

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

Fumiaki Toyoshima (Université de Sherbrooke)

jww: Adrien Barton (IRIT, CNRS, Université de Toulouse)

& Jean-François Ethier (Université de Sherbrooke)

ICBO2022

September 25-28, 2022



Background: Aging



- Central to many domains: biology, medicine, demography, etc.
- A very heterogeneous phenomenon. Hard to define.
 - Z.A. Medvedev’s classification of more than 300 theories
 - “ageing exists in many diverse forms and variations”
- Problem: Lack of a unifying framework for various theories of aging
 - Previous work: C. López-Otín et al.’s “nine hallmarks of aging”

Purpose and methodology

- *Purpose*: To develop an ontology of aging that can serve as a unified and interdisciplinary framework for investigating aging
 - *Methodology*: By giving an ontological analysis of the six defining features of aging based on Basic Formal Ontology (BFO)
- Six defining features of aging: (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

Homeostasis and aging



- Important for aging
 - Very roughly, aging is part of life.
 - And life is a matter of maintaining homeostasis while facing a “hostile environment” (e.g. infectious agents).
- More specifically: The loss of homeostasis is linked with some increase of the probability of death
 - It’s a defining feature of aging: When an organism ages, it tends to have a higher probability of death.

Two ways of homeostasis relating to the increase of the probability of death

1. How far an organism is from the homeostatic state owing to some factors (e.g. mutations and infections)
 - Each kidney in your old body has lost too many nephrons.
 - Even if the remaining nephrons can recuperate from insults.
2. How efficient the organism is at correcting “drifts” from the homeostatic state
 - Your kidneys still have a good number of nephrons.
 - But each nephron is insufficiently efficient at repairing itself.

