there must be some change to its physical structure. In this sense, instances of Disposition are not optional for bearers. Realizations of instances of Disposition occur, moreover, owing to the physical structure of the bearer – determined by its qualities (Spears, Smith, 2016) - and that fact that the bearer is in some special environment, where “special” is means an environment the material bearer is not always in. Turning again to the solubility of a piece of sodium chloride, the realization of its disposition occurs owing to the lattice structure and bonding forces of the material when placed in unsaturated water with its own bonding forces which facilitate the manifestation of solubility.

Machine generated alternative text:
NaC1 bearer of 
dissolving 
disposition 
H20 molecule 
bearing 
electronegative 
attraction disposition 
NaC1 molecule 
bearing 
electropositive 
attraction disposition 
NaC1 dissolving in H20 Process 
Realizations of electronegative and 
electropositive attraction dispositions 
Macroscopic 
Microscopic 

*Figure 1: Sodium Chloride manifesting disposition to dissolve in H2O*

Role is a disjoint sibling class of Disposition, and so a Realizable Entity, but one with characteristics sharply distinguishing it from its sibling. Role is defined as:

r is a role =def

r is a realizable entity &

r exists because there is some single bearer that is in some special physical, social, or institutional set of circumstances in which this bearer does not have to be

& r is not such that, if it ceases to exist, then the physical make-up of the bearer is thereby changed

In contrast to Disposition, instances of Role are thus optional in the sense that bearers may gain or lose them without alteration to their physical structure. A student, for example, who graduates from a university no longer bears the role of student at that institution. That does not, however, imply any physical change in the student. The individual, moreover, need not have been involved in that social circumstance at all. Put another way, whether an entity bears a role or not depends largely on what happens external to the entity.

Altogether, the BFO characterization of Disposition and its disjoint sibling class Role tracks the following distinctions:

1. Optional vs Non-optional
2. Actual vs Possible vs Probable
3. Internal vs External Grounding
4. Tracking vs Manifesting

Call this the *BFO Treatment*. Each of these features have been discussed above. Dispositions are not optional, while Roles are. Both instances of Role and instances of Disposition are intended to contrast with instances of Quality, insofar as the latter class represents actually manifesting instances of Specifically Dependent Continuant, while the former classes – being instances of Realizable Entity – represents potential manifestations. Instances of Role are claimed to be grounded in the external environment, while instances of Disposition are grounded internally to bearers, while both subclasses of Realizable Entity are meant to accommodate that researchers typically observe manifestations then infer to the best explanation about what dispositions entities must have to cause them, from which we derive mechanisms used in prediction and tracking of instances of Realizable Entity.

The *BFO Treatment* is an elegant way to track the preceding – important – distinctions. This treatment is, however, incomplete:

* Constellations - The system composed of sodium chloride, hydrogen, and oxygen is an instance of Material Entity and so exhibits some material structure based on its constituents. This material entity – before sodium chloride dissolves – presumably bears dispositions, e.g. solution pH. Realization of the disposition of sodium chloride results in changes to dispositions inhering in the solution, and so changes to its material base that is the solution. But then realization of a disposition is a complex phenomenon, resulting in what we might call *constellations* (Williams, 2020) of disposition pairs interacting. This complexity is not part of extant discussions of the *BFO Treatment*.
* Grounding - While, for example, the use of “internally” and “externally” grounds to distinguish these entities is intuitive, this language is also imprecise. Presently, this distinction is drawn by observing if there is realizable entity change that requires material basis change, then the realizable entity is a disposition; roles may be changed without material change. Consider a student leaving a university. The student loses this role without undergoing material change. The student has this role, however, as a member of the university – which in BFO is understood as a mereological part. Whenever the university gains or loses a student it undergoes material change. The BFO line is that universities are instances of Object Aggregate, which bear instances of Role. Here, however, we have a case in which whenever member parts of the aggregate bearing roles leave, the whole undergoes a material change. That suggests either the university bears a disposition and a role – in which case the relationship between them should be explained – or just a role – in which case the grounding constraint does not distinguish dispositions and roles – or just a disposition – in which case extant literature has mistakenly attributed roles to universities. Presumably, the first option aligns best with BFO. Consider that the heart of a gazelle might bear a disposition to pump blood, but in other circumstances may play the role of dinner for a carnivore. In this respect, a given entity may bear instances of Role and instances of Disposition. In any event, this leads to the next issue:
* Relationships – Little has been said about the relationship between roles and dispositions in general, and even less about how roles and relationships are related across levels of granularity (Bittner & Smith; Bittner, Smith, & Donnelly, ). The molecules comprising a functional group bear some relation to the larger molecules they compose; the student bears some relation to the university. Moreover, little has been said about relationships borne *among* roles, e.g. the relationship between an employee role and a teacher role in a university.

