An Ontological Approach to Developing a Unified and Interdisciplinary Framework for Aging

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Abstract

Aging is a central notion in various domains, including biomedicine. There is an urgent need for a unified and interdisciplinary framework for articulating the multifaceted character of aging. To take initial steps towards such a framework, we provide an ontological analysis of the six defining features of aging based on Basic Formal Ontology (BFO): functional decline, structural damage, reserve depletion, cellular senescence, phenotypic change, and the increase in the probability of death or disease. Our proposal leverages the BFO dispositional account of function as well as a BFO-compliant theory of dispositions and dispositional approach to causation. We also briefly discuss premature aging, disease, health, and homeostasis in relation with aging.

Keywords

aging, disposition, causation, function, Basic Formal Ontology (BFO)

1. Introduction

1.1. Background and purpose

Aging is a central notion in various domains, ranging from biology and medicine to evolutionary ecology, demography, and epidemiology. Defining aging is nonetheless a thorny issue. Medvedev's [1] classical work classifies more than 300 existing accounts of aging and concludes that: "we need many theories [of aging] because in nature ageing exists in many diverse forms and variations" (ibid., p. 391). In a similar vein, Cohen et al. [2] have recently argued that aging is such a heterogeneous phenomenon that it may be undesirable to attempt a single unitary notion of aging.

This line of reasoning leads a different team [3] to propose that, for further advancement, aging biology should develop an interdisciplinary framework for comparing and unifying different theories of aging in different domains. As a matter of fact, López-Otín et al.'s [4] "nine hallmarks of aging" may be traditionally taken and utilized as a promising candidate for such a framework. However, this nine-hallmark view of aging is not without difficulty. For instance, Gems & de Magalhães [5] maintain that, despite its usefulness in biogerontology, this hallmark-based approach to aging fails to constitute an explanatory paradigm for understanding the mechanistic causes of the diverse aging-related pathological phenomena.

In this paper we put forward the idea that ontology can offer an alternative way of developing such a unified and interdisciplinary framework for investigating aging. In information science, an ontology is an explicit representation of a certain domain that is given in formal language and it has been used as a tool for enhancing the integration of data and knowledge that are dispersed in different information systems (e.g. databases). An ontology of aging is expected to specify a common ground for various theories

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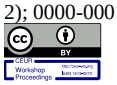
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of aging because it serves to make implicit assumptions of these theories transparent and to facilitate the comparison among their commonalities and differences.

The paper is organized as follows. Section 1.2 specifies the methodology. Section 2 is devoted to preliminaries. Section 3 provides an ontological analysis of several defining features of aging. Section 4 offers discussion. Section 5 concludes the paper.

1.2. Methodology

To embark on the development of a unified ontological framework for aging, we will analyze ontologically six defining features of aging that are extracted from the relevant literature: (1) functional decline, (2) structural damage, (3) reserve depletion, (4) cellular senescence, (5) phenotypic change, and (6) the increase in the probability of death or disease.

Several clarificatory caveats are in order. First, we are using the term "defining feature" that is looser than the term "definition", by which we mean giving a set of individually necessary and jointly sufficient conditions for something being the entity in question (aging, in our case). This is motivated by Lemoine's [6] similar word preference that is based on his observation that, instead of defining aging, many existing works state what aging *is associated with*.

Second, we do not think that these six defining features can exhaust all the key characteristics of aging, since it is considerably complex and multifaceted (see, for instance, Cagan et al.'s [7] recent finding that somatic mutation rates may be a contributory factor in aging). At the same time, we contend that they are an integral part of a solid foundation for an ontology of aging because they can be found and causally linked in what we may call the "canonical case of aging" (if not in all particular aging phenomena): roughly, the idealized case that is synthetically described by general biomedical observations of aging.[2] For that matter, Lemoine [6] reviews the literature on aging and discusses the five defining features of aging, which we will scrutinize in addition to cellular senescence.[3]

Moreover, we will concentrate on one particular scenario of aging in which processes that are defining features of aging are causally connected. This scenario is visualized in Figure 1 (in the appendix) and the processes therein will be written in boldface (e.g. "**process1**", which refers to a particular process of functional decline). In addition, there are multiple interpretations of the causal links among these processes. But in principle, we will provide one compelling interpretation thereof with recourse to the second dispositional approach to causation given in Section 2.3 (which appeals to dispositions and their causal bases) because this approach may serve to provide one unifying perspective on causal relations between what we may call "aging processes", as illustrated by the six defining features of aging.