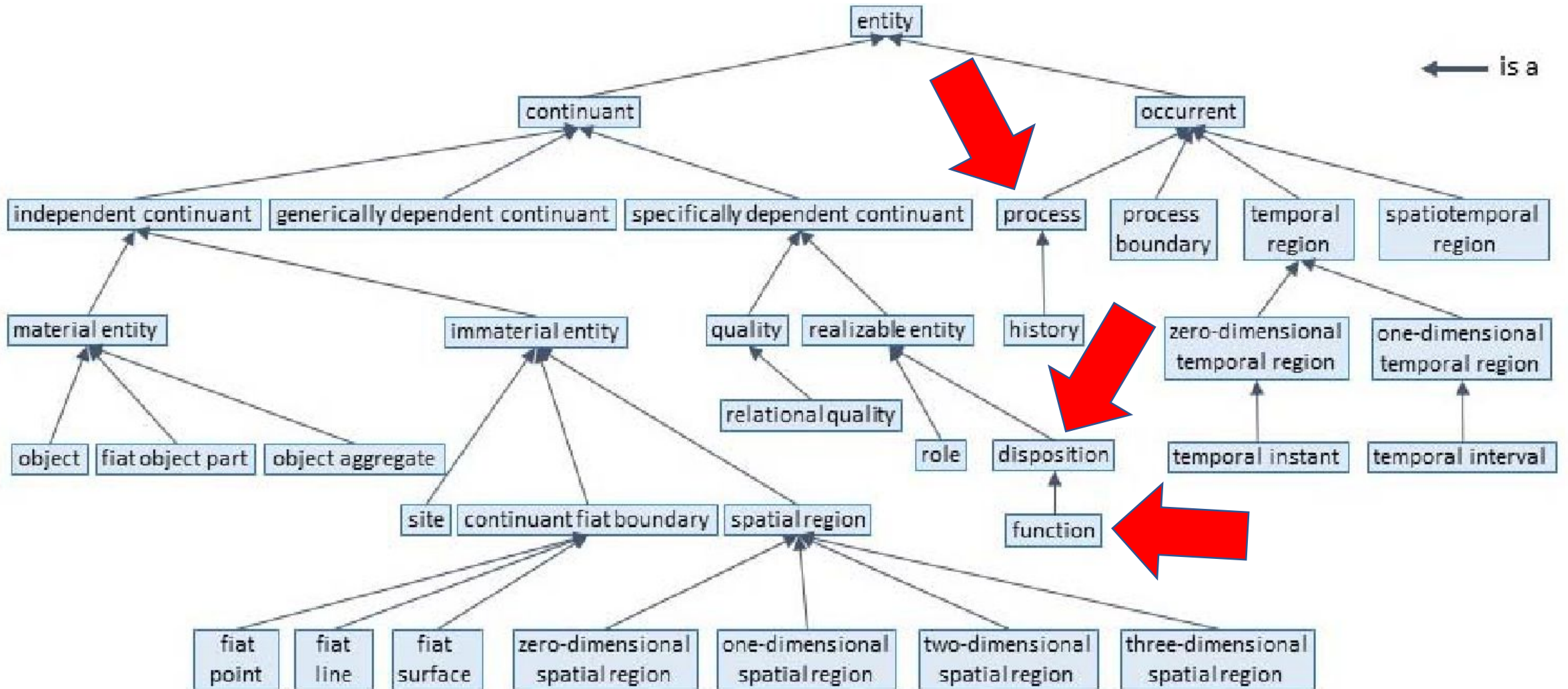


Towards an ontology of aging

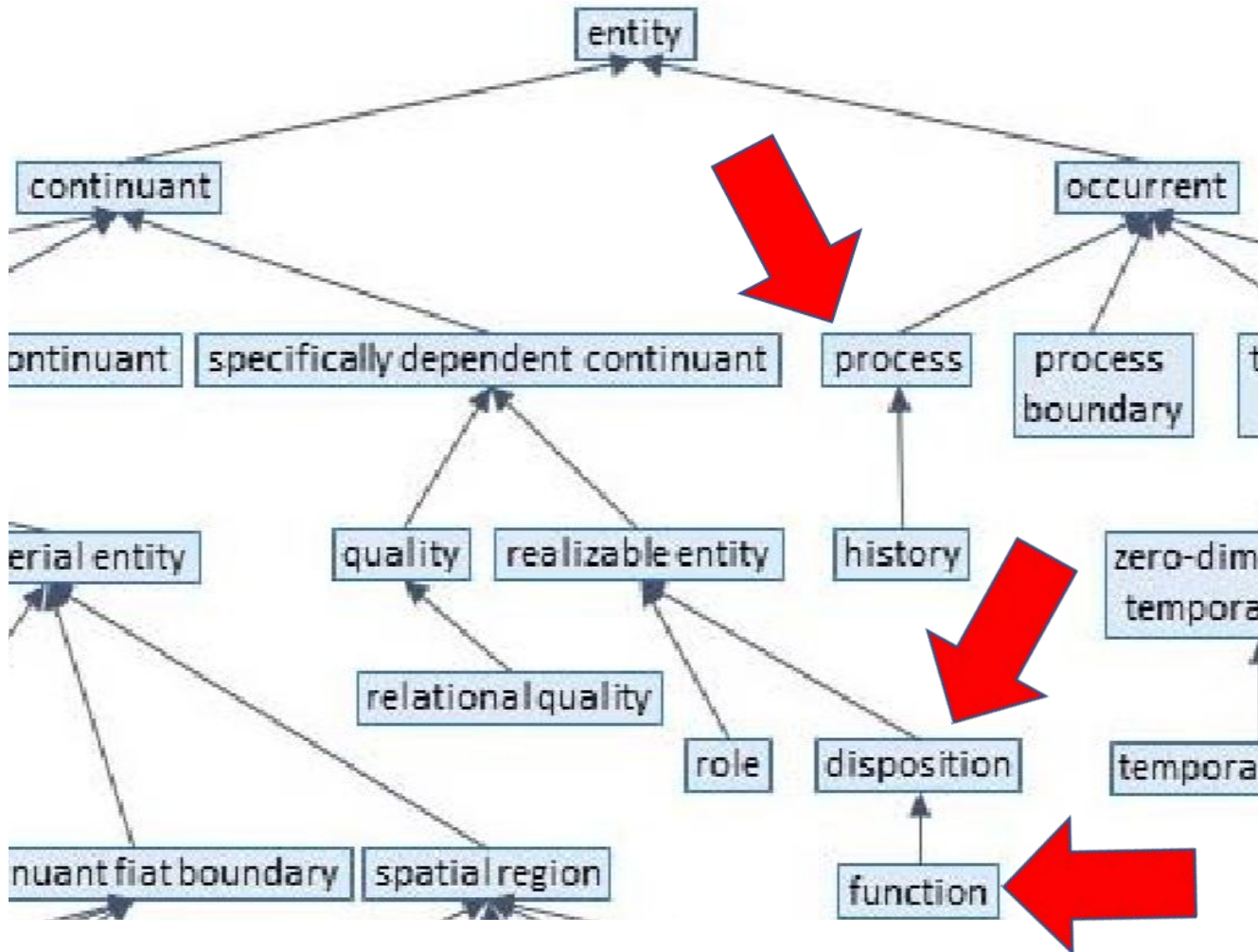
- A BFO-based ontological analysis of the increase of the probability of death
- *Preliminary*: Basic Formal Ontology (BFO)
 - An upper ontology that is based on the “realist methodology”
 - Recognized by the ISO (ISO/IEC PRF 21838-2.2)
 - Widely used in the context of the Open Biological and Biomedical Ontologies (OBO) Foundry



BFO hierarchy



Dispositions, functions, and processes



blood pumping



fragility



solubility



the function of the heart to pump blood

Homeostasis and the increase of the probability of death

- Homeostasis is a disposition of the whole organism to regulate its bodily processes in some associated way.