In what follows, we add to discussions of realizable entities in the ontological literature by addressing these concerns. More specifically, we build on the *BFO Treatment* to provide a formal explication of the notions of internal and external grounding which respects BFO’s treatment of the entities mentioned in the preceding, which will in turn address constellation and relationship issues. Our specification of these nuanced scenarios will provide further clarification of the normative standards for ontological modeling with BFO’s realizable entities, and so provide researchers modeling recipes.

**Results**

*Varieties of Grounding*

As discussed, dispositions are internally-grounded realizable entities, and the dispositions that an object has are determined by its pattern of qualities.[[1]](#footnote-1) While the definition of Role in BFO requires grounding in the “physical make-up” of a material entity bearer, material bearers at every point have some quality or other. There is no reference to “bare matter”[[2]](#footnote-2) in BFO.[[3]](#footnote-3) Indeed, material entities are continuants with matter as parts, and so bear shape and size qualities at least. Whatever disposition a material entity thus has will at least be grounded in such qualities.

For all x, t: If x is a material entity at time t then there is some y such that y is a disposition and y inheres in x at t[[4]](#footnote-4)

In BFO, the relation *hasMaterialBasisIn* is used to relate a given disposition and the material in which it inheres at a given time. The *inheresIn* relation holds between – among other things – instances of quality and instances of material entity. There is not, however, a relation holding between a given disposition and qualities in which it is grounded.

**Internal-Grounding.** There is one type of grounding to consider here:

* *Internal-Grounding in Quality*: The solubility of sodium chloride is a disposition inhering in – roughly speaking – the lattice structure of the salt. The salt has this disposition because of its lattice structure. Importantly, the salt may lose its particular lattice structure at a given time and still maintain its solubility disposition. We capture this by requiring the lattice structure changes be minimal, not deviating from the determinate structure of some determinable lattice shape quality class. In short, a solubility disposition inhering in an instance of salt will be grounded in the salt’s shape, and this shape may change slightly while maintaining a solubility disposition inhering in the salt. There is nevertheless some point after which the disposition will no longer inhere in the salt, since its shape will have changed too drastically to ground the disposition. Where this cutoff lies in an assumed arrangement of determinate shapes is an empirical question; that there may be no sharp cutoff is a feature of determinates, cp. Color qualities.

**External Grounding and Mereology.** There are two sub-types of external grounding to consider:

* *External*-*Grounding and Mereology #1*: Consider a relation holding between an instance of Object Aggregate and a proper mereological part of that aggregate. A University is – among other things an Object Aggregate comprised of administrative staff, educators, custodial staff, students, etc. A given student of a University is a proper object part of that aggregate. In this case, an individual bears a student role, correlated with potential manifestations of, say, duties. As a role, this realizable entity is optional, and so no change to the physical qualities of the student need arise if the student loses this role. Note, however, that while the individual need not physical change after the loss of this role, the University does, since it loses a material part. That is, the student bears a mereological parthood relation to the University, and the Object Aggregate that is the University is physically changed following the loss of this part. This may be reflected by a University headcount. On this proposal then, roles are grounded insofar relevant entities bear parthood relations to aggregates, while instances of Disposition are grounded in instances of Quality. The former characterizes external grounding, while the latter characterizes internal grounding.
* *External*-*Grounding and Mereology #2*: Consider two organisms engaged in commensalism. Each bears a commensal role realized in processes associated with commensalism. One organism gains benefit from interacting with the other, while the second neither gains nor loses anything. One might understand this relationship in mereological terms. There is an aggregate composed of these entities, and each organism bears as role insofar as they are members of that aggregate. If one organism loses this membership, it need not physically change the other organism, but the aggregate will lose a mereological part, and thus be physically changed. On this proposal then, roles are grounded insofar relevant entities bear parthood relations to aggregates, while instances of Disposition are grounded in instances of Quality. The former characterizes external grounding, while the latter characterizes internal grounding.