Third, it is not the case that the six defining features of aging are specific only to aging phenomena. For example, not all function declines are associated with aging: if you are involved in a serious car accident, you could lose the function of your right arm to grab something, totally irrespective of aging. In employing the term "functional decline", we therefore refer to a phenomenon of functional decline of a specific kind (where this kind may be expected to be defined or elucidated in the future, as an ontology of aging is furthered). All the terms representing defining features of aging should be understood in this way.

Fourth and finally, functional decline is of paramount importance among the six defining features of aging. We will hypothesize that all the other five features can be well explicated in relation with functional decline. (We will explain the centrality of function and functional decline to aging phenomena in Section 3.1.) Thus, we will develop a disposition-centered approach to aging. For one thing, we adopt a dispositional perspective on the causal import of aging (see Section 2.3). For another, functional decline plays a critical role in our analysis of aging (see Section 3.1) and function is a subtype of disposition (see Section 2.2).

[2] Our elucidation of the term "canonical case of aging" takes a cue from Rosse & Mejino's [8] notion of "canonical anatomy": "a field of anatomy (science) that comprises the synthesis of generalizations based on anatomical observations that describe idealized anatomy (structure)" (ibid., p. 480).

[3] Lemoine [6] argues that "aging is associated with at least one of the following features: structural damage, functional decline, depletion, a progressive increase of the probability of death, or the phenotypic traits typical of old age." In this paper, by contrast, we presuppose that aging refers to a heterogeneous phenomenon (cf. [2]) in which his five defining features of aging ("aging processes", which we will introduce later) are causally connected, which we will analyze ontologically below.

2. Preliminaries

2.1. Basic Formal Ontology (BFO)

In order to give an ontological characterization of aging, we will deploy Basic Formal Ontology (BFO)[9][10]. BFO is an upper ontology that is theoretically underpinned by the idea (often called the "realist methodology") that (scientific) ontologies should represent what exists in reality [11] and it is recognized by the International Standards Organization [12]. BFO is also arguably one of the most widespread upper ontologies in the context of the Open Biological and Biomedical Ontologies (OBO) Foundry [13][14]: a collaborative project to coordinate interoperable biomedical ontologies.

BFO endorses a top-level distinction between continuants and occurrents, the former being further divided into independent continuants and dependent continuants. Continuants continue to exist in time (while having no temporal parts), whereas occurrents extend through time.

Regarding continuants, a material entity is an independent continuant that has some portion of matter as part (e.g. organisms and an aggregate of cells). A specifically dependent continuant is a dependent continuant that depends (existentially) on at least one independent continuant. A quality is a specifically dependent continuant that does not require any further process in order to be realized (e.g. color, shape, and mass).

Notably, a realizable entity is a specifically dependent continuant that inheres in some independent continuant and is of a type such that some instances thereof are realized in processes of a correlated type. We will delineate two specific subtypes of realizable entities below: dispositions and functions (refer to Toyoshima et al. [15] for a global view of realizable entities in BFO).

Regarding occurrents, a process is an occurrent that exists in time by occurring, has temporal parts, and depends on at least one independent continuant as participant (e.g. the process of cell division).

2.2. Disposition and function

Two subtypes of realizable entities in BFO will be pivotal to our investigation into aging: dispositions and functions. A disposition is: "A realizable entity (…) that exists because of certain features of the physical makeup of the independent continuant that is its bearer" ([9], p. 178). Paradigmatic examples of dispositions include fragility (the disposition to break when pressed with sufficient force) and solubility (the disposition to dissolve when put in a solvent).

We will leverage a BFO-compliant enriched theory of dispositions that has been elaborated in line with Röhl & Jansen's [16] and Barton et al.'s [17] works. A disposition can be realized in some process and to be realized in a process, a disposition needs to be triggered by another process. By way of illustration, the fragility of this glass can be realized in a process of glass-breaking and it can be triggered by a process of pressing the glass with force above a certain threshold.

A disposition has some causal basis: roughly, something of the disposition bearer that renders the disposition causally relevant to its realization (refer to Toyoshima et al. [15] for details on causal bases of dispositions, or more broadly of realizable entities). There are two kinds of causal bases of dispositions: (1) a material basis of a disposition, which is a material entity of the disposition bearer; and (2) a categorical basis of a disposition, which is one or more qualities of the disposition bearer. For instance, the fragility of this glass has as material basis some molecules and as categorical basis the relevant molecular structure.