□ The Ontology for General Medical Science (OGMS)

- The increase of the probability of death is a process.

□ One analysis: A process of increase in the probability of death involves a disposition to die that is associated with the probability.

- Open question: What is the relationship between these dispositions?

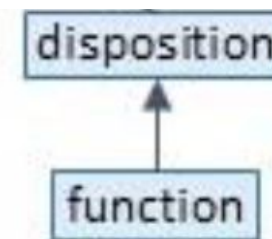
Six defining features of aging

1. functional decline
 2. structural damage
 3. reserve depletion
 4. cellular senescence
 5. phenotypic change
 6. the increase in the probability of death or disease
- Analysis in terms of dispositions, functions, and processes

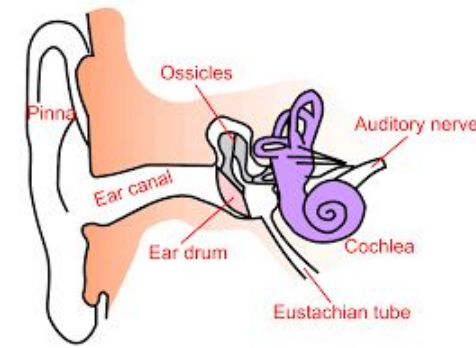
Causation and aging



- A satisfactory definition of aging can be expected to analyze aging by determining cause-and-effect relationships. (M. Lemoine)
- We'll take a dispositional approach to the causal import of aging
 1. A dispositional approach to causation
 - A disposition has the causal import to bring about some process.
 2. A function-centered approach to aging
 - Functional decline is a central feature of aging.



What is functional decline?



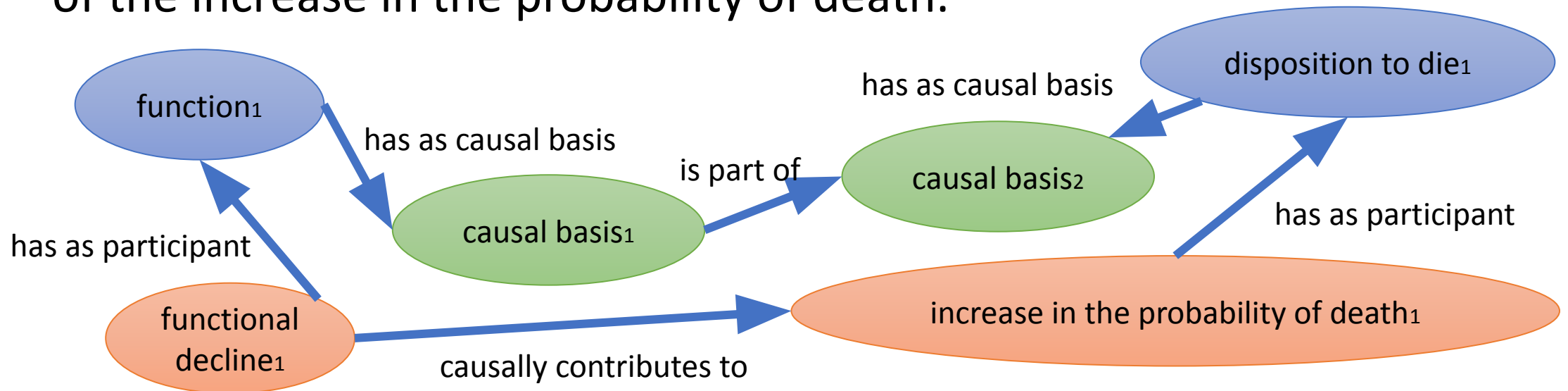
- A process. It has as participant an independent continuant that bears a function at least at the beginning point of this process.
- A function has a “causal basis”, because it’s a disposition.
 - Ex. The function of the ear to detect sounds has, as (part of its) causal basis, hair in the ear canal



- Functional decline comes in degrees.
 - Ex. A partial hearing loss and the total lack of awareness of sounds

The causal import of the increase of the probability of death

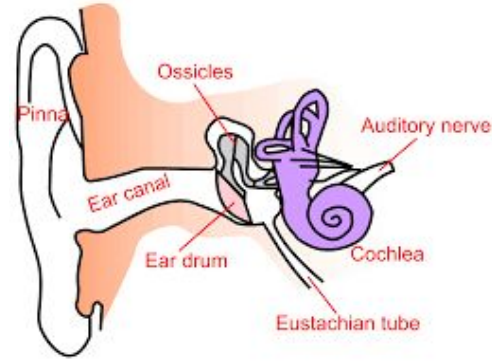
- This process of functional decline causally contributes to this process of the increase in the probability of death.