**External Grounding and Dependence.** There are again, two types of external grounding to consider:

* *External*-*Grounding and Dependence #1*: Alternatively, a case might be made for claiming there is a Relational Quality holding between the student and the University, which grounds the role the former has. Taken together as an aggregate, once the individual is no longer a student, the relation between the individual and the University is changed or eliminated. That is, there is a qualitative change to the University. Indeed, in any case of a student leaving University there will be such qualitative change. On this proposal then, roles are grounded in instances of Relational Quality, and distinguished from instances of Disposition which are grounded in instances of Quality. The former characterizes external grounding, while the latter characterizes internal grounding.
* *External-Grounding and Dependence #2*: Alternatively, we might say the grounds of each role is best understood as a relational quality holding between the organisms. The organisms together comprise an object aggregate in which the relational quality inheres. This relational quality is the grounds for each commensal role. Thus, when we describe an organism as bearing a commensal role, this is to say it bears a realizable entity grounded externally, in the sense that it is a proper part of some aggregate and other members of that aggregate partially ground the realizable entity. On this proposal then, roles are grounded in instances of Relational Quality, and distinguished from instances of Disposition which are grounded in instances of Quality. The former characterizes external grounding, while the latter characterizes internal grounding.

**Mereological and Dependence Grounding**. We have uncovered two options for grounding, each of which allows for distinguishing internal from external varieties. The difference, however, is that in one case we require that all instances of Role be dependent on some instance of Specifically Dependent Continuant, a feature we observe when reflecting on instances of Disposition. That said, in the other case we do not require such dependence on instances of Specifically Dependent Continuant, but instead appeal to relations of parthood to distinguish grounds. More succinctly, our options are:

*Dependence Grounding* =def x is a realizable entity and y is a specifically dependent continuant of type T, and if x inheres in material entity b at a time t, then determinates of y inhere in b at t, and x inheres in b at t because determinates of y inhere in b at t

*Mereological Grounding* =def x is a realizable entity and x inheres in material entity y at a time t, and x inheres in y at t and if y losing x is associated with the loss of proper parts of y

According to Dependence Grounding, Roles are externally grounded because they are grounded in instances of Relational Quality, inhering in relevant instances of Object Aggregate. Dispositions are, however, internally grounded because they are grounded in instances of Quality borne by material entities. On the other hand, according to Mereological Grounding, Roles are externally grounded because bearers are mereological parts of Object Aggregates, while Dispositions are internally grounded because they are again grounded in instances of Quality borne by material entities.

One concern arises over the use of Dependence Grounding worth addressing here. This notion of grounding is analogous to what philosophers call “Cambridge” change. Consider, Socrates losing a limb is a more substantial change to Socrates than Socrates being admired by a student. Dependence Grounding is more like the second sort of change. This, however, conflicts with treating relevant grounds as instances of Relational Quality, since in BFO these instances are first-class entities.

*Varieties of Role Dependence*

Given the definitions of Role and Disposition in BFO, it seems clear that the latter can exist without the former. This, moreover, seems intuitive. A portion of water, for instance, bears many dispositions, but may not bear any role at a given time. That said, any given instance of Role does seem to depend on some instance of Disposition. Consider an instance of sodium chloride being used to increase the salinity of water, or enhance the flavor of a dish. Salt is used in these respective fashions because of its dispositions.

For all x, y, t: If x is a Role and x inheres in material entity y at time t, then there is some y such that y is a disposition and y inheres in x at t

The preceding is a consequence of either proposal offered above.

**Blocking Dispositions and Roles.** Manifestations of one disposition often excludes the realizations of other dispositions. Call the former a *blocking disposition* and the latter *blocking dispositions*. Focusing on blocking-blocked disposition pairs forefronts a broader array of background dispositions. D2 counts as a blocking disposition for D1 only if the realization of D2 prevents the realization of D1, and this might arise in various ways. For example, realizations of dispositions result in occurrents, such as processes. D2 might realize process P2, which is incompatible with P1 realized by D1. More concretely, a piece of sodium chloride realizing a process of dissolving in unsaturated water, is incompatible with that portion of water realizing an increase in pH.

Another way in which realization may be prevented is when the presence of a quality Q2 is incompatible with the quality of another Q1. For example, a square entity bears a shape quality that is incompatible with circular shape properties. What we have then are material entities such as sodium chloride, bearing qualities such as shape, volume, lattice structure, etc. In many cases, as a consequence of these qualities, material entities bear dispositions as well. For instance, the lattice structure of sodium chloride is a quality, and sodium chloride bears a disposition to dissolve in unsaturated water which is grounded in that lattice structure. Examining parts of the lattice structure in more detail would reveal, of course, atomic particles bearing qualities, such as charge, force, etc. grounding dissolving dispositions. Following BFO, however, we attend to the level of granularity fitting for our domain, in this case, sodium chloride and water. Our analysis reveals, moreover, how incompatible dispositions may be ground in incompatible qualities. Though in common parlance, we do not say that a round entity cannot be square because round entities realize processes incompatible with processes realized by round entities, this seems due largely to never having the opportunity to experience conflict. A car built with round tires realizes rolling processes incompatible with those associated with a car built with square tires.