In BFO, a function is a disposition of a bearer with a specific kind of historical development [18] (for more thoughts, see Röhl & Jansen's [19] and Jansen's [20] criticism of such a dispositional account of function). In more detail: "a function is a disposition that exists in virtue of the bearer's physical make-up, and this physical make-up is something the bearer possesses because of how it came into being — either through natural selection (in the case of biological entities) or through intentional design (in the case of artifacts)" [9](pp. 102-103). Examples of functions include the function of this heart to pump blood and the function of this screwdriver to turn screws.

2.3. Causation and disposition

Causation is pertinent to the study of aging. Lemoine [6] says that a satisfactory definition of aging for biomedical research can be expected to articulate the main features of aging by determining cause-and-effect relationships. To explore the causal import of aging, we focus on the linkage between causation and dispositions, partly because of the utility of a dispositional

approach to causation in biomedical ontologies [21].

We specify two possible ways of connecting causation and dispositions, while leaving a full-fledged dispositional account of causation for future work. For this purpose, we adopt the assumption that is accepted by many theories of causation in formal ontology: causation involves a binary relation between processes [21]. We will call such two causally related processes a "causing process" and a "resulting process".

One way of linking causation with dispositions is that a causing process triggers a disposition, which is in turn realized in a resulting process. To take a simple example, when this process of pressing this glass with force caused this process of glass-breaking, the former process triggered the fragility of the glass, which was in turn realized in the latter process. This dispositional perspective on causation coheres with the prevailing view that a causing process temporally precedes a resulting process [21]. It may also correspond to what BFO calls the "causality of processes triggering dispositions" [12] (Section A.1.1).

Another possibility is that a causing process is a change in a causal basis of a disposition and a resulting process is a change in this disposition. Suppose for instance that Mary's heart has an arial septal defect (a hole in the heart between the atria) and it can pump blood better after some surgery has closed the hole. In this case, we can say that this process of closing the hole in Mary's heart caused this process of Mary's heart becoming capable of pumping blood better. Seen dispositionally, the former process is such that the four-chambered structure that is a causal basis of the disposition (or function) of Mary's heart to pump blood was restored and the latter process is such that this disposition was improved

It is this second dispositional analysis of causation that will be vital for our characterization of aging. As we will see below, causal relations among many aging phenomena might be explicable in terms of dispositions and their causal bases. It is also worth noting that, according to this dispositional interpretation of causation, a causing process may be (partially) simultaneous with a resulting process. By way of example, the restoration of the four-chambered structure of Mary's heart may coincide with the improvement of the disposition of Mary's heart to pump blood. This disposition-based idea of simultaneous causation merits foundational consideration, but it falls outside the scope of our present article (for initial thoughts, see Mumford & Anjum's [22] argument for simultaneous causation in their dispositional theory of causation).

3. An ontological analysis of the six defining features of aging

3.1. Functional decline

Functional decline refers to a phenomenon in which a function is damaged (e.g. the decline of the function of the ear to detect sounds). We submit that function and functional decline can serve as a hub for an ontological approach to aging. According to Medvedev's [1] classification of theories of aging, "theories related to age changes" pertain to "the deterioration of structures or *functions* in aged organisms or tissues" (ibid., p. 378, emphasis added). López-Otín et al. [4] speak of the "*functional* interconnections between the hallmarks of aging" (ibid., p. 1207, emphasis added). They also characterize the third group of the hallmarks of aging ("integrative hallmarks") — stem cell exhaustion and altered intercellular communication — as being ultimately responsible for functional decline.

In ontological parlance, functional decline is a process (as illustrated by **process1**) and has as participant an independent continuant that bears a function at least at the beginning point of this process. A function is a disposition and it has a causal basis: for example, the function of the ear to detect sounds has as (part of its) causal basis hair in the ear canal. While almost always a continuum, we can identify two sections on the functional decline continuum. (1) A process leading to a reduced function but which level is deemed still relevant. (2) A process leading to a function decline so profound that it is deemed that the function ceases to exist as far as the individual's activities are concerned. An example of the former would be a partial hearing loss where an individual might have difficulty discerning certain words in a crowed, busy environment while an example of the latter would be the complete lack of awareness of sounds in one's daily activities (even though with specialized testing, some frequencies might still register if amplified).