- When **causal basis₁** of **function₁** changes through **functional decline₁**, the associated probability of death increases.

Structural damage

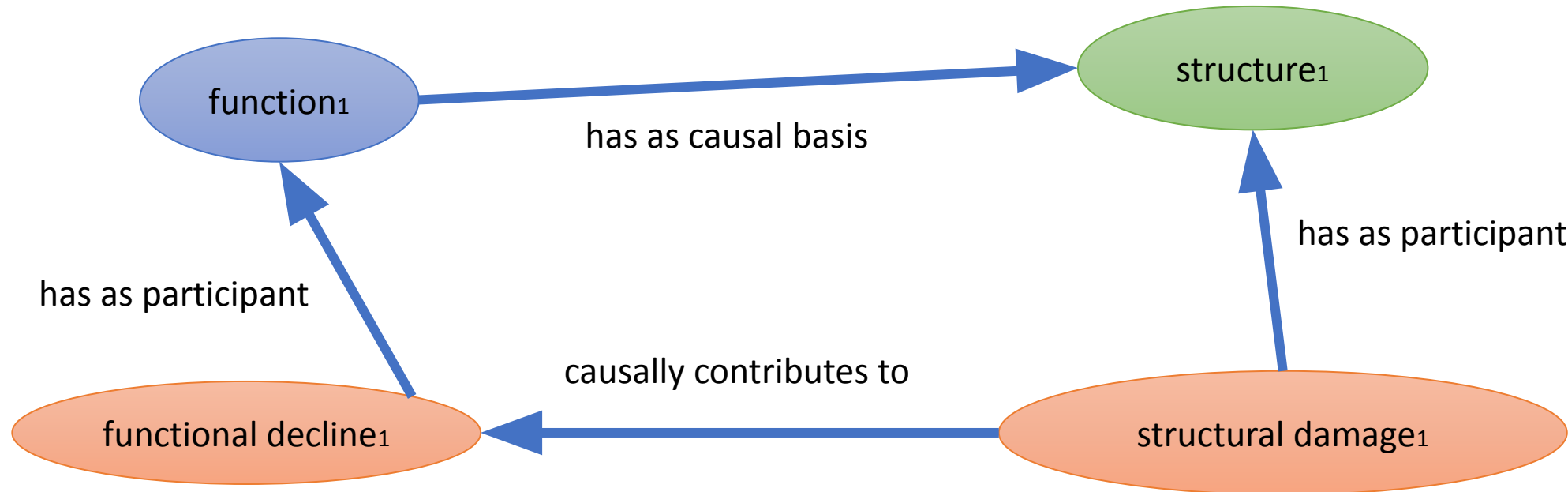
- Another defining feature of aging



- A phenomenon in which some physical structure deteriorates
 - Ex. the deterioration of the spiral structure of the cochlea inside the ear
- A process in which some physical structure deteriorates.
- Structural damage causally contributes to functional decline.

The causal import of structural damage

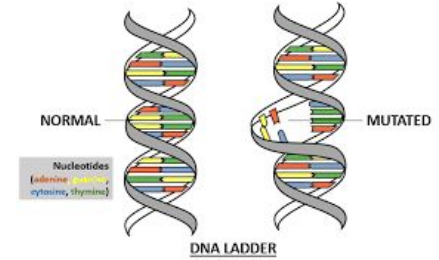
- This process of structural damage causally contributes to this process of functional decline.



Disease and aging

- We are generally concerned with aging to prevent aging-related diseases, improve the quality of life, and expand lifespan.
- But what is an “aging-related 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. (OGMS)
 - A disease has as material basis some disorder(s) in the organism.
 - Ex. Epilepsy and an abnormal neuronal circuitry of the brain

Disease and aging (cont'd)



- One interpretation: an aging-related disease is a result of some “aging process”, as illustrated by any of the six defining features of aging.

- etiological process =_{def.}

A process in an organism that leads to a subsequent disorder. (OGMS)

- Some aging-related diseases have as material bases disorders that result from etiological processes that are either parts of aging processes or caused by them.

Summary

- First steps towards an ontology of aging that can serve as a unified and interdisciplinary framework for investigating aging
- A BFO-based analysis of the six defining features of aging
 - functional decline, structural damage, reserve depletion, cellular senescence, phenotypic change, and the increase in the probability of death or disease
 - A dispositional approach to the causal import of aging

Thank you for your attention!

Fumiaki Toyoshima, Adrien Barton and Jean-François Ethier

University of Sherbrooke, Sherbrooke, Canada

IRIT/CNRS, Toulouse, France

ICBO2022, September 25-28, 2022



- FT acknowledges financial support by the SPOR Canadian Data Platform (CIHR).