Though not previously discussed, similar points apply to *roles*, starting by observing that – much like dispositions – roles often operate against and in conflict with other roles. Call a role that blocks the manifestation of another role, a *blocking role*, and the role blocked a *blocked role*. We again can identify two natural ways in which this might occur. Roles are – like dispositions – realized in occurrents which may themselves conflict with other occurrents. For example, the role of an enzyme to break down protein is incompatible with the process of synthesizing protein, itself grounded in a role. On the other hand, a tree cannot bear a student role, since trees lack qualities needed for being students. Our analysis reveals a further way in which roles may be incompatible with other roles, namely, insofar as they are grounded in dispositions which are themselves incompatible. That is, we observe the following relationships: Roles may be grounded in dispositions; dispositions may be grounded in qualities; qualities may be grounded in material entities.

This suggests that qualities may be incompatible with other qualities, but also dispositions and roles. Similarly, dispositions may be incompatible with other dispositions, and also with other roles.

*Use Case 1: Coronavirus*

As indicated in the introduction, BFO is a general ontology, from which more specific ontologies extend by downward population. The Infectious Disease Ontology (IDO) Core, is an example of a downward extension ontology. IDO covers terms relevant to the investigation of infectious diseases, broadly speaking, and itself boast several extensions to specific diseases such as the Virus Infectious Disease Ontology (VIDO) and the Coronavirus Infectious Disease Ontology (CIDO). We examine applications of the preceding discussion in domains covered by each.

Of particular interest here, IDO Core provides terms needed to represent pathogens, where “pathogen” should be understood as indexed either to a species or to stages in the developmental cycle of a species. Motivation for the former stems from the fact that some viruses may engage in mutual symbiosis with one species, while exhibiting pathogenic behavior towards others. With respect to the latter, mature plants are often susceptible to different pathogens than developing plants. We capture virus pathogenic behavior in VIDO in steps. From IDO Core:

*pathogenic disposition* =def Disposition borne by a material entity to establish localization in or produce toxins that can be transmitted to an organism or acellular structure, either of which may form disorder in the entity or immunocompetent members of the entity’s species.

Borne by instances of the class *pathogen*, and:

*infectious disposition* =def Pathogenic disposition borne by a pathogen to be transmitted to a host and then become part of an infection in that host or immunocompetent members of the same species as the host.

The complexity of the definitions of *pathogenic disposition* and *infectious disposition* reflect the variety of pathogen examples in contemporary literature. Three preliminaries are in order before examining illustrative examples. First, note the term *establishment of localization* used in *pathogenic disposition* is imported from GO, and is tethering or adhesion to a host, while ‘formation of disorder’ abbreviates two imported IDO Core terms: *appearance of disorder,* which is a *process* that *results in the formation of* a *disorder*. Second, there is an implicit temporal ordering in the textual definition of *pathogenic disposition*, which is reflected explicitly in the associated logical axioms. Similarly, there is an implicit temporal ordering in the definition of *infectious disposition* between transmission to a host – represented by *pathogen transmission process* imported from the Pathogen Transmission Ontology (<https://bioportal.bioontology.org/ontologies/PTRANS>) - and becoming part of an infection – represented by the IDO Core *process of establishing an infection*. A pathogen bearing an *infectious disposition* that generates disorder in a host, will have been transmitted to the host prior to establishing localization in the host and will have established an infection prior to the appearance of disorder.

Now to illustrate pathogen and infectious entity examples from the literature. Consider, *s. aureus* is an opportunistic pathogen in humans, becoming harmful to its host under changes in its environment. We count *s. aureus* as a pathogen, even when it does not realize disorder in a host, since it is nevertheless disposed to localize in a human host and generate disorder, if given the opportunity. This is a disposition of *s. aureus* – following BFO – because it is an “internally-grounded” property of the entity. That is, it is part of the material basis of *s. aureus* to generate disorder in human hosts if given the chance. This is analogous to the way salt has a disposition to dissolve, based on its lattice structure, whether it ever realizes this disposition. Salt thrown in unsaturated water had a disposition to dissolve before it was immersed; just because an environmental change triggered manifestation does not mean salt lacked the disposition. Similarly, for *s. aureus*. More generally, opportunistic pathogens are not pathogens because of an opportunity, but because they are disposed to localize and cause disorder in a host.