3.2. Structural damage

Structural damage refers to a phenomenon in which some physical structure deteriorates (e.g.

the deterioration of the spiral structure of the cochlea inside the ear). Based on Medvedev's [1] classification, "theories related to age changes" relate to "the deterioration of *structures* or functions in aged organisms or tissues" (ibid., p. 378, emphasis added). López-Otín et al. [4] characterize the first group of hallmarks ("primary hallmarks") — genomic instability, telomere attrition, epigenetic alteration, and loss of proteostasis — as being causes of cellular damage and the second group ("antagonistic hallmarks") — deregulated nutrient sensing, mitochondrial, and cellular senescence — as being responses to cellular damage. In this respect, cellular damage is highly relevant to the hallmark view of aging and cellular damage is a kind of structural damage.

From an ontological perspective, structural damage is a process in which some physical structure (which is taken here to be a quality) deteriorates (as illustrated by **process2**). In the canonical case of aging, structural damage causally contributes to functional decline. Because causation involves a binary relation between processes, this process of structural damage **process2** causes this process of functional decline **process1**.

Given the second dispositional construal of causation, the causality involved here might be considered in such a way that the structure that is a categorical basis of a function figuring in this process of functional decline **process1** is damaged in this process of structural damage **process2** (alternatively, according to the first dispositional analysis of causation, **process2** might trigger some disposition which is in turn realized in **process1**; as explained earlier, such alternative interpretations of causal connections might hold also for the analysis of the connection between other processes and will not be repeated later).

3.3. Reserve depletion

Reserve depletion refers to a phenomenon in which the reserve decreases, where the term "reserve" roughly means something that helps to repair or compensate for functional decline. This understanding of reserve is given e.g. by Lemoine [6], who takes reserve depletion as one of his five defining features of aging. Two subtypes of depletion can be identified: 1) a "fixed stock of materials" (e.g. stem cells, oocytes, and nephrons) or 2) a "limited number of repair/compensation actions" (e.g. replication, protein, synthesis, and the elimination of damage proteins).

To put it ontologically, reserve depletion is a process in which the reserve diminishes. We can represent the first subtype of reserve (namely, as a fixed stock of materials) by introducing a reserve that is a subtype of material entity and illustrate a process of the depletion of the first subtype of reserve with **process3**. In the canonical case of aging, reserve depletion causally contributes to functional decline. That is to say, this process of reserve depletion **process3** causes this process of functional decline **process1**.

The causality involved here can be dispositionally viewed as follows: (at least part of) one or more material entities in the reserve that is a material basis of a function figuring in this process of functional decline **process1** is depleted in this process of reserve depletion **process3**.

The second subtype of reserve proposed by Lemoine, as "limited number of repair/compensation actions", would be more difficult to ontologize, though. Indeed, in this case, the reserve would be constituted by *possible* individual actions, and BFO only considers *actual* individuals because of its realist methodology (see Section 2.1). It might be represented by a disposition to be realized in a process of repair/compensation action such that, when this disposition is realized in a certain number of times, it disappears or cannot be realized anymore.

3.4. Cellular senescence

Cellular senescence refers to an irreversible cell cycle arrest. In Medvedev's [1] classification, "theories related to primary change" are: "based on the study of or suggestion of the nature of possible internal or external damage factors which generate *irreversible changes in cells* and tissues" (ibid., p. 378, emphasis added). As said in Section 3.2, cellular senescence is one of López-Otín et al.'s [4] "antagonistic hallmarks".

Ontologically speaking, cellular senescence is a process of the cessation of cell division. In the canonical case of aging, cellular senescence causally contributes to functional decline: let us consider a process of cellular senescence **process4** that causes this process of functional decline **process1**.

The causality involved here can be dispositionally analyzed in either of the following two ways: cells figuring in the process of cellular senescence **process4** are (i) parts of the reserve

(which we take to be a material entity; see Section 3.3) which is a material basis of a function involved in the process of functional decline **process1** or (ii) parts of the bearer of the structure (cf. Section 3.2) where this structure is a quality that is a categorical basis of such a function; and these cells are no longer capable of progressing through the cell cycle.

3.5. Phenotypic change

Phenotypic change refers to a phenomenon of change in phenotypic traits. It is one of Lemoine's [6] five defining features of aging. His examples of phenotypic traits include the level of inflammation and frailty.

From an ontological point of view, phenotypic change is a process of change in phenotypical traits (as illustrated by **process5**). We take it that a phenotypic trait is a subtype of quality or disposition. For one thing, the term "phenotype" refers to a quality or an aggregate of qualities within the Ontology for General Medical Science (OGMS) [23], which has been developed in alignment with BFO and the OBO principles. In fact, it is plausible to think of the level of inflammation as a quality. For another, we have good reason to see some phenotypic traits as dispositions, as frailty is closely akin to fragility, which is an exemplar of dispositions.

In the canonical case of aging, some functional decline causally contributes to some phenotypical change: in our illustrative example, this process of functional decline **process1** causes this process of phenotypic change **process5**.

The causality involved here can be dispositionally seen as follows. The categorical basis of a function figuring in a process of functional decline **process1** is part either (i) of the phenotypic trait figuring in a process of phenotypic change **process5** when the phenotypic trait is a quality or (ii) of the causal basis of the phenotypic trait figuring in a process of phenotypic change **process5** when the phenotypic trait is a disposition; and when the causal basis of the involved function changes, the associated phenotypic trait accordingly changes.

3.6. The increase in the probability of death or disease

The increase in the probability of death or disease here refers to a phenomenon of the progressive increase in the probability of death, or sometimes of disease, throughout the lifetime of the individuals in a population. We owe this explanation to Lemoine [6], among whose five defining features of aging is the increase in the probability of death or disease.

Seen ontologically, the increase in the probability of death or disease is a process. In the canonical case of aging (at least in molecular biology, as Lemoine says), functional decline causally contributes to the increase in the probability of death or disease: in our example, the process of functional decline **process1** causes a process of increase in the probability of death or disease **process6**.

The causality involved here can be dispositionally examined as follows. The categorical basis of the function figuring in this process of functional decline **process1** is part of the causal basis of a disposition to die or to contract a disease, where **process6** is the process of increase of the probability associated to this disposition; and when the causal basis of the involved function changes through **process1**, the associated probability of death or disease accordingly increases (refer to Barton et al. [24] for details on how we can assign probabilities to some dispositions).

4. Discussion

We will briefly discuss premature aging (Section 4.1) as well as disease (Section 4.2), health (Section 4.3), and homeostasis (Section 4.4) in connection with aging. The relationship between disease or health and aging deserves consideration because we are generally concerned with aging to prevent aging-related disease, improve the quality of life, and expand lifespan. Homeostasis is also closely intertwined with aging because it can provide a more fine-grained perspective on some defining features of aging.

4.1. Premature aging

Premature aging is somewhat elusive to define, as it requires the use of a group of reference which is said to have "usual" or "average" aging. The implications might therefore vary based on the characteristics of the chosen group like sex, genetic background, etc. Nevertheless, one can postulate that premature aging refers to a phenomenon in which typical characteristics of old age manifest themselves earlier than usually.

Function decline is often gradual and so is the process of aging. In particular, in case of premature aging, the functional decline is more pronounced than in the group of reference.

Following the approach presented in this work, we can give two examples of how premature functional decline could be described. If an individual is born with a less advantageous biological characteristic, for example, shorter telomers than the "standard" or "average" individual from a group of interest, all else being equal, they will present a faster functional decline than an individual with average length telomers. Similarly, the repair capabilities of the organism are also at play. If an individual starts with telomers of average length but cannot repair the UV damage as effectively as average of individuals in the group of reference, he will also suffer from a more pronounced functional decline linked with very short telomers faster. Both phenomena, individually or in combination, can contribute to premature aging.

4.2. Disease and aging

We will address two questions about disease and aging that are inspired by Lemoine [6]. First, is aging a disease? Second, what is a so-called "disease associated with aging" or, more simply, an "aging-related disease"? To tackle them, we will introduce the dispositional theory of disease that is provided by the OGMS [23].

The OGMS definition of disease employs two technical terms: "disorder" and "pathological process". Roughly, a disorder is a material entity which is a clinically abnormal part of an organism. A pathological process is a bodily process that is a manifestation of a disorder, where a bodily process is a process in which one or more material entities within or on the surface of an organism participate. Pathological processes can be recognized through symptoms and signs.