Consider now, *c. botulinum*, a pathogen which produces toxin spores sometimes ingested by humans. This bacterium counts as a pathogen for adult humans since the toxins often result in disorder when ingested. That said, *c. botulinum* may cause infection in human infants if, say honey colonized by *c. botulinum* is ingested. The sugar content of honey inhibits *c. botulinum* growth, but in the low-oxygen, low-acid intestines of human infants, spores can localize, grow, and produce toxins resulting in disorder. This of course counts *c. botulinum* as a human infant pathogen. We do not, however, take the further step and say *c. botulinum* bears an *infectious disposition* towards human infants, however, since it is not disposed to invade or be transmitted to them. We leave open whether *c. botulinum* may become part of an infection in an infant. Compatibility with either characterization stems from the fact that being part of an infect*ion* is not itself sufficient to be counted as infect*ious*. Pathogens bearing an *infectious disposition* must be disposed to *both* transmit *and* become part of an infection. Many opportunistic pathogens for example, are not infectious.

Immunocompetence and species membership clauses in the respective definitions of *infectious disposition* and *pathogenic disposition* are included to address instances where mutations in hosts may block realization of disorder or infection. In such cases, a pathogen may nevertheless be transmissible and cause disorder or infection in others. For example, HIV-1 is a pathogen that may localize in a host with CCR-5 mutations that block the virus from attaching to host cells, and so block pathogenesis to AIDS. Similarly, *p. falciparum* may be transmitted to a host with a sickle-cell trait that blocks manifestation of the disease malaria. In each case, however, the relevant pathogen may be transmitted to immunocompetent members of the same species as the host. Our definitions count these entities as pathogens, as they should be. It is worth noting, moreover, our claim that *p. falciparum* and HIV-1 count as a pathogen even if they do not result in the formation of disorders for hosts with a sickle-cell trait or CCR-5 mutation, respectively, does not entail there are *no* clinical abnormalities associated with these traits or mutations. Individuals, for example, with CCR-5 mutations do exhibit clinical abnormalities, and so disorders. Importantly, however, this is not *because* of the HIV-1 virus. Rather, it is because of the genetic mutation. Related, it has been hypothesized that evolutionary fitness pressure due to the presence of *p. falciparum* resulted in the presence of sickle-cell trait in certain populations. Consequently, the clinical abnormality associated with the sickle-cell trait is – in a broad sense – because of *p. falciparum*. Similar remarks would apply to the relationships between CCR-5 mutations and *y. pestis* or *v. major*, if suggested selection pressure explanations involving these pathogens are true.

Altogether, *infectious dispositions* are realized in localization in a host, transmission to a host, and generation of infection and disorder in a host or immunocompetent member of the host’s species, and *infectious structures* – such as viruses – bear this disposition. The virus SARS-CoV-2 – characterized in CIDO - for example, is disposed – as a matter of its material composition – to be transmitted to hosts, localize, cause infection, and result in disorder.

We have mentioned “host” at several points in the preceding, and collaboration with the IDO Core team resulted in a ready import for this term to VIDO and CIDO. Construction of the term was guided by recent shifts in researcher focus on host-pathogen interactions. Until recently, microbiologists, immunologists, virologists, and others studying pathogenesis have engaged in either host-centered or pathogen-centered pathogenesis research. Each approach has its merits and has led to impressive research results. Nevertheless, emphasizing one aspect of host-pathogen interactions at the expense of the other may leave valuable questions unanswered. Emphasis, for example, solely on pathogenic factors of SARS-CoV-2 will provide only a partial explanation of various pathogenesis pathways observed in clinical settings; focusing solely on host immune response is similarly limiting. IDO Core, VIDO, and CIDO prioritize neither host nor pathogen in representation of pathogens and associated diseases, adopting the Damage Response Framework (DRF) for guidance in development of relevant terms, which recognizes the importance of both pathogen and host to pathogenesis:

1. Pathogenesis results from interactions between host and pathogen, and attributable to neither alone
2. Host and pathogens interact primarily through damage to the host
3. Host damage is a function of the intensity and degree of host response and pathogen factors, each determined by genetic and phenotypic profiles

Host and pathogen engage in – metaphorically – a tug of war, the results of which influence manifestations of signs, symptoms, and disease.