The OGMS provides the following definition of disease:

> disease $=_{def.}$ A disposition (i) to undergo pathological processes that (ii) exists in an organism because of one or more disorders in that organism. [23](p. 118)

Disease is a disposition that inheres in an organism and that has as material basis some disorder(s) in the organism. To take one example, epilepsy is a disposition to undergo the occurrence of seizures (pathological processes) that exists because of some clinically abnormal[4], neuronal circuitry (disorder) of the brain.

As for the realization of disease, the OGMS introduces the term "disease course": a disease course is the totality of all processes through which a disease is realized. The disease course ranges widely from potentially asymptomatic early stages of the disease to its recognizable, pathological processes. For example, the disease course of epilepsy can comprise pathological processes of seizures and processes of loss of consciousness.

Consider now the first question of whether aging is a disease or not. We can certainly answer it negatively: in the OBO Foundry framework, aging is not a disease. The OGMS says that disease is a disposition, whereas we analyzed any of the six defining features of aging as a process (see Section 3). However, the term "disease" is ambiguously used in medical discourse and it may sometimes refer to a pathological process or a process in the disease course. Thus, the statement that "aging is a disease" may be understood as meaning that aging is a pathological process, a process in the disease course, or perhaps an aggregate of such processes. A complete answer to this question will warrant the disambiguation of both terms "aging" and "disease".

Let us turn to the second question of what an aging-related disease is. There can be many answers to it because disease can be associated with aging in so many ways. We provide merely one possible interpretation for being an aging-related disease. The basic idea is that an aging-related disease is a result of some "aging process", as illustrated by any of the six defining features of aging.

One way to concretize this idea is to utilize the entity that the OGMS calls an "etiological process". This term is explained as follows:

> etiological process $=_{def.}$ A process in an organism that leads to a subsequent disorder.
>
> Example: toxic chemical exposure resulting in a mutation in the genomic DNA of a cell. [23](p. 118)

[4] The definition of "being clinically abnormal" in OGMS remains somewhat elusive, with a risk of circularity if it is defined as leading to a pathological process. A more involved exploration of this notion lays outside the scope of this paper.

An etiological process is a process at the end point of which a disorder comes into existence. Moreover, because the "etiological process creates the physical basis of (…) the disease" (ibid.), it can be thought of as a process that produces a disorder and its concomitant disease (which has this disorder as material basis).[5]

We can now conjecture that some (if not every) type of aging-related disease is a disease that has as material basis a disorder that results from an etiological process that is either a (proper or improper) part of some aging process or caused by it. Note that we leave open the nature of the causal relation between aging processes and etiological processes of aging-related diseases, especially how it can be dispositionally construed.

To illustrate this hypothesis, consider the fact that presbycusis is commonly caused by gradual changes in the inner ear as we age. Assuming that Mary was an aged woman and contracted presbycusis, this process of the damage of the spiral structure of the cochlea inside Mary's right ear is part of some etiological process, which in turn produces the clinically abnormal cochlea therein (which is a disorder) and brings about Mary's presbycusis (which has as material basis this cochlea).

4.3. Health and aging

The relationship between health and aging may be all the more difficult to analyze because the notion of health remains largely unexplored from an ontological viewpoint. To consider the connection between them, we introduce Werkhoven's [25] philosophical account of health, while leaving for future work its full-development in the context of formal ontology.

Werkhoven develops a dispositional theory of health. The guiding idea is that pathological phenomena reduce what an organism is capable of doing, or the number of dispositions that the organism has. For instance, Mary will lose a disposition to move from one place another when she suffers from locomotive disability. This observation leads to the view that health is a measure of the set of an organism's dispositions ("disposition set") relative to the maximum set of dispositions ("maximum dispositional set") that the organism could have. To elucidate the maximum dispositional set, Werkhoven borrows Boorse's [26] notion of the "reference class" that is specified by species, sex, and age. Hence, he defines health as: "the ratio of a living organism's dispositional set compared to the maximum dispositional set belonging to its reference class" [25](p. 934).

Given Werkhoven's dispositional conception of health, we will briefly consider the linkage between health and aging. To be concrete, let us focus on the fact that, in the canonical case of aging, a process of functional decline (as illustrated by **process1**) causally contributes to a process of being less healthy (as illustrated by **process7**) (note our usage of the term "causally contributes to" rather than "causes" for the reason to appear below). For example, this process of the decline in the function of Mary's right ear to detect sounds causally contributed to this process of Mary being less healthy. The Werkhoven-style dispositional account of health enables us to analyze the latter process as a process of Mary losing her disposition to hear sounds.

It should be however noted that we may not be able to say straightforwardly that a process of functional decline *causes* a process of being less healthy in accordance with the standard view of causation as involving a binary relation between processes. This is because these two different processes may reside at different granular levels of reality, as a process of function decline has as participant one or more parts of an organism but a process of being less healthy has as participant the organism as a whole. Therefore, close scrutiny of the causality involved in the two processes requires a granularity-laden approach to causation. For pointers into this line of inquiry, see Vogt's [27] granularity framework for the life sciences. See also Barton et al.'s [28] theory of disposition-parthood as it may be helpful in analyzing the interrelationships among dispositions at different granular levels of reality, such as the connection between the function (which is a disposition) of Mary's right ear to detect sounds and Mary's disposition to hear sounds.

4.4. Homeostasis and aging

Homeostasis is pertinent to aging because, very roughly, aging is part of life and life is a matter of maintaining homeostasis while facing what can be described as a hostile environment.

[5] "The etiological process creates the physical basis of that disposition to pathological processes which is the disease. (…) Etiological processes do not form a natural kind. To be etiological is to be such as to have brought about an outcome of a certain sort: pathological processes realizing one disease may lead to dysfunction that gives rise to the further disease of depression." [23](p. 118)

To be more concrete, the intuitive notion of homeostatic state is involved in two phenomena relevant to the probability of death (cf. Section 3.6): (1) how far an organism is from the homeostatic state owing to some factors (e.g. mutations and infections) and (2) how effective and efficient is the organism at correcting "drifts" from the homeostatic state. Generally speaking, when an organism ages, it tends to have a higher probability of death because of both factors. For example, if you are too old and each kidney have lost too many nephrons, you may have a higher probability of death because of the first phenomenon as you might not be able to get rid of toxic substances quickly enough — but not necessarily in the second sense since the remaining nephrons could be functioning correctly and be able to recuperate from insults. The converse situation is obviously also possible where the number of nephrons might not have diminished but each nephron is less efficient at repairing itself following some insult.

The OGMS takes "homeostasis" to be a primitive term but elucidates it in such a way that homeostasis is a disposition of the whole organism to regulate its bodily processes in some associated way. [6] Although lack of space precludes a careful study of exactly how homeostasis is relatable to aging, we will pose several important questions to facilitate this direction of future work.

First, what is the relationship between homeostasis and the disposition to die or to contract a disease (articulated in Section 3.6)? Given that homeostasis is a disposition, what kind of relationship can hold between these two dispositions? How can we ontologize the aforementioned observation about homeostasis and the increasing probability of death?

Second, what is the relationship between homeostasis and health? As we said in Section 4.3, health can be characterized in terms of an aggregate of dispositions of the whole organism. Because homeostasis is a disposition of the whole organism, how can we link homeostasis with such health-related dispositions and further with aging?

5. Conclusion

We laid down the basic groundwork for an ontology of aging by providing an ontological analysis of the six defining features of aging which centers around functional decline and the dispositional account of function that is adopted by the BFO upper ontology. Our proposal is built upon a BFO-compliant theory of dispositions and dispositional approach to causation. We also briefly discussed premature aging as well as disease, health, and homeostasis *vis-à-vis* aging, with reference to the OGMS dispositional conception of disease and homeostasis, and in addition, Werkhoven's dispositional theory of health.

In our canonical case of aging, we identified six processes (**process1 — process6**) that might each be qualified as being an "aging process" in some theory of aging. We also outlined an ontological framework that has the potential to encompass those six processes in a unifying way. Further development of this framework will require a systematic, ontological comparison of existing theories of aging.

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[3] Cohen AA, Kennedy BK, Anglas U, et al. Lack of consensus on an aging biology paradigm? A global survey reveals an agreement to disagree, and the need for an interdisciplinary framework. *Mech Ageing*

[6] "We use 'homeostasis' to designate a disposition of the whole organism (or of some causally relatively isolated part of the organism, such as a single cell) to regulate its bodily processes in such a way as (1) to maintain bodily qualities within a certain range or profile and (2) to respond successfully to departures from this range caused by internal influences or environmental influences such as poisoning. When bodily processes yield qualities outside the homeostatic range, the organism initiates processes designed to return the qualities to a value within this range. In some cases, homeostasis can be lost and then re-gained at a level that is clinically abnormal, for example in the case of adaptation to major injury. In other cases the organism will pass a point where it falls irreversibly outside the realm of homeostasis" [23](p. 117). It is interesting to note that aging seems to represent an exemplar of the case in which "the organism will pass a point where it falls irreversibly outside the realm of homeostasis".

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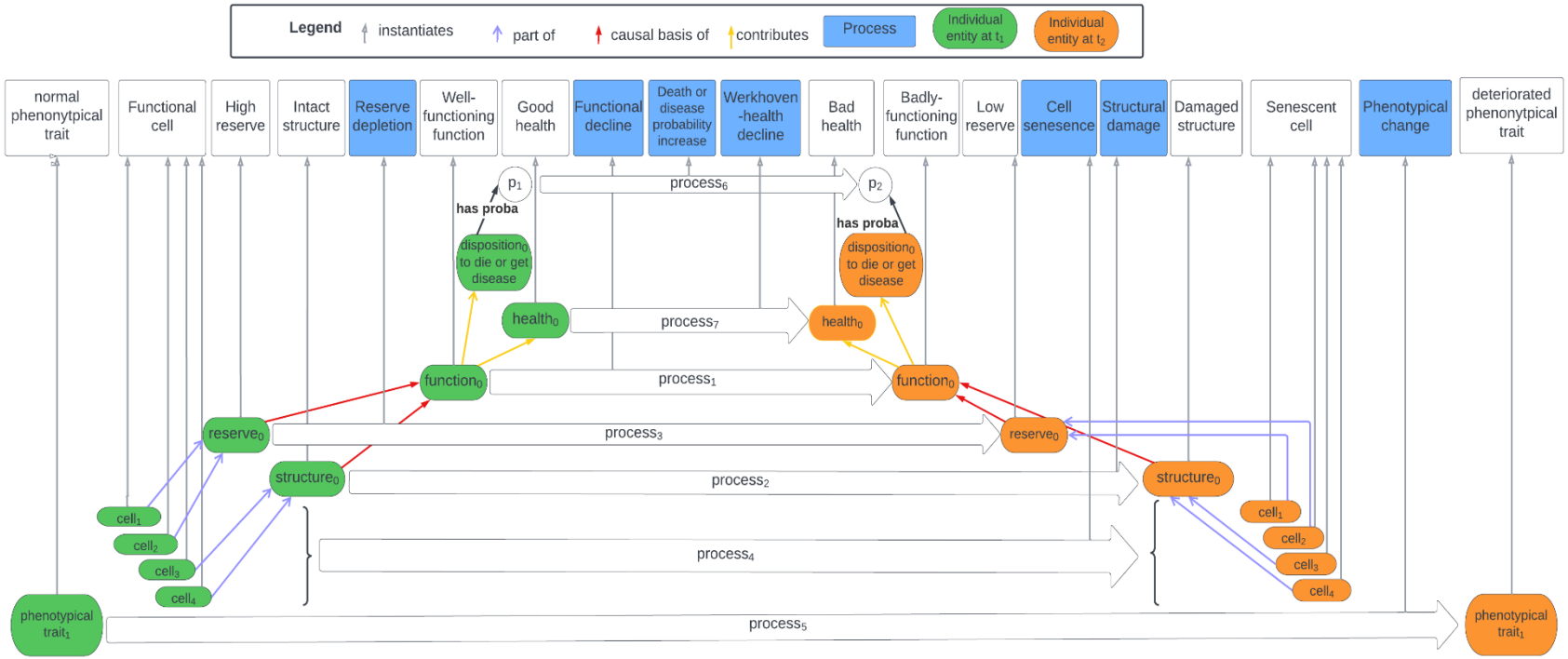
Legend
instantiates
part of
causal basis of
contributes
Process
Individual entity at t1
Individual entity at t2
normal phenonytpical trait
Functional cell
High reserve
Intact structure
Reserve depletion
Well-functioning function
Good health
Functional decline
Death or disease probability increase
Werkhoven-health decline
Bad health
Badly-functioning function
Low reserve
Cell senesence
Structural damage
Damaged structure
Senescent cell
Phenotypical change
deteriorated phenonytpical trait
p1
p2
has proba
has proba
disposition0 to die or get disease
disposition0 to die or get disease
process6
process7
process1
process3
process2
process4
process5
health0
health0
function0
function0
reserve0
reserve0
structure0
structure0
cell1
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cell1
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phenotypical trait1
phenotypical trait1