These principles provided support for the development of host terms in IDO Core, which were then imported to VIDO and CIDO:

*host role*=def Role borne by an acellular structure containing a distinct material entity, or organism whose extended organism contains a distinct material entity, realized in use of that structure or organism as a site of reproduction or replication.

*pathogen host role* =def Host role borne by an organism having a pathogen as part of its extended organism.

*symptomatic carrier role* =def Pathogen host role borne by an organism whose extended organism contains a pathogen bearing an infectious disposition towards the host, and the host has manifested symptoms of the infectious disease caused by the pathogen.

Where symptomatic cases of virus infection can be represented by importing terms from the Symptom Ontology (<https://bioportal.bioontology.org/ontologies/SYMP>), such as *dry cough*, *fever*, *taste alteration*, *smell alteration*, among others. Given the importance of asymptomatic carriers in viral infection spread, moreover, special attention should be given to:

*asymptomatic carrier role* =def Pathogen host role borne by an organism whose extended organism contains a pathogen bearing an infectious disposition towards the host, and the host has no symptoms of the infectious disease caused by the pathogen.

*subclinical infection* =def Infection that is part of an asymptomatic carrier.

The term *subclinical infection* reflects standard – if somewhat obscure – use of the terms “subclinical” and “asymptomatic” while nevertheless allowing for cases in which hosts with clinically abnormal infections exhibit no symptoms. For VIDO and CIDO, this term is straightforwardly extended to *subclinical virus infection*, which is an infection caused by a virus that is part of an asymptomatic carrier.

*Use Case 2: Superposition*

Principles of quantum mechanics have been applied with growing frequency to the domain of biology in recent years. Processes within scope of biology often involve energy conversion and chemical transformations which rely on quantum phenomena. Perhaps surprisingly, our extension of the BFO Treatment of roles and dispositions leads naturally to explication of several aspects of quantum biology.

To illustrate, we must first clear up terminology. Physicists frequently speak of quantum phenomena as involving wave-like particles. Waves are tricky to model. A wave crashing on a beach is arguably composed of water and debris, but dissipates on the beach, while the sea remains. There are waves in ponds that emerge when fish strike upwards from the deep. Sound waves transmit information to hearers through air or perhaps through other waves, e.g. under water.

Waves are not their material bearers. Waves, for example, are not composed of the same, say, water as they proceed towards a beach, but undergo changes in composition throughout. Waves, moreover, are superimposable, whereas material entities in BFO are not. Any two material entities that occupy the same space at all times they exist are identical. Waves are, moreover, not merely shapes, since they must be borne by bearers.

We argue – pace other ontologists (Batchelor & Hastings, ) – that waves have disposition and role features. Some argue waves cannot be dispositional because – citing (Mumford & Anjum, 2010) – manifestations of dispositions always lead to the creation of new dispositions. Mumford and Anjum merely assert this is so, however, without argument. It is consistent (Williams, 2020) for a theory of dispositions to allow for cases in which a disposition manifests without creating a new disposition, e.g. two cards stacked against each other on a table (Martin, 1994). Additionally, BFO remains neutral on this matter. In any event, dispositions are superimposable in the sense that manifestations can be blocked as described above.

One wrinkle here is that dispositions are always grounded in some material entity. This is particularly troubling since quantum waves – photons – are sometimes claimed to lack material features. This is because photons are claimed to be energy and massless. But note, energy is the capacity to do work, and that means it is a disposition. Note too that photons may lack mass but that need not imply they lack material parts. Photons have spin, for instance, which implies they have angular momentum, and so are extended. But this in turn implies they have material parts.

On our proposal, quantum waves are best understood as dispositional and so having material bases, and realized in various processes. Superposition is explained by appealing to the fact that wave realizations may block others. This provides a basis for discussion of quantum tunneling, which where roles and dispositions both come into play.

Bring in slit experiment to illustrate photon has light and wave like features

role understood as completed process may provide wave aspect and disposition is particle

Should we say waves have dispositional and role like properties, much like physicists say photons have wave and particle properties?

**Discussion**

Summary and what to do next for future work

Compare work that’s been done with the work of others, as a way to clarify

Discussions of superposition in philosophical, physics, etc. literature. We are the *first* to discuss superpositions through the lens of applied ontology.

Limitations

**Concluding Remarks**

Briefer summary of just the most significant points (highlights), one paragraph

**Acknowledgements**